

**Early-life characterization and assessment
of risk factors for the classification
of growth-restricted piglets**

Pau Salgado López

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Early-life characterization and assessment of risk factors for the classification of growth-restricted piglets

TESIS DOCTORAL PRESENTADA PER:

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PER ACCEDIR AL GRAU DE DOCTOR DINS EL PROGRAMA DE DOCTORAT
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El **Dr. David Solà Oriol**, professor i investigador del Departament de Ciència Animal i dels Aliments de la Facultat de Veterinària de la Universitat Autònoma de Barcelona i el **Dr. Josep Gasà Gasó**, catedràtic del Departament de Ciència Animal i dels Aliments de la Facultat de Veterinària de la Universitat Autònoma de Barcelona,

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Que la memòria titulada ***"Early-life characterization and assessment of risk factors for the classification of growth-restricted piglets"***, presentada per en Pau Salgado López amb la finalitat d'optar al grau de Doctor en Veterinària amb menció internacional, ha estat realitzada sota la seva direcció i, considerant-la acabada, autoritzen la seva presentació perquè sigui jutjada per la comissió corresponent.

I perquè consti als efectes oportuns, signen la present a Bellaterra, 2 de Desembre de 2025.

Dr. David Solà Oriol

Dr. Josep Gasà Gasó

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Summary

Variability in body weight (BW) at slaughter is a major determinant of overall efficiency in pig production, with tail-end pigs in the herd distribution contributing most to reduced productivity. Continuous genetic selection and improvement over recent decades focused on increasing sow prolificacy has led to a decrease in average birth weight (BtW), resulting in a higher proportion of lightweight piglets experiencing varying degrees of intrauterine growth restriction (IUGR) and increased within-litter BtW variability. Therefore, addressing BW variability at birth and identifying early-life risk factors associated with delayed growth are essential, as these pigs largely drive performance variability within the herd.

Chapter 3 aimed to identify morphological, physiological, and behavioral indicators of varying degrees of IUGR in piglets classified by BtW. A total of 1,990 piglets were categorized as IUGR (< 0.75 kg), restricted low BtW (R-LBW; 0.75–0.95 kg), non-restricted low BtW (NR-LBW; 0.95–1.15 kg), and normal ($\geq$ 1.15 kg). Piglets classified as IUGR exhibited the most severe impairments in postnatal growth, vitality, and survival, associated with reduced colostrum intake, limited energy reserves, altered metabolic profiles, and gastrointestinal dysfunction. Although R-LBW piglets showed significantly lower average daily gain from birth to weaning than NR-LBW piglets, no metabolic or physiological differences were found between these two low BtW categories, suggesting that BtW alone is insufficient for classifying piglets with different growth and survival potentials.

Chapter 4 therefore focused on organ and skeletal characteristics to detect varying degrees of IUGR within low BtW piglets and refine the classification of growth-restricted newborns. Correlations between external and internal measures were also assessed to identify simple, on-farm indicators of internal development. A total of 24 piglets were categorized by BtW and head morphology as severely IUGR (< 0.75 kg with characteristic head morphology), low BtW (LBW; 0.75–1.00 kg), moderate BtW (MBW; 1.00–1.25 kg), and high BtW ($\geq$ 1.25 kg). Piglets with growth restriction showed asymmetrical organ growth prioritizing the brain, impaired ossification and longitudinal bone growth, and enhanced tibial mechanical properties, mainly due to increased manganese and zinc content. Only relative brain weight and bone density differed consistently between LBW and MBW piglets. Strong correlations were identified between BtW, morphological characteristics, and internal organ and skeletal traits, suggesting that external measurements have potential to describe internal development at birth.

While Chapters 3 and 4 highlighted the challenges of classifying low BtW piglets with differing growth and survival potentials during lactation, Chapter 5 aimed to identify early-life risk factors associated with poor growth and mortality, ultimately developing a multi-criteria predictive model for classifying compromised piglets. A total of 3,253 piglets from two commercial farms were monitored from birth to weaning, with detailed records of farrowing traits, BW, body conformation indicators, colostrum intake, and survival. Body weight on day 7 was a stronger predictor of weaning weight ($R^2 > 0.60$) than BW on day 1 ($R^2 \approx 0.30$). The final model for predicting compromised piglets on day 7 included BW on day 1, the piglet's relative BW within the litter on day 1, colostrum intake, and sow parity, achieving an area under the curve (AUC) of 0.910. Each 100 g increase in BW on day 1 reduced the odds of being classified as compromised by 27.6%. Similarly, higher relative BW on day 1 and greater colostrum intake were linked to a reduced risk.

Chapters 3, 4, and 5 collectively focused on the earliest stages of life (birth to weaning). To gain a broader understanding of growth variability across the production cycle, Chapters 6 and 7 applied machine learning methods as alternatives to classical ordinary least squares regression to classify pigs at risk of growth retardation at different production stages and to identify the key factors associated with low BW at each phase. These algorithms were evaluated using both a purebred nucleus and a commercial crossbred dataset. Across all production stages and cut-off points, random forest and boosting algorithms consistently achieved the highest AUC values, with improvements observable from the second decimal place onward. For weaning weight, birthweight-related factors accounted for more than 60% of predictive importance for identifying light pigs. At later stages, these factors were replaced by the BW immediately preceding the target stage, indicating that BW becomes increasingly predictive the closer it is to the stage being evaluated. Similar results were obtained in both datasets, underscoring the potential of machine learning algorithms as valuable tools for evaluating risk factors affecting efficiency and uniformity in swine production and for identifying pigs at risk of growth retardation.

In Chapter 8, the persistent challenges of classifying light piglets at birth that later exhibit different growth and survival trajectories were discussed, and future research directions to improve the diagnosis of varying degrees of growth restriction were highlighted. Key risk factors contributing to BW variability, particularly those in the first week of lactation, and the potential of machine learning tools for the swine industry were also evaluated. Based on these results, it is concluded that classifying light piglets based solely on birth weight

is insufficient for distinguishing degrees of growth restriction that explain performance differences during lactation. A successful switch-on of lactation is critical for supporting piglet growth and survival from the first week through weaning and beyond, highlighting a window of opportunity for targeted interventions. Finally, machine learning algorithms show strong potential for identifying pigs at risk of growth retardation and enhancing decision-making in swine production.

Resumen

La variabilidad en el peso vivo (PV) al sacrificio es un determinante clave de la eficiencia general en la producción porcina, siendo los cerdos situados en la cola de la distribución del rebaño los principales contribuyentes a la reducción de la productividad. La selección y mejora genética continua durante las últimas décadas, dirigida a aumentar la prolificidad de las cerdas, ha provocado una disminución del peso al nacimiento (PN) promedio, lo que ha resultado en una mayor proporción de lechones de bajo peso con distintos grados de restricción de crecimiento intrauterino (RCIU) y un incremento de la variabilidad del PN dentro de la camada. Por lo tanto, abordar la variabilidad del PV al nacimiento e identificar factores de riesgo tempranos asociados con un crecimiento retrasado es esencial, ya que estos lechones son los que principalmente impulsan la variabilidad del desempeño en el rebaño.

El Capítulo 3 tuvo como objetivo identificar indicadores morfológicos, fisiológicos y de comportamiento de distintos grados de RCIU en lechones clasificados según su PN. Se categorizaron 1,990 lechones como RCIU (< 0.75 kg), restringidos con bajo PN (R-BPN; $0.75\text{--}0.95$ kg), no restringidos con bajo PN (NR-BPN; $0.95\text{--}1.15$ kg) y normales (≥ 1.15 kg). Los lechones clasificados como RCIU mostraron las mayores afectaciones en crecimiento postnatal, vitalidad y supervivencia, asociadas con una menor ingesta de calostro, reservas energéticas limitadas, perfiles metabólicos alterados y disfunción gastrointestinal. Aunque los lechones R-BPN mostraron una ganancia media diaria significativamente menor que los NR-BPN desde el nacimiento hasta el destete, no se encontraron diferencias metabólicas o fisiológicas entre estas dos categorías de lechones con bajo PN, lo que sugiere que el PN por sí solo es insuficiente para clasificar lechones con diferentes potenciales de crecimiento y supervivencia.

El Capítulo 4 se centró en las características de órganos y esqueleto para detectar grados variables de RCIU dentro de los lechones de bajo PN y refinar la clasificación de los recién nacidos con restricción de crecimiento. También se evaluaron las correlaciones entre medidas externas e internas para identificar indicadores simples y prácticos de desarrollo interno. Se categorizaron 24 lechones según su PN y morfología de la cabeza como RCIU severa (< 0.75 kg con morfología característica de la cabeza), bajo PN (BPN; $0.75\text{--}1.00$ kg), moderado PN (MPN; $1.00\text{--}1.25$ kg) y alto PN (≥ 1.25 kg). Los lechones con restricción de crecimiento mostraron un crecimiento asimétrico de los órganos priorizando el cerebro,

una osificación y crecimiento longitudinal óseo disminuidos, y unas propiedades mecánicas tibiales mejoradas, principalmente debido a un aumento en el contenido de manganeso y zinc. Solo el peso relativo del cerebro y la densidad ósea se diferenciaron de manera consistente entre BPN y MPN. Se identificaron fuertes correlaciones entre PN, características morfológicas y rasgos internos de órganos y esqueleto, sugiriendo que las mediciones externas tienen potencial para describir el desarrollo interno del lechón al nacimiento.

Mientras los Capítulos 3 y 4 resaltaron los desafíos de clasificar lechones de bajo PN con distintos potenciales de crecimiento y supervivencia durante la lactación, el Capítulo 5 tuvo como objetivo identificar factores de riesgo tempranos asociados con crecimiento reducido y mayor mortalidad, desarrollando finalmente un modelo predictivo multicriterio para clasificar lechones comprometidos. Se monitorearon 3,253 lechones de dos granjas comerciales desde el nacimiento hasta el destete, registrando detalladamente características del parto, PV, indicadores de conformación corporal, ingesta de calostro y supervivencia. El PV al día 7 fue un mejor predictor del peso al destete ($R^2 > 0.60$) que el PV al día 1 ($R^2 \approx 0.30$). El modelo final para predecir lechones comprometidos al día 7 incluyó el PV al día 1, el PV relativo del lechón dentro de la camada al día 1, la ingesta de calostro y la paridad de la cerda, alcanzando un área bajo la curva (AUC) de 0.910. Cada incremento de 100 g en el PV al día 1 redujo las probabilidades de ser clasificado como comprometido en un 27.6%. De manera similar, un mayor PV relativo al día 1 y una mayor ingesta de calostro se asociaron con un riesgo reducido.

Los Capítulos 3, 4 y 5 se centraron colectivamente en las etapas más tempranas de vida (nacimiento a destete). Para obtener una comprensión más amplia de la variabilidad del crecimiento a lo largo del ciclo de producción, los Capítulos 6 y 7 aplicaron métodos de aprendizaje automático como alternativa a la regresión clásica de mínimos cuadrados ordinarios para clasificar lechones con riesgo de retraso de crecimiento en diferentes etapas de producción y para identificar los factores clave asociados con bajo PV en cada fase. Estos algoritmos se evaluaron tanto en una base de datos de un núcleo puro como de un cruce genético en condiciones comerciales. En todas las etapas de producción y puntos de corte, los algoritmos de bosque aleatorio y “boosting” alcanzaron consistentemente los valores más altos de AUC, con mejoras observables desde el segundo decimal. Para el peso al destete, los factores relacionados con el PN representaron más del 60% de la importancia predictiva para identificar lechones ligeros. En etapas posteriores, estos factores fueron reemplazados por el PV inmediatamente anterior a la etapa evaluada, indicando que el PV se vuelve cada vez más

predictivo a medida que se aproxima a la etapa objetivo. Se obtuvieron resultados similares en ambos conjuntos de datos, destacando el potencial de los algoritmos de aprendizaje automático como herramientas valiosas para evaluar factores de riesgo que afectan la eficiencia y la uniformidad en la producción porcina y para identificar lechones con riesgo de retraso de crecimiento.

En el Capítulo 8 se discutieron los desafíos persistentes de clasificar lechones ligeros al nacimiento que posteriormente pueden exhibir diferentes trayectorias de crecimiento y supervivencia, y se destacaron líneas de investigación futuras para mejorar el diagnóstico de distintos grados de restricción de crecimiento. También se evaluaron los factores de riesgo clave que contribuyen a la variabilidad del PV, particularmente durante la primera semana de lactación, así como el potencial de las herramientas de aprendizaje automático para la industria porcina. En base a estos resultados, se concluyó que clasificar lechones de bajo peso únicamente por el PN es insuficiente para distinguir los grados de restricción de crecimiento que pueden explicar las diferencias de desempeño durante la lactación. Un buen arranque de la lactación es crítico para apoyar el crecimiento y la supervivencia del lechón desde la primera semana hasta el destete y más allá, destacando una ventana de oportunidad para intervenciones dirigidas. Finalmente, los algoritmos de aprendizaje automático muestran un gran potencial para identificar lechones con riesgo de retraso de crecimiento y mejorar la toma de decisiones en la producción porcina.

Resum

La variabilitat en el pes viu (PV) al sacrifici és un determinant clau de l'eficiència global en la producció porcina, on els porcs situats a l'extrem de la distribució del ramat són els que més contribueixen a reduir la productivitat. La selecció i millora genètica contínua durant les últimes dècades, enfocada a incrementar la prolificitat de les truges, ha provocat una disminució del pes mitjà al naixement (PN), fet que ha resultat en una proporció més elevada de garrins de baix pes amb diferents graus de restricció de creixement intrauterí (RCIU) i en un augment de la variabilitat de PN dins la garrinada. Per tant, abordar la variabilitat de PV al naixement i identificar factors de risc associats al creixement retardat és essencial, ja que aquests garrins són els principals responsables de la variabilitat del rendiment dins del ramat.

El Capítol 3 va tenir com a objectiu identificar indicadors morfològics, fisiològics i de comportament de diferents graus de RCIU en garrins classificats segons el seu PN. Es van categoritzar 1,990 garrins com a RCIU (< 0.75 kg), restringits amb baix PN (R-BPN; $0.75\text{--}0.95$ kg), no restringits amb baix PN (NR-BPN; $0.95\text{--}1.15$ kg) i normals (≥ 1.15 kg). Els garrins amb RCIU van mostrar els pitjors nivells de creixement post natal, vitalitat i supervivència, associats a una menor ingestió de calostre, reserves energètiques limitades, perfils metabòlics alterats i disfunció gastrointestinal. Tot i que els garrins R-BPN van mostrar un menor guany mig diari que els NR-BPN des del naixement fins al deslletament, no es van observar diferències metabòliques o fisiològiques entre aquestes dues categories de garrins de baix PN, suggerint que el PN per si sol és insuficient per classificar garrins amb diferents potencials de creixement i supervivència.

El Capítol 4 es va centrar en les característiques dels òrgans i l'esquelet per detectar graus variables de RCIU dins dels garrins amb baix PN i refinar la classificació dels nounats amb restricció de creixement. També es van avaluar les correlacions entre mesures externes i internes per identificar indicadors simples i pràctics del desenvolupament intern. Es van categoritzar 24 garrins per PN i morfologia del cap com a garrins amb RCIU severa (< 0.75 kg amb morfologia característica del cap), baix PN (BPN; $0.75\text{--}1.00$ kg), moderat PN (MPN; $1.00\text{--}1.25$ kg) i alt PN (≥ 1.25 kg). Els garrins amb restricció de creixement van mostrar desenvolupament asimètric d'òrgans prioritzant el cervell, ossificació i creixement ossi longitudinal reduïts, i propietats mecàniques tibials millorades, principalment a causa d'un augment del contingut de manganès i zinc. Només el pes relatiu del cervell i la densitat òssia

van diferir de manera consistent entre garrins de BPN i garrins de MPN. Les fortes correlacions identificades entre PN, característiques morfològiques i característiques d'òrgans i esquelet suggereixen que les mesures externes tenen potencial per descriure el desenvolupament intern del garrí al naixement.

Mentre els Capítols 3 i 4 van destacar les dificultats de classificar garrins de baix PN amb diferents potencials de creixement i supervivència durant la lactació, el Capítol 5 va tenir com a objectiu identificar factors de risc precoços associats al mal creixement i l'elevada mortalitat, desenvolupant finalment un model predictiu multi criteri per classificar garrins compromesos. Es van monitoritzar 3,253 garrins de dues granges comercials des del naixement fins al deslletament, amb registres detallats dels trets del part, PV, indicadors de conformació corporal, ingestió de calostre i supervivència. El PV al dia 7 va ser un millor predictor del pes al deslletament ($R^2 > 0.60$) que el PV al dia 1 ($R^2 \approx 0.30$). El model final per predir garrins compromesos al dia 7 va incloure el PV al dia 1, el PV relatiu del garrí dins de la garrinada al dia 1, la ingestió de calostre i la paritat de la truja, assolint una àrea sota la corba (AUC) de 0.910. Cada augment de 100 g en el PV al dia 1 reduïa les probabilitats de ser classificat com a compromès en un 27.6%. De la mateixa manera, un PV relatiu més alt al dia 1 i una major ingestió de calostre es van associar amb un risc inferior de ser classificat com a compromès.

Els Capítols 3, 4 i 5 es van centrar en les primeres etapes de vida (del naixement al deslletament). Per obtenir una visió més àmplia de la variabilitat de creixements al llarg del cicle productiu, els Capítols 6 i 7 van aplicar mètodes d'aprenentatge automàtic com a alternativa a la regressió clàssica de mínims quadrats ordinaris per classificar porcs amb risc de retràs de creixement en diferents etapes productives i identificar els factors clau associats a baix PV a cada fase. Aquests algoritmes es van avaluar tant en una base de dades d'un nucli genètic pur com d'un creuament genètic en condicions comercials. En totes les etapes productives i punts de tall, els boscos aleatoris i "boosting" van aconseguir de manera consistent els valors d'AUC més elevats, amb millores perceptibles des del segon decimal. Pel pes al deslletament, els factors relacionats amb el PN van representar més del 60% de la importància predictiva. En etapes posteriors, aquests factors van ser substituïts pel PV immediatament anterior a l'etapa d'interès, indicant que el PV esdevé progressivament més predictiu com més proper és a la fase objectiu. Es van obtenir resultats similars en ambdós bases de dades, destacant el potencial dels algoritmes d'aprenentatge automàtic per avaluar factors de risc que afecten l'eficiència i la uniformitat en la producció porcina i per identificar garrins amb risc de retard en el creixement.

Al Capítol 8 es van discutir les dificultats persistents en la classificació de garrins de baix pes al naixement que posteriorment poden mostrar trajectòries de creixement i supervivència diferents, així com les futures línies de recerca per millorar el diagnòstic dels diversos graus de restricció del creixement. També es van avaluar els factors de risc clau que contribueixen a la variabilitat del PV, especialment durant la primera setmana de lactació, i el potencial de les eines d'aprenentatge automàtic pel sector porcí. En base a aquests resultats, es va concloure que classificar garrins de baix pes únicament pel PN és insuficient per distingir graus de restricció de creixement que puguin explicar les diferències de rendiment durant la lactació. Una bona arrancada de la lactació és fonamental per donar suport al creixement i la supervivència del garrí des de la primera setmana fins al deslletament i més enllà, oferint una finestra d'oportunitat per a intervencions dirigides. Finalment, els algoritmes d'aprenentatge automàtic mostren un gran potencial per identificar porcs amb risc de retard de creixement i millorar la presa de decisions en la producció porcina.

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List of abbreviations

AA	amino acid	FOV	field of view
AC	abdominal circumference	FPR	false positive rate
ADG	average daily gain	HBW	high birth weight
AIAO	all-in-all-out	HU	hounsfield unit
AIC	akaike information criterion	ICP-MS	inductively coupled plasma mass spectrometry
AUC	area under the curve	IGF-I	insulin-like growth factor I
BMI	body mass index	IgG	immunoglobulin G
BtW	birth weight	IUGR	intrauterine growth restriction
BW	body weight	LBW	low birth weight
Ca	calcium	MBW	moderate birth weight
CD	crypt depth	ML	machine learning
CI	colostrum intake	Mn	manganese
CRL	crown-to-rump length	N	normal birth weight
CT	computed tomography	NCC	number of completed circles around enclosure
Cu	copper	NMR	nuclear magnetic resonance
CUG	catch-up growth	NR-LBW	non-restricted low birth weight
CV	coefficient of variation	OR	odds ratio
DB	difference between the piglet's birth weight and the average litter weight at birth	P	phosphorus
DC	difference between the piglet's birth weight and the average litter weight after cross-fostering	PBS	phosphate-buffered saline
DS	dataset	PCA	principal component analysis
EBV	entire bone volume	PI	ponderal index
FDR	false discovery rate	PLS-DA	partial least squares discriminant analysis
		PPV	positive predictive value

RBW	relative body weight
R-LBW	restricted low birth weight
ROC	receiver operating characteristic
ROI	regions-of-interest
RT	rectal temperature
SEM	standard error of the mean
SID	standardized ileal digestible
sIUGR	severe intrauterine growth restriction
SD	standard deviation
TPR	true positive rate
U	udder stimulation
UTM	universal test machine
VB	within-litter variance of body weight at birth
VC	within-litter variance of body weight after cross-fostering
VH	villus height
VIF	variance inflation factor
VIP	variable importance for projection
WW	weaning weight
Zn	zinc

Chapter 1

General introduction

1.1 Introduction: The Pig Production Industry

1.1.1 Current Situation and Challenges

World meat production has grown steadily over the past few decades, reaching 379 million tons (carcass weight equivalent) in 2024 (FAO, 2025), driven mainly by the expansion of poultry meat supply. Poultry meat production surpassed pork production around 2018, largely due to a sharp decline in global pork output caused by African swine fever outbreaks in major producing countries such as China (OECD/FAO, 2025). Pork production began to recover from this shock starting in 2021 as herd inventories were gradually rebuilt. As the second most produced livestock species, global pig meat output reached 125.1 million tons in 2024 (Fig. 1.1; FAO, 2025), remaining largely stable from the previous year, as decline in China's production offset gains in the next five largest producers (*i.e.*, United States, Spain, Brazil, Germany, and Russia). In Spain, pork production totaled 4.92 million tons in 2024. This overall growth in meat production has been accompanied by rising global demand, with total meat consumption projected to increase by 47.9 million tons over the next decade (OECD/FAO, 2025). Global pig meat consumption is expected to rise by around 5% by 2034, particularly in upper middle-income countries, where rapid population and income growth are driving demand (OECD/FAO, 2025). This expansion in pig production capacity has been driven primarily by advances in genetics, while improvements in nutrition, animal health and welfare, and breeding providing important complementary support.

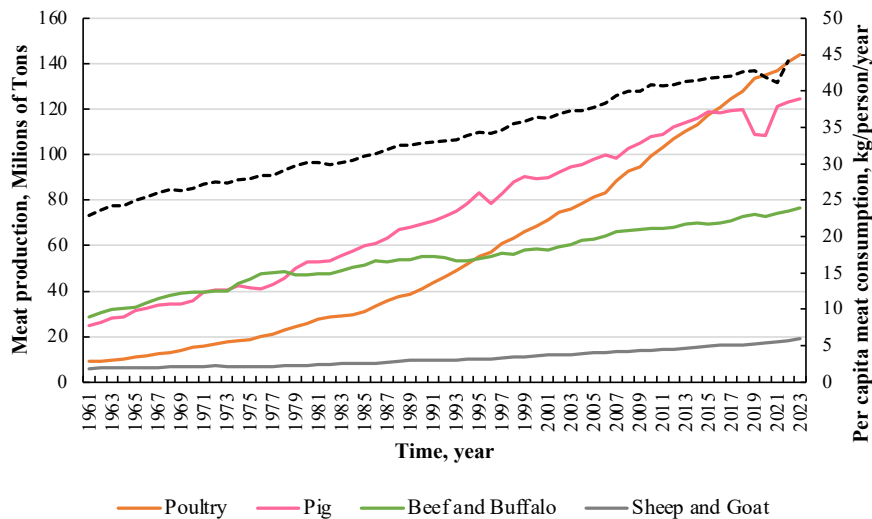


Fig. 1.1 Evolution of worldwide meat production for the four main livestock species from 1961 to 2023 (OECD/FAO, 2025). The black dashed line represents per capita meat consumption, expressed in kilograms per person per year (values shown on the right vertical axis).

World meat production is projected to rise by 13% by 2034. More than half of this growth (55%) is expected to occur in Asia, driven primarily by a 15-million-ton increase in poultry production. Poultry is therefore set to expand its dominance in the global meat sector, accounting for 62% of the additional meat produced over the next decade (OECD/FAO, 2025). Poultry benefits from short production cycles, high feed conversion efficiency, lower overall production costs, and the absence of cultural or religious dietary restrictions, making it easier to meet growing demand. In contrast, pig meat is projected to contribute about 13% of this additional production worldwide by 2034, with trends varying across countries and regions (Fig. 1.2; OECD/FAO, 2025).

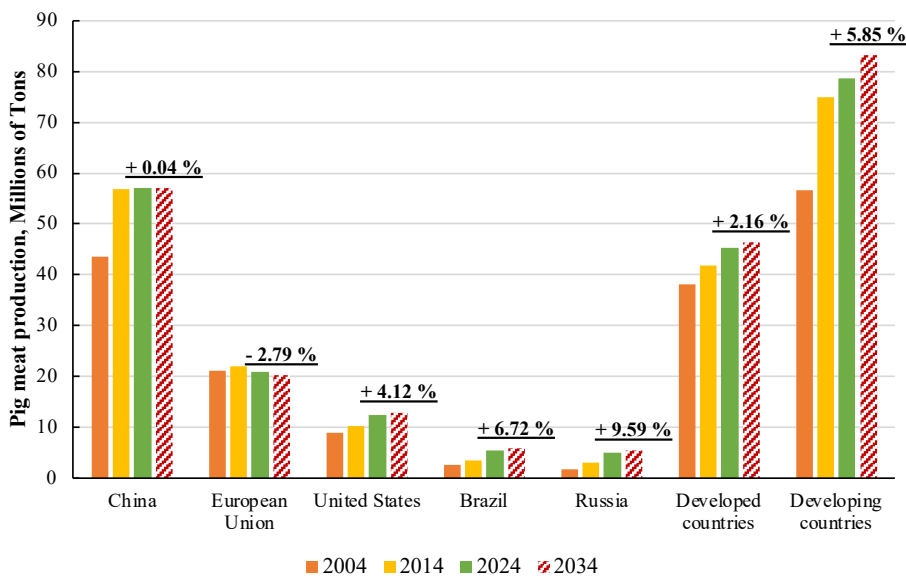


Fig. 1.2 Pig meat production in the five largest global producers, as well as in developed and developing countries, from 2004 to 2024, and projected production from 2024 to 2034 (OECD/FAO, 2025). Percentages above the last two bars indicate the expected change in pig meat production between 2024 and 2034.

Recent forecasts indicate that Asia (*i.e.*, African swine fever-affected regions such as Vietnam) will lead global pork production between 2024 and 2034 (Mateos et al., 2024), with an expected increase of 3.7% (OECD/FAO, 2025). Growth in other regions is projected to range from 4.1% in North America and 14.7% in Latin America to 33.3% in Africa (OECD/FAO, 2025). This expected expansion in production share in regions like Latin America and Africa is not only driven by robust global demand, but also supported by competitive advantages in land availability, feed resources, and animal genetics, as well as their relatively low starting point in production compared with Asia and Europe. In Europe, pig meat production rebounded in 2024

after two consecutive years of contraction, supported by abundant piglet supply, higher slaughter numbers, and lower feed costs (FAO, 2025). However, it is expected to remain relatively stable (+ 0.86%) through 2034, with a 2.79% decline in the European Union (OECD/FAO, 2025). The largest increases in pig production are expected in developing countries, driven by the need to meet the demands of a growing global population, projected to reach 8.82 billion (+ 8.1%) by 2034 (OECD/FAO, 2025).

The global meat industry is facing growing challenges on multiple fronts. In recent years, producers worldwide have had to deal with rising production costs, stricter environmental and animal health regulations, and outbreaks of various diseases (OECD/FAO, 2025). In the European Union, pig meat production faces several specific difficulties: competition from increasing pig production in Asia, which could reduce exports from other countries; instability in the global economic and political environment; new outbreaks of African swine fever and other diseases that threaten productivity; declining per capita pork consumption due to inflation and changing consumer preferences for healthier or more ethically produced food; market distortions caused by rising energy prices (both as a general input for production and as a component of feed costs) and pork prices, which increase costs and reduce profits; reduced availability of feed ingredients, labor, and energy; and limited awareness among farmers of consumers expectations regarding pork quality, as well as the growing demands for food safety, sustainability, and animal welfare (Mateos et al., 2024).

Text box 1: Under these circumstances, improving production and feed efficiency is essential to address these major challenges and to ensure the economic viability of the pig industry. This is especially relevant in the European Union, where pig production is predominantly export-oriented and has reached a plateau, limiting opportunities for further growth. As a result, overall production may decline, with a portion relocating to emerging regions with expanding markets.

1.1.2 Production Efficiency in the Swine Industry

In general terms, production efficiency refers to improving the ratio between input and output. In livestock production, it involves making better use of resources to meet the growing demand for animal products through technological innovation and improved management practices. This includes enhancing land productivity, energy efficiency, waste reduction, feeding,

breeding, and herd management (Nova and González-Schnake, 2014). Greater production efficiency not only generates economic benefits for farms but also reduces environmental pollution per unit of product. Improving the efficiency of pork production is a critical goal for pig producers and supporting scientists. However, production efficiency varies across major pig producing countries, mainly due to differences in market weight, feed composition, genetics, management practices, mortality, morbidity, and environmental conditions. For example, compared with China, the European Union raises only 29.7% as many pigs but produces 41.5% of the pork output. This means that, in terms of efficiency, the European Union produces about 40% more pork per the same number of pigs than China (Kim et al., 2024).

1.1.3 Impact of Body Weight Variability

Current swine production systems maintain contemporary pigs in the same batch, as this practice is recommended for optimal animal health (Maes et al., 2004). In all-in-all-out (AIAO) production systems, one of the main factors affecting production efficiency is the variability in body weight (BW) at slaughter, particularly the substantial differences in target BW among pigs of the same age (Patience et al., 2004). High variability in market weights lowers carcass value by worsening quality classification and price quotation, reduces the effectiveness of slaughterhouse equipment, and increases the time pigs occupy finishing farm facilities (López-Vergé et al., 2018). Furthermore, Calderón Díaz et al. (2017b) reported that delaying pigs from the normal production flow is negatively associated with both health and performance. Altogether, these challenges represent the main shadow production cost for the swine industry.

The main contributors to this variability are slow-growing pigs, which generally reach slaughter weight later than their faster-growing counterparts (Douglas et al., 2014; He et al., 2016). It is estimated that, within a given batch, 10 to 15% of pigs are slow-growing (Calderón Díaz et al., 2017b). These pigs are typically defined as individuals with low birth and/or weaning BW, falling within the lower quartile of the BW population distribution, and requiring extra time to reach target slaughter weight (Douglas et al., 2014; He et al., 2016; Montoro et al., 2020). Specifically, Douglas et al. (2014) and López-Vergé et al. (2018) demonstrated that pigs with low BW at entry into the grow-finishing barn tend to reach market weight later than heavier pigs. This delay is largely attributed to the limited effectiveness of strategies designed to help lighter pigs catch up with their heavier pen mates, particularly from weaning onwards (Blavi et al., 2021).

The variability among pigs, commonly measured as the coefficient of variation (CV), tends to decrease with age (Patience et al., 2004; López-Vergé et al., 2018). This reduction is mainly due to the application of different management (e.g., cross-fostering, segregation by BW or sex) and nutritional practices implemented on farms. Nevertheless, most of the variability originates at birth (CV = 20-25%), and usually increases slightly during lactation or up to 14 days post-weaning (López-Vergé et al., 2018).

Text box 2: Overall, these results suggest that addressing piglet BW variability at birth is essential for minimizing variability throughout the production cycle.

1.2 Developments in Piglet Production per Sow

1.2.1 Sow Prolificacy

One of the main economic drivers in pig production is reproductive efficiency, typically measured as the number of piglets weaned per sow per year. Optimizing this factor is critical for the sustainability and productivity of the global pork industry. Over recent decades, genetic progress has focused largely on increasing sow prolificacy to raise the annual number of piglets produced per sow (Rutherford et al., 2013). Consequently, much of the productivity gain has been achieved through years of genetic selection of hyperprolific lines, supported by the widespread use of Best Linear Unbiased Prediction methodologies and advances in genomic selection, both of which have markedly improved the accuracy of breeding programs (Bolet et al., 2001; Wongwaipisitkul et al., 2024). Modern production systems therefore emphasize maximizing the number of piglets weaned per sow as a key breeding and management objective (Hansen et al., 2019). In the European Union, the number of piglets weaned per sow per year showed a steady upward trend between 2010 and 2022 (Fig. 1.3; Sanz-Fernández et al., 2024), with an average annual increase of + 0.48. Spain followed a similar but more moderate trajectory, with an average annual increase of + 0.27 piglets per sow per year. In terms of efficiency, it is also important to consider the kilograms of piglet weaned per sow per year, which reflects the combined influence of both litter size and weaning weight. In Spain, de Andrés et al. (2022) reported that in 2019 the weaning yield reached 186.73 kg per sow per year, emphasizing the need not only to increase litter size but also to ensure adequate piglet growth to maintain overall productivity.

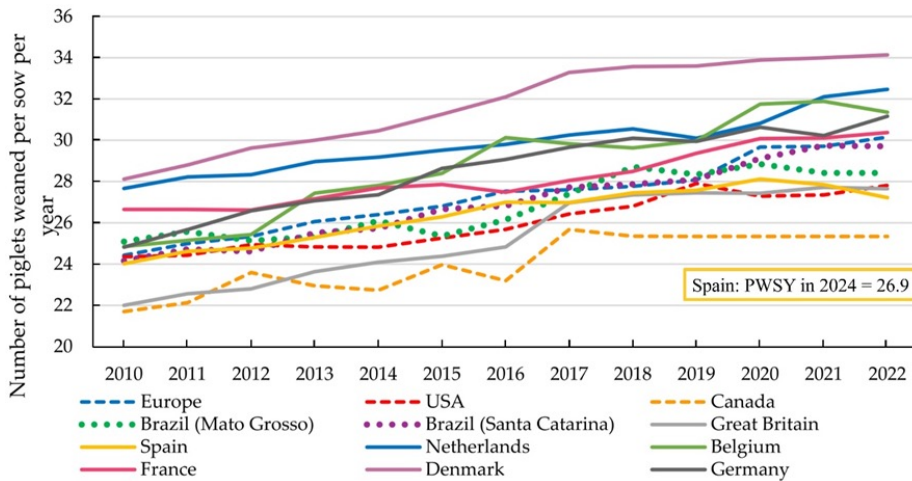


Fig. 1.3 Evolution of the number of piglets weaned per sow per year in selected countries. Fig. adapted from Sanz-Fernández et al. (2024). This figure is based on an InterPIG report that includes data from a limited number of representative farms; therefore, the values should be interpreted as indicative rather than exact. Abbreviation: PWSY = piglets weaned per sow per year.

Interestingly, as litter size has increased over time, producing the same number of weaned piglets now requires fewer litters, particularly if piglet mortality can be simultaneously reduced. However, reducing piglet mortality remains a major challenge with today's hyperprolific sows. As a direct result, since 2000, most European countries have decreased their sow herds, while the number of pigs slaughtered has risen by a comparable proportion. This shift has contributed to lowering the environmental footprint per kilogram of pig meat (Knap et al., 2023).

1.2.2 Effect of Litter Size on Piglet Quality

Increases in prolificacy have led to a significant reduction in average birth weight (BtW), resulting in a higher number of lightweight piglets at birth (Fig. 1.4; Quiniou et al., 2002; Beaulieu et al., 2010; Riddersholm et al., 2021) and in piglets experiencing varying degrees of intrauterine growth restriction (IUGR) (Foxcroft et al., 2006; Amdi et al., 2013; Hales et al., 2013; Hansen et al., 2019). Douglas et al. (2014) and He et al. (2016) defined low BtW piglets as those weighing ≤ 1.25 kg, whereas more recent studies reported that 15–25% of newborn piglets weigh under 1.1 kg (Wang et al., 2017), which compromises their subsequent growth and development, and, consequently, places them at greater risk of not reaching target

slaughter weight (Montoro et al., 2020). Other authors have suggested that piglets born weighing < 1 kg are at higher risk of poor growth throughout the production cycle (Larriestra et al., 2006; Calderón Díaz et al., 2017a). Similarly, Paredes et al. (2012) reported that piglets with a BtW more than 2.5 SD below the population mean are unlikely to achieve adequate growth under current commercial conditions.

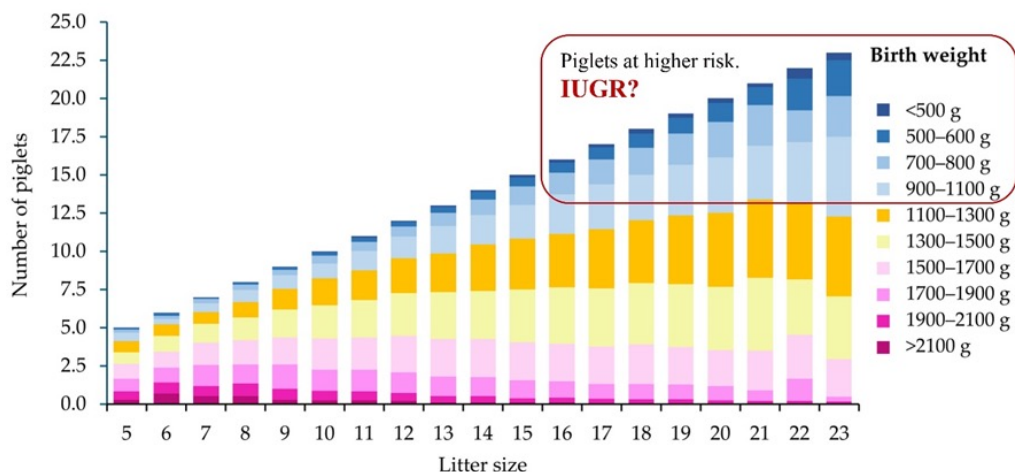


Fig. 1.4 Effect of litter size on birth weight distribution. The data were collected at Schothorst Feed Research B.V. (Lelystad, The Netherlands) from 2011 to 2019, based on 97,552 piglets born alive from 7,888 litters. Fig. adapted from Huting et al. (2021).

Moreover, it is estimated that approximately 20% of piglets within a litter (Krueger et al., 2014), and even 30–40% in hyperprolific sows (Edwards et al., 2019), naturally exhibit some degree of IUGR. Both low BtW and IUGR piglets are considered at higher risk, as they are less likely to catch up with their heavier littermates throughout the production cycle (Quiniou et al., 2002; Beaulieu et al., 2010; Fix et al., 2010). Consequently, the increasing proportion of low BtW and IUGR piglets, driven by larger litter sizes in recent decades, has led to complications in animal management, health, and welfare, as reflected in higher rates of morbidity and prenatal and neonatal mortality (Rutherford et al., 2013). Knap et al. (2023) demonstrated that the effect of BtW on lactation mortality is non-linear, with most of its impact occurring below a specific threshold. Although some studies have estimated this threshold (e.g., 1.1 kg; Feldpausch et al., 2019; 1.0 kg; Roehe and Kalm, 2000; Quiniou et al., 2002), Knap et al. (2023) noted that it can vary between pig populations and may also change over time due to genetic selection.

1.2.3 Effect of Litter Size on Piglet Mortality

In polytocous species such as pigs, a certain level of mortality at birth is considered normal. However, the increased prolificacy of hyperprolific sows has led to a substantial rise in perinatal piglet mortality (Baxter et al., 2020). Prolonged farrowing duration (Oliviero et al., 2019), together with higher incidences of stillbirths and hypoxia in piglets (Langendijk et al., 2018), are recognized as major contributors to mortality in large litters. In such farrowings, reduced vitality immediately after birth, combined with intense litter competition at the udder, may decrease the amount of colostrum ingested and delay its intake following the onset of parturition (Oliviero et al., 2019). Adequate colostrum consumption is essential for survival and development, as it provides immunoglobulins for immune protection as well as energy for thermoregulation and growth (Devillers et al., 2004). Additionally, increased prolificacy can further compromise piglet survival during lactation (Ward et al., 2020). Preweaning mortality on European farms, which averaged around 12% in the first decade of the 21st century, representing a loss of approximately 39 million born alive piglets per year (Muns et al., 2013a), now ranges between 15% and 20% (Farmer, 2022). In Spain, according to the Spanish Porcine Reference Database (Bdporc; www.bdporc.irta.es), the increase in prolificacy has been accompanied by a rise in piglet mortality during lactation, reaching 18.21% in 2023. This corresponds to an average annual increase of 0.65% in preweaning mortality since 2014 in commercial farms. Altogether, piglets born into these larger litters are at higher risk of mortality throughout the production cycle (Larriestra et al., 2006; Calderón Díaz et al., 2017a). This trend is a growing concern for the sector, posing challenges for both animal welfare and sustainability of farms, and underlining the need for developing more effective and sustainable management strategies (Rutherford et al., 2013).

Text box 3: Hyperprolific sows pose a major challenge in modern swine production, as the increase in litter size has resulted in a substantial reduction in average BtW, a higher proportion of low BtW piglets, and increased preweaning mortality. Therefore, balancing prolificacy with piglet viability is essential to achieving more sustainable pig production.

1.3 Intrauterine Growth Restricted Piglets

1.3.1 Intrauterine Growth Restriction – Definition

Intrauterine growth restriction is defined as the failure of the fetus to reach its genetically determined growth potential during gestation, resulting in impaired organ development (Wu et al., 2006). Birth weight, head shape, and indicators of body conformation are commonly used as criteria to identify IUGR (as described in Section 1.3.3). It is important to distinguish between the terms IUGR and low BtW, which are often used interchangeably. Unlike IUGR, low BtW is defined solely based on the piglet's BtW. Piglet maturity is a separate concept from both IUGR and low BtW, referring to the degree of development required for survival at birth (Lefort et al., 2020). An immature piglet not only fails to reach its genetically expected growth during gestation (as in IUGR) but may also have a genetically determined lower baseline for its developmental stage at birth. The terms "mature" or "immature piglets" will not be used in this thesis.

1.3.2 Risk Factors Associated with Intrauterine Growth Restricted Piglets

In livestock animals, both naturally occurring and environmentally induced IUGR are well documented (Wu et al., 2006). The key determinant of fetal growth and development is placental growth, including placental angiogenesis and vascular growth (Gootwine, 2004; Reynolds et al., 2005). As highlighted by Farmer and Edwards (2022), IUGR is a condition observed in newborn piglets, especially those from highly prolific sows, because of insufficient placental transfer of oxygen and nutrients from the mother to the fetus. Reynolds et al. (2005) reported that uterine and placental blood flows increase progressively throughout gestation to meet the metabolic demands of the growing conceptus, emphasizing that uteroplacental circulation is a major factor influencing the supply of nutrients and oxygen to the fetus. These blood flow rates depend largely on placental vascular growth, which is driven by angiogenesis (the formation of new vessels from existing ones) and vascularization (Vonnahme and Ford, 2004; Reynolds et al., 2005).

Uteroplacental insufficiency is therefore recognized as the primary factor limiting fetal growth (Bauer et al., 2003; Town et al., 2004) and may arise naturally or due to breeding practices. Naturally occurring IUGR is common in pigs (Bauer et al., 1998) and is characterized by a reduction in placental weight per fetus, resulting in relative placental insufficiency (Town et al., 2004). The region of the placenta primarily affected by this impaired development, located at the junction of the second and third segments of the uterine horns (Bauer et al., 1998), is

particularly susceptible to vascular compression (Chand et al., 2022). Placental development can also be influenced by breed-specific traits, as certain breeds (e.g., Meishan sows) show superior placental vascularization, more consistent placental weights, and improved nutrient transfer to the fetus, thereby mitigating uterine overcrowding and lowering the incidence of stillbirths (Canario et al., 2006; Bonnet et al., 2024). Regarding breeding practices, both breeding at an immature BW and breeding at an advanced age can contribute to uteroplacental insufficiency. In first-parity sows bred before reaching full physical maturity, maternal and fetal growth occur simultaneously, resulting in competition for nutrients during gestation and potentially insufficient nutrient supply for both (Ruggeri et al., 2025b). Conversely, breeding older sows can impair placental growth, as age-related increases in ovulation rates may produce more conceptuses than the uterus can support, resulting in intrauterine overcrowding (Foxcroft et al., 2006).

Uteroplacental insufficiency occurs around day 35 of gestation, when the number of embryos surviving post-implantation period may exceed uterine capacity, leading to intrauterine overcrowding and placental insufficiency (Town et al., 2004; Wu et al., 2006). From this point until day 90 of gestation, which coincides with the muscle fiber development in the pig (Foxcroft et al., 2006), fetal growth is largely determined by the uterine environment (Wilson et al., 1998; Biensen et al., 1999), whereas the later phase of gestation is primarily controlled by genetic factors. Consequently, adverse influences occurring before day 90 can disrupt the uterine environment and predispose fetuses to IUGR (Felicioni et al., 2018). Bazer et al. (1969) defined uterine capacity as the physiological and biochemical limitations imposed by the uterus on conceptus growth and development. The finite capacity of the uterus ultimately limits litter size (Wilson et al., 1998) and can become a major constraint on fetal growth, particularly in highly prolific sows, even when fetuses are relatively evenly distributed along the uterine horns (Knight et al., 1977).

In addition to the genetic contribution from both parents, several studies (Wu et al., 2004; Wu et al., 2006; Van Ginneken et al., 2023; Ruggeri et al., 2025b) have identified multiple factors that can influence fetal development. These include maternal nutrition (e.g., low or high feed intake and nutrient imbalances), maternal intestinal malabsorption, exposure to toxins, environmental temperature and stress, fetal infections (e.g., Circovirus or Porcine Reproductive and Respiratory Syndrome infections), disturbances in maternal or fetal metabolic and homeostatic mechanisms, and maternal and fetal genetics (e.g., variations in genes regulating placental development and nutrient transport to the fetus). Among all these factors, maternal nutrition is considered the second major determinant of fetal growth, following insufficient uterine capacity (Wu et al., 2006). While days 30 to 40 of gestation

are defined as the critical period during which uterine capacity exerts its effects (Knight et al., 1977), available evidence indicates that the prenatal growth trajectory of all placental mammals is sensitive to the direct and indirect effects of maternal nutrition at every stage from oocyte maturation to birth (Robinson et al., 1999; Rehfeldt et al., 2004).

1.3.3 Diagnosis of Intrauterine Growth Restriction in Newborn Piglets

In pigs, the identification of IUGR is only possible after birth and relies on evaluating various parameters, including BtW and piglet morphology. Although BtW is considered the main criterion, several studies have emphasized that morphological characteristics provide an additional and essential basis for identifying IUGR piglets (Baxter et al., 2008; Douglas et al., 2016; Riddersholm et al., 2021). In this thesis, the following parameters are applied to identify IUGR piglets at birth.

1.3.3.1 Birth Body Weight

Birth BW is commonly used on farms as a criterion for detecting IUGR (Wu et al., 2006), although different thresholds have been proposed in the literature. Early studies classified animals with a BW below the 10th percentile of the population distribution as IUGR (Bauer et al., 1998). Similarly, Wollmann (1998) and Mamelle et al. (2001) reported that within the group of small for gestational age newborn piglets (defined as those with a BtW below the 10th percentile for their gestational age), fetuses failing to reach their genetically determined growth potential were considered growth restricted. Felicioni et al. (2018) suggested that to establish the weight range representing IUGR piglets, it is convenient to record the BtW of approximately 1,000 piglets from a given farm and determine a range from mean – 2 standard deviations (SD) to mean – 1 SD as the IUGR category. Because the pig is a polytocous species, other studies generated reference values based on BtW within individual litters. Wang et al. (2016) categorized piglets as IUGR if their BtW ranged between 0.75 and 0.90 kg and fell within the lower quartile of the litter's BtW distribution. Quiniou et al. (2002) classified piglets as IUGR if their BtW was below the 11th percentile. D'Inca et al. (2010) and Van Tichelen et al. (2021) defined IUGR newborns as those with a BtW 1.5-2 SD below the litter mean. Finally, Ji et al. (2017) proposed a higher threshold than previously reported, considering piglets with a BtW of less than 1.1 kg as IUGR in a population with a mean BtW of 1.4 kg.

1.3.3.2 Head Shape

Chevaux et al. (2010) was the first study to suggest head morphology as a distinctive qualitative morphological indicator of immaturity. Building on this finding, Hales et al. (2013)

defined three head morphology criteria to characterize growth-restricted piglets: 1) a steep, dolphin-like forehead, 2) wrinkles perpendicular to the mouth, and 3) bulging eyes (Fig. 1.5). Based on these criteria, piglets were classified into three categories: IUGR (all three criteria present), light IUGR (one or two criteria present), and normal (none of the criteria present). Similarly, Amdi et al. (2013) defined severe IUGR piglets as those displaying two or three of these characteristics, mildly IUGR piglets as those showing one, and normal piglets as those showing none. In subsequent studies, the characteristic of hair with no defined growth direction was added, and IUGR piglets were defined as those displaying a steep, dolphin-like forehead along with at least one additional feature (Engelsmann et al., 2019; Amdi et al., 2020; Amdi et al., 2023).

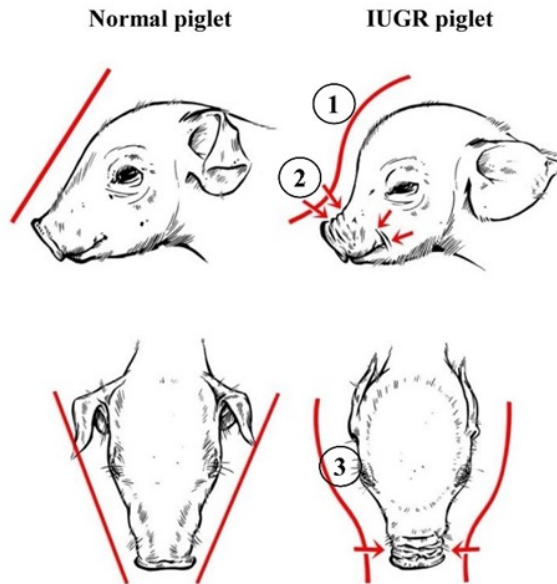


Fig. 1.5 Illustrations of a normal (left) and a growth-restricted piglet (right). Criteria for growth restriction: 1) steep, dolphin-like forehead, 2) wrinkles perpendicular to the mouth, and 3) bulging eyes. IUGR = intrauterine growth restriction. Fig. adapted from Hales et al. (2013).

Text box 4: In the present thesis, piglets classified as severely affected by IUGR are defined by a BtW threshold of 0.75 kg, corresponding to more than 1.5 SD below the mean litter weight in the studied populations, together with the presence of the three characteristic head morphology criteria (a steep, dolphin-like forehead; wrinkles perpendicular to the mouth; bulging eyes).

1.3.3.3 Indicators of Body Conformation

Indicators of body conformation, reflecting body proportionality, were first described in the literature as complementary predictors to BtW for survival and growth performance (Baxter et al., 2008; Baxter et al., 2009; Hales et al., 2013). Baxter et al. (2008) demonstrated that body mass index (BMI; BtW (kg)/[crown to rump length (m)]²) and ponderal index (PI; BtW (kg)/[crown to rump length (m)]³) were highly significant indicators of stillbirth in piglets. In human medicine, PI and BMI are commonly used together to distinguish neonates that are naturally small from those whose reduced size is a result of IUGR (Ruggeri et al., 2025b). Hales et al. (2013) were the first to link body conformation indicators to growth restriction. They found that piglets suffering from IUGR had a markedly higher risk of dying within the first days of life (1.8 times greater risk of death on days 0-1 compared with days 2-26), with the degree of growth restriction explaining differences only between piglets that survived to weaning and those that died on days 0-1. Moreover, BMI differed significantly between piglets alive at weaning and those that died on days 0-1, suggesting a correlation between BMI and growth restriction and indicating improved survivability in piglets with higher BMI. Interestingly, Hales et al. (2013) also reported that the smallest piglet within a litter was at greater risk of dying shortly after birth, but not of being stillborn. The strong influence of IUGR score on morphological characteristics was further confirmed by Amdi et al. (2013), who observed that normal piglets had higher crown to rump length (CRL; the supine length from the crown of the head to the base of the tail), higher BMI, and higher PI compared with both mild and severe IUGR piglets. Similarly, Hansen et al. (2019) identified differences in CRL, BMI, and PI among the same categories of liveborn piglets (normal, mild IUGR, and IUGR). These parameters were significantly reduced in litters of ≥ 17 piglets (Ngo et al., 2024), where the proportion of IUGR

Table 1.1 Postnatal consequences of intrauterine growth restriction in piglets during the preweaning period. The conditions reviewed will be further evaluated in this thesis.

Consequences of IUGR ¹	
Prewaning performance	↓ growth rates (↓ average daily gain)
	↓ feed efficiency (by 5–10%)
	↑ mortality rate (primarily occurring in the first 2-3 days after birth)
Behavior	↓ vitality
	↓ ability to compete effectively with littermates for early and sufficient CI (↓ CI)

piglets increases substantially compared with smaller litters of 7-14 piglets (Chaiyapatmaetee et al., 2025). Regarding CRL, Hales et al. (2013) found that it did not explain differences in preweaning survival, thus highlighting the superiority of BMI as a predictor of survival (Baxter et al., 2008), because it accounts for both piglet weight and length. Douglas et al. (2016) also reported that BMI was the strongest predictor of postnatal growth in piglets with low BtW. Another body conformation measure proposed as a reliable predictor of postnatal growth performance is abdominal circumference (AC; Douglas et al., 2016). In this regard, IUGR piglets have been shown to consume insufficient colostrum within the first 24 hours after birth, with most having half-full or less than half-full stomachs (Amdi et al., 2013), a condition that may be reflected in AC. Consistently, Baxter et al. (2008), Hales et al. (2013) and Riddersholm et al. (2021) reported that piglets affected by growth restriction are characterized by a thin body profile.

1.3.4 Consequences of Intrauterine Growth Restriction

Piglets affected by IUGR represent a major challenge to achieving the primary goals of pig production, which include improving feed efficiency and producing abundant, high-quality meat for increasingly health-conscious consumers (Wu et al., 2006). Numerous studies have shown that IUGR has lasting detrimental effects on neonatal adaptation, preweaning survival, postnatal growth, feed efficiency, lifetime health, time to reach market BW, body composition, and meat quality. Understanding these outcomes is essential to accurately diagnose IUGR in newborn piglets based on external traits and to distinguish different degrees of growth restriction. A summary of the main postnatal consequences of IUGR during the preweaning period is presented in Table 1.1.

