Universitat Autònoma de Barcelona

TESIS DOCTORAL

# Investigación epidemiológica sobre pacientes nonagenarios no traumáticos intervenidos de urgencia

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*A mi familia,*

*a Victoria y  a Francisco*

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Vista la instància presentada per en/na Andrés Pelavski Atlas de sol·licitud de presentació de tesi doctoral com a compendi de publicacions,

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**RESOLC**

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- Pelavski, A.; Lacasta, A. [*et al.*] "Mortality and surgical risk assessment among the extreme old undergoing emergency surgery". A: *The American Journal of Surgery* (acceptat per a publicació).
- Pelavski, A.; Lacasta, A. [*et al.*] "Observational study of nonogenarians undergoing emergency, non-trauma surgery". A: *British Journal of Anaesthesia* (2011; 106:189-193).

La publicació següent podrà formar part de la tesi com a annex o part no fonamental, tot i que els treballs fets en aquesta publicació es poden comentar en la discussió de resultats.

- Pelavski, A.; Miguel, M. de [*et al.*] "Perioperative transfusion in nonagenarians undergoing non-elective, non-traumatic surgery" (en revisió).

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# 1. INTRODUCCIÓN

Junto con Japón y Suecia, España es uno de los países con mayor esperanza de vida. Si esta tendencia continúa, la mayoría de los niños nacidos a partir del año 2000 vivirán para celebrar su centenario.[1] No es necesario, sin embargo, proyectar un futuro tan lejano; durante las últimas décadas el segmento poblacional que más se ha desarrollado es el de las edades más avanzadas (mayores de 85 años). Tanto es así que la representación tradicional de la distribución de la población con forma piramidal está cambiando, y está adquiriendo una forma trapezoidal/rectangular. En ella, el numero de individuos jóvenes es cada vez más similar al de los ancianos.[2] Así pues, en los últimos años la OMS (Organización Mundial de la Salud) ha dividido a la población anciana en dos categorías: la tercera edad o ancianos

jóvenes (de 65 a 85 años), y la cuarta edad o ancianos añosos, (mayores de 85 años).[1,3]

Todos estos cambios demográficos plantean desafíos en el área de la salud a distintos niveles: desde un punto de vista económico, la cuarta edad consume –en forma progresiva- recursos cada vez más escasos.[4] Desde un punto de vista social surgen problemas discriminatorios y en los hospitales se alude a estos pacientes como 'bloqueadores de camas',[5] o se habla de 'ageism'.[6] En esta misma esfera social también se plantean los problemas de dependencia y de carga familiar. Otros dilemas, cuyas soluciones son aún más complejas, surgen en el plano ético: las cuestiones sobre cuánto debe prolongarse la vida, o hasta qué punto se debe evitar la mortalidad sin tener en cuenta la morbilidad son fundamentales y sus respuestas, muy controvertidas.[5,7] Finalmente, desde la perspectiva médica, el principal problema con esta población es la falta de conocimiento: se estudian mucho más las enfermedades relacionadas con la vejez, que a los pacientes ancianos como grupo individual y con características propias.[8]

Para intentar comprender el alcance, la interacción y las consecuencias de este conjunto de factores en los pacientes ancianos añosos, es útil recurrir a una definición del envejecimiento. Tal definición pretende articular los hallazgos clínicos y patológicos con las realidades económica y social de estos pacientes, a fin de conseguir una visión

más general de los problemas que se plantean, y poder ofrecer así una aproximación terapéutica integral.

## 1.1 Definición de envejecimiento

Desde el punto de vista biológico, el envejecimiento se ha definido como la pérdida de la *entropía*, de la *homeostasis,* y de la *fractalidad.*[9] La *entropía* refleja la habilidad de un sistema para generar energía; consecuentemente, el descenso en su producción ocasiona un declive progresivo en la capacidad de un individuo para funcionar independientemente y soportar el estrés. La *homeostasis*, a su vez, está relacionada con el poder autorregulatorio de un sistema, es decir, la capacidad de regresar a sus condiciones basales después de su alteración. De esta manera, la desregulación de ciertos parámetros como la tensión arterial, la glicemia, la cortisolemia –característicos de la vejez- son utilizados en los estudios de 'carga alostérica' –junto con otros parámetros (en total 12)- para calcular la edad fisiológica.[10] Por último, la *fractalidad* es la capacidad de un organismo de generar fractales. Los fractales son unidades que se ramifican y se dividen en subunidades menores del mismo tipo, cuyo número y longitud son impredecibles. Los fractales pueden ser estáticos, como la ramificación progresiva del sistema bronquial, vascular, nervioso; o dinámicos, como la maduración y diferenciación progresiva del sistema hematopoyético a partir de células pluripotenciales. Tanto los

fractales estáticos como los dinámicos mantienen la funcionalidad del cuerpo humano. Resulta evidente que ni la entropía ni la fractalidad son cuantificables, sólo la homeostasis se podría medir a través de la carga alostérica. Por lo tanto no existen tests de laboratorio para determinar la edad fisiológica de una persona. De todos modos, sí es manifiesto que el declive de estos tres aspectos biológicos tienen su correlato clínico y social en estos pacientes.

En efecto, sólo contamos con la definición clínica (que es más una valoración que una definición) para cuantificar el grado del envejecimiento; y esta se basa en la evaluación de ciertas funciones –incorporadas al 'Comprehensive Geriatric Assessement'-[11] que característicamente declinan con la edad. Entre ellas están la fragilidad, la dependencia, la disminución de la reserva funcional, el deterioro cognitivo, la mayor incidencia de comorbilidades y la polifarmacia. Ninguna de ellas es, en forma aislada, diagnóstica de envejecimiento, sino la combinación de varias dan la pauta del grado de deterioro que acompaña al proceso. En cualquier caso, las definiciones de envejecimiento resultan algo vagas, y en consecuencia, los estudios en ancianos se basan en la edad cronológica, y no en el declive clínico-biológico. Aún así, como se mencionó más arriba, los estudios en pacientes de la cuarta edad son escasos; hasta tal punto, que se trata a este grupo poblacional extrapolando las conclusiones obtenidas en estudios con pacientes más jóvenes y más sanos.[12] Este fenómeno resulta aún más paradójico

teniendo en cuenta que estos pacientes requieren cuidadados médicos y cirugía en forma más frecuente –proporcionalmente- que los individuos más jóvenes.[13]

Todas estas cuestiones se ponen particularmente en evidencia con la patología de urgencia;[14] especialmente con la patología quirúrgica urgente. Aunque existe cierta bibliografía sobre el colectivo de pacientes nonagenarios con fractura de cadera,[15-19] todo el resto de cirugía urgente en esta población no ha recibido tanta atención. La mayoría de trabajos realizados en nonagenarios y centenarios o bien tratan la patología traumática, o bien son series retrospectivas.[19,20] Por otro lado, los pocos estudios prospectivos que existen suelen incluir tanto procedimientos programados como urgentes.[12] Es decir, prácticamente no se ha investigado en forma prospectiva a la población "anciana añosa" que requiere cirugía no traumática urgente.

## 1.2 Justificación de la unidad temática de la tesis

Es sabido que uno de los factores más importantes que empeora el pronóstico de la cirugía en pacientes ancianos, es el hecho de que sea urgente.[21] Más aún, en muchas ocasiones, se decide operar en forma urgente a pacientes cuya cirugía se descartaría en una situación programada; especialmente en cirugía intra-abdominal y vascular.[21] Es por esto que resulta particularmente importante estudiar las características demográficas de esta población. Algunas revisiones han

intentado entender y explicar el *cómo* y el *por qué* de los cambios asociados a la edad, y su relevancia en el período perioperatorio.[22,23] Sin embargo, una de las áreas prioritarias de investigación actual es cuantificar cuáles son las consecuencias de esos cambios. Es decir, conocer en qué condiciones concretas llegan estos enfermos al quirófano, determinar la prevalencia real de comorbilidades en estos enfermos, saber cuáles son las intervenciones más frecuentes, disponer de cifras de morbi-mortalidad, y desarrollar herramientas para valorar el riesgo quirúrgico.[24]

El presente trabajo considera a los pacientes nonagenarios intervenidos de urgencia como un grupo poblacional específico, individual y con características propias. A fin de analizar en profundidad ciertos aspectos del mismo, se ha dividido el estudio de esta población en 3 ejes temáticos: en primer lugar se presenta un análisis demográfico preliminar que define la situación actual. A continuación, una evaluación del riesgo quirúrgico y de las diferentes herramientas existentes para valorarlo en estos pacientes. Por último, se realiza una descripción de la política transfusional perioperatoria, y un análisis de los factores asociados a la transfusión. En definitiva, la población de pacientes nonagenarios intervenidos de urgencia de cirugía no traumática constituye el hilo conductor que da unidad temática al presente trabajo. De esta población se realiza una descripción demográfica exhaustiva; y se plantean dos cuestiones controvertidas y prioritarias para su manejo perioperatorio: una

relacionada con el riesgo quirúrgico; y la otra con la práctica transfusional.

### 1.3 Análisis demográfico preliminar

Si bien intuitivamente parece evidente que los pacientes nonagenarios tienen mayor riesgo para la cirugía de urgencias que el resto de la población, no está claro cuál es la morbilidad y la mortalidad real de estos pacientes. En consecuencia, la evaluación del riesgo/beneficio resulta sumamente subjetiva, y muchas veces no queda claro si la morbi-mortalidad asociada al procedimiento, sumada a la ya de por si reducida esperanza de vida, justifica la intervención. Más aún, ni siquiera está bien documentado cuáles son las patologías no traumáticas que suelen requerir cirugía urgente en este grupo etario, ni cuáles los procedimientos más frecuentes.

Por ello, el estudio demográfico descriptivo se ha planteado en términos de: estado basal de estos enfermos (edad, sexo, ASA, patologías asociadas), diagnósticos y procedimientos más frecuentes (se han dividido según las especialidades quirúrgicas, y se ha analizado también la técnica anestésica), y resultados postquirúrgicos. En esta categoría se han analizado la estancia hospitalaria, la morbilidad (las complicaciones más prevalentes en el postoperatorio inmediato) y la mortalidad durante los primeros 30 días después de la intervención.

El conocimiento sobre el tiempo medio de estancia hospitalaria, los diagnósticos y las intervenciones más frecuentes es fundamental para la planificación de los recursos. El análisis sobre la incidencia y el tipo de complicaciones, junto con la determinación de la tasa de mortalidad resultan útiles, no sólo para la planificación, sino también para tomar decisiones basadas en la evidencia científica, y no en la mera intuición.

### 1.4 Riesgo quirúrgico

Mucho se ha insistido sobre el riesgo quirúrgico de estos enfermos, sin embargo, ninguna de las escalas existentes para valorar dicho riesgo ha sido probada en nonagenarios. La clasificación de la ASA (American Society of Anaesthesia) es sin duda un herramienta útil, pero poco específica, y no tiene en cuenta ni la edad, ni el tipo de cirugía, datos particularmente importantes en este tipo de pacientes. El POSSUM (Physiological and Operative Severity Score for the enUmeration of the Mortality and morbidity) fue desarrollado originalmente como una herramienta para medir calidad, y utilizado para auditar y comparar los resultados de la práctica quirúrgica en distintos centros.[25] Sin embargo, recientemente se ha sugerido su utilización como escala para medir el riesgo quirúrgico.[26,27] La ventaja principal del POSSUM consiste en ser una escala sencilla y precisa en muchos tipos de cirugía no cardíaca.[28,29]

Dado que se demostró que el POSSUM sobreestimaba la mortalidad en pacientes con bajo riesgo, se ha desarrollado el P-POSSUM (Portsmouth POSSUM) que, utlizando las mismas variables pero cambiando la ecuación, demostró tener un poder de predicción más preciso.[30] Siguiendo este ejemplo, han aparecido otras escalas basadas en el POSSUM, algunas específicas para ciertas especialidades quirúrgicas. Últimamente, también se ha publicado un E-POSSUM (Elderly POSSUM) específico para pacientes mayores de 65 años intervenidos de cirugía colorrectal.[31] La novedad que ofrece esta escala en relación con las demás, aparte de una ecuación diferente para determinar el riesgo quirúrgico, es una estratificación más detallada de la edad. El POSSUM original, y todos los scores que surgieron a partir de él distinguían 3 grupos etarios: pacientes menores de 61 años, entre 61 y 70 años, y mayores de 70; a los que atribuían los coeficientes de 1, 2, y 4 respectivamente. El grupo de Tran Ba Loc, basados en la clasificación de la OMS, validaron para el E-POSSUM un grupo de edad extra; el de los mayores de 85 años, a los que atribuyeron un coeficiente de 8. De esta manera, el E-POSSUM considera a la cuarta edad como una categoría separada y con mayor riesgo.

