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Original Article

Three-year survival follow-up of patients with gastrointestinal cancer treated during the COVID-19 pandemic in Spain: data from the PANDORA-TTD20 study

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Abstract

Introduction: The initial SARS-CoV-2 pandemic wave in Spain in 2020 precipitated significant paradigm shifts in gastrointestinal oncology patient management. This study captures the "Zeitgeist" of this period by analyzing adaptive strategies, treatment modifications, and survival outcomes, leveraging a 3-year follow-up perspective to extract insights from this unprecedented experience.

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Methods: We conducted a multicenter, retrospective cohort study utilizing the RETUD-TTD registry, encompassing 703 patients across 19 Spanish centers in April 2020. We evaluated alterations in clinical practice, therapeutic approaches, coronavirus disease 2019 (COVID-19)-related impacts, and patient survival. A Bayesian hierarchical model was employed to identify potential regional-specific frailties.

Results: The peak of the pandemic in April 2020 catalyzed substantial shifts in oncological care delivery. Outpatient consultations decreased by 13%, with a notable selection bias toward cases with more favorable prognostic indicators. Multidisciplinary tumor board discussions were significantly curtailed (eg, mean monthly colorectal cancer cases discussed was reduced from 40 to 23), compromising qualitative care measures. This occurred concurrently with an average of over 3 oncologists per center on medical leave. Contrary to initial concerns, the healthcare system demonstrated remarkable resilience. The majority of patients received standard-of-care therapies with regulatory approval, albeit with regimen modifications in 15% of cases. These adaptations included extended dosing intervals, dose intensity modulations, and transitions to oral formulations while maintaining unexpectedly stable long-term survival outcomes. The Bayesian frailty model detected minimal unmeasured prognostic factors related to geographic location, and the type of pandemic-induced adaptation did not significantly impact survival. The model revealed that coronavirus disease 2019's impact was less pronounced than other core prognostic variables.

Conclusions: The decentralized Spanish healthcare system exhibited substantial robustness in managing pre-pandemic diagnosed gastrointestinal malignancies, despite asymmetrical, and occasionally severe organizational disruptions. The insights gleaned from this experience could inform future crisis preparedness strategies and optimize care provision during subsequent public health emergencies.

Key words: gastrointestinal cancer; coronavirus disease 2019; Spain; PANDORA-TTD20; RETUD registry; spatial frailties.

Implications for practice

The impact of coronavirus disease 2019 (COVID-19) on gastrointestinal cancer care in Spain was examined, revealing a "test laboratory" scenario. This study highlighted asymmetric changes in treatment strategies during the pandemic. Despite challenges, most centers maintained oncology care, witnessing only a slight 13% consultation drop. The data showed stable survival outcomes, mirroring figures from the pre-COVID-19 era. Spain's healthcare displayed strong resilience, emphasizing the adaptability of its systems in crisis.

Introduction

Spain was severely affected by the coronavirus disease 2019 (COVID-19) pandemic in 2020, ranking third in Europe for confirmed cases with nearly 30 000 deaths.[1-3] An estimated 6% of the population was infected during the first 2 waves, resulting in over 100 000 hospital admissions.[3,4] The impact varied regionally,[5,6] with areas like Madrid and Catalonia experiencing higher case fatality rates.[6-9]

The nationwide state of emergency, declared in March 2020, led to regional lockdowns[10] and a decentralized crisis management approach.[3] This stressed the healthcare system, hampering its capacity to diagnose, and treat non-COVID-19 diseases.[11] Cases of chronic pathologies, including neoplastic diseases, decreased markedly during the first 2 waves.[12-14]

Gastrointestinal cancer screening in Spain was significantly disrupted, leading to many undiagnosed patients. Compared to 2019, diagnoses of digestive cancers,[15-17] including colorectal cancer, fell by 17%.[18] This underdiagnosis persisted in some regions until 2022.[19] High COVID-19 mortality among oncology patients led to hesitancy in seeking medical consultation,[20] exacerbated by longer waiting times for diagnostic tests and reduced surgical activity.[17,21-23]

The impact on Medical Oncology Services, particularly on perioperative cancer management and treatment in advanced age, has not been thoroughly documented. New visits to medical oncology departments dropped by around 20% between February and June 2020 across Spain.[17] Management protocols for advanced tumors were modified swiftly, promoting preoperative therapies to delay surgeries,[22] and telemedicine consultations became more prevalent.[24] Scientific societies published consensus documents on cancer patient management, particularly for gastrointestinal tumors.[25-27] However, there was a noticeable decline in medical day hospital activity, including lower administration of chemotherapy and a 13% reduction in clinical trial recruitment.[17]

This study aims to document the alterations in structure and care provision for gastrointestinal cancer in Spain's oncology departments affiliated with a national cooperative group. It evaluates the impact of pandemic-related policies on research, treatment, and survival across different geographical regions of Spain during the peak of the pandemic in April 2020. The findings will provide insights into healthcare resilience and adaptations in oncology care during unprecedented disruptions.