References

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- Hansen et al., 2019; Lynegaard et al., 2020
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- Bérard et al., 2008; Bérard et al., 2010; Schinckel et al., 2010
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- Roehe and Kalm, 2000; Baxter et al., 2008; Hansen et al., 2019; Matyba et al., 2021; Chaiyapatmaetee et al., 2025
-
- Muns et al., 2013b; Vanden Hole et al., 2019
-
- Amdi et al., 2013; Farmer and Edwards, 2022; Chaiyapatmaetee et al., 2025
-

Organ development	"Brain-sparing" effect: vital functions of the brain preserved; compromised development of other organs (e.g., liver, kidneys, intestine, pancreas) ↑ brain-to-heart and brain-to-liver weight ratios ↓ absolute organ weights ↑ relative weights of heart and brain; ↓ relative liver weight ↓ absolute organ weights and ↑ relative brain weight at weaning
Gastrointestinal tract development	↓ intestinal length and weight ↓ VH and ↓ VH:CD ratio ↓ numbers of goblet cells (particularly in the ileum and jejunum) and ↓ lymphocytes in the ileum Delayed enterocyte maturation ↓ expression of genes related to glucose and lipid metabolism ↓ expression of antioxidant enzyme genes (e.g., SOD2m) ↓ expression of immune-related genes (e.g., FAXDC2, HSPB1, PPARGC1α, IL-2, IL-10) ↑ expression of stress-related genes (HSD11β1) ↓ expression of IGF-I and its receptor in the intestinal mucosa Impaired tight junctions: ↓ expression of Occludin, Claudin-1, ZO-1 → ↑ intestinal permeability Abnormal digestion and nutrient absorption
Bone development	↑ bone mineral density at weaning
Muscle fiber development	Impaired muscle hyperplasia (↓ ratio of secondary to primary muscle fibers) ↓ number of skeletal muscle fibers ↓ skeletal muscle cross-sectional area ↓ skeletal muscle fiber diameter ↓ protein deposition in skeletal muscle
Adipose tissue development	↓ development and proliferation of adipocytes ↑ fat deposition and excessive adiposity
Energy reserves	↓ hepatic glycogen reserves and impaired glycogen utilization during the first 8 hours after birth ↓ capacity to accumulate and mobilize muscle glycogen ↑ loss of body temperature after birth

Bauer et al., 1998; Cohen et al., 2015; Felicioni et al., 2018

Amdi et al., 2013; Hansen et al., 2019; Ruggeri et al., 2024b

Xu et al., 1994; Amdi et al., 2013; Hansen et al., 2019

Amdi et al., 2013; Hansen et al., 2019

Lynegaard et al., 2020

Xu et al., 1994; Wang et al., 2005; Wang et al., 2008; D’Inca et al., 2010;

Dong et al., 2014; Huang et al., 2019; Chen et al., 2021

Xu et al., 1994; Wang et al., 2005; Wang et al., 2008; D’Inca et al., 2010; Dong et al., 2014; Huang et al., 2019; Chen et al., 2021; Tang and Xiong, 2022

Dong et al., 2014

Wang et al., 2005; Ferenc et al., 2017

Yao et al., 2017

Villagómez-Estrada et al., 2022

Dong et al., 2014; Yao et al., 2017; Amdi et al., 2020; Villagómez-Estrada et al., 2022

Villagómez-Estrada et al., 2022

Wang et al., 2005

Dong et al., 2014; Wang et al., 2016; Chen et al., 2021; Olszewski et al., 2021;

Tang and Xiong, 2022

Wang et al., 2005; Wang et al., 2008; D’Inca et al., 2010; Santos et al., 2022

Ruggeri et al., 2025a

Handel and Stickland, 1987; Bauer et al., 2003; Foxcroft et al., 2006; Bérard et al., 2010

Bérard et al., 2010; Alvarenga et al., 2013; Wang et al., 2013

Bérard et al., 2010; Alvarenga et al., 2013

Bérard et al., 2010; Alvarenga et al., 2013

Wu et al., 2010

Attig et al., 2008; Gondret et al., 2011; Sarr et al., 2012

Attig et al., 2008; Sarr et al., 2012

Amdi et al., 2013; Vanden Hole et al., 2019

Voillet et al., 2014; Vanden Hole et al., 2019

Amdi et al., 2016; Chaiyapatmaetee et al., 2025

Blood parameters	Altered amino acid and protein metabolism (at birth and on day 21):
	↑ threonine and glycoproteins; ↓ proline, arginine, leucine, tyrosine (representative examples)
	↑ purine metabolism: ↑ xanthine, deoxyinosine, hypoxanthine (day 7);
	↑ xanthosine (day 28)
	Impaired energy metabolism: ↓ glucose and citrate concentrations;
	↑ plasma lactate (at birth and on day 21)
	Altered lipogenesis and lipid oxidation (on day 21):
	↓ concentrations of unsaturated lipids, <i>myo</i> -inositol, and choline
	↓ antioxidant capacity (on day 21): ↓ T-AOC, GSH-Px, and SOD activity
	↑ levels of pro-inflammatory cytokines (TNF- α , IL- β , IFN- γ)
	↓ concentrations of anti-inflammatory cytokines (IL-10, IL-2)
	and immunoglobulins (IgG, IgA)

¹All postnatal consequences reviewed were assessed at birth (within a maximum of 24-48 hours postpartum). When they occur at a different time point, this is specifically indicated in the table. Abbreviations: CD = crypt depth; CI = colostrum intake; FAXDC2 = Fatty Acid Hydroxylase Domain Containing 2; GSH-Px = Glutathione Peroxi-dase; HSD11 β 1 = Hydroxysteroid 11-Beta Dehydrogenase 1; HSPB1 = Heat Shock Protein Family B (Small) Member 1; IFN- γ = Interferon

Table 1.1 reviews the main conditions associated with IUGR in piglets from birth to weaning, which will be further examined in the present thesis. Regarding performance, numerous studies have consistently shown that IUGR piglets exhibit slower growth rates compared with their normal littermates across all production stages. Reduced average daily gain (ADG) has been reported in IUGR piglets from birth to weaning (Hansen et al., 2019; Lynegaard et al., 2020), but also from birth to the growing phase (Bérard et al., 2010; Alvarenga et al., 2013; Ruggeri et al., 2024b), and from birth to slaughter (Bérard et al., 2008; Santos et al., 2022). Consequently, and in the best-case scenario, these piglets require additional time to reach the same slaughter weight as their heavier littermates (Quiniou et al., 2002; Gondret et al., 2005), resulting in increased production costs and reduced overall production efficiency (Calderón Díaz et al., 2017b). Another major performance issue in IUGR piglets is their elevated preweaning mortality rate, which occurs predominantly within the first 2-3 days after birth (Roehe and Kalm, 2000; Baxter et al., 2008; Hansen et al., 2019; Matyba et al., 2021; Chaiyapatmaetee et al., 2025). Low vitality at birth (Muns et al., 2013b), and consequently a reduced ability to compete effectively with littermates for early and sufficient colostrum intake (CI) to obtain energy (Amdi et al., 2013; Farmer and Edwards, 2022; Chaiyapatmaetee et al.,

He et al., 2011; Huang et al., 2019; Tang et al., 2022

Tang et al., 2022

He et al., 2011; Amdi et al., 2013; Amdi et al., 2016

He et al., 2011

He et al., 2011; Tang and Xiong, 2022

Huang et al., 2019

Huang et al., 2019

Gamma; IGF-I = Insulin-like Growth Factor 1; IgA = immunoglobulin A; IgG = immunoglobulin G; IL = interleukin; PPARGC1 α = PPARG Coactivator 1 Alpha; SOD2m = Superoxide Dismutase 2; T-AOC = Total Antioxidant Capacity; TNF- α = Tumor Necrosis Factor-alpha; VH = villus height; ZO-1 = Zonula Occludens 1.

2025), together with limited glycogen reserves in both the liver and muscles and an impaired capacity to mobilize glycogen during the first hours after birth to maintain body temperature (Amdi et al., 2013; Voillet et al., 2014; Vanden Hole et al., 2019), have been identified as the main factors contributing to the higher neonatal mortality observed in IUGR piglets.

Piglets exposed to IUGR prioritize brain development due to the “brain sparing effect”, a fetal adaptive response to placental insufficiency (Roza et al., 2008). To adapt to chronic oxygen and nutrient deprivation, primarily resulting from a reduction in placental size per fetus, the fetus redirects cardiac output predominantly toward the brain (Cohen et al., 2015). Although this redirection of blood flow ensures fetal survival by preserving vital brain functions, it compromises the development of other organs due to reduced general vascularization (e.g., liver, kidneys, intestine, and pancreas; Bauer et al., 1998; Cohen et al., 2015; Felicioni et al., 2018). Several studies have assessed organ development in IUGR piglets at birth, reporting decreased absolute organ weights, increased brain-to-heart and brain-to-liver ratios, and greater relative weights of brain and heart (Xu et al., 1994; Amdi et al., 2013; Hansen et al., 2019). At weaning, Lynegaard et al. (2020) observed consistent findings with those reported at birth.

The development of the gastrointestinal tract has been widely studied, as delayed gastrointestinal maturation is a major factor contributing to the slower growth of piglets with IUGR compared to those with normal intrauterine development (Wang et al., 2005). Intrauterine growth restriction can impair intestinal growth and appropriate morphology, resulting in reduced intestinal length and weight, decreased villus height, and a lower villus height-to-crypt depth ratio (Xu et al., 1994; Wang et al., 2005; Wang et al., 2008; D'Inca et al., 2010; Dong et al., 2014; Huang et al., 2019; Chen et al., 2021; Tang and Xiong, 2022), which consequently leads to abnormal digestion and nutrient absorption (Wang et al., 2005; Wang et al., 2008; D'Inca et al., 2010; Santos et al., 2022). This impaired gastrointestinal development has also been associated with altered expression of growth-related genes (Wang et al., 2005) as well as other functional genes, as summarized in Table 1.1. Additionally, growth restriction in the uterus affects gut microbiota composition, with dynamic shifts observed in IUGR pigs compared to normal pigs across various developmental stages (Ruggeri et al., 2025b). Variations in microbial composition during the lactation period, particularly among families linked to short-chain fatty acid production and gut health (Ruggeri et al., 2025a), may contribute to the compromised health and growth of IUGR piglets. Altogether, as noted by Santos et al. (2022), gastrointestinal health and function are essential for the physiology, metabolism, and growth of pigs.

Metabolic alterations induced by intrauterine growth restriction have also been shown to contribute to the impaired development and postnatal growth observed in affected pigs. The distinctive metabolic profile of IUGR piglets, compared with their normal-weight counterparts, is mainly characterized by alterations in lipogenesis and lipid oxidation (He et al., 2011), energy supply and utilization (He et al., 2011; Amdi et al., 2013; Amdi et al., 2016), amino acid and protein metabolism (He et al., 2011; Huang et al., 2019; Tang and Xiong, 2022). Moreover, Huang et al. (2019) reported that IUGR piglets exhibited increased levels of pro-inflammatory cytokines (e.g., TNF- α , IL- β , and IFN- γ) and decreased concentrations of anti-inflammatory cytokines (e.g., IL-10, IL-2) and immunoglobulins (e.g., IgA and IgG) compared with piglets of normal BtW. Although metabolomic data in IUGR piglets are still limited, metabolomic approaches hold great potential for identifying biomarkers that enable the accurate classification of IUGR piglets and for elucidating the underlying mechanisms of this condition (Bahado-Singh et al., 2019).

A series of studies in pigs has demonstrated that intrauterine overcrowding is a critical factor influencing muscle development, as it restricts nutrient availability to the

embryo during a key period of myogenesis (Foxcroft et al., 2006). Handel and Stickland (1987), Bauer et al. (2003), Foxcroft et al. (2006) and Bérard et al. (2010) reported that such overcrowding significantly impairs muscle hyperplasia, particularly affecting the formation of secondary myofibers. Additional studies have shown that piglets subjected to growth restriction during gestation exhibit a reduced total number of muscle fibers, smaller fiber diameters, and decreased skeletal muscle cross-sectional area at birth (Bérard et al., 2010; Alvarenga et al., 2013; Wang et al., 2013). Because muscle fiber hyperplasia is completed by day 90 of gestation, alterations in fiber number observed at birth are permanent (Dwyer et al., 1994). However, Gondret et al. (2006) and Alvarenga et al. (2013) demonstrated that IUGR pigs often display myofiber diameters equal to or even larger than those of their heavier littermates when reaching a constant slaughter weight, suggesting that postnatal muscle hypertrophy may not be compromised by intrauterine growth restriction. Overall, Dwyer et al. (1993) established a positive correlation between the total number of muscle fibers and postnatal growth potential, showing that littermates with a higher number of fibers grew faster and more efficiently than those with fewer fibers.

Although bone development in IUGR piglets has not been extensively investigated, studies in humans have shown that placental insufficiency and maternal metabolic dysfunction can restrict the availability of substrates essential for normal skeletogenesis, thereby impairing endochondral ossification (Briana and Malamitsi-Puchner, 2016; Pastor et al., 2024). Consequently, neonates affected by IUGR exhibit altered biochemical markers of bone formation, including lower circulating concentrations of osteocalcin and 1.25-dihydroxyvitamin D, compared with appropriate-for-gestational-age infants (Briana and Malamitsi-Puchner, 2016). Impaired endochondral ossification has been associated with reduced postnatal growth velocity and lower bone strength during early childhood (Chen et al., 2013). In pigs, Ruggeri et al. (2025a) reported no differences in bone mass at weaning but observed a higher bone mineral density in IUGR piglets compared with normal-weight counterparts.

Text box 5: To understand the mechanisms underlying IUGR, it is essential to comprehensively assess piglet quality at birth, considering physiological, behavioral, and internal developmental characteristics. This approach may allow for the accurate identification of at-risk piglets, which typically exhibit impaired growth and survival throughout all production stages, particularly from birth to weaning.

1.3.5 Small “Normal” Piglets versus Intrauterine Growth Restricted Piglets

The previous sections have shown that IUGR piglets, which can be identified after birth, represent a major challenge to achieving the primary objectives of modern pig production. These piglets are considered to have failed to reach their normal intrauterine growth potential and exhibit asymmetrical organ development, characterized by preserved brain growth at the expense of internal organs (Ashworth, 2013). In contrast, low BtW piglets that display normal allometric growth are considered to have achieved their genetic growth potential (Ashworth, 2013). Distinguishing between these categories is important, as constitutionally normal low BtW piglets may have greater capacity for postnatal recovery when provided with targeted management or nutritional interventions, whereas IUGR piglets present additional developmental abnormalities that limit their viability (Rutherford et al., 2013).

Cui et al. (2022) reported that piglets with a BtW more than two SD below the average BtW of the total population may exhibit either catch-up growth (CUG; weaning weight greater than the average BW of 80 litters of weaned piglets) or non-catch-up growth (weaning weight remains below that average). No significant differences between CUG and normal BtW piglets were observed at the weaning. Catch-up growth has been described in the literature as the body's rapid growth after a period of growth inhibition, particularly during early postnatal life (Faenza et al., 2013; Finkielstein et al., 2013). Limited evidence in pigs also indicates that early postnatal CUG piglets exhibit similar morbidity and growth potential to normal BtW counterparts throughout the growing-fattening period (Montoro et al., 2020). These findings suggest that understanding and promoting CUG before weaning may be critical to mitigating economic losses associated with growth restriction in swine production. Blavi et al. (2021) showed similar findings, indicating that during the early growth stages (*i.e.*, up to the end of lactation), BW categories in pigs tend to fluctuate. This was evidenced by the low correlation observed between BW and the number of days required to reach a market weight of 105 kg, suggesting that a proportion of pigs shift between weight categories over time. Consequently, achieving a high BW at weaning is crucial, as the window of opportunity for lighter pigs to effectively compensate and reach the performance of their heavier counterparts narrows considerably after this stage (López-Vergé et al., 2018; Blavi et al., 2021).

A comprehensive overview of growth patterns throughout the production cycle was provided by Font (2020), who selected pairs of piglets at birth that were 50% siblings of the

same sex, and with a maximum BtW difference of 60 g. The mean difference between paired animals in the number of days required to reach a target BW of 105 kg was 18 ± 13 days. Approximately 80% of the pairs differed in BW at day 163 of age, with differences of up to 14 kg, while the remaining pairs reached similar final BW, differing by only about 2 kg. Differences in BW between the paired animals became apparent between the two groups by the end of the nursery phase and remained significant throughout the fattening period. Therefore, these results indicate that piglets with comparable characteristics at birth can display divergent growth trajectories across subsequent production stages.

Text box 6: Developing a practical and effective on-farm classification system to assess piglet variability and quality at birth is essential, as not all low BtW piglets are affected by IUGR. Such a system may help identify those at higher risk and enable timely, targeted interventions during the early postnatal period, ultimately improving subsequent performance and reducing overall variability.

1.4 Classification of Piglets at Higher Risk

1.4.1 Statistical Learning

Statistical learning encompasses a set of tools designed for modeling and interpreting complex datasets. It is a relatively recent branch of statistics that overlaps with developments in computer science, particularly in machine learning (ML). Since the late 1970s, substantial advances in computing power and classification algorithms have provided robust alternatives to traditional parametric linear models, which dominated from the early 19th century to the 1940s (e.g., linear and logistic regression). Consequently, statistical learning has emerged as a subfield of statistics focused on modeling and prediction, inspired by the development of ML and related disciplines (James et al., 2017).

Artificial intelligence is a field that integrates computer science and large datasets to develop intelligent systems capable of performing tasks that typically require human intelligence (Sarker, 2022). Machine learning and deep learning are specific methods of achieving this goal. Specifically, ML focuses on the learning aspect of artificial intelligence by developing algorithms

that best represent a given dataset. In this process, a computer is provided with a dataset and associated outputs, enabling it to learn and generate an algorithm that describes the relationship between them. This algorithm can then be used to make inferences on new, unseen data (Choi et al., 2020). In ML, four main learning methods are commonly used: supervised, unsupervised, semi-supervised, and reinforcement learning (Hastie et al., 2009; James et al., 2017).

The statistical learning methods applied in the present thesis operate within the supervised learning domain, in which each observation of the predictor variable(s) is associated with a corresponding response measurement. Accordingly, the model relates the response to the predictors, with the aim of accurately predicting the response for future observations (prediction) or improving the understanding of the relationship between the response and the predictors (inference) (James et al., 2017). The most common supervised learning tasks are regression, which involves predicting numerical data, and classification, which entails predicting the category to which a case belongs (Hastie et al., 2009; James et al., 2017). It is important to note that some ML algorithms (*i.e.*, decision trees, random forests, boosting) are also considered part of statistical learning. However, statistical learning also encompasses more classical and formal statistical methods, such as linear and logistic regression. There is some debate regarding this classification, as certain authors consider linear and logistic regression to be classic ML methods (Choi et al., 2020).

Performance evaluation of ML algorithms aims to assess how well a model generalizes to unseen data. In supervised learning, the dataset is typically split into three parts: a training set used to fit the model, a validation set used to tune the algorithm and monitor learning progress, and a test set used to evaluate final performance (Choi et al., 2020). During training, the algorithm iteratively learns the relationship between features and target variables, with its performance on the training set compared to the validation set. This process allows for tuning while avoiding overfitting the training data. True generalizability is assessed using the test dataset, which contains instances the model has never seen. An ideally fitted model is one that performs strongly on training and test datasets, suggesting it is generalizable (*i.e.*, it will perform well on other similar datasets) (Hastie et al., 2009; James et al., 2017).

A receiver operating characteristic (ROC) curve is a technique used to visualize, organize, and compare classifiers based on their performance (Fawcett, 2006). It graphically represents the performance of a classifier by plotting the true positive rate (TPR; sensitivity or recall, *i.e.*, positives correctly identified out of all actual positives) against the false positive rate

(FPR; $1 - \text{specificity}$, *i.e.*, negatives incorrectly identified as positive out of all actual negatives) across different decision thresholds (Fawcett, 2006; Choi et al., 2020). The curve starts at the point (FPR = 0, TPR = 0), where all samples are classified as negative, and ends at the point (FPR = 1, TPR = 1), where all are classified as positive. The intermediate points, which form the curve, are obtained by computing the TPR and FPR for various decision thresholds between 1 and 0, illustrating the trade-off between sensitivity and specificity (Nayeri et al., 2019; Choi et al., 2020). The area under the curve (AUC) quantifies the overall performance of the classifier: an AUC value of 0.50 indicates performance equivalent to a random chance, whereas an AUC of 1.00 represents perfect classification (Hosmer and Lemeshow, 2000; Choi et al., 2020).

1.4.1.1 Linear Regression

Linear regression is a simple approach in supervised learning. The primary goal of regression analysis is to model the relationship between one or more numerical features and a single numerical target, making it a valuable tool for predicting quantitative outcomes (Hastie et al., 2009; James et al., 2017). Simple linear regression predicts a quantitative response Y based on a single predictor variable X , assuming an approximately linear relationship between X and Y . This relationship can be expressed mathematically as $Y = \beta_0 + \beta_1 X + \epsilon$, where β_0 and β_1 represent the intercept and slope, respectively, and ϵ is a random error term with mean zero. The terms β_0 and β_1 are the model's coefficients or parameters (James et al., 2017). Linear regression models a dataset using this slope-intercept form, with the goal of estimating the coefficients that allow the resulting line to best capture the relationship between the input values X and the corresponding outputs Y (Choi et al., 2020). When there is more than one predictor, the model can be extended to multiple linear regression, which accommodates multiple predictors by assigning each one a separate slope coefficient within a single model. The multiple linear regression model can be expressed as $Y = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \dots + \beta_p X_p + \epsilon$, where X_j represents the j -th predictor, and β_j quantifies the association between that predictor and the response, holding all other predictors constant (James et al., 2017). To assess how well a linear regression model fits the data, the residual standard error, which measures the average difference between the predicted and actual values, and the R^2 statistic, which indicates the proportion of variability in the outcome that the model explains, are commonly used. In general, a low residual standard error or an R^2 close to 1 suggests a good fit (James et al., 2017). However, the R^2 value alone does not guarantee that the model is appropriate. It is convenient to evaluate multicollinearity among the predictors and thoroughly examine the residuals to ensure the adequacy and reliability of the model fit.

1.4.1.2 Logistic Regression

Logistic regression is a statistical classification method used to model the relationship between one or more predictor variables and the probability of a specific outcome (Choi et al., 2020). Unlike linear regression, which fits a straight line to the data and may yield predicted values outside the $[0, 1]$ range, logistic regression uses a logistic function that constrains predicted probabilities between 0 and 1 (James et al., 2017; Choi et al., 2020). The logistic function in simple logistic regression is defined as $p(X) = [e^{(\beta_0 + \beta_1 X)}] / [1 + e^{(\beta_0 + \beta_1 X)}]$, where $p(X)$ represents the probability of the outcome given the predictor X , β_0 is the intercept, and β_1 is the coefficient associated with X . This function generates an S-shaped curve that ensures all estimated probabilities are bounded between 0 and 1, providing meaningful and interpretable results regardless of the value of X (James et al., 2017). In logistic regression, the effect of each predictor variable is interpreted in terms of *odds*, defined as the ratio of the probability of the event occurring to the probability of it not occurring (Fonseca Martinez et al., 2017). The model can be extended from a simple to a multiple logistic regression framework, analogous to the transition from simple to multiple linear regression, allowing the inclusion of several predictor variables to model a binary response (James et al., 2017). Moreover, logistic regression can be generalized to handle binomial outcomes (two categories) or multinomial outcomes (> 2 categories) (James et al., 2017; Choi et al., 2020). Overall, the main advantages of logistic regression are that it produces bounded and interpretable probability estimates, provides a solid statistical foundation for classification problems, and can effectively handle a variety of categorical response types (James et al., 2017; Choi et al., 2020).

1.4.1.3 Decision Trees

Decision trees are primarily used for classification tasks, although they can also be applied to regression problems. They are simple, intuitive, and highly interpretable; however, they often do not reach the same predictive accuracy as more advanced and complex supervised learning algorithms (James et al., 2017; Nayeri et al., 2019). A decision tree begins with a root node, representing the initial decision point and containing the feature that best divides the dataset into distinct groups. Each split creates either another decision node (or internal node), which further partitions the data based on another feature, or a terminal node (or leaf), which provides the final prediction (James et al., 2017; Choi et al., 2020). Decision trees are typically drawn upside down, with the leaves positioned at the bottom of the tree. The connections between nodes are called branches (James et al., 2017). This stepwise division of the data into binary subsets is known as recursive partitioning. It

begins with all observations in a single group and successively splits them into two smaller groups according to the variable and cutoff point that most effectively reduce prediction errors. This approach selects the best split at each step without considering future potential splits (Hastie et al., 2009; James et al., 2017; Choi et al., 2020). Despite their simplicity, decision trees can outperform classical statistical methods when the relationship between predictors and the response variable is highly non-linear or involves complex interactions among features. Regarding the main disadvantages, decision trees are prone to overfitting, unstable to changes and noise in the data, biased when working with unbalanced datasets, and computationally expensive on large datasets (Attard, 2023).

1.4.1.4 Random Forests

Random forests are a supervised ensemble learning method that generates multiple decision trees to build a classification or regression model capable of predicting future responses when the target class is known *a priori* (Bakoev et al., 2020; Choi et al., 2020). Unlike standard decision trees, which use all available features for every split, random forests introduce randomness by selecting a subset of predictors at each decision point (Choi et al., 2020). Specifically, when a split is considered, a random sample of m features (from the full set of p predictors) is chosen as potential candidates for splitting, and only one of these m predictors is used to perform the split. A new random subset of features is selected at each subsequent split. By restricting the set of predictors considered at each split, random forests reduce the likelihood that all trees rely on the same dominant predictor, which would make them highly correlated (James et al., 2017). This strategy increases tree diversity, reduces correlation among trees, and improves the overall stability and predictive performance of the ensemble (Bakoev et al., 2020). Each tree independently produces a class prediction (in classification) or a numerical estimate (in regression), and the final model output is obtained by aggregating the predictions of all trees, through majority voting for classification tasks or averaging for regression tasks (Choi et al., 2020). A major advantage of random forests is their robustness and their ability to handle missing data, a common challenge in biological studies (Nayeri et al., 2019).

1.4.1.5 Boosting

Boosting is a general ensemble learning approach that can be applied to many statistical learning methods for both regression and classification tasks (James et al., 2017). It combines a large number of weak learners, typically small decision trees, to build a strong predictive model (Nayeri et al., 2019). Unlike random forests, where trees are built independently, in

boosting the trees are grown sequentially. Each new tree is trained using the residuals from the previous model as the response variable, allowing the algorithm to focus on observations that were previously predicted poorly. The new tree is then added to the existing model to update the residuals and improve overall prediction accuracy. Because each tree depends on those already grown, boosting typically requires smaller and simpler trees, making the learning process gradual but highly effective (James et al., 2017; Nayeri et al., 2019; Bakoev et al., 2020). Boosting has three main tuning parameters: (1) The number of trees (B): increasing B improves model performance up to a point, but excessively large values can lead to overfitting. (2) The shrinkage parameter (λ): which controls the learning rate. Smaller values slow down the learning process, requiring more trees but often yielding better generalization. (3) The number of splits per tree (d): which determines tree complexity. Often $d = 1$ works well, but larger values allow the model to capture higher-order interactions among predictors (Friedman, 2001; Chen and Guestrin, 2016; James et al., 2017). By fitting small trees to the residuals, boosting gradually improves model accuracy in areas where predictions are weak. This slow learning process tends to produce models that are both robust and accurate. Additionally, the use of small trees enhances interpretability (James et al., 2017).

1.4.2 Application in the Pig Industry and Future Perspectives

The current lack of an accurate, effective, and non-invasive method to identify piglets at higher risk (e.g., those affected by IUGR) during early-life stages presents a major challenge for the modern pig industry, as it limits the development of effective intervention strategies (Felicioni et al., 2018). Linear regression models have been widely used for decades as a valuable tool for predicting quantitative responses. In the pig industry, one of their main applications has been the characterization of IUGR piglets by examining relationships between BtW and organ weights, for example (Bauer et al., 1998). More recently, Ruggeri et al. (2024a) demonstrated that linear regression models based on morphometric traits extracted from images of newborn piglets are effective for predicting brain and liver weights and diagnosing IUGR at birth. Furthermore, these models can also be applied to predict BW at different stages of production (Paredes et al., 2012). Similarly, logistic regression models play a key role in pig research because they are well-suited for modeling binary or categorical outcomes such as survival and growth performance. These models have been primarily used to assess the influence of parameters measured at birth on piglet mortality and growth performance during the early postnatal period and up to weaning (Panzardi et al., 2013; Gourley et al., 2020; Geiping et al., 2022). Additionally, other studies have employed logistic regression to identify

potential risk factors for poor postnatal growth and to investigate changes in BW categories throughout the production cycle (Douglas et al., 2013; Huting et al., 2018).

While the studies described above have advanced the understanding of the biological challenges faced by IUGR piglets, as well as the risk factors associated with this subset and their early-life identification, the utility of prior performance information to accurately and timely identify piglets at the highest risk of growth retardation remains largely unexplored. Addressing this challenge requires a shift in the analytical paradigm, from focusing primarily on the goodness of fit in cause-effect models toward evaluating the predictive power of methodologies designed to anticipate outcomes (Steyerberg et al., 2010). Such a perspective opens the door for the application of more advanced predictive approaches with potential contributions to the swine industry (Quinlan, 1987; Friedman, 2001; Chen and Guestrin, 2016; Wright and Ziegler, 2017). The ability of these approaches to generate predictions and insights from large datasets produces information that can support decision-making (Rutten et al., 2013), potentially contributing to more sustainable and efficient pig production. However, large datasets with high quality data are essential for applying these methods and for determining the most effective classification tool based on a representative population while avoiding sampling biases, which poses a challenge when working with animals (Ruggeri et al., 2025b). This issue can be addressed with emerging techniques such as transfer learning, where pretrained models are fine-tuned on smaller, domain-specific datasets, or with data augmentation, which generates synthetic data to expand dataset size and improve model robustness (Han et al., 2018).

Several livestock studies demonstrated the successful application of ML approaches in multiple areas, including health, production, fertility, mortality, nutrition, and breeding. Although ML methods are not new, particularly in the field of reproduction (Firk et al., 2002; Rorie et al., 2002), recent advances in computational power, as well as in data collection and storage, have significantly accelerated their development and practical implementation. Nayeri et al. (2019) provided a comprehensive review of ML methods applied in various areas of animal science in recent years, highlighting that some algorithms exhibit remarkable predictive and discriminative performance, enabling more accurate classification and decision-making compared with traditional statistical approaches. The development of deep learning models, particularly convolutional neural networks, holds considerable promise for identifying pigs at higher risk. These networks are capable of automatically learning complex hierarchical representation from data, enabling precise differentiation between normal and abnormal features (Anwar et al., 2018). By analyzing traits

such as body size, shape, and other morphological characteristics, these models could potentially detect at-risk piglets at birth with greater accuracy than conventional methods, supporting earlier and more targeted interventions. Other techniques, such as support vector machines, may also aid in diagnosing this subset of problematic piglets through the analysis of image data (Zhang et al., 2017).

Text box 7: New algorithms show strong potential to outperform traditional statistical methods in identifying pigs at higher risk across all production stages. By using large and complex datasets, these models can achieve greater diagnostic accuracy and predictive capacity, representing a crucial step toward the early detection of at-risk animals and the implementation of more effective, targeted interventions.

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Chapter 2

Background, hypothesis and objectives

The growing global demand for meat requires the production of high-quality products through competitive and sustainable livestock and industrial systems. An optimal production system must achieve the highest biological efficiency while ensuring optimal welfare conditions for both animals and employees and maintaining maximum respect for the environment. Variability in BW at slaughter is a key factor influencing the overall efficiency of pig production, with tail-end pigs within the population distribution being the main contributors to reduced productivity. The economic impact of low BW pigs is critical in AIAO production systems, as they tend to exhibit higher mortality rates throughout the production cycle, and survivors often pose management challenges, ultimately reducing overall production efficiency and farm profitability. The closer a low BW pig is to the end of the production cycle, the greater the probability it will be sent to slaughter at a later stage. This is due to the limited opportunity to implement effective strategies that enable lighter pigs to catch up with their heavier pen mates, particularly from weaning onwards. Therefore, there is a need to address BW variability at birth and to identify potential risk factors associated with the occurrence of pigs exhibiting delayed growth, which are largely responsible for performance variability within the herd.

In response to the swine industry's interest in finding solutions to the above mentioned challenges and contributing to improved production efficiency and sustainability, along with the need for more basic research to address these issues, the Animal Nutrition and Welfare Service (SNiBA) of the Department of Animal and Food Science at the Universitat Autònoma de Barcelona (UAB), obtained public funding for a four-year research project (Spanish Innovation Agency, Ministry of Science, Innovation and Universities; project code PID2019-103915GB-I00). The Vall Companys Group supported and collaborated in the project by providing their facilities for the trials conducted.

Chapter 1 introduces the effects of increasing sow prolificacy on piglet BtW and mortality, as well as the prevalence and consequences of IUGR in modern swine production systems. Moreover, the relevance of IUGR and low BtW piglets, which exhibit differential growth potential and survivability depending on their degree of growth restriction, highlights the need for further research focusing on their early-life differentiation. Consequently, it was hypothesized that distinct categories of piglets could be established at birth according to their degree of growth restriction. In addition, piglets with low body metrics at birth may present impaired internal physiological status, which could help develop practical on-farm criteria to identify different piglet types at birth. It was also hypothesized that reducing piglet BW variability at birth and throughout the production cycle requires identifying clear differences

among piglets with varying degrees of growth restriction. Accordingly, the first general objective of the present thesis was to describe newborn piglets according to their degree of growth restriction.

Moreover, advances in computing power and classification algorithms, which offer robust alternatives to traditional parametric linear models and hold significant potential for application in the swine industry, are also described in Chapter 1. However, little is known about the use of such algorithms to classify pigs at risk of growth retardation or to identify the main production factors associated with low pig BW. Furthermore, there is growing interest in developing accurate, effective, and non-invasive methods to identify piglets at higher risk during early-life stages, which could facilitate the implementation of targeted and timely intervention strategies. Consequently, it was hypothesized that applying these algorithms to large and comprehensive datasets could outperform classical methodologies in prediction and classification tasks. In addition, early-life risk factors could be more accurately identified, thereby enabling the prediction of early-life survivability and growth performance. Therefore, the second general objective of this thesis was to investigate the potential of recently developed machine learning algorithms applied to large-scale swine production databases, which could be implemented in commercial operations to support data-driven decision-making based on previously recorded information. To achieve the main objectives and test the hypotheses defined above, five specific objectives were formulated:

1. To describe the effects of varying degrees of growth restriction on the internal and external development of newborn piglets and to investigate the correlations between these characteristics (Results presented in Chapters 3 and 4).
2. To determine how internal characteristics differ among piglets classified into different birth weight categories according to their degree of growth restriction, and to assess whether these traits determine their differential growth and survival potential (Results presented in Chapters 3 and 4).
3. To find a multi-criteria model for general on-farm application based on birth-related risk factors, aimed at differentiating piglets with varying early-life survivability and growth potential (Results presented in Chapter 5).

4. To evaluate the potential of machine learning methods to classify pigs at risk of growth retardation throughout the production cycle and to identify the main production factors underlying low body weight at each stage (Results presented in Chapters 6 and 7).
5. To assess the applicability of machine learning methods in the swine industry using large datasets from purebred nucleus and commercial crossbred herds (Results presented in Chapters 6 and 7).

The following chapters describe the methodology used to assess the hypothesis and objectives outlined above, as well as the main findings of this thesis. To achieve the objectives of Chapters 3, 4, and 5, three experiments were conducted under commercial conditions. For Chapters 6 and 7, two large datasets (one from purebred nucleus and one from commercial production) were provided by DNA Swine Genetics, which also collaborated on the project. The findings and conclusions from each chapter are further discussed in Chapter 8.

Chapter 3

Linking the degree of intrauterine growth restriction to alterations in metabolism, energy reserves, and gut health in newborn piglets

Linking the degree of intrauterine growth restriction to alterations in metabolism, energy reserves, and gut health in newborn piglets

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Lay Summary

Piglets with intrauterine growth restriction (IUGR) negatively affect overall swine production efficiency, as they exhibit stunted postnatal growth, reduced feed conversion efficiency, and poorer carcass quality. Classifying piglets at birth according to their degree of IUGR enables farmers to implement targeted strategies for the subset of pigs at higher risk. In this study, piglets were classified based on their birth weight (BtW) into four categories: IUGR, restricted low BtW (R-LBW), non-restricted low BtW (NR-LBW), and normal (N). Overall, IUGR piglets were lighter at birth and showed impaired growth throughout lactation. This growth retardation could be attributed to low vitality and reduced colostrum intake, metabolic alterations affecting amino acid and energy metabolism, gastrointestinal dysfunction characterized by altered morphology and upregulation of pro-inflammatory and stress-related genes, and limited energy reserves. Piglets classified as R-LBW and NR-LBW also exhibited reduced growth performance compared to N piglets and displayed distinct morphological characteristics, although few differences were observed in internal traits between the two categories. Understanding the biological challenges faced by IUGR and low BtW piglets, as well as how to differentiate them, could help farmers improve survival, growth, and overall health, ultimately enhancing farm efficiency and animal welfare.

Teaser Text

Accurate characterization of piglets across different birth weights provides detailed morphological, behavioral, and physiological insights into varying degrees of intrauterine growth restriction, thereby supporting targeted interventions for pigs at risk of growth retardation or poor survivability.

Abstract

In modern swine production, increasing litter size has reduced average birth weight (BtW) and increased the prevalence of intrauterine growth restriction (IUGR). This study aimed to classify piglets according to their degree of IUGR and to evaluate associated morphological, physiological, and behavioral traits. A total of 1,990 piglets were categorized by BtW as IUGR (< 0.75 kg), restricted low BtW (R-LBW; 0.75–0.95 kg), non-restricted low

BtW (NR-LBW; 0.95–1.15 kg), and normal (N; ≥ 1.15 kg). A subset of 48 piglets (12 piglets/category) was euthanized within 24 h of birth for tissue and blood collection. Piglets with IUGR exhibited the lowest body weights from birth to weaning, not differing from R-LBW piglets at d 7 and weaning, while N piglets were the heaviest ($P < 0.001$). Average daily gain was lower ($P \leq 0.027$) in IUGR and R-LBW piglets compared with NR-LBW and N piglets throughout lactation. Colostrum intake (CI) differed ($P < 0.001$), with IUGR piglets consuming 285 g less than N piglets. Consequently, NR-LBW and N piglets showed higher immunoglobulin G concentrations compared with the other categories ($P \leq 0.028$). Morphological indicators confirmed growth restriction, with IUGR piglets showing the lowest values. Vitality scores were lowest in IUGR piglets ($P < 0.001$), with 62.4% scoring the worst. Piglets with IUGR had the lowest albumin concentrations compared with N piglets ($P < 0.001$), whereas N piglets exhibited the highest insulin-like growth factor I concentrations ($P < 0.001$). Metabolomic profiling revealed distinct clustering of IUGR piglets compared with the other categories ($P \leq 0.008$), indicating alterations in amino acid and energy metabolism. Glycogen concentrations at birth were impaired in IUGR piglets, averaging $\sim 55\%$ lower than in N piglets ($P = 0.022$). Intestinal function and development were altered in IUGR and low BtW piglets, which exhibited a lower villus height:crypt depth ratio compared with N piglets ($P \leq 0.029$), along with a gene expression profile characterized by upregulation of genes associated with inflammatory response and stress. In conclusion, IUGR piglets exhibited impaired growth during lactation, which was associated with low vitality, reduced CI, metabolic alterations, gastrointestinal dysfunction, and limited energy availability at birth. Further indicators should be investigated to better understand the differences among low BtW piglets, which also exhibited poorer growth performance than N piglets.

Key words: birth weight, gut development, intrauterine growth restriction, metabolomics, neonatal traits, piglets

3.1 Introduction

The number of pigs weaned per sow per year is a critical determinant of economic efficiency in swine production. In modern production systems, increasing litter size and the number of piglets weaned per sow are major breeding and management objectives (Hansen et al., 2019), with producers expecting up to 30 pigs weaned per sow annually (Knox, 2005). However, it is widely reported that the increase in litter size has resulted in uterine crowding and greater nutrient demands during gestation (Foxcroft et al., 2009). Consequently, average birth weight (BtW) has decreased, resulting in a higher proportion of lightweight piglets at birth (Quiniou et al., 2002; Beaulieu et al., 2010; Riddersholm et al., 2021) that are subject to varying degrees of intrauterine growth restriction (IUGR; Amdi et al., 2013; Hansen et al., 2019). Wu et al. (2006) defined IUGR as impaired fetal growth during gestation, primarily caused by placental insufficiency, which limits the appropriate supply of oxygen and nutrients to the fetus (Cohen et al., 2015). It is estimated that approximately 20% of piglets within a litter exhibit naturally occurring some degree of IUGR (Krueger et al., 2014).

Intrauterine growth restriction is a key factor that negatively affects overall pig production efficiency (Wu et al., 2006). It is associated with an increased risk of neonatal morbidity and mortality, as well as long-term consequences of fetal programming, including stunted postnatal growth, reduced feed conversion efficiency (Wu et al., 2006; Krueger et al., 2014), and poor carcass quality (Foxcroft et al., 2007). Although fetal and birth weight relative to gestational age are often used to define IUGR (Wu et al., 2006), several studies have emphasized that morphological characteristics provide an additional and necessary criterion for identifying IUGR piglets (Baxter et al., 2008; Douglas et al., 2016; Riddersholm et al., 2021). Reported features include distinctive head morphology (dolphin-like head shape, bulging eyes, and wrinkles perpendicular to the mouth; Chevaux et al., 2010; Hales et al., 2013; Hansen et al., 2019), low body mass index (BMI) and ponderal index (PI; Hales et al., 2013; Douglas et al., 2016), reduced crown-to-rump length (CRL; Salgado-López et al., 2025), and a thin body profile (Baxter et al., 2008; Hales et al., 2013; Riddersholm et al., 2021). While severely IUGR piglets exhibiting all these traits are unable to survive, a major challenge for the pig industry lies in identifying piglets that lack these morphological characteristics at birth but subsequently display poor growth, persistently remaining in the lower quartile of the body weight (BW) distribution (Montoro et al., 2020).

In addition to these morphological traits, IUGR piglets prioritize brain development as part of a fetal adaptive response to placental insufficiency (Roza et al., 2008; Amdi et al., 2013), which occurs at the expense of normal development of other organs (Lynegaard et al.,

2020). Consequently, IUGR piglets are characterized by gastrointestinal dysfunction (Xu et al., 1994; Yeung and Smyth, 2003; Wang et al., 2005), impaired liver development with reduced glycogen concentrations (Vanden Hole et al., 2019), and a lower number of muscle fibers due to a decreased ratio of secondary to primary fibers (Handel and Stickland, 1987; Cerisuelo et al., 2007) compared with their normal counterparts. In terms of behavioral variables, Amdi et al. (2013) reported that IUGR piglets consume significantly less colostrum within the first 12 h after birth compared with normal piglets. This reduction has been linked to lower vitality immediately after birth (Herpin et al., 1996; Muns et al., 2013), which compromises the piglet's ability to effectively ingest colostrum (Oliviero et al., 2019).

Nevertheless, most of these morphological, physiological, and behavioral traits have been well characterized primarily in comparisons between severely IUGR and normal piglets. Developing effective management and nutritional interventions for pigs at risk of growth retardation or poor survivability requires reliable tools to identify piglets with any degree of IUGR (Amdi et al., 2013). Accurate characterization of piglets across different BtW offers the potential to provide detailed physiological insights and valuable information on piglets affected by varying degrees of IUGR. This study aimed to establish a classification of piglets at birth according to their degree of IUGR, thereby enabling the implementation of targeted strategies for those at higher risk. To achieve this, we comprehensively evaluated morphological, physiological, and behavioral traits across piglets with varying BtW to identify early-life indicators associated with impaired growth and development.

3.2 Materials and Methods

The study was approved by the Animal Ethics Committee of the Universitat Autònoma de Barcelona (CEEAH2788M2) and was conducted in accordance with European Union guidelines for the care and use of animals in research (European Parliament, 2010).

3.2.1 Animals, Housing, and Experimental Design

This experiment was conducted on a 1,050-sow commercial farm (Landrace x Yorkshire) in Spain. A total of 1,990 live-born crossbred piglets (Pietrain x [Landrace x Yorkshire]; 994 females and 996 males) from 102 litters across 11 consecutive batches were included. Sow parity ranged from 1 to 9 (mean $\pm$ SD: 3.5 ± 2.09). The mean litter size was 22.2 ± 4.18 piglets, and the mean BtW was 1.24 ± 0.32 kg.

The sows were housed in individual farrowing pens (2.7 x 1.7 m²), starting 5 d before the expected farrowing date. Farrowing pens had slatted metal flooring in the sow area and slatted plastic flooring in the rest of the pen, with a heating plate provided for the piglets. During the first few days after parturition, a heat lamp was placed above the heating plate. The temperature in the farrowing room was maintained at 24 °C using electronically controlled forced ventilation, with natural light supplemented by artificial lighting from 0600 h to 1400 h. During farrowings, the lights remained on until the last monitored sow had completed farrowing, typically around 0100 h or 0200 h.

On the day of birth (d 0), prior to litter equalization, piglets were collected, individually ear-tagged (LeeO®, MSD Animal Health, Spain), and weighed. Piglets were classified based on their BtW as follows: IUGR (BtW < 0.75 kg), restricted low BtW (R-LBW; BtW ≥ 0.75 kg and < 0.95 kg), non-restricted low BtW (NR-LBW; BtW ≥ 0.95 and < 1.15 kg), and normal BtW (N; BtW ≥ 1.15 kg). Within 24 h of birth, a subset of 48 piglets (12 per category; one from each category per sow across 12 sows) was euthanized. To identify severely IUGR piglets exhibiting clear signs of restriction, head morphological characteristics (Chevaux et al., 2010; Hales et al., 2013; Hansen et al., 2019) were evaluated at birth. Severe IUGR piglets were defined by the following morphological characteristics of the head: pronounced, dolphin-like head shape, bulging eyes, hair with no direction of growth, and wrinkles perpendicular to the mouth. Only IUGR piglets presenting all these characteristics were selected for euthanasia, whereas piglets selected from the other 3 categories showed none of these characteristics.

3.2.2 Management Routines

Cross-fostering was performed within the first 24 h after birth, once it was ensured that all piglets had consumed colostrum. Special care was provided to IUGR piglets within 1 h of birth to stimulate them to start suckling. The cross-fostering protocol for this study included the following steps: (1) all litters were equalized to 15 piglets to ensure each piglet had access to a teat, (2) when litter size exceeded 15 piglets, those with the lowest and highest BtW were fostered to off-test sows, (3) if more than 15 piglets still remained after step two, average-weight piglets were fostered to multiparous sows (parity 2-5), and (4) piglets were only fostered into litters with fewer than 15 piglets on d 1 of life. Steps two and three were designed to maintain approximately half of the litter above the average BtW, stimulating colostrum and milk production by the sow, while ensuring that the remaining half, with below-average BtW, had access to a teat and thus reducing within-litter competition. Overall, this protocol aimed to maximize the number of piglets remaining with their biological sow. Tail docking and iron

injection (Uniferon®, Intervet International B.V., Boxmeer, The Netherlands) were performed on d 3 after farrowing. Piglets had *ad libitum* access to water, and creep feed (crude protein = 16.91%, ether extract = 4.8%, lactose = 7.69%, net energy = 2,423 kcal/kg, and standardized ileal digestible Lys = 1.2%) was offered *ad libitum* starting 10 d before weaning. Piglets were weaned 4 wk after farrowing (mean $\pm$ SD: 26.1 $\pm$ 0.44 d). Apart from the measurements recorded for this study, all animals were managed according to standard farm routines.

3.2.3 Data and Sample Collection

All piglets were assessed for morphological, behavioral, and physiological traits. At birth, sex, BW, and CRL were recorded, and rectal temperature (RT) was measured within 30 min. Body mass index (birth weight (kg)/[CRL (m)²]), PI (birth weight (kg)/[CRL (m)³]), and relative birth weight (RBW, [(piglet birth weight – mean birth weight of litter)/mean birth weight of litter] x 100) were calculated. Vitality was scored on a scale from 0 to 3 based on udder stimulation (U, score of 0 or 1) and the number of completed circles around enclosure (NCC, score of 0, 1, or 2), according to Muns et al. (2013). For U, a score of 0 was assigned when the piglet showed no head movements (e.g., no U or searching behavior within 30 s), and a score of 1 when head movements were observed. For NCC, a score of 0 was assigned when the piglet was unable to rotate its body axis 360° from its initial orientation and could not walk along the limits of the bucket (55-cm diameter x 60-cm height, solid plastic enclosure, open at the bottom and top); a score of 1 when the piglet was able to either rotate 360° or walk once along the limits within 30 s; and a score of 2 when the piglet was able to either rotate 360° or walk along the limits at least twice within 30 s. Piglets were weighed again on d 1 (after cross-fostering), d 7, and at weaning. Piglet BW gain within the first 24 h after birth was used to estimate individual colostrum intake (CI), based on the equation developed by Theil et al. (2014). Survival was recorded throughout lactation.

The mean $\pm$ SD BtW of piglets selected for physiological analyses (n = 12 piglets/category) were: 0.57 $\pm$ 0.114 kg for IUGR, 0.86 $\pm$ 0.067 kg for R-LBW, 1.02 $\pm$ 0.051 kg for NR-LBW, and 1.36 $\pm$ 0.086 kg for N piglets. First, the piglets were sedated by intramuscular injection of azaperone (Sediron 40 mg/mL; Livisto Int'l, S.L.) and ketamine (Ketamidol 100 mg/mL; VetViva Richter GmbH). Subsequently, blood samples (10 mL) were collected from the jugular vein using BD Vacutainer™ plastic serum tubes. Samples were kept on ice for 1-2 h, centrifuged at 2,000 x g for 10 min at 4 °C to separate serum, and stored at -80 °C until analysis. Because of the limited blood volume collected from

IUGR piglets, only 6 samples were available for serum metabolite analyses in this category. The animals were humanely euthanized by intravenous injection of sodium pentobarbital (Euthasol 400 mg/ml; Dechra Pharmaceuticals PLC), after which tissue samples from the liver, jejunum, and ileum were collected. The liver sample (~ 60 g) consisted of a pooled pieces from each of the six lobes (lobus sinister lateralis and medialis, lobus dexter lateralis and medialis, lobus quadratus and lobus caudatus). Immediately after dissection, the samples were snap-frozen and stored at -80 °C until glycogen concentration analysis. Portions of jejunal and ileal tissue (~ 1.5 cm²) were collected at 30 cm and 2 cm from the ileo-cecal valve, respectively. Jejunal sections were rinsed in phosphate-buffered saline (PBS) and immediately snap-frozen in 1.5 mL of RNAlater (Deltalab, Rubí, Spain), then stored at -80 °C until gene expression analysis. Ileal sections were also rinsed in PBS, placed in individual tubes containing formaldehyde solution for histomorphology analysis, and maintained at room temperature.

3.2.4 Serum Immunoglobulin G, Albumin, and Insulin-like Growth Factor I Concentrations

Serum samples were analyzed for immunoglobulin G (IgG) using Pig IgG ELISA kit (ref. E101-104, Bethyl Laboratories, Inc., USA), albumin using OSR reagents (Bromos cresol Green Method) with AU480 analyzer (Beckman Coulter®, Germany), and insulin-like growth factor I (IGF-I) concentrations using an IGF-I ELISA kit (Ref. E20, Mediagnost, Reutlingen, Germany). Analyses were conducted according to the kit's manual. ELISA plates were read at 450 nm using the Multiskan Sky (ThermoFisher Scientific) and software Skanlt 6.0.1.

3.2.5 Serum Metabolite Analysis

For nuclear magnetic resonance (NMR) sample preparation, an aliquot (500 µL) of each serum sample was thawed on ice, vortexed and centrifuged through 0.5-ml 3kDa Amicon® ultracentrifuge filters at 13,000 x g for 60 min at 4 °C. Prior to use, the filters were prewashed four times with 500 µL of HPLC-grade water by centrifugation at 13,000 x g for 5 min at 4 °C. The eluted fraction (300 µL) was then mixed with 100 µL of PBS (containing 10% D₂O with 0.33% DSS, pH 7.4; Merch KgaA, Darmstadt, Germany) and transferred into a 5-mm Wilmad® NMR tube (Merch KgaA). An additional 150 µL of D₂O was added prior to acquisition of the ¹H NMR profile.

^1H NMR spectra were obtained using a Bruker 600-MHz Avance III NMR spectrometer (Bruker Biospin, Rheinstetten, Germany) operating at a ^1H frequency of 600.13 MHz. The sample temperature was set to 298 K, with an equilibration period of 10 min prior to each spectra acquisition. The 1D- ^1H -nuclear Overhauser effect spectroscopy (1D-NOESY) pulse sequence with presaturation during relaxation delay and mixing time and spoil gradient from the Bruker library was utilized (noesygppr1d). Acquisition parameters were set as follows: mixing time, 100 ms (d8); recovery delay, 2 s (d1); 90° pulse, 11.77 μs (p1); spectral width, 7211.539 Hz (swh); spectral size, 32 k (td); number of scans, 256 (ns); and acquisition time, 2.27 s (aq).

Spectra were processed and analyzed using Chenomx 8.0 profiler software (Chenomx Inc., Edmonton, Canada). This software contains tools for automatic phase, baseline correction, reference calibration, and a library of metabolites for spectral profiling. Automatic tools were used, with manual corrections performed when required. The concentration of each identified metabolite was determined based on internal TSP concentration in the NMR tube (4.3 mM). Metabolic assignments and ^1H spectral images are provided in Supplemental Figs. 3.5, 3.6 and 3.7.

3.2.6 Liver Glycogen Concentration

Frozen liver tissue samples were weighed and minced into small pieces. Each sample (200 mg of tissue) was homogenized in 1 mL of Assay Buffer (1X) from the Glycogen Assay Kit (Cayman Chemical, MI, USA, Item No. 700480) containing protease inhibitors: Nuclear Extraction Protease Inhibitor Cocktail (100X) (Cayman Chemical, MI, USA, Item No. 100009303) diluted 100-fold in the diluted Assay Buffer. The homogenate was centrifuged at $800 \times g$ for 10 min at 4°C , and the resulting supernatant was transferred to a new tube and stored on ice. Immediately after, glycogen concentrations were determined according to the manufacturer's instructions for the Glycogen Assay Kit (Cayman Chemical, MI, USA, Item No. 700480). Plates were read fluorometrically in Spark 10 m (TECAN Austria GmbH) and software Sparkcontrol 2.1.