Independientemente del POSSUM, Donati y colaboradores han publicado otro sistema diferente, basado principalmente en la edad y

en el ASA; que también ha sido validado para estimar el riesgo quirúrgico.[32]

Sin embargo ninguna de estas escalas ha sido probada en esta población, que presumiblemente tiene un riesgo quirúrgico elevado; ni se ha demostrado si alguna de ellas podría resultar útil para valorar el riesgo quirúrgico de estos pacientes nonagenarios intervenidos de urgencia de cirugía no cardíaca ni traumática. Es por esto que en el presente trabajo se ha valorado cada score individualmente, a fin de determinar la precisión de cada uno para predecir la mortalidad de esta población.

Una herramienta que pueda pronosticar –con una cierta confianza- el riesgo quirúrgico, según el tipo de paciente y el tipo de cirugía resultará sumamente útil desde un punto de vista práctico a la hora de tomar las decisiones; desde una perspectiva ética facilitará una evaluación basada en la evidencia científica acerca de cuáles serían las consecuencias de determinada conducta terpeútica; y, por otro lado, permitirá –a la hora de informar a los pacientes y sus familias- que estos tomen una decisión consciente, y den un consentimiento fundado en el conocimiento de las consecuencias más probables.

## 1.5 Política transfusional

Otro aspecto importante del tratamiento perioperatorio de estos enfermos, que –dadas las peculiaridades de la urgencia- suelen llegar a quirófano en condiciones subóptimas, es el de la política transfusional. Al igual que con las características demográficas de la población, escasean los datos relativos a este tema. En efecto, hay cierta bibliografía con alusiones a la anemia en la población añosa sana,[33,34] algún trabajo relativo a las transfusiones en los pacientes de este colectivo con fractura de cadera.[18,35] Pero, nuevamente, no existen datos acerca de las características transfusionales de los nonagenarios operados de urgencia de cirugía no traumática. Más aún, debido a la escasez de evidencia científica de clase I (estudios prospectivos randomizados), las guías clínicas sólo se limitan a sugerir determinadas prácticas. De hecho la ASA (Sociedad Americana de Anestesiología) directamente no menciona a los pacientes de edad avanzada en sus guías de práctica transfusional.[36] La Asociación de Anestesiólogos de Gran Bretaña e Irlanda (AAGB&I) es un poco más concreta al respecto y establece una hemoglobina de 8 g/dl como umbral transfusional para los ancianos.[37] Sin embargo, no distingue entre pacientes de 3º y 4º edad. La Sociedad Española de Transfusión Sanguínea (SETS) es un poco más concreta al definir a la población, pero utiliza un umbral más restrictivo de 7g/dl.[38] Finalmente, la Sociedad Navarra de Salud sugiere una política intermedia entre las sugerencias británicas y las españolas. Establece unos niveles preoperatorios deseables de 8-9 g/dl de hemoglobina para pacientes mayores de 70 años.[39]

Por otro lado, los criterios para decidir la reserva de sangre preoperatoria (cross-match) no están claros en los pacientes nonagenarios, y ciertos estudios señalan la edad como factor individual e independiente que aumenta el riesgo transfusional.[40,41] En consecuencia, no es infrecuente que se cruce sangre innecesariamente en pacientes de esta población que van a ser intervenidos en forma urgente.[42]

Por consiguiente, el tercer eje temático de este estudio está dedicado a la política transfusional. Se ha realizado un análisis observacional descriptivo para caracterizarla; se ha desarrollado un modelo de regresión logística para dilucidar los factores predictivos de las transfusiones en estos pacientes, a fin de poder desarrollar a posteriori una política más racional para el cross-match; y por último, se han comparado las características transfusionales de los nonagenarios con las de una población control de ancianos jóvenes. Es decir, pacientes en la tercera edad que fueron intervenidos durante el mismo período de las mismas cirugías.

La aplicabilidad de esta información es, indudablemente, una utilización más racional de los recursos. El conocimiento de los factores asociados a la transfusión en esta población reducirá el cruce de sangre indiscriminado en estos pacientes; y con ello, el gasto. Por

otro lado, tanto desde el punto de vista clínico, como desde una perspectiva logística será interesante saber si la idea intuitiva de que los pacientes más ancianos se transfunden más[43] es verdadera o no.

# 2. OBJETIVOS

## 2.1 Objetivo general:

Avanzar en el conocimiento de las características distintivas, particulares y específicas de los pacientes nonagenarios intervenidos de urgencia de cirugía no traumática

## 2.2 Objetivos específicos

2.2.1 Describir las características demográficas de dichos pacientes en términos de patología asociada más prevalente, diagnósticos y tipos de intervención más frecuentes, estancia hospitalaria, incidencia de complicaciones postquirúrgicas y mortalidad postoperatoria.

2.2.2 Valorar el riesgo quirúrgico a partir de la tasa de mortalidad postoperatoria a 30 días; y analizar individualmente la exactitud de cada una de las siguientes escalas –POSSUM, P-POSSUM, E-POSSUM, Donati- para medir el riesgo quirúrgico en esta población.

2.2.3 Caracterizar la política transfusional en estos pacientes a fin de determinar la incidencia de la transfusión perioperatoria, y los principales factores predictores de dichas transfusiones. Asimismo, comparar los hallazgos acerca de la política transfusional en pacientes de la 4º edad, con pacientes de la 3º edad.

# 3. PLAN DE TRABAJO

Esta tesis ha sido realizada por compilación de 3 artículos que dan respuesta a cada uno de los objetivos específicos:

1. Observational study of nonagenarians undergoing emergency, non-trauma surgery. *Br J Anaesth 2011; **106**: (2) 189-93*

2. Mortality and surgical risk assessment among the extreme old undergoing emergency surgery *Am J Surg*
*doi:10.1016/j.amjsurg.2012.03.008*

3. Anaemia and transfusion in nonagenarians undergoing emergency, non-traumatic surgery**:** a prospective observational study

Los primeros dos artículos han sido aceptados para su publicación en revistas internacionales, y el tercero está en proceso de revisión

## 3.1 PUBLICACIONES QUE COMPONEN EL CUERPO DE LA TESIS DOCTORAL

### 3.1.1 Análisis demográfico:

Observational study of nonagenarians undergoing emergency, non-trauma surgery

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BJA

# Observational study of nonogenarians undergoing emergency, non-trauma surgery

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## Editor's key points

- This mono-centre observational study describes general caracteristics of a nonagenarian population requiring emergency surgery.
- Surgery was for acute limb arterial thrombosis, incarcerated hernia, and bowel occlusion.
- Confusion, renal failure, and abdominal problems were frequent causes of morbidity.
- Abdominal complications, pulmonary oedema, aspiration, stroke, and renal failure were associated with mortality.

**Background.** Nonagenarian population is growing, and so is the number of them needing emergency surgery. Yet, their treatment is often based on the outcomes of younger patients: although old age is known to be a risk factor for surgery, its level is not clear. This is a prospective, observational study to describe the population. It is aimed at providing quantified scientific evidence of the current procedures and their outcomes.

**Methods.** All non-traumatic nonagenarians who underwent surgery between July 2006 and September 2010 in our University Hospital were recruited and followed up over a month after discharge. A descriptive statistical analysis was performed.

**Results.** Of the approximately 12 660 surgical emergencies, 102 were nonagenarians: 69.6% were women, who mostly had an ASA score III (62.7%). Perioperative morbidity and mortality rates of 61.8% [95% confidence interval (CI): 52.33–71.19%] and 35.3% (95% CI: 26.01–44.57%), respectively, were found statistically associated with preoperative neoplasms. The most frequent causes of surgery were acute limb arterial thrombosis (20), incarcerated hernia (17), and bowel occlusion (14). Confusion, renal failure, and abdominal problems accounted for the most frequent causes of morbidity. Among them, abdominal complications, cardiogenic pulmonary oedema, aspiration, stroke, and renal failure were associated with mortality.

**Conclusions.** The study gave scientific support and actual figures to many intuitive beliefs: morbidity and mortality are high and are associated with many preoperative comorbidities. All this, combined with an already reduced life expectancy, and a presumably low physiological reserve makes these patients particularly vulnerable to emergency surgery.

Keywords: aged, 80 and over; emergencies; surgical procedures, operative

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Nonagenarians are still a small but rapidly emerging population. Although their surgical rates have notoriously increased during the last few decades,[1] much of their medical and surgical treatment depends on the experience and results of treating younger patients.[2] Furthermore, emergency surgery is carried out more frequently on the elderly than on younger generations, and often in cases where elective surgery might appear unreasonable.[3 4] Nevertheless, most published work dealing with emergencies among 90-yr-olds is based on hip fracture cohorts,[4–8] whereas information about all other kinds of emergency procedure is scarce.

Not surprisingly, these patient characteristic changes are raising some controversial issues: it is clear that the benefits of surgical treatment should always be balanced against nonagenarians' morbidity and mortality rates, as well as their generally shorter life expectancy. However, apart from the general idea that old age is a risk factor for emergency surgery, little is known from literature. In addition, strong economic and ethical concerns have been pointed out.[3]

As a result, we performed a prospective, observational study in order to understand the current situation. Our aim was to describe the main characteristics of this population in terms of basal status, types of surgery, and perioperative outcomes. With this information, the decision as to whether surgery is the best available treatment can be based on actual figures and not on mere intuitive speculation. We concentrated on non-traumatic patients because the need for surgical repair has been well established in hip fractures.[4 5]

## Methods

The study was conducted between July 2006 and September 2010 in Vall d'Hebron University Hospital, one of the largest hospitals in Barcelona, Spain, which provides medical and surgical care for residents of the city and its surroundings. One of its three major departments, the General Care Hospital, has 643 beds. In its two emergency operating theatres (OTs), an average of 3100 patients annually undergo surgery.

From them, we recruited all patients aged 90 yr and above who underwent an emergency surgical procedure during the study period. Only information from the initial operation on each individual was included in the analysis. Colonoscopies, bronchoscopies, and other diagnostic procedures unattended by anaesthetists were excluded.

The senior anaesthetist on call interviewed each patient before entering the OT. Baseline characteristics and preoperative medical conditions were registered, and patients were classified according to the American Society of Anesthesia (ASA) score. In addition, we asked for a contact telephone number in order to enable the follow-up after discharge.

Information about the major diagnosis, surgical procedures, and anaesthetic technique was collected. We considered every new disease or complication derived from the surgical procedure as postoperative morbidity, if it occurred during admission or within 30 days after discharge. To define them, we used the criteria established in the POSSUM score.[9] Deaths that occurred during that same period were recorded as perioperative mortality. Every complication was diagnosed by the investigators involved in the study, except for postoperative confusional states (confusion, disorientation, and delirium). Because of their sudden and unpredictably transient nature, the surgeon in charge diagnosed and registered these states when the patients were in the ward, and the anaesthetist on call, when the patients were in the post-anaesthesia care unit.

A descriptive statistical analysis was performed with SPSS 11.0. Absolute frequencies, percentages, and 95% confidence intervals (95% CI) were calculated for categorical variables; means, SDs, and 95% CI, for continuous ones. The statistical relation between qualitative variables was studied with Pearson's $x^2$ test, or Fisher's exact test when necessary. Mantel and Hanzel's $x^2$ was used to assess linear association. In all cases, a two-tailed P-value of , 0.05 was considered evidence not attributable to chance.

## Results

A total of 119 nonagenarians were operated on in the emergency OT of the General Care Hospital during the study period (about 0.90% of the total emergency surgery volume). Of them, nine were placed an emergency pleural drain, and eight patients were referred to another hospital immediately after the procedure (they had all undergone a limb embolectomy to treat acute arterial thrombosis). Consequently, results are based on the 102 patients who could be followed up.

There were 71 (69.6%) females and 31 (30.4%) males, with a median age of 92 yr (range 90–100). Sixty-four patients (62.7%) were categorized as ASA III, whereas only seven (6.9%) were ASA IV and the rest, 31 patients (30.4%), ASA II. The overall mean hospital length of stay was 10.6 (7.4) days (there was no significant difference in the length of stay between those who died in hospital and those who survived until discharge, P¼0.97). Preoperative interviews showed that they had a median of four comorbidities per patient (range 1–12). The main findings concerning morbidity and mortality are shown in Table 1.

As far as preoperative conditions are concerned, Table 2 shows the main comorbidities and their frequencies. A statistically significant increase in postoperative morbidity (P¼0.02) and mortality rates (P¼0.001) was only demonstrated in patients who had a neoplasm. In addition, we found a higher morbidity rate (P¼0.03) in patients who had a history of stroke, and a tendency towards higher morbidity (P¼0.053) in patients with myocardial ischaemia. As expected, higher ASA scores were linearly associated with higher morbidity (P¼0.005) and mortality (P¼0.006) rates.