Method

This study utilized data from the Spanish Registry of Digestive Tumors (RETUD), establishing PANDORA-TTD20 as a retrospective cohort involving 19 TTD-affiliated centers. The study population comprised patients seen between April 20, 2000 and 24, 2020, during the peak of Spain's first COVID-19 wave. Eligible participants were adults diagnosed with gastrointestinal cancer who were treated at the Oncology Department. Outcome analyses focused on patients with localized tumors under active treatment and all patients with advanced disease stages. A 3-year survival assessment was conducted with a follow-up in April 2023. An additional survey investigated staffing, tumor committee activity, and patient volume in participating centers. The primary aim was to examine changes in organization, structures, staffing, and committees that affect digestive cancer management, and identify potential spatial frailties associated with regional disparities.[28] The primary endpoint was overall survival (OS) from April 22, 2020, to any-cause death or censoring. Secondary aims sought to gain insight into cancer management patterns during the pandemic. Variables included medical factors (ECOG-PS, comorbidities, age, sex, disease stage, tumor location, treatment goals, clinical trial participation), management patterns, SARS-CoV-2 infection rates and consequences, center-specific data, and regional COVID-19 information from the Spanish Ministry of Health.[3] Statistical analysis employed a Bayesian semiparametric proportional hazards model, with spatial location modeled via frailties using an independent identically distributed non-informative Gaussian prior.[28,29] An additional analysis used a Gaussian random field prior based on geographic coordinates.[30] A multivariable model incorporated all mentioned covariates.

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Exponentiated frailties were represented on a geographic map, with correlation between regional frailties and COVID-19 situation quantified using Tjostheim's coefficient.[31] Basic summary statistics, Kaplan-Meier estimator for survival modeling, and 2-tailed Wilcoxon test for paired data were also utilized. Analyses were performed using R v4.3.1 with relevant libraries.[30,32-34] The study adhered to ethical regulations, obtained informed consent from living participants and received approval from the Drug Research Ethics Committee of all participating centers. A comprehensive description of the materials and methods employed in this study, including detailed protocols, statistical analyses, and Supplementary Data, is provided in the Supplementary Appendix.

Results

Patient care during the pandemic

A cohort of 703 patients, seen in-person at 19 participating Medical Oncology services between April 20, 2000 and 24, 2020, was consecutively recruited for the PANDORA-TTD20 study. Table 1 provides baseline characteristics, with Supplementary Table S1 showing study recruitment by participating regions and centers and Supplementary Tables S3 and S4 depicting participating oncology departments' characteristics and patient baseline characteristics per center, respectively. Of the cohort, 31% ($n = 221$) had localized tumors, with 55% (121/221) of those under follow-up without active intervention. Of the patients with localized cancers requiring evaluation (100/221), 79% (79/100) were recommended for systemic antineoplastic treatment. Of those recommended, 93% (74/79) received the treatment. Standard adjuvant therapy was administered to 95% (70/74) of treated patients, with 18% (13/74) undergoing regimen modifications. Oncology consultation appointments were affected in 9% of cases (Table 2). Of the rectal cancer surgeries ($n = 16$), one case (6%) was postponed by 3 weeks.

Metastatic disease was present in 68% (482/703), with 65% (313/482) of those indicated for active treatment. Despite challenges, 87% (272/313) initiated or continued treatment. The pandemic was the sole reason for stopping therapy in 2% (7/313) of cases. Among treated patients ($n = 272$), pandemic-related adjustments included: lengthened intervals among cycles (6%, 17/272), dose adjustments (5%, 15/272), both modifications (2%, 6/272), and switching to oral forms (1%, 3/272). Appointments were transitioned to telephone consultations in 11% (31/272) and spaced out for 6% (16/272) of cases. Table 2 lists these modifications.

Regarding clinical research, 18% (56/313) of eligible patients could not participate in trials due to pandemic-linked causes. Of pre-enrolled patients ($n = 76$), 84% (64/76) maintained experimental treatment, 14% (11) withdrew due to progression, and one discontinued due to the pandemic. For metastatic cancer patients eligible for surgery (9%, 27/313), 74% (20/27) underwent the operation as planned. Supplementary Table S5 provides a detailed overview of metastatic cancer patient management per center.

By April 20–24, 2020, 4.3% (30/703) of subjects had acquired COVID-19, with 83% (25/30) having metastatic cancer. The infection-related mortality was 7% (2/30). COVID-19 indirectly impacted patient care, with 30% (9/30) experiencing progression after treatment interruption, and 23% (7/30) requiring treatment adjustments or halting. Supplementary Table S6 details COVID-19's impact on these patients.

Table 1. Baseline characteristics (April 2020)

Baseline characteristics	N (%)
Age, mean (range)	65 (30-89)
Sex, women	260 (36.9)
Performance status, ECOG-PS	
0	209 (29.7)
1	341 (48.1)
2	66 (9.3)
3	16 (2.2)
4	5 (0.7)
Unknown	66 (9.3)
Comorbidities that limit systemic treatment *	128 (18.1)
Patient referred from another area or health center	138 (19.6)
Primary cancer site	
Esophagus	41 (5.8)
Stomach	47 (6.6)
Pancreas	150 (21.3)
Liver and bile duct	64 (9.1)
Colon	266 (37.8)
Rectum	127 (18.0)
Anus	8 (1.1)
Tumor stage	
Non metastatic	221 (31.4)
Metastatic	482 (68.5)
Clinical trial participants	76 (10.8)

Organizational changes and status of centers

The characteristics of the 19 centers are displayed in Supplementary Table S3. Of these, 17 serve population areas exceeding 300 000 inhabitants. Typically, medical oncology departments have a median of 28 oncologists (range 16-65), with 5 (range 2-12) specializing in digestive tumors. Twelve hospitals had specific committees for pancreatohepatobiliary, colorectal, and esophagogastric tumors, while 7 had a single gastrointestinal tumor committee.