3.2.7 Jejunal Gene Expression Analysis

Frozen jejunal tissue samples were homogenized in Lysing Matrix D 2 mL tubes (MP Biomedicals, Irvine, CA, US) using a Precellys Evolution tissue homogenizer (Bertin Technologies, Montigny-le-Bretonneux, IDF, FR) coupled with a Cryolys Evolution cooling

system (Bertin Technologies, Montigny-le-Bretonneux, IDF, FR), under a homogenization cycle of 6,500 rpm for 30 s at 4 °C. Total RNA was extracted with the Maxwell® RSC simplyRNA Tissue Kit (Promega Corporation, Madison, WI, US) on a Maxwell® RSC instrument (Promega Corporation, Madison, WI, US), following the manufacturer's instructions. RNA quantity and purity were determined with a NanoDropND-1000 spectrophotometer (NanoDrop products, Wilmington, DE, USA), and RNA integrity was evaluated with an Agilent Bioanalyzer-2100 (Agilent Technologies, Santa Clara, CA, USA). All samples had an RNA integrity number greater than 7. Approximately 1 µg of total RNA was reverse transcribed to double-stranded cDNA using random primers and the High-Capacity cDNA Reverse Transcription kit (Applied Biosystems, Foster City, CA) in a 20 µL reaction. Thermal cycling conditions were 25 °C for 10 min, 37 °C for 120 min, 85 °C for 5 min, followed by a 4 °C hold.

Gene expression was assessed by high-throughput real-time qPCR using a 96.96 Dynamic Array™ IFC for Gene Expression (Standard Biotech Inc., South San Francisco, CA, US) on a Biomark™ HD system (Standard Biotech Inc., South San Francisco, CA, US). A pooled cDNA sample, representative of all the experimental conditions, was used to evaluate qPCR efficiency for each gene following the relative standard curve method. Triplicates of two-fold (1/5, 1/10, 1/20, 1/40, 1/80, 1/160) and four-fold (1/320, 1/1280, 1/5120) serial dilutions were included. Samples were analyzed in duplicate at a 1/20 dilution for the quantification of 44 genes (40 target genes and 4 housekeeping genes) related to intestinal health, selected based on published literature. Primer sequences and gene details are available in González-Solé et al. (2020) and Villagómez-Estrada et al. (2022). Additionally, four genes not previously reported in those studies were analyzed: Myeloid Differentiation Primary Response 88 (*MyD88*) and Nuclear Factor Kappa-light-chain-enhancer of activated B cells (*NF-κB*), both involved in immune and inflammatory responses; SH3 Domain Containing Ringer Finger 2 (*SH3RF2*), involved in protein regulation and degradation; and Proline-Rich AKT1 Substrate 1 (*AKT1S1*), a nutrient transport coding gene. Primer sequences and gene details for these four genes are presented in Supplemental Table 3.6.

Data collection and quality control were conducted using the Fluidigm Real-Time PCR Analysis software (v4.8.1; Standard Biotech Inc., South San Francisco, CA, US). Gene expression analysis was then performed with DAG Expression software (v1.0.5.6) (Ballester et al., 2013). The relative standard curve method was applied to account for gene-specific qPCR efficiency, which was obtained from a serial dilution of a representative cDNA pool, yielding quantity values. Gene expression was normalized using the geometric mean of four

housekeeping genes (*ACTB*, *B2M*, *GAPDH* and *TBP*), generating normalized quantity values. Gene expression data were analyzed by applying the $2^{-\Delta\Delta C_t}$ method for relative quantification and using the sample with the lowest expression as a calibrator.

3.2.8 Ileal Histomorphometry

Ileal tissue samples were dehydrated, embedded in paraffin wax, sectioned at 4 μm , and stained with hematoxylin and eosin. Morphological measurements were performed using a light microscope (BHS, Olympus, Barcelona Spain) following the method described by Nofrarías et al. (2006). Villus height (VH), crypt depth (CD), and the VH:CD ratio were measured in a blinded manner on 10 well-oriented villi and crypts per sample by the same person.

3.2.9 Statistical Analysis

All calculations and statistical analyses were conducted using the open-source software R v.4.4.0 (R Core Team, 2024). Residuals were tested for normality with the Shapiro-Wilk test using the *ols_test_normality* function from the *olsrr* package (Hebbali, 2024) and visually evaluated with normal probability plots. Production performance data and piglet traits at birth were analyzed by ANOVA within a linear mixed-effects model (*lmer* function, *lme4* package; Bates et al., 2015). The model included piglet category (IUGR, R-LBW, NR-LBW, and N) as a fixed effect and sow as a random effect. Piglet vitality was analyzed using a cumulative link model (*c/m* function, *ordinal* package; Christensen, 2023), with vitality scores (0–3) treated as an ordered categorical response. The model included piglet category as a fixed effect, and threshold parameters were estimated under a flexible structure. Vitality distributions for each piglet category were visualized using stacked proportional bar plots generated with the *ggplot2* package (Wickham, 2016).

Laboratory data (*i.e.*, serum IgG, albumin, and IGF-I concentrations; serum metabolites; liver glycogen; and ileal histomorphology) were analyzed using the same modeling approach as production performance data and piglet traits at birth. Variables that did not follow a normal distribution were log₁₀-transformed. Individual metabolites data were normalized using logarithmic transformation (log₁₀) and mean centering. Although logarithmic transformations were performed to compare the metabolic concentrations between categories, original means are presented in Supplemental Table 3.7. Therefore, results are expressed as least squares means $\pm$ SEM, except for metabolites, which are expressed as means $\pm$ SEM from transformed data. The experimental unit was the individual pig. The *P*-values < 0.050 were considered

significant for all data, and $P < 0.100$ were considered trends. Metabolomics data were analyzed using the web-based platform MetaboAnalyst (<https://www.metaboanalyst.ca>). Differences among piglet categories were assessed using a PERMANOVA test. Partial least squares discriminant analysis (PLS-DA) was performed to explore differential metabolites among groups. The Variable Importance for Projection (VIP) score was used to determine the influence of every single component on the principal scores.

Relative gene expression quantification values were checked for normalization using a log10 transformation, and all statistical analyses were performed with R v.4.4.0 (R Core Team, 2024) and Bioconductor (Gentleman et al., 2004). A one-way ANOVA with piglet category as a fixed effect was conducted, and the Benjamini-Hochberg false discovery rate (FDR q -value) was calculated to control for multiple testing (Benjamini and Hochberg, 1995). Pairwise post hoc category comparisons between categories were carried out using Tukey's honest significant difference test (Tukey, 1949). Statistical differences were considered significant at P -values and q -values below 0.050 for the ANOVA and Tukey's analyses and for the FDR, respectively. A principal component analysis (PCA) was performed with samples as cases and gene log10-expressions as variables. The PCA function from the FactoMineR library (Lê et al., 2008) was used for dimensionality reduction and visualization of the first two principal components. The variables factor map was restricted to genes showing cos2-qualities greater than 0.45 and showing significant differences. Two samples from IUGR piglets were excluded from the analysis due to low gene expression and insufficient quantification quality.

3.3 Results

3.3.1 Growth Performance

Growth performance from birth to weaning and CI are presented in Table 3.1. Body weight at birth differed among categories ($P < 0.001$), with IUGR piglets being the lightest and N piglets the heaviest. Differences in BW remained at d 1, d 7, and weaning ($P < 0.001$). However, the numerical differences between IUGR and R-LBW piglets were no longer statistically significant at d 7 and weaning ($P = 0.091$ and $P = 0.493$, respectively). Average daily gain (ADG) was lower ($P < 0.05$) in IUGR and R-LBW piglets compared with NR-LBW and N piglets throughout all periods. Colostrum intake also differed among categories ($P < 0.001$), with IUGR piglets consuming the least on average and N piglets the most, while R-LBW and NR-LBW piglets had intermediate intake levels.

In terms of survival, significant differences were observed among categories ($P < 0.001$) throughout lactation (results not shown). Mortality was highest in IUGR piglets (78.5%), followed by R-LBW piglets (33.1%), NR-LBW piglets (10.9%), and N piglets (5.88%).

Table 3.1 Body weight (BW) and average daily gain (ADG) from birth to weaning, and colostrum intake for four categories of pigs classified by birth weight as intrauterine growth restricted (IUGR), restricted low birth weight (R-LBW), non-restricted low birth weight (NR-LBW), and normal birth weight (N).

Item	Category				SEM	P =
	IUGR	R-LBW	NR-LBW	N		
BW, ¹ kg						
Birth	0.65 ^d	0.88 ^c	1.06 ^b	1.44 ^a	0.017	< 0.001
D 1	0.73 ^d	0.92 ^c	1.13 ^b	1.54 ^a	0.033	< 0.001
D 7	1.22 ^c	1.47 ^c	1.84 ^b	2.49 ^a	0.102	< 0.001
Weaning	4.08 ^c	4.69 ^c	5.68 ^b	7.27 ^a	0.411	< 0.001
ADG, ² kg						
First week, d 0 to 7	78.8 ^c	87.2 ^c	117 ^b	158 ^a	13.73	< 0.001
D 7 to weaning	146 ^c	166 ^c	200 ^b	249 ^a	17.46	< 0.001
Lactation, d 0 to weaning	128 ^c	142 ^c	174 ^b	220 ^a	15.07	< 0.001
Colostrum intake, ³ g/piglet	208 ^d	272 ^c	354 ^b	493 ^a	17.45	< 0.001

¹BW at birth (n = 107 IUGR, 216 R-LBW, 383 NR-LBW, 1,284 N); BW d 1 (n = 35 IUGR, 170 R-LBW, 318 NR-LBW, 980 N); BW d 7 (n = 19 IUGR, 136 R-LBW, 301 NR-LBW, 958 N); BW at weaning (n = 14 IUGR, 115 R-LBW, 286 NR-LBW, 929 N). ²ADG first week (n = 19 IUGR, 134 R-LBW, 298 NR-LBW, 951 N); ADG d 7 to weaning (n = 14 IUGR, 114 R-LBW, 285 NR-LBW, 921 N); ADG lactation (n = 14 IUGR, 113 R-LBW, 284 NR-LBW, 922 N). ³Colostrum intake (n = 35 IUGR, 168 R-LBW, 312 NR-LBW, 970 N).

3.3.2 Piglet Traits at Birth

Piglets morphological (*i.e.*, CRL, BMI, PI, RBW) and physiological (*i.e.*, RT) characteristics at birth differed among the four categories (Table 3.2). Crown-to-rump length increased progressively from IUGR to N piglets ($P < 0.001$), with R-LBW and NR-LBW showing intermediate values, which differed from each other and from the other categories ($P < 0.001$). Body mass index followed a similar pattern, with IUGR piglets having the lowest values and N piglets the highest ($P < 0.001$). Ponderal index differed between IUGR and N piglets ($P < 0.001$), but no significant differences were observed between R-LBW and NR-LBW piglets ($P = 1.00$) or between R-LBW and N piglets ($P = 0.109$). Relative birth weight also differed among categories

($P < 0.001$). Rectal temperature recorded within 30 min of birth was lowest in IUGR piglets and highest in N piglets ($P < 0.001$), with R-LBW and NR-LBW piglets showing intermediate values.

The probability distribution of vitality scores at birth is shown in Fig. 3.1. Intrauterine growth restricted piglets exhibited the lowest vitality, with a greater proportion scoring 0 (62.4%) and 1 (21.5%) compared with the other categories ($P < 0.001$). In contrast, R-LBW, NR-LBW, and N piglets showed similar distributions ($P > 0.05$), with most piglets scoring 1 (40.8, 44.6, and 42.9%, respectively) or 2 (38.8, 35.0, and 36.4%, respectively). Only a small proportion of piglets in these three categories scored 0 ($< 18\%$) or 3 ($< 8\%$). The proportion of high-vitality piglets (score of 3) was low overall but was slightly greater in NR-LBW (6.1%) and N piglets (7.5%) compared with IUGR piglets (1.1%).

Table 3.2 Birth traits of piglets across four categories based on birth weight: intrauterine growth restricted (IUGR), restricted low birth weight (R-LBW), non-restricted low birth weight (NR-LBW), and normal birth weight (N).

Item	Category				SEM	$P =$
	IUGR	R-LBW	NR-LBW	N		
<i>n</i>	107	216	383	1,284		
Physical characteristics						
Crown-to-rump length, cm	19.1 ^d	20.5 ^c	21.9 ^b	24.0 ^a	0.123	< 0.001
Body mass index, kg/m ²	17.5 ^d	20.7 ^c	22.1 ^b	24.7 ^a	0.225	< 0.001
Ponderal index, kg/m ³	92.0 ^c	101a ^b	101 ^b	103 ^a	1.27	< 0.001
Relative birth weight, %	-49.8 ^d	-30.1 ^c	-14.3 ^b	13.8 ^a	1.36	< 0.001
Rectal temperature (RT)						
RT at birth, ¹ °C	35.0 ^d	35.8 ^c	36.3 ^b	37.0 ^a	0.169	< 0.001

¹The rectal temperature of each piglet was measured within 30 minutes of birth.

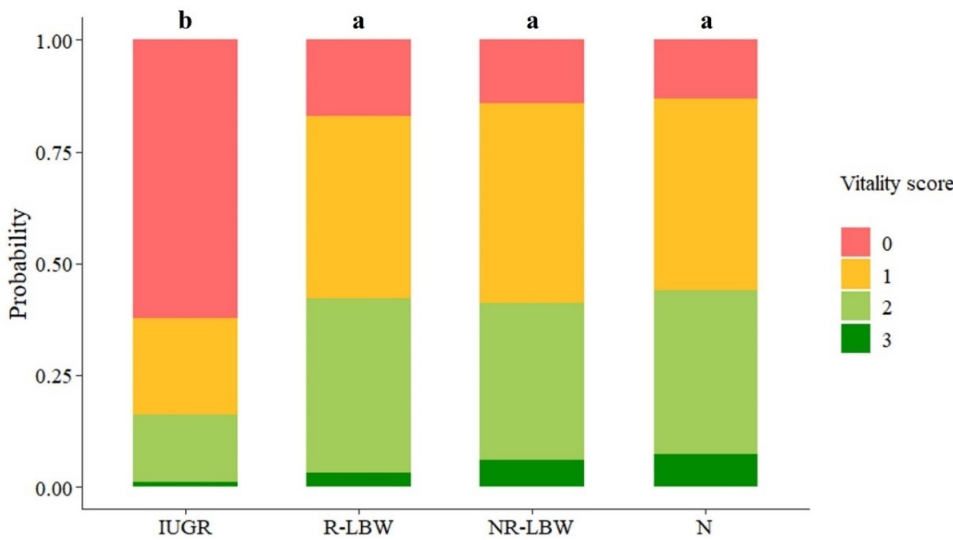


Fig. 3.1 Probability distribution of Vitality scores at birth for four categories of pigs classified by birth weight as intrauterine growth restricted (IUGR, $n = 93$), restricted low birth weight (R-LBW, $n = 152$), non-restricted low birth weight (NR-LBW, $n = 294$), and normal birth weight (N, $n = 939$). Significant differences among groups ($P < 0.05$) are indicated by different letters.

3.3.3 Serum Immunoglobulin G, Albumin, and Insulin-like Growth Factor I

Serum concentrations of IgG, albumin, and IGF-I at birth differed among piglet categories (Table 3.3). Immunoglobulin G concentrations were lowest in IUGR piglets and greatest in NR-LBW and N piglets ($P < 0.001$), with R-LBW piglets showing intermediate values. No differences were observed between NR-LBW and N piglets ($P = 1.00$). Albumin concentrations were lower in IUGR piglets compared with N piglets ($P < 0.001$), whereas R-LBW and NR-LBW piglets did not differ significantly from each other or from either extreme group ($P > 0.05$). Insulin-like growth factor I concentrations were lowest in IUGR piglets and highest in N piglets ($P < 0.001$), with R-LBW and NR-LBW piglets showing intermediate values. Restricted-LBW piglets did not differ significantly from IUGR ($P = 0.057$) or NR-LBW piglets ($P = 0.265$).

Table 3.3 Concentrations of immunoglobulin G (IgG), albumin, and insulin-like growth factor I (IGF-I) at birth for four categories of pigs classified by birth weight as intrauterine growth restricted (IUGR), restricted low birth weight (R-LBW), non-restricted low birth weight (NR-LBW), and normal birth weight (N).

Item	Category				SEM	P =
	IUGR	R-LBW	NR-LBW	N		
<i>n</i>	12	12	12	12		
Blood						
IgG, mg/mL	1.281 ^c	16.12 ^b	27.94 ^a	28.24 ^a	3.180	< 0.001
Albumin, g/dL	0.510 ^b	0.618 ^{ab}	0.636 ^{ab}	0.731 ^a	0.037	< 0.001
IGF-I, ng/mL	23.97 ^c	31.22 ^b	37.11 ^b	54.02 ^a	3.352	< 0.001

3.3.4 Overall Metabolomic Profile

The PLS-DA 2D score plot of serum metabolites revealed distinct clustering among the piglet categories (Fig. 3.2a), with clear separation between IUGR piglets and the other categories. The PERMANOVA test confirmed a significant difference in the metabolic profile of IUGR piglets compared to the other categories ($P \leq 0.008$), whereas no significant differences were observed among the remaining three groups ($P > 0.05$) (results not shown). Metabolites with VIP scores > 1 are presented in Fig. 3.2b, with amino acids (AA) contributing most to the cluster separation, followed by metabolites related to energy metabolism. Amino acids (*i.e.*, Pro, His, Tyr, Asn, Met, Val, Thr, Phe, and Leu) were upregulated in N piglets compared to IUGR piglets ($P \leq 0.031$). Glucose concentrations also differed among categories ($P < 0.001$), being higher in N and NR-LBW piglets than in IUGR piglets. In contrast, hypoxanthine was upregulated in IUGR piglets compared to the other three categories ($P < 0.001$). Detailed metabolite concentrations for each category are provided in Supplemental Table 3.7.

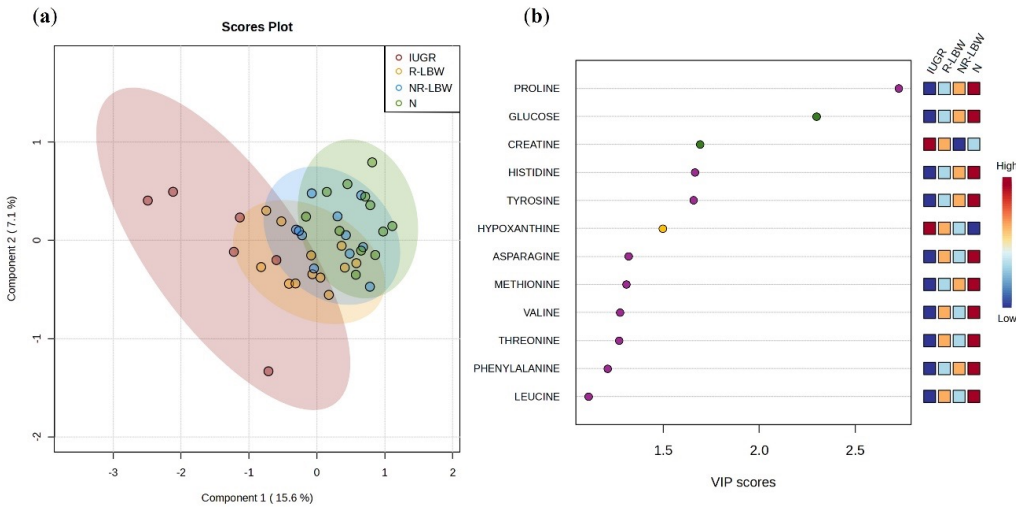


Fig. 3.2 (a) PLS-DA 2D scores plot of serum metabolites from intrauterine growth restricted (IUGR, $n = 6$), restricted low birth weight (R-LBW, $n = 12$), non-restricted low birth weight (NR-LBW, $n = 12$), and normal birth weight (N, $n = 12$) piglets. Shaded areas in different colors indicate the 95% confidence intervals. (b) Metabolites with VIP scores > 1 . Metabolites are color-coded according to their biochemical category: amino acids (purple), energy metabolism-related metabolites (green), and purine metabolism-related metabolites (yellow). Abbreviations: PLS-DA = partial least squares discriminant analysis; VIP = Variable Importance for Projection.

3.3.5 Liver Glycogen

The results of liver glycogen concentrations are presented in Fig. 3.3. Significant differences were observed among the four categories ($P = 0.014$), with a linear increase from piglets with the lowest BtW to those with the highest. Intrauterine growth restricted piglets exhibited the lowest concentrations, whereas N piglets had the highest ($P = 0.022$). Restricted-LBW and NR-LBW piglets presented intermediate values that did not differ significantly from each other or from the other categories ($P > 0.05$), due to the high variability within groups.

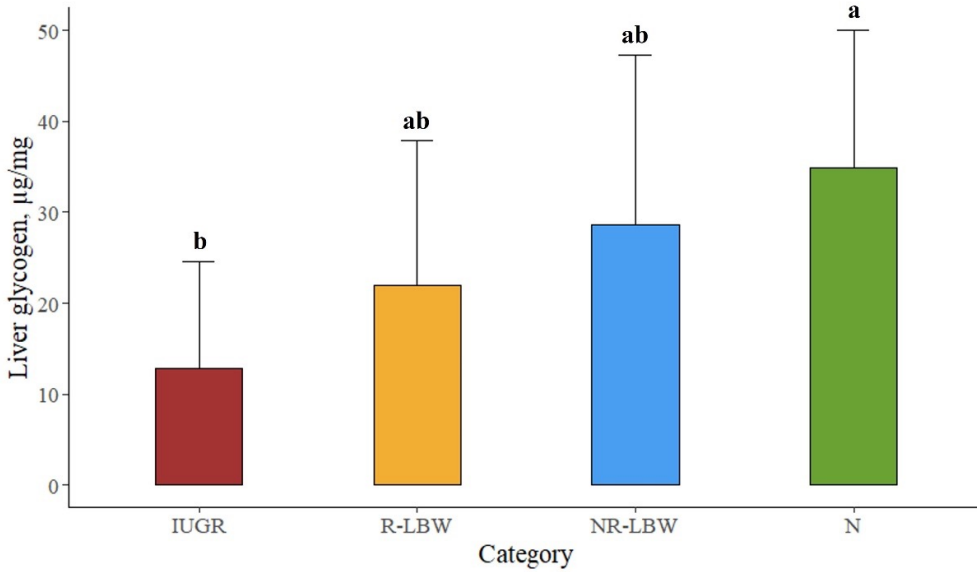


Fig. 3.3 Liver glycogen concentration at birth for four categories of pigs classified by birth weight as intrauterine growth restricted (IUGR, $n = 12$), restricted low birth weight (R-LBW, $n = 12$), non-restricted low birth weight (NR-LBW, $n = 12$), and normal birth weight (N, $n = 12$). Significant differences ($P < 0.05$) are indicated by different letters.

3.3.6 Jejunal Gene Expression

The results of the jejunal gene expression analysis are presented in Table 3.4. Among antioxidant enzymes, *GPX2* was upregulated in N piglets compared with all other categories ($P < 0.001$), with IUGR piglets showing the lowest values and R-LBW and NR-LBW being intermediate and not different from each other ($P = 0.849$). In contrast, *SOD2m* expression was downregulated in NR-LBW piglets compared with IUGR piglets ($P = 0.023$). Genes associated with barrier function (*OCLN* and *ZO1*) were upregulated in IUGR piglets relative to all other categories ($P < 0.001$). A similar pattern was observed for *SH3RF2*, which was highest in IUGR piglets and lowest in NR-LBW and N piglets ($P < 0.001$). For digestive function, *ALPI* expression was upregulated in IUGR piglets compared with NR-LBW and N piglets ($P \leq 0.031$), while *DAO1* showed a comparable pattern. The *IGF1R* gene transcription was downregulated in NR-LBW and N piglets relative to IUGR piglets ($P < 0.001$), whereas R-LBW piglets displayed intermediate values that differed from the other three categories ($P \leq 0.034$). Immune-related genes also exhibited differential expressions: *GBP1* was downregulated in IUGR piglets compared with all other categories ($P \leq 0.008$), while *IFNGR1*, *IL1 β* , *NF-K κ* , *PPARGC1 α* , *TGF β 1*, and *TLR4* were upregulated in IUGR piglets relative to N

piglets ($P < 0.05$). Restricted-LBW and NR-LBW piglets showed intermediate expression levels that did not differ from each other. Several nutrient transport genes were upregulated in IUGR piglets, while N piglets consistently displayed the lowest expression ($P \leq 0.042$). Stress-related genes (*HSD11B1* and *CRHR1*) were upregulated in IUGR piglets compared with NR-LBW and N piglets ($P \leq 0.016$).

A PCA was performed to evaluate correlations in gene expression among samples from the four piglet categories. The individuals factor map (Fig. 3.4a) displays sample identifiers colored by category, whereas the variables factor map (Fig. 3.4b) illustrates the correlation structure of genes across samples. The 2D representation explained 47.35% of the total variance. Overall, the PCA revealed clear patterns in gene expression. All significant genes, except *GBP1* and *GPX2*, were well represented in the 2D space (long arrows) and were in the first and fourth quadrants. Samples from IUGR piglets (dark red) were also positioned in these quadrants, indicating medium to high expression levels. In contrast, *GBP1* and *GPX2* were positioned in the second quadrant, where samples from N and NR-LBW piglets (green and blue, respectively) were predominantly located. Samples from R-LBW piglets were dispersed across all quadrants.

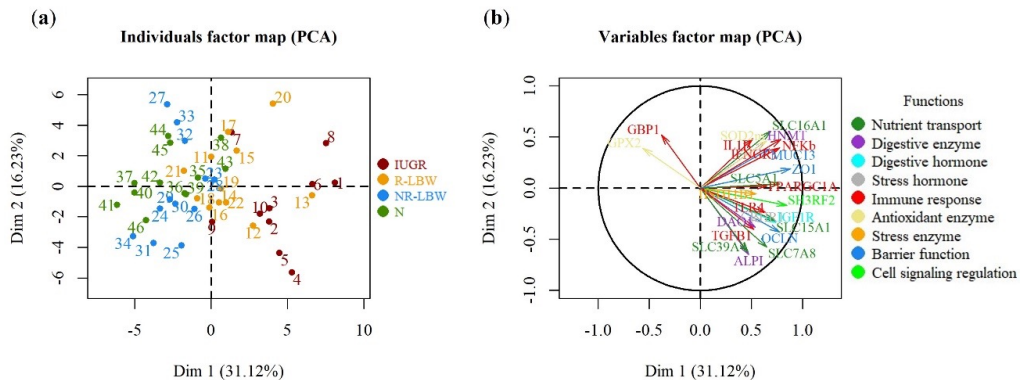


Fig. 3.4 Principal component analysis (PCA): (a) Individuals factor map of jejunal samples, color-coded by category: IUGR = intrauterine growth restricted piglets ($n = 10$); R-LBW = restricted low birth weight piglets ($n = 12$); NR-LBW = non-restricted low birth weight piglets ($n = 12$); N = normal birth weight piglets ($n = 12$). (b) Variables factor map of gene expression in the jejunum. Only genes with $P < 0.05$ and represented by a long arrow are displayed. Each arrow color denotes a different functional group.

Table 3.4 Relative gene expression on jejunal mucosa at birth for four categories of pigs classified by birth weight as intrauterine growth restricted (IUGR, $n = 10$), restricted low birth weight (R-LBW, $n = 12$), non-restricted low birth weight (NR-LBW, $n = 12$), and normal birth weight (N, $n = 12$). Gene expression values are presented as ratios of cycle relative threshold value for each gene normalized to that of the reference sample. P-values come from the ANOVA test and FDR is the false discovery rate.

Function	Genes ¹	Category				SEM	P =	q-value (FDR) =
		IUGR	R-LBW	NR-LBW	N			
Antioxidant enzyme	GPX2	0.04 ^c	0.39 ^b	0.58 ^b	1.81 ^a	0.147	< 0.001	< 0.001
	SOD2m	1.31 ^a	1.18 ^a	0.75 ^b	0.80 ^{ab}	0.054	0.007	0.019
Barrier function	OCLN	1.44 ^a	1.14 ^a	0.88 ^b	0.79 ^c	0.030	< 0.001	< 0.001
	ZO1	1.32 ^a	0.88 ^b	0.55 ^c	0.51 ^c	0.038	< 0.001	< 0.001
Cell signaling regulation	SH3RF2	1.66 ^a	0.92 ^b	0.66 ^c	0.68 ^c	0.032	< 0.001	< 0.001
Digestive enzyme	ALPI	1.50 ^a	1.07 ^{ab}	0.94 ^b	0.95 ^b	0.041	0.016	0.036
	DAO1	1.28 ^a	1.17 ^{ab}	0.83 ^b	0.97 ^{ab}	0.040	0.015	0.036
Digestive hormone	IGF1R	1.57 ^a	1.05 ^b	0.75 ^c	0.61 ^c	0.035	< 0.001	< 0.001
Immune response	GBP1	0.46 ^b	0.91 ^a	0.89 ^a	1.25 ^a	0.069	< 0.001	0.001
	IFNGR1	1.13 ^a	1.08 ^a	0.76 ^{bc}	0.73 ^c	0.043	0.004	0.012
	IL1 β	2.03 ^a	0.42 ^{ab}	0.36 ^b	0.28 ^{ab}	0.137	0.035	0.063
	NF-K κ	1.06 ^a	0.88 ^{ab}	0.72 ^b	0.67 ^b	0.037	0.004	0.012
	PPARGC1 α	1.65 ^a	1.16 ^{ab}	0.91 ^b	0.94 ^b	0.057	0.018	0.037
	TGF β 1	1.51 ^a	1.20 ^{ab}	1.13 ^{ab}	1.13 ^b	0.032	0.036	0.063
	TLR4	1.32 ^a	1.14 ^{ab}	0.86 ^b	0.87 ^b	0.036	0.002	0.006
Nutrient transport	AKT1S1	1.55 ^a	1.07 ^{ab}	1.03 ^{ab}	0.87 ^b	0.059	0.042	0.070
	SLC15A1/PEPT1	1.91 ^a	1.40 ^{ab}	1.01 ^b	0.99 ^b	0.045	0.001	0.002
	SLC16A1/MCT1	1.16 ^a	0.99 ^{ab}	0.78 ^b	0.73 ^b	0.048	0.016	0.036
	SLC39A4/ZIP4	1.87 ^a	1.21 ^{ab}	1.04 ^{ab}	0.93 ^b	0.057	0.027	0.052
	SLC5A1/SGLT1	1.69 ^a	1.01 ^{ab}	0.54 ^b	0.55 ^b	0.088	< 0.001	0.001
Stress enzyme	SLC7A8	2.49 ^a	1.09 ^b	0.78 ^{bc}	0.52 ^c	0.077	< 0.001	< 0.001
	HSD11B1	1.41 ^a	1.16 ^{ab}	0.90 ^b	0.89 ^b	0.041	0.007	0.019
Stress hormone	CRHR1	3.20 ^a	1.91 ^a	1.65 ^{bc}	1.14 ^c	0.067	< 0.001	0.001

¹Genes: GPX2 = glutathione peroxidase 2; SOD2m = superoxide dismutase 2; OCLN = occludin; ZO1 = zonula occludens 1; SH3RF2 = SH3 domain containing ring finger 2; ALPI = intestinal alkaline phosphatase; DAO1 = D-amino acid oxidase; IGF1R = insulin like growth factor I receptor; GBP1 = guanylate binding protein 1; IFNGR1 = interferon gamma receptor 1; IL1 β = interleukin 1 beta; NF-K κ = nuclear factor kappa-light-chain-enhancer of activated B cells; PPARGC1 α = PPARG coactivator 1 alpha; TGF β 1 = transforming growth factor beta 1; TLR4 = toll like receptor 4; AKT1S1 = proline-rich AKT1 substrate 1; SLC15A1/PEPT1 = solute carrier family 15 member 1; SLC16A1/MCT1 = solute carrier family 16 member 1; SLC39A4/ZIP4 = solute carrier family 39 member 4; SLC5A1/SGLT1 = solute carrier family 5 member 1; SLC7A8 = solute carrier family 7 member 8; HSD11B1 = hydroxysteroid 11-beta dehydrogenase 1; CRHR1 = corticotropin releasing hormone receptor 1. ^{a,b,c} Different letters in the same row indicate significant statistical mean differences in the four categories (Tukey's test P -value < 0.05).

3.3.7 Ileal Histomorphology

The ileal histomorphology results (Table 3.5) indicated significant differences in VH, CD, and the VH:CD ratio among piglets classified by BtW ($P < 0.001$). Normal piglets exhibited the greatest VH and CD values, whereas IUGR piglets showed the lowest values. Restricted-LBW and NR-LBW piglets had intermediate values. Specifically, NR-LBW piglets differed from IUGR piglets for both VH and CD ($P < 0.05$), while R-LBW piglets differed from IUGR and N piglets for VH ($P < 0.05$) and from N piglets for CD ($P = 0.033$). For the VH:CD ratio, IUGR piglets had the lowest value, N piglets had the highest, and both R-LBW and NR-LBW piglets exhibited intermediate values that did not differ significantly from each other or from IUGR piglets.

Table 3.5 Ileal histomorphology at birth for four categories of pigs classified by birth weight as intrauterine growth restricted (IUGR), restricted low birth weight (R-LBW), non-restricted low birth weight (NR-LBW), and normal birth weight (N).

Item	Category				SEM	P =
	IUGR	R-LBW	NR-LBW	N		
<i>n</i>	12	12	12	12		
Ileal morphology						
VH, μm	332 ^c	426 ^b	459 ^{ab}	537 ^a	23.3	< 0.001
CD, μm	39.3 ^c	43.4 ^b	46.1 ^{ab}	47.7 ^a	1.70	< 0.001
VH:CD ratio	8.3 ^b	9.6 ^b	9.9 ^b	11.7 ^a	0.49	< 0.001

Abbreviations: CD = crypt depth; VH = villus height.

3.4 Discussion

Fetal growth restriction is often caused by chronic placental insufficiency, which limits the supply of oxygen and nutrients to the developing fetus and ultimately impairs its growth and development (Cohen et al., 2015; Chand et al., 2022). In recent decades, the incidence of this condition has increased, primarily driven by larger litter sizes that result in uterine crowding and elevated nutrient demands during gestation (Foxcroft et al., 2009).

Consequently, IUGR piglets pose a significant challenge to swine production efficiency, affecting both growth performance and overall herd productivity (Wu et al., 2006). This subset of piglets has been well characterized in the literature for their low BtW and distinctive morphology (Chevaux et al., 2010; Hales et al., 2013; Douglas et al., 2016; Riddersholm et al., 2021), facilitating their early identification and the implementation of targeted management strategies. The authors emphasize the importance of identifying low BtW piglets that lack distinctive morphological traits at birth but exhibit poor subsequent growth, consistently remaining in the lower quartile of the BW distribution and requiring extra time to reach target slaughter weight (Douglas et al., 2014; He et al., 2016; Montoro et al., 2020). Font (2020) demonstrated that pairs of half-brothers with the same low BtW can exhibit significant differences in weight by the end of the nursery phase, and these differences persist through the fattening phase. This indicates that such piglets may experience varying degrees of growth restriction, which can substantially affect group homogeneity over the production cycle.

To examine the full range of BtW within the study population, piglets were classified into four categories based on BtW. The IUGR category included piglets with a BtW more than 1.5 SD below the mean litter weight (Wang et al., 2016; Van Tichelen et al., 2021), corresponding to a BtW of less than 0.75 kg in the study population. The cut-off value of 1.15 kg for the low BtW category was determined based on previous literature (He et al., 2016; Wang et al., 2017; Montoro et al., 2020) and the lower 30th percentile of the BtW distribution in the study population. Within the low BtW population without morphological signs of IUGR, two subcategories were defined to evaluate varying degrees of growth restriction. Piglets with a BtW ≥ 1.15 kg were classified as normal and served as the reference category. There is a plethora of scientific literature aiming to characterize IUGR at birth (Chaiyapatmaetee et al., 2025), its effects on preweaning performance (Van Ginneken et al., 2023), organ function (Bauer et al., 2003), and gastrointestinal health and development (Wang et al., 2005; Tang and Xiong, 2022; Villagómez-Estrada et al., 2022), among others. However, to the author's knowledge, no previous studies have investigated different categories of low BtW piglets to accurately characterize them at birth and identify early-life indicators of growth restriction that may explain subsequent differences in growth performance.

Differences in BtW among the four piglet categories were also reflected in distinct physical characteristics at birth (*i.e.*, CRL, BMI, RBW), consistent with previous findings

from our group (Salgado-López et al., 2025), which reported strong correlations between BtW and these traits. Several studies have identified BtW as a key predictor of postnatal performance (Gondret et al., 2005; Rehfeldt et al., 2008; Fix et al., 2010) and survival (Van der Lende and De Jager, 1991; Roehe and Kalm, 2000), whereas others have suggested that indicators of body conformation may provide more accurate predictions of both survival and growth (Hales et al., 2013; Huting et al., 2018; Hansen et al., 2019). In agreement with these findings, survival and growth performance during lactation differed among categories. The high mortality observed in IUGR piglets (78.5%) compared to the other categories may be attributed to their low vitality scores, consistent with the results of Muns et al. (2013). Regarding growth performance, no differences in ADG during the first week or across the entire lactation period were observed between IUGR and R-LBW piglets, which reached similar BW at d 7 and at weaning. This underscores the importance of investigating additional indicators to better understand the biological challenges faced by low BtW piglets and reflects that changes in piglets' BW categories are common during the lactation period (Douglas et al., 2013; Blavi et al., 2021).

Rectal temperature was measured immediately after birth to better reflect intrauterine conditions rather than the piglet's body temperature after exposure to the external environment. Rectal temperature also differed among categories, with N piglets averaging 2 °C higher than IUGR piglets and about 1 °C higher than R-LBW and NR-LBW piglets. These findings align with those of Baxter et al. (2008, 2009), who reported higher birth temperatures in surviving compared with non-surviving piglets, but contrast with other studies in which RT was not associated with piglet survival or growth (Tuchscherer et al., 2000; Casellas et al., 2004; Panzardi et al., 2013).

Results regarding CI confirmed previous findings that piglet colostrum consumption increases with BtW (Devillers et al., 2007; Declerck et al., 2017; Hasan et al., 2019; Quesnel et al., 2023), showing a linear increase from IUGR to N piglets. Moreover, other piglet characteristics, such as vitality immediately after birth, have been identified as important factors influencing their ability to ingest colostrum (Peltoniemi et al., 2021; Oliviero, 2023). This helps explain why IUGR piglets in this study consumed the lowest amounts of colostrum, on average, 285 g less than N piglets. Adequate colostrum ingestion is crucial for neonatal survival and development, as it provides immunoglobulins for immune protection and energy for thermoregulation and growth (Devillers et al., 2004). Colostrum is particularly rich in IgG (Le Dividich et al., 2005; Peltoniemi et al., 2021), which is essential for piglets to acquire passive immunity. Consistent with Oliviero (2023), who reported that piglets with higher BtW have

increased IgG concentrations in the blood, the highest IgG levels in this study were observed in NR-LBW and N piglets, followed by R-LBW (with approximately half the concentration) and IUGR piglets, whose values were close to zero. This finding suggests that, while IUGR piglets are unable to achieve adequate colostrum intake, low BtW piglets exhibit variable initial suckling behaviors. Colostrum intake in this subset of piglets is critical for their future survival, as they have reduced energy reserves and a lower capacity for thermoregulation (Ward et al., 2020).

Quesnel et al. (2023) demonstrated positive associations of albumin and IGF-I with CI, partially explained by the fact that concentrations of these variables are positively correlated with BtW. In line with these findings, we observed higher albumin and IGF-I concentrations in N piglets compared with IUGR piglets, with R-LBW and NR-LBW piglets exhibiting intermediate values. Albumin plays a key role in transporting various proteins in the blood, and reduced levels have been associated with compromised growth, overall health, nutritional status, and liver function (Doornenbal et al., 1986; Wang et al., 2020; Rymut et al., 2021). Insulin-like growth factor I promotes mitogenic activity in target tissues and plays a critical role in the regulation of tissue and organ development (Morise et al., 2008). Concentrations of both albumin and IGF-I have been recognized as reliable indicators of fetal growth and maturity at birth (Herpin et al., 1993; Canario et al., 2007; Gondret et al., 2018), with low levels potentially reflecting impaired developmental maturity.

Another consequence of this reduced maturity at birth, often resulting from fetal malnutrition and inadequate CI (Sanz-Cortés et al., 2013), was the lower hepatic glycogen concentration observed in IUGR piglets compared with N piglets, consistent with the findings of Vanden Hole et al. (2019). In our study, IUGR piglets exhibited hepatic glycogen concentrations approximately 60% lower than those of N piglets. Such low glycogen levels at birth may compromise the piglet's ability to mobilize their energy reserves, likely because these reserves are already critically low at birth. Consequently, impaired gluconeogenesis combined with poor glycogen stores results in low blood glucose concentrations, which have been associated with reduced viability and increased mortality (Panzardi et al., 2013). In agreement with these findings, we observed higher blood glucose concentrations in NR-LBW and N piglets compared with IUGR piglets, whereas R-LBW piglets showed intermediate values that did not differ from the other categories. Additionally, the lack of energy substrates in IUGR piglets appeared to numerically activate creatine metabolism, a by-product of phosphocreatine turnover. The non-significant elevated creatine levels observed in IUGR piglets may reflect a metabolic adaptation to compensate for insufficient energy availability

(Sanz-Cortés et al., 2013), given that creatine is a key metabolite in energy metabolism through ATP production. In the present study, both glucose and creatine emerged as key metabolites associated with energy metabolism.

The main differences in the metabolic profile of IUGR piglets compared with the other categories were primarily due to a downregulation of AA. This finding aligns with Huang et al. (2019), who reported disturbances in AA metabolism in IUGR piglets 12 h after birth, which may contribute to the development of metabolic diseases later in life. Proline exhibited the highest VIP score, with N, NR-LBW, and R-LBW piglets showing higher concentrations than IUGR piglets. Proline plays a pivotal role in cell structure, antioxidative reactions, immune responses, energy metabolism and protein synthesis (Wu et al., 2011). Its higher levels in piglets with greater BtW may be linked to CI, as Pro is one of the most abundant AA in sow colostrum (Wang et al., 2021). Phenylalanine and Tyr (synthesized from the essential AA Phe) were also reduced in IUGR piglets. Similarly, studies on severe IUGR cases reported decreased Phe levels (Paolini et al., 2001), attributed to impaired placental transport, likely resulting from placental tissue damage and the hypercatabolic state inherent to IUGR (Paolini et al., 2001; Lin et al., 2012). In agreement with Cetin et al. (1990) and Sanz-Cortés et al. (2013), the branched-chain AA Leu and Val were significantly reduced in IUGR piglets. The literature identified chronic malnutrition and increased glucocorticoid exposure as potential mechanisms underlying the reduction in these AA concentrations (Hiroshige et al., 2001; Palova et al., 2007). Interestingly, the low concentrations of Leu and Tyr observed in IUGR piglets have been associated with reduced growth, altered metabolism, and impaired maturation of the nervous system (Ruggeri et al., 2025). Lower concentrations of Asn may also be linked to the reduced growth of IUGR piglets and their increased susceptibility to disease (Wu et al., 2006; Farmer and Edwards, 2022). Although not observed within the first 24 h after birth, Ruggeri et al. (2025) reported lower Asn concentrations in IUGR compared with N piglets at the end of the starter period. Asparagine participates in energy and AA metabolism and protein synthesis (Wang et al., 2015) and supports immune function, benefiting the intestine and liver during inflammation (Wu et al., 2015; Chen et al., 2016). Other AA, such as His, Met, and Thr, which play crucial roles in protein synthesis and immune responses and possess antioxidative, anti-inflammatory, and immunomodulatory properties (Zhang et al., 2019a; Souza et al., 2023; Zheng et al., 2024) were also downregulated in IUGR piglets. Altogether, these AA are important for growth, protein synthesis, and neuromuscular development. Their reduced concentrations in IUGR piglets compared with the other categories likely reflect impaired placental transport of nutrients during gestation and decreased intestinal absorption. Additionally, alterations in liver

and muscle metabolism may occur, as evidenced by reduced protein synthesis and changes in AA oxidation (Sanz-Cortés et al., 2013).

Conversely, hypoxanthine was upregulated in IUGR piglets compared with the other three categories. Hypoxanthine, a byproduct of purine metabolism, serves as a marker of hypoxia and oxidative stress. Elevated concentrations have been reported in hypoxic tissues of IUGR piglets, as blood flow tends to prioritize vital organs such as the brain and heart over peripheral tissues (Choi et al., 2025).

The integrity of intestinal morphology and function was also assessed at birth, as both are critical for intestinal health and nutrient utilization. Several studies have indicated that IUGR is associated with impaired intestinal development (Wang et al., 2005; Zhang et al., 2019b; Niu et al., 2021), linking the slow growth of IUGR piglets to intestinal injury (Tang and Xiong, 2022). In the present study, IUGR and R-LBW piglets exhibited decreased VH and CD compared with N piglets, whereas the VH:CD ratio was higher in N piglets than in the other three categories. The results for VH and the VH:CD ratio are consistent with previous studies that also reported IUGR-related damage to the intestinal morphology of piglets at birth (D'Inca et al., 2010; Dong et al., 2014). In contrast, those studies observed either no differences or an increase in CD in IUGR piglets. Interestingly, Cui et al. (2022) and Tang and Xiong (2022) reported similar intestinal morphological differences by the end of the suckling period, suggesting that the impaired intestinal development and function observed at birth may have a lasting effect.

The maintenance of intestinal function is closely associated with normal intestinal morphology and structure, as well as with the integrity of the intestinal barrier and redox status (Chen et al., 2021). Consequently, impaired morphology can lead to altered intestinal function, as reflected by the disrupted gene expression patterns observed in IUGR piglets, which were similar to those of R-LBW piglets but differed from NR-LBW and N piglets. Newborns are particularly vulnerable to oxidative stress due to their immature antioxidant systems (Robles et al., 2001; Friel et al., 2004), with low BtW piglets being the most affected, as they exhibit reduced antioxidant enzyme activity compared with N piglets (Chen et al., 2021; Tang and Xiong, 2022). Consistent with these findings, in the present study, N piglets showed the highest mRNA expression of the antioxidant enzyme *GPX2*, which helps eliminate reactive oxygen species and thus prevent oxidative stress (Circu and Aw, 2010). However, no differences between IUGR and N piglets were observed for *SOD2m*, another gene involved in the detoxification of reactive oxygen species. Along with the oxidative

stress observed in the small intestine of low BtW piglets, intestinal gene expression at birth showed an overexpression of stress-related (*HSD11B1* and *CRHR1*) and pro-inflammatory genes (*IL1 β* and *NF-K κ B*). These findings suggest that the first 24 h after birth represent a particularly stressful period for low BtW piglets, triggering an intestinal inflammatory response. Villagómez-Estrada et al. (2022) reported an overexpression of the stress-related gene *HSD11B1* in low BtW piglets. This gene encodes the enzyme that converts inactive cortisone into active cortisol, thereby regulating tissue glucocorticoid levels and playing a pivotal role in both metabolism and inflammatory response (Nixon et al., 2012). Although some studies have reported increased expression of pro-inflammatory pathways in IUGR piglets compared with N piglets (Tang et al., 2022; Villagómez-Estrada et al., 2022), their activation remains unclear, as other reports have described reduced levels of pro-inflammatory genes in IUGR neonates (Zhong et al., 2012; Dong et al., 2014). The simultaneous upregulation of stress-related and pro-inflammatory genes observed in our study suggests that low BtW piglets experience considerable physiological stress at birth. Interestingly, the *AKT1S1* gene, which encodes a subunit of mTORC1 (Wang et al., 2008), was upregulated in IUGR piglets compared with N piglets. This gene interacts with and inhibits mTORC1 activity (Yang et al., 2017), potentially disrupting mTORC1-dependent processes, thereby impairing protein synthesis, cell growth, and nutrient sensing and utilization in the jejunum (Wang et al., 2008). Similarly, the *SH3RF2* gene, which is involved in protein breakdown, was downregulated in NR-LBW and N piglets compared with the other categories. Remus et al. (2022) reported that this gene was downregulated in pigs with high protein deposition, suggesting that reduced expression favors protein synthesis while limiting protein breakdown.

Several studies have shown that oxidative stress is associated with intestinal barrier dysfunction and various gastrointestinal diseases (Navarro-Yepes et al., 2014; Zha et al., 2020; Chen et al., 2021). Wang et al. (2016) reported that neonates with IUGR exhibited increased tight-junction permeability and markedly reduced expression of occludin. In contrast, we observed an upregulation of tight-junction proteins (*OCLN* and *ZO1*) in IUGR piglets. These proteins form the intestinal mucosal barrier and are essential for regulating intestinal permeability (Chen et al., 2021). Moreover, in contrast with previous studies (Huang et al., 2020; Villagómez-Estrada et al., 2022), we found higher mRNA expression of digestive enzymes and hormones (*ALPI*, *DAO*, *IGF1R*), as well as nutrient transport genes, in IUGR piglets. Although no previous studies have directly supported our findings, most research has examined newborn piglets before CI, whereas we assessed gene expression about 24 h after birth, when piglets had already consumed colostrum. In this context, Wang et al.

(2018) demonstrated that intestinal proteins modulated by colostrum feeding play key roles in enhancing intestinal integrity, nutrient transport, energy metabolism, protein synthesis, and immune response. Nevertheless, colostrum only partially improved the compromised status of the jejunal mucosa in low BtW neonates, which still showed reduced expression levels compared with N counterparts. Further studies are needed to investigate compensatory mechanisms during early life, as evidence suggests that some low BtW piglets can catch up with their normal BtW counterparts by weaning (Cui et al., 2022).

3.5 Conclusions

This study provides a comprehensive characterization of piglets across different birth weights, highlighting the biological and physiological challenges associated with intrauterine growth restriction. Piglets classified as intrauterine growth restricted exhibited the most severe impairments in postnatal growth, vitality, and survival, which were linked to reduced colostrum intake, limited energy reserves, altered metabolic profiles, and gastrointestinal dysfunction. Restricted and non-restricted low birth weight piglets also showed impaired growth and distinct morphological traits compared with normal birth weight piglets, although their physiological alterations were less pronounced and differences between these two categories were minimal. Our findings indicate that early-life classification based on birth weight provides valuable insights into the developmental status and growth potential of piglets. Future research should aim to refine predictive indicators of growth potential by considering not only intrinsic factors but also external influences, such as sow characteristics and competition within the litter. Early identification of low birth weight piglets at risk of growth retardation enables targeted management and nutritional interventions, potentially improving survival, growth performance, and overall production efficiency.

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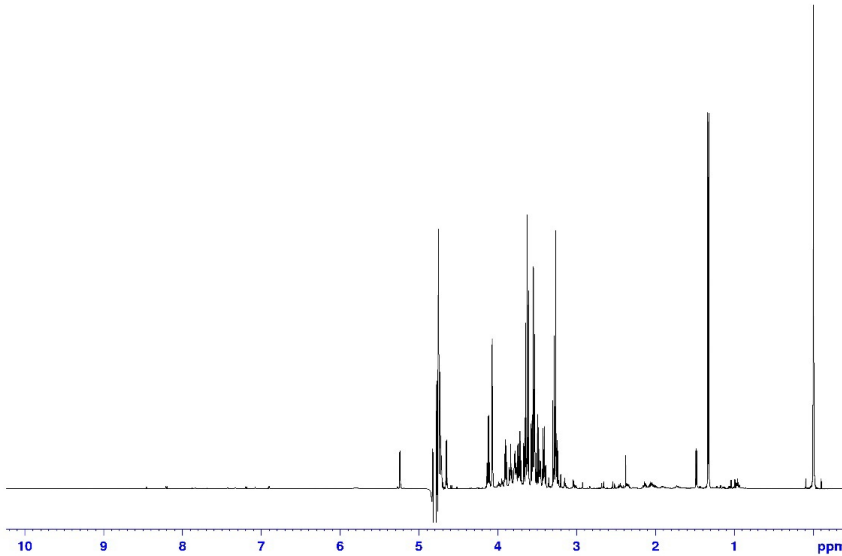
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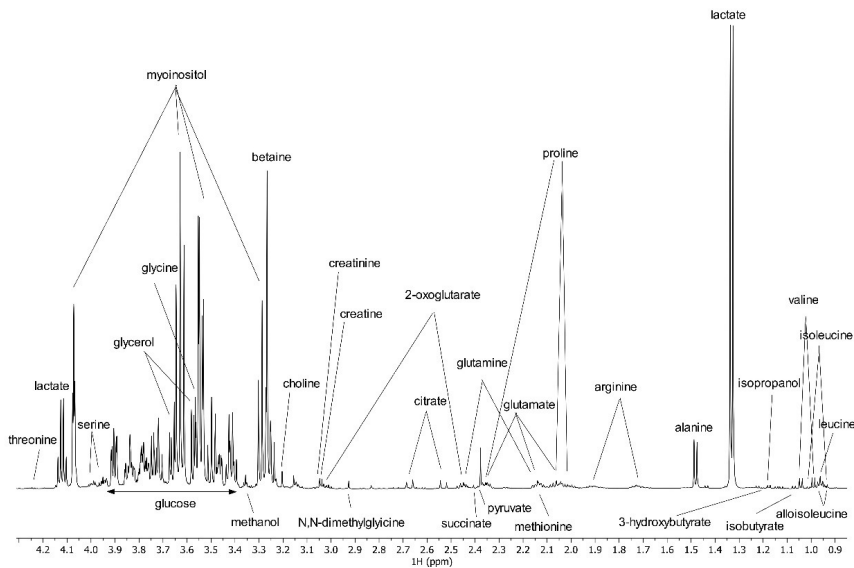
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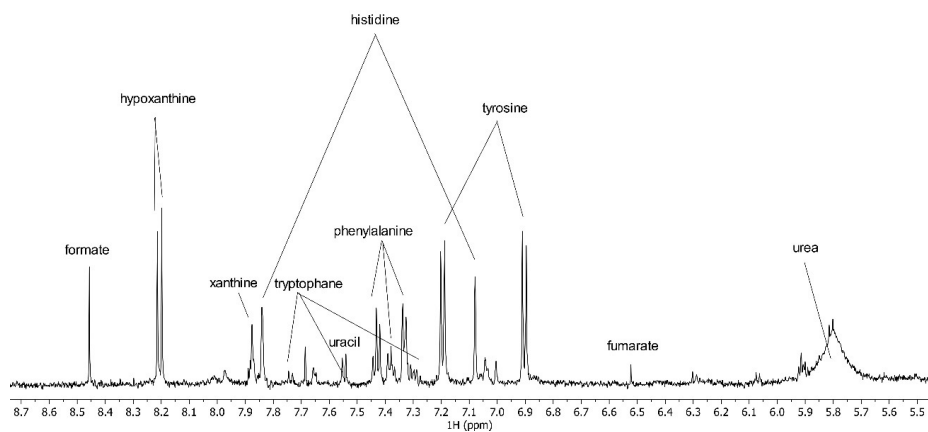
3.7 Supplemental Material



Supplemental Fig. 3.5 ^1H -NMR spectrum (noesygppr1d) acquired at 600.13 MHz, 298 K, with a recovery delay of 2 s (d1), 256 scans (ns), and a mixing time of 100 ms (d8). Abbreviation: NMR = nuclear magnetic resonance.