Data regarding the distribution of patients according to their diagnosis and procedures are shown in Table 3. Interestingly, the most common diagnoses were incarcerated hernia (17 patients), acute arterial thrombosis of a limb (20 patients), and intestinal occlusion (14 patients). Altogether, they accounted for 50% of all the diagnosis. Only mortality rates of general and vascular surgery should be considered in the analysis, as the 95% CI of all other specialities resulted too wide to draw any conclusion.

Regarding anaesthesia, few cases required unusual techniques for the procedure: one of the colectomies and one

Table 1 General findings

| | Number of patients (%) | 95% CI |
|---|---|---|
| Morbidity | 63 (61.6) | 52.33–71.19% |
| Need to re-operate | 7 (6.9) | 1.95–11.76% |
| In-hospital mortality | 30 (29.4) | 20.56–38.25% |
| Mortality after discharge | 5 (4.9) | 0.71–9.09% |
| Need to be readmitted to hospital | 14 (13.7) | 7.04–20.40% |
| Total perioperative mortality | 36 (35.3) | 26.01–44.57% |

Table 2 Comorbidities

| Comorbidities | Number of patients (%) | 95% CI |
|---|---|---|
| Hypertension (HT) | 59 (57.8) | 48.25–67.42% |
| Atrial fibrillation (AF) | 37 (36.3) | 26.94–45.60% |
| Congestive heart failure (CHF) | 29 (28.4) | 19.68–37.18% |
| Cancer | 23 (22.5) | 14.43–30.66% |
| Dementia | 24 (23.5) | 15.30–31.76% |
| Chronic obstructive pulmonary disease (COPD) | 21 (20.6) | 12.74–28.43% |
| Diabetes (DM) | 21 (20.6) | 12.74–28.43% |
| Stroke | 19 (18.6) | 11.07–26.18% |
| Myocardial ischaemia (MI) | 16 (15.7) | 8.63–22.74% |
| Peripheral vascular disease | 15 (14.7) | 7.83–21.58% |
| Prostatic hyperplasia | 13 (12.7) | 6.27–19.21% |
| Chronic renal failure | 11 (10.8) | 7.76–16.8% |

Table 3 Distribution of patients according to surgical specialities, diagnosis, procedures, and outcomes. *Results are expressed as total number of patients and percentage calculated from the whole population. †Results are expressed as total number of patients and percentage calculated from the total speciality sample. ‡Plastic surgery, maxillofacial surgery, ENT

| Speciality* | ASA score† | Diagnosis* | Mortality† [n (%), 95% CI] |
|---|---|---|---|
| General surgery 56 (54.9%) | II 20 (35.7%) | Incarcerated hernia 17 (16.7%) | 24 (42.9%) |
| | III 33 (58.9%) | Occlusive syndrome 14 (13.7%) | 29.89–55.82% |
| | IV 3 (5.4) | Cholecystitis 12 (11.8%) | |
| | | Appendicitis 5 (4.9%) | |
| | | Intestinal perforation 5 (4.9%) | |
| | | Wound dehiscence, intestinal bleeding, or ischaemia 3 (2.9%) | |
| Vascular surgery 30 (29.4%) | II 7 (23.3%) | Acute arterial thrombosis 20 (19.6%) | 6 (20%) |
| | III 21 (70%) | Infected ischaemic wound/diabetic foot 10 (9.8%) | 5.69–34.31% |
| | IV 2 (6.7%) | | |
| Urology 11 (10.78%) | II 1 (9.1%) | Obstructive pyelonephritis 3 (2.9%) | 5 (45.4%) |
| | III 7 (63.6%) | Haematuria 7 (6.9%) | 16.03–74.88% |
| | IV 3 (27.3%) | Orchi-epididymitis 1(0.9%) | |
| Other specialities‡ 5 (4.9%) | II 2(40%) | Other diagnoses | 1 (20%) |
| | III 3 (60%) | | 0.58–76.49% |

of the bowel resections were carried out under epidural instead of general anaesthesia; and one of the hernioplasties with local anaesthesia and sedation. Similarly, for the periodontal abscess drainage, the anaesthetist decided to sedate the patient instead of using general anaesthesia.

Table 4 shows the main postoperative complications, the most frequent ones being confusion/delirium, renal failure, and abdominal complications (this category includes anastomotic leak, wound dehiscence, and persistent ileus).

The complications that were statistically associated with mortality in the bivariate analysis were cardiogenic pulmonary oedema ($P=0.003$), aspiration ($P=0.001$), renal failure ($P=0.016$), stroke ($P=0.03$), and abdominal complications ($P=0.001$). It should be underlined that only one of the patients who died as a result of cardiac complications had previously been diagnosed with heart disease; none of the patients who suffered aspiration were either demented or had a documented deglutition disturbance; furthermore, aspiration (mainly after abdominal surgery) never occurred during induction of anaesthesia. Finally, stroke was not associated with preoperative atrial fibrillation or neoplasms, and acute renal failure was associated—in only one patient—with previously known chronic renal failure. There were two other complications associated with death, respiratory insufficiency ($P=0.042$) and sepsis ($P=0.003$). On the other hand, confusional states were registered mainly in patients who had a previous diagnosis of dementia (16 cases).

Table 4 Postoperative morbidity and mortality

| Complication | Number of patients (%) | 95% CI |
|---|---|---|
| Acute postoperative confusional states | 18 (17.6) | 10.24–25.04% |
| Acute renal failure | 16 (15.7) | 8.63–22.74% |
| Abdominal complications | 14 (13.7) | 7.04–20.40% |
| Acute cardiogenic pulmonary oedema | 10 (9.8) | 4.03–15.57% |
| Sepsis | 8 (7.8) | 2.62–13.06% |
| Urinary tract infection (UTI) | 6 (5.9) | 1.32–10.45% |
| Aspiration | 6 (5.9) | 1.32–10.45% |
| Pneumonia | 6 (5.9) | 1.32–10.45% |
| Stroke | 5 (4.9) | 0.71–9.09% |
| Haemorrhage | 5 (4.9) | 0.71–9.09% |
| Arrhythmia | 4 (3.9) | 0.15–7.69% |
| Wound infection | 4 (3.9) | 1.12–10.12% |
| Myocardial infarction | 3 (2.9) | 0.52–6.22% |
| Acute exacerbation of COPD | 2 (2.0) | 0.12–4.65% |
| Respiratory insufficiency | 2 (2.0) | 0.12–4.65% |
| Pulmonary embolism | 0 | — |

## Discussion

This is the first study to shed light on the condition in which nonagenarians undergoing emergency surgical procedures are admitted to hospital, and describes their most frequent diagnosis and procedures. Our main achievement was to measure and quantify their perioperative outcomes, that is, although old age had been recognized as an important risk factor, an actual figure is given here to morbidity and mortality rates. As a result, it could be a valuable tool when making decisions as to whether to operate on these patients or not. (Other factors, such as ethical concerns, must also be taken into account.)

Regarding the sample size, the low percentage of surgical nonagenarians in this series (0.90%) compared with others (about 5% in Mitsunaga's cohort),[10] is mainly due to the fact that all traumatic patients were excluded from this study and not from the others (hip fractures usually account for almost half of all surgical volume in this population).

As far as the baseline characteristics are concerned, the patients did not substantially differ from an equivalent but healthy population: Formiga and colleagues[11] presented in the Nona-Santfeliu study a sample of nonagenarians whose characteristics were similar to ours in both their sex distribution and comorbidity rates. Some comorbidities in this population, however, were 10% more frequent than those in Formiga's group (DM, MI, CHF, and COPD). Only stroke and dementia were virtually identical in both series. Furthermore, like the Nona-Santfeliu study and unlike the Danish 1905 cohort survey,[12] the number of comorbidities in these patients was correlated with mortality.

Most findings are difficult to compare or contextualize, as other published series are retrospective or include elective procedures: both Ackermann and colleagues[2] and Hosking and colleagues[13] report similar perioperative mortality rates for their emergency patients (19.8% and 17.4%, respectively), which are significantly lower than our 35.3%. Note, however, that they have included hip fractures in their results, and these have much lower mortality rates.[2 5–7] On the contrary, Adkins and Scout[14]—who did not include trauma cases—found a mortality rate for emergency procedures of about 43%. Again, their results are difficult to correlate with those presented here, as their study was published in 1984, when surgical and anaesthetic techniques were presumably less developed. Similarly, most diagnosis and procedures reported by Ackermann and colleagues[2] coincided with ours, but there was a significant difference in their frequencies. Like certain authors' reports,[13] intra-abdominal surgery had high mortality rates.

With respect to postoperative morbidity, the fact that most of the patients who suffered a fatal complication had not had a previously known history of that disease could be an indication of the low functional reserve among nonagenarians:[1 8 15] although their basal function might seem relatively normal, they lack the capacity to compensate for physiological or surgical stress. As a result, they can develop severe unexpected complications in the perioperative period.

A most unexpected finding was the lack of association between cognitive impairment and mortality. Other studies[13 16] pointed out dementia as a major independent predictor of mortality, whereas here it was only associated with postoperative confusional states. A possible explanation for this could be the difference in the study designs: this association was present in large cohorts of healthy patients followed up for years, and this conclusion only became clear after the second year.[11] In this study, where patients are only assessed during their immediate perioperative period, the influence of cognitive impairment on mortality is not evident. Nevertheless, from an ethical point of view, guidelines that determine the degree of cognitive impairment whereby aggressive procedures should be precluded would be very useful.

The main limitation to this study is the low number of patients; a larger sample would enable further stratification, and a multivariate analysis of risk factors. However, although the population is increasing, nonagenarians are still very few. Moreover, those who undergo emergency surgery are a further minority among this minority. Other limitations include: the rate of postoperative confusional states might be overestimated—especially for demented patients—because in most cases, the surgeon diagnosed it clinically. Also, due to the emergency setting, certain risk factors for postoperative mortality in the elderly surgical patients could not be checked.[17] Moreover, the population includes only those patients who actually underwent a surgical procedure, but not those where surgery was precluded because of their condition. As a result, we should take into account this selection bias when interpreting these findings.

To sum up, we should bear in mind, when treating these patients, that their morbidity and mortality rates are high even for simple procedures, and that although cognitive impairment is not associated with immediate perioperative mortality, it does reduce the already short life expectancy. Considering the rapid increase of their number, and the amount of healthcare resources they consume,[17] understanding the current situation of this population should help in making conscientious decisions, and also in planning future strategies within the Health Care System.

## Conflict of interest

None declared.

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### 3.1.2 Riesgo Quirúrgico:

Mortality and surgical risk assessment among the extreme old undergoing emergency surgery

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**Abstract:**

Background: Although longevity is becoming frequent, there are no scores to assess nonagenarians undergoing emergency surgery. This prospective observational study determines the 30-day mortality; and the individual performance of POSSUM and other scores in predicting their risk of death.

Methods: 126 patients were included (2006 -2011) and followed up for 30 days. We calculated their risk of death with different scores. The accuracy of each score was assessed with exponential and linear methods, and with the area under the receiver operating characteristic (ROC) curve (AUC).

Results: Overall mortality was 34.9%. The POSSUM, with a modification in the age category (modPOSSUM) had an AUC of 7.1 and a ratio of observed to predicted deaths of 1.07 and 1.22 respectively in the linear and exponential analysis.

Conclusion: In a population with as high a risk as nonagenarians, the modPOSSUM proved accurate to audit surgery and assess the mortality risk.

**Key words:**

Aged, 80 and over; Emergency medicine; Risk assessment; Surgical procedures;; operative

**Short Summary**: The population is ageing, but very little is known about the extreme old. This prospective observational study shows that their mortality is high and POSSUM score is a valuable and accurate tool to assess nonagenarians undergoing emergency surgery.

## Introduction

Longevity is becoming less and less exceptional, and accordingly the number of nonagenarians is increasing. So much so, that some authors have started to distinguish between third age or young old (65-84 years old), and fourth age or oldest old (>85 years old).[1] This emergent segment of the population poses serious challenges to the medical team, as information about them is still scarce. Furthermore, it is sometimes difficult to decide whether emergency surgery in these patients is a viable option, because there are no validated tools to audit the surgical outcomes, or to assess their mortality risk.

The Physiological and Operative Severity Score for enUmeration of Mortality and morbidity (POSSUM) was first developed to audit surgical practice[25], and has recently been suggested as a useful tool to assess risk.[26,27,56] Based on the variables analysed by the POSSUM (see appendix), a number of other scoring systems –some of them specific for certain specialities- have been described. Among them, the Portsmouth POSSUM (P-POSSUM), introduced by Whiteley and co-workers[30], proved to predict deaths better than POSSUM, especially for patients with low risk.[26,30,57] The Elderly POSSUM (E-POSSUM), on the other hand, succeeded in predicting mortality and morbidity in elderly patients (older then 65 years old) undergoing colorectal surgery.[31] Furthermore, another age based system, the Donati score[32] (see appendix), is also in use to assess operative risk. It has some advantages over the POSSUM-based ones; namely, it requires fewer variables, and they can all be assessed preoperatively. However, none of these scales have been tested in nonagenarians, a particularly vulnerable population, with many commorbidities and high risk, a risk that becomes even higher when they need emergency surgery.[8]

This study aims to determine the 30-day mortality rate in nonagenarians undergoing emergency surgery, in order to assess the individual performance of each of the above mentioned scores in predicting the risk of death.