In April 2020, centers averaged 3.2 COVID-19-related absences (range 0-9), with 2.3 due to staff contracting COVID-19 and 0.8 (range 0-4) due to preventive quarantine. Total leaves increased from 0.4 to 3.8 per center between February and April 2020 (Wilcoxon test, $P = .0016$). Adaptations are shown in Supplementary Table S7. Among centers, 37% ($n = 7$) maintained regular activity, 58% ($n = 11$) made adjustments, and 5% ($n = 1$) suspended many oncological activities. Supplementary Table S8 presents patient characteristics grouped by adaptation type.

Staff relocation occurred at 58% (11/19) of the centers (Figure 1). Patient consultations decreased by 13% from February to April 2020 (176-153, Wilcoxon test, $P = .002$). Multidisciplinary committee meetings saw significant declines (Wilcoxon test, $P < .01$): colorectal committees from 40 to 23 cases, esophagogastric from 17 to 9, and pancreatohepatobiliary from 24 to 16 (Figure 1B). Committee participation also dropped, with colorectal tumor committees decreasing from 14.8 to 6.7 specialists per center (Wilcoxon test, $P = .008$). Only 3/12 colorectal cancer committees continued in-person

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Table 2. Management of patients with non-metastatic or metastatic cancer during the COVID-19 pandemic (April 2020).

Management of patients with non-metastatic cancer	*N* (%) 221 (100)
Treatment and follow-up management	
Follow-up visits	121 (54.7)
Treatment visits	100 (45.3)
Adjuvant treatment not indicated	21 (9.5)
Adjuvant chemotherapy indicated by oncologic criteria	79 (35.7)
Prescribed despite the pandemic	74 (33.4)
Not prescribed due to the pandemic	1 (0.45)
Not prescribed for other reasons	4 (1.8)
Treatment strategies	
Standard regimen	70 (31.76)
Modification of the standard regimen	13 (5.9)
Standard regimen adjusting dose	6 (2.7)
Standard regimen adjusting interval	5 (2.2)
Standard regimen adjusting dose and interval	1 (0.4)
Change the route of administration of any drug from IV to oral	1 (0.4)
Modification of visits	21 (9.5)
In-person and telephone visits were alternated	13 (5.8)
Only telephone visits were conducted	6 (2.7)
Visits were spaced out	2 (0.9)
Management of patients with metastatic cancer	***N*** **(%) 482 (100)**
Treatment and follow-up management	
Follow-up visit	109 (22.6)
Decision on treatment	373 (87.4)
Alternative to systemic treatment *	60 (12.5)
Systemic treatment indicated by medical criteria	313 (64.9)
Prescribed despite the pandemic	272 (56.4)
Not prescribed due to the pandemic	7 (1.4)
Not prescribed for other reasons	33 (6.8)
Reasons for not initiating or continuing systemic treatment	
Improved supportive care as systemic treatment is contraindicated	10 (2.0)
Improved supportive care favored by the pandemic	8 (1.6)
Mixed reasons	23 (4.7)
Type of systemic treatment	***N*** **(%) 272 (100)**
First-line chemotherapy with palliative intention	126 (46.3)
First-line chemotherapy with intention to convert	40 (14.7)
Second-line chemotherapy	67 (24.6)
Third-line chemotherapy or beyond	31 (11.4)
Adjuvant chemotherapy for metastasis resection	8 (2.9)
Treatment strategies	
Standard therapy	222 (81.7)
Modification of the regimen	50 (18.3)
Alternative antineoplastic agents to the standard	9 (1.8)
Standard regimen adjusting dose	15 (3.1)
Standard regimen adjusting interval	17 (3.5)
Standard regimen adjusting dose and interval	6 (1.2)
Change the route of administration of any drug from IV to oral	3 (0.6)
Modification of visits	51 (18.7)
Several cycles were scheduled without visits and without blood tests	3 (0.6)
In-person and telephone visits were alternated	31 (6.4)
Only telephone visits were conducted	3 (0.6)
Visits were spaced out	16 (3.3)
Suitability for metastasis surgery	27 (9.9)
Performed as scheduled	20 (4.1)
Delayed due to COVID-19	4 (0.8)
Chemotherapy was continued	4 (0.8)
Rejected due to disease progression	1 (0.2)
Replaced by locoregional treatments (yttrium microspheres)	2 (0.4)

meetings, and similar trends were observed in other committees (Figure 2).

In gastroesophageal tumor committees, 4/12 switched to non-face-to-face meetings, and 3/12 alternated. Meeting frequency changed from weekly to every 2-4 weeks, conducted primarily via video conference. Regarding management protocols, 58% (11/19) of centers adopted SEOM recommendations for COVID-19, 16% (3/19) followed ESMO guidelines, and 26% (5/19) developed their own protocols.