Supplemental Fig. 3.6 ^1H -NMR spectrum (600.13 MHz). Expanded area from 0.8 to 4.3 ppm. Metabolite assignments were performed using the Chenomx 8.0 database. Abbreviation: NMR = nuclear magnetic resonance.



Supplemental Fig. 3.7 ^1H -NMR spectrum (600.13 MHz). Expanded area from 5.5 to 8.7 ppm. Metabolite assignments were performed using the Chenomx 8.0 database. Abbreviation: NMR = nuclear magnetic resonance.

Supplemental Table 3.6 List of newly designed primers used for the gene expression analysis of 48 genes using the 96.96 Dynamic ArrayTM IFC qPCR custom design.

Gene	Name	Forward Primer (5' → 3')	Reverse Primer (5' → 3')	Target/ Housekeeping
AKT1S1	Proline-Rich AKT1 Substrate 1	CCACACAGCAGTATGCCAAGT	AGGAGGGCGGCCCAT	Target
MyD88	Myeloid Differentiation Primary Response 88	GATTACCTGCAAAGCAAGGAATG	TCTGATGGGCACCTGGAGAG	Target
NF-Kb	NuclearFactor Kappa-light-chain -enhancer of activated B cells	CCCCACAGACGTTTCATAGACAATTT	GAGGCTGGTTTTGTAATGTTGACA	Target
SH3RF2	SH3 Domain	CCGAACGTCAGAATCCACATG	AGGATGACGTCTCCCTTATTGAAC	Target

Supplemental Table 3.7 Serum metabolite concentrations at birth in four categories of piglets classified by birth weight as intrauterine growth restricted (IUGR, n = 6), restricted low birth weight (R-LBW, n = 12), non-restricted low birth weight (NR-LBW, n = 12), and normal birth weight (N, n = 12).

Item	Category					P =
	IUGR	R-LBW	NR-LBW	N	SEM	
2-Hydroxybutyrate	0.012	0.015	0.014	0.012	0.003	0.788
2-Oxoglutarate	0.038	0.039	0.041	0.038	0.005	0.944
3-Hydroxybutyrate	0.007 ^b	0.012 ^a	0.014 ^a	0.010 ^{ab}	0.002	0.001
Alanine	0.243 ^b	0.414 ^a	0.358 ^{ab}	0.356 ^{ab}	0.040	0.008
Alloisoleucine	0.011	0.020	0.024	0.020	0.004	0.041
Asparagine	0.019 ^b	0.055 ^a	0.062 ^a	0.064 ^a	0.010	< 0.001
Aspartate	0.027	0.031	0.030	0.032	0.007	0.959
Betaine	0.266	0.347	0.384	0.261	0.051	0.028
Choline	0.022	0.022	0.022	0.021	0.003	0.954
Citrate	0.139 ^b	0.155 ^{ab}	0.185 ^{ab}	0.195 ^a	0.014	0.011
Creatine	0.084	0.059	0.053	0.054	0.022	0.477
Creatinine	0.048	0.052	0.048	0.052	0.004	0.548
Formate	0.037 ^b	0.041 ^{ab}	0.055 ^{ab}	0.058 ^a	0.006	0.005
Glucose	0.059 ^b	1.43 ^{ab}	2.57 ^a	2.82 ^a	0.567	< 0.001
Glutamate	0.120	0.151	0.170	0.171	0.023	0.364
Glutamine	0.150 ^b	0.276 ^a	0.289 ^a	0.336 ^a	0.040	< 0.001
Glycerol	2.24	2.13	1.74	1.98	0.307	0.361
Glycine	0.257 ^b	0.423 ^a	0.397 ^a	0.406 ^a	0.037	0.003
Histidine	0.034 ^c	0.075 ^b	0.096 ^{ab}	0.117 ^a	0.014	< 0.001
Hypoxanthine	0.062 ^a	0.031 ^b	0.021 ^b	0.021 ^b	0.010	< 0.001
Isobutyrate	0.008 ^b	0.018 ^a	0.018 ^a	0.018 ^a	0.002	< 0.001
Isoleucine	0.017	0.031	0.028	0.025	0.005	0.048
Isopropanol	0.008	0.012	0.012	0.009	0.001	0.019
Lactate	3.21	2.99	3.08	2.79	0.378	0.726
Leucine	0.027 ^b	0.075 ^a	0.068 ^a	0.083 ^a	0.011	< 0.001
Lysine	0.072 ^b	0.134 ^a	0.133 ^a	0.152 ^a	0.020	0.002
Methanol	0.065	0.069	0.066	0.075	0.012	0.869
Methionine	0.016 ^b	0.028 ^{ab}	0.031 ^{ab}	0.039 ^a	0.007	0.031
Myoinositol	3.29	1.88	2.94	1.86	1.41	0.439
N,N-Dimethylglycine	0.024	0.018	0.024	0.026	0.004	0.116
Phenylalanine	0.028 ^b	0.061 ^a	0.059 ^a	0.067 ^a	0.007	< 0.001
Proline	0.082 ^b	0.354 ^a	0.415 ^a	0.530 ^a	0.073	< 0.001
Pyruvate	0.168	0.211	0.199	0.178	0.027	0.525

Serine	0.106 ^b	0.142 ^{ab}	0.143 ^{ab}	0.170 ^a	0.016	0.013
Succinate	0.011	0.010	0.011	0.010	0.001	0.696
Threonine	0.040 ^b	0.059 ^{ab}	0.084 ^a	0.090 ^a	0.012	< 0.001
Tyrosine	0.056 ^b	0.171 ^a	0.167 ^a	0.186 ^a	0.031	< 0.001
Urea	0.582	0.797	0.637	0.765	0.097	0.227
Valine	0.066 ^b	0.169 ^a	0.169 ^a	0.196 ^a	0.025	< 0.001

Chapter 4

Evaluation of organ and skeletal physiological characteristics for improved classification of growth-restricted newborn piglets

Evaluation of organ and skeletal physiological characteristics for improved classification of growth-restricted newborn piglets

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Abstract

The identification of potentially slow-growing pigs at birth, using both external and internal traits, would enable the early implementation of targeted management and feeding strategies to optimize herd management and improve production efficiency. Twenty-four piglets from six hyperprolific sows were classified into four categories based on birth body weight (BW), body mass index (BMI), and crown-to-rump length (CRL): severe intrauterine growth restriction (sIUGR), low birth weight (LBW), moderate birth weight (MBW), and high birth weight (HBW). Organ weights, computed tomography (CT) measurements, bending tests to assess tibial mechanical and geometric properties, and tibial mineral content analysis were performed to evaluate organ and skeletal physiological characteristics. Severe IUGR piglets exhibited higher brain-to-organ ratios and relative brain weights, which decreased linearly across categories. High birth BW piglets demonstrated 70% more bone volume and a greater proportion of high-density bones than sIUGR piglets, along with the largest cortical area and thickness in tibia measurements. On the other hand, sIUGR showed higher maximum stress, stiffness values, and manganese content in their tibiae compared to other categories. These findings reveal that piglets with varying degrees of IUGR prioritize brain development, exhibit asymmetrical organ growth, and experience impaired ossification and longitudinal bone growth. This study underscores the need to incorporate complementary birth indicators to refine the classification of newborn piglets with different degrees of restriction.

Keywords: bending tests, computed tomography, intrauterine growth restriction, mineral content, organ and skeletal physiological characteristics, swine

4.1 Introduction

One of the primary economic drivers in pig production is the reproductive efficiency, which is typically defined as the number of piglets produced per sow per year. Optimizing this factor is crucial for the sustainability and productivity of the global pork industry. In recent decades, continuous genetic advancements have focused on increasing sow prolificacy, aiming to raise the number of slaughtered pigs produced per sow per year (Rutherford et al., 2013). However, this increase in prolificacy has led to a significant reduction in average birth body weight (BW), resulting in a higher number of lightweight piglets at birth (Quiniou et al., 2002; Beaulieu et al., 2010). Piglets born small may experience varying degrees of intrauterine

growth restriction (IUGR) (Amdi et al., 2013; Hales et al., 2013; Foxcroft et al., 2014; Hansen et al., 2019) and are likely to struggle to catch up with their heavier counterparts throughout the production cycle (Beaulieu et al., 2010; Fix et al., 2010; Quiniou et al., 2002).

It is estimated that approximately 10–15% of pigs in any given batch exhibit slow growth (Calderón Díaz et al., 2017). Recent studies have highlighted the identification of this subset of pigs at different production stages by applying different machine learning algorithms to robust and powerful databases (Casellas et al., 2024; Salgado-López et al., 2024). These pigs are at a higher risk of mortality throughout the production cycle (Larriestra et al., 2006; Calderón Díaz et al., 2017). Those that survive present significant management challenges in modern swine production systems, which aim to group contemporary pigs within the same batch to ensure optimal animal health and performance (Maes et al., 2004). In addition, it is also reported that as pigs near the end of the production cycle, the likelihood of lighter pigs being sent to the slaughterhouse at a later stage increase (López-Vergé et al., 2018). Therefore, early identification of slow-growing pigs and the implementation of effective preventive measures are essential to enhance their performance and reduce variability. This is further supported by studies emphasizing that changes in pigs' BW category are more frequent during the lactation period (Montoro et al., 2020; Blavi et al., 2021).

Potentially slow-growing pigs can be easily identified at birth if they exhibit severe IUGR and display a distinctive head morphology previously described (Chevaux et al., 2010). However, identifying piglets that lack these traits at birth but experience poor subsequent growth performance, persistently remaining in the lower quartile of the birth weight population distribution, becomes a greater challenge. Birth BW is widely recognized as one of the most critical determinants of lifetime growth performance (Douglas et al., 2014) and survivability (Roehe and Kalm, 2000) in pigs. However, extensive scientific literature research has also explored other individual traits influencing pre-weaning mortality and growth. These include morphometric attributes (Hales et al., 2013; Huting et al., 2018; Hansen et al., 2019) physiological characteristics (Amdi et al., 2016; Vanden Hole et al., 2019; Lynegaard et al., 2020) and behavioral features (Muns et al., 2013). In addition, risk factors related to the sow, the environment, and BW variability (Douglas et al., 2013; López-Vergé et al., 2018; Riddersholm et al., 2021) among others, have also been examined highlighting their collective impact on piglet growth and survival.

The identification of slow-growing pigs at birth would facilitate the implementation of targeted management and feeding strategies during early life, allowing farmers to optimize herd management and enhance overall farm production efficiency (Montoro et al., 2020). Within

these strategies, particular attention should be given to those focusing on piglet care during their first days of life. A common practice in pig production, particularly for supporting low-birth weight piglets, is colostrum supplementation. For example (Muns et al., 2014), reported that orally supplementing weaker piglets with freshly milked colostrum from sows within the same herd helped stabilize their body temperature and enhanced litter performance within the first 24 h. Another strategy is split suckling prior to cross-fostering, which has been shown to improve daily weight gain and litter uniformity at weaning (Donovan and Dritz, 1996). Equally important is the feeding management of piglets during the early stages. One widely used strategy is creep feeding, which stimulates feed intake and promotes post-weaning growth. This practice has been associated with increased total weight gain in eater pigs (Sulabo et al., 2010; Kuller et al., 2007; Sulabo et al., 2010) reduced weight variability at weaning (Solà-Oriol and Gasa, 2017) and improved growth during the early post-weaning period (Bruininx et al. 2002; Bruininx et al. 2004; Sulabo et al., 2010). Although less common than creep feeding, milk replacer supplementation has also demonstrated significant benefits, including higher weaning weights, increased total litter weight (Zijlstra et al., 1996; Dunshea et al., 1999) and enhanced weight gain after weaning (Blavi et al., 2021) .

Among the performance criteria described in the literature for identifying these growth-restricted piglets, birth BW, along with other indicators of body conformation, such as body mass index (BMI) (Hales et al., 2013) and crown-to-rump length (CRL; the piglet's supine length measured from the crown of the head to the base of the tail), stand out as the most widely studied. Despite extensive investigation, little is known about their correlation with internal measurements, such as those related to the physiological status of organs and bones, which are key factors in postnatal growth. The interest in assessing bone characteristics in piglets at birth lies in finding a more specific indicator of skeletal development than birth weight alone. This could help identify neonates at greater risk of compromised postnatal growth trajectories. In humans, several studies have demonstrated that neonates with IUGR exhibit altered biochemical markers of bone formation, such as lower circulating osteocalcin and 1.25-dihydroxyvitamin D concentrations, relative to appropriate-for-gestational-age infants (Briana and Malamitsi-Puchner 2016). These alterations arise in part from impaired endochondral ossification under conditions of placental insufficiency and maternal metabolic dysfunction, which limit the availability of substrates necessary for normal skeletogenesis (Briana and Malamitsi-Puchner, 2016; Pastor et al., 2024). Importantly, bone physiological status has been linked to growth and bone mass accretion during infancy. For example (Chen et al., 2013), showed that IUGR-associated reductions in endochondral ossification correlate with impaired postnatal growth velocity and lower bone strength in early childhood.

We hypothesized that piglets with low body metrics at birth exhibit impaired organ and bone physiological status compared to their heavier counterparts. Identifying strong correlations between external and internal measures is essential for reliably identifying potentially slow-growing piglets at an early stage. This early identification would enable the timely implementation of effective intervention strategies for this subset of pigs. In this context, the objectives of this study were to (1) characterize piglets at the level of organ and bone physiological status at birth, and (2) investigate whether these characteristics correlate with individual external physical metrics currently used as indicators of survivability and growth performance in suckling piglets.

4.2 Materials and Methods

All animal experimentation procedures were approved by the Ethics Committee of the Universitat Autònoma de Barcelona (CEEAH2788M2) in accordance with the European Union guidelines for the care and use of animals in research (European Parliament. Directive 2010/63/EU). This study is reported in accordance with ARRIVE guidelines.

4.2.1 Animals and experimental design

This study was conducted with 24 piglets (*Pietrain* x [*Danish Landrace* x *Danish Yorkshire*]) from 6 multiparous sows of the same batch, sourced from a commercial farm in Lleida, Spain. The average total litter size was 20.2 ± 1.20 piglets, and the average total litter weight was 26.8 ± 2.00 kg. On the day of parturition (day 0), before litter equalization, piglets were individually weighed, and the BMI and CRL were measured. The degree of IUGR was determined based on the head morphology criteria described by (Chevaux et al., 2010). Four piglets per sow were selected according to the previously described measures to generate four different groups ($n = 6$ piglets/group): severe intrauterine growth restricted (sIUGR), low birth weight (LBW), moderate birth weight (MBW), and high birth weight (HBW). Piglets classified as sIUGR exhibited a steep, dolphin-like forehead, bulging eyes, and wrinkles perpendicular to the mouth. Piglets with a birth BW between 0.75 and 1.0 kg, without morphological signs of sIUGR, were categorized as LBW, while those with a birth BW between 1.0 and 1.25 kg were considered MBW. Piglets with a birth BW exceeding 1.25 kg were classified as HBW. All descriptive statistics by group are provided in Table 4.1. After classifying the piglets, they were euthanized with an intramuscular injection of azaperone

(Sediron 40 mg/ml; Livisto Int'l, S.L.) and ketamine (Ketamidor 100 mg/ml; VetViva Richter GmbH), followed by an intravenous injection of sodium pentobarbital (Euthasol 400 mg/ml; Dechra Pharmaceuticals PLC).

Table 4.1 Descriptive statistics for birth body weight (BW), body mass index (BMI), and crown-to-rump length (CRL) [Mean $\pm$ Standard deviation (SD)] for piglets ($n = 6$ piglets per group) classified as severe intrauterine growth restricted (sIUGR), low birth weight (LBW), moderate birth weight (MBW), and high birth weight (HBW).

	sIUGR		LBW		MBW		HBW		P-value ¹
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Birth BW (kg)	0.49 ^d	0.037	0.97 ^c	0.042	1.18 ^b	0.027	1.69 ^a	0.121	< 0.001
BMI (kg/m ²)	14.35 ^c	1.368	18.00 ^b	2.806	18.48 ^b	1.107	22.71 ^a	1.771	< 0.001
CRL (cm)	18.57 ^c	0.673	23.40 ^b	1.817	25.25 ^{ab}	0.880	27.30 ^a	1.397	< 0.001

¹P-value obtained from ANOVA test. ^{a,b,c,d}Different superscripts within row indicate significant differences ($P \leq 0.05$).

4.2.2 Computed tomography (CT), post-mortem examination, and organ and tibiae sampling

Piglets were fully scanned post-mortem after birth with a Philips Brilliance 16 scanner (Philips Healthcare, Madrid, ES). The CT scanner undergoes daily internal calibration prior to use. The acquisition conditions were as follows: 120 kV, 200 mA, field of view (FOV) 150 mm, 512 $\times$ 512 matrix, collimation 16 $\times$ 1.5, helical 3 mm-thick images every 3 mm (pitch 0.938). The reconstruction algorithm used was the standard.

Image analysis was performed with software Matlab 2008b (The MathWorks Inc., Natick, MA, USA) using a customized script. From all the images of each piglet, frequency of voxels (3D pixels) associated with each Hounsfield unit (HU) value, were obtained and transformed into volume using the image thickness, matrix size and FOV values (Font-i-Furnols et al., 2009). The volume corresponding to HU values between + 140 and + 1,700 was classified as bone tissue (Font-i-Furnols et al., 2015) and this range was used to calculate the total volume of bones. Moreover, four bone density ranges were defined in order to obtain volume measurements of bones with different densities: low dense bones between HU values + 140 and + 499, medium dense bones between HU values + 500 and + 999, high dense bones between HU values + 1,000 and + 1,499, and very high dense bones between HU

values + 1,500 and + 1,700, following (Fabà et al., 2019) but including an additional range. Based on the volume of each range and the total bone volume, the proportion corresponding to each density range was determined.

Measurements were taken axially in the central part of the left tibia using VisualPork software (Bardera et al., 2012). External and internal cortical bone areas were manually selected as regions-of-interest (ROI), and the area of the cortical bone was obtained as a difference between the two areas. Moreover, the average HU value of the cortical area and the thickness of the cortical bone were also determined (Fig. 4.1).

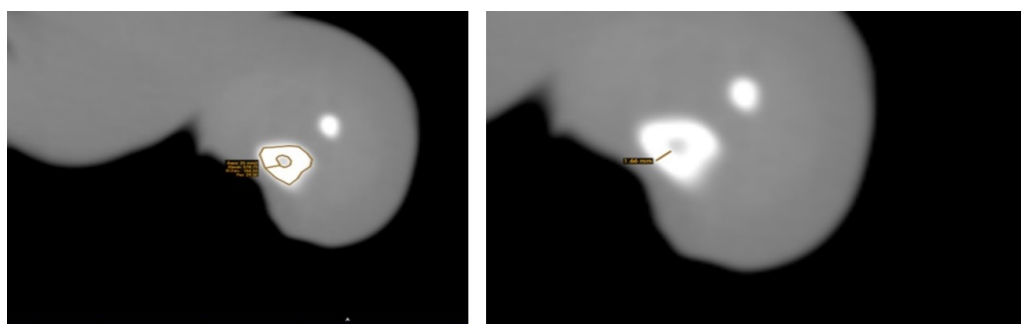


Fig. 4.1 The area of the cortical bone (left) and thickness of the cortical bone (right) measured in tibia bone.

Afterwards, the brain, heart, liver, lungs, kidneys, and spleen were harvested and blotted dry before these were weighed on a precision scale (Sartorius AG, Model ED224S, Germany). The intestine and stomach were carefully removed intact, rinsed thoroughly and weighed. The hind legs of each piglet were separated from the rest of the body and individually frozen for subsequent tibiae analyses (mechanical and geometric properties and mineral determination).

4.2.3 Bending tests for mechanical properties of piglet tibiae determination

The left hind leg of each piglet was thawed and placed in the autoclave at 121 °C for 30 min. Then, the flesh was removed from those hind legs to obtain only the clean left tibiae. The tibia density (ρ) of each specimen was determined from two measurements, the unsubmerged weight (P_{air}) and the weight of the same sample submerged (P_{sum} , the latter measurement being equal to the weight in air plus the buoyant force of the fluid). The geometric magnitudes, including the cross-sectional area and moment of inertia, were calculated and subsequently used to

determine the following properties. The mechanical properties of porcine bone (left piglet tibiae) were determined from three point bending tests using a Universal Test Machine (UTM) Zwick All-around table-top 5 kN (ZwickRoell S.L., Ulm, Germany), equipped with a load cell of 500 N. The real values of cross-section (A) and area moment of inertia (I_z) of the fractured cross-section were computed for each specimen from an image using ImageJ® software. Specifically, the mechanical properties calculated were the following: stiffness (Young's modulus) (E), maximum stress ($\sigma_{\max}$), ultimate strain (ϵ_u), proof resilience (W_e), and toughness (W_u). The mechanical properties E , $\sigma_{\max}$, W_e and W_u were determined through analytical approximations from the final stress-strain curves. The ϵ_u was calculated from the maximum displacement.

All tibia specimens were tested at the same displacement rate ($v = 0.5$ mm/min). This rate was controlled by the UTM, which simultaneously recorded both displacement and applied force. Due to differences in specimen size and strength, displacement at failure consistently ranged between 0.4 and 1.0 mm, resulting in total test durations of 75 to 125 s. Both the strain rate ($d\epsilon/dt$) and the loading rate (dF/dt) increased linearly with the imposed displacement rate (v), although they were also influenced by the cross-sectional dimensions and strength of each tibia. The calculated strain rate values ranged from 2.0×10^{-4} to 1.0×10^{-5} s⁻¹, depending on the specimen geometry. These values fall within the quasi-static regime, ensuring that the mechanical behavior corresponds to a rigid-elastic model with brittle failure. Higher testing speeds would induce viscoelastic effects, which would hinder meaningful comparisons between specimens. The loading rate, in turn, was affected not only by the displacement rate but also by the stiffness and strength of the individual tibiae. In all cases, the loading rate ranged from 1.0 to 4.0 N/s.

4.2.4 Inductively coupled plasma mass spectrometry (ICP-MS) for piglet tibiae mineral determination

For the right hind legs, as with the left, they were thawed and placed in an autoclave at 121 °C for 30 min to obtain clean right tibiae. Tibiae bones were then dried at 103 °C for 12 h, followed by immersion in acetone for 48 h to remove any remaining fat residues. Finally, to obtain the tibiae ash, they were heated again at 103 °C for 12 h and then placed in a muffle furnace at 550 °C for 12 h.

Concentrations of phosphorus (P), calcium (Ca), zinc (Zn), copper (Cu), and manganese (Mn) were determined in the ash obtained from the right tibiae samples according to the AOAC 984.27 method, using a mass spectrometer ICP-MS 7900 (Agilent Technologies, Santa Clara, California, USA).

To validate the accuracy of the analytical method, a standard was added to the samples (spiked samples). The recovery percentages for these spiked samples were 98% for P, 97% for Ca, 105% for Mn, 101% for Cu, and 93% for Zn. Furthermore, the minimum concentrations quantifiable in the sample using the described methodology were 8 mg/g for P, 10 mg/g for Ca, 0.2 mg/g for Mn, 2 mg/g for Cu, and 2 mg/g for Zn.

4.2.5 Statistical analysis

All calculations and statistical analyses were performed with open-source software R v.4.4.084. Pig was used as the experimental unit in all data analyses. Residuals were tested for normality using the Shapiro-Wilk test (*ols_test_normality* function, *olsrr* package) and assessed with normal probability plots. Birth BW, BMI, and CRL measures were analyzed using a linear mixed-effect model (*lmer* function, *lme4* package), with piglet category as a fixed effect and sow as a random effect. All other examined variables, except those related to the proportion of bones with different densities, were similarly analyzed using a linear mixed-effect model (*lmer* function, *lme4* package), including category of piglet as fixed effect and sow as random effect. The variables related to the proportion of bones with different densities were analyzed using a generalized linear mixed-effect model (*glmer* function, *lme4* package) with a binomial family, also including piglet category as fixed effect and sow as random effect. Multiple means comparisons were done using Tukey-Kramer's correction. Results for the fixed effects are presented as least squares means with the standard error of the mean (SEM). Results were considered significant at $P \leq 0.05$ and a tendency when $0.05 < P \leq 0.10$. Pearson correlations were calculated using the *cor.test* function.

4.3 Results

4.3.1 Descriptive results

Average birth BW of sUGR, LBW, MBW and HBW piglets were 0.49 ± 0.037 kg, 0.97 ± 0.042 kg, 1.18 ± 0.027 kg, and 1.69 ± 0.121 kg, respectively. Significant differences in birth BW between these four categories of piglets were also reflected in BMI and CRL measurements, likely due to the strong correlation among these variables. Pearson's correlation coefficient analysis showed that birth BW was significantly positively correlated with BMI ($R = 0.870$; $P \leq 0.001$) and CRL ($R = 0.935$; $P \leq 0.001$). The HBW piglets exhibited the highest BMI and CRL values, while the MBW and LBW piglets had intermediate values that did not differ significantly from each other. The sUGR piglets showed the lowest values for both BMI and CRL.

4.3.2 Organ weights

Relative organ weights and the different organ ratios calculated are shown in Table 4.2. The relative brain weight was higher in sIUGR piglets ($P < 0.001$) and progressively decreased across categories, reaching the lowest values in HBW piglets. The brain: heart, brain: liver, and brain: lungs ratios were also significantly higher in sIUGR piglets compared to all other categories ($P \leq 0.009$), which showed no significant differences among themselves. These differences revealed that sIUGR piglets had a significantly larger relative brain size compared to the other categories. The spleen was significantly larger ($P = 0.027$) in the lowest weight categories (sIUGR and LBW) compared to MBW and HBW piglets, while the relative stomach weight showed only a tendency ($P = 0.068$) to be greater in the lowest weight categories (sIUGR and LBW).

Table 4.2 Effect of piglet type (sIUGR, LBW, MBW, or HBW) on organ weights at birth.

Items ¹	Piglet type ²				SEM	P-value ³
	sIUGR	LBW	MBW	HBW		
<i>n</i>	6	6	6	6		
<i>ROW (g/kg BW)</i>						
Brain	54.13 ^a	32.10 ^b	27.23 ^c	20.65 ^d	1.401	< 0.001
Heart	11.35	11.80	8.56	8.05	1.573	0.170
Liver	23.72	26.50	21.24	21.86	2.866	0.451
Lungs	26.51	29.14	23.34	23.75	2.209	0.157
Kidneys	9.39	10.13	7.85	8.58	1.547	0.626
Stomach	7.34	7.75	5.33	6.60	0.724	0.068
Spleen	1.45 ^{ab}	1.82 ^a	0.98 ^b	1.05 ^{ab}	0.206	0.027
Intestine	44.05	59.43	50.14	48.70	7.657	0.493
<i>Organ ratios</i>						
Brain:heart	5.19 ^a	2.82 ^b	3.27 ^b	2.58 ^b	0.596	0.009
Brain:liver	2.37 ^a	1.25 ^b	1.32 ^b	0.96 ^b	0.210	< 0.001
Brain:lungs	2.06 ^a	1.11 ^b	1.22 ^b	0.88 ^b	0.130	< 0.001

¹ROW = Relative organ weights. ²sIUGR = Severe intrauterine growth restricted, LBW = Low birth weight, MBW = Moderate birth weight, HBW = High birth weight. ³P-value obtained from ANOVA test. ^{a,b,c,d}Different superscripts within row indicate significant differences ($P \leq 0.05$).

4.3.3 Computed tomography measurements

Results of the CT measurements are presented in Table 4.3. As expected, there was a significant difference in the total bone volume at birth among the four categories of piglets ($P < 0.001$). The HBW piglets exhibited the largest bone volume, with values ranging from 173.25 to 193.34 cm³ while the sIUGR piglets had approximately 70% lower volumes. No significant differences were detected between the LBW and MBW piglets, which had intermediate bone volumes. No differences were observed in the relative total bone volume across the four piglet categories. Furthermore, the proportion of bones with different densities also differed significantly depending on the piglet category ($P < 0.001$). Specifically, piglets with lower bone volume had a higher percentage of low dense bones (low HU values), whereas piglets with higher bone volume had a higher percentage of high dense bones (high HU values).

Specific measurements of the left tibiae revealed that HBW piglets had a higher cortical area ($P < 0.001$) compared to the other categories, with an average value of 35.67 mm². The cortical area of the left tibia was reduced by approximately 60% in sIUGR piglets ($P < 0.001$), while LBW and MBW piglets exhibited intermediate values, showing a tendency to differ from each other ($P = 0.069$). HBW piglets also showed greater tibial thickness ($P = 0.01$) compared to the lower weight categories (sIUGR and LBW), with an average value of 2.66 mm. Both sIUGR and LBW piglets had the lowest left tibial thickness, whereas MBW piglets exhibited values not different from other piglets. Similarly, the mean HU values differed significantly among categories ($P = 0.041$), although no differences were observed between individual categories. The mean HU values for sIUGR and LBW piglets, as well as for MBW and HBW piglets, were numerically similar.

Table 4.3 Effect of piglet type (sIUGR, LBW, MBW, or HBW) on computed tomography measurements at birth.

Items ¹	Piglet type ³				SEM	P-value ⁴
	sIUGR	LBW	MBW	HBW		
<i>n</i>	6	6	6	6		
EBV (cm ³)	57.13 ^c	105.97 ^b	122.07 ^b	182.79 ^a	4.932	< 0.001
REBV (cm ³ /kg BW)	114.99	109.11	103.87	108.43	6.189	0.558
<i>(%) of bones between</i>						
HU ² 140 and HU 499	92.85 ^a	90.88 ^b	90.19 ^c	88.29 ^d	0.041	< 0.001
HU 500 and HU 999	6.95 ^d	8.73 ^c	9.35 ^b	11.18 ^a	0.040	< 0.001
HU 1000 and HU 1499	0.20 ^d	0.39 ^c	0.45 ^b	0.52 ^a	0.009	< 0.001
HU 1500 and HU 1700	0.00 ^b	0.00 ^b	0.01 ^{ab}	0.01 ^a	0.001	< 0.001
<i>Left tibia measures</i>						
Cortical area (mm ²)	13.40 ^c	20.25 ^b	26.40 ^b	35.67 ^a	1.920	< 0.001
Mean HU	578.9 ⁸	573.00	661.16	680.44	33.348	0.041
Thickness (mm)	1.50 ^b	1.48 ^b	2.19 ^{ab}	2.66 ^a	0.237	0.004

¹EBV = Entire bone volume, REBV = Relative entire bone volume, HU = Hounsfield unit. ²Hounsfield units are a standardized, dimensionless unit used in computed tomography scans to quantify the density of tissues and fluids.

³sIUGR = Severe intrauterine growth restricted, LBW = Low birth weight, MBW = Moderate birth weight, HBW = High birth weight. ⁴P-value obtained from ANOVA test. ^{a,b,c,d}Different superscripts within row indicate significant differences ($P \leq 0.05$).

4.3.4 Mechanical and geometric magnitudes of piglet tibiae

The results of the mechanical and geometric properties of piglet tibiae are presented in Table 4.4. The maximum stress values ($\sigma_{C' \max}$ and $\sigma_{T' \max}$) were significantly higher ($P = 0.002$ and $P = 0.001$, respectively) in the tibiae of sIUGR piglets compared to those of the other piglet categories. The Young's modulus values also differed significantly ($P = 0.006$) among the piglet categories, with sIUGR piglets exhibiting higher values than both MBW and HBW piglets ($P < 0.05$) (differences reaching up to 7281.40 MPa). In contrast, significant differences ($P < 0.001$) in the area moment of inertia and cross-section of the tibiae were observed in the opposite direction, with HBW piglets showing the highest values for both variables.

Table 4.4 Effect of piglet type (sIUGR, LBW, MBW, or HBW) on mechanical and geometric properties of piglet tibiae at birth.

Items ¹	Piglet type ³				SEM	P-value ⁴
	sIUGR	LBW	MBW	HBW		
<i>n</i>	6	6	6	6		
$\sigma_{C,max}$ (MPa) ²	113.1 ^a	77.7 ^b	67.5 ^b	74.9 ^b	8.436	0.002
$\sigma_{T,max}$ (MPa)	104.6 ^a	69.8 ^b	61.1 ^b	66.7 ^b	7.970	0.001
<i>E</i> (MPa)	7886 ^a	5279 ^{a,b}	4378 ^b	5053 ^b	747.25	0.006
ε_u (%)	1.80	2.03	2.04	2.00	0.166	0.611
W_e (J/m ³)	53.15	49.35	41.08	38.86	10.608	0.699
W_u (J/m ³)	105.28	92.43	76.74	77.65	15.979	0.453
ρ (g/cm ³)	1.32	1.33	1.32	1.29	0.028	0.670
<i>A</i> (mm ²)	9.33 ^c	18.32 ^b	21.24 ^{ab}	25.88 ^a	1.510	< 0.001
I_z (mm ⁴)	11.20 ^b	42.47 ^{ab}	51.49 ^a	72.34 ^a	9.480	< 0.001

¹ $\sigma_{C,max}$ = Maximum compression stress, $\sigma_{T,max}$ = Maximum tensile stress, *E* = Young's modulus, ε_u = Ultimate strain, W_e = Proof resilience, W_u = Toughness, ρ = Density, *A* = Area of the cross-section, I_z = Area moment of inertia for the cross-section. ²MPa = Megapascal. ³sIUGR = Severe intrauterine growth restricted, LBW = Low birth weight, MBW = Moderate birth weight, HBW = High birth weight. ⁴P-value obtained from ANOVA test. ^{a,b,c}Different superscripts within row indicate significant differences ($P \leq 0.05$).

4.3.5 Mineral content in piglet tibiae

The mineral content of piglet tibiae is shown in Table 4.5. The P, Ca, and Cu content in the tibiae of piglets did not differ among the four categories studied. However, the Mn content varied depending on the piglet category ($P = 0.028$), with sIUGR piglets exhibiting the highest levels and HBW piglets the lowest, showing differences of up to 15.4 mg/g ($P = 0.031$). The Mn content in LBW and MBW piglets was intermediate, not different from that of either sIUGR or HBW piglets. Additionally, there was a tendency toward decreasing Zn content ($P = 0.067$) from sIUGR piglets to HBW piglets, although the differences among the piglet categories were not statistically significant.

Table 4.5 Effect of piglet type (sIUGR, LBW, MBW, or HBW) on the mineral content of piglet tibiae at birth.

Items ¹	Piglet type ²				SEM	P-value ³
	sIUGR	LBW	MBW	HBW		
<i>n</i>	6	6	6	6		
<i>Mineral content (mg/g)</i>						
P	186.2	184.9	186.8	185.3	1.940	0.887
Ca	392.4	388.7	390.4	391.1	2.766	0.723
Mn	16.41 ^a	12.30 ^{ab}	12.22 ^{ab}	10.90 ^b	1.386	0.028
Cu	2.89	3.07	3.37	2.76	0.283	0.370
Zn	213.5	201.6	185.1	170.2	12.17	0.067

¹P = Phosphorus, Ca = Calcium, Mn = Manganese, Cu = Copper, Zn = Zinc. ²sIUGR = Severe intrauterine growth restricted, LBW = Low birth weight, MBW = Moderate birth weight, HBW = High birth weight. ³P-value obtained from ANOVA test.

^{a,b}Different superscripts within row indicate significant differences ($P \leq 0.05$).

4.3.6 Correlations between external physical characteristics (birth BW, BMI, CRL) and internal parameters

The correlations between the three external physical characteristics used to classify piglets at birth (birth BW, BMI, and CRL) and the internal parameters analyzed post-mortem are presented in Table 4.6. Four correlations involving various organ weight measures and external parameters had strong negative correlation coefficients below -0.63 ($P < 0.01$). Among these, the relative brain weight exhibited the strongest negative correlations with external parameters (-0.93 for birth BW, -0.88 for BMI, and -0.93 for CRL), followed by the organ weight ratios of brain: lungs, brain: liver, and brain: heart. Similarly, the mechanical properties of maximum compression stress, maximum tensile stress, and Young's modulus also showed negative correlations with external parameters, with coefficients ranging from -0.62 to -0.47 ($P < 0.05$). The Mn and Zn content in the piglet tibiae also demonstrated negative correlations with external parameters, with coefficients ranging from -0.56 to -0.48 ($P < 0.05$).

Conversely, the parameters mainly related to skeletal development were positively correlated with the external parameters. Specifically, the entire bone volume (EBV) showed the strongest positive correlation with birth BW (0.98 , $P < 0.001$), CRL (0.92 , $P < 0.001$), and BMI (0.84 , $P < 0.001$). Bone density was also correlated with external parameters, with the proportion of high and very high-density bones exhibiting positive correlation coefficients

ranging from 0.50 to 0.77 ($P < 0.05$). Furthermore, regarding piglet tibiae measures and geometric magnitudes, the cortical area (0.74 for BMI to 0.91 for birth BW), area (0.74 for BMI to 0.88 for birth BW), and inertia of the Sect. (0.64 for CRL to 0.74 for BMI) were also positively correlated with external parameters ($P < 0.001$).

Table 4.6 Correlation coefficients between birth body weight, crown-to-rump length, body mass index, and internal body variables.

Traits ¹	Organ ratios				
	Brain:heart	Brain:lungs	Brain:liver	Liver	Heart
Birth BW ²	-0.64	-0.83	-0.79	-0.17	-0.47
CRL ³	-0.63	-0.82	-0.78	-0.18	-0.46
BMI ⁴	-0.65	-0.85	-0.82	-0.08	-0.40

(% of bones between					
Traits	EBV	REBV	HU 140 and HU 499	HU 500 and HU 999	HU 1000 and HU 1499
Birth BW	0.98	-0.21	-0.50	0.47	0.76
CRL	0.92	-0.20	-0.56	0.54	0.77
BMI	0.84	-0.21	-0.28	0.25	0.67

Traits	Mechanical properties				
	E	ε_u	W_e	W_u	ρ
Birth BW	-0.52	0.22	-0.24	-0.28	-0.16
CRL	-0.56	0.29	-0.19	-0.23	-0.12
BMI	-0.47	0.15	-0.26	-0.32	-0.16

¹EBV = Entire bone volume, REBV = Relative entire bone volume, HU = Hounsfield unit, $\sigma C_{\max}$ = Maximum compression stress, $\sigma T_{\max}$ = Maximum tensile stress, E = Young's modulus, ε_u = Ultimate strain, W_e = Proof resilience, W_u = Toughness, ρ = Density, A = Area of the cross-section, I_z = Area moment of inertia for the cross-section, P =

Relative organ weights						
Lungs	Brain	Kidneys	Intestine	Spleen	Stomach	
-0.29	-0.93	-0.21	0.14	-0.41	-0.48	
-0.31	-0.93	-0.14	0.19	-0.41	-0.44	
-0.13	-0.88	-0.34	0.12	-0.37	-0.47	
Left tibia measures				Mechanical properties		
HU 1500 and HU 1700	Cortical area	Mean HU	Thickness	σC_{max}	σT_{max}	
0.60	0.91	0.55	0.69	-0.57	-0.60	
0.50	0.92	0.58	0.69	-0.56	-0.59	
0.68	0.74	0.33	0.49	-0.59	-0.62	
Geometric magnitudes		Mineral content				
A	I_z	P	Ca	Mn	Cu	Zn
0.88	0.72	-0.06	-0.11	-0.56	-0.02	-0.55
0.88	0.64	-0.08	-0.09	-0.55	0.03	-0.51
0.74	0.74	-0.01	-0.16	-0.55	0.01	-0.48

Phosphorus, Ca = Calcium, Mn = Manganese, Cu = Copper, Zn = Zinc. ²BW = Body weight. ³CRL = Crown-to-rump length. ⁴BMI = Body mass index. Note: bold $P \leq 0.05$ and italic $0.05 < P \leq 0.10$.

4.4 Discussion

Birth BW is a critical indicator of postnatal performance, as piglets born small often remain stunted and are unable to catch up to their larger counterparts throughout the entire production cycle (Gondret et al., 2005; Rehfeldt et al., 2008; Fix et al., 2010). Some studies have defined pigs with a birth BW of less than 1.0–1.25 kg and without organ growth restriction as low birth BW pigs (Milligan et al., 2001a; Milligan et al., 2001b; Douglas et al., 2014; Montoro et al., 2020). Accordingly, in the current study, piglets were selected within the lower and upper thresholds of these established cut-off points to identify differences among those considered small at birth. Piglets within the lower threshold had a mean birth BW of 0.97 ± 0.037 kg and were considered LBW, while those within the upper threshold had a mean birth BW of 1.18 ± 0.027 kg and were considered MBW. As some studies suggest that pigs born small may have the potential to compensate during suckling (Quiniou et al., 2002; Montoro et al., 2020; Blavi et al., 2021) and subsequent growth stages (Paredes et al., 2012; Douglas et al., 2013; He et al., 2016) it is important to evaluate and differentiate their characteristics at birth. To encompass the entire birth BW distribution of the population, piglets with the characteristic head morphology of severe IUGR (Chevaux et al., 2010) along with those with a birth BW exceeding 1.25 kg, were also evaluated.

While the link between birth BW and survivability is well established (Roehe and Kalm, 2000) additional measures of body conformation, such as BMI and CRL, also serve as important indicators of survivability (Baxter et al., 2008; Baxter et al., 2009; Hales et al., 2013). Furthermore, body shape at birth has been identified as a reliable predictor of postnatal growth in piglets born with low birth BW (Douglas et al., 2013). In this context, it is suggested that not all light pigs are similar and that their performance is more strongly influenced by body shape than by birth BW (Huting et al., 2018). In this study, we found high correlation coefficients between BMI and CRL and birth BW (0.870 and 0.935, respectively). However, no significant differences in these body shape metrics were observed between LBW and MBW piglets. These findings suggest that differentiating light piglets at birth based just on morphometric characteristics is challenging, and that internal physiological status likely may play a critical role in their subsequent growth performance.

Despite the strong interest in extensively studying the internal physiological status of newborn piglets, these traits are difficult to estimate non-invasively, often requiring euthanasia and expensive analytical techniques. The main limitation of this study is the

relatively small sample size, with only 6 piglets per category. Consequently, the findings should be regarded as a preliminary step toward understanding the physiological status of organs and bones in newborn piglets based on their birth characteristics, which may significantly impact their future growth performance. Further research involving a larger sample size is crucial to improve the reliability and generalizability of these results. Assessing organ and bone characteristics at birth could aid in identifying neonates at greater risk of compromised postnatal growth trajectories. Similarly, other traits, such as the number and size of muscle fibers, have been extensively studied as critical factors influencing postnatal growth potential. Low birth weight piglets tend to have fewer muscle fibers due to a reduced ratio of secondary to primary fibers (Handel and Stickland, 1987; Cerisuelo et al., 2009). Notably, since muscle fiber hyperplasia is completed by day 90 of gestation, the alterations in fiber number observed at birth are permanent (Dwyer et al., 1994). These effects directly affect the concept of fetal programming, which may significantly influence neonatal survival, as well as subsequent growth and efficiency in pigs (Ji et al., 2017).

The increased litter size in pigs over the past decades has led to uterine crowding. This, in turn, limits nutrient availability to the embryos during critical periods of development, compromising placental development in surviving fetuses and increasing the likelihood of having runt fetuses (Bazer et al., 1969; Vallet, 2000; Foxcroft et al., 2014) demonstrated that intrauterine crowding becomes a limiting factor when the number of embryos exceeds 14. In this way, piglets affected by IUGR experience asymmetrical organ growth during gestation as part of a fetal adaptative response to placental insufficiency (Wang et al., 2005; Roza et al., 2008; Amdi et al., 2013). The brain and heart are identified as the organs most protected from growth restriction compared to others. Consistent with these studies, the relative brain weight was significantly greater in sIUGR piglets at birth, showing a significant linear decrease as the piglets exhibited better external physical metrics. However, these differences among piglet categories were not reflected in organ ratios, where significant differences were observed only between the sIUGR group and the other categories (Bauer et al., 2003; Lynegaard et al., 2020). This was most likely due to what has been described as the “brain-sparing effect” (Roza et al., 2008) which primarily affects piglets with the most severe degree of IUGR. Another study revealed that the preferential growth of the nervous and cardiovascular systems in small fetuses can be detected as early as day 45 of gestation (Lyderik et al., 2023). Interestingly, most relative organ weights were comparable between sIUGR and LBW piglets but differed numerically from those of MBW and HBW piglets, which were also similar to each other.

Differences in bone growth and development were also observed among the 4 categories of piglets. The growth in bone length is stated that depends on body size and, consequently, on nutritional status (Adams, 1971). Restricted and undernourished fetuses are smaller than normal and possess bones that are anatomically less developed compared to well-nourished fetuses of the same age (Adams, 1971). In agreement with that, HBW piglets exhibited the highest EBV at birth, which was approximately 70% greater than that of the sIUGR piglets. In humans was described that skeletal ossification is more advanced than normal in large fetuses and delayed in those small for their gestational age (Berridge and Bruce Eton, 1958). This observation could be related to differences in the proportions of bones with higher or lower densities identified in our study. In this context, sIUGR piglets exhibited a higher percentage of low-density bones and a lower percentage of high-density bones compared to their heavier counterparts. Regarding LBW and MBW piglets, differences in bone density were observed between these two categories, indicating that not all light piglets at birth (< 1.25 kg) exhibit the same physiological status. The proportions of bones with different densities were determined using the HU value cut-off ranges originally described for adult pigs (Gaundré et al., 2014; Fabà et al., 2019) where higher HU values indicate greater bone density (Batawil and Sabiq, 2016). Despite this, these ranges successfully differentiated between bones of varying densities in newborn piglets, demonstrating the sensitivity of this method and its applicability to small piglets.

These findings on organ development, ossification, and bone growth in newborn piglets support the statement that the lower preweaning growth observed in runt pigs cannot be fully explained by their lower birth BW. This suggests that IUGR exerts a more complex influence on development potential (Van der Lende and De Jager, 1991). This influence likely originates during gestation, where growth-retarded pig fetuses are associated with smaller placentas characterized by slower blood flow (Wootton et al., 1977) and fewer, less dense areolae (Baxter et al., 2008) compared to their littermates. The placenta plays a pivotal role in fetal growth and development as it facilitates the transport of nutrients and respiratory gases between maternal and fetal circulation (Godfrey, 2002). Consequently, fetuses associated with smaller placentas exhibit alterations in fetal organ development, changes in the number and type of muscle fibers (Foxcroft et al., 2014) and impaired endochondral ossification (Briana and Malamitsi-Puchner, 2016; Pastor et al., 2024) thereby compromising their future developmental potential. Within-litter variation in fetal weight is reported to be detectable as early as day 28 of gestation and increases as gestation progresses and fetuses grow (Lyderik et al., 2023). This finding suggests that small fetuses identified early in gestation are likely to

maintain a reduced growth rate, may experience further compromise in later gestation, and are ultimately born as low-weight or IUGR piglets. The differences we observed, primarily in brain weight, EBV, and bone density among the various categories of piglets, may help identify varying degrees of restriction likely established during gestation. These intrauterine growth restrictions seem to have a direct impact on the piglets' postnatal growth and development.

To gain a deeper understanding of the differences among these growth-restricted piglets at birth, we also analyzed various parameters related to their tibiae. The tibia was selected as the optimal long bone for analysis for several reasons. First, it allows for the most precise measurements using CT, facilitating the calculation of specific metrics previously described in the literature (Fabà et al., 2019). Additionally, the tibia is well-known as a significant mineral reservoir, particularly for Ca and P. Its mineral content and mechanical properties have been studied in pigs in previous research (Vanderschueren et al., 1992; Pointillart et al., 1995). Proper bone growth, along with normal joint structure and function, is essential for the overall development of the organism (Tomaszewska et al., 2012). Therefore, piglets with a larger cortical area and greater tibial thickness are likely to exhibit better development at birth compared to their littermates, as demonstrated in our study. High birth BW piglets had the largest cortical area, approximately 60% greater than that of sIUGR piglets. Similarly, HBW piglets exhibited greater tibial thickness compared to the lower weight categories (sIUGR and LBW). These two measures are influenced by the process of bone growth, which is regulated by a complex system of endocrine signals. It is described that the growth of long bones is influenced by growth factors, dietary factors, and other cellular signals that are essential for chondrocyte differentiation (Orth, 1999; Ytrehus et al., 2007; Athanasiou et al., 2009). Among those factors that can damage the growth plate, IUGR piglets are being associated with impaired plasma IGF-1 levels (Chriett et al., 2016). Since insulin/IGF-1 signaling plays a pivotal role in early development and fetal growth, IUGR pigs are more prone to skeletal disorders caused by disruptions in the endocrine regulation of the growth plate (Tomaszewska et al., 2012). Indeed, IGF-1 not only stimulates longitudinal bone growth but also has demonstrated direct effects on bone modeling, supported by both in vivo (Spencer et al., 1991) and in vitro (Mccarthy et al., 1989) evidence.

Although our results suggest that piglets born light are more likely to experience impaired ossification, the mechanical properties of the tibiae, including maximum stress in compression and tension, as well as rigidity, were highest in the sIUGR group compared to the other categories. This could be supported by the following: (1) these mechanical properties

are intrinsic to the bone itself and, therefore, remain independent of both its size and the piglet's birth BW, and (2) as part of a fetal adaptive response to placental insufficiency and limited access to nutrients from the sow, similar to the "brain-sparing effect", piglets affected by IUGR may prioritize intrinsic bone quality over longitudinal bone growth. Although this specific physiological phenomenon has not been extensively studied in the literature (Adams, 1971), described that full-term runts had bones and epiphyses with a chemical composition more aligned with their age than their size. This implies that, regardless of weight, piglets can achieve chemical maturation of their bones as a function of age. Moreover, this study identified differences in the mineral content of the tibiae, which correlate with the observed variations in mechanical properties. Greater bone mineralization is associated with improved intrinsic bone quality. Ca and P, both essential for optimal bone formation and mineralization (Pointillart et al., 1995) displayed similar levels in both sIUGR and HBW piglets. Hydroxyapatite ($\text{Ca}_5(\text{PO}_4)_3(\text{OH})$), a mineral form of Ca and P that provides bones with their rigidity and strength, is the primary and essential component of bones in animals (Siris et al., 2004; Zhao et al., 2019). Differences were observed in the Mn and Zn content, both of which play crucial roles in bone and cartilage development (Veum et al., 2009; Van Riet et al., 2013; Skiba et al., 2022). The highest Mn and Zn levels were found in sIUGR piglets, with a linear decrease observed toward the HBW piglets. Given that Ca and P levels were consistent across piglet categories, and sIUGR exhibited higher Mn and Zn content in their bones, the impaired ossification identified in these sIUGR piglets did not lead to changes in intrinsic bone properties, such as rigidity and strength. Mn plays a role in bone and cartilage matrix formation through its involvement with proteoglycans (Van Riet et al., 2013) while Zn influences bone mass and is critical for matrix quality (Veum et al., 2009; Skiba et al., 2022). Regarding the mechanical properties and mineralization of the bone, it is important to note that no differences were found between LBW and MBW piglets. Since piglets were euthanized immediately after birth without having access to colostrum, this suggests the existence of an anticipated fetal adaptive response in bone quality that appears to be evident only in piglets with a severe degree of IUGR.

This characterization of piglets at organ and skeletal development levels will enable a more precise assessment of their susceptibility and subsequent risk of mortality due to their IUGR status at birth. Previous studies (Bauer et al., 1998; Amdi et al., 2013) noted that some small piglets can still achieve their genetic growth potential, exhibiting normal growth, whereas piglets affected by IUGR do not. These differences in genetic growth potential and survivability among low birth BW may be attributed to the asymmetrical organ and skeletal growth experienced by IUGR piglets during gestation. In the present study, the most pronounced

differences were observed between HBW and sIUGR piglets, while less significant differences were noted between LBW and MBW piglets. LBW piglets exhibited greater similarity to sIUGR piglets, whereas MBW piglets were more comparable to HBW piglets. This suggests that although light piglets at birth (LBW and MBW piglets) may be affected to varying degrees by a "mild-moderate" form of IUGR, distinguishing them clearly across different categories remains challenging. These two categories of light piglets studied align with the findings of (Montoro et al., 2020) which identified two distinct populations among piglets born with low BW based on their future growth performance. The authors further propose that incorporating additional variables measured at birth, especially in population with high birth BW variability, could allow for the identification and study of additional piglet categories. Other easily measurable on-farm indicators, such as the piglet's relative birth BW within its litter (Hales et al., 2013) the difference between the piglet's birth BW and the average litter weight at birth or after cross-fostering (Casellas et al., 2024; Salgado-López et al., 2024) and colostrum intake (Amdi et al., 2013) among others, should be used as complementary indicators alongside those employed in this study. Incorporating these measures would enable a more precise and robust classification of light piglets at birth.

Identifying piglets with some degree of IUGR at birth using easily measurable on-farm indicators offers farmers a quick and practical method to determine which piglets require additional support to optimize neonatal survival and growth performance. Our study demonstrates that birth BW, BMI, and CRL are strongly correlated with most of the internal characteristics analyzed, confirming their reliability as indicators of survivability and growth potential. Specifically, these morphological traits showed strong negative correlations with relative brain weight and organ ratios, and strong positive correlations with total bone volume and the longitudinal growth of the tibia. The results of the present study indicate that these external indicators can explain the organ and skeletal physiological status of piglets at birth but are not precise or accurate enough to distinguish between light piglets at birth (LBW and MBW piglets). The interest in this pig population lies in their varying growth performance potential and their ability to transition between categories of weight during the early stages of life. Some authors have highlighted the potential benefits of prediction methods using large data sets to identify pigs at risk of growth retardation (Casellas et al., 2024; Salgado-López et al., 2024). Further research is needed to improve the early identification of piglets affected by varying degrees of IUGR.

4.5 Conclusions

This study provides a deeper understanding of organ and bone physiological status in newborn piglets classified by birth weight, body mass index, and crown-to-rump length. Piglets experiencing some degree of IUGR exhibit asymmetrical organ growth favoring brain development, along with impaired ossification and longitudinal bone growth. Furthermore, these piglets show enhanced mechanical properties of the tibia, attributed to increased manganese and zinc content. The findings of this study reveal that the strong correlation between morphological characteristics at birth and organ and skeletal physiological characteristics is insufficient to accurately identify piglets classified as LBW or MBW, which are small at birth and with a “mild-moderate” degree of IUGR. Improving this classification criterion by incorporating complementary indicators at birth could enable pig farmers to design specific management and nutritional strategies targeted at this vulnerable population, ultimately enhancing their performance and survivability.