## Materials and methods

*Patients:* The study was conducted in the general surgical area of our Tertiary Care University Hospital, between July 2006 and February 2011. We prospectively recruited all patients aged 90 yrs and above undergoing emergency surgery. Hip fracture repairs, and other orthopaedic procedures are normally performed in a separate trauma area; therefore, these patients were excluded. For those individuals who were admitted to hospital more

than once during the study period, the analysis only includes information about their first admission. As a matter of fact, most patients who had to be readmitted to hospital, did it within a short time period, and for a reason related to their first admission. As a result, unless they underwent another surgical procedure (in which case the POSSUM related scores take it into account), we did not consider the second admission independently.

To calculate the sample size we used the equation needed to estimate a proportion:

$(Z_\alpha^2 * p * q)/d$

where $Z_\alpha$ is the confidence coefficient (1- α), i.e 1.96 (for a confidence level of 95%). *p* is the expected proportion, we assumed an expected proportion of 30% for the 30-day mortality rate (we estimated this value with data from other series[15] and our own preliminary descriptive demographic study of this population[58]). *q* is (1- p), 0.7 in this case. And *d* is the precision; we chose a precision of 0.08 for this study. As a result, 126 patients were necessary for a confidence level of 95% and a precision of 8%.

*Scores and endpoints:* The postoperative mortality rate (up to 30 days) was the endpoint. The senior anaesthetist on call was in charge of informing the patients and their relatives about this study, and getting their informed consent. He also recorded the physiological variables (preoperative) required for the POSSUM-based scores, and those needed for the Donati score, before entering the operating theatre. Finally, he asked for a contact telephone number, in order to assess mortality after discharge. The chief investigator was in charge of the follow-up, of registering the operative variables, and of calculating the POSSUM, P-POSSUM, E-POSSUM and Donati scores for each patient. In all cases, the 30 day follow-up call was not considered valid until the patient or a close relative could verify his death or survival.

Early on in the analysis we observed that all scores underpredicted deaths in the lower risk strata. To improve this, we tried introducing the extra age class –validated by Tran Ba Loc and co-workers[31] for the E-POSSUM- to the other scores (see appendix). This group adapted the WHO age classification[59] to the POSSUM original coefficients, i.e. instead of using 3 coefficients to quantify the risk associated with age, they used 4; the last one including patients older than 85. We used the same weighted age class to calculate the POSSUM and the P-POSSUM. In other words, we recalculated the POSSUM and P-POSSUM for every patient, with a coefficient of 8 in the age category. They will be referred to in the results section as modified

POSSUM (modPOSSUM), and modified P-POSSUM (mod-P-POSSUM) respectively.

*Statistics:* The statistical analysis was performed with SPSS version 17.0 (SPSS Inc., Chicago, IL, USA). In order to test the performance of a score in a new cohort two aspects are important: calibration and discrimination. To asses the calibration of each score (the ability to predict the risk of death for a certain patient or a small group of them), we used the exponential and linear analysis described by Wijesinghe and co-workers.[57] Discrimination is a rank order statistic for predictions versus actual outcome[60]. To assess discrimination, we used the area under the receiver operating characteristic (ROC) curve (AUC).

Both exponential and linear analysis aim at obtaining a ratio of observed to predicted deaths (O:E ratio). The difference between them lies in the way each method groups the patients according to their risk levels –as predicted by each score- to obtain such a ratio. In the exponential method, patients whose predicted risk falls above certain cut-offs are grouped together in order to calculate the O:E ratio. The linear method, on the other hand, which is based on Hosmer and Lemeshow´s goodness-of-fit test, stratifies the sample according to the risk level by using deciles, and the O:E ratio is analysed within each band separately. (In a nutshell, what these calibration methods actually test is that in a group with a POSSUM score of –for example- 20%; mortality is also about 20%.) The exponential analysis was first described to assess the calibration of the POSSUM equation; it is not a standard statistical technique –unlike the linear analysis- and has been criticised for its difficulty in attributing a risk score to an individual.[61] For this reason, we used it only to assess the POSSUM-based scores, but not the Donati score.

We also used the findings of the linear analysis to make contingency tables. This way, we were able to calculate sensitivity, specificity, and positive and negative predictive values of the different scores. Unlike Copeland et al.[25] these values do not consider the sample as a whole; instead we calculated true positives (TP), true negatives (TN), false positives (FP) and false negatives (FN) stratum by stratum.

**Results**

Of all the nonagenarians who underwent an emergency procedure, 8 were referred to another hospital immediately after surgery, and 2 could not be followed up. In the end 126 patients were included. The in-hospital mortality

rate was 29.4% (37 patients) and the 30-day mortality rate 34.9% (44 patients). 14.3% (18 patients) had to be readmitted after discharge during the first postoperative month, and 4 of these died (they were included within the 30-day mortality rate). The mean length of hospital stay was 10±7.14 days (range 2-26), thus all in-hospital mortality occurred within 30 days or not at all.

Figure 1 shows the ROC analysis to compare the discrimination ability of the different scores, and table 1, the AUCs.

*Linear analysis:* Table 2 shows the linear analysis for POSSUM, P-POSSUM, E-POSSUM, modPOSSUM, and Donati score (the mod-P-POSSUM proved to be most inaccurate in all the analyses, hence results are omitted for this score). Inaccuracies occurred for most scores in the lower strata; which happened to be the deciles with larger number of patients: according to the POSSUM almost 40% of the patients had a mortality risk between 0 and 20%; according to the E-POSSUM, around 50%; and according to the P-POSSUM about 60% of the patients had this risk. In all these cases the O:E ratio was significantly higher than 1. The modPOSSUM, on the contrary, proved accurate for nonagenarians with both, low and high mortality risk, with an O:E ratio close to 1 in most deciles. The Donati score performed poorly, as it underestimated mortality in all ranges. Based on the linear analysis, table 3 shows the results calculated from the contingency tables.

*Exponential analysis:* The outcomes of the exponential analysis are summarized in table 4.

**Discussion**

Nonagenarians are often treated according to the results and experience gained with younger patients.[12] By the same token, the tools used to audit the outcomes and assess their surgical risk are the same as those used with the general population. However, the extreme old are at higher risk of morbidity and mortality, especially when they undergo emergency surgery.[58] In this context, the high mortality rate found in our sample might be partly explained as a consequence of the lack of scores to assess these patients: as the actual risk of surgery in each patient is not clear, many individuals –who would not be eligible for surgery with an accurate cost-benefit analysis- end up being operated on. Furthermore, a sensible risk assessment may prompt a deferral of surgery until the patient´s condition is improved, or even a reduction in the severity of the procedure.[32] As a result, a validated score

enables an objective risk-adjusted comparison of surgical results, as well as an estimation of the risk of death. Regarding the scores discussed in this study, they are all cost-effective tools, as the variables used in them are normally obtained as the basic assessment of the patient in the emergency ward (no extra tests are needed).

The modPOSSUM had an acceptable performance in both, the discrimination analysis (AUC of 0.71), and in the calibration analysis. The most likely explanation for this finding is based on the high risk of this population: the POSSUM equation proved to be accurate in various studies,[25,28,62,63] except for patients with low risk, and elderly patients with a hip fracture,[29] where it tended to overestimate mortality. Nonagenarians, however, even healthy ones, are a group of patients with higher risk of death than the rest of the population.[64] As a result, the POSSUM score proved accurate, and it was further improved when the extra age category –validated by Tran Ba Loc and co-workers[31]- included a higher coefficient for nonagenarians; i.e. when it was modified to consider fourth-age patients as a separate, more vulnerable group (modPOSSUM). Accordingly, the P-POSSUM, which was developed to improve the accuracy of the POSSUM with low risk patients,[65] did not have an optimum performance (especially in the calibration tests) with this high risk population. Regarding the E-POSSUM, its poor predictive power might reflect either the fact that it was also developed for the young olds; or its specificity for colorectal surgery. At this point we might suggest that a population-specific score rather than a procedure-specific one seems more reasonable for nonagenarians.

As far as the Donati score is concerned, its poor outcomes can be ascribed to two causes: on the one hand, the first of the four variables it is based on –age- was virtually constant in our population (all the patients were in their nineties). On the other hand, the second and most important variable in this scale, the ASA score;[32] which has a big impact in the final result; is fairly subjective. Especially in this population, anaesthetists tend to grade the patients with a higher score, just because they are old, and seem fragile.

It is particularly surprising, that both POSSUM and modPOSSUM had good outcomes in both calibration tests, the linear and the exponential analysis. Normally POSSUM shows better outcomes with the exponential method, whereas P-POSSUM does so with the linear one.[61] Furthermore, in our findings, the O:E ratios of POSSUM and modPOSSUM were closer to 1

with the linear analysis (1.07 and 0.85) than with the exponential one (1.69 and 1.22).

The accuracy of these scores, particularly the modPOSSUM, was further confirmed with sensitivity, specificity and positive and negative predictive values. The advantage of the analysis stratum by stratum is that it illustrates how many TP, TN, FP and FN there were in each decile of risk predicted by the scores. In this way it explains the apparent lack of consistency between the discrimination and calibration methods. The ROC analysis yielded a similar AUC for most POSSUM-based scores, however; by calculating the number of accurate and false predictions in each stratum, two phenomena become clear: on the one hand, most scores underestimate risk in the lower strata –where they allocate most of the patients- (in table 2 all the scores except modPOSSUM have an O:E ratio $\geq 2$ in the first two deciles); but on the other, they compensate for these inaccuracies by overestimating the risk in higher deciles. As a result, the overall inaccuracies are balanced and the curves seem similar. On the contrary, the modPOSSUM shows both a good AUC in the ROC analysis, and good sensitivity, specificity, positive and negative predictive values. Considering that the tool is useful as long as it can be applied in a case-by-case manner; apart from a good discrimination, good calibration is crucial. Only the modPOSSUM has proved it in this population.

In order to illustrate how the different scores function, it is useful to analyse a few cases. We will look at a patient with low risk, and another with high risk. The first case was a woman aged 91, ASA II, operated on an incarcered hernia that arrived at the OR in a fairly stable condition (slightly hypertensive, 13,800 leucocytes and BUN 4.65 mmol/l.) The procedure was uneventful, total blood loss between 100-300 ml, and minor peritoneal soiling. This woman had a POSSUM 6%, P-POSSUM 2%, E-POSSUM 3%, modPOSSUM 8%, and Donati 2%. The patient survived the first postoperative month. This case illustrates how, for these very low risk patients, all scores predicted a mortality rate below 10%. Furthermore, when being informed about the risk, the family can be told that the best case-scenario has a mortality below 10%; nevertheless, this percentage can increase if unexpected findings or complications occur. e.g if the procedure required a bowel resection due to ischemia, or intestinal content was found in the abdomen, the risk could increase considerably: POSSUM would raise

upto 18%, P-POSSUM 5%, E-POSSUM 8%, and modPOSSUM 30% (Donati score would remain unchanged).

Our second case highlights the other end of the spectrum: it was also a woman aged 91, ASA III, who underwent an exploratory laparotomy. In the preoperative examination she was found tachycardic (117 beats/min), normal blood preassure, anaemic (Hb 8 mg/dl), leucocytes 24,200 and plasma Na of 135mmol/l. During the procedure, an occlusive abscessed neoplasm was found in the colon, with local peritoneal pus. The surgeon decided to perform a right hemicolectomy with latero-lateral anastomosis. Intraoperative bleeding was 700 ml. The scores were calculated as follows: POSSUM 48%, P-POSSUM 31%, E-POSSUM 30%, modPOSSUM 60%, and Donati 26%. The postoperative period was complicated by an anastomotic leak, and the patient died of sepsis 17 days after the procedure. In this situation, if the surgeon had been able to quantify the risk, perhaps he would have chosen a less aggressive procedure.

In any case, the low performance of Donati´s score –as stated above- is mainly based on the subjectivity of the ASA classification, and on the fact that it is purely preoperative. Regarding the other scores, although they do take into account the operative severity, they underestimate the age-dependent increase in risk, and explain why the modPOSSUM showed to be more accurate. In other words, the advantage of the modPOSSUM over the others is the steeper increase in the predicted risk, which is probably excessive for a younger population but not for these elderly patients.