Survival-based outcomes and frailties

Median survival rates by tumor type, center, and stage over 3 years are shown in Figure 3 and Supplementary Table S9. No definitive association was found among organizational adaptations, committee modifications, and survival outcomes.

A spatial multivariable model revealed minimal variations in hazard rates associated with geographical locations, both regionally and center-wise (Figure 4), with frailties approaching zero. This suggests a low probability of unobserved variables influencing prognosis. The effect of known covariables is presented in Supplementary Table S10, showing the expected association of ECOG-PS, line number, and stage with prognosis. Supplementary Figure S1 illustrates the posterior probability distribution for hazard ratios in each autonomous community, emphasizing the relative uniformity among regions.

Data showed minimal correlation with regional COVID-19 incidence, with a Tjostheim's coefficient of −0.056 (standard error, 0.33). Supplementary Figure S2 displays the regional distribution of cumulative COVID-19 incidences in April 2020. In a multivariable Cox model, adaptation type did not significantly influence survival ($P = .346$), while the main prognostic factors were ECOG-PS, tumor location, line of treatment, and stage.

Discussion

This study investigated the varying impact of COVID-19 on gastrointestinal cancer management across Spain's regions. The pandemic significantly transformed organizational structures, affecting staffing, consultation modalities, and

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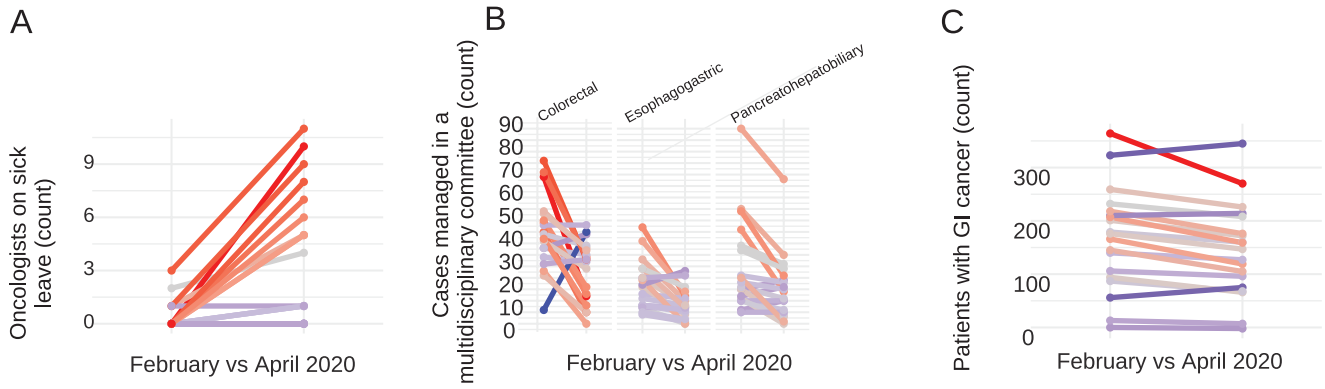

Figure 1. Oncologist leaves and patient management in committees and consultations during the COVID-19 pandemic. The colors and gradient of the arrows indicate the intensity of the changes.