4.6 Literature Cited

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Chapter 5

Early-life risk factors predicting growth retardation and mortality in pigs:
a multi-criteria approach

Early-life risk factors predicting growth retardation and mortality in pigs: a multi-criteria approach

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Lay Summary

Pigs at risk of growth retardation or poor survival pose a significant management challenge and can cause economic losses for pig producers. Early identification of risk factors associated with survival and growth performance during the initial stages of the production cycle is essential for the timely implementation of effective preventive strategies. This research evaluated binomial logistic regression models to identify early-life factors associated with poor postnatal growth and mortality. Body weight on d 7 was the strongest predictor of weaning weight, followed by average daily gain during the first week. Body weight on d 1, relative body weight after cross-fostering, colostrum intake, and sow parity were significantly associated with the probability of being classified as compromised during early-life stages by the logistic regression model. The model trained using data up to d 7 retained its predictive capacity when applied to classify pigs at weaning using the same variables. Consistent performance across datasets was achieved. In conclusion, the development of a multi-criteria model incorporating relevant birth-related risk factors shows strong potential as a practical tool to improve production efficiency by enabling better management of factors affecting pig uniformity and growth outcomes in swine production.

Teaser Text

The development of a multi-criteria model based on easily measurable birth-related risk factors, with broad applicability across different pig populations, could enable the swine industry to identify pigs at risk of growth retardation or early mortality. In turn, this could facilitate timely interventions, improve efficiency, and reduce body weight variability at slaughter.

Abstract

Body weight (BW) variability throughout the production cycle remains a major challenge for the swine industry, particularly due to the negative impact of slow-growing pigs on production efficiency and batch uniformity. This study aimed to identify early-life risk factors associated with poor postnatal growth and mortality, and to develop a multi-criteria predictive model for classifying pigs based on their early growth and survival potential. Data from 2,138 pigs (Pietrain × [Landrace × Yorkshire]) and 1,115 pigs (Pietrain × [Landrace ×

Large White]), collected from two commercial farms, were analyzed. Pigs were monitored from birth to weaning, with detailed records of farrowing traits, BW, body conformation indicators, colostrum intake (CI), and survival outcomes. Body weight on d 7 was the strongest predictor of weaning weight ($R^2 > 0.60$), highlighting the critical influence of the first week on later growth. Logistic regression models were used to classify pigs as either compromised (defined as dead or alive with a BW below the 15th percentile of the BW distribution on d 7 of life and at weaning) or normal. The classification performance of the competing models, as well as the selection of the final model, was evaluated using the area under the curve (AUC) of the receiver operating characteristic curve. Subsequently, the optimal classification threshold was adjusted to balance sensitivity and positive predictive value. The final model, trained on d 7 data, achieved a high AUC (0.910), with BW on d 1, relative BW (RBW) on d 1, CI, and sow parity all significantly associated with the probability of being classified as compromised ($P < 0.05$). Each 100 g increase in BW on d 1 was associated with a 27.6% decrease in the odds of being compromised. Similarly, greater RBW on d 1 and CI were linked to a reduced risk. Pigs falling within the 10th percentile for BW on d 1, with low CI and negative RBW on d 1, showed the highest probability of being compromised by d 7. The model's robustness was confirmed through consistent performance across datasets. Density plots further validated the model, illustrating clear distributional differences between compromised and normal pigs. These findings suggest that a model based on easily measurable birth-related indicators can reliably identify pigs at risk of poor early-life performance. Such a tool holds strong potential for on-farm application to enhance pig management and reduce BW variability at slaughter.

Key words: binomial logistic regression, body weight, colostrum intake, growth performance, preweaning survival, swine

5.1 Introduction

One of the main factors affecting the efficiency of global pig production is the variability in body weight (BW) throughout the production cycle. For sanitary reasons, it is recommended to maintain contemporary pigs in the same batch (Maes et al., 2004), making BW variability a limiting factor in optimizing current all-in-all-out swine production systems (Patience et al., 2004). The main contributors to this variability are slow-growing pigs, which are expected to reach slaughter weight later than their faster-growing counterparts (Douglas et al., 2014; He et al., 2016). This subset of pigs has increased in recent decades due to continuous genetic advancements aimed at increasing sow prolificacy and, consequently, the number of pigs produced per sow per year (Rutherford et al., 2013). Calderón Díaz et al. (2017) estimated that, in any given batch, 10 to 15% of pigs are slow-growing pigs.

Based on an epidemiological approach, López-Vergé et al. (2018) suggested that the closer a light pig is to the end of the production cycle, the greater the probability it will be sent to slaughter at a later stage. This is due to the decreasing opportunity to implement effective strategies that enable lighter pigs to catch up to their heavier pen mates, particularly from weaning onwards (Blavi et al., 2021). Identifying potential risk factors associated with the survivability and growth performance of these pigs during the early stages of the production cycle is crucial for the timely implementation of effective preventive measures aiming to enhance their overall performance. Previous studies showed that weaning weight (WW) has a significant impact on postweaning growth, the number of days required to reach the target slaughter BW, and rates of morbidity and mortality (Wolter and Ellis, 2001; Douglas et al., 2013). Furthermore, Casellas et al. (2024) and Salgado-López et al. (2024) highlighted the substantial contribution of including WW as a prediction factor for subsequent BW in enhancing the performance of different machine learning models used to classify pigs at risk of growth retardation across the different stages of the production cycle, until slaughter. Achieving a high BW at weaning is crucial, as changes in pigs' BW category beyond this point are uncommon (Blavi et al., 2021).

Several studies have identified birth BW as a key indicator of postnatal performance, with pigs born underweight often remaining stunted throughout their life and unable to catch up with their faster-growing counterparts (Gondret et al., 2005; Rehfeldt et al., 2008; Fix et al., 2010). The relationship between birth BW and survivability is also well established in the literature (Van der Lende and De Jager, 1991; Roehe and Kalm, 2000). However, other

studies have shown that some pigs with low birth BW can exhibit compensatory growth during early stages (e.g., until the end of lactation), suggesting that birth BW alone may not be the best predictor of subsequent growth performance (Douglas et al., 2013; Montoro et al., 2020). This highlights the potential for targeted management strategies to enhance their lifetime growth.

Many studies have examined additional factors influencing pig growth and survival during the lactation period. Casellas et al. (2024) demonstrated that the probability of being small at weaning is not solely determined by birth BW at the beginning of the period. Other factors such as the difference between an individual pig's birth BW and the average litter weight, as well as within-litter birth BW variance, also play a role. These findings highlight the importance of cross-fostering for the classification of low BW pigs at weaning. Some authors have suggested that indicators of body conformation, such as body mass index (BMI) and ponderal index (PI), may serve as better predictors of survivability than birth weight alone (Baxter et al., 2008; Baxter et al., 2009; Hales et al., 2013). Other authors have linked pig neonatal vitality to both survival and growth performance during lactation (Herpin et al., 1996; Baxter et al., 2008; Muns et al., 2013). Moreover, all these factors can influence colostrum intake (CI), which is critical for postnatal survival and growth up to weaning (Quesnel et al., 2023).

All the studies mentioned above evaluated the individual impact of specific risk factors. To effectively develop early-life management and nutritional strategies for pigs at higher risk of poor growth performance and reduced survivability, the swine industry would benefit from identifying generalizable risk factors associated with compromised pigs. Building on this background, the following sections describe the present study and the work conducted to address these issues. Two distinct pig populations were characterized from birth to weaning, generating two datasets used to (1) identify key factors associated with low growth performance and early-life mortality, and (2) characterize different pig populations based on these risk factors, which are critical for predicting early-life mortality or poor growth. The objective of this research was to propose a multi-criteria model, based on the most relevant birth-related risk factors, for general on-farm application. The goal is to improve the future performance of the most vulnerable pigs by focusing on easily measurable on-farm criteria. We hypothesize that integrating multiple birth-related and early-life risk factors into a single multi-criteria model, derived from robust and powerful datasets, would enable accurate prediction of early-life mortality and poor growth, providing a practical tool to identify at-risk pigs and guide timely interventions during the early postnatal period.

5.2 Materials and Methods

The study was conducted with the approval of the Animal Ethics Committee of the Universitat Autònoma de Barcelona (CEEAH2788M2), in accordance with the European Union guidelines for the care and use of animals in research (European Parliament, 2010). Two independent populations of pigs were studied from birth to weaning on two commercial farms in Spain. A summary of each dataset (DS) is presented in Table 5.1. Dataset 1 was collected from 11 consecutive batches on a 1,050-sow farm (Landrace × Yorkshire) with a weekly batch management system. Dataset 2 was collected from 6 consecutive batches on a 600-sow farm (Landrace × Large White) with a 4-wk batch management system.

Table 5.1 Summary of the two datasets analyzed, including the number of pigs, genetic lines, average lactation length, and management practices.

Item	Dataset 1	Dataset 2
Number of pigs, n	2,138	1,115
Data collection	March 2022 – July 2022	January 2024 – June 2024
Pig crossbred line	(P × [Ld × Y])	(P × [Ld × Lw])
Sex	Males and females	Males and females
Length of lactation, d	26.1 ± 0.44	21.2 ± 1.25
Type of management	Weekly	4 wk
BW recording	Birth to weaning	Birth to weaning

Abbreviations: BW = Body weight; Ld = Landrace; Lw = Large white; P = Pietrain; Y = Yorkshire.

5.2.1 Animals, Diets and Housing

In DS 1, 2,138 crossbred pigs (Pietrain × [Landrace × Yorkshire]) from 102 litters were used, whereas in DS 2, 1,115 crossbred pigs (Pietrain × [Landrace × Large White]) from 86 litters were included. In both DS 1 and DS 2, sow parities ranged from 1 to 9, with means ± SD of 3.5 ± 2.09 and 4.4 ± 2.41 , respectively.

Sows in both datasets were fed commercial pelleted diets. During gestation, the diets consisted of corn, wheat, and wheat middlings (15.5% crude protein), while during lactation, they were primarily composed of corn, wheat, wheat middlings (15.5% crude protein), and soybean meal. The gestation diets provided 2,200 kcal/kg of feed and 0.500% standardized

ileal digestible (SID) Lys, whereas the lactation diets supplied 2,412 kcal/kg of feed and 0.804% SID Lys. In DS 1, each female received 2.2 kg of feed per day throughout gestation (from d 30 until placement in the farrowing pens). During the pre-farrowing period, gilts and sows were provided 2.6 kg and 3.0 kg of feed per day, respectively. Starting the day after farrowing, the daily feed allowance was increased by 400 g per day until d 9 post-farrowing, after which females were fed *ad libitum*, reaching a maximum intake of up to 9 kg of feed per sow per day. In DS 2, each female also received 2.2 kg of feed per day throughout gestation (from d 30 until placement in the farrowing pens). Before farrowing, gilts and sows received 2.8 kg and 3.2 kg of feed per day, respectively. For gilts, the daily allowance was reduced to 2.6 kg around farrowing and gradually increased to 5 kg/d by d 10 of lactation, reaching 7.5 kg/d at weaning. For sows, the feeding rate was maintained at 3.2 kg/d around farrowing and progressively increased to 6.0 kg/d by d 7, 8.0 kg/d by d 14, and 9.0 kg/d at weaning.

During gestation, sows were housed in groups of 30 to 35 in pens with concrete slatted floors. Five days before the expected farrowing date, sows were moved to the farrowing unit. The farrowing rooms were diffuse ventilated, with a room temperature of approximately 24 °C. Artificial lighting was provided from 0600 h to 1400 h in DS 1 and from 0700 h to 1800 h in DS 2. During farrowing, the lights remained switched on until the last monitored sow had finished farrowing, typically around 0100 h or 0200 h. Individual farrowing pens had slatted metal flooring in the sow's area and slatted plastic flooring in the rest of the pen. During the first days after parturition, a heat lamp was placed above the heat pad.

5.2.2 Management Routines

Cross-fostering was performed within the first 24 h after birth, once it was ensured that all pigs had consumed colostrum. A different protocol was followed on each of the farms under study. In the farm from DS 1, the protocol included the following steps: (1) all litters were equalized to 15 pigs, (2) when litter sizes exceeded 15 pigs, those with the lowest and highest birth weights were fostered to smaller litters, (3) pigs were cross-fostered only into litters with fewer than 15 pigs on d 1 of life. In the farm from DS 2, the protocol included the following steps: (1) all litters were equalized to a number of pigs equal to or greater than 12, (2) when litter sizes exceeded functional teat count + 1, pigs were fostered to smaller litters, (3) pigs were cross-fostered only into litters with fewer than 12 pigs on d 1 of life. These protocols aimed to keep the maximum number of pigs with their biological sow. Tail docking and iron injection (Uniferon®, Intervet Internation B.V., Boxmeer, The Netherlands) were performed on d 3 after farrowing. Pigs had free access to water, and creep feed (crude protein = 16.91%, net

energy = 2,423 kcal/kg, SID Lys = 1.2 g/kg) was offered — starting 10 d before weaning. In DS 1, pigs were weaned 4 wk after farrowing (mean $\pm$ SD: 26.1 $\pm$ 0.44 days), while in DS 2, pigs were weaned 3 wk after farrowing (mean $\pm$ SD: 21.2 $\pm$ 1.25 days). Pigs deemed unlikely to survive until weaning due to trauma, disease, or other causes were humanely euthanized by blunt-force trauma. Apart from the recordings made for the study, all animals were managed according to the standard routines of the farms.

5.2.3 Recordings

All live-born pigs were subjected to measurements of farrowing and morphological traits (Table 5.2). On the day of birth, prior to litter equalization, each pig was individually identified with an ear tag (LeeO®, MSD Animal Health, Spain). Birth order and the time of birth for each pig (stillborn and born alive) were recorded during farrowing supervision. Farrowing traits included birth order and cumulative birth interval, defined as the interval elapsed from the birth of each pig to that of the first pig in the litter. In cases where pigs were cross-fostered, both the date of transfer and the identity of the receiving sow were recorded. Sex, BW, and crown-to-rump length (CRL, the supine length of the pig from the crown of the head to the base of the tail) were recorded at birth. Rectal temperature of each pig was measured within the first 30 min after birth. From these measurements, the following indicators of body conformation were calculated: BMI (birth weight (kg)/[CRL (m)]²), PI (birth weight (kg)/[CRL (m)]³), and relative BW (RBW) at birth $\left(\frac{\text{[pig birth weight - mean birth weight of litter]}}{\text{mean birth weight of litter}} \times 100\right)$ and on d 1 $\left(\frac{\text{[pig BW on d 1 - mean weight of litter d 1]}}{\text{mean weight of litter d 1}} \times 100\right)$. The vitality score at birth was assessed on a 0–3 scale, calculated as the sum of two behavioral variables described by Muns et al. (2013). Udder stimulation: score of 0 if the pig showed no head movements (e.g., no udder stimulation or searching behavior within 30 s), and 1 if head movements were observed. Number of completed circles around enclosure: score of 0 if the pig was unable to rotate its body axis 360° from its initial orientation or walk along the limits of the bucket (55-cm diameter x 60-cm height, solid plastic enclosure, open at the bottom and top); 1 if it could either rotate 360° or walk once along the limits within 30 s; and 2 if it could either rotate 360° or walk along the limits at least twice within 30 s. Pigs were weighed again on d 1 (after cross-fostering), d 7, and at weaning. Body weight at birth and on d 1 were used to calculate 24-h weight gain and to estimate individual CI using the equation developed by Theil et al. (2014). Pig survival throughout the lactation period was monitored and recorded.

Table 5.2 List of additional individual variables evaluated in pigs at birth and on the first day of life, used in the logistic regression analysis of survivability and growth performance.

Item	Variables	Measuring unit
Farrowing traits	Birth order	n
	Cumulative birth interval	min
	Cross-fostering	yes/no
Pig traits at birth	Sex	male/female
Physical characteristics	Crown-to-rump length	cm
	Body mass index	kg/(m) ²
	Ponderal index	kg/(m) ³
	Relative birth weight	%
Rectal temperature	Rectal temperature at birth	°C
Vitality	Vitality score	U + NCC = Score 0, 1, 2, 3
	Udder stimulation (U) ¹	Score 0, 1
	No. of completed circles around enclosure (NCC) ²	Score 0, 1, 2
Pig performance after birth	BW gain for 24 h after birth	g
	Relative body weight on day ¹	%
	Colostrum intake	g/pig
Pig survival	Survival within the first week	yes/no
	Survival within the lactation period	yes/no

¹U: score of 0 if the pig showed no head movements (e.g., no udder stimulation or searching behavior within 30 s), and 1 if head movements were observed. ²NCC: score of 0 if the pig was unable to rotate its body axis 360° from its initial orientation or walk along the limits of the bucket; 1 if it could either rotate 360° or walk once along the limits within 30 s; and 2 if it could either rotate 360° or walk along the limits at least twice within 30 s. Abbreviation: BW = Body weight.

5.2.4 Calculations and Statistical Analyses

All calculations and statistical analyses were performed using the open-source software R v.4.4.0 (R Core Team, 2024). Simple linear regression models, implemented via the *lm()* function, were used to identify which early-life growth performance variables (BW on d 1, BW on d 7, and average daily gain (ADG) during the first week) best predicted pig WW individually. The coefficient of determination (R^2) was used to compare the models.

To identify potential risk factors associated with pig short survival and poor postnatal growth during the first week of life and throughout the lactation period, binomial logistic regression analysis (*glm()* function) was performed. A binary (1|0) outcome variable was

created, classifying each pig as either compromised (1: dead or alive with a BW below the 15th percentile of the BW distribution at a fixed time point for its respective farm) or normal (0: alive with a BW above the 15th percentile). This classification was applied for both time points: d 7 of age and the end of the lactation period. Percentiles were calculated separately for each farm, as the populations in DS 1 and DS 2 differed. The 15th percentile was selected as the cut-off point to balance between avoiding focusing on extreme values (e.g., outliers) that may arise from using lower percentiles and preventing excessive inclusion of pigs as compromised when using higher percentiles. The final DS used in the models had an unbalanced partition, which is common in cases involving death or compromised pigs, as these are typically minority outcomes. Stillborn pigs or those excluded from the study because they were cross-fostered to off-test sows were not included in the final DS. Moreover, to train the model, edge cases (pigs between the 15th and 16th percentiles) that could complicate the training process were removed and were reinserted once predicted with the selected model.

A subset of variables described in Table 5.2 (*i.e.*, farrowing traits, pig traits at birth, and pig performance after birth), together with BW on d 1 and sow farrowing traits, were included as predictors in the multiple logistic regression model. Initially, a stepwise backward selection procedure based on the Akaike Information Criterion (AIC), where a lower AIC indicates a better model, was applied using the *step()* function to identify potential risk factors for inclusion in the candidate models. Secondly, an ANOVA F-test (using the *anova()* function) for nested models was conducted to confirm whether certain groups of variables were not jointly significant at the 5% level; such variables were then removed. Simultaneously, multicollinearity among predictors was assessed by calculating the Variance Inflation Factor (VIF) using the *vif()* function from the *car* package (Fox and Weisberg, 2019). Variance Inflation Factor values greater than 5 or 10 were considered indicative of moderate and severe multicollinearity, respectively. In such cases, one or more variables with high VIF were considered for exclusion to mitigate multicollinearity.

After selecting candidate models based on multiple criteria (AIC, VIF, and coefficient interpretability), we evaluated the predictive performance of each model to determine the final selection. Once a candidate model was defined, predicted probabilities of belonging to the compromised category were obtained for each observation in the full DS using the *predict()* function. The classification ability was then evaluated using the area under the curve (AUC) of the receiver operating characteristic (ROC) curve (Egan, 1975), which plots sensitivity against specificity. Sensitivity referred to the proportion of compromised pigs classified as such by the classification rule, whereas specificity referred to the proportion of normal pigs correctly

classified as normal. The ROC curve was drawn, and the AUC was calculated using *roc()* and *auc()* functions of the pROC library (Robin et al., 2011). The candidate model with the highest AUC was selected as the final model.

Based on the ROC curve of the final selected model, a threshold-dependent classification analysis was performed to assess how varying decision thresholds influenced classification metrics. For each threshold (Ψ) in (0, 1), predicted probabilities were binarized such that observations with probabilities equal to or exceeding Ψ were classified as compromised, while those below Ψ were classified as normal. A confusion matrix was generated for each Ψ to calculate the numbers of true positives, false positives, true negatives, and false negatives, with compromised pigs considered positives and normal pigs considered negatives (Supplemental Table 5.6A). Various metrics derived from the confusion matrix were used to evaluate the classification models and identify the optimal Ψ . Among these metrics, accuracy refers to the proportion of pigs correctly classified, whether normal or compromised; the Youden statistic is defined as sensitivity + specificity – 1; and positive predictive value (PPV) is the proportion of pigs classified as compromised that are truly compromised (Trevethan, 2017), increasing as the number of false positives decreases. In our study, the Ψ based on Youden's statistic resulted in a high number of false positives, greatly exceeding the number of false negatives. The final Ψ was selected to balance PPV and sensitivity, while also balancing the number of false positives and false negatives, with the justification provided in the Discussion section. The Ψ demonstrating the best overall performance was selected to generate the final predicted classifications up to d 7 of life (Supplemental Table 5.6B). Predicted values from the final model were visualized using the *plot_model* function from the sjPlot package (Lüdtke, 2024). Predictions were displayed along with their corresponding 95% confidence intervals.

Predictive performance of the final model and threshold was evaluated using *k*-fold cross-validation with *k* = 3, 4, 5, and 10, implemented via the caret package (Kuhn, 2008). The DS was partitioned into *k* folds, with *k* – 1 folds used for training and the remaining fold for validation; this process was repeated *k* times. Performance metrics, accuracy and Cohen's kappa (which accounts for agreement beyond chance), were calculated for each fold and averaged to provide overall estimates of predictive performance (Supplemental Table 5.6C).

Additionally, without training the model to weaning, the same model trained to detect compromised pigs on d 7 was used to evaluate its ability to identify compromised pigs at weaning. Therefore, pigs classified as compromised by the non-balanced model at d 7 were

followed until weaning. The results of the logistic models gave odds ratios (OR) as well as 95% confidence intervals (Fonseca Martinez et al., 2017). The OR represents the change in the odds of the outcome occurring associated with a one-unit increase in the predictor variable, assuming all other variables in the model are held constant.

To evaluate the effect of the “pig category” factor on the most relevant variables identified in the logistic regression model (BW on d 1, RBW on d 1, CI, and parity), beyond differences in mean values, density plots were used to illustrate the full distribution of responses across categories. Sample percentiles (10th, 25th, 50th, 75th, and 90th) were calculated to position cumulative percentages of individuals within the response distribution. Percentiles, which are robust to outliers, indicate the response level below which a given percentage of animals are found (e.g., the 10th percentile, denoted Q10, indicates that 10% of animals fall below this value). To determine if the differences in quantiles were significant, a quantile test (Johnson et al., 1987) was used separately for each pair among the pig categories and each response. This nonparametric approach was implemented in R (Millard, 2013). Statistical significance was accepted at $P < 0.05$ and $P < 0.10$ was considered a trend.

5.3 Results

5.3.1 Descriptive Statistics

The descriptive statistics of farrowing traits and growth performance from birth to weaning in the two DS are presented in Table 5.3. Regarding farrowing traits, the results differ between DS 1 and DS 2 due to differences in sow prolificacy (hyperprolific sows in DS 1 vs. non-hyperprolific sows in DS 2). The total number of pigs born was higher in DS 1 (mean $\pm$ SD: 22.2 $\pm$ 4.18) than in DS 2 (mean $\pm$ SD: 16.0 $\pm$ 4.39). Consequently, DS 2 showed a higher percentage of live born pigs, with an average increase of 2.68% compared to DS 1. Gestation length was the same in both DS, while the number of pigs after cross-fostering differed by an average of 1.5 pigs due to the different cross-fostering protocols followed on each of the farms.

Regarding BW, pigs in DS 1 had a lower average birth weight (mean $\pm$ SD: 1.24 $\pm$ 0.32) compared to those in DS 2 (mean $\pm$ SD: 1.38 $\pm$ 0.36), which is attributed to the higher total number of pigs born per litter in DS 1. This initial difference of 140 g at birth was maintained on d 1 of life and increased to 410 g by d 7, with DS 1 pigs averaging 2.23 $\pm$ 0.60 kg and DS

2 pigs 2.64 ± 0.68 kg. However, as pigs in DS 1 experienced an average of 5 additional days of lactation, they ended the lactation period with a 1.22 kg greater BW (mean $\pm$ SD: 6.67 ± 1.89 kg) compared to those in DS 2 (mean $\pm$ SD: 5.45 ± 1.44 kg). It was observed that the SD increased with age, reflecting greater variability in BW by the end of the lactation period. In terms of ADG, the pattern observed was similar to that of BW. During the first week, ADG was greater in DS 2 (mean $\pm$ SD: 0.182 ± 0.079 kg/d) compared to DS 1 (mean $\pm$ SD: 0.141 ± 0.067 kg/d). This difference was no longer evident from d 7 to weaning or over the entire lactation period, likely due to the longer lactation duration in DS 1. The mean ADG for the whole lactation period was 0.206 ± 0.067 kg/d in DS 1 and 0.209 ± 0.066 kg/d in DS 2.

Table 5.3 Descriptive statistics for Dataset 1 and Dataset 2 during the lactation period, including the total number of sows and pigs, mean, and SD.

Item	Dataset 1			Dataset 2		
	Total n	Mean	SD	Total n	Mean	SD
Farrowing traits (sows)						
Parity, n	102	3.5	2.09	86	4.4	2.41
Total born, n	102	22.2	4.18	86	16.0	4.39
Live born, %	102	88.63	8.83	86	91.31	9.37
Stillborn, %	102	7.18	7.47	86	7.94	9.04
Mummified, %	102	4.19	5.09	86	0.74	2.90
Gestation length, d	102	116	0.76	86	116	0.99
Pigs after CF, ¹ n	102	15.0	0.00	86	13.5	1.64
Growth performance (pigs)						
BW, kg						
Birth	2,138	1.24	0.32	1,115	1.38	0.36
D 1	1,493	1.36	0.33	1,001	1.51	0.37
D 7	1,405	2.23	0.60	931	2.64	0.68
Weaning	1,336	6.67	1.89	870	5.45	1.44
ADG, kg						
First week, d 0 to 7	1,405	0.141	0.067	931	0.182	0.079
D 7 to weaning	1,336	0.230	0.077	870	0.231	0.077
Lactation, d 0 to weaning	1,336	0.206	0.067	870	0.209	0.066

¹Number of pigs per litter after cross-fostering.

Abbreviations: ADG = Average daily gain; BW = Body weight.

5.3.2 Early-Life Growth Performance Variables as Predictors of Weaning Weight

All early-life growth performance variables studied showed a positive and significant association with WW (Fig. 5.1). Among them, BW on d 7 emerged as the most powerful predictor of WW, explaining the largest proportion of variability in both DS ($R^2 = 0.64$ and 0.66 for DS 1 and DS 2, respectively). In contrast, BW on d 1 exhibited the weakest relationship with WW, with lower explanatory power in DS 2 ($R^2 = 0.28$) than in DS 1 ($R^2 = 0.32$). Average daily gain during the first week was also strongly associated with WW ($R^2 = 0.54$ and 0.59 for DS 1 and DS 2, respectively), although its predictive capacity remained below that of BW on d 7. The slightly weaker relationships observed in DS 1 for BW on d 7 and ADG during the first week may be attributed to the longer lactation period (one week longer than in DS 2). Nevertheless, both BW on d 7 and ADG during the first week proved to be strong early indicators of weaning performance in both datasets. Although BW on d 1 remained significant, its predictive capacity was notably lower compared with BW on d 7.

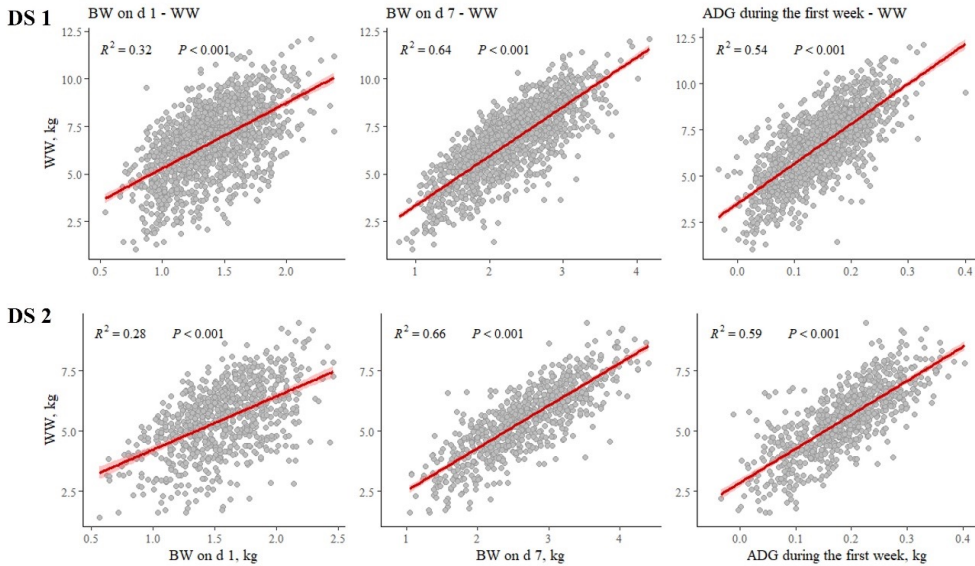


Fig. 5.1 Weaning body weight (WW) in relation to body weight (BW) on d 1, BW on d 7, and average daily gain (ADG) during the first week in Dataset (DS) 1 and DS 2. Each grey dot represents an individual pig. The red line depicts the fitted linear regression model, with the shaded area representing the 95% confidence interval.

5.3.3 Logistic Regression Model

Prediction of compromised pigs on d 7 of life using a binomial logistic regression model achieved an AUC of 0.910 (Fig. 5.2A). A final threshold of 0.416 (Fig. 5.2B) was chosen to achieve a balance between sensitivity and PPV, resulting in accuracy = 0.876, sensitivity = 0.700, specificity = 0.922, and PPV = 0.703. On d 7, the model correctly classified 1,726 pigs as normal and 346 as compromised, while misclassifying 146 normal pigs as compromised (false compromised) and 148 compromised pigs as normal (false normal). The confusion matrix and model performance are presented in Supplemental Table 5.6. Among all pigs classified as compromised by the model, 24.2% died before d 7 and 46.1% had a BW below the 15th percentile of the BW distribution at d 7 (24.2% + 46.1% = 70.3% PPV). Although the model was trained only up to d 7, follow-up of the pigs classified as compromised revealed the following outcomes by weaning: 34.8% died before weaning, and 29.9% had a BW below the 15th percentile of the weaning BW distribution (34.8% + 29.9% = 64.6% PPV). Model performance at weaning was slightly lower than on d 7.

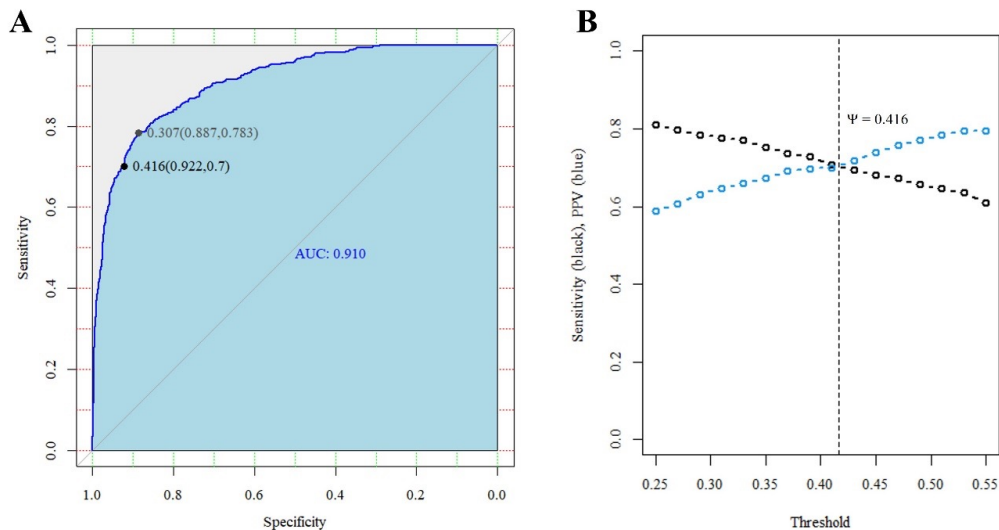


Fig. 5.2 (A) Receiver operating characteristic curve and area under the curve (AUC) for predicting compromised pigs at d 7 of life using a multiple logistic regression model. The threshold (Ψ) based on Youden's statistic was 0.307, whereas balancing sensitivity and positive predictive value (PPV) yielded a Ψ of 0.416. The coordinates of the point associated with each Ψ , including specificity and sensitivity, are shown in parentheses. (B) Sensitivity (black) and PPV (blue) of the multiple logistic regression model across a range of classification thresholds. Each point represents the model's performance at a given Ψ value.

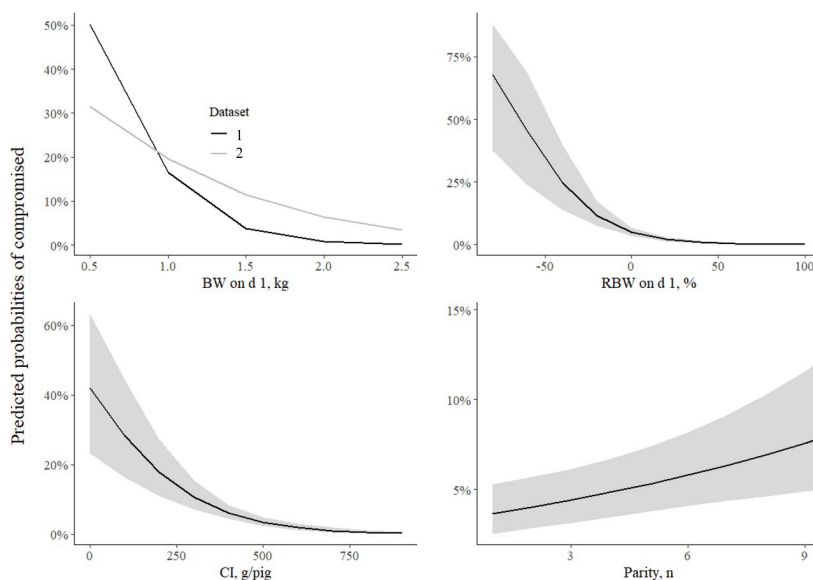
The variables that were significant in the multiple logistic regression model on survivability and growth during the first week of life were BW on d 1 ($P < 0.001$), RBW on d 1 ($P < 0.001$), CI ($P < 0.001$), and parity ($P = 0.002$) (Table 5.4); all other variables included in the model were not significant. According to the logistic regression model, each 1 kg increase in BW on d 1 was associated with a 96% reduction in the odds of being classified as compromised (OR = 0.04). For a 100 g increase in BW on d 1, the odds of being classified as compromised decreased by approximately 27.6% (results not shown). Similarly, each 1% increase in RBW on d 1 and each 1 g increase in CI were associated with lower odds of being compromised (OR = 0.95 and OR = 0.99, respectively). Parity was positively associated with risk, with each additional parity increasing the odds of a pig being compromised by 10% (OR = 1.10). A significant interaction between BW on d 1 and DS was detected, indicating that the relationship between BW on d 1 and the likelihood of being compromised differed by DS. In DS 1, lower BW on d 1 was associated with a higher probability of being compromised (Estimate = -3.26, $P < 0.001$). In contrast, in DS 2, the negative effect of BW on d 1 was attenuated or even reversed due to the positive interaction term (Estimate = 1.99, $P = 0.002$).

Figure 5.3 presents the predicted probabilities of being classified as compromised by d 7 of life based on the significant variables identified in the logistic regression model. For BW on d 1, lower values were associated with a higher risk of being compromised. In DS 1, the probability of compromise was higher below 1 kg compared to DS 2. However, due to the sharp decline in risk observed in DS 1 up to 1 kg, the trend reversed above this threshold, with DS 2 showing a higher probability of compromise beyond 1 kg. This illustrates the significant interaction between BW on d 1 and DS. A strong negative association was also observed for RBW on d 1, where pigs with lower values had a substantially higher risk of being compromised. A value of around 0% RBW on d 1 appeared to be a critical threshold below which the probability of compromise increased to 75%. Regarding CI, the probability of being compromised decreased as intake increased. A threshold of approximately 250 g per pig was associated with a probability of compromise below 20%, with further increases in CI leading to only marginal additional reductions in risk. Although the effect parity was moderate, pigs from older sows tended to have a higher risk of being compromised compared to those from younger sows.

Table 5.4 Multiple logistic regression model evaluating the association between morphological and farrowing traits and the probability of pigs being compromised by day 7 of lactation in terms of survivability and growth performance.

Item		Normal	Compromised
Total	n (%)	1,872 (79.1)	494 (20.9)
Intercept			
BW on d 1, kg	Mean (SD)	1.52 (0.30)	1.04 (0.26)
RBW on d 1, %	Mean (SD)	6.21 (17.2)	-23.3 (16.9)
CI, g/pig	Mean (SD)	483 (125)	286 (113)
Parity, n	Mean (SD)	3.84 (2.24)	4.27 (2.33)
Dataset			
1 (ref)	n (%)	1,178 (79.9)	297 (20.1)
2	n (%)	694 (77.9)	197 (22.1)
BW on d 1 × Dataset			
BW on d 1 × Dataset 2	-	-	-

Abbreviations: BW = Body weight; CI = Colostrum intake; OR = Odds Ratio; RBW = Relative body weight; 95%-CI = 95%-Confidence Interval.

**Fig. 5.3** Predicted probabilities of being compromised on d 7 of life as a function of the most relevant variables that significantly influenced this outcome in the logistic regression model. Abbreviations: BW on d 1 = Body weight on d 1; CI = Colostrum intake; RBW on d 1 = Relative body weight on d 1.

Multiple model				
Estimate	OR	95%-CI		P-value
		Low	Up	
	-	-	-	-
3.93				
-3.26	0.04	0.01	0.15	< 0.001
-0.05	0.95	0.94	0.97	< 0.001
-0.01	0.99	0.99	1.00	< 0.001
0.10	1.10	1.04	1.17	0.002
-	1	-	-	-
-1.78	0.17	0.04	0.80	0.025
1.99	7.30	2.05	26.5	0.002

5.3.4 Probability of Early-Life Risk Classification

Based on the odds ratios obtained from the logistic regression model, predicted probabilities of pigs with a BW on d 1 below the 30th percentile being classified as compromised on d 7 were calculated, considering different combinations of BW on d 1, RBW on d 1, and CI, with parity fixed at three (Table 5.5). Because pigs with low BW on d 1 are at higher risk of being compromised by d 7, this subset of pigs was selected to explore how the other significant variables included in the final model influenced the predicted probabilities. In general, the probability of being compromised decreased as BW on d 1 increased from the 10th to the 30th percentile. Within each BW on d 1 percentile, pigs with low CI and negative RBW on d 1 consistently exhibited the highest risk of being compromised. For example, at the 10th percentile of BW on d 1, a pig with low CI and negative RBW on d 1 had a predicted probability of being compromised exceeding 0.80 in both DS. In contrast, a pig at the same BW on d 1 percentile but with high CI and positive RBW on d 1 showed a lower predicted risk (below 0.25 in both DS). Similar patterns were observed at the 20th and 30th percentiles of BW on d 1. At the 30th percentile, predicted probabilities dropped considerably, particularly for pigs with adequate or high CI and neutral or positive RBW on d 1. The lowest predicted probabilities (0.09 in DS 1 and 0.11 in DS 2) were observed in pigs with high CI and positive RBW on d 1. Notably, the consistency of predictions across both DS supports the robustness of the model.

Table 5.5 Predicted probabilities of pigs below the 30th percentile for body weight on day 1 of life being classified as compromised on day 7, for each dataset. Predictions are based on significant variables identified through multiple logistic regression, with parity fixed at three.

BW on d 1, ¹ kg	CI, ² g/pig	RBW on d 1, ³ %	Prob. (DS 1)	Prob. (DS 2)
P10	Low	Negative	0.87	0.83
		Neutral	0.75	0.73
		Positive	0.63	0.60
	Adequate	Negative	0.72	0.67
		Neutral	0.55	0.53
		Positive	0.41	0.38
	High	Negative	0.51	0.45
		Neutral	0.33	0.31
		Positive	0.22	0.20
P20	Low	Negative	0.80	0.77
		Neutral	0.65	0.65
		Positive	0.50	0.50
	Adequate	Negative	0.61	0.58
		Neutral	0.43	0.43
		Positive	0.29	0.29
	High	Negative	0.40	0.36
		Neutral	0.23	0.23
		Positive	0.14	0.14
P30	Low	Negative	0.70	0.72
		Neutral	0.52	0.59
		Positive	0.38	0.44
	Adequate	Negative	0.49	0.51
		Neutral	0.31	0.37
		Positive	0.20	0.24
	High	Negative	0.28	0.30
		Neutral	0.15	0.19
		Positive	0.09	0.11

¹BW on d 1 = Body weight on day 1 (P10 = 10th percentile; P20 = 20th percentile; P30 = 30th percentile).

²CI = Colostrum intake (Adequate = 160 g/kg BW; Low = Adequate – 150; High = Adequate + 150).

³RBW on d 1 = Relative body weight on day 1 (Negative = 25th percentile; Neutral = 50th percentile; Positive = 75th percentile).

Abbreviations: DS = Dataset.

5.3.5 Quantile Analysis of Day 1 Body Weight, Relative Body Weight, Colostrum Intake, and Parity by Pig Category

To better understand the pig populations misclassified by the logistic regression model (false compromised and false normal), density plots of BW on d 1, RBW on d 1, CI, and parity across pig categories (true normal, false normal, true compromised, and false compromised) are shown in Fig. 5.4. Statistical details are provided in Supplemental Table 5.7, and descriptive statistics for all variables included in the model by pig category are presented in Supplemental Table 5.8. Regarding the well-classified populations, true compromised pigs exhibited a higher density in the left tail, indicating the lowest BW on d 1, RBW on d 1, and CI among all categories. In contrast, true normal pigs showed a higher density in the right tail, reflecting the greatest BW on d 1, RBW on d 1, and CI across all categories. Regarding the misclassified populations, false normal pigs showed significantly higher BW on d 1, RBW on d 1, and CI than false compromised pigs across all evaluated percentiles. This observed shift in density estimates, where false normal pigs outperformed false compromised pigs in key variables included in the model, was the primary reason for misclassification between these two populations.

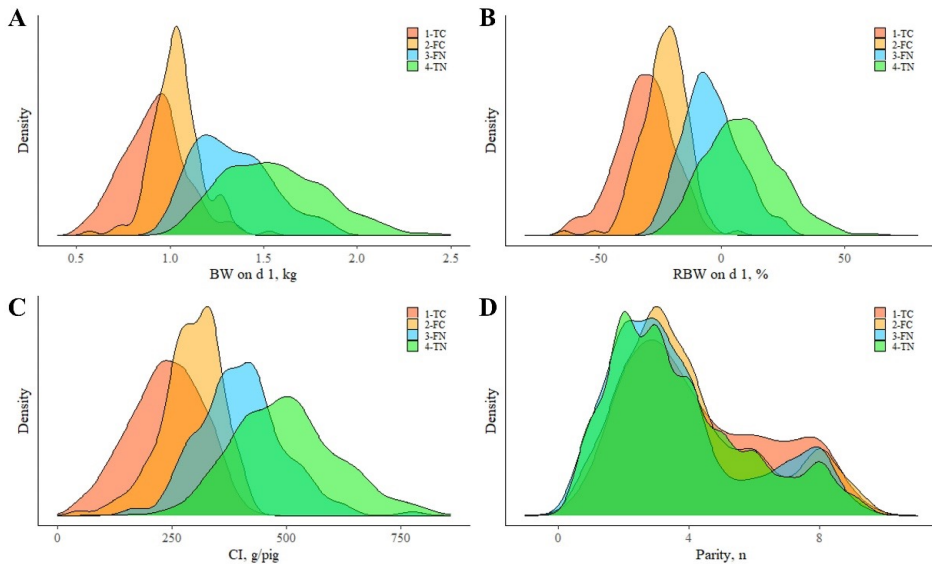


Fig. 5.4 Density plots showing: (A) body weight (BW) on d 1, (B) relative body weight (RBW) on d 1, (C) colostrum intake (CI), and (D) parity for pigs classified into four categories based on the logistic regression model: True compromised (TC, $n = 346$), False compromised (FC, $n = 146$), False normal (FN, $n = 148$), and True normal (TN, $n = 1,726$).

5.4 Discussion

This study investigated the most influential early-life risk factors affecting growth performance and survival in pigs during the first week of life and throughout lactation. The objective was to develop a multi-criteria model for practical on-farm application, aimed at identifying the optimal timing of interventions to enhance the performance of pigs at higher risk during the lactation period. This is particularly relevant for the pig industry, where uniformity and growth performance are critical, as variability in pig size significantly impacts profitability, with financial, welfare, and environmental consequences (Patience et al., 2004). Body weight variation often comes from a subset of pigs that exhibit markedly slower growth from birth to slaughter, posing significant management challenges and reducing system efficiency (Douglas et al., 2013). Pig performance across the production system results from a complex interaction of factors, with early-life conditions playing a key role in determining lifetime performance (Douglas et al., 2014).

Understanding which early-life conditions most influence subsequent pig performance can help improve survival during the lactation period and increase WW. To identify general indicators of growth performance and survivability, and to ensure the robustness of the proposed model, two independent DS from pig populations with differing levels of prolificacy were characterized and analysed. The descriptive statistics from both DS were consistent with previous studies (Paredes et al., 2012; Douglas et al., 2013; López-Vergé et al., 2018), supporting the reliability of our data. In line with previous studies suggesting that the predictive value of a factor increases the closer it is to the target weight record (Casellas et al., 2024; Salgado-López et al., 2024), the present results confirm that BW on d 7 and ADG during the first week outperformed BW on d 1 as predictors of WW. These variables therefore serve as strong early indicators of weaning performance in both DS. Additionally, early lactation and the peripartum are when most pre-weaning mortality occurs, with approximately 15 to 20% of all pigs born dying during this time (Baxter and Edwards, 2018; Tucker et al., 2021). This finding is both novel and highly significant, as it demonstrates that events occurring during the first week of life can be as important, or even more important, than birth BW, which has previously been identified as the primary indicator of postnatal performance (Gondret et al., 2005; Rehfeldt et al., 2008; Fix et al., 2010). This may represent a paradigm shift, suggesting that pigs born underweight are not necessarily irreversibly compromised and that early-life interventions in high-risk pigs can improve their subsequent performance. From a practical standpoint, weighing pigs is not a routinely performed on farms. Therefore, producers should

recognize the critical importance of the early lactation period rather than focusing solely on birth BW or BW on d 7. Providing targeted care during the first week of life, including ensuring the successful onset of lactation, during which the interaction between the sow and pigs is crucial, has the potential to enhance growth and overall performance up to weaning. Although no interventions during the first week of life were evaluated in this study, the key factors influencing early-life growth performance and survival are discussed below.

While most studies focus on the individual associations between early-life risk factors and pig survival or growth during the preweaning period (Hales et al., 2013; Panzardi et al., 2013; Quesnel et al., 2023) or throughout the production cycle (Paredes et al., 2012; Douglas et al., 2013; He et al., 2016), few publications consider these factors collectively to identify which are most critical to classifying a newborn pig as compromised (low chances of survival and growth) or as normal (Pandolfi et al., 2017; Ward et al., 2020; Geiping et al., 2022). To the authors' knowledge, no previous studies have proposed a multi-criteria model based on measurable on-farm risk factors within the first 24 h after birth to predict whether a pig is likely to be compromised or normal by d 7 of life. The cut-off weight used to classify a pig as compromised was defined in accordance with previous studies reporting that the incidence of slow-growing pigs on commercial farms ranges from 10 to 15% of the population (Larriestra et al., 2006; He et al., 2016; Calderón Díaz et al., 2017). While other studies have defined slow-growing pigs as those falling within the lower quartile of the BW population distribution (Montoro et al., 2020), a more conservative cut-off was chosen in the present study to avoid excessive inclusion of pigs in the compromised category, thereby reducing the risk of false positives in the model.

The final model on d 7 of life achieved a maximum AUC of 0.910, indicating outstanding discriminatory performance (Hosmer and Lemeshow, 2000). Sensitivity and specificity were adjusted to obtain a balance between predictive values (*i.e.*, PPV) and sensitivity, which is particularly relevant when classifying or screening animals (Fawcett, 2006; Trevethan, 2017). Given that the model based on pre-lactation indicators cannot capture causes of mortality or poor growth that occur during lactation, it is expected that some cases will not be detected. Therefore, authors accepted a small increase in false negatives in exchange for a non-negligible reduction in false positives. A moderate to high PPV was considered desirable to minimize false positive outcomes from the model, thus supporting the targeted application of specific management strategies (Blavi et al., 2021) or costly supplements (Threadgold et al., 2021) to pigs at highest risk. A PPV of 0.703 indicated that 70.3% of the pigs classified

as compromised by the model were indeed truly compromised. When pigs classified as compromised by the model trained only up to d 7 were followed until weaning, the PPV of this model decreased, likely due to the time elapsed between early-life factors and the recording of WW (Casellas et al., 2024; Salgado-López et al., 2024). Nevertheless, a still meaningful PPV of 0.647 was obtained at weaning, indicating that 64.7% of pigs identified as compromised by the early-life model were confirmed as such at weaning.

Poor growth performance and survival during the first week of life and throughout the lactation period were associated with several variables, including BW on d 1, RBW on d 1, CI, and parity. Consistent with the findings of Douglas et al. (2013) and Montoro et al. (2020), who reported that pigs with lower birth weights were able to shift to higher BW categories from birth or weaning to slaughter, our results indicate that BW on d 1 is not the sole determinant of postnatal growth. This also aligns with López-Vergé et al. (2018) and Blavi et al. (2021), who noted that changes in BW category are common during early growth phases, indicating the pig's potential for compensatory postnatal growth. In terms of survivability, Hales et al. (2013) demonstrated that birth weight alone is not a good indicator of the risk of dying prenatally or shortly after birth. These concepts are supported by the identification of two subsets of pigs (false compromised and false normal) by our model, both of which showed early-life growth performance and survivability independent of their birth characteristics. Specifically, the subset of pigs capable of changing BW category over time had BW on d 1 values ranging from 1.04 ± 0.13 kg to 1.33 ± 0.21 kg. A similar pattern was observed for RBW on d 1 and CI, with pigs showing RBW on d 1 values between $-23.5 \pm 9.31\%$ and $-4.18 \pm 11.3\%$, and CI ranging from 292 ± 66 g to 402 ± 93 g, indicating early-life growth performance that appeared independent of these birth weight-related variables.

Although a proportion of pigs demonstrated the capacity to shift categories during the early growth phases, a negative association between BW on d 1 and the probability of being classified as compromised was observed in the remainder of the population. This finding aligns with numerous studies reporting a positive relationship between higher birth weight and improved survival (Van der Lende and De Jager, 1991; Roehe and Kalm, 2000), with pigs born underweight being at greater risk of mortality (Rehfeldt and Kuhn, 2006) and more likely to remain stunted throughout the production cycle (Quiniou et al., 2002; Gondret et al., 2005; Rehfeldt and Kuhn, 2006). Pigs with a BW below 1 kg on d 1 were at a higher risk of being classified as compromised in litters from hyperprolific sows. This may be attributed to the increased proportion of low-birth-weight pigs (Quiniou et al., 2002; Beaulieu et al., 2010),

the decreased amount of colostrum available per pig, and the number of pigs born alive often exceeding the number of functional teats (Bortolozzo et al., 2023). However, appropriate care during the first days of life, particularly through the implementation of targeted cross-fostering protocols, which is a practice especially relevant in large litters (Muns et al., 2016), significantly reduced the risk, especially among pigs with increasing BW on d 1.

Relative weight of pigs is associated with their position within the litter and can therefore be used to identify low-birth-weight individuals. Greater RBW on d 1 values were associated with lower odds of being classified as compromised. In agreement with Milligan et al. (2002a) and Hales et al. (2013), who reported that pigs with low relative birth weight have an increased risk of early mortality, a strong negative association was observed between RBW on d 1 and the predicted probability of being compromised. Relative weight was thus identified as an important indicator of early growth performance and survivability. Similarly, Casellas et al. (2024) found that the difference between BW after cross-fostering and average litter weight was the most important factor in classifying light pigs at weaning using machine learning algorithms. In the present logistic regression model, RBW on d 1 was included instead of BMI, contrasting with the findings of Van der Lende and De Jager (1991) and Hales et al. (2013), who indicated that birth weight and BMI were more reliable predictors of survivability than RBW. Notably, a critical threshold around 0% RBW on d 1 was identified, below which the likelihood of being classified as compromised increased substantially. This highlights the importance of providing immediate care to the lightest pigs in the litter and implementing an appropriate cross-fostering protocol aimed at balancing litter sizes and reducing pre-weaning mortality (Wattanaphansak et al., 2002; Muns et al., 2014).

The RBW of each pig within the litter can be visually assessed on-farm by identifying individuals that are noticeably above or below the average weight of the litter. The identification of these extreme pigs is crucial, as those with the lowest BW are most at risk of pre-weaning mortality (Milligan et al., 2002a; Milligan et al., 2002b; Quesnel et al., 2012). Three important recommendations for an effective cross-fostering protocol are: (1) identify viable and non-viable pigs, assigning the smallest ones to the best sows (Muns et al., 2014), (2) ensure that all pigs receive adequate colostrum from their own mother before any movement takes place (Wattanaphansak et al., 2002), (3) minimize the number and frequency of movements, trying to keep the maximum number of pigs with their own mother (Wattanaphansak et al., 2002). Based on these recommendations and our results, the authors highlight the importance of fostering the smallest pigs to achieve low variation within their litters, without the need to

minimize within-litter variation across all litters. This approach would allow farmers to keep pigs with their birth mothers as much as possible.

Colostrum consumption significantly contributes to the survival and development of pigs, providing immunoglobulins for immune protection as well as energy for thermoregulation and growth (Devillers et al., 2004). In this study, we observed a reduction in the odds of being classified as compromised with each unit increase in CI, highlighting the critical importance of adequate colostrum consumption for pig survival after birth and growth until weaning, as also noted by Quesnel et al. (2023). Interestingly, a threshold of approximately 250 g per pig was associated with a probability of being classified as compromised below 20%, with further increases in intake yielding only marginal additional reductions in risk. This finding aligns with the recommendation by Quesnel et al. (2012), who suggested that pigs should consume at least 250 g of colostrum within the first 24 h to ensure survival. Other authors have proposed an intake of 150 to 170 g/kg BW as the minimum required to ensure neonatal survival, particularly in low-birth-weight pigs (Le Dividich et al., 2005; De Vos et al., 2014). In hyperprolific sows, prolonged farrowing duration combined with intense litter competition at the udder may reduce the amount of colostrum ingested and delay its intake after the onset of parturition (Oliviero et al., 2019). In such farrowings, reduced vitality immediately after birth can also significantly impair pigs' ability to ingest colostrum (Oliviero et al., 2019), which is one of the most important factors influencing their initial suckling behavior (Peltoniemi et al., 2021). A 27 g CI difference in favor of DS 2 compared to DS 1 aligns with these results regarding hyperprolific sows. Thus, ensuring sufficient CI for survival until weaning remains a major challenge, especially for low-birth-weight pigs born to hyperprolific sows.