Some limitations to this study are worth mentioning: firstly, the number of patients. Most studies use larger samples,[31,65,66] however, nonagenarians are a fast-growing, but still a small group. As a result it took our team –in one of the biggest hospitals in Barcelona- 4.5 years to collect a sample with acceptable statistical power. In fact, a larger sample would allow to make actual comparisons between the different scores. Secondly, the study was not designed or powered to formulate a new score. However, the modPOSSUM is not a new score, but a broader version of an existing and validated one. Furthermore, the addition of an extra coefficient to the age category had been previously described and validated. Thirdly, the value of this score to predict postoperative mortality before the actual procedure is limited because it depends on intraoperative variables. Nevertheless, it does provide the medical team with a tool to assess the risk in possible alternative case-scenarios. This way, the patients can be informed of the treatments available,

their risk, and the added risk of death when complications occur. Although this is not always possible in the emergency setting, it is important to offer the patient and his family the clearest picture, so that they can give a responsible consent. Furthermore, the quantification of the risk might help them understand why a procedure should be postponed, or why the surgery should be less severe. Fourthly, the ability of the score to predict mortality might seem modest compared to other studies; however it is the first score ever tested for nonagenarians. In this respect, Dalton and coworkers[67] have recently published an interesting index for risk quantification. It is simple, straightforward and accurate, but it covers the age range between 10 and 90 years old; i.e. nonagenarians are not considered.

To sum up, mortality among nonagenarians undergoing emergency surgery is high, and the POSSUM score –with a modification in the age category (referred to as modPOSSUM in this paper)- proved to be both an accurate and cost-effective tool to assess their risk of death. Although the decision as to whether to operate or not should not be based on it, it could help to objectively assess (and inform) the risk of the different possible case-scenarios arising from such a decision. Furthermore, as an audit tool, it can help to compare the surgical outcomes for this population within different teams of different hospitals, and to plan resources. This is particularly relevant in a fast-growing group so scarcely studied, and with such high morbidity and mortality as this one has.

**Appendix:**

The POSSUM and related systems are all based in two groups of variables, which are listed below: 12 physiological, which are recorded preoperatively and yield the physiological score; and 6 operative, recorded during or post surgery, which yield the operative score.

Physiological variables:

Age

Cardiac signs

Respiratory history

Blood pressure

Pulse

Glasgow coma score

Haemoglobin

White cell count

Urea

Sodium

Potasium

Electrocardiogram

Operative variables

Operative severity

Multiple procedures

Total blood loss

Peritoneal soiling

Presence of malignancy

Mode of surgery

Each variable is given a coefficient 1, 2, 4 or 8, according to the degree of alteration: 1 is the normal weighted class for the variable; and 2, 4, and 8 represent progressive degrees of distortion.

In the POSSUM and the P-POSSUM, the age category can only receive 3 coefficients; 1 (age $\leq$ 60), 2 (61-71), and 4 ($\geq$ 71). Tran Ba Loc and co-workers have added an extra age class to the E-POSSUM. In their system, all patients older than 85 were given a coefficient of 8.

With the physiologic and operative scores, the different scales calculate the mortality risk through the following equations:

**POSSUM**: $1/(1+e^{X})$ where X = -7.04 + (0.13 x Physiological score) + (0.16 x Operative score)
**P-POSSUM**: $1/(1+e^{Y})$ where Y = -9.37 + (0.19 x Physiological score) + (0.15 x Operative score)
**E-POSSUM**: $1/(1+e^{Z})$ where Z = -7.69 + (0.14 x Physiological score) + (0.11 x Operative score)

The Donati score assesess 4 preoperative variables:

ASA score
Age
Severity of the procedure
Mode of surgery

ASA and age are continuous variables, whereas severity and mode of surgery are both categorical, and each is divided into 3 weighted classes.
The severity of the procedure can be minimal to moderately invasive (grade I); moderate to significantly invasive (grade II) or highly invasive (grade III). The mode of surgery can be elective, urgent or emergency.

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Figure 1

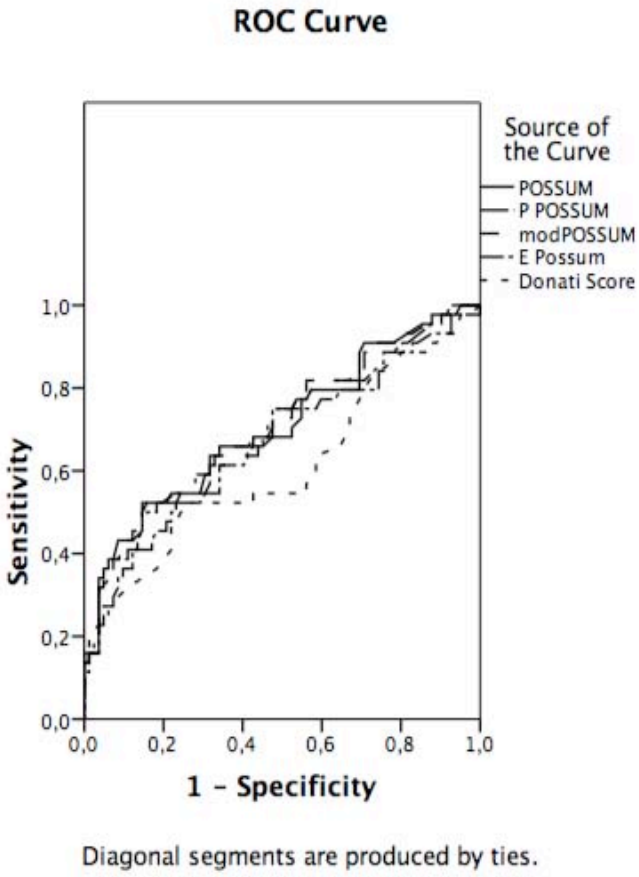
ROC Curve
Source of the Curve
POSSUM
P POSSUM
modPOSSUM
E Possum
Donati Score
Sensitivity
1,0
0,8
0,6
0,4
0,2
0,0
0,0
0,2
0,4
0,6
0,8
1,0
1 – Specificity
Diagonal segments are produced by ties.

**Table 1. AUC values for the different scores.**

| | AUC | 95% Confidence Interval |
|---|---|---|
| **POSSUM** | 0.70 | 0.60-0.80 |
| **P-POSSUM** | 0.70 | 0.59-0.80 |
| **modPOSSUM** | 0.71 | 0.61-0.80 |
| **modP-POSSUM** | 0.64 | 0.56-0.77 |
| **E-POSSUM** | 0.69 | 0.59-0.79 |
| **Donati** | 0.60 | 0.50-0.72 |

**Table 2: Linear analysis of mortality predicted by the different scores**

| | POSSUM | | | | P-POSSUM | | | | E-POSSUM | | | | modPOSSUM | | | | Donati Score | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Decile Risk | *n* | Deaths | Pred. Mort | O:E ratio | *n* | Deaths | Pred. Mort | O:E ratio | *n* | Deaths | Pred. Mort | O:E ratio | *n* | Deaths | Pred. Mort | O:E ratio | *n* | Deaths | Pred. Mort | O:E ratio |
| **0-10** | 14 | 2 | 1 | 2.00 | 50 | 11 | 2 | 5.50 | 37 | 8 | 2 | 4.00 | 7 | 1 | 0 | - | 69 | 21 | 3 | 7 |
| **10.1-20** | 35 | 10 | 5 | 2.00 | 28 | 8 | 4 | 2.00 | 28 | 8 | 4 | 2.00 | 21 | 4 | 3 | 1.33 | 21 | 5 | 3 | 1,67 |
| **20.1-30** | 19 | 3 | 5 | 0.60 | 14 | 4 | 3 | 1.33 | 22 | 6 | 5 | 1.20 | 18 | 5 | 5 | 1.00 | 30 | 12 | 7 | 1,71 |
| **30.1-40** | 19 | 6 | 7 | 0.86 | 6 | 2 | 2 | 1.00 | 16 | 6 | 6 | 1.00 | 20 | 5 | 7 | 0.71 | 0 | - | - | - |
| **40.1-50** | 16 | 6 | 7 | 0.86 | 11 | 6 | 5 | 1.20 | 8 | 5 | 4 | 1.25 | 15 | 5 | 7 | 0.71 | 3 | 3 | 1 | 3 |
| **50.1-60** | 8 | 5 | 4 | 1.25 | 4 | 3 | 2 | 1.50 | 6 | 4 | 3 | 1.33 | 17 | 5 | 9 | 0.55 | 2 | 2 | 1 | 2 |
| **60.1-70** | 4 | 4 | 3 | 1.33 | 5 | 3 | 3 | 1.00 | 3 | 2 | 2 | 1.00 | 10 | 5 | 6 | 0.83 | 0 | 0 | - | - |
| **70.1-80** | 5 | 2 | 4 | 0.50 | 3 | 2 | 2 | 1.00 | 2 | 1 | 1 | 1.00 | 8 | 7 | 6 | 1.16 | 1 | 1 | 1 | 1 |
| **80.1-90** | 5 | 5 | 4 | 1.25 | 3 | 3 | 3 | 1.00 | 4 | 4 | 3 | 1.33 | 7 | 4 | 6 | 0.66 | 0 | 0 | - | - |
| **90.1-100** | 1 | 1 | 1 | 1.00 | 2 | 2 | 2 | 1.00 | 0 | - | - | - | 3 | 3 | 3 | 1.00 | 0 | - | - | - |
| **0-100** | 126 | 44 | 41 | **1.07** | 126 | 44 | 28 | **1.57** | 126 | 44 | 30 | **1.47** | 126 | 44 | 52 | **0.85** | 126 | 44 | 16 | **2.75** |

***n:*** number of patients in each decile for each score.

**Deaths:** actual number of deaths.

**Mort. Pred.:** number of deaths predicted by each score (in all cases, the figures were rounded to the nearest whole number.)

**Table 3. Results of the contingency table based on the linear analysis**

| | Sensitivity | Specificity | Positive Predictive value | Negative Predictive Value |
|---|---|---|---|---|
| POSSUM | 0,80 | 0,93 | 0,85 | 0,89 |
| P-POSSUM | 0,64 | 1,00 | 1,00 | 0,84 |
| E-POSSUM | 0,68 | 1,00 | 1,00 | 0,85 |
| modPOSSUM | 0,94 | 0,86 | 0,71 | 0,97 |
| Donati score | 0,36 | 1,00 | 1,00 | 0,75 |

**Table 4. Summary of the outcomes obtained through the exponential analysis**

| | O:E ratio |
|---|---|
| POSSUM | 1.69 |
| P-POSSUM | 2.20 |
| E-POSSUM | 2.09 |
| modPOSSUM | 1.22 |

# 4 RESULTADOS GLOBALES Y DISCUSIÓN

## 4.1. Análisis demográfico preliminar

El estudio demográfico preliminar está incluido, en forma completa, en la sección 3.1.1 A continuación se presentará un resumen global de los principales resultados y la discusión de los mismos.

Como ya se ha mencionado al principio, este es el primer estudio prospectivo en que se cuantifican los resultados quirúrgicos en este tipo de pacientes; y donde se obtienen cifras concretas de morbi-mortalidad. En consecuencia resulta difícil comparar estos resultados con la escasa bibliografía existente: sólo se puede contrastar estos hallazgos con series prospectivas de nonagenarios sanos de la comunidad,[44] o con series retrospectivas, algunas publicadas hace más

de 20 años,[45] otras que incluyen tanto cirugía urgente como cirugía programada;[20] y otras donde se presentan tanto pacientes traumáticos como no traumáticos.[12,19] Es decir, ninguno de los investigadores ha estudiado una población como esta en forma prospectiva.