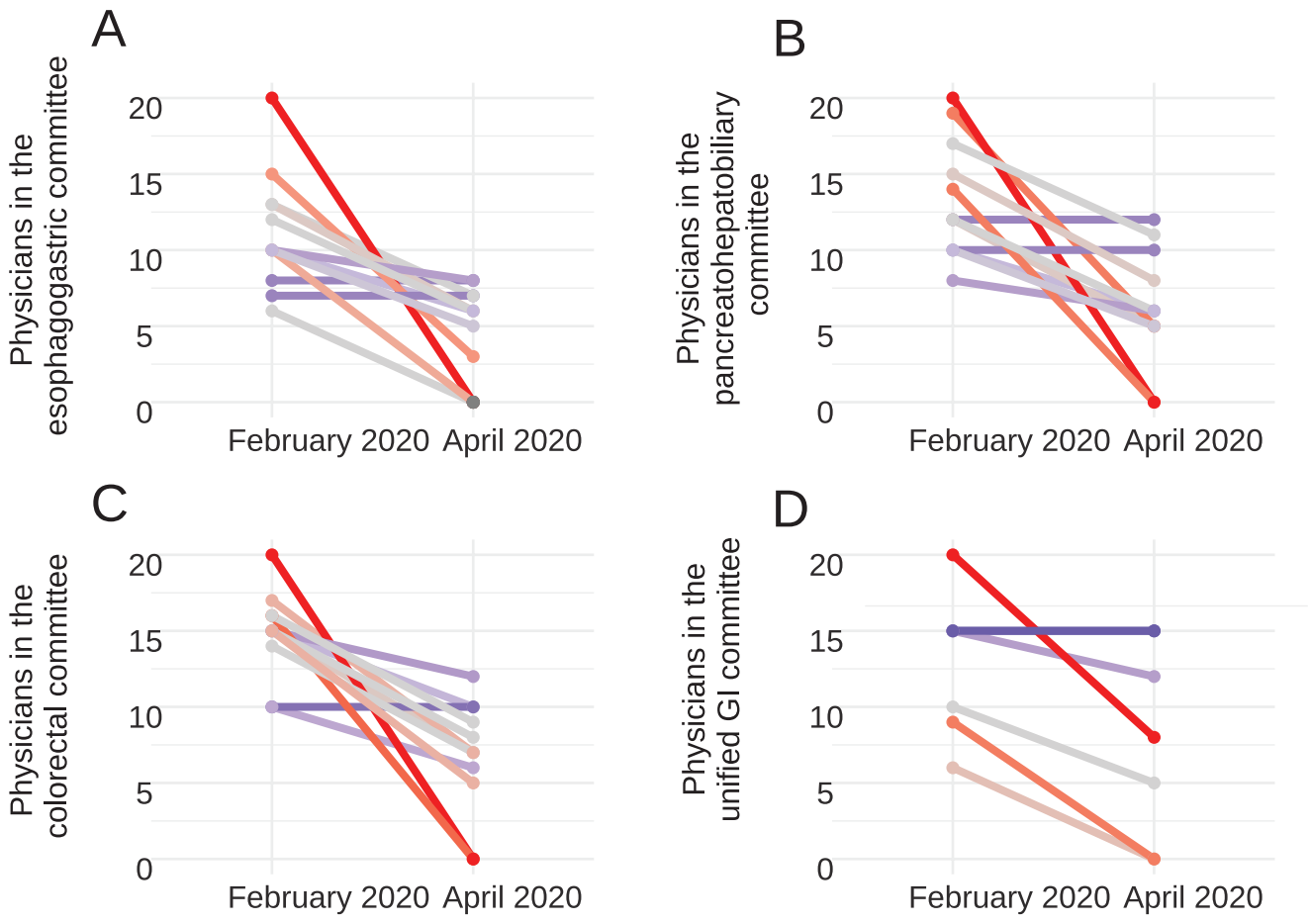

Figure 2. Staff involvement in multidisciplinary committees for patients with gastrointestinal cancer: a comparison of February and April 2020. The colors and gradient of the arrows indicate the intensity of the changes.

committee discussions.[35] Despite these disruptions, most centers maintained oncology patient care with necessary adjustments.

During April 20–24, 2020, patient consultations decreased by 13% compared to February 10–14, 2020. This reduction was achieved by prioritizing patients with better functional status, evidenced by the absence of ECOG-PS > 2 cases in 8 centers, cases with complicating comorbidities in 4 centers, and patients eligible for clinical trials in 6 hospitals. Most patients eligible for treatment received care without substantial alterations, even during the pandemic's peak.

OS outcomes remained like pre-pandemic historical controls. Median OS from April 2020 was 28.1 months (95% CI, 19.6-32.8) for advanced colorectal cancer, comparable to 27.6 months (95% CI, 25.9-29.2) in the 2018-2019 PROMETEO registry.[36,37] For advanced gastric cancer, median OS was 9 months (95% CI, 5.5-16.4), similar to the pre-pandemic AGAMENON-SEOM registry's 10.8 months (95% CI, 10.5-11.1) (Z-test, $P = .518$).[36] For advanced pancreatic

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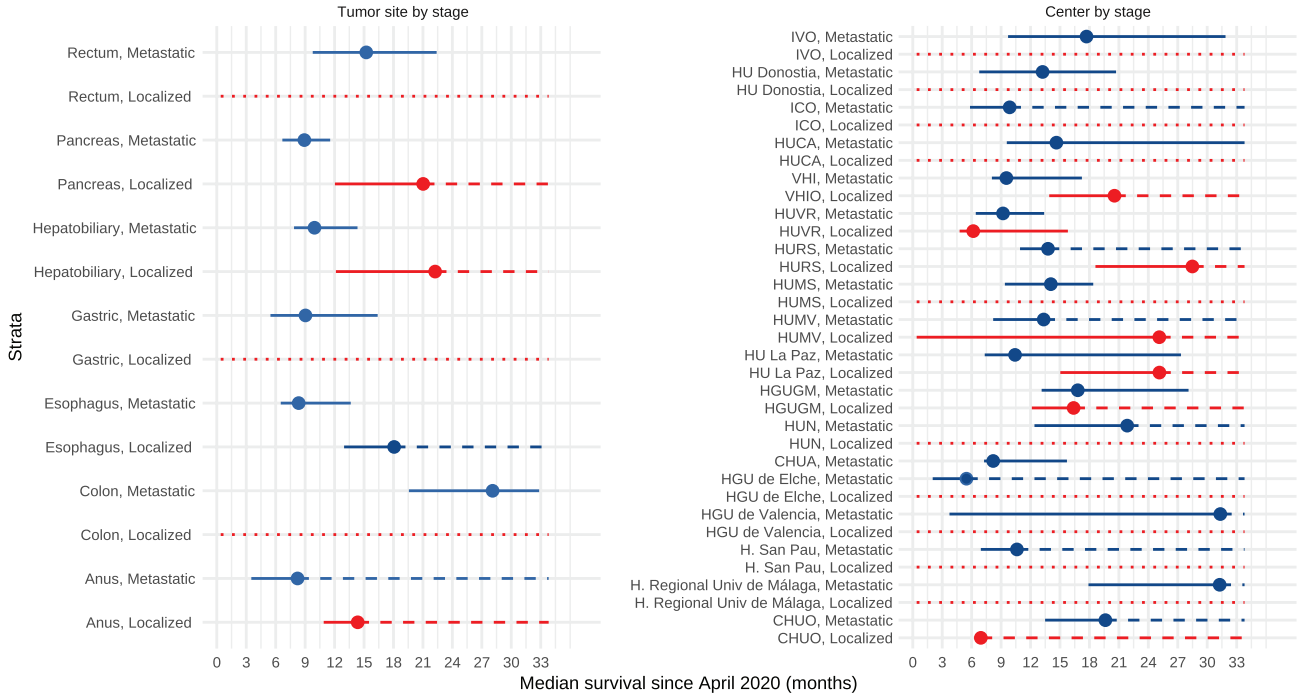