Colostrum intake can be easily assessed on-farm by palpating the abdomen to determine fullness (Geiping et al., 2022). Several management strategies can be implemented to support proper colostrum consumption. Oral supplementation with colostrum recently milked from sows within the same herd has been shown to increase immunoglobulin G blood levels in weaker pigs, promoting better thermoregulation and improving overall litter performance within the first 24-h (Muns et al., 2014). Additionally, split suckling (Rutherford et al., 2013; Solà-Oriol and Gasa, 2017), performed just prior to cross-fostering, has proven effective in ensuring CI in less vital pigs, resulting in improved daily weight gain and greater litter homogeneity at weaning (Donovan and Dritz, 1996).

Parity was the final significant variable included in the logistic regression model. In this study, each additional parity increased the odds of a pig being classified as compromised by 10%, which is in accordance with Roehe and Kalm (2000), who reported a greater risk of mortality among pigs born to sows of parity 2 to 5 compared to those born to parity 1 sows. Similarly, other studies have shown increased pig mortality and a higher prevalence of crushing with increasing parity (Roehe and Kalm, 2000; Weber et al., 2009). Douglas et al. (2013) also identified parity as a significant factor for growth in all periods of pig life, although the pattern across the consecutive parities was unclear. In the same way, several authors have highlighted parity number as a key determinant of pig performance, with pigs born to gilts being lighter at birth than those born to sows (Smith et al., 2007; Quesnel et al., 2008). In contrast, Wulbers-Mindermann et al. (2002) and Hales et al. (2013) reported a greater risk of mortality among pigs born to primiparous sows compared to those born from multiparous sows. Additionally, the effect of parity on colostrum yield, and consequently on early-life growth performance, appears inconsistent across studies (Quesnel and Farmer, 2019; Quesnel et al., 2023).

The results were consistent across the two DS, providing confidence that the conclusions drawn may have broader applicability. This consistency highlights the potential utility of the model as a predictive tool for the early identification of pigs at risk. Nonetheless, it is important to note that the inclusion of DS as a significant fixed effect in the final model may limit the generalizability of the results to other DS. If a new DS shares the same descriptive characteristics as those used to develop the model, DS can be treated as a fixed effect. Conversely, if the new DS differs in its descriptive characteristics, it may be more appropriate to include DS as a random effect, which could influence some of the predictive performance of the final model. Another limitation of the model is that it was not validated using an independent third DS, which could have further strengthened the generalizability of the findings. Nevertheless, predictive performance was rigorously assessed through *k*-fold cross-validation, yielding high accuracy and substantial agreement, thereby supporting the model's robustness and reliability.

When focusing on pigs inherently at higher risk (BW on d 1 below the 30th percentile), the model demonstrated how early postnatal factors can either exacerbate or mitigate this vulnerability. As expected, greater BW on d 1 was associated with a general decline in the predicted probability of being classified as compromised, confirming the strong association between greater BW on d 1 and improved survival and growth performance identified in the logistic regression model. However, even within each BW on d 1 percentile group, the influence of RBW on d 1 and CI remained evident. Pigs with poor CI and a negative position within the

litter consistently showed the highest predicted risk, underscoring the critical importance of both CI and relative BW position within the litter, particularly among the most vulnerable individuals. In contrast, pigs with high CI and a positive RBW on d 1 exhibited significantly lower predicted risks. These findings suggest that early-life interventions aimed at enhancing CI and promoting immediate postnatal growth may be effective in reducing early-life risk, even in pigs with low-birthweights.

Farmers could benefit from using the variables identified in the logistic regression model as a guideline for determining when to implement interventions and which pigs to target, thereby enhancing their future growth performance and survival. This approach is particularly relevant in hyperprolific populations, where increased prolificacy often leads to a significant reduction in average birth weight, resulting in a higher number of low-birth-weight pigs (Quiniou et al., 2002; Beaulieu et al., 2010). In the swine industry, the greatest proportion of BW variability originates at birth, increasing slightly during lactation and in the first days post weaning until pigs adapt to solid feed (López-Vergé et al., 2018). From this point until slaughter, variability tends to decrease, mainly due to routine management practices implemented on farms (López-Vergé et al., 2018). The lactation period represents the most appropriate window of opportunity to implement strategies that enable lighter pigs to successfully catch up to their heavier pen mates, thereby reducing BW variability within the population.

5.5 Conclusions

This study provides a better understanding of key early-life indicators associated with pig survival and postnatal growth from birth to weaning under commercial conditions. Among the early growth performance variables analyzed, body weight at d 7 and average daily gain during the first week emerged as the strongest predictors of weaning weight, underscoring the critical importance of early lactation for subsequent postnatal performance. Using logistic regression, a model with good predictive ability was developed to identify pigs at risk of poor growth or mortality by d 7 of life, based on body weight on d 1, relative body weight on d 1, colostrum intake, and sow parity. The consistency of model's performance across two independent populations, despite differences in farm management and prolificacy, supports the generalizability and robustness of this risk classification approach. Integrating these risk factors into a predictive framework may offer swine producers a valuable tool to target interventions more precisely during the neonatal period.

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5.7 Supplemental Material

Supplemental Table 5.6 (A) Confusion matrix comparing the predicted results and real conditions of the proposed model trained up to day 7. (B) Model performance metrics (Accuracy, Sensitivity, Specificity, and Positive Predictive Value) across different thresholds. (C) Accuracy and Cohen's kappa obtained from k-fold cross-validation.

A)

Day 7 Model		True condition	
	Total population = 2,366	1	0
Predicted condition	1	346	146
	0	148	1,726

B)

Threshold criterion	Threshold	Accuracy ¹	Se ²	Sp ³	PPV ⁴
Youden statistic ⁵	0.307	0.866	0.783	0.887	0.647
Se $\approx$ PPV	0.416	0.876	0.700	0.922	0.703

C)

Cross-validation folds	3-fold	4-fold	5-fold	10-fold
Accuracy	0.891	0.886	0.889	0.890
Cohen's kappa ⁶	0.648	0.634	0.641	0.646

¹Accuracy = (TC + TN) / n = (346 + 1,726) / 2,366.

²Se = Sensitivity = TC / (TC + FN) = 346 / (346 + 148).

³Sp = Specificity = TN / (TN + FC) = 1,726 / (1,726 + 146).

⁴PPV = Positive Predictive Value = TC / (TC + FC) = 346 / (346 + 146).

⁵Youden statistic = Se + Sp - 1.

⁶Cohen's kappa = measure of agreement beyond chance, calculated as $(P_o - P_e) / (1 - P_e)$,

where P_o is the observed agreement and P_e the agreement expected by chance.

Abbreviations: FN = False normal; FC = False compromised; TN = True normal; TC = True compromised.

Supplemental Table 5.7 Effect of the predicted category from the logistic regression model on quantile change (Q10, Q25, Q50, Q75, and Q90) according to body weight on day 1 (A), relative body weight on day 1 (B), colostrum intake (C), and parity (D). The reference groups used in this analysis are the True normal (TN), True compromised (TC), and False compromised (FC).

A)

Item	Q10	P Q10	Q25	P Q25	Q50	P Q50	Q75	P Q75	Q90	P Q90
TN	1.22		1.34		1.54		1.75		1.92	
FN	1.1	< 0.001	1.17	< 0.001	1.31	< 0.001	1.46	< 0.001	1.6	< 0.001
TN	1.22		1.34		1.54		1.75		1.92	
FC	0.89	< 0.001	0.956	< 0.001	1.03	< 0.001	1.1	< 0.001	1.19	< 0.001
TC	0.695		0.8		0.915		1		1.12	
FC	0.89	< 0.001	0.956	< 0.001	1.03	< 0.001	1.1	< 0.001	1.19	0.004
TC	0.695		0.8		0.915		1		1.12	
FN	1.1	< 0.001	1.17	< 0.001	1.31	< 0.001	1.46	< 0.001	1.6	< 0.001
FC	0.89		0.956		1.03		1.1		1.19	
FN	1.1	< 0.001	1.17	< 0.001	1.31	< 0.001	1.46	< 0.001	1.6	< 0.001

B)

Item	Q10	P Q10	Q25	P Q25	Q50	P Q50	Q75	P Q75	Q90	P Q90
TN	-10.3		-2.11		8.06		18.3		28.1	
FN	-17.9	< 0.001	-11.8	< 0.001	-5.57	< 0.001	2.45	< 0.001	11.8	< 0.001
TN	-10.3		-2.11		8.06		18.3		28.1	
FC	-35	< 0.001	-28.6	< 0.001	-22.8	< 0.001	-17.7	< 0.001	-13.3	< 0.001
TC	-46.1		-38.2		-30.9		-24		-17	
FC	-35	< 0.001	-28.6	< 0.001	-22.8	< 0.001	-17.7	< 0.001	-13.3	0.001
TC	-46.1		-38.2		-30.9		-24		-17	
FN	-17.9	< 0.001	-11.8	< 0.001	-5.57	< 0.001	2.45	< 0.001	11.8	< 0.001
FC	-35		-38.6		-22.8		-17.7		-13.3	
FN	-17.9	< 0.001	-11.8	< 0.001	-5.57	< 0.001	2.45	< 0.001	11.8	< 0.001

C)

Item	Q10	P Q10	Q25	P Q25	Q50	P Q50	Q75	P Q75	Q90	P Q90
TN	355		417		495		570		655	
FN	288	< 0.001	347	< 0.001	402	< 0.001	448	< 0.001	524	< 0.001
TN	355		417		495		570		655	
FC	205	< 0.001	258	< 0.001	298	< 0.001	338	< 0.001	367	< 0.001
TC	126		183		238		294		338	
FC	205	< 0.001	258	< 0.001	298	< 0.001	338	< 0.001	367	0.001
TC	126		183		238		294		338	
FN	288	< 0.001	347	< 0.001	402	< 0.001	448	< 0.001	524	< 0.001
FC	205		258		298		338		367	
FN	288	< 0.001	347	< 0.001	402	< 0.001	448	< 0.001	524	< 0.001

D)

Item	Q10	P Q10	Q25	P Q25	Q50	P Q50	Q75	P Q75	Q90	P Q90
TN	1		2		3		5		7.5	
FN	1	0.503	2	0.526	3	0.361	5	0.672	8	0.834
TN	1		2		3		5		7.5	
FC	2	0.947	3	0.995	3.5	0.889	5	0.818	8	0.848
TC	2		3		4		6		8	
FC	2	0.953	3	0.705	3.5	0.888	5	0.963	8	0.776
TC	2		3		4		6		8	
FN	1	0.999	2	0.997	3	0.995	5	0.870	8	0.792
FC	2		3		3.5		5		8	
FN	1	0.920	2	0.977	3	0.899	5	0.684	8	0.588

Abbreviations: FN = False normal; P = P-value.

Supplemental Table 5.8 Descriptive statistics (mean, SD, minimum, maximum) for pigs classified into four categories based on the logistic regression model: True compromised (n = 346), False compromised (n = 146), False normal (n = 148), and True normal (n = 1,726).

Item	True compromised				False compromised			
	Mean	SD	Min.	Max.	Mean	SD	Min.	Max.
Significant variables								
BW on d 1, kg	0.91	0.17	0.50	1.38	1.04	0.13	0.57	1.53
RBW on d 1, %	-31.6	11.4	-64.3	1.55	-23.5	9.31	-64.2	6.36
CI, g/pig	237	79	29	433	292	66	46	416
Parity, n	4.5	2.3	1	9	4.1	2.1	1	9
Pig additional variables								
Traits at birth								
CRL, cm	21.0	1.48	18.1	26.0	21.5	1.28	18.4	26.0
BMI, kg/m ²	20.6	2.50	13.9	27.6	21.6	2.25	14.2	29.3
PI, kg/m ³	98.6	13.7	60.8	130.5	100.6	12.6	57.8	138.5
RBW on d 0, %	-26.3	12.2	-60.2	17.4	-20.5	10.8	-62.9	25.8
RT, °C	35.8	1.6	32.1	40.4	36.2	1.7	32.6	39.8
Vitality ≥ 2, %	38.0	-	-	-	44.8	-	-	-
BW on d 0, kg	0.91	0.17	0.54	1.35	1.01	0.15	0.55	1.58
Performance after birth								
BW gain 24h, g	1.85	61.6	-200	160	28.5	59.4	-300	130

Abbreviations: BMI = Body mass index; BW = Body weight; CI = Colostrum intake;
 CRL = Crown-to-rump length; PI = Ponderal index; RBW = Relative body weight;
 RT = Rectal temperature.

False normal				True normal			
Mean	SD	Min.	Max.	Mean	SD	Min.	Max.
1.33	0.21	0.99	1.84	1.56	0.27	0.91	2.46
-4.18	11.3	-27.8	25.0	8.72	15.2	-28.1	82.5
402	93	165	776	499	115	144	845
3.8	2.4	1	9	3.8	2.2	1	9
23.3	1.94	14.4	28.0	24.1	1.69	18.5	32.0
23.1	2.88	16.6	37.4	24.7	2.85	15.0	38.9
100.4	19.3	65.5	241.1	102.8	14.0	51.7	210.1
-1.85	13.5	-40.5	43.2	9.39	15.8	-33.6	87.2
36.4	1.3	33.0	39.0	36.8	1.4	32.0	40.6
44.4	-	-	-	42.1	-	-	-
1.26	0.22	0.72	1.81	1.44	0.26	0.79	2.44
69.7	78.3	-180	450	114	75.7	-310	360

Chapter 6

Classification of light Yorkshire pigs
at different production stages using ordinary
least squares and machine learning methods

Classification of light Yorkshire pigs at different production stages using ordinary least squares and machine learning methods

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Abstract

Pig homogeneity and growth are major concerns for the pig industry today. Variability in pigs' size has a strong impact on profitability as uniformity plays a key role in the overall economic value of pigs produced. This research focused on statistical methods to identify pigs at risk of growth retardation at different stages of production. Data from 125,083 Yorkshire pigs at weaning (18–28 d), 59,533 pigs at the end of the nursery period (70–82 d) and 48,862 pigs at slaughter (155–170 d) were analyzed under three different cut-points (lowest 10, 20 and 30%) to characterize light animals. Records were randomly split into 2:1 training:testing sets, and each training data set was analyzed through an ordinary least squares approach and four machine learning algorithms (decision tree, random forest, and two alternative boosting approaches). A wide range of weighting functions were applied to give increased relevance to lighter pigs. Each resulting classification norm was used to classify light pigs in the testing data set. Both sensitivity and specificity were retained to construct the receiver operating characteristic curve, and the statistical performance of each analytical approach was evaluated by the area under the curve (AUC). In all production stages and cut-points, the random forest machine learning algorithm provided the highest AUC, closely followed by boosting procedures. For weaning BW (WW), factors related to birth BW and litter size accounted for more than 75% of the important prediction factors for light pigs. BW at the end of the nursery period and slaughter BW analyses revealed a similar pattern where WW and BW at the end of the nursery period accounted for more than 40 and 50% of statistical importance among the prediction factors, respectively. Machine learning algorithms are useful tools to easily evaluate the risk factors affecting the efficiency and homogeneity in swine. Since the BW at birth and weaning are key factors, sow nutrition and feeding management during gestation and lactation, along with piglet management during lactation, are identified as important influences on pig weight variability.

Implications

Providing robust tools to identify pigs at risk of growth retardation will help to develop better management strategies for this subset of pigs. This research has tested five different classification algorithms (ordinary least squares regression; decision tree; random forest; two alternative boosting approaches) to determine their ability to classify lightweight pigs at different production stages. The random forest technique had the best performance,

followed closely by boosting approaches. The classification ability of these methods increased when focused on more extreme individuals. Weight-related traits at previous ages played the key role in the classification of light animals.

Keywords: area under the curve, artificial Intelligence, growth retardation, live weight, swine

6.1 Introduction

The current swine production systems maintain contemporary pigs in the same batch as it is recommended for optimal animal health (Maes et al., 2004). One of the main important factors affecting the efficiency of pig production in these all-in-all-out systems is the variability of BW at slaughter (Patience et al., 2004). High variability in market weight reduces the value of the carcasses by worsening their quality classification and price quotation, reduces the effectiveness of slaughterhouse equipment and increases the occupation time in finishing farm facilities (López-Vergé et al., 2018), although with relevant economic consequences on earlier stages (Larriestra et al., 2006). These effects represent the main shadow production cost for the swine industry. There is a plethora of scientific literature aiming to identify the environmental (Botermans et al., 2000; Quiniou et al., 2002), behavioral (Georgsson and Svendsen, 2002; Carcò et al., 2018), nutritional and feeding (Brossard et al., 2009; Solà-Oriol and Gasa, 2017; Blavi et al., 2021), and genetic factors (Ibañez-Escriche et al., 2008; Peltoniemi et al., 2021), among others, that contribute to variability in pig weights under commercial conditions.

Pigs with a low BW at the beginning of the grow-finishing barn are expected to reach market BW later than their faster-growing counterparts (Douglas et al., 2014; López-Vergé et al., 2018). Nevertheless, little is known about the usefulness of prior performance information to effectively identify those animals at greatest risk of growth retardation in sufficient time for intervention to improve outcome. Indeed, this implies a change in the analytical paradigm, moving from a goodness of fit of cause-effect parametrizations, to the predictive ability of methodologies aimed at the outcome (Steyerberg et al., 2010).

Advances in both computer performance and classification algorithms have been significant in recent decades, and these advances are providing reliable alternatives to the well-known parametric linear model for the analysis of continuous traits. Machine learning, a branch of the artificial intelligence research field, must be viewed as a paradigmatic example

that allow computers to evolve behavior based on empirical data (Mitchell, 1997). There are many prediction methods with potential contributions to the swine industry (Quinlan, 1987; Friedman, 2001; Chen and Guestrin, 2016; Wright and Ziegler, 2017), although little is known about their ability to identify pigs at risk of growth retardation. Large data sets become mandatory to apply these methods and to determine the best classification tool based on a representative population and avoiding sampling biases.

In order to confidently intervene with effective management strategies for low BW and low growth pigs, the industry would benefit from robust tools to identify these pigs. In that sense, the present study was conducted based on a robust and powerful database available to accurately classify (1) the piglets that would be the main cause of variation within a population and (2) linking and identifying the main production factors that explain low pig BW at each phase within the pig production cycle with accuracy and robustness.

The objective of this research focused on the classification of light pigs at different production stages. More specifically, we tested five different classification algorithms on BW data from more than 100,000 Yorkshire pigs, evaluating three independent weight cut-off points for light pigs and their performance across different production stages. The patterns of sensitivity and specificity were characterized for each method by constructing receiver operating characteristic (ROC) curves. Factors with higher contributions to the final category were identified and discussed.

6.2 Materials and Methods

Animal Care and Use Committee approval was not necessary for this study because analyses were performed on existing field data obtained under standard farm management from Andrimner Genética Aplicada (Barcelona, Spain) and DNA Genetics (Columbus, NE, USA) selection farms. Both productive and pedigree data were collected by trained technicians within the context of the genetic selection program of the Yorkshire population involved in this study.

6.2.1 Selection nuclei pig data

All analyses focused on Line 200 Yorkshire (DNA Genetics) nucleus data set, collected in four farms from both North America and Europe from January 2014 to March 2021. Animals were kept under standard intensive farming conditions, and weighed at: birth (BtW), weaning

(WW, 18–28 d), the end of the nursery period (70–82 d), and slaughter (155–170 d). The distribution of WW, BW at the end of the nursery period, and slaughter BW, as well as cut-points (lowest 10, 20 and 30%) are presented in Fig. 6.1. Age-related differences at each weigh point were removed for WW, BW at the end of the nursery period and slaughter BW by a standard linear adjustment based on total data at 21 d, 75 d and 160 d, respectively (Table 6.1). For BW at the end of the nursery period and slaughter BW, there was a 3.7-fold increase in data from females compared to males. This discrepancy arose because all females were retained for the grow-finisher period, whereas only a certain number of maternal boars were selected to continue in that phase. Additional data for each piglet (*i.e.*, sex, death cause and date, and cross-fostering date and adoption litter after cross-fostering, if any), sow (*i.e.*, parity number and farm) and litter levels (*i.e.*, birth date, litter size at birth and after cross-fostering, if any) were systematically collected by trained farm staff.

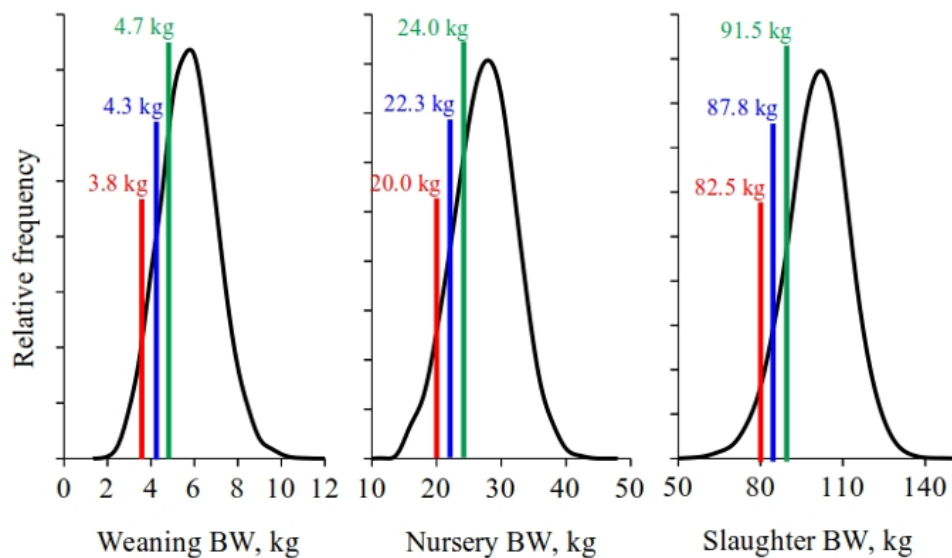


Fig. 6.1 Distribution of weaning (125,083), end of the nursery period (59,533), and slaughter (48,862) BWs from Yorkshire pigs, as well as cut-points for the lowest 10% (red), 20% (blue) and 30% (green). Abbreviation: Nursery BW = BW at the end of the nursery period.

Table 6.1 Summary of weaning BW, BW at the end of the nursery period, and slaughter BW in the Yorkshire pig population.

	Weaning BW, kg		BW at the end of the nursery period, kg		Slaughter BW, kg	
	n	Mean $\pm$ SE	n	Mean $\pm$ SE	n	Mean $\pm$ SE
Overall	125,083	5.456 $\pm$ 0.007	59,533	26.391 $\pm$ 0.021	48,862	96.820 $\pm$ 0.045
Sex						
Male	63,079	5.606 $\pm$ 0.009	12,551	27.259 $\pm$ 0.047	10,309	98.334 $\pm$ 0.098
Female	62,004	5.304 $\pm$ 0.009	46,982	26.159 $\pm$ 0.024	38,553	96.416 $\pm$ 0.050
Cross-fostered						
No	117,495	5.470 $\pm$ 0.007	55,292	26.380 $\pm$ 0.022	45,448	96.737 $\pm$ 0.046
Yes	7,588	5.239 $\pm$ 0.026	4,241	26.523 $\pm$ 0.079	3,414	97.930 $\pm$ 0.169
Sow parity						
1	64,594	5.255 $\pm$ 0.009	31,714	25.762 $\pm$ 0.029	25,908	95.745 $\pm$ 0.061
2	32,725	5.657 $\pm$ 0.013	14,693	27.145 $\pm$ 0.043	11,815	98.141 $\pm$ 0.091
3	15,171	5.642 $\pm$ 0.019	6,926	27.034 $\pm$ 0.063	5,883	98.345 $\pm$ 0.129
4	7,061	5.750 $\pm$ 0.029	3,554	27.149 $\pm$ 0.180	3,026	97.793 $\pm$ 0.087
5	3,693	5.684 $\pm$ 0.039	1,720	26.888 $\pm$ 0.125	1,429	96.927 $\pm$ 0.260
>5	1,839	5.829 $\pm$ 0.056	926	27.303 $\pm$ 0.172	801	97.039 $\pm$ 0.349
Farm ¹						
A	8,522	5.317 $\pm$ 0.025	4,117	25.740 $\pm$ 0.079	2,438	94.361 $\pm$ 0.197
B	14,951	5.143 $\pm$ 0.019	2,647	23.527 $\pm$ 0.094	1,418	91.881 $\pm$ 0.255
C	17,574	5.434 $\pm$ 0.018	11,170	27.207 $\pm$ 0.049	9,898	98.428 $\pm$ 0.100
D	84,036	5.530 $\pm$ 0.008	41,599	26.418 $\pm$ 0.025	35,108	96.738 $\pm$ 0.053

¹Farms were anonymized due to privacy concerns and sorted by the number of available weaning BWs.

6.2.2 Cross-fostering protocol

Cross-fostering is a management technique which could be performed in several ways. The cross-fostering protocol for the present study was based on the following steps: (1) fostering took place within the first 24 hours of birth and after 24 hours any fostering was only because of a lactation failure, (2) loading as many sows as possible to nurse a number of pigs equal to their functional teat count + 1 more pig and (3) when litter sizes exceeded functional teat count + 1, piglets were fostered to smaller litters (this determination was made within the first 24 hours). The biggest piglets were the first ones to be moved, as they seem to be able to withstand easier the changes in the environment. This process is similar to the protocols used in high-health farms; recommending keeping litters intact as much as possible, doing the minimum number of changes and applying an intervention only to balance the number of pigs per litter (Muns et al., 2014). Within this context, 73.4% of litters had no fostered pigs in this Yorkshire line, whereas 9.6, 7.2 and 9.2% of the litters had 1, 2 or more than two fostered pigs, respectively. Protocols for lower health status farms usually make litters including only or mainly small piglets to help and protect those animals during lactation (Alexopoulos et al., 2018). Other strategies such as creep feeding or milk replacers, together with the piglet's good vitality, may help to reduce the risk factors to become a slow-growing pig at weaning and thereafter (Muns and Tummaruk, 2016).

6.2.3 Operational models

Prediction of WW data focused on the following model,

$$WW_{ijklmnopq} = BtW_i + Sex_j + Cross-fostered_k + DB_i + DC_i + VB_i + VC_i + Stillbirths_m + Parity\ number_n + Litter\ size_o + Farm_p + Season_q$$

where BtW_i was the birth BW of the i th piglet, Sex_j was the sex of the j th piglet (male or female), $Cross-fostered_k$ identified if cross-fostered or not, DB_i (DC_i) was the difference between its BtW and the average litter weight at birth (after cross-fostering), VB_i (VC_i) was the within-litter variance of BW at birth (after cross-fostering), $Stillbirths_m$ were the number of stillbirths in the litter (0, 1, 2, 3, 4 or >4), $Parity\ number_n$ was the parity number of the sow (1, 2, 3, 4, 5 or >5), $Litter\ size_o$ was the litter size after cross-fostering (<6, 6–7, 8–9, 10–11, 12–13, 14–15, 16–17, 18–19, 20–21, 22–23, or >23), $Farm_p$ was the farm with four levels, and $Season_q$ was the season of birth on a 2π -radian scale. The same was assumed for the remaining traits, after including WW_i as a predictor in the model for the analysis of BW at the end of the nursery period $ijklmnopq'$ and WW_i and BW at the end of the nursery period i as predictors in the model for the analysis of slaughter BW $ijklmnopq''$, unless otherwise stated. Weight data were predicted by incorporating the inherent systematic effects associated with each individual pig.

The statistical importance of the prediction factors was assessed by quantifying the improvement in the performance measure associated with each attribute split point, weighted by the number of observations assigned to the respective node. The Gini index was used as a performance measure.

6.2.4 Weighting function

The main target of this research was the classification of light piglets at different growing stages. Given this objective, data from lighter animals is likely more informative than weights from heavier littermates, although there is not a standardized approach to appropriately weigh these records. To avoid bias, the following weighting function was applied,

$$\Psi^{-\delta/100}$$

where $\Psi = \{\text{WW, BW at the end of the nursery period, slaughter BW}\}$, and δ started from $\delta = 0$ and increased by one until the relative weight of average Ψ minus two SDs was 10 times larger than the relative weight of average Ψ (see Fig. 6.2 as an example plot of the weighting function $\Psi^{-\delta/100}$). Average Ψ referred to the average of the individual WW of the data set (BW at the end of the nursery period, slaughter BW in subsequent analyses). Within this context, analyses were repeated 144 times (WW data), 703 times (BW at the end of the nursery period data), and 801 times (slaughter BW data) to create each ROC curve.

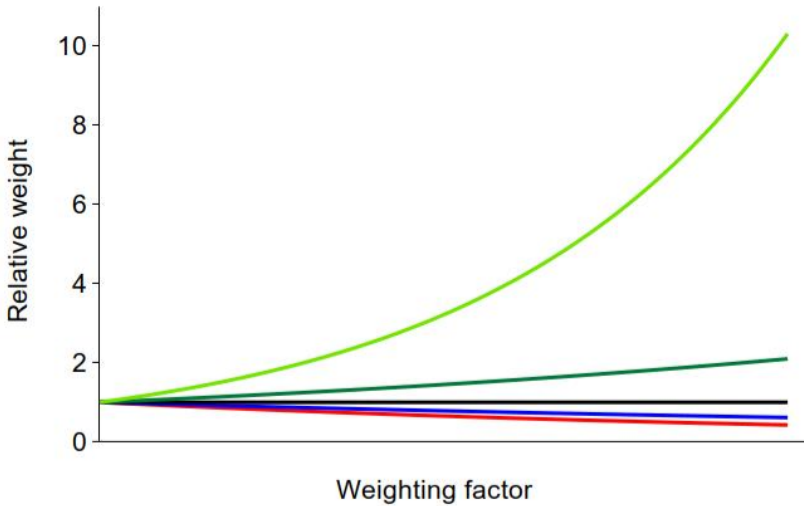


Fig. 6.2 Plot of the weighting function $\Psi^{-\delta/100}$ applied to classification models for Yorkshire pigs. Note that black line was taken as reference ($\Psi = \psi$) whereas red ($\Psi = \psi + 2k$), blue ($\Psi = \psi + k$), dark green ($\Psi = \psi - k$) and fair green ($\Psi = \psi - 2k$) lines were obtained by adding or subtracting a constant amount (k).

6.2.5 Analytical approaches

All analyses were performed with R v.4.1.2 (R Core Team, 2020). Within a parametric space, a weighted linear model was fitted by ordinary least squares (*lm* function, stats package; R Core Team, 2020), and all factors were assumed continuous except for Stillbirths_m, Parity number_n, Litter size_o, Farm_p and Season_q. This last one was categorized by each $\pi/4$ radians.

Four machine learning approaches with varying levels of complexity were also implemented. From lower to higher complexity, we fitted a decision tree (*rpart* package, *anova* method; Quinlan, 1987), random forest with 1,000 trees (*ranger* package; Wright and Ziegler, 2017) and two boosting approaches, the Generalized Boosted Regression model (*gbm* package; Friedman, 2001) and the Extreme Gradient Boosting (*xgboost* package; Chen and Guestrin, 2016). Both boosting approaches were set with identical parameters for number of trees (1,000), maximum interaction depth (5) and shrinkage (0.01), following Elith et al. (2008). These two boosting methods were employed because assuming identical analytical performance was not feasible and determining the superior one required their application to the data set.

The same parameters were set for all machine learning methods to establish a consistent framework for comparative purposes. Preliminary analyses were conducted on the data sets to ensure their utility and performance. Although this entailed higher computational costs, both the number of trees and interaction depth were fitted in excess to guarantee model fit in all cases. The same principle was applied to the shrinkage parameter, which was undervalued (see below). It is important to note that 1,000 trees exceeded the predicted number of trees with minimum cross-validation error (*i.e.*, which.min function) in all cases (results not shown). Using more trees resulted in a better fit, but the rate of improvement decreased as the number of trees increased, and marginal enhancements became negligible when approaching 1,000 trees. The maximum interaction depth is directly related to the number of relevant factors evaluated by the prediction rule, and typically behaves in a similar way to that of the number of trees (*i.e.*, the fit marginally increases with interaction depth). Within this context, preliminary analyses tested for interaction depths of 3, 5, 7, and 9. However, the area under the curve (AUC) matched the second decimal place from interaction depth 5 and above. Four different shrinkage parameters were preliminarily tested in all data sets and boosting approaches (0.1, 0.05, 0.01, and 0.001). The AUC did not differ beyond the fourth decimal place when comparing 0.01 and 0.001, whereas only the extreme gradient boosting revealed differences in the third decimal place for WW when comparing 0.05 and 0.1.

6.2.6 Cross-validation for classification ability

Each model was evaluated by a three-fold cross-validation approach. Each data set was randomly split into three subsets of equal size (33.3%). Two of them merged as training data set to fit the model, and its classification ability was evaluated against the remaining subset (*i.e.*, testing data set). Once the upper threshold for light pigs (Ψ_l) was defined, and the analysis was conducted for each value resulting from this threshold, classification ability was evaluated as the AUC when plotting sensitivity against 1 – specificity, *i.e.*, a receiver operating characteristic curve (Woodward, 1953; Peterson et al., 1954). Note that sensitivity referred to the proportion of light pigs (*i.e.*, $\Psi_i \leq \Psi_l$) classified as such by the classification rule, whereas specificity was the proportion of non-light pigs (*i.e.*, $\Psi_i > \Psi_l$) correctly classified as non-light pigs. Both sensitivity and specificity are standard parameters. The AUC characterizes the performance of the discrimination rule and fluctuates between 0.5 (*i.e.*, successful classifications are occurred by chance) and 1 (*i.e.*, perfect sensitivity and specificity). In general, the classification performance of any rule measured by the AUC can be categorized as worthless (<0.7), acceptable (0.7–0.8), excellent (0.8–0.9) and outstanding (>0.9) (Hosmer and Lemeshow, 2000).

6.3 Results

6.3.1 Classification of light BW pigs at weaning

The parametric linear model reached an intermediate classification ability when compared with machine learning methodologies, regardless of the cut-point assumed for WW. The single decision tree provided remarkably lower AUC estimates, whereas both boosting and random forest approaches increased AUC at the second decimal place (Table 6.2).

Classifications from random forest reached the highest AUC in all scenarios and increased AUC between 1.08% (cut-point, 4.7 kg) and 2.53% (cut-point, 3.7 kg) when compared with the second highest AUC (*i.e.*, extreme gradient boosting; Table 6.2). It is important to note that the advantage of random forest extended to all specificity values, and ROC curves only converged under complete or null specificity (Fig. 6.3). Moreover, AUC increased when reducing the cut-point for WW, although changes were smaller for methods with higher AUC estimates (Table 6.2).

When examining the importance of various values, only BtW_p, DB_p, DC_p, VB_p, VC_p, and Litter size_o accounted for 5% or more as shown in Fig. 6.4. Indeed, importance changed along the specificity space, although these six factors always captured more than 80%. Five of them were birthweight-related factors that, when combined, explained more than 75% of the specificity space for high specificity values, or even more than 80% (moderate to low specificity values). Dependence plots for all these factors were provided in Fig. 6.5.

Table 6.2 Area under the curve for five classification models used as discrimination tools to identify light pigs at weaning (i.e., live weight standardized to 21 d of age) under three different weight cut-points.

	Testing data set			Mean ± SE
	1	2	3	
Cut-point < 3.7 kg (10%)				
Linear model	0.729	0.732	0.732	0.731 ± 0.001
Decision tree	0.608	0.609	0.614	0.610 ± 0.002
Random forest	0.766	0.771	0.772	0.770 ± 0.002
Generalized boosted regression	0.748	0.746	0.748	0.747 ± 0.001
Extreme gradient boosting	0.752	0.752	0.750	0.751 ± 0.001
Cut-point < 4.3 kg (20%)				
Linear model	0.725	0.721	0.717	0.721 ± 0.002
Decision tree	0.579	0.582	0.584	0.582 ± 0.002
Random forest	0.762	0.759	0.761	0.761 ± 0.001
Generalized boosted regression	0.742	0.745	0.742	0.743 ± 0.001
Extreme gradient boosting	0.749	0.745	0.744	0.746 ± 0.002
Cut-point < 4.7 kg (30%)				
Linear model	0.721	0.722	0.727	0.723 ± 0.002
Decision tree	0.530	0.535	0.535	0.533 ± 0.002
Random forest	0.748	0.745	0.747	0.747 ± 0.001
Generalized boosted regression	0.735	0.736	0.739	0.736 ± 0.001
Extreme gradient boosting	0.738	0.742	0.738	0.739 ± 0.001

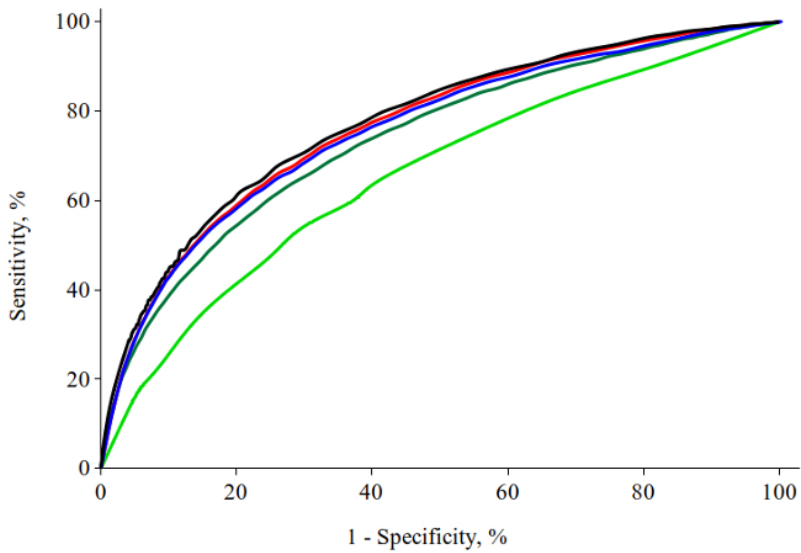


Fig. 6.3 Receiver operating characteristic curve for the classification of light pigs at weaning (< 4.3 kg) calculated by a parametric linear model (dark green) and four machine learning procedures (single decision tree, fair green line; random forest, black line; generalized boosted regression, blue line; extreme gradient boosting, red line).

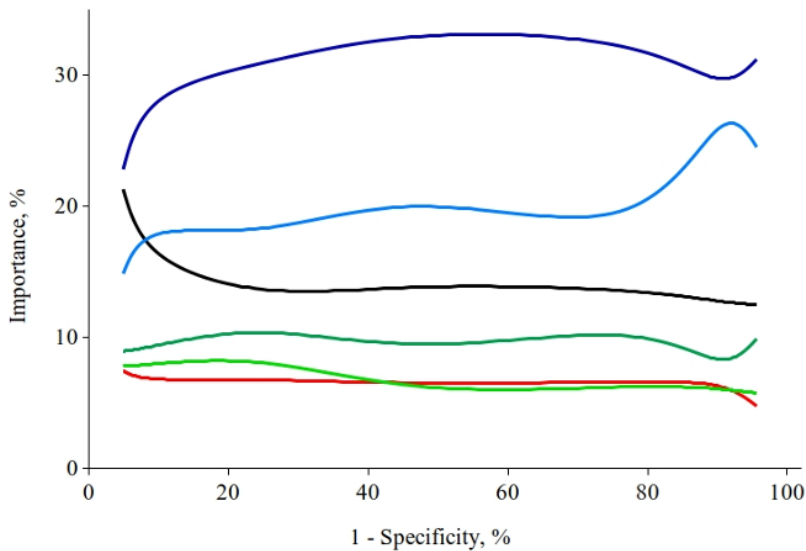


Fig. 6.4 Importance evolution for factors accounting for more than 5% when classifying light pigs at weaning (< 4.3 kg) with random forest. Green lines were for within-litter birth BW variance, and blue lines referred to the difference between birth BW and average litter weight, both at birth (fair lines) and after cross-fostering (dark lines). The black and red lines were for birth BW and litter size after cross-fostering, respectively.

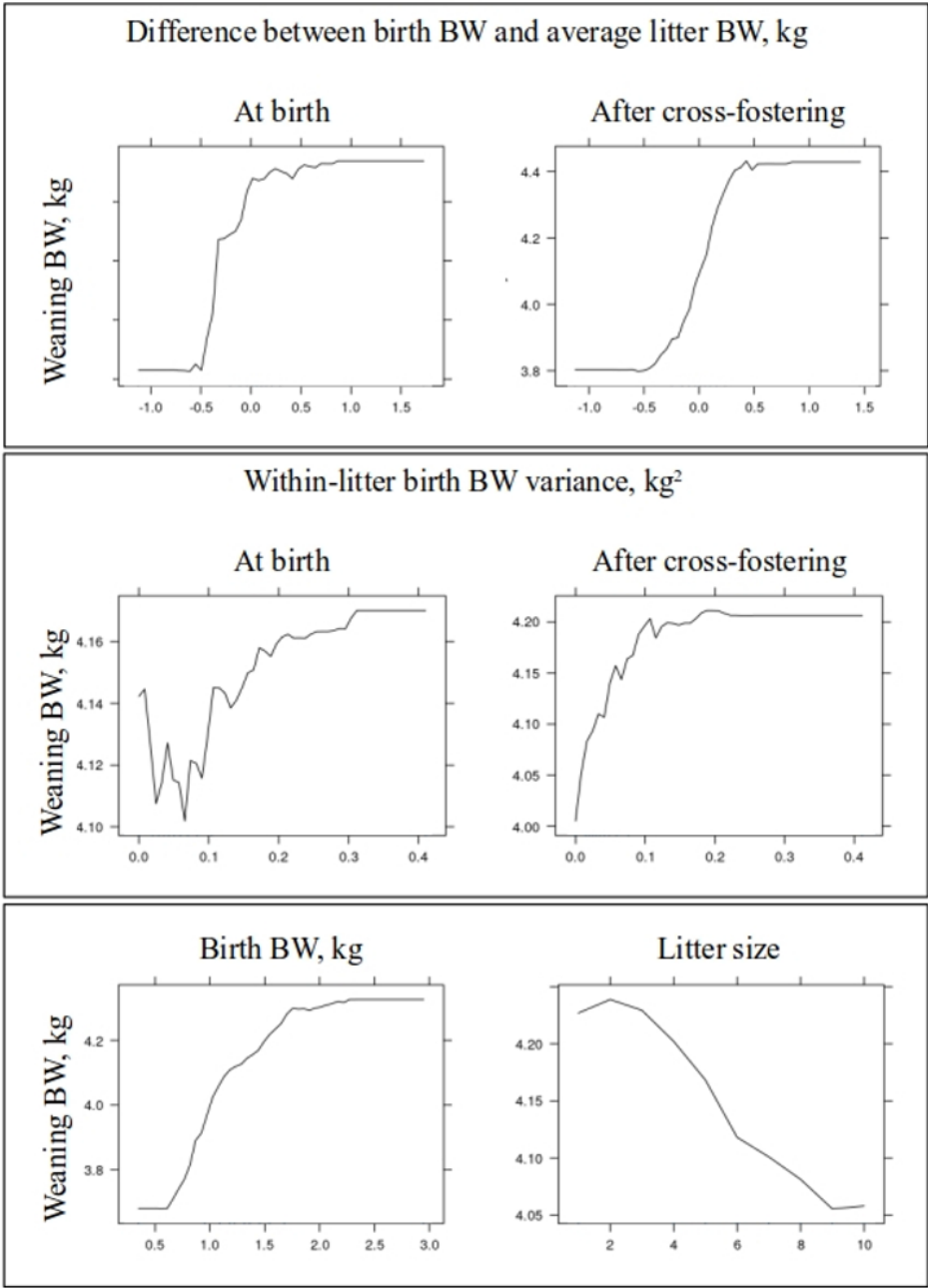


Fig. 6.5 Partial dependence plots for factors accounting for more than 5% importance when classifying light pigs at weaning (< 4.3 kg) with random forest (sensitivity, 82%; specificity, 60%). Abbreviation: Nursery BW = BW at the end of the nursery period.

6.3.2 Classification of light BW pigs at the end of the nursery period and slaughter

The random forest technique maintained its superiority when classifying light pigs at older stages, with an advantage between 1 and 3% of AUC when compared with the next highest methodology based on the AUC (*i.e.*, extreme gradient boosting; Tables 6.3 and 6.4). Higher AUC was observed for smaller cut-points for BW at the end of the nursery period and slaughter BW, and older production stages (*i.e.*, slaughter BW vs. BW at the end of the nursery period).

The inclusion of WW as a prediction factor for the analysis of BW at the end of the nursery period had a substantial impact on the final performance of the discrimination rule. This is demonstrated by the importance plot shown in Fig. 6.6. When excluded, the AUC reduced between 0.05 (cut-point, 24.0 kg) and 0.07 (cut-point, 22.0 kg), and the importance of birthweight-related factors substantially increased (results not shown). A similar pattern was observed for the analysis of slaughter BW with regard to WW and BW at the end of the nursery period as prediction factors. Given the highest contribution of BW at the end of the nursery period (Fig. 6.7), its arbitrary exclusion from the model generated a remarkable reduction of the AUC, between 0.11 (cut-point, 91.5 kg) and 0.17 (cut-point, 82.5 kg). Dependence plots for factors accounting for more than 5% importance when classifying light pigs at the end of the nursery period and slaughter were provided in Figs. 6.8 and 6.9. When BW at the end of the nursery period and WW were excluded together, these reductions increased up to 0.18 and 0.24, respectively (results not shown).

Thus, the impact on the ROC curves when BtW is only considered as main factor on the prediction for the slaughter BW is reported in Fig. 6.10, showing a reduction of the AUC when the BWs for the intermediate phases are not considered (WW and BW at the end of the nursery period).

Table 6.3 Area under the curve for five classification models used as discrimination tools to identify light pigs at the end of the nursery period (i.e., live weight standardized to 75 d of age) under three different weight cut-points.

	Testing data set			Mean $\pm$ SE
	1	2	3	
Cut-point < 20.0 kg (10%)				
Linear model	0.771	0.767	0.767	0.768 $\pm$ 0.001
Decision tree	0.672	0.675	0.675	0.674 $\pm$ 0.001
Random forest	0.823	0.822	0.817	0.821 $\pm$ 0.002
Generalized boosted regression	0.794	0.792	0.795	0.794 $\pm$ 0.001
Extreme gradient boosting	0.803	0.805	0.806	0.805 $\pm$ 0.001
Cut-point < 22.3 kg (20%)				
Linear model	0.759	0.760	0.762	0.760 $\pm$ 0.001
Decision tree	0.639	0.644	0.643	0.642 $\pm$ 0.002
Random forest	0.812	0.814	0.816	0.814 $\pm$ 0.001
Generalized boosted regression	0.781	0.776	0.777	0.778 $\pm$ 0.001
Extreme gradient boosting	0.796	0.796	0.791	0.794 $\pm$ 0.002
Cut-point < 24.0 kg (30%)				
Linear model	0.751	0.753	0.749	0.751 $\pm$ 0.001
Decision tree	0.600	0.601	0.596	0.599 $\pm$ 0.001
Random forest	0.781	0.780	0.776	0.779 $\pm$ 0.001
Generalized boosted regression	0.766	0.768	0.766	0.767 $\pm$ 0.001
Extreme gradient boosting	0.769	0.773	0.774	0.772 $\pm$ 0.002

Table 6.4 Area under the curve for five classification models used as discrimination tools to identify light pigs at slaughter (i.e., live weight standardized to 160 d of age) under three different weight cut-points.

	Testing data set			
	1	2	3	Mean ± SE
Cut-point < 82.5 kg (10%)				
Linear model	0.871	0.874	0.877	0.874 ± 0.002
Decision tree	0.781	0.782	0.780	0.781 ± 0.001
Random forest	0.898	0.897	0.902	0.899 ± 0.001
Generalized boosted regression	0.870	0.873	0.878	0.874 ± 0.002
Extreme gradient boosting	0.875	0.873	0.869	0.872 ± 0.002
Cut-point < 87.8 kg (20%)				
Linear model	0.851	0.849	0.847	0.849 ± 0.001
Decision tree	0.723	0.720	0.717	0.720 ± 0.002
Random forest	0.874	0.876	0.873	0.874 ± 0.001
Generalized boosted regression	0.859	0.855	0.858	0.858 ± 0.001
Extreme gradient boosting	0.860	0.863	0.866	0.863 ± 0.002
Cut-point < 91.5 kg (30%)				
Linear model	0.839	0.835	0.838	0.837 ± 0.001
Decision tree	0.661	0.659	0.661	0.660 ± 0.001
Random forest	0.861	0.860	0.860	0.860 ± 0.001
Generalized boosted regression	0.848	0.844	0.845	0.846 ± 0.001
Extreme gradient boosting	0.852	0.848	0.852	0.851 ± 0.001

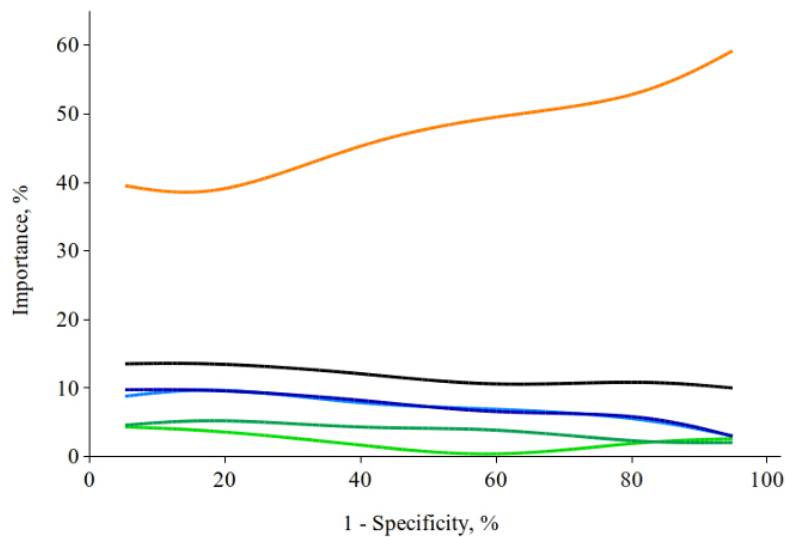


Fig. 6.6 Importance evolution for factors accounting for more than 5% when classifying light pigs at 75 d old (< 22.3 kg) with random forest. Green lines were for within-litter birth BW variance, and blue lines referred to the difference between birth BW and average litter weight, both at birth (fair lines) and after cross-fostering (dark lines). Remaining lines referred to birth (black) and weaning BW (orange).

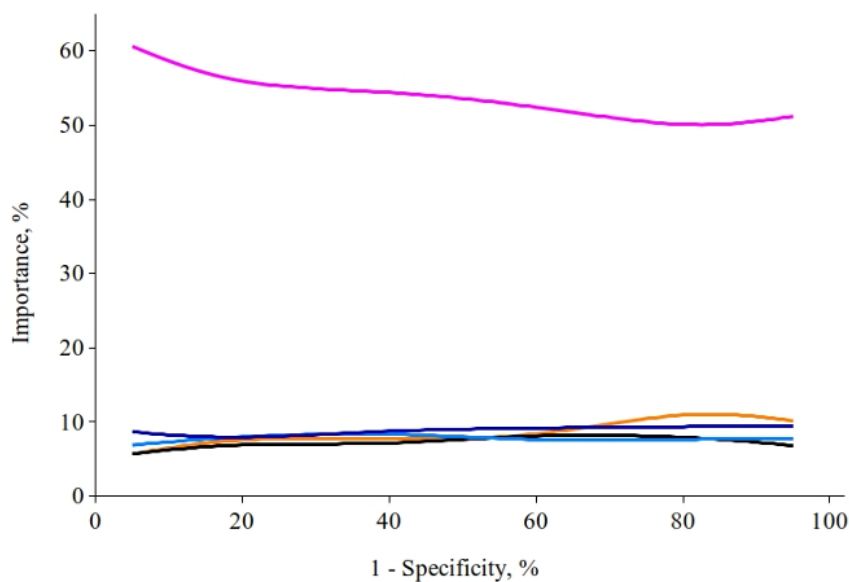


Fig. 6.7 Importance evolution for factors accounting for more than 5% when classifying light pigs at 160 d old (< 87.8 kg) with random forest. Blue lines referred to the difference between birth BW and average litter weight, both at birth (fair line) and after cross-fostering (dark line). Remaining lines referred to birth (black), weaning (orange) and end of the nursery period BWs (pink).