Las características demográficas al ingreso más destacadas de estos nonagenarios fueron un predominio de mujeres (70.6%) y una alta prevalencia de patología asociada (se ha obtenido una mediana de 4 comorbilidades por paciente con un rango de 1-12). Entre ellas, las más características fueron hipertensión arterial (57.8%), fibrilación auricular (36.3%), insuficiencia cardíaca congestiva (28.4%) y neoplasias (23.5%). Consecuentemente, la mayoría de los pacientes fueron clasificados como ASA III (62.7%). Al comparar estos pacientes con una población similar pero de la comunidad,[44] se observó que no había grandes diferencias ni en la distribución por género ni en la prevalencia de comorbilidades. Más aún, en nuestra serie, al igual que en el estudio Nona-Sanfeliú, el número de patologías asociadas estaba correlacionado con la mortalidad.[44]

La cirugía del aparato gastrointestinal y la cirugía vascular fueron las especialidades más recurrentes; de hecho, al analizar las indicaciones quirúrgicas, se observó que el 50% de la población fue intervenida por una hernia incarcerada, una trombosis arterial aguda, o un síndrome oclusivo intestinal. La comparación con otros estudios evidenció que el tipo de cirugía y los diagnósticos eran similares, aunque la

prevalencia de cada procedimiento fue diferente en las diversas series.[12] Por otro lado, varios estudios coinciden con el nuestro en que la mortalidad de la cirugía intra-abdominal urgente en nonagenarios es elevada y ronda el 30%.[19,20]

Los hallazgos postoperatorios más destacados fueron una estancia hospitalaria media de 10.6 días (DS 7.4), una elevada mortalidad 35.3% a los 30 días, y una elevada morbilidad: el 62% de los pacientes sufrió algún tipo de complicación. De estas, las más frecuentes fueron los síndromes confusionales (17.6%), la insuficiencia renal aguda (16%) y las complicaciones abdominales –dehiscencia de sutura, evisceración, íleo paralítico persistente- (13.7%). Sorprendentemente, varias complicaciones que en el estudio bivariante estuvieron asociadas con una mayor mortalidad –tales como el fallo cardíaco, el fallo renal, los accidentes vásculo-cerebrales o la broncoaspiración- se presentaron principalmente en pacientes sin antecedentes de dichas patologías, y no en aquellos cuya patología previa de dichos órganos era conocida. Este hallazgo podría interpretarse como una indicación indirecta de la baja reserva funcional de estos pacientes:[22,23] aunque en estado basal la función de los distintos órganos pueda parecer normal, carecen de la capacidad de responder ante situaciones de estrés fisiológico. Siguiendo la definición biológica de envejecimiento mencionada al comienzo, este hallazgo confirmaría el declive en la *homeostasis* de estos enfermos. En consecuencia, desarrollarían complicaciones perioperatorias

severas e inesperadas debidas a la dificultad para responder al estrés quirúrgico.

La alta tasa de morbi-mortalidad al mes de estos pacientes subraya la necesidad de cuidados postoperatorios rigurosos. Más aún, teniendo en cuenta ciertos estudios que sugieren que, de los ancianos ingresados postoperatoriamente en unidades de críticos, los que reciben un tratamiento agresivo de las complicaciones son los que tienen mayores posibilidades de sobrevida.[46] Sin embargo, también hay datos que demuestran que la agresividad del tratamiento de los pacientes más ancianos suele ser menor comparada con los más jóvenes; y que la decisión de limitar el esfuerzo terapéutico es mucho más frecuente.[47,48] Por lo tanto, es importante mantener una conducta coherente, y una vez tomada una decisión terapéutica, se debe ser consecuente con ella. Así pues, si se optó por la opción quirúrgica agresiva, se debe persistir con el tratamiento agresivo también durante el postoperatorio. Para ello, es importante que la decisión se base en una medición objetiva del riesgo, en las posibilidades reales de supervivencia; y que sea tomada consensuadamente entre los distintos servicios implicados en el pre, el intra y el postoperatorio.

## 4.2 Valoración del riesgo quirúrgico

La sección 3.1.2 contiene el análisis detallado sobre este punto. Lo que sigue es la presentación y discusión de los resultados más relevantes.

Para determinar la precisión de una escala de riesgo en una cohorte nueva es importante verificar tanto su poder de discriminación como su calibración. La discriminación determina la capacidad global del score para predecir la mortalidad en la totalidad de la muestra, contrastada con la mortalidad real. Para estudiar la discriminación de los diferentes scores en la población de nonagenarios se utilizó el área bajo la curva (AUC) ROC (receiver operating characteristic). La calibración, en cambio, se refiere a la capacidad de cada escala para predecir el riesgo específico para un determinado paciente o para un grupo pequeño de ellos. La calibración fue estudiada mediante los análisis lineal y exponencial.[30] Tanto uno como el otro comparan –utilizando diferentes formas de estratificar a la población- la mortalidad observada con la mortalidad esperada en cada estrato, según las diferentes escalas de riesgo. En definitiva, ambos métodos buscan determinar en qué medida el cociente mortalidad observada/mortalidad esperada (O:E) se aleja de 1; que constituye el valor ideal en que las predicciones de la escala (valores esperados) serían idénticas a la mortalidad observada.

Ya desde las primeras fases del análisis, los estudios de calibración demostraron que todas las escalas existentes infravaloraban el riesgo

quirúrgico en los estratos de bajo riesgo para la población de nonagenarios. En consecuencia, se intentó recalcular el POSSUM (la que presentaba mejor calibración de las cuatro), utilizando la categoría extra de edad validada por Tran Ba Loc y colaboradores.[31] Es decir, para cada paciente, además del POSSUM, el P-POSSUM, el E-POSSUM y el Donati; se volvió a calcular el riesgo según la ecuación del primero, pero utilizando un coeficiente de 8 en la edad, tal como lo establece el E-POSSUM para los nonagenarios. Se aludirá a esta variación como POSSUM modificado o mod-POSSUM.

Los análisis de discriminación de las escalas estudiadas demostraron AUCs muy similares para todas las escalas basadas en las variables del POSSUM, con una ventaja muy sutil para el mod-POSSUM (AUC 0.71). Los estudios de calibración, en cambio, evidenciaron una superioridad más clara del POSSUM y el mod-POSSUM para el estudio lineal; y sólo del mod-POSSUM, para el estudio exponencial. Esta aparente contradicción se explica cuando se comparan las tablas de calibración estrato por estrato. Entonces, resulta evidente que los deciles de riesgo bajo, que son los que concentran la mayor proporción de la población estudiada, son los que presentan peores resultados en todas las escalas salvo en el mod-POSSUM. De hecho, los deciles de riesgo entre 0-20% concentran el 40% de la población según el POSSUM, el 50% según el P-POSSUM, y el 60% según la escala de Donati; y en todas ellas el cociente O:E es superior o igual a 2. Sin embargo, esta infravaloración del riesgo es compensada con su

sobrevaloración en los estratos de riesgo más elevados. En consecuencia las inexactitudes se compensan y las curvas ROC acaban resultando similares. El mod-POSSUM, por otro lado, presenta una distribución más homogénea de la población a través de los diferentes deciles de riego; y una menor variación entre ellos, pues todos son cercanos a 1. Para evitar este error, se han trazado las tablas de contingencia, y se ha calculado –estrato por estrato- los verdaderos positivos, verdaderos negativos, falsos positivos y falsos negativos. Estas evidenciaron, al valorar la sensibilidad, la especificidad, y los valores predictivos positivo y negativo, la superioridad del mod-POSSUM en esta población.

Una posible explicación para estos hallazgos se basa en el riesgo elevado de estos pacientes nonagenarios intervenidos de urgencia. En efecto, los nonagenarios, inclusive los que son sanos, tienen un riesgo más alto que el resto de la población;[44] por ello, de las escalas originales, la que mejor predijo el riesgo fue el POSSUM; y esta fue aún mejorada cuando se agregó la categoría extra de edad validada por Tran Ba Loc y cols.[31] Es decir, cuando el POSSUM fue modificado para considerar a los individuos de la cuarta edad como un grupo separado, con mayor riesgo quirúrgico.

En definitiva, el mod-POSSUM parece ser una herramienta útil y coste-efectiva en dos aspectos principales: para realizar comparaciones objetivas –ajustadas según el riesgo- de los resultados

quirúrgicos en diferentes instituciones (tal fue el objetivo original para el cual el POSSUM fue desarrollado);[25] y como escala para estimar el riesgo de mortalidad.[26,27] A partir de esta segunda aplicación surgen nuevas perspectivas; un riesgo inadmisiblemente elevado puede servir para diferir la cirugía hasta que las condiciones del paciente sean mejores, para decidir un procedimiento menos agresivo,[32] e inclusive, para plantear al paciente y su familia los diferentes escenarios que podrían presentarse, en caso de que ocurrieran complicaciones;[26] permitiendo, de esta manera, mayor independencia e información en las decisiones que estos tomen.

## 4.3 Práctica transfusional

El análisis completo sobre la práctica transfusional se encuentra en el ANEXO (sección 7.1) . Los hallazgos más destacados se discuten a continuación.

La prevalencia de la anemia en esta población –definida según los criterios de la OMS- fue del 54% y el Coeficiente Transfusional (pacientes transfundidos /total de pacientes) dio un valor de 0.35. Sorprendentemente, en el análisis bivariante la anemia no estuvo asociada a una mayor morbilidad ni mortalidad. Los pacientes transfundidos, en cambio, presentaron mayor morbilidad perioperatoria ($p$<0.001), mayor estancia hospitalaria ($p$<0.001), y tendencia a mayor mortalidad ($p$ 0.06). Más aún, el número de

concentrados de hematíes (CCHH) estuvo linealmente correlacionado con los días de estancia hospitalaria (*Rho de Pearson* 0.48, $p<0.001$).

La prevalencia de la anemia no varió sustancialmente respecto a otras series;[35,49] sin embargo, la falta de asociación entre anemia y morbi-mortalidad sí es llamativa. La única explicación posible es que los estudios que presentaron este hallazgo, a diferencia del nuestro, sólo incluyeron cirugía electiva.[50,51] De hecho, el estudio de Wu, que incluye pacientes de la tercera y cuarta edad, tampoco encontró esta asociación en los casos urgentes, mientras que sí la constató en los casos de cirugía electiva.[52] Por otro lado, a diferencia de otro estudio de Wu y cols. –también realizado con una cohorte retrospectiva similar a la anterior- en que los pacientes transfundidos presentaban peores condiciones basales que los no transfundidos;[53] en el presente estudio los pacientes que recibieron transfusiones no presentaron diferencias significativas en cuanto al ASA ni a la mayoría de las patologías asociadas, respecto de los que no las recibieron. Es decir, excepto por la mayor prevalencia de demencia y neoplasias, los nonagenarios que fueron transfundidos presentaban condiciones basales bastante similares a los que no lo fueron.

Los factores de riesgo independientes para la transfusión fueron la anemia preoperatoria, las neoplasias y la necesidad de laparotomía exploradora. La anemia ya era un predictor conocido de las transfusiones en procedimientos electivos[51] y en otras poblaciones de ancianos,[43] pero no en el contexto de la urgencia. En forma similar, la

asociación entre transfusión y determinados procedimientos ya había sido demostrada para la cirugía vascular,[54] las fracturas de cadera[42] y la cirugía intrabdominal.[41] Sin embargo, a diferencia de otros estudios en que la transfusión dependía de varias comorbilidades,[40] en estos nonagenarios intervenidos de urgencia sólo las neoplasias estuvieron independientemente relacionadas con la transfusión. En efecto, aunque no parezca un hallazgo novedoso el hecho de que los pacientes anémicos, con cáncer o en los que se practican procedimientos más agresivos requieran transfusiones; sí es sorprendente que otras patologías que habitualmente están relacionadas con la transfusión –tales como la enfermedad coronaria,[55] la insuficiencia renal, o la EPOC-[40] en esta población no lo estuvieran. Asimismo, al agrupar los pacientes que presentaban cualquiera de los 3 factores mencionados se observó que el Índice Transfusional IT (número de CCHH/paciente) y el Coeficiente Transfusional CT (pacientes transfundidos/población) resultaban persistentemente superiores a 0.5, lo cual indica la necesidad de realizar reserva preoperatoria de hemoderivados.[42] Aunque otros estudios plantean que la edad avanzada y la cirugía de urgencias son, en sí mismas, factores predictores potentes de las transfusiones,[40,41] el CT de toda la población fue de 0.35; por lo tanto, no parece aconsejable realizar el cross match de todos los nonagenarios intervenidos de urgencia.

Respecto a la comparación entre los nonagenarios con pacientes de la tercera edad, los hallazgos principales fueron diferencias significativas

en la distribución por género, peores condiciones basales de los nonagenarios (mayor número de pacientes ASA III y mayor prevalencia de la mayoría de comorbilidades), y mayor mortalidad entre los pacientes de la cuarta edad; pero sin diferencias en la política transfusional. De hecho, tanto la proporción de pacientes transfundidos (CT) como el número de concentrados por paciente (IT) fueron similares, y las prevalencias de la anemia pre- y postoperatoria también lo fueron. Sólo se observaron diferencias en el umbral transfusional, lo cual puede explicarse dadas las peores condiciones basales en que se hallaban los nonagenarios. En definitiva, parece desprenderse de estos hallazgos que la política transfusional fue similar para los dos grupos en estudio; y que la diferencia en el umbral transfusional fue debida a las diferencias de las poablaciones. En efecto, en ambos casos se puede hablar de una política transfusional restrictiva.

# 5. CONCLUSIONES

1- La población de nonagenarios que requiere cirugía no traumática urgente se caracteriza por presentar una alta prevalencia de comorbilidades; por ser intervenida predominantemente debido a patología de la pared abdominal, a isquemia aguda de una extremidad (secundaria a embolia), y a patología del tubo digestivo; y por presentar una alta incidencia de complicaciones post-quirúrgicas, así como una elevada mortalidad a los 30 días.