Figure 3. Overall survival stratified by tumor type, center, and stage (unadjusted). Abbreviations: CHUA, Complejo Hospitalario Universitario de A Coruña; CHUO, Complejo Hospitalario Universitario de Orense; H. San Pau, Hospital de la Santa Creu i Sant Pau; HGU de Elche, Hospital General Universitario de Elche; HGU de Valencia, Hospital General Universitario de Valencia; HGU, Hospital General Universitario; HGUGM, Hospital General Universitario Gregorio Marañón; HU La Paz, Hospital Universitario La Paz; HU, Hospital Universitario; HUCA, Hospital Universitario Central de Asturias, HUMS, Hospital Universitario Miguel Servet; HUMV, Hospital Universitario Marqués de Valdecilla; HUN, Hospital Universitario de Navarra; HURC, Hospital Universitario Ramón y Cajal; HURS, Hospital Universitario Reina Sofía; HUVR, Hospital Universitario Virgen del Rocío ICO L'Hospitalet, Instituto Catalán de Oncología; IVO, Instituto Valenciano de Oncología; VHIO, Hospital Universitario de la Vall d'Hebron y Vall d'Hebron Instituto de Oncología;. Dashed lines represent the upper limits of the confidence intervals that were not reached. The dotted lines indicate that there are no available events for that stratum. The color red identifies patients with localized cancer, and the color blue identifies patients with metastatic cancer. Hospital Universitario Ramón y Cajal provided only organizational information but did not report direct patient data.

cancer, median OS was 8.9 months (95% CI, 6.7-11.5), aligning with the ANICE-PAC study's 7.2 months (95% CI, 6.0-8.5).[38] For localized esophageal cancer, our findings of 18.1 months (95% CI 13—not reached) were not significantly different from the AGAMENON registry's 22.5 months (95% CI, 18.5-31.1).[39] The most significant change was the reduction in multidisciplinary committee evaluations; however, the impact on prognosis appears minimal, as decisions were made through alternative channels that ensured process efficacy.

Our results reveal stable OS outcomes in cancer patients treated during the first COVID-19 wave peak, highlighting the Spanish healthcare system's resilience. This contrasts with previously described trends in diagnostic management.[40,41] Literature has suggested that the pandemic underscored chronic issues in the system's decentralized structure,[15-17] with decreased attention during initial cancer diagnostic phases documented across healthcare domains.[42,43] Patient surveys indicated a perceived decline in care,[44] yet this trend is not confirmed in our study of pre-pandemic diagnosed patients with gastrointestinal cancer. After a 3-year follow-up, we found no definitive evidence linking survival outcomes with organizational adaptations, committee modifications, or therapeutic decisions at each center. Analysis of spatial frailties[45] suggests that regional disparities due to unobserved variables are unlikely to have influenced patient prognosis. Adjustments and impacts were relatively uniform across regions, with mechanisms mitigating effects on most patients.

Limitations include the retrospective design, albeit strengthened by a 3-year follow-up, and the limited number of participating centers, though nationally representative. Our study focused on major organizational changes during the pandemic, attempting to uncover hidden aspects through unobserved variable analysis. We did not assess the prognosis of patients who discontinued consultations due to the pandemic, with uncertain impact on cancer prognosis and COVID-19 exposure. The study's focus on survival outcomes does not address the psychological impact on cancer patients, though research suggests they demonstrated resilience.[46,47] The brief study period in April 2020 may not capture the full picture of longer-lasting, regionally varied contingency plans. Our study demonstrates healthcare system resilience for patients accessing care during the pandemic peak but cannot fully address the overall impact on gastrointestinal cancer outcomes. The 13% reduction in consultations suggests that many patients did not access care and may present later with advanced disease. The high proportion of metastatic cases (68%), although compatible with the treatment duration dynamics and workload differences between metastatic and non-metastatic cancer patients, still warrants careful consideration. This limitation in generalizability, likely influenced by screening suspensions and potential selection bias, necessitates a cautious interpretation of our findings. Furthermore, our study's follow-up period, while adequate for assessing outcomes in metastatic disease with relatively mature and precise estimates, may not