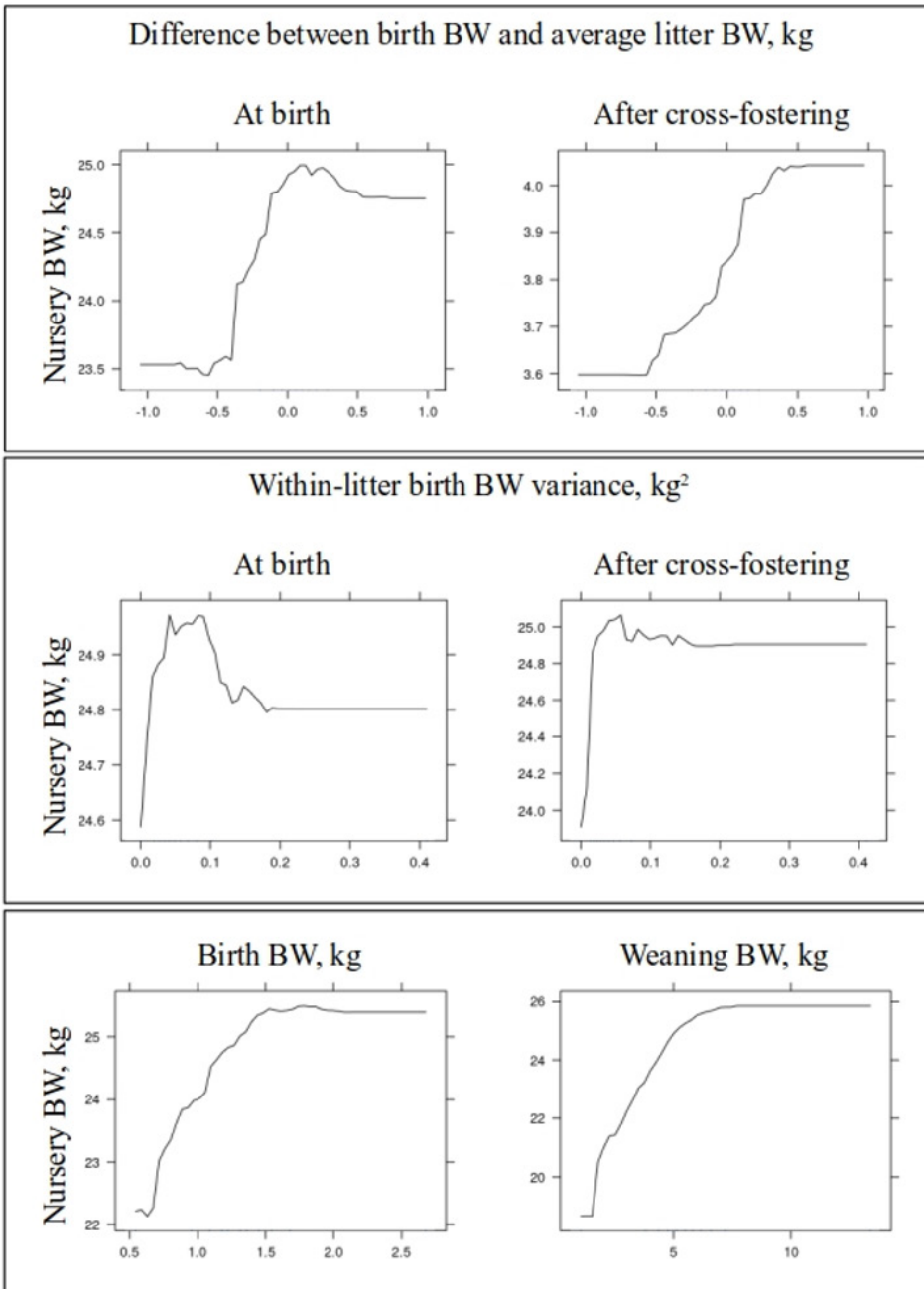


Fig. 6.8 Partial dependence plots for factors accounting for more than 5% importance when classifying light pigs at 75 d old (< 22.3 kg) with random forest (sensitivity, 84%; specificity, 60%). Abbreviation: Nursery BW = BW at the end of the nursery period.

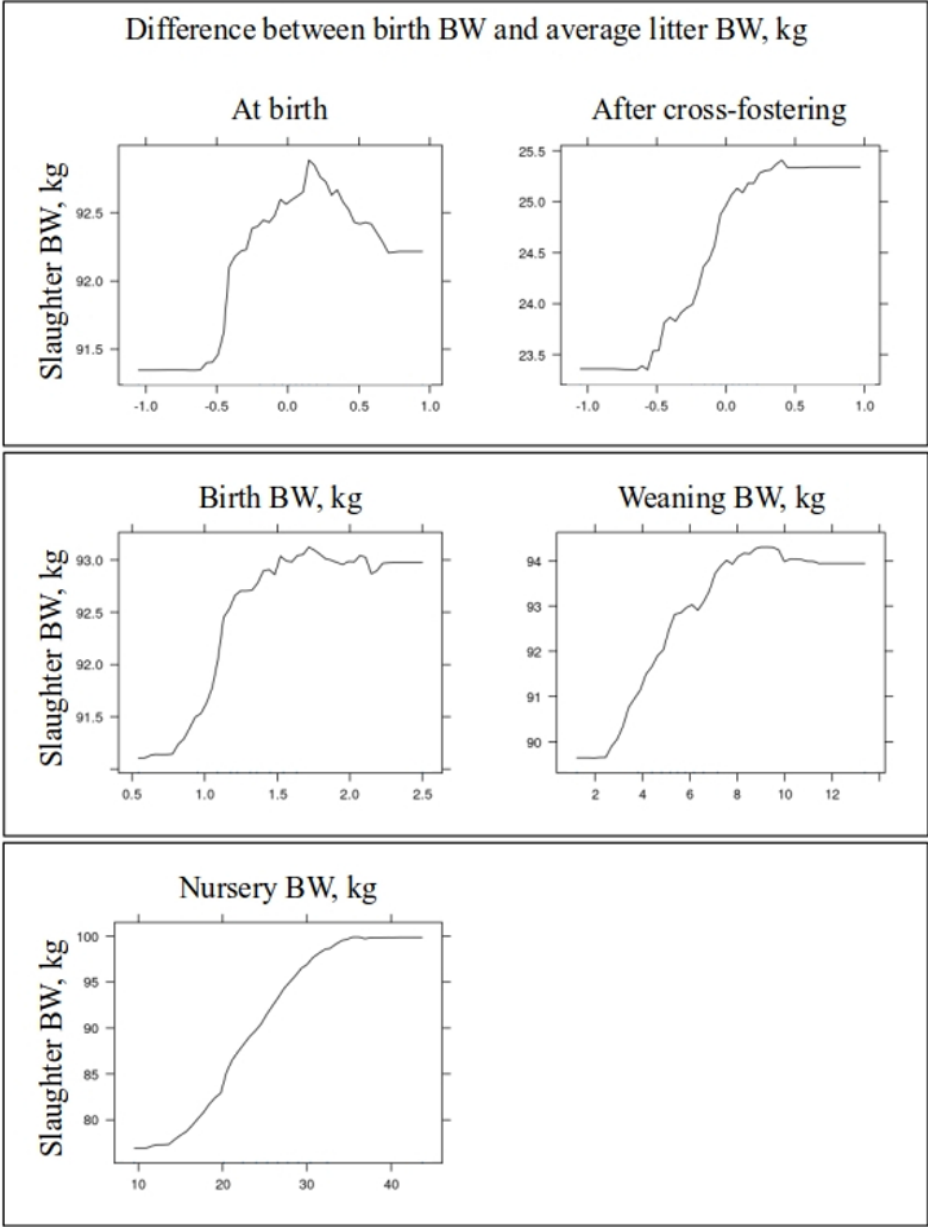


Fig. 6.9 Partial dependence plots for factors accounting for more than 5% importance when classifying light pigs at 160 d old (< 87.8 kg) with random forest (sensitivity, 87%; specificity, 60%). Abbreviation: Nursery BW = BW at the end of the nursery period.

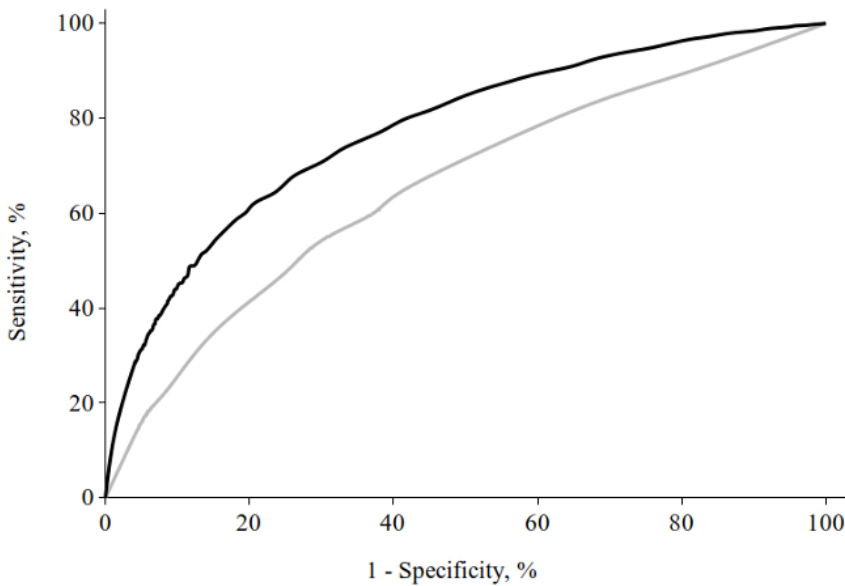


Fig. 6.10 Receiver operating characteristic curve for predicting the marketing BW of Yorkshire pigs based on BW at birth, weaning BW, and BW at the end of the nursery period (black line), compared to considering only the BW at birth (gray line).

6.4 Discussion

6.4.1 Classification ability trade-off for pig weight models

The ROC curve was initially developed for operators of military radar receivers during the decade of the 1940s (Woodward, 1953). This curve illustrates the relationship between sensitivity (Y-axis) and 1 – specificity (X-axis) of a binary classifier system as its discrimination threshold varies (*i.e.*, light vs. non-light pig). The overall performance of the classification rule is typically evaluated by the AUC, thus summarizing all possible scenarios combining sensitivity and specificity. Nevertheless, the performance of AUC as an evaluation criterion for classification ability would suffer from statistical inconsistency if two or more ROC curves intersect at a given point. The ROC curve with higher sensitivity at a given interval of 1 – specificity values becomes preferable in that region, even if its overall AUC is smaller than those for competing ROC curves (Fawcett, 2006). It is important to highlight that this behavior has not been observed in our analyses and all ROC curves from different analytical methodologies did not intersect when calculated on the same data set. The classification

advantage (or disadvantage) regarding each analytical methodology persisted along the curve and could be effectively captured by the AUC in our data sets.

Maximum AUC for all analyses showed acceptable discrimination performance (Hosmer and Lemeshow, 2000) with values ranging between 0.7 and 0.8, and even excellent (0.8–0.9) in some specific cases, although the trade-off between sensitivity and specificity was remarkable. Far from being a penalty for this research, this must be viewed as a flexible framework where the optimum combination of sensitivity and specificity can be defined according to management practices for light pigs during different production stages. A higher rate of false positives (*i.e.*, lower specificity) could be assumed for cheap management practices such as cross-fostering (Calderón-Díaz et al., 2018), where (almost) all potentially light animals would be managed according to appropriate management practices. On the other hand, time-consuming individual treatments, or expensive supplements (Casellas et al., 2005; Threadgold et al., 2021) must focus on those pigs who were truly light, avoiding false positives (*i.e.*, high specificity) and accepting a higher rate of false negatives (*i.e.*, low sensitivity), even if they suffered a commercial penalty.

6.4.2 Area under the curve across cut-points and production stages

The AUC increased when reducing the weight cut-point for light pigs and indicated a superior classification ability when focusing on more extreme individuals. This could be anticipated because of the increase in the average difference between both groups of animals, as previously reported by Steyerberg et al. (2010). Nevertheless, differences were remarkably small for classification methods with higher AUC, which suggested negligible benefit for more restrictive weight cut-off points. This stability of the AUC for methods with higher estimates is of special interest for the implementation of these methodologies in the swine industry, providing a wide range of cut-point values without relevant departures from the expected power of discrimination.

The increase of AUC along production stages is directly related to the inclusion of additional sources of information in the analytical model. It must be noted that WW contributed strongly to the prediction of BW at the end of the nursery period and slaughter BW, and BW at the end of the nursery period was a strongly determinant factor for the prediction of slaughter BW. Indeed, the AUC fell below values calculated at weaning for any classification model and weight cut-point used if WW and BW at the end of the nursery period were arbitrarily removed

from the model. This is directly linked to the time elapsed between birth and BW at the end of the nursery period and slaughter BW recording, where birth-related factors must be less informative than weight records collected closer in time to the event being predicted. Thus, the influence of a prediction factor increases the closer it is to the weight record. Although weighing animals at later phases of production could be a time-consuming practice, our results suggest that this source of information is the most useful for optimizing a classification tool for lightweight animals.

6.4.3 Pig weight classification techniques

The random forest methodology was the approach that obtained the best performance among the five models evaluated in this research. This technique systematically outperformed all other methodologies across all testing data sets, production stages and cut-points for light pigs. This demonstrated the stability of random forest for light pig classification at different production stages and revealed a useful tool for the swine industry. The superior statistical performance of random forest was previously reported in pigs, although with other data sources (Bakoev et al., 2020), and has also been seen in other livestock species such as sheep (Sant'Ana et al., 2021). This indicates the existence of methods, specifically those based on machine learning, which can out-perform traditional ordinary least squares regression as predictive tools for weight traits in pigs.

One must be cautious with the extrapolation of these results to other pig populations or breeds because of the slight advantage reported for random forest in relation with other machine learning algorithms such as boosting. Indeed, the objective of this research did not focus on the identification of a specific analytical method or any "golden rule" based on the optimum combination of factors, sensitivity, and specificity, but the evaluation of several approaches under different levels of stringency (*i.e.*, weight cut-points), characterizing the behavior of each classification method along the analytical space.

6.4.4 Factors influencing light pig classification

Under commercial conditions, the results obtained from the random forest procedure agree with those reported by López-Vergé et al. (2018) based on an epidemiological approach. López-Vergé et al. (2018) indicated that the probability for a light piglet to be sent to the slaughterhouse late increases with age, and increases closer to the end of the cycle, probably

due to the short time available to implement preventive measures. The relative importance of factors that impact the classification of low BW pigs at weaning (difference between BtW and average litter weight, both at birth and after cross-fostering, accounting for >20%), decreased at the entrance of the growing-finishing barn only six weeks later. The contribution of BtW also decreases from weaning to 160 days old pigs and most of the evaluated factors (sex, parity, farm, or season) become residual as the marketing weight approaches. By contrast, the importance of the pig BW at each previous step remains the most important factor and increases with age, accounting for 30, 40, and 50% of relative importance for weaning, end of the nursery (72 d) or slaughterhouse (160 d), respectively. However, a significant reduction of the AUC in the ROC curve is observed when only BtW is considered to predict the final marketing weight. In that sense, lower sensitivity and specificity are obtained independently of the classification model used.

This indicates that the main effect on nursery and grow-finish is accumulated and best described by BW at the beginning of each period (weaning and end of the nursery period, respectively) and it follows that the possibility of low BW pigs to recover BW is reduced with age or approaching the end of the cycle. Factors not considered, for example, sex (Douglas et al., 2013; Paredes et al., 2012), genetic line (Damgaard et al., 2003), birth season (Douglas et al., 2013; Paredes et al., 2012) or sanitary status of the farm (van der Meer et al., 2016; 2020) may influence the risk of being a slow-growing pig. Nevertheless, the influence of these factors in the analysis becomes marginal, as the inclusion of BW in the model reduces the significance of the other factors, given that it already incorporates a portion of their impact. As in the present study, WW has been shown to have a high impact on postweaning growth and the time to reach the desirable slaughter BW (Collins et al., 2017; Wolter and Ellis, 2001). Larriestra et al. (2006), by fitting a logistic mixed model, reported a threshold of 3.6 kg of BW at weaning (17 ± 2 d), which maximizes sensitivity and specificity to correctly predict the likelihood of dying or of being lightweight when exiting the nursery stage. Moreover, He et al. (2016) stated that 80% of pigs weaned at 28 days of age at <6.4 kg of BW became slow-growing pigs at slaughter age. Similarly, López-Vergé et al. (2019) reported that 6.9 kg of BW at a minimum of 26 days of age at weaning was a threshold that predicted better growth performance in the grow-finish period. With lower lactation length (ranging between 21 and 28 d), the cut-point of 5.0 kg at weaning may account for >25% of a weaning batch, showing that piglet BW at weaning is essential. Based on our observed response, and extrapolating to the weaning BWs previously reported by He et al. (2016) and López-Vergé et al. (2019), it may be assumed that these pigs will differ by >10–15 kg of BW at marketing as compared to the pigs with the WW < 3.6 kg reported by Larriestra et al. (2006).

In contrast with the end of the nursery or grow-finisher periods, the probability of being small at weaning is less related to the BW at the beginning of the period (birth or after cross-fostering BW), indicating that other factors are involved, and that action may be taken at those early stages on these factors. This study shows the relative importance of cross-fostering for the classification of the low BW piglets at weaning, ranging from 40 to 30% with specificities of 40 and 80%. One of the main predictive factor is the within-litter weight variance after cross-fostering, showing the importance of performing a proper adoption management in order to reduce WW variability.

6.5 Conclusions

Classification of light pigs at different production stages can be effectively carried out by both ordinary least squares and machine learning algorithms, although with a balance between realized sensitivity and specificity. The random forest machine learning algorithm reached the highest statistical performance at weaning, end of the nursery period, and slaughter, with weight-related traits at previous ages playing the key role in classifying light animals. In terms of farm decision making, the machine learning models could become a key tool for improving efficiency. We have demonstrated that the probability to stop being a low BW pig decreases with age and becomes progressively worse as the pig approaches the final BW. The BW and variation of the newborn and weaned piglets, as well as on-farm handling techniques (*i.e.*, cross-fostering), are key factors to reduce weight gain variability and to achieve maximum return.

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Chapter 7

Applicability of machine learning
methods for classifying lightweight pigs
in commercial conditions

Applicability of machine learning methods for classifying lightweight pigs in commercial conditions

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Abstract

The varying growth rates within a group of pigs present a significant challenge for the current all-in-all-out systems in the pig industry. This study evaluated the applicability of statistical methods for classifying pigs at risk of growth retardation at different production stages using a robust dataset collected under commercial conditions. Data from 26,749 crossbred pigs (Yorkshire × Landrace) with Duroc at weaning (17 to 27 d), 15,409 pigs at the end of the nursery period (60 to 78 d), and 4,996 pigs at slaughter (151 to 161 d) were analyzed under three different cut points (lowest 10%, 20%, and 30% weights) to characterize light animals. Records were randomly split into training and testing sets in a 2:1 ratio, and each training dataset was analyzed using an ordinary least squares approach and three machine learning algorithms (decision tree, random forest, and generalized boosted regression). The classification performance of each analytical approach was evaluated by the area under the curve (AUC). In all production stages and cut points, the random forest and generalized boosted regression models demonstrated superior classification performance, with AUC estimates ranging from 0.772 to 0.861. The parametric linear model also showed acceptable classification performance, with slightly lower AUC estimates ranging from 0.752 to 0.818. In contrast, the single decision tree was categorized as worthless, with AUC estimates between 0.608 and 0.726. Key prediction factors varied across production stages, with birthweight-related factors being most significant at weaning, and weight at previous stages becoming more crucial later in the production cycle. These findings suggest the potential of machine learning algorithms to improve decision-making and efficiency in pig production systems by accurately identifying pigs at risk of growth retardation.

Lay Summary

Body weight (BW) variability at slaughter is mainly due to the presence of slow-growing pigs in the herd, which reach market weight later than their faster-growing counterparts. Implementing machine learning algorithms to identify pigs at risk of growth retardation offers significant potential for improving decision-making, production efficiency, and profitability in the swine industry. This research evaluated four different classification algorithms (ordinary least squares regression; decision tree; random forest; and generalized boosted regression) to evaluate their ability to classify commercial lightweight pigs at various production stages. Among these, generalized boosted regression and random forest exhibited the best

performance when classifying lightweight pigs at any stage. Thus, the robust performance of these models highlights their practical utility under commercial conditions. These methods could facilitate the identification of lightweight pigs, enabling targeted interventions to optimize growth and reduce variability. As a result, adopting these tools could improve herd management, optimize the use of farm facilities, and ultimately increase overall productivity while reducing shadow production costs in pig farming operations.

Keywords: area under the curve, classification algorithms, efficiency, growth retardation, live weight, swine.

7.1 Introduction

Body weight (BW) variability is a primary factor affecting production efficiency and profitability, presenting a costly problem for the pig industry (Patience et al., 2004). Though it has been studied that slow-growing pigs play a relevant role in this issue, the early and reliable identification of this subset of pigs is often inconsistent. Such pigs are expected to reach target slaughter weights later than their faster-growing counterparts (López-Vergé et al., 2018), which poses a challenge in swine production systems that aim to maintain contemporary pigs in the same batch to ensure optimal animal health and management efficiency (Maes et al., 2004). Calderón Díaz et al. (2017) reported that delaying pigs from the normal production flow in current all-in-all-out systems is negatively associated with pig health and performance. Moreover, significant variability in market weight lowers carcass value and reduces the operational efficiency of slaughterhouse equipment (López-Vergé et al., 2018).

The incidence of pigs at risk of growth retardation has increased over the past decade, primarily due to ongoing genetic advancements that have increased litter sizes at birth. Consequently, a higher percentage of piglets are born with low birth weights (Beaulieu et al., 2010), contributing to increases of up to 25% in BW variability at birth, as measured by the coefficient of variation (López-Vergé et al., 2018). Although pigs' BW categories during the initial growth phases can change (Blavi et al., 2021), and the implementation of different management and nutritional practices (Patience et al., 2004; Solà-Oriol and Gasa, 2017) tends to reduce variability with age, it is estimated that 10% to 15% of pigs in any given batch remain classified as slow-growing (Calderón Díaz et al., 2017). Identifying these pigs is crucial for optimizing efficiency and profitability in the swine industry.

Artificial intelligence is a field that integrates computer science and large datasets to develop intelligent systems capable of performing tasks typically requiring human intelligence (Sarker, 2022). Machine learning, a branch of artificial intelligence, utilizes subsets of data to generate algorithms that use different combinations of features, enabling the prediction of outputs based on what the algorithm has learned from the data (Choi et al., 2020). Many machine learning approaches have been developed since the early 1960s, with significant impact on various types of problems, such as classification (Nayeri et al., 2019). Therefore, the application of artificial intelligence in the animal production field is not new (Firk et al., 2002; Rorie et al., 2002). The advancements in computer performance in recent decades have accelerated the pace of development of several methodologies (Curti et al., 2023) with potential contributions to the swine industry. The development of robust tools to identify slow-growing pigs, along with identifying potential risk factors associated with their occurrence, will help develop effective strategies to ensure homogeneity and optimal growth among pigs. Casellas et al. (2024) stated that machine learning algorithms applied to a large dataset from a pure-bred nucleus provide reliable alternatives to parametric linear models for analyzing continuous traits. However, the ability of these algorithms to identify pigs at risk of growth retardation under commercial conditions has not been tested.

Therefore, the objective of this research was to evaluate the applicability of machine learning algorithms for classifying light pigs at each phase within the pig production cycle, using a powerful and robust dataset collected from a single commercial breeding herd. Specifically, we aimed to 1) classify pigs that would be the main contributors to variation within a population and 2) identify the main production factors that explain low pig BW at each stage of production.

7.2 Materials and methods

Approval from the Animal Care and Use Committee was not required for this study, as the analyses were conducted on existing field data collected under standard farm management practices from a commercial farm operated by Andrimner Genética Aplicada (Barcelona, Spain) and DNA Genetics (Columbus, NE, USA).

7.2.1 Commercial Pig Farm Data

All data were collected from a single farm in the United States between March 2019 and May 2023, focusing on Line 246 (Yorkshire × Landrace) × Duroc (DNA Genetics). The animals were housed under standard intensive farming conditions and were individually weighed at the following stages: birth (BtW), weaning (WW, 17 to 27 d), the end of the nursery period (60 to 78 d), and slaughter (151 to 161 d). Three different cut points were established at each production stage, corresponding to the lowest 10%, 20%, and 30% of weights. These thresholds were selected because they effectively represent light pigs, as supported by studies (Douglas et al., 2014; He et al., 2016; Montoro et al., 2020), which indicate that pigs in the lower quartile of the BW population distribution typically require additional time to reach target slaughter weights and are often classified as slow-growing pigs. Moreover, although identifying a smaller percentage of very light pigs can be a useful statistical approach, it may have a limited impact on improving the overall homogenization of the batch. Therefore, the cut points at weaning were 4.31 kg, 4.90 kg, and 5.33 kg; at the end of the nursery period, they were 16.00 kg, 18.20 kg, and 19.80 kg; and at slaughter, they were 92.80 kg, 100.00 kg, and 105.00 kg. These cut points can be adjusted according to the specific needs of each user. Age-related differences at each weigh point were corrected for WW, BW at the end of the nursery period, and slaughter BW using a standard linear adjustment based on total data at 21 d, 65 d, and 155 d, respectively (Table 7.1). Trained farm staff systematically collected additional data for each piglet (including sex, cause and date of death, cross-fostering date, and adoption litter after cross-fostering, if any), for each sow (parity number), and for each litter (birth date, litter size at birth and after cross-fostering, if any).

Table 7.1 Summary of weaning BW, BW at the end of the nursery period, and slaughter BW in the (Yorkshire x Landrace) x Duroc pig population.

	Weaning BW, kg		BW at the end of the nursery period, kg		Slaughter BW, kg	
	n	Mean ± SE	n	Mean ± SE	n	Mean ± SE
Overall	26,749	6.01 ± 0.008	15,409	22.18 ± 0.037	4,996	110.82 ± 0.196
Sex						
Male	13,539	6.07 ± 0.011	7,668	22.13 ± 0.053	2,447	112.83 ± 0.279
Female	13,210	5.96 ± 0.011	7,741	22.23 ± 0.052	2,549	108.89 ± 0.270

Cross-fostered						
No	25,871	6.01 ± 0.008	14,619	22.17 ± 0.038	4,748	110.78 ± 0.201
Yes	878	6.04 ± 0.043	790	22.49 ± 0.158	248	111.49 ± 0.864
Sow parity						
1	9,042	5.68 ± 0.012	6,306	22.11 ± 0.057	3,234	111.94 ± 0.225
2	7,134	6.27 ± 0.016	4,376	22.21 ± 0.070	1,459	111.15 ± 0.386
3	4,865	6.11 ± 0.020	2,341	21.97 ± 0.103	297	97.32 ± 0.777
4	3,433	6.19 ± 0.024	1,220	22.23 ± 0.133	6	96.77 ± 4.051
>4	2,275	6.12 ± 0.028	1,166	22.87 ± 0.130		

Abbreviation: BW, body weight.

7.2.2 Operational models

The prediction of WW data was based on the following model,

$$WW_{ijklmnopq} = \text{BtW}_i + \text{Sex}_j + \text{Cross-fostered}_k + \text{DB}_i + \text{DC}_i + \text{VB}_i + \text{VC}_i + \text{Stillbirths}_m \\ + \text{Parity number}_n + \text{Litter size}_o + \text{Season}_q$$

where BtW_i represented the birth BW of the i th piglet, Sex_j denoted the sex of the j th piglet (male or female), and Cross-fostered_k indicated whether the piglet was cross-fostered or not. DB_i and DC_i were the differences between the piglet's BtW and the average litter weight at birth and after cross-fostering, respectively. VB_i and VC_i were the within-litter variances of BW at birth and after cross-fostering, respectively. Stillbirths_m referred to the number of stillbirths in the litter (0, 1, 2, 3 or >3), Parity number_n represented the sow's parity number (1, 2, 3, 4 or >4), Litter size_o indicated the litter size after cross-fostering (<10, 10, 11, 12, 13, 14, 15, 16, 17 or >17), and Season_p specified the season of birth (winter, spring, summer, autumn). In addition to the described variables, the model for analyzing BW at the end of the nursery period $ijklmnop$ also included WW_i as a predictor, while the model for analyzing slaughter BW $ijklmnop$ included both WW_i and BW at the end of the nursery period $ijklmnop'$ as predictors. Weight data were predicted by considering the inherent systematic effects linked to each pig individually. Thus, the prediction of WW $ijklmnop'$ BW at the end of the nursery period $ijklmnop'$, and slaughter BW $ijklmnop$ in relation to the upper threshold for light pigs served as the outcome variables in these operational models, which were designed to develop multiclass classification algorithms for identifying lightweight pigs at each stage of the pig production cycle.

The statistical importance of the prediction factors was evaluated by measuring the performance improvement associated with each attribute's split point, adjusted for the number of observations assigned to the corresponding node. The Gini index served as the performance metric for this assessment. Partial dependence plots were examined for factors accounting for more than 5% importance when classifying light pigs at weaning, the end of the nursery period, and slaughter.

7.2.3 Weighting function

The same weighting function ($\Psi^{-\delta/100}$) applied by Casellas et al. (2024) was used in this study to appropriately adjust the weighting of all recorded data and mitigate any biases. In this context, Ψ represented the variables WW, BW at the end of the nursery period, and slaughter BW. The parameter δ started from $\delta = 0$ and increased by 1 until the relative weight of the average Ψ minus two standard deviations was 10 times larger than the relative weight of the average Ψ .

The analyses were repeated 1,000 times (for WW, BW at the end of the nursery period, and slaughter BW data) to achieve the necessary number of iterations for the iterative process. While this repetition count exceeded the minimum required in some cases to assess the stability and variability of the results under different weight adjustments, it was standardized across all analyses to ensure consistent model fitting and to generate the corresponding receiver operating characteristic (ROC) curves. This approach aimed to strike a balance between computational efficiency and the need for robust, comprehensive ROC curve generation.

7.2.4 Analytical approaches and model hyperparameter optimization

All analyses were performed with open-source software R v.4.4.0 (R Core Team, 2024) following the analytical approaches established by Casellas et al. (2024), with specific adjustments for the commercial dataset. In a parametric framework, a weighted linear model was fitted by ordinary least squares (*lm* function, *stats* package), with all variables considered continuous except for Stillbirths_m, Parity number_n, Litter size_o, and Season_p. Three different machine learning approaches of varying complexity were also implemented. From lower to higher complexity, we fitted a decision tree (*rpart* package, *anova* method; Quinlan, 1987), a random forest with 1,000 trees (*ranger* package; Marvin and Ziegler, 2017), and a boosting

approach, specifically the generalized boosted regression model (*gbm* package; Friedman, 2001). The boosting approach was set with the following parameters: 1000 trees, a maximum interaction depth of 6, and shrinkage set to 0.01.

The hyperparameters for the machine learning models were tuned following the suggestions of Elith et al. (2008) and Casellas et al. (2024) and were standardized across all approaches to provide similar starting points. This methodology provided a consistent framework for comparative purposes. The random forest and generalized boosted regression models were ultimately fitted with 1,000 trees. Preliminary tests with alternative values (*i.e.*, 100, 500, 5,000, 10,000 trees) indicated that fewer than 1,000 trees did not consistently ensure an adequate model fit, while using more than 1,000 trees yielded only marginal improvements in performance. Although the 1,000-tree configuration slightly exceeded the predicted optimal number of trees based on minimum cross-validation error in all cases and entailed higher computational costs, it was necessary to guarantee a reliable model fit across all scenarios. The maximum interaction depth for each tree in the generalized boosted regression models was set to 6, enabling the capture of complex decision boundaries. The models were initially tested and compared with alternative values (*i.e.*, 3, 5, 7, 9) for interaction depth. While the differences in performance across the tested values in all datasets were almost null, the area under the curve (AUC) matched the second decimal place starting from an interaction depth of 6 and higher. A shrinkage parameter of 0.01 was selected after testing different alternatives (*i.e.*, 0.1, 0.05, 0.001, 0.005) in the generalized boosted regression models. This value ensured optimal model fit in all cases, as the AUC for WW, BW at the end of the nursery period, and slaughter BW remained consistent beyond the fourth decimal place when comparing 0.01 with smaller shrinkage parameters. The minimum number of observations per terminal node was set to the default value of 10 in the *gbm* package, as it provided a suitable balance between model complexity and generalization.

7.2.5 Cross-validation for classification ability

Each model was evaluated using a 3-fold cross-validation method. The dataset was randomly divided into three equal and balanced subsets (33.3% each). Two subsets were combined to form the training dataset for fitting the model, and its classification ability was evaluated against the remaining subset (referred to as the testing dataset). Each training dataset was analyzed using an ordinary least squares approach and three machine learning algorithms, applied under three different cut points (lowest 10%, 20%, and 30% weights)

for each phase within the pig production cycle. A total of 1,000 individual repetitions of the 3-fold cross-validation method were performed for each approach. While the training and testing datasets remained constant across iterations, different weights were applied to the models in each repetition, controlled by the weighting function. Once the upper threshold for light pigs (Ψ_u) was defined, the analysis was conducted for each value resulting from this threshold. Classification ability was evaluated using the AUC of the ROC curve, which plots sensitivity against 1 – specificity, following the methodology outlined by Casellas et al. (2024). Sensitivity, defined as the proportion of light pigs correctly classified, and specificity, defined as the proportion of nonlight pigs correctly classified, were calculated for each repetition. Both metrics are standard parameters for assessing model performance. The classification performance of a model, as measured by the AUC, can generally be categorized as follows: worthless (<0.7), acceptable (0.7 to 0.8), excellent (0.8 to 0.9), and outstanding (>0.9) (Hosmer and Lemeshow, 2000).

7.3 Results

7.3.1 Comparison of classification ability across models

The parametric linear model achieved intermediate classification performance compared to the machine learning approaches, regardless of the cut point assumed for WW (AUC estimates ranging from 0.786 to 0.818; Table 7.2) and for older stages (AUC estimates ranging from 0.752 to 0.801; Tables 7.3 and 7.4). The single decision tree provided the lowest AUC estimates for each phase within the pig production cycle, with values ranging from 0.608 to 0.652 for WW (Table 7.2) and from 0.638 to 0.726 for older stages (Tables 7.3 and 7.4). In contrast, the random forest and generalized boosted regression approaches demonstrated acceptable to excellent classification performance, achieving the highest AUC values in all scenarios (Tables 7.2, 7.3, and 7.4).

The generalized boosted regression achieved slightly higher AUC estimates than the random forest for the lowest cut points (20% and 10%). At weaning, the AUC increased by 0.25% (cut point, 4.90 kg) and 0.73% (cut point, 4.31 kg), while at older stages, the advantage ranged from 0.00% to 1.13%. The random forest exhibited the best classification performance for the highest cut point (30%), with AUC estimates increasing by 0.75% at weaning, and by 0.52% to 1.10% for older stages, compared with the second highest AUC (*i.e.*, generalized

boosted regression). The slight advantage of generalized boosted regression at low specificity values and random forest at high specificity values is shown in Figure 7.1, where the ROC curves converged only under conditions of nearly complete or null specificity. Furthermore, generalized boosted regression and random forest achieved higher AUC values for smaller cut points for WW, BW at the end of the nursery period, and slaughter BW.

Table 7.2 AUC for four classification models used as discrimination tools to identify light pigs at weaning (*i.e.*, live weight standardized to 21 d of age), evaluated using three different weight cut points.

	Testing data set			Mean ± SE
	1	2	3	
Cut point < 4.31 kg (10%)				
Linear model	0.823	0.823	0.809	0.818 ± 0.005
Decision tree	0.675	0.604	0.638	0.639 ± 0.021
Random forest	0.829	0.823	0.827	0.826 ± 0.002
Generalized boosted regression	0.837	0.833	0.827	0.832 ± 0.003
Cut point < 4.90 kg (20%)				
Linear model	0.812	0.807	0.802	0.807 ± 0.003
Decision tree	0.622	0.647	0.686	0.652 ± 0.019
Random forest	0.815	0.816	0.817	0.816 ± 0.001
Generalized boosted regression	0.819	0.818	0.816	0.818 ± 0.001
Cut point < 5.33 kg (30%)				
Linear model	0.791	0.782	0.784	0.786 ± 0.003
Decision tree	0.685	0.526	0.612	0.608 ± 0.046
Random forest	0.800	0.801	0.792	0.798 ± 0.003
Generalized boosted regression	0.801	0.796	0.792	0.796 ± 0.003

Table 7.3 AUC for four classification models used as discrimination tools to identify light pigs at the end of the nursery period (i.e., live weight standardized to 65 d of age), evaluated using three different weight cut points.

	Testing data set			Mean ± SE
	1	2	3	
Cut point < 16.00 kg (10%)				
Linear model	0.765	0.756	0.790	0.770 ± 0.010
Decision tree	0.716	0.682	0.609	0.669 ± 0.032
Random forest	0.807	0.787	0.804	0.799 ± 0.006
Generalized boosted regression	0.811	0.792	0.820	0.808 ± 0.008
Cut point < 18.20 kg (20%)				
Linear model	0.781	0.767	0.787	0.778 ± 0.006
Decision tree	0.714	0.612	0.664	0.663 ± 0.029
Random forest	0.806	0.793	0.804	0.801 ± 0.004
Generalized boosted regression	0.807	0.793	0.804	0.801 ± 0.004
Cut point < 19.80 kg (30%)				
Linear model	0.755	0.742	0.760	0.752 ± 0.005
Decision tree	0.657	0.651	0.606	0.638 ± 0.016
Random forest	0.780	0.770	0.778	0.776 ± 0.003
Generalized boosted regression	0.778	0.761	0.776	0.772 ± 0.005

Table 7.4 AUC for four classification models used as discrimination tools to identify light pigs at slaughter (i.e., live weight standardized to 155 d of age), evaluated using three different weight cut points.

	Testing data set			Mean $\pm$ SE
	1	2	3	
Cut point < 92.80 kg (10%)				
Linear model	0.839	0.746	0.745	0.777 $\pm$ 0.031
Decision tree	0.659	0.772	0.626	0.686 $\pm$ 0.044
Random forest	0.889	0.849	0.835	0.858 $\pm$ 0.018
Generalized boosted regression	0.895	0.863	0.824	0.861 $\pm$ 0.019
Cut point < 100.00 kg (20%)				
Linear model	0.806	0.779	0.817	0.801 $\pm$ 0.011
Decision tree	0.707	0.756	0.714	0.726 $\pm$ 0.015
Random forest	0.842	0.848	0.858	0.849 $\pm$ 0.005
Generalized boosted regression	0.850	0.856	0.865	0.857 $\pm$ 0.004
Cut point < 105.00 kg (30%)				
Linear model	0.782	0.760	0.799	0.780 $\pm$ 0.011
Decision tree	0.730	0.645	0.739	0.705 $\pm$ 0.030
Random forest	0.822	0.836	0.845	0.834 $\pm$ 0.007
Generalized boosted regression	0.820	0.816	0.840	0.825 $\pm$ 0.007

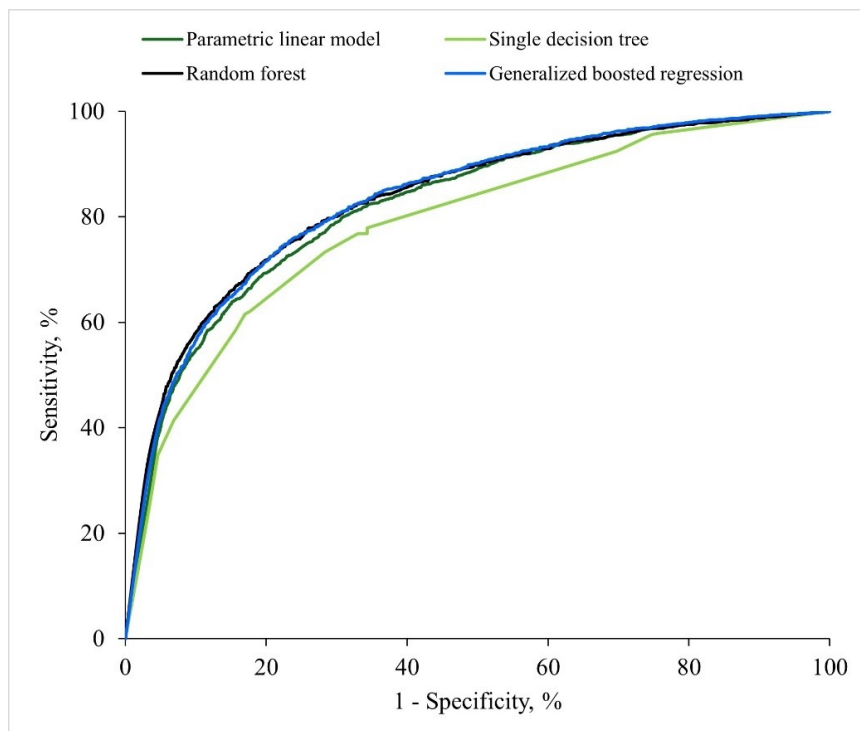


Fig. 7.1 ROC curve for the classification of light pigs at weaning (< 4.90 kg) calculated by a parametric linear model and three machine learning procedures (single decision tree, random forest, and generalized boosted regression).

7.3.2 Importance of prediction factors

When evaluating the importance of prediction factors for WW analysis, factors BtW_i , $Litter\ size_o$, DB_i , DC_i , VB_i , VC_i , and $Season_p$ individually contributed at least 5% at certain points across the specificity space (Figure 7.2). The combined importance of all these factors consistently exceeded 85%, with BtW_i standing out as the most relevant factor, particularly for high specificity values. Additionally, when birthweight-related factors were combined, they explained more than 60% of the specificity space. The predictor $Litter\ size_o$ remained the second most important factor along the specificity space. Dependence plots for all these factors were provided in Figure 7.3.

In the analysis of BW at the end of the nursery period, the prediction factor WW_i replaced birthweight-related factors as the most relevant, accounting for more than 50% of the importance for high specificity values (Figure 7.4). When excluded, the AUC reduced between

0.027 (cut point, 19.80 kg) and 0.040 (cut point, 16.00 kg) (results not shown). Moreover, the prediction factor Season_p always captured more than 10% of the importance along the specificity space. Similarly, the prediction factor BW at the end of the nursery period, was the primary contributor in the analysis of slaughter BW (Figure 7.5). Excluding this factor from the slaughter BW model resulted in a decrease in AUC ranging from 0.056 (cut point, 92.80 kg) and 0.060 (cut point, 105.00 kg) (results not shown). Dependence plots for factors with more than 5% importance in classifying light pigs at the end of the nursery period and at slaughter were provided in Figs. 7.6 and 7.7. Furthermore, when the BW for the intermediate phases (weaning and the end of the nursery period) were not considered in predicting slaughter BW, the reduction of the AUC was significant (Figure 7.8).

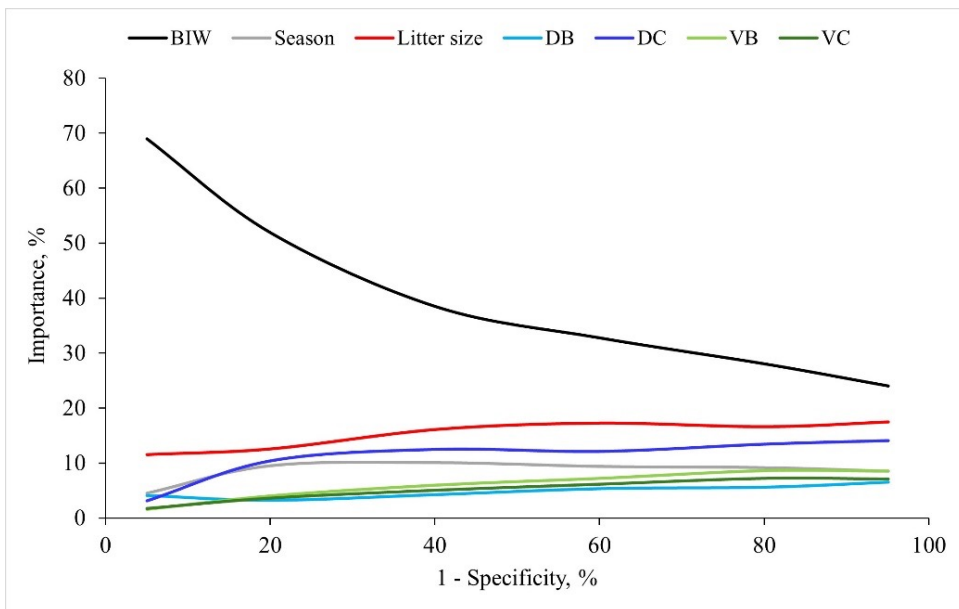


Fig. 7.2 Importance evolution for factors accounting for more than 5% when classifying light pigs at 21 d old (< 4.9 kg), with generalized boosted regression. Abbreviations: DB, difference between the piglet's birth weight and the average litter weight at birth; DC, difference between the piglet's birth weight and the average litter weight after cross-fostering; BtW, birth weight; VB, within-litter variance of body weight at birth; VC, within-litter variance of body weight after cross-fostering.

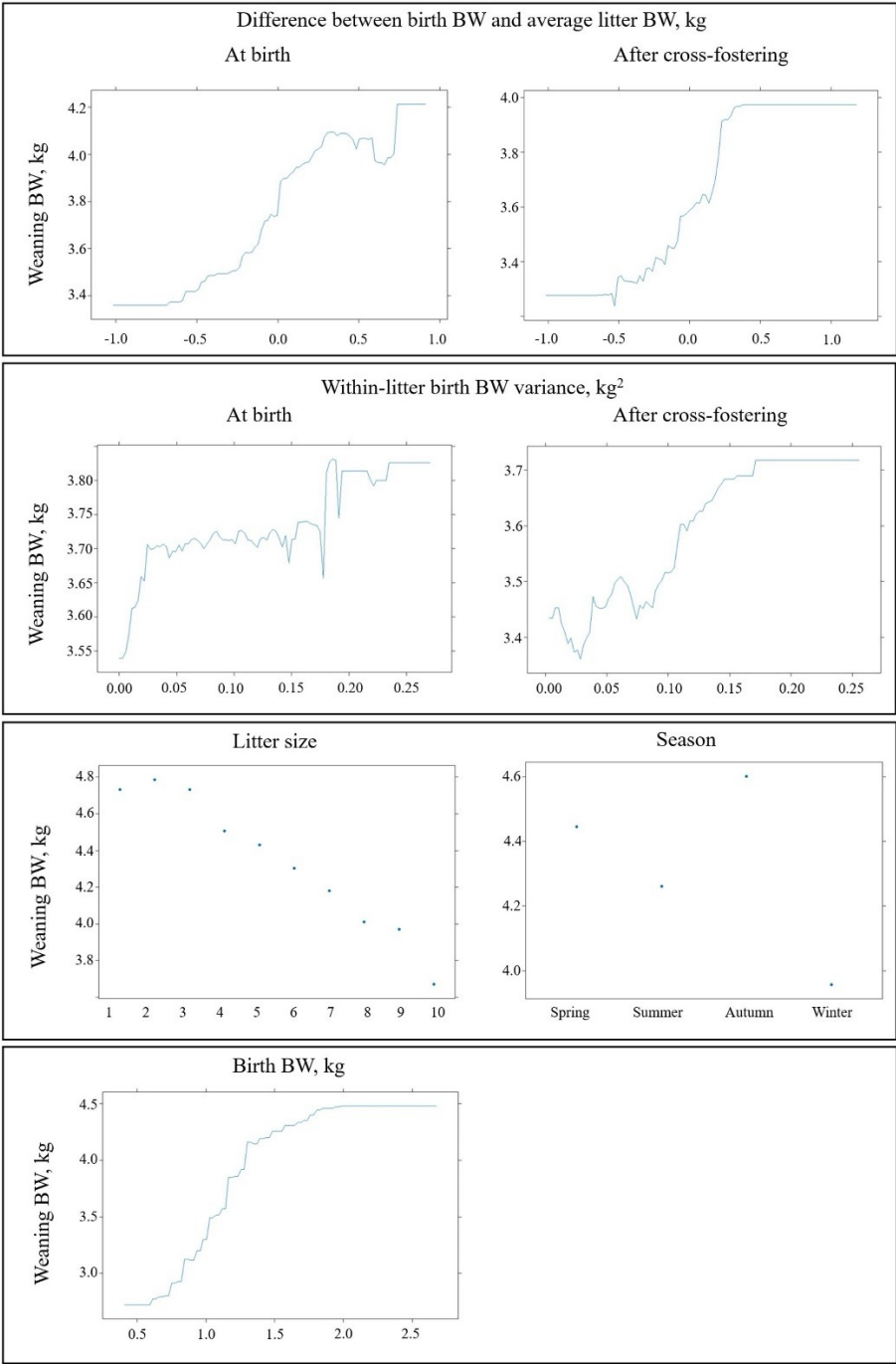


Fig. 7.3 Partial dependence plots for factors accounting for more than 5% importance when classifying light pigs at weaning (< 4.9 kg) with generalized boosted regression (sensitivity, 86%; specificity, 60%).

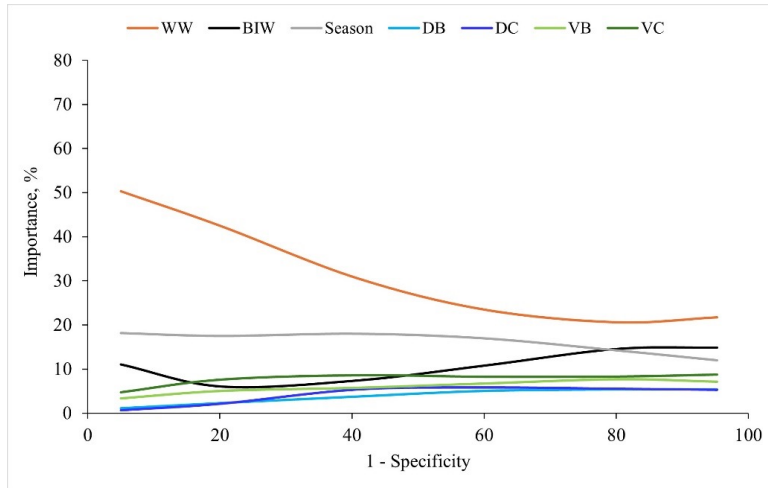


Fig. 7.4 Importance evolution for factors accounting for more than 5% when classifying light pigs at 65 d old (< 18.2 kg), with generalized boosted regression. Abbreviations: DB, difference between the piglet's birth weight and the average litter weight at birth; DC, difference between the piglet's birth weight and the average litter weight after cross-fostering; BtW, birth weight; VB, within-litter variance of body weight at birth; VC, within-litter variance of body weight after cross-fostering; WW, weaning weight.

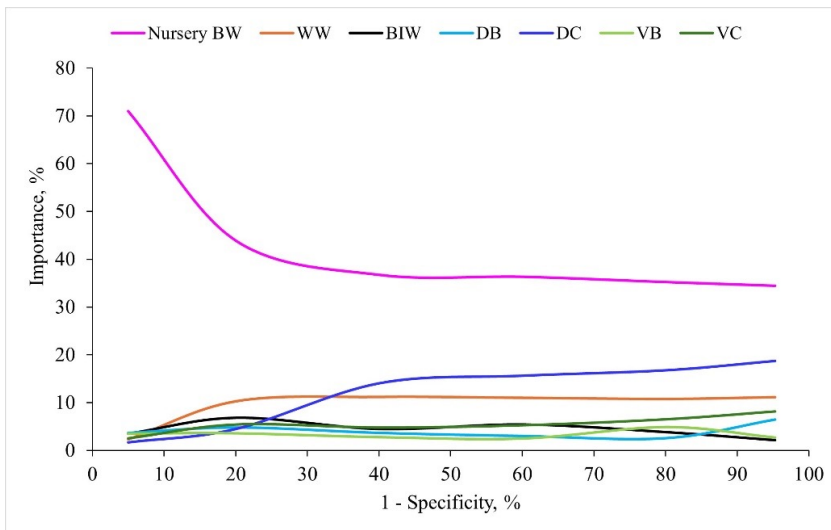


Fig. 7.5 Importance evolution for factors accounting for more than 5% when classifying light pigs at 155 d old (< 100.0 kg), with generalized boosted regression. Abbreviations: DB, difference between the piglet's birth weight and the average litter weight at birth; DC, difference between the piglet's birth weight and the average litter weight after cross-fostering; BtW, birth weight; Nursery BW, body weight at the end of the nursery period; VB, within-litter variance of body weight at birth; VC, within-litter variance of body weight after cross-fostering; WW, weaning weight.

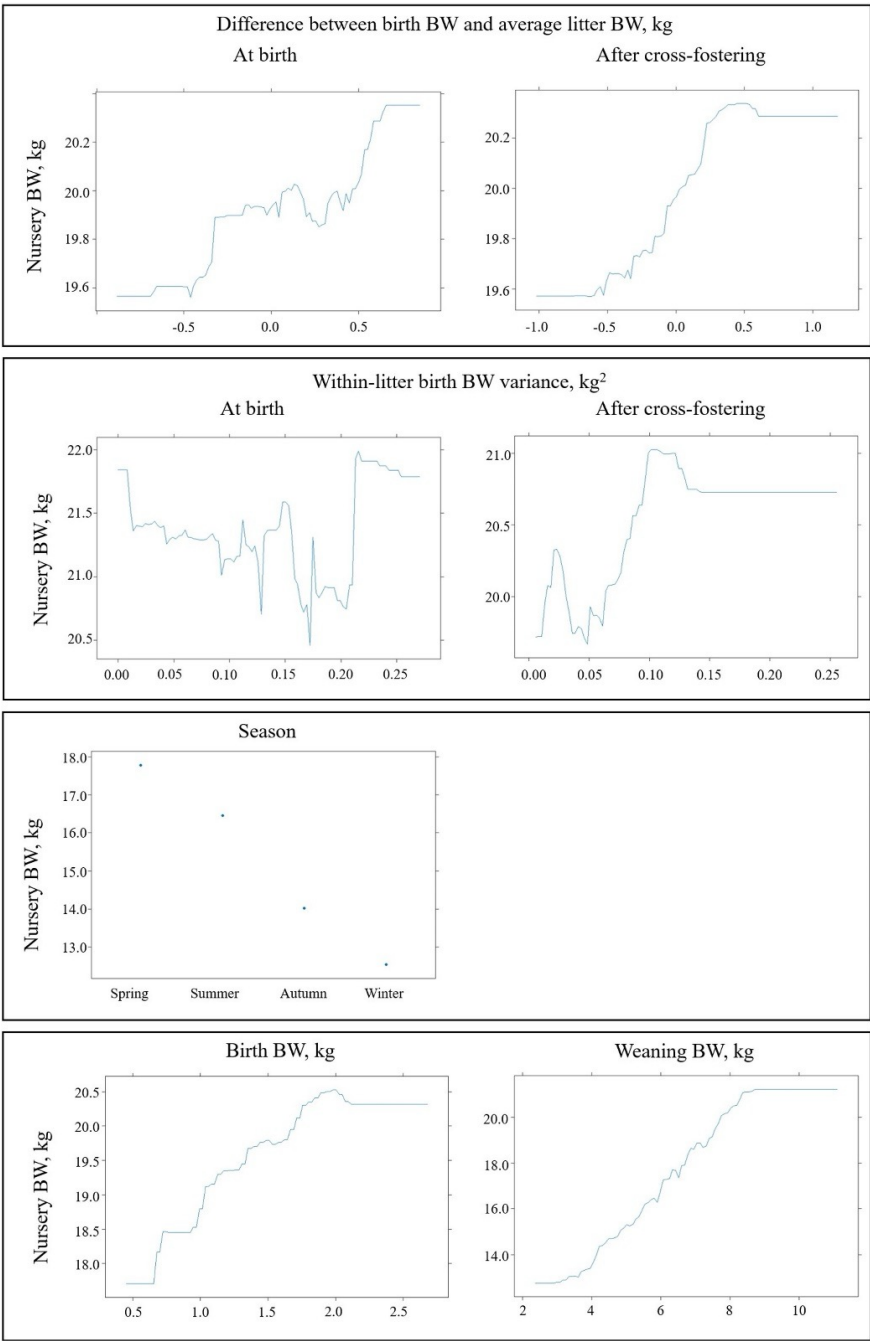


Fig. 7.6 Partial dependence plots for factors accounting for more than 5% importance when classifying light pigs at 65 d old (< 18.2 kg) with generalized boosted regression (sensitivity, 85%; specificity, 60%). Abbreviation: Nursery BW, BW at the end of the nursery period.