2- El POSSUM, con la modificación en la categoría de la edad –*mod-POSSUM*- destinada a incluir a los pacientes de la 4º edad como un grupo separado de mayor riesgo, demostró ser una herramienta útil para valorar el elevado riesgo quirúrgico de estos pacientes.

3- La anemia y los requerimientos transfusionales son elevados en estos pacientes. Los factores independientes asociados a la necesidad de transfusión son: la anemia preoperatoria, la presencia de alguna neoplasia, y la necesidad de una laparotomía exploradora. Los mismos deberían ser tenidos en cuenta a la hora de decidir la reserva de sangre prequirúrgica. En cuanto a las diferencias halladas al comparar pacientes de la tercera edad con pacientes de la cuarta, estas se debieron a las características poblacionales y no a una política transfusional diferenciada; pues en ambos casos, se puede considerar que se trata de una política restrictiva.

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# 7. ANEXO

## 7.1 Práctica transfusional

Anaemia and transfusion in nonagenarians undergoing emergency, non-traumatic surgery: a prospective observational study

En Revisión

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**Abstract**

**Context**: Perioperative anemia and transfusion are currently topical, but little is known about them in nonagenarians undergoing emergency, non traumatic surgery.

**Objectives**: the primary goal was to characterise transfusion in this population and determine its main predictors. As a secondary goal, we compared nonagenarians to a similar, but younger sample, as far as the transfusional policy is concerned.

**Design**: Prospective observational study

**Setting**: The study was performed between 2006- 2011, in a tertiary care university hospital in Barcelona, Spain

**Patients**: the study group included 135 patients older than 90 who underwent, a non-elective, non-traumatic procedure. As a control sample, we used a similar number of patients in their 3rd age (between 65 and 85 years old), who underwent the same procedure, during the same period of time.

**Main outcome measures**: transfusional rate, pre and postoperative haemoglobin, number of concentrate per patient, morbidity, mortality.

**Results**: 35% of the nonagenarians were transfused. The main independent factors associated with transfusion were anemia ($p<0.01$, OR 6.77), a coexisting neoplasm ($p<0.01$, OR 10.99) and the need for an exploratory laparotomy ($p=0.01$, OR 3.05).

When comparing the nonagenarians to the younger group, we found a significant difference in their basal health status and the mortality rate ($p<0.01$), but the transfusion policy did not differ substantially except for the haemoglobin threshold ($p=0.01$).

**Conclusions**: the independent transfusion predictors in nonagenarians should be taken into account for cross-matching. Transfusional policy being similar between nonagenarians and 3rd aged patients; the differences in thresholds were due to the differences in the populations.

**Key words:** Aged, 80 and over; Blood transfusion; Surgical procedures, operative; Emergency medicine

## Introduction

Elderly patients are expanding rapidly in developed countries. According to the WHO, the chronological age of 65 years defines an 'old person';[1] however, this definition includes a wide age range. As a result the elderly population has lately been stratified into 2 smaller categories: 3rd age (65 to 85) and 4th age (older than 85)[1 2]. Among them, nonagenarians are the fastest-growing segment.[3] Still, clinical evidence about this segment is scarce, and most of the medical care they receive is based on studies with younger patients.

On the one hand, nonagenarians need urgent and emergency surgery proportionally more often than the rest of the population, and their prevalence of anemia is higher.[3] Nevertheless, very few studies have addressed perioperative anemia and transfusion in nonagenarians within the non-elective setting:[4] except for traumatic cases, predominantly comprised of hip fractures repairs,[5-8] most studies about these topics are based on elective surgery.[9] In addition, over-cross-matching is common practice for these patients.[5]

On the other hand, most studies do not distinguish between 3rd and 4th age; instead, they consider the elderly as a single category.[4 10-12] Thus, it is not clear whether perioperative differences do exist between these two groups; or how they actually differ

Consequentley, we performed a prospective observational study: our primary goal was to characterise transfusion practise in nonagenarians undergoing non-traumatic urgent and emergency surgery. Specifically, the main endpoints were to determine the incidence of transfusions (transfusion rate), and to elucidate the main transfusional determinants. This work can be considered as a first step towards a rational cross-matching policy for these patients. As a secondary goal, we tried to compare our findings among the 90-year olds (4th age), to a similar but younger population, patients in their 3rd age. The purpose was to determine in which aspects nonagenarians are different or similar to them, as far as transfusion policy is concerned.

## Materials and methods

All eligible patients and their accompanying relatives were informed about the study. In order to be included, every patient –from both the study and the

control groups- or their relative in charge (if the patient was impeded) agreed to sign an informed consent.

Every non-traumatic patient older than 90, who underwent urgent or emergency surgery in our tertiary care University Hospital, between July 2006 and June 2011, was prospectively recruited and followed up. Our primary outcome variable was whether or not the patient received a transfusion.

As cross-matching in the emergency setting needs to be decided early on, we chose to study those potential predictors for transfusion that had shown to be relevant in previous studies, and which are routinely checked in any patient undergoing emergency surgery.[13 14] We registered demographic variables; preoperative comorbid conditions (including atrial fibrillation, hypertension, heart failure, heart ischaemia, COPD, diabetes, chronic renal failure, stroke, peripheral vasculopathy, neoplasms and dementia); and type of procedure (specialty, site of surgery, open versus laparoscopic) The variables recorded to assess transfusion were pre- and postoperative Hb values, transfusion threshold (defined as the lowest Hb value before the first transfusion was decided), and number of red blood cell (RBC) units transfused. With this variables we calculated the Transfusion Rate (TR), defined as the number of transfused patients/total number of patients; the Transfusion index (TI), defined as the number of RBC units/total number of patients; and the Actual Transfusion Index (ATI), i.e., number of RBC units/ number of patients transfused.[3] Bleeding was recorded as a dichotomous variable: it was considered positive when more than 500cc of blood were accounted for in the aspiration liners (significant bleeding). Anemia was defined according to the WHO criteria (Hb<13 g/dL for males and Hb<12 g/dL for females);[3] and was studied both, as a dichotomous and as a continuous variable (preoperative Hb). Finally, we followed the patients up, and collected information about postoperative morbidity (the complications considered were heart failure, angina/infarction, arrhythmia, exacerbation of COPD, pneumonia, pulmonary embolism, acute renal failure, urinary infections, stroke hemorrhage, surgical site infection, abdominal complications and sepsis); length of hospital stay; and 30-day postoperative mortality.

Simultaneously, a control group was recruited. It was comprised of the same number of patients, who underwent the same procedures, but who belonged to the 3rd age. In other words, the control group was chosen from among patients between 65 and 85 years old, who were operated on due to the same

pathology, and during the same period as the nonagenarians. To avoid bias and have the same *n* in both groups, for the control sample, we included the first eligible patient after each nonagenarian that underwent the same operation: e.g if a nonagenarian underwent an incarcerated hernia operation, the first patient aged 65-85 after him, who underwent the same procedure, was included.

The statistical analysis was performed with SPSS 15.0 (SPSS Inc., Chicago, IL, USA). To determine the sample size we assumed an expected transfusion rate of 0.34, based on our preliminary descriptive demographic study of this population[15]. As a result, 135 patients yielded a confidence level of 95% and a precision of 8%.

The univariate relation between each factor and transfusion was studied with an independent sample *t* test for continuous variables, and either a $\chi^2$ or Fisher´s exact test for categorical ones. All the variables associated with transfusion in the univariate analysis ($p < 0.05$), were consecutively examined in the multivariate analysis using forward stepwise logistic regression. We chose this low *p* value in order to achieve a parsimonious model. This way, we were able to adjust the data more effectively and use as few predicting variables as possible. The advantage of this approach is that predictions are more accurate and the model is more robust. We used a Pearson´s test for linear correlations. A $p < 0.05$ was considered significant.

**Results**

135 patientes in their nineties and 135 3rd-aged controls were recruited.

*Transfusional characteristics of nonagenarians:*

Amongst nonagenarians, 68.1% were females; 64.4% were classified as ASA III; and their median age was 92 (range 90-100). Table 1 shows the pre- and intraoperative variables assessed as potential risk factors for transfusion; table 2 shows the postoperative outcomes: 54.8% of all nonagenarians were anemic upon admission (20% of them were men, and 34.8% women), 34.8% were transfused (TR 0.35). The mean transfusional threshold was Hb 8.1 g/dl, SD 0.84; their 30-day mortality rate was 36.3%, and their mean hospital length of stay was 10 days, SD 7.04.

Independent risk factors associated with transfusion were neoplasm, exploratory laparotomy and preoperative anemia. (see table 3). When we analyzed each group of patients with any of these factors separately, it

became clear that the TI and the TR were both persistently higher than 0.5 in all cases.

Regarding outcomes, no increased morbidity (*p* 0.969) was found for patients with baseline anemia. Similarly, the association between mortality and preoperative anaemia was nether demonstrated when anaemia was mild (Hb 10.01-12 g/dL): *p* 0.528, moderate (Hb 8.01-10-0 g/dL): *p* 0.418, nor severe (Hb < 8.0 g/dL): *p* 0.137. Accordingly, when analyzing anaemia as a continuous variable, no difference was found in preoperative Hb between patients who suffered a complication and those who did not (*p* 0.30), nor between patients who died and those who survived (*p* 0.85). On the other hand, as shown in table 2, transfused nonagenarians had a higher 30-day postoperative morbidity ($p<0.001$), a strong trend towards increased mortality ($p=0.06$), and a longer hospital stay than the nontransfused elderly patients ($p<0.001$). Furthermore, the number of RBC units transfused was linearly correlated with the days of hospital stay (Pearson's *Rho* 0.48, $p < 0.001$).

*Comparison of nonagenarians and control group:*

Results of the comparison between nonagenarians and younger patients are shown in Table 4. Interestingly, the study population and the control group differed in the gender distribution, the basal health status (the ASA score and the prevalence of certain comorbidities), and the mortality rate.

The main finding, as far as transfusion policy is concerned, was a more restrictive threshold Hb in the control group. The number of patients transfused did not differ significantly (the TR was similar in both groups), neither did the pre or post operative rate of anemia, nor the other indexes we calculated.

**Discussion**

In view of the lack of clinical evidence regarding transfusional policy in nonagenarians, these findings are the first prospective attempt at characterising it. Furthermore, this study elucidates the main transfusion predictors in such an elderly group of patients, and attempts to compare these nonagenarians to a similar, but younger group. The reason for choosing only the emergency setting is that there are virtually no published studies in this domain, whereas there is some information about elective patients.

*Transfusion in nonagenarians*

Our TC was 0.35, which –as stated above- is difficult to compare with other series, due to the scarcity of studies addressing this type of patient. Regarding the independent risk factors found to be associated with transfusion, preoperative Hb and anemia were already known to be strong predictors of transfusions in elective procedures[9] on other elderly populations,[11] but not in this non-traumatic emergency setting. Similarly, the association between transfusion and certain procedures has been proved for vascular surgery,[16] pertrochanteric fracture repair,[5] and intraabdominal surgery[17] in younger groups. Nevertheless, unlike other series where transfusion was associated with various comorbidities;[14] our sample showed that only cancer was independently associated with transfusions in these nonagenarians.

Although it might come as no surprise that nonagenarians who are anemic, have cancer, or undergo bigger surgeries need more transfusions than the rest; it is surprising that in our findings, other comorbid conditions or indicators of poor basal status were not associated as well with transfusion. In fact, except for dementia and neoplasms transfused nonagenarians were similar to the non-transfused; consequently, we cannot be sure that the former were in worse shape than the latter. Conversely, other studies have found coronary disease,[13] renal impairment and COPD as important predictors;[14] in our outcomes, however, these factors were not even associated with transfusion in the bivariate analysis -$p$>0.2 in all cases- (as shown in table 1). Also remarkable is the high odds ratio (OR) of the exploratory laparotomy, which indicates a high relative risk of transfusion for patients undergoing that type of surgery. This finding, supports previous work, where abdominal procedures also showed a similarly increased risk of transfusion (OR 10.9).[17]

Groups of patients with any of the 3 independent factors mentioned above had TI and TR values above 0.5 therefore indicating the need for a routine cross-match.[5] Other studies proposed age[14 17] and emergency surgery as strong predictors for transfusion, however the overall TR of the whole group was 0.35, hence routine cross-matching in all nonagenarians undergoing emergency surgery should be discouraged.