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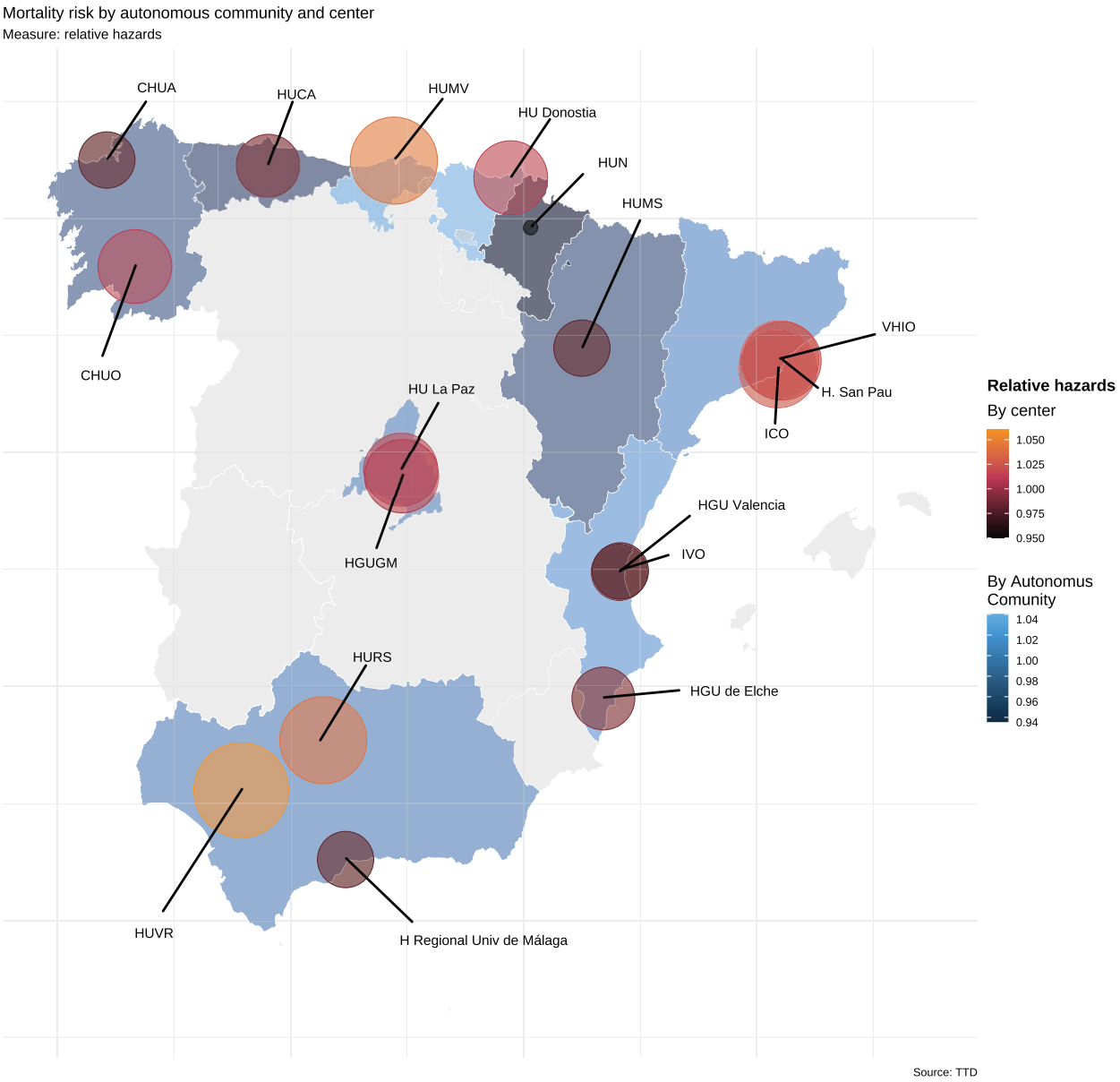

Figure 4. Mortality risk by autonomous community and center. Abbreviations: CHUA, Complejo Hospitalario Universitario de A Coruña; CHUO, Complejo Hospitalario Universitario de Orense; H. San Pau, Hospital de la Santa Creu i Sant Pau; HGU de Elche, Hospital General Universitario de Elche; HGU de Valencia, Hospital General Universitario de Valencia; HGU, Hospital General Universitario; HGUGM, Hospital General Universitario Gregorio Marañón; HU La Paz, Hospital Universitario La Paz; HU, Hospital Universitario; HUCA, Hospital Universitario Central de Asturias, HUMV, Hospital Universitario Marqués de Valdecilla; HUMS, Hospital Universitario Miguel Servet; HUN, Hospital Universitario de Navarra; HURC, Hospital Universitario Ramón y Cajal; HURS, Hospital Universitario Reina Sofía; HUVR, Hospital Universitario Virgen del Rocío.; ICO L'Hospitalet, Instituto Catalán de Oncología; IVO, Instituto Valenciano de Oncología; VHIO, Hospital Universitario de la Vall d'Hebron y Vall d'Hebron Instituto de Oncología*Note*: The bluer or more orange it is, the higher the hazard rate. Hospital Universitario Ramón y Cajal provided only organizational information but did not report direct patient data.

fully capture the potential increase in recurrence rates for localized cancers. These initially localized cases could potentially progress to metastatic disease in the years following our study, thereby affecting long-term survival outcomes. As evidenced in Figure 3, the survival estimates for localized cancers show considerable imprecision, which limits our ability to draw firm conclusions about how the pandemic impacted early-stage disease outcomes. Given these limitations, follow-up studies are crucial to examine delayed presentations, long-term recurrence patterns, and provide a more comprehensive view of COVID-19's enduring impact on cancer care across all disease stages.