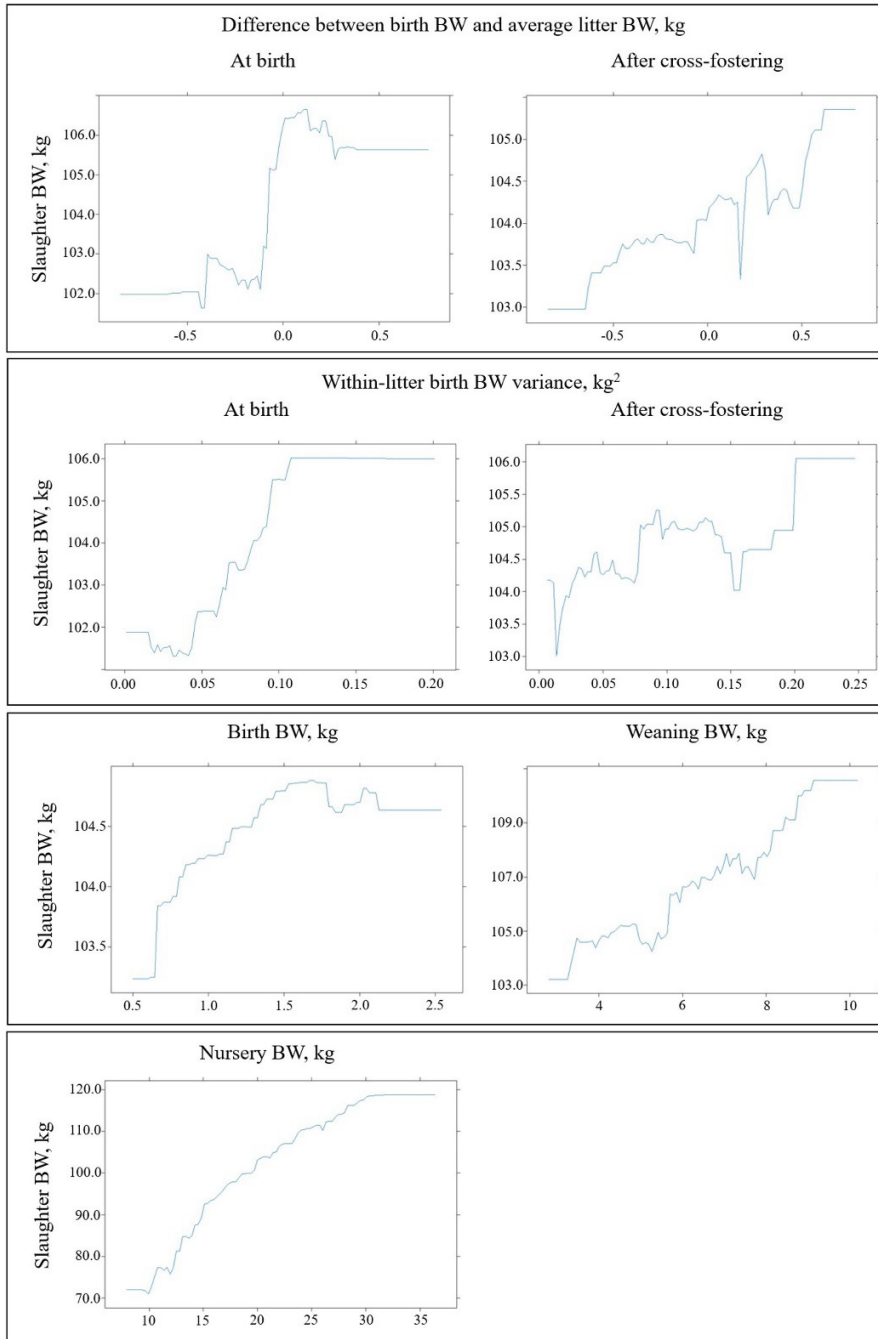


Fig. 7.7 Partial dependence plots for factors accounting for more than 5% importance when classifying light pigs at 155 d old (< 100.0 kg) with generalized boosted regression (sensitivity, 90%; specificity, 60%). Abbreviations: Nursery BW, BW at the end of the nursery period.

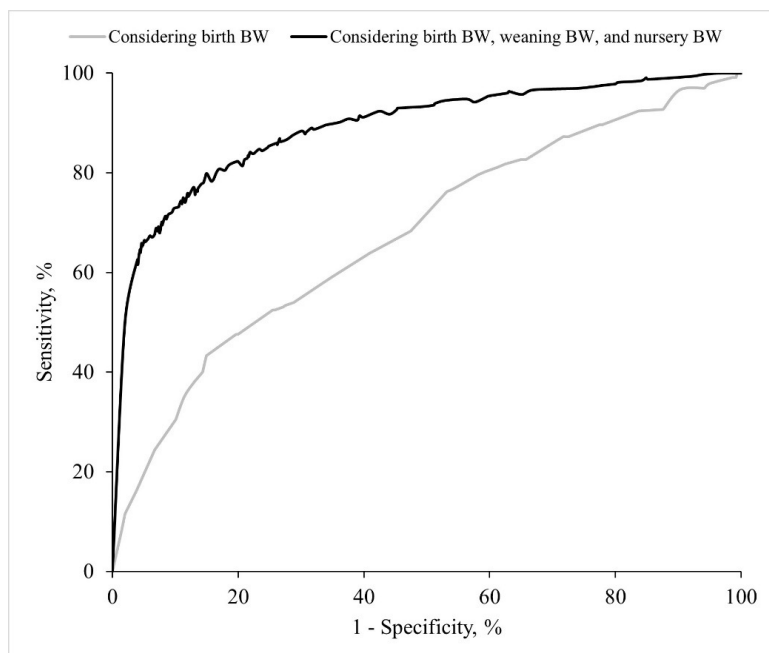


Fig. 7.8 ROC curve for predicting the market BW of (Yorkshire x Landrace) x Duroc pigs based on birth BW, weaning BW, and BW at the end of the nursery period, compared to using only birth BW. Abbreviations: Nursery BW, BW at the end of the nursery period.

7.4 Discussion

Pigs at risk of growth retardation are the main contributors to BW variability throughout the production cycle. It is estimated that, in any given batch, these pigs represent 10% to 15% of the total, leading to inefficient pen utilization and poor carcass grading (Calderón Díaz et al., 2017). Thus, the pig industry would greatly benefit from robust tools to identify these problematic pigs, enabling the development of effective strategies to improve homogeneity and growth within pig production systems.

In recent decades, classification algorithms based on machine learning have emerged as alternative methods with potential applications to the swine industry (Friedman, 2001; Marvin and Ziegler, 2017). In this study, the random forest and generalized boosted regression models achieved the highest classification performance among the four models evaluated. Their classification advantage persisted throughout the ROC curve and was effectively

captured by the AUC in our commercial dataset. The AUC values for these models indicated an acceptable to excellent discrimination performance (Hosmer and Lemeshow, 2000), ranging from 0.772 to 0.861. These results are in accordance with findings from Lee et al. (2019) and Casellas et al. (2024), who indicated that machine learning methods can outperform traditional ordinary least squares regression in predicting weight traits in pigs.

In our study, we observed a slight advantage for generalized boosted regression in classifying more extreme pigs, which we attributed to its fine-tuning capability for extreme observations (Friedman, 2001; Chen and Guestrin, 2016). At higher cut points, random forest demonstrated the best classification performance (Su et al., 2022; Casellas et al., 2024). One of the reasons why generalized boosted regression and random forest performed better is their ability to handle heterogeneous features, such as the quantitative and categorical variables in our dataset (Su et al., 2022). Rather than being a disadvantage for this research, the different behavior of these two models depending on the defined cut point should be seen as an opportunity, where the selection of one method over the other can be defined according to the specific needs of each user.

Random forest and generalized boosted regression models demonstrated increased AUC with reduced weight cut points, indicating superior classification performance when focusing on extreme individuals. This result is consistent with previous studies (Steyerberg et al., 2010; Casellas et al., 2024), which have shown that focusing on more extreme cases (*i.e.*, pigs that are much lighter or heavier) increases the difference between the two groups, making them easier to classify. However, regardless of the cut points and the classification models, the differences in classification ability were remarkably small, suggesting minimal benefit from the chosen method and stricter weight cut points. The acceptable to excellent and stable classification performance of random forest and generalized boosted regression across the analytical space is particularly noteworthy for their potential implementation in the swine industry.

In the database of commercial terminal pigs used in this study, the primary influence on the weaning, nursery, and grow-finish stages is best described by the BW at the beginning of each respective period (birth, weaning, and end of the nursery period). As reported by Casellas et al. (2024), the importance of each of these factors decreases throughout the production cycle in favor of the weights recorded at each subsequent stage, indicating that the influence of a prediction factor increases the closer it is to the weight measurement. Consequently, a

significant decrease in the AUC of the ROC curves is observed when final marketing weight predictions are based solely on BtW. Several studies have proposed thresholds to identify low BtW piglets (*i.e.*, ≤ 1.1 kg by Wang et al., 2017; ≤ 1.15 kg by Montoro et al., 2020; ≤ 1.25 kg by Beaulieu et al., 2012; He et al., 2016, Douglas et al., 2014), although the results regarding subsequent growth performance remain controversial. Our findings align with studies by Huting et al. (2018), Zeng et al. (2019), Surek et al. (2019), and Montoro et al. (2020), which reported that light BtW piglets are capable of catching up to their heavier counterparts, achieving comparable BW by the end of the production cycle. Conversely, our results differ from those of Quiniou et al. (2002), Douglas et al. (2013), and He et al. (2016), who concluded that lightweight pigs at birth exhibit inferior growth performance compared to their heavier counterparts. Weights recorded at weaning and at the end of the nursery period have been shown to significantly influence subsequent growth performance. Thus, pigs with lower BW at later stages of the production cycle are generally expected to reach market weight later than their faster-growing counterparts (Douglas et al., 2014; Collins et al., 2017; López-Vergé et al., 2018). These findings suggest that farmers would benefit from systematically weighing animals at different stages of production to maintain a robust and updated database, which would be useful for efficiently identifying lighter animals. Interestingly, the importance of weight records along the specificity space increased notably for high specificity values. Therefore, weighing animals is crucial when implementing time-consuming individual treatments or expensive supplements, as these strategies should focus on truly underweight pigs, thereby avoiding false positives (*i.e.*, high specificity).

It should be noted that incorporating additional prediction factors beyond BW into the analytical models could slightly improve AUC estimates, as these factors may influence the risk of a pig being slow-growing. One of the main factors influencing piglet growth performance during the lactation period is competition with littermates (Blavi et al., 2021; Riddersholm et al., 2021). In this context, litter size and the difference between birth BW and the average litter weight after cross-fostering appeared as the second and third most important factors, respectively, in classifying pigs at weaning. The within-litter weight variance also emerged as a main prediction factor during early growth stages, highlighting the importance of implementing effective management strategies such as cross-fostering (Patience et al., 2004). Additionally, practices like segregating piglets by BW or gender can help minimize subsequent weight variability, promoting more uniform growth within the batch. When classifying pigs at the end of the nursery period, birthweight-related factors were replaced not only by the WW but also by the season of birth. Interestingly, the season of birth demonstrated

greater predictive significance for BW at the end of the nursery period than for WW. Douglas et al. (2013) highlighted the role of seasonality, suggesting that the month of birth can influence subsequent growth performance. Similarly, Paredes et al. (2012) identified the season of birth as one of the most important factors influencing the BW of pigs at the end of the nursery phase. The prediction of slaughter BW was strongly influenced by the BW at the end of the nursery period, resulting in the model achieving the highest AUC estimates across different production phases, as noted by Casellas et al. (2024). These results are consistent with the findings of López-Vergé et al. (2018), who observed that the probability of light pigs being sent to the slaughterhouse later increases as they approach the end of the production cycle.

In this study, generalized boosted regression and random forest consistently ranked highest in classification performance across all analyses. However, it is important to be careful when extrapolating these results to other datasets, as the performance of machine learning algorithms can vary significantly depending on the specific application and data types involved. The inclusion of additional prediction factors in the models could potentially enhance the classification ability of the algorithms. In our case, some limitations of the models were the inclusion of data from a single farm and only features up to weaning. However, as noted by Casellas et al. (2024), factors beyond the BW of pigs at each production stage may influence the risk of being slow-growing, but their impact on the analysis tends to be marginal, as the weight factors capture most of the critical information within the specificity space.

From a practical standpoint, we recommend evaluating a range of candidate algorithms (*i.e.*, linear model, random forest, generalized boosted regression) for each application, rather than relying solely on a single approach. Once the best model is adjusted to a specific pig population and breed, the algorithm could be regularly updated without needing to monitor the entire population. Instead, updates could be based on sentinel animals within each batch. This approach could be highly useful for both decision-making within the herd and assessing the impact of specific management practices and nutritional interventions (*i.e.*, cross-fostering, ensuring adequate colostrum intake, and providing creep-feed, among others) aimed at target variables, such as reducing the risk of low BW at various stages of the production system. Notably, these interventions are particularly effective during the early growth phases, especially during the lactation period, which has been identified as a critical window for influencing pigs' BW category and enhancing the growth performance of lighter piglets (Blavi et al., 2021).

7.5 Conclusions

In conclusion, our study demonstrates that machine learning algorithms are reliable and effective tools for classifying commercial pigs at risk of growth retardation across different production stages. Both random forest and generalized boosted regression models exhibited the highest classification performance. Their applicability in commercial herds may form the basis for decision-making on management strategies in the swine industry.

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Chapter 8

General discussion

The continuous genetic improvement over recent decades aimed at increasing sow prolificacy to raise the number of slaughtered pigs produced per sow per year (Rutherford et al., 2013) has led to a considerable decrease in average BtW, thereby increasing both the proportion of lightweight piglets (Quiniou et al., 2002; Beaulieu et al., 2010) and within-litter BtW variability (Foxcroft et al., 2007). Consequently, this has also resulted in a greater number of piglets experiencing varying degrees of IUGR (Amdi et al., 2013; Hales et al., 2013). As reviewed in Chapter 1, such increased variability poses major management challenges with significant economic, welfare, and environmental implications for pig producers, particularly in AIAO production systems (Patience et al., 2004). Previous research projects conducted by our group have provided essential background information to better understand the root causes of the problem and its main consequences for pig production (Fig. 8.1).

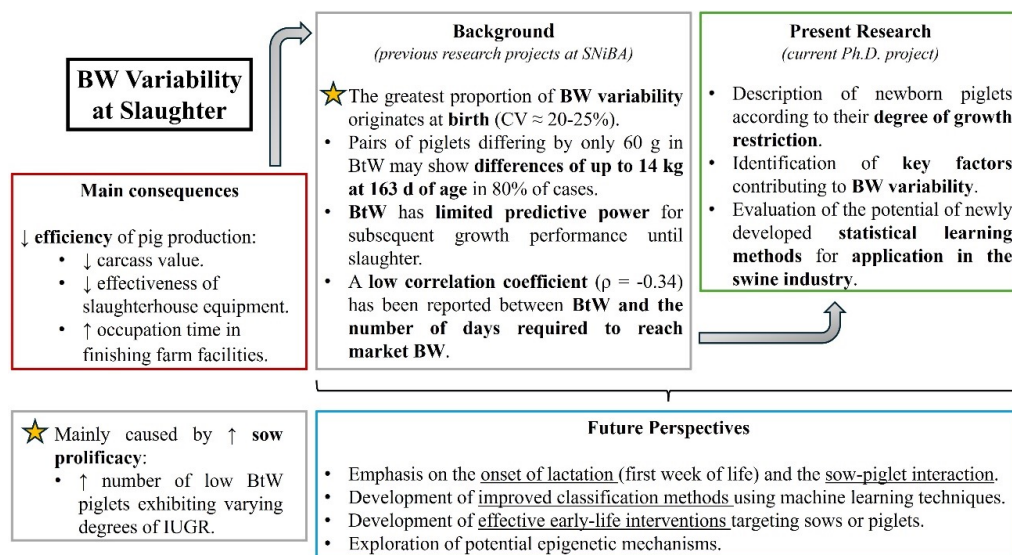


Fig. 8.1 Summary of the main problem explored, the background supporting the research topics addressed in the present thesis, and future directions.

Based on these previous findings, the hypothesis and objectives outlined in Chapter 2 focused on: (1) describing the effects of varying degrees of growth restriction in newborn piglets and how these influence differential growth and survival potential; (2) developing a multi-criteria model based on easily measurable on-farm risk factors to identify piglets with differing early-life survivability and growth potential; and (3) evaluating the potential of statistical learning algorithms to classify pigs at risk of growth retardation within the swine

industry. Addressing these objectives provides the foundation for a broader and future goal: to effectively develop intervention strategies that can be implemented at the optimal time, targeted towards high-risk pigs, and focused on the most relevant risk factors. As the results derived from this thesis are discussed in detail in the previous chapters (Chapters 3 and 4 examined the physiological characteristics of piglets affected by varying degrees of IUGR, Chapter 5 identified key risk factors that compromise early-life growth and survival, and Chapters 6 and 7 applied ML algorithms to classify light pigs throughout the production cycle), the present section aims to provide an integrated discussion across the different studies, emphasizing the practical implications of the findings. Accordingly, the following pages address: (1) insights into growth restriction in newborn piglets; (2) key risk factors affecting BW variability; (3) the potential applications of statistical learning methods in the swine industry; and (4) the broader implications of the present results and future research directions.

8.1 Understanding Growth Restriction in Newborn Piglets

Slow growing pigs are well defined in the literature as individuals with low birth and/or weaning BW, typically falling within the lower quartile of the population BW distribution and requiring additional time to reach target slaughter weight (Douglas et al., 2014; He et al., 2016; Montoro et al., 2020). These pigs, which represent approximately 10-15% of animals within a given batch, are the main contributors to increased BW variability within groups of pigs and a leading cause of prolonged farm occupancy, thereby generating substantial shadow costs for the swine industry due to reduced efficiency (He et al., 2016; Calderón Díaz et al., 2017). However, not all low BtW piglets exhibit slow postnatal growth. A proportion of them can display varying degrees of compensatory growth, particularly during early life (*i.e.*, ADG during lactation above the average; Montoro et al., 2020). The number of muscle fibers present at birth (Handel and Stickland, 1987; Dwyer et al., 1993) and morphometric characteristics at birth (Huting et al., 2018) are key factors explaining why some piglets exhibit different capacities for compensatory growth. This suggests a heterogeneous growth potential within the low BtW population (Font, 2020; Blavi et al., 2021; Cui et al., 2022).

To effectively manage this subset of pigs, it is essential to understand the biological mechanisms underlying differential growth potential among low BtW piglets. This requires (1) identifying and characterizing different degrees of IUGR and (2) establishing relationships between internal developmental parameters and external morphometric traits that can serve

as practical early-life indicators of growth capacity and survival potential. These were the main objectives of Chapters 3 and 4.

In the present thesis, the characterization of piglets across different BtW categories provided valuable insights into varying degrees of IUGR. Severely affected IUGR piglets were identified primarily by their distinctive head morphology (dolphin-like head shape, bulging eyes, and wrinkles perpendicular to the mouth; Chevaux et al., 2010; Hales et al., 2013; Hansen et al., 2019). A BtW threshold of 0.75 kg was used to define this group, corresponding to more than 1.5 SD below the mean litter weight (Wang et al., 2016; Van Tichelen et al., 2021). Selecting an appropriate BtW cut-off point to define low BtW piglets is complex, as different studies have used variable criteria. In this thesis, a value of 1.15 kg was established in Chapter 3, corresponding to the lower 30th percentile of the population BtW distribution, while a threshold of 1.25 kg was used in Chapter 4 based on previous literature (Douglas et al., 2014; He et al., 2016). As expected, compared with normal BtW piglets (> 1.15 or 1.25 kg), those with severe IUGR exhibited the most pronounced impairments in postnatal growth, vitality, and survival, likely driven by reduced colostrum intake, limited energy reserves, altered metabolic profiles, gastrointestinal dysfunction, and impaired ossification and longitudinal bone growth. These findings are consistent with the existing literature on IUGR, which suggests that the reduced postnatal growth rate observed in affected pigs is programmed during fetal development (Foxcroft et al., 2006).

While differences between severe IUGR and normal BtW piglets are well documented and persist through to slaughter (Ruggeri et al., 2024), the most intriguing biological question concerns the intermediate range of low BtW piglets, approximately between 0.75 and 1.25 kg, which display markedly variable postnatal growth trajectories. The differential growth performance of low BtW piglets originating from a hyperprolific sow population is illustrated in Fig. 8.2.

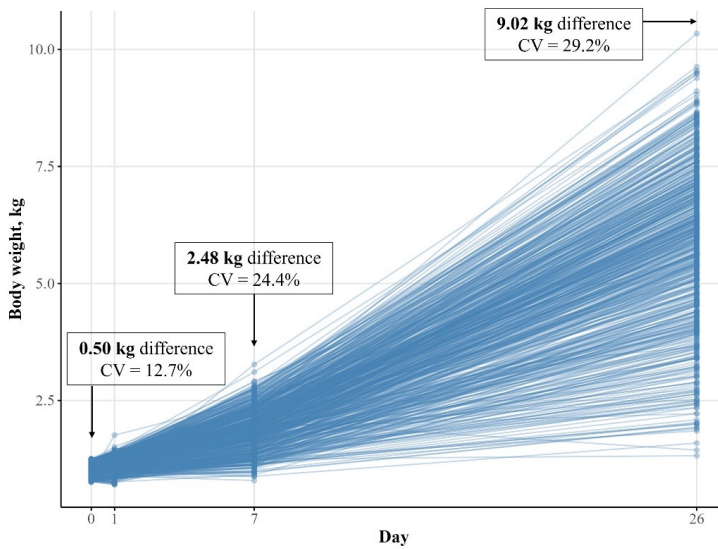


Fig. 8.2 Representation of the BW evolution in low BtW piglets (0.75–1.25 kg) throughout the lactation period (26.1 ± 0.42 days). The data correspond to the dataset described in Chapter 3, comprising 924 low BtW piglets born alive from 99 litters. Text boxes indicate the difference between the lightest and heaviest piglets and the CV for each day.

Although some studies have reported catch-up growth in piglets before weaning (Cui et al., 2022) and shown that low BtW does not necessarily indicate IUGR (Gupta, 2007), the mechanisms underlying these differences remain poorly understood. In Chapters 3 and 4, a BtW cut-off of approximately 1.00 kg was used to define two categories of low BtW piglets. Despite an initial mean difference of only 0.20 kg at birth, the gap widened to nearly 1.00 kg by weaning, accompanied by differences in colostrum intake, resulting in lower blood immunoglobulin G concentrations in piglets with lower BtW, and in survivability (approximately 20%). Yet few internal physiological traits could account for these divergent outcomes. Among the variables assessed, significant differences were limited to relative brain weight, greater in lighter piglets, and bone density, with the lowest BtW piglets showing a higher proportion of low-density bones. These findings align with the concept of the “brain-sparing effect”, whereby nutrient and oxygen supply is preferentially directed toward vital organs (*i.e.*, brain and heart) at the expense of peripheral tissues in growth-restricted fetuses (Wang et al., 2005; Roza et al., 2008; Amdi et al., 2013). Despite pronounced morphological differences at birth (*i.e.*, CRL and BMI) and their strong correlation with internal developmental parameters, no significant differences were observed in gut health, energy reserves, or metabolomic profiles among low BtW categories. This indicates that classifying piglets solely by BtW is insufficient to capture the true biological diversity within this group. The findings from Chapters 3 and

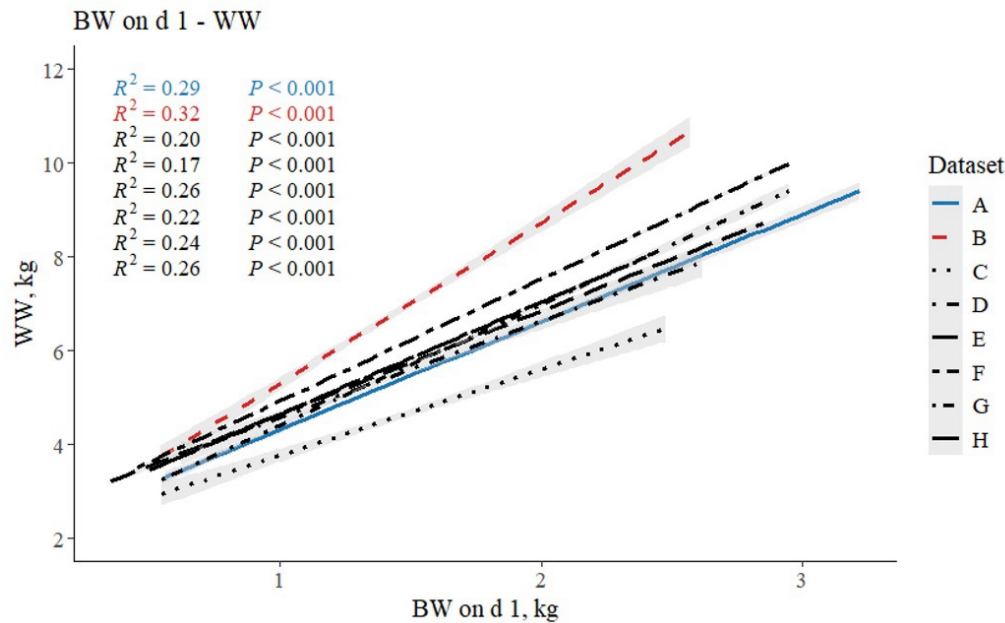
4 support the hypothesis that low body metrics at birth are associated with compromised internal physiological status, indicating that specific morphometric traits can serve as reliable indicators of internal development, enabling a non-invasive diagnosis of IUGR. Moreover, they confirm that BtW remains a strong but incomplete predictor of performance, capable of distinguishing between the extreme categories but inadequate for differentiating among degrees of restriction within the low BtW range. Overall, the physiological profiles of the lighter low BtW piglets more closely resembled those of severely IUGR piglets, whereas the heavier low BtW piglets exhibited values closer to those of normal BtW counterparts. This indicates that low BtW piglets do not represent a homogeneous group in terms of developmental status. Therefore, identifying reliable, non-invasive early-life indicators beyond BtW remains a key challenge for the future, with the goal of better characterizing biological diversity and predicting growth potential.

8.2 Early-Life Risk Factors Influencing Body Weight Variability

Body weight variability at birth can reach CV of up to 25%, with increases during lactation or up to approximately 14 days postweaning, when piglets are fully adapted to solid feed (López-Vergé et al., 2018). Although variability among pigs tends to decrease with age (Patience et al., 2004; López-Vergé et al., 2018) due to the application of various management and nutritional strategies on farms, the opportunity to effectively implement these interventions, enabling lighter pigs to catch up with their heavier pen mates, diminishes as pigs grow, particularly after weaning (Blavi et al., 2021). Therefore, achieving a high BW at weaning (WW) is critical, as it significantly affects postweaning growth, the time required to reach target slaughter weights, and the incidence of morbidity and mortality (Wolter and Ellis, 2001; Douglas et al., 2013). While Chapter 5 focused on identifying risk factors associated with low growth performance and early-life mortality, Chapters 6 and 7 examined the main production factors influencing low pig BW at different stages of the production cycle, extending the analysis beyond weaning.

Birth BW has been extensively investigated in the literature as a key indicator of postnatal performance (Gondret et al., 2005; Rehfeldt et al., 2008; Fix et al., 2010) and is strongly associated with piglet survivability (Van der Lende and De Jager, 1991; Roehe and Kalm, 2000). In Chapter 5, simple linear regression models identified BW on day 7 as the most powerful predictor of WW, explaining the largest proportion of variability across the two datasets analyzed ($R^2 > 0.60$) and clearly outperforming the predictive capacity of BW on day 1 ($R^2 \approx 0.30$). This

finding is both novel and significant, as it highlights the importance of the first week of lactation, particularly the successful switch-on of lactation, during which the interaction between the sow and her piglets plays a crucial role. The importance of this finding lies not in what interventions should be applied, but rather when they should be implemented. Providing targeted care during the first week of life has the potential to enhance growth and overall performance up to weaning, indicating that piglets born underweight are not necessarily irreversibly compromised if they are identified early. The swine industry should therefore recognize the critical value of the early lactation period rather than focusing solely on BtW. A review of the relationship between BW on day 1 and WW, and between BW on day 7 and WW, across multiple datasets collected in Spain and the United States over the past decade confirms that the predictive capacity of BW on day 1 is approximately half that of BW on day 7 (Fig. 8.3), regardless of lactation length. These findings align with those of Montoro et al. (2020), who reported that BtW has limited predictive value for subsequent growth until slaughter, largely because BW categories can shift during lactation. Moreover, Gasa et al. (2020) observed greater apathy in piglets housed in hot environments compared to those kept under temperature conditions, which negatively affected their BW on day 7, mainly due to reduced BW gain within the first 24 hours after birth. This impaired switch-on of lactation resulted in piglets reared under hot conditions having a lower BW at weaning than those raised under temperature conditions.



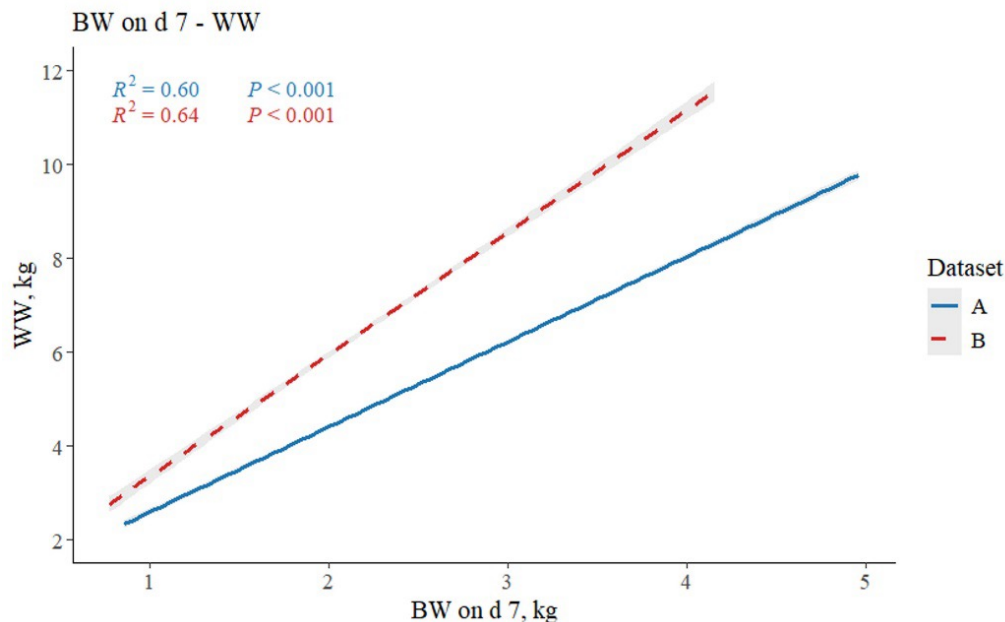


Fig. 8.3 Weaning body weight (WW) in relation to BW on d 1 and BW on d 7 across eight different datasets: A (n = 4,394; lactation = 21.1 ± 2.26 d), B (n = 1,412; lactation = 26.1 ± 0.44 d), C (n = 785; lactation = 24.8 ± 1.92 d), D (n = 1,102; lactation = 21.4 ± 3.12 d), E (n = 15,861; lactation = 22.8 ± 1.89 d), F (n = 90,240; lactation = 22.0 ± 2.95), G (n = 9,844; lactation = 21.0 ± 2.47 d), H (n = 20,464; lactation = 20.4 ± 2.26 d). Datasets A – D were collected in Spain, while datasets E – H were collected in the United States. Each line represents a fitted linear regression model.

Once the importance of ensuring a successful onset of lactation has been established, it becomes essential to identify the main risk factors that may compromise this outcome, thereby enabling targeted interventions in populations at higher risk. In Chapter 5, the results showed that BW on day 1, relative BW (RBW) on day 1, and CI were the primary variables influencing survivability and growth during the first week of life. Among these, BW on day 1 appeared to play a pivotal role, with each 100 g increase reducing the odds of being classified as compromised by approximately 27.6%. Although Knap et al. (2023) reported that the genetic potential for piglet BtW increased by 0.27 kg from 2012 to 2022, direct manipulation of BtW is difficult. Therefore, the main strategies based on our findings should focus on (1) implementing cross-fostering protocols to ensure a RBW on day 1 above 0%, and (2) providing special care during the first 24 hours after birth to guarantee adequate CI, with a theoretical threshold of approximately 250 g per pig. Low RBW has been associated with an increased risk of early mortality (Milligan et al., 2002; Hales et al., 2013), while CI is essential for piglet

survival and development, providing both immunoglobulins for immune protection and energy for thermoregulation and growth (Devillers et al., 2004; Quesnel et al., 2023). The results from Chapters 6 and 7 consistently highlight the central role of birthweight-related factors in determining piglet performance and classification outcomes up to weaning. Among these variables, which together explained more than 60% of the specificity space in all cases, BtW and the difference between individual BtW and average litter weight (at birth and after cross-fostering) emerged as the most influential predictors. Altogether, these findings underscore the importance of both absolute BtW and its relative position within the litter in shaping early-life outcomes, confirming the hypothesis that statistical learning models can effectively capture the main determinants of piglet survival and growth, thereby enabling accurate identification of individuals at greatest risk.

The influence of a predictive factor, such as BW, increases the closer it is to the target weight record, emphasizing the critical role of pig weight immediately prior to each stage in predicting subsequent growth performance (Chapters 6 and 7). While birthweight-related factors contribute to early predictions, their influence diminishes as the production cycle advances, gradually being replaced by more recent weight measurements. Consistent with Paredes et al. (2012) and Douglas et al. (2013), WW emerged as the strongest predictor for classifying light pigs at the end of the nursery period, whereas nursery-end weight was the main determinant for predicting slaughter weight. Excluding these intermediate weight records from predictive models markedly reduced classification accuracy, underscoring the importance of temporal proximity in growth prediction. Although weighing pigs is a time-consuming practice and may not be feasible on all farms, the findings reported in Chapters 5, 6, and 7 indicate that such information remains the most valuable for optimizing classifications tools aimed at identifying animals at greatest risk. Farmers may therefore benefit from using the identified risk factors as practical guidelines for determining when to intervene and which pigs to target, ultimately improving growth performance and survival rates and minimizing the negative effects of piglets at risk.

However, the models presented in this thesis are inherently dependent on the datasets used, which may limit the generalizability of the identified risk factors to other populations, farms, or breeds. Therefore, validation in larger and more diverse populations is essential to confirm the robustness and applicability of the models across different production systems, ensuring that these risk factors can reliably guide interventions in a variety of commercial settings.

8.3 Potential Applications of Machine Learning in Swine Production

The absence of reliable, efficient, and non-invasive tools to identify piglets at elevated risk, particularly during the earliest stages of life, remains a major constraint for the swine industry. This limitation hinders the timely implementation of targeted management or nutritional interventions aimed at mitigating poor growth performance and improving survivability (Felicioni et al., 2018; Ruggeri et al., 2025). Given that pigs at risk of growth retardation represent a major source of within-batch variability, developing robust tools to detect this subset of vulnerable animals is essential for enhancing batch uniformity, improving production efficiency, and ultimately increasing overall farm profitability. Recent advances in computational power, together with the availability of increasingly complex classification algorithms, provide a valuable alternative to classical statistical learning approaches. Numerous prediction methods, including decision trees (Quinlan, 1987), boosting algorithms (Friedman, 2001; Chen and Guestrin, 2016), and random forests (Wright and Ziegler, 2017), have demonstrated strong potential for application in animal production systems. In this thesis, various machine learning algorithms were evaluated for their ability to identify pigs at risk of growth retardation throughout the production cycle.

In Chapter 6, which used a purebred nucleus dataset, the random forest methodology consistently achieved the best performance among the five models evaluated (ordinary least squares regression, decision tree, random forest, generalized boosted regression, and extreme gradient boosting). Random forest outperformed all alternative approaches across all production stages and cut-off points for lightweight pigs, followed closely by boosting methods. Maximum AUC values ranged from 0.70 to 0.80, indicative of acceptable discrimination, and reached 0.80 to 0.90 in some specific cases, indicating excellent classification performance (Hosmer and Lemeshow, 2000). Similarly, Chapter 7, which used a commercial crossbred dataset, revealed that random forest and generalized boosted regression achieved the highest classification performance. Both models exhibited acceptable to excellent AUC values, with generalized boosted regression showing a slight advantage in identifying extreme individuals, likely due to its enhanced fine-tuning capabilities for rare or extreme observations (Friedman, 2001; Chen and Guestrin, 2016). Notably, in both Chapters the best-performing algorithms were boosted approaches and random forest, regardless of dataset origin. This consistency underscores the strengths of these methods in handling heterogeneous datasets that include both quantitative and categorical variables (Su et al., 2022). Altogether, these results are

consistent with previous studies and confirm that machine learning methods can surpass traditional ordinary least squares regression as predictive tools for weight-related traits in pigs (Bakoev et al., 2020).

Additionally, the stability of AUC values across different cut-off points for the top-performing models is of particular interest for practical implementation in the swine industry. This stability indicates that the algorithms maintain strong discriminatory power across a wide range of classification thresholds, thereby offering producers flexibility when defining economically meaningful weight cut-off points. In this context, the ability of these models to accommodate different trade-offs between sensitivity and specificity becomes a notable advantage. Such flexibility provides a decision-making framework in which producers can adjust the optimal balance between sensitivity and specificity according to the management or nutritional practices applied to lightweight pigs at each production stage. For example, when implementing low-cost management practices such as cross-fostering (Calderón Díaz et al., 2018), highlighted in Chapter 5 for its role in ensuring a positive relative weight balance within the litter, a higher rate of false positives (*i.e.*, lower specificity) may be acceptable, as nearly all potentially lightweight pigs can be managed with minimal economic cost.

Despite their advantages, several limitations must be considered when implementing machine learning approaches in swine production. Traditional regression models require relatively small datasets, are computationally inexpensive, and are simple to implement (James et al., 2017). In contrast, machine learning algorithms typically require large datasets to perform effectively and avoid overfitting or sampling biases (Sarker, 2022). This requirement represents a challenge in contexts where data availability is limited, a common situation when working with animals. Moreover, more complex algorithms (*i.e.*, extreme gradient boosting) demand substantially higher computational time, which limits their practical use when the expected improvement in classification performance is marginal. For this reason, extreme gradient boosting was not implemented in Chapter 7, as the results obtained in Chapter 6 were nearly identical to those generated by the generalized boosted regression model across all thresholds and phases of the production cycle. These considerations also highlight the need for caution when extrapolating results to other farms, environments, or genetic lines. The slight advantage observed between the best-performing models (random forest vs. boosting approaches) may vary depending on the specific characteristics of the dataset. Therefore, their generalizability should be confirmed through external validation in large, independent populations representing diverse production conditions.

Overall, these findings indicate that classification models based on machine learning represent a promising approach for the early identification of IUGR piglets and individuals at greatest risk of growth retardation. Importantly, they confirm the hypothesis that applying machine learning algorithms to large and comprehensive datasets can outperform classical methodologies in prediction and classification tasks. Therefore, the use of robust machine learning algorithms within large-scale swine datasets offers a valuable tool for data-driven decision-making, with the potential to enhance both the sustainability and profitability of modern pig production systems. Their application could improve diagnostic precision, support timely interventions, and ultimately contribute to improved animal welfare and production efficiency.

8.4 Implications and Future Research Directions

Neonatal piglets face major challenges during the earliest stages of life, being highly vulnerable to mortality or impaired growth due to their inherent physiological limitations. These limitations are further exacerbated in modern hyperprolific sow lines, which increase the prevalence of IUGR and consequently the number of low BtW piglets at risk (Farmer and Edwards, 2022). This thesis has made progress in advancing our understanding of the physiological characteristics of piglets affected by varying degrees of IUGR (Chapters 3 and 4), in identifying key risk factors that compromise early-life growth and survival (Chapter 5), and in applying machine learning algorithms to classify at-risk piglets throughout the production cycle (Chapters 6 and 7).

Translating the findings of this thesis into practice highlights the need for targeted early-life management strategies aimed at ensuring an optimal switch-on of lactation, which is essential for achieving a high WW. Farrowing supervision and timely assistance to piglets are essential during the first hours after birth, particularly to ensure adequate CI. This need is even more critical in hyperprolific sows, where prolonged farrowing, intense litter competition at the udder, and reduced piglet vitality can collectively decrease the amount of colostrum ingested and delay its consumption after parturition begins (Oliviero et al., 2019). As reported by Suárez-Trujillo et al. (2020), the quantity of colostrum a piglet consumes during the first 24 hours postpartum influences its thermoregulation, growth, and passive immune acquisition, with effects that extend well beyond this early period. Furthermore, to ensure proper transfer of antigen-specific immune components, piglets should remain with their biological dam for at least 12 hours, and not fewer than 6 hours, to effectively acquire

passive immunity from colostrum (Bandrick et al., 2011). Although under optimal sanitary conditions it is recommended to minimize the number and frequency of movements and to keep as many piglets as possible with their biological dam (Wattanaphansak et al., 2002), cross-fostering remains a necessary practice in cases of very large litters or when sanitary conditions are suboptimal. It allows piglets to be distributed according to teat availability and their vitality (Farmer and Edwards, 2022). Muns et al. (2014) emphasized the importance of identifying viable and non-viable piglets at birth and allocating the smallest or least viable piglets to the best-performing sows. In this context, the correlations observed in Chapter 4 between body metrics at birth and internal physiological status can support the practical, on-farm identification of at-risk piglets. It is also crucial to ensure that an adequate number of functional teats are available, as unsuckled teats begin to regress shortly after birth, ultimately reducing milk production throughout lactation (Theil et al., 2005). This is particularly important in first-parity sows, because early teat stimulation enhances colostrum and milk production in subsequent lactations (Farmer and Edwards, 2022). Further research in this area is therefore needed to develop strategies specifically adapted to modern sow genotypes, ensuring optimal survival and growth of their piglets.

Despite these advancements, several knowledge gaps remain. Key areas that require further investigation include the physiological differences among low BtW piglet categories with varying growth and survival potentials, as well as the specific role of the sow and the dynamics of the sow-piglet interaction in the switch-on of milk production during the first days after farrowing. A deeper understanding of the intrinsic factors that cause certain piglets to fall behind, despite adequate management, is essential for developing more effective interventions.

In the present thesis, the blood metabolomic profile of pigs with different BtW revealed specific metabolite changes among categories, primarily highlighting a downregulation of amino acid metabolism in IUGR piglets compared with the other categories, consistent with the findings of Huang et al. (2019). Emerging evidence also emphasizes that studying the microbiota composition of pigs may reveal specific differences in microbial taxa among piglets with varying degrees of IUGR, potentially serving as a biomarker for diagnosing this condition (Ruggeri et al., 2025). The concept of the microbiota-gut-brain axis has recently been established, demonstrating that microbiota plays a key role in modulating gut-brain signaling, which is critical not only for long-term survival but also for maintaining gut-brain homeostasis (Margolis et al., 2021). The establishment of the microbiota-gut-brain axis during early life is particularly significant, as this period coincides with the maturation of both the brain (Cowan

et al., 2019) and the enteric nervous system (Obata and Pachnis, 2016). Consequently, the first days postpartum represent a sensitive window for microbial colonization, during which the microbiota shifts toward communities optimized for supporting the neonate's rapid growth and neurodevelopment (Koenig et al., 2011). Although these differences in microbiota may reflect the piglet's growth-restricted state rather than being causal, they still hold potential as early biomarkers for identifying individual variability. Another promising area of research involves epigenetic modifications to better understand the regulatory mechanisms underlying IUGR in piglets. A common epigenetic mechanism is DNA methylation. Studies have identified tissue-specific genome-wide methylation differences between IUGR and normal BtW piglets in pathways regulating growth and tissue development, energy and carbohydrate metabolism, lipid metabolism, protein turnover, immune function, detoxification and oxidative stress, and cell death (Hu et al., 2018; Tao et al., 2019). These findings suggest that IUGR has long-lasting developmental and metabolic consequences mediated not only by nutrient availability but also by persistent epigenetic alterations established during gestation. Combining epigenetic biomarkers and microbiota-based indicators may allow for earlier and more accurate identification of piglets at higher risk than is currently possible.

The role of the sow and her interaction with the piglets during the first days of lactation must also be considered. During this period, piglet feeding behavior is determined by milk intake and the initial transition to solid feed consumption. Specifically, feeding behavior is strongly influenced by social interactions, both with littermates and with the sow, as well as by environmental quality (Blavi et al., 2021). Piglet vitality and activity during the first five days after farrowing play a key role in shaping social behavior and are critical for triggering milk production and ensuring proper piglet growth (Muns et al., 2013). For instance, Gasa et al. (2020) demonstrated that litter apathy impairs the proper switch-on of lactation. Therefore, it is essential to ensure the presence of high-vitality piglets in every litter, as proactive litters help stimulate the sow and support the proper onset of milk production. Additionally, sow recovery during the first days postpartum is highly important not only for ensuring milk production but also because this is the period when most piglet deaths occur (Farmer, 2022). Providing targeted care during the first week of life, including ensuring the successful onset of lactation, when sow-piglet interactions are crucial, has the potential to improve piglet growth and overall performance up to weaning.

All this knowledge should contribute to a framework that supports the development of statistical learning models, including machine learning algorithms, capable of identifying piglets at higher risk. Incorporating new inputs into these models should enhance their

classification ability, particularly when such inputs capture meaningful differences among piglet categories based on their future growth performance and survivability. Improving these approaches would be highly valuable both for on-farm decision-making and for evaluating the impact of specific management practices or nutritional interventions aimed at key objectives, such as reducing the risk of low BW at various stages of the production cycle.

In summary, addressing growth restriction in pigs is not only a matter of enhancing biological performance but also of responding to broader economic, ethical, and environmental challenges. With global meat demand continuing to rise, and global pig meat consumption projected to increase over the next decade (OECD/FAO, 2025), the swine industry must simultaneously improve efficiency, reduce its environmental impact, and guarantee high welfare standards. The development of advanced risk assessment models for the early and accurate identification of vulnerable piglets, along with the implementation of effective and refined strategies to support those at greatest risk, represents a crucial step toward more sustainable production systems. This Ph.D. dissertation provides primary evidence and the initial steps toward the long-term goal outlined at the beginning of the Discussion section: to develop and implement timely, targeted intervention strategies for high-risk piglets, emphasizing the accurate identification of individuals with varying degrees of IUGR and the management of the most critical risk factors to maximize survival and growth.

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Chapter 9

Conclusions

Based on the results presented in Chapters 3 to 7 and their interpretation, the following conclusions were drawn:

1. Severely intrauterine growth restricted piglets, identified by their characteristic head morphology and lowest birth weights, exhibit impairments in postnatal growth, vitality, and survival. These deficits are primarily associated with limited energy reserves, altered metabolic profiles, gastrointestinal dysfunction, and reduced colostrum intake. However, classifying light piglets solely based on birth weight (threshold around 1.00 kg) fails to capture these metabolic and physiological differences and is therefore insufficient to distinguish the varying degrees of growth restriction that explain performance differences during lactation.
2. Assessing organ development and skeletal traits may help refine the classification of light piglets with differing degrees of growth restriction, as lighter piglets exhibit a lower relative brain weight and a higher proportion of low-density bones. Although these parameters are strongly correlated with both birth weight and external physical characteristics, the differences observed remain insufficient to accurately differentiate categories of light piglets using a threshold based solely on birth weight.
3. Body weight on day 7 is a stronger predictor of weaning weight than body weight on day 1, accounting for more than twice the proportion of explained variability ($R^2 > 0.60$ vs. $R^2 \approx 0.30$). A successful switch-on of lactation is therefore critical to support piglet growth from the first week of life through weaning and beyond.
4. The main factors influencing piglet survivability and early postnatal growth during the first week of life are body weight on day 1, the piglet's relative body weight within the litter on day 1, colostrum intake, and sow parity. A 100 g increase in body weight on day 1 reduces the odds of poor growth or compromised survival by approximately 27.6%. Critical thresholds for relative body weight on day 1 and for colostrum intake are estimated at approximately 0% and 250 g per pig, respectively.

5. Machine learning models (*i.e.*, random forest and boosting) consistently outperform parametric linear models in classifying lightweight pigs across all production stages, with increases in the area under the curve observable from the second decimal place onward. Their applicability is demonstrated in both purebred nucleus and commercial crossbred datasets.
6. The influence of body weight as a predictive factor increases the closer it is to the weight record of interest. Birthweight-related factors are the most important when classifying lightweight piglets at weaning, explaining more than 60% of the specificity space in all cases. At subsequent stages, these factors are replaced by the weight measurement immediately preceding each stage. Incorporating additional predictors into the models further increases the area under the curve across production stages.

Chapter 10

About the author

10.1 Scientific Peer Reviewed Publications

Casellas, J., **P. Salgado-López**, J. Lorente, I. S. Diaz, T. Rathje, J. Gasa, and D. Solà-Oriol. 2024. Classification of light Yorkshire pigs at different production stages using ordinary least squares and machine learning methods. *Animal*. 18. doi:10.1016/j.animal.2023.101047.

Salgado-López, P., J. Casellas, I. Solar Diaz, T. Rathje, J. Gasa, and D. Solà-Oriol. 2024. Applicability of machine learning methods for classifying lightweight pigs in commercial conditions. *Transl Anim Sci*. 8. doi:10.1093/tas/txae171.

Salgado-López, P., E. Llauradó-Calero, S. García-Vilana, D. Sánchez-Molina, A. Brun, M. Font-I-Furnols, J. Gasa, and D. Solà-Oriol. 2025. Evaluation of organ and skeletal physiological characteristics for improved classification of growth-restricted newborn piglets. *Sci Rep*. 15:34328. doi:10.1038/s41598-025-16687-x.

Suppi, J., **P. Salgado-López**, E. Llauradó-Calero, J. Coma, A. Pelegrí-Pineda, Y. Saco, A. Bassols, M. Farré, and D. Solà-Oriol. 2025. Faecal inflammatory biomarkers as non-invasive indicators of feed intake status in weaned piglets. *Animal*. 19. doi:10.1016/j.animal.2025.101684.

Salgado-López, P., K. N. Gaffield, M. D. Tokach, J. Coma, J. Gasa, M. Farré, and D. Solà-Oriol. 2025. Early-life risk factors predicting growth retardation and mortality in pigs: a multi-criteria approach. *J Anim Sci*. doi:10.1093/jas/skaf402.

Huenul, E., S. M. Martin-Orúe, L. Fabà, R. Forsten, **P. Salgado-López**, M. J. Rodríguez-Lagunas, F. Llobet-Cabau, M. Fornós, and J. F. Pérez. 2025. Early-Life Stages Impact Later Feeding Behavior and Metabolic Status in Light-Born Piglets. *J Anim Sci*. doi:10.1093/jas/skaf437.

10.2 Scientific Publications Currently with Journal Editors

Salgado-López, P., J. Suppi, K. N. Gaffield, M. D. Tokach, J. Coma, J. Gasa, and D. Solà-Oriol. 2025. Linking the Degree of Intrauterine Growth Restriction to Alterations in Metabolism, Energy Reserves, and Gut Health in Newborn Piglets. *Submitted to Journal of Animal Science*.

10.3 Conference Oral Presentations

Salgado-López, P., P. Aymerich, J. Gasà, J. Casellas, and D. Solà-Oriol, 197 Evaluating the Associations Between Piglet's Characteristics at Birth and Growth Performance During Lactation Period on Piglets from Hyperprolific Sows, *Journal of Animal Science*, Volume 101, Issue Supplement_2, November 2023, Pages 235–236, <https://doi.org/10.1093/jas/skad341.266>

Salgado-López, P., E. López, P. Aymerich, J. Gasà, and D. Solà-Oriol. 2023. Efectos de incrementar los días de transición en cerdos de bajo peso al destete. XX Jornadas de Producción Animal AIDA. June 13-14- Zaragoza, Spain.

Salgado-López, P., P. Aymerich, F. Llobet-Cabau, A. Castelló, J.M. Folch, J. Gasà, and D. Solà-Oriol, 25. Umbilical cord gene expression in newborn piglets with different birth body weight and lactation growth, *Animal - science proceedings*, Volume 14, Issue 7, 2023, Pages 839–840, ISSN 2772–283X, <https://doi.org/10.1016/j.anscip.2023.09.026>.

Salgado-López, P., E. Llauradó-Calero, J. Gasà, and D. Solà-Oriol. 2025. Caracterización del desarrollo de órganos y esqueleto en lechones con diferente conformación corporal al nacimiento. XXI Jornadas sobre Producción Animal AIDA. June 3-4. Zaragoza, Spain.

Salgado-López, P., J. Suppi, C. Soldevila, J. Gasà, and D. Solà-Oriol, 247 Impact of lactation growth on individual piglet's entry into solid feed consumption and its implications for post-weaning growth, *Journal of Animal Science*, Volume 103, Issue Supplement_1, May 2025, Pages 242–243, <https://doi.org/10.1093/jas/skaf102.265>

Salgado-López, P., J. Coma, M. Farré, J. Gasà, and D. Solà-Oriol. 2026. Identifying early-life risk factors for predicting pig survival and growth in commercial farms. 2026 Midwest Section Meeting. March 8-11. Omaha, Nebraska, USA.

Salgado-López, P., J. Suppi, J. Coma, J. Gasà, and D. Solà-Oriol. 2026. Changes in metabolism, energy reserves, and gut health in newborn piglets with different degrees of intrauterine growth restriction. 2026 Midwest Section Meeting. March 8-11. Omaha, Nebraska, USA.

Salgado-López, P., J. Bonet, C. Soldevila, J. Coma. 2026. Effects of reducing dietary energy density by modifying fat or fiber inclusion on growth performance and carcass characteristics of finishing pigs. 2026 Midwest Section Meeting. March 8-11. Omaha, Nebraska, USA.

Salgado-López, P., J. Bonet, C. Soldevila, J. Coma. 2026. Effects of wheat middlings inclusion, grinding, and carbohydrase supplementation in isoenergetic diets on growth performance and carcass characteristics of grow-finish pigs. 2026 Midwest Section Meeting. March 8-11. Omaha, Nebraska, USA.

10.4 Conference Poster Presentations

Salgado-López, P., P. Aymerich, J. Gasa, and D. Solà-Oriol. 2023. Intestinal gene expression patterns reveal differences between low-birthweight piglets with different degrees of growth restriction. 14th European Symposium of Porcine Health Management. May 31-June 2. Thessaloniki, Greece.

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10.5 Technical Reports

Salgado-López, P., and D. Solà-Oriol. 2025. Eficiencia en riesgo: Comprendiendo el impacto de los lechones de bajo peso al nacer en la producción porcina actual. *Revista porciNews*.

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10.6 Awards

International Australasian Pig Science Association (APSA) Travel Scholarship Award. 19th biennial Australasian Pig Science Association Conference. November 13-16, 2023. Brisbane, Australia.