As far as the relationship between anemia and poor outcomes, the cohorts that found this association only included elective procedures.[9 18] Our findings, therefore, support the only study that tested anemia and mortality in emergency patients, which also found no such association among men older

than 65.[4]

A few studies have reported the association between transfusion and different markers of poor outcomes: increased postoperative mortality,[10 11] longer hospital stays,[12 16] and specific postoperative complications.[11] Our findings support most of these conclusions; however, the association between transfusion and negative outcomes highlights the difficulty in separating the actual effects of transfusion from the effects arising from the "need for transfusion".[19] With this in mind, the linear association we found between the number of RBC units transfused and length of hospital stay can be reasonably explained by assuming that patients with longer hospitalizations were those who sustained more complications and hence, became more anaemic. Under no circumstance can we deduce from these findings that the statistical association found between transfusion and poor outcomes necessarily indicates a causal relation.

*Nonagenarians versus 3rd aged-patients*

Although our study population did present a lower basal status than the control group –the prevalence of ASA score III, atrial fibrillation, heart failure and dementia were significantly higher- the transfusional characteristics did not vary substantially among them: the proportion of patients transfused (TR), the number of RBC units (TI and ATI), and the prevalence of pre- and postoperative anemia were similar. This finding partly reinforces the lack of relation we observed between basal physical status and transfusion among nonagenarians. On the other hand, the poorer basal status found amongst nonagenarians –as compared to the control group- can also probably explain the higher threshold for transfusion used in them. In other words, it seems like a similar transfusion policy was applied to two different populations, and that the poorer basal status of the study group conditioned a higher transfusion threshold, rather than a difference in the TR, or the transfusion indexes. Nevertheless, although the threshold for transfusion among the nonagenarians was higher than for the younger elderly, it can still be considered restrictive.

Some limitations to this study are worth mentioning: this is a single center study, and therefore our population might not fully represent all of the nonagenarians that undergo this kind of procedures. Moreover, it could be biased because this is a tertiary care University Hospital that receives complicated cases from peripheral hospitals. On the other hand, the fact that many patients are transferred to our institution has enabled us to collect a

significant sample; otherwise it would have been difficult, considering that nonagenarians –though growing fast- are still a minority. The main limitation is related to the matching of the control group, in which the patients were only adjusted for type of surgery and basal Hb, but not for weight, gender, or basal physiscal status. Regarding the weight, emergency patients are not routinely weighed before an emergency procedure in our institution, hence we could not collect those data. As far as gender distribution is concerned, the difference found between the study and the contol group is an important issue that complicates their comparison. However it should be noted that there is a significantly larger number of males among the 3$^{rd}$ aged patients than among the 4$^{th}$ aged ones, and as a result, -though unadjusted- the gender distribution in our control groups reflects the actual gender distribution in the population. Lastly, although stratification according to comorbidities would have been interesting, it would have made the selection of controls extremely complicated, as every patient has a different combination of several comorbidities. Another weakness of the study is that it was purely observational, and the transfusions were based on the criterion of each anaesthetist. However, despite the lack of a rigid protocol, the analysis of the threshold Hb shows that all transfusions were decided with values between 6.10 and 9.50 g/dl, which are normally recommended in international guidelines. Thus, even without a standarised transfusion policy, the transfusion indications were done in accordance with accepted clinical standards. Finally, although we did register the transfusional threshold used, and the intraoperative bleeding, other criteria might have influenced the decision, which were not recorded.

To conclude, our findings show that the general principles which guide transfusion policy in the younger elderly patients are also valid for nonagenarians. However, due to the specificities of this population, anaesthetists have had to adapt their standard transfusional approach to the nonagenarians' specific characteristics; namely, a poorer basal status, numerous preoperative comorbidities, frequent complications and high mortality rate. In a nutshell, a similar restrictive transfusional policy was applied to a significantly different population. On the other hand, the knowledge of the factors associated with transfusion in this population should reduce indiscriminate cross-matching, and spare important expenses.

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**Table 1**: Bivariate analysis: demographics

| | Other procedures § | Transfused7 (24.9) | Nontransfused29 (33.0) | 0.024+ |
|---|---|---|---|---|
| | | N (%) | N (%) | |
| | | 47 (34.8%) | 88 (65.3%) | p |
| Patient-depending variables | Female/male | 34 (72.3)/13 (27.7) | 58 (65.9)/30 (34.1) | 0.445 |
| | ASA II | 11 (23.4) | 26 (29.5) | 0.446 |
| | ASA III | 31 (66.0) | 56 (63.6) | 0.788 |
| | ASA IV | 5 (10.6) | 6 (6.8) | 0.322 |
| | Atrial Fibrillation | 16 (34.0) | 35 (39.8) | 0.513 |
| | Hypertension | 31 (66.0) | 50 (56.8) | 0.302 |
| | Heart Ischaemia | 10 (21.3) | 12 (13.6) | 0.252 |
| | Heart failure | 9 (19.1) | 26 (29.5) | 0.189 |
| | COPD | 10 (21.3) | 13 (14.8) | 0.338 |
| | Diabetes | 8 (17.0) | 17 (19.3) | 0.743 |
| | Renal failure | 6 (12.8) | 9 (10.2) | 0.655 |
| | Stroke | 6 (12.8) | 20 (22.7) | 0.162 |
| | Peripheral vasculopathy | 11 (23.4) | 11 (12.5) | 0.102 |
| | Neoplasm | 20 (42.6) | 11 (12.5) | **<0.001*** |
| | Dementia | 5 (10.6) | 24 (27.3) | **0.025*** |
| Transfusional variables | Preoperative anemia | 33 (70.2) | 41 (46.6) | **0.009*** |
| | Preoperative Hb | 11.14±2.04 | 12.34±1.74 | **<0.001*** |
| | Postoperative anemia | 43 (91.5) | 57 (64.8) | 0.001+ |
| | Intraop. blood loss >500cc | 10 (21.3) | 2 (2.3) | **<0.001*** |
| Surgery-depending variables | Exploratory laparotomy | 15 (31.9) | 6 (6.8) | **<0.001*** |
| | Laparoscopic procedure | 4 (3.0) | 0 | 0.176 |
| | Thrombectomy | 6 (12.8) | 18 (20.4) | 0.266 |
| | Herniorraphy | 4 (8.5) | 17 (9.13) | 0.099 |
| | Cholecystectomy | 5 (10.6) | 8 (9.1) | 0.772 |
| | TUR | 6 (12.8) | 4 (4.5) | 0.096 |
| | Amputation | 4 (8.5) | 6 (6.8) | 0.721 |
| | Appendectomy | 5 (3.7) | 0 | 0.113 |

* $p<0.05$ the number of transfused patients is significantly higher than the number of nontransfused patients.

+ $p<0.05$ the number of nontransfused patients is significantly higher than the number of transfused patients.

§ Other procedures include: tracheostomy, abscess drainage, peripheral by-pass, diabetic foot debridation, pleural drain, urether catheterization, percutaneous nephrostomy, orchiectomy, abdominal wall repair, infected wound debridation, wound debridation + grafting.

**Table 2**: Bivariate analysis: outcomes

| | | Transfused N (%) 47 (34.8%) | Nontransfused N (%) 88 (65.3%) | p |
|---|---|---|---|---|
| Postoperative outcomes | Heart failure/pulm edema | 7 (14.9) | 6 (6.8) | 0.130 |
| | Angina/infarction | 2 (4.3) | 1 (1.1) | 0.242 |
| | Arrhythmia | 2 (4.3) | 5 (5.7) | 0.722 |
| | COPD exacerbation | 0 | 2 (2.3) | 0.423 |
| | Pneumonia | 3 (6.4) | 3 (3.4) | 0.347 |
| | Pulmonary embolism | - | - | - |
| | Acute renal impairment | 12 (25.5) | 9 (10.2) | **0.019*** |
| | Cerebro-vascular accident | 4 (8.5) | 1 (1.1) | **0.031*** |
| | Urinary tract infection | 6 (12.8) | 3 (3.4) | **0.038*** |
| | Hemorrhage | 5 (10.6) | 2 (2.3) | 0.050 |
| | Surgical site infection | 4 (8.5) | 0 | **0.013*** |
| | Abdominal complications ¶ | 12 (25.5) | 5 (5.7) | **0.001*** |
| | Sepsis | 7 (14.9) | 3 (3.4) | **0.015*** |
| | Discharge Hb | 9.89±1.4 | 10.96±1.7 | **0.001*** |
| | Mortality | 22 (46.8) | 27 (30.7) | 0.06 |
| | Length of Hospital stay | 14.4±7.6 | 7.6±5.5 | **<0.001*** |

***** $p<0.05$ the number of transfused patients is significantly higher than the number of nontransfused patients.

+ $p<0.05$ the number of nontransfused patients is significantly higher than the number of transfused patients.

¶ Included in this category: anastomotic leak, wound dehiscence, persistent ileus.

**Table 3**: Multivariate analysis of transfusion predictive factors

| | Regression Coeficient | Odds Ration | 95% CI | P |
|---|---|---|---|---|
| Neoplasm | 1.91 | 6.77 | 2.51-18.2 | <0.001 |
| Exploratory laparotomy | 2.39 | 10.99 | 8.86-34.82 | 0.008 |
| Anaemia | 1.11 | 3.05 | 1.26-7-28 | 0.013 |

**Table 4**: Bivariate Comparison between nonagenarians and 3rd aged patients

| | | Nonagenarians | 3rd Age | p |
|---|---|---|---|---|
| Basal status | Female/male | 92(68.1)/43(31.9) | 73(54.1)/62(46.0) | **>0.001*** |
| | ASA II | 37 (27.4) | 78 (57.8) | **>0.001**+ |
| | ASA III | 87 (64.4) | 51 (37.8) | **0.001*** |
| | ASA IV | 11 (8.1) | 6 (4.4) | 0.306 |
| | Atrial Fibrillation | 51 (37.8) | 27 (20.0) | **0.003*** |
| | Hypertension | 81 (60.0) | 86 (63.2) | 0.586 |
| | Heart Ischaemia | 22 (16.3) | 22 (16.3) | 0.992 |
| | Heart failure | 35 (25.9) | 17 (12.6) | **0.010*** |
| | COPD | 23 (17.0) | 21 (15.6) | 0.732 |
| | Diabetes | 25 (18.5) | 44 (32.6) | **0.012**+ |
| | Renal failure | 15 (11.1) | 10 (7.4) | 0.374 |
| | Stroke | 26 (19.3) | 26 (19.3) | 0.996 |
| | Peripheral vasculopathy | 22 (16.3) | 23 (17.3) | 0.835 |
| | Neoplasm | 31 (23.0) | 26 (19.3) | 0.485 |
| | Dementia | 29 (21.5) | 9 (6.7) | **0.002*** |
| Trasnfusion | Intraop. blood loss >500cc | 12 (8.89) | 9 (6.7) | 0.542 |
| | Preoperative Hb | 11.92±1.93 | 12.18±2.19 | 0.340 |
| | Preoperative anemia | 74 (54.81) | 64 (47.4) | 0.238 |
| | Postoperative anemia | 100 (74.1) | 84 (62.2) | 0.055 |
| | Threshold Hb | 8.08±0.87 | 7.23±1.74 | **0.012*** |
| | RBCU/Total pts (Transfusion Index) | 0.99 | 1.14 | 0.540 |
| | RBCU/ Transf pts (Actual Transfusion Index) | 2.89 | 3.15 | 0.588 |
| | Pt Transf/Total pts (Transfusion Rate) | 0.35 | 0.35 | 0.974 |

| | | | | |
|---|---|---|---|---|
| Outcomes | Heart failure/pulm edema | 13 (9.6) | 8 (5.9) | 0.274 |
| | Angina/infarction | 3 (2.2) | 6 (4.4) | 0.271 |
| | Arrhythmia | 7 (5.2) | 13 (9.7) | 0.186 |
| | COPD exacerbation | 2 (1.5) | 6 (4.4) | 0.131 |
| | Pneumonia | 6 (4.4) | 10 (7.4) | 0.289 |
| | Pulmonary embolism | - | - | - |
| | Acute renal impairment | 21 (15.6) | 21 (15.6) | 0.971 |
| | Cerebro vascular accident | 5 (3.7) | 1 (0.7) | 0.179 |
| | Urinary tract infection | 9 (6.7) | 1 (0.7) | **0.026*** |
| | Hemorrage | 7 (5.2) | 9 (6.7) | 0.614 |
| | Surgical site infection | 4 (3.0) | 9 (6.7) | 0.168 |
| | Abdominal complications | 17 (12.6) | 21 (15.6) | 0.535 |
| | Sepsis | 10 (7.4) | 13 (9.6) | 0.541 |
| | Mortality | 49 (36.3) | 22 (16.3) | **0.001*** |
| | Length of Hospital stay | 9.99±7.04 | 12.01±14.21 | 0.154± |

***** $p<0.05$ the number of nonagenarians is significantly higher than the number of younger olds.

+ $p<0.05$ the number of young olds is significantly higher than the number of nonagenarians.

RBCU: Red blood cell units

Pt: patients. Transf pt.: transfused patients, Total pts.: total number of patients