While acknowledging the limitations, this study reveals important findings. Notably, most patients who were recommended treatment successfully received standard regimens, despite highly variable regional pandemic responses in Spain's communities. Adaptations were modest, indicating healthcare resilience. Cross-community cooperative groups likely mitigated the impact, enabling consistent patient care. Uniform patient outcomes across regions thus spotlights the adaptability and robustness of Spain's healthcare infrastructure during the pandemic. These findings show that coordinated efforts between healthcare providers and administrative systems can minimize the negative impacts of future public health crises

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on cancer patient management and outcomes. However, it is vital that such strategies extend to all patients, including the most vulnerable, to prevent disease progression during crises.

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Author contributions

Pilar García-Alfonso, Enrique Aranda and Paula Jimenez-Fonseca have contributed to the conceptualization, investigation. Alberto Carmona-Bayonas, and Paula Jimenez-Fonseca have performed formal analysis, methodology, and writing—original draft, and Pilar García-Alfonso, has participated in writing—original draft. Alberto Carmona-Bayonas, Pilar García-Alfonso and Paula Jimenez-Fonseca have provided support in project administration. Javier Soto-Alsar, Iosune Baraibar, Cristina Santos, Adelaida La Casta, Ismael Ghanem, Gema Pulido Cortijo, Axel Mariño Méndez, Roberto Pazo-Cid, Ruth Vera, Marcos Melián, Julia Alcaide, Begoña Graña, David Páez, Inmaculada Gallego, Miriam Lobo, Miguel Borregón, Ana Fernández Montes, Eva Martínez de Castro, have been involved in data curation. All authors have carried out resources, supervision, validation, visualisation, writing—review and editing.

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Conflicts of interest

P.G.A. has received honoraria for speakers' bureaus from Amgen, Roche, Merck-Serono, Sanofi-Aventis, Pierre Fabre and Servier; advisory activities from Amgen, Roche, Merck-Serono, Sanofi-Aventis, Pierre Fabre and Servier and support for attending meetings and travel from Amgen, Roche, Merck-Serono, Sanofi-Aventis, Pierre Fabre and Servier. P.J.F. has received honoraria for speakers' bureaus or advisory boards from Astellas, AstraZeneca, Brystol Myes Squibb, Lilly, Merck, Novartis, and support for attending meetings and travel from Amgen. I.B. has received honoraria for speakers' bureaus from Astra Zeneca and support for attending meetings and travel from Amgen, Merck, Sanofi, and Servier. CS has received honoraria for speakers' bureaus from Amgen, Pierre Fabre, and support for attending meetings and travel from Merck, Amgen, and MSD. R.P.C. has received honoraria for medical writing and processing charges of publication from Astellas and Ipsen; contracts from Beigene, Celgene; speakers' bureaus from Eisai, Roche, BMS, Astellas; expert testimony from AstraZeneca and Lilly; advisory board from AstraZeneca, Roche and Ipsen and support for attending meetings and travel from Lilly, BMS and Roche. M.M. has received honoraria for speakers' bureaus from Amgen, Merck, Pierre-Fabre, Servier; advisory board from Merck, Servier and support for attending meetings and travel from Merck, Pierre-Fabre, Servier. I.G. has received honoraria for speakers' bureaus, expert testimony, and support for attending meetings and travel from AstraZeneca and Servier. M.L. has received honoraria for speakers' bureaus from Leo Pharma, Vifor Pharma, Fresenius Kabi, Pfizer, Servier, and support for attending meetings and travel from Novartis, Servier, Pharma Mar, AstraZeneca, and Roche. AFM. A.C.B. has received honoraria for speakers' bureaus or advisory boards from Astellas, Brystol Myes Squibb, Eisai, Lilly, MSD, Merck, Novartis, and support for attending meetings and travel from Novartis. E.A. has received honoraria for the advisory board from Amgen, Bayer, Celgene, Merck, Roche, and Sanofi. J.S.A., A.L.C., I.G., G.P.C., A.M.M., R.V., J.A., B.G., D.P., M.B., A.F.M., and E.M.C. have no conflict of interest related to the scope of this article.

Research involving human participants

This study was conducted in accordance with the ethical regulations of each participating center, ensuring the protection of rights and safety of patients in accordance with local laws and international ethical principles. The study was approved by the Drug Research Ethics Committee of the Principality of Asturias (Code 2020.317).

Consent to participate

Signed informed consent was obtained from all patients.

Consent to publish

Informed consent and approval by the national competent authorities including permission for publication and diffusion of the data was obtained.

Data availability

The analyses were carried out with the statistical package R v4.3.1, including the survival, spBayesSurv, and SpatialPack libraries. The R code for data analysis is in **Supplementary Table 2**.

Supplementary material

Supplementary material is available at *The Oncologist* online.

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