



End-of-life care for patients with pancreatic cancer in France: a nationwide population-based cohort study

Ugo Marchese, Vanessa Pauly, Anna Pellat, Yasmina Richa , Guillaume Fond, Stylianos Tzedakis , Martin Gaillard, Basile Fuchs, Veronica Orleans, David Fuks, Mehdi El Amrani and Laurent Boyer 

Abstract

Background: Pancreatic cancer, a frequently fatal disease with severe symptoms, can require high-intensity end-of-life (HI-EOL) care, posing challenges to patients' well-being. The examination of HI-EOL care to develop tailored interventions in the management of pancreatic cancer is a critical, yet underexplored area.

Objectives: The objective of this study was to assess the factors that influence the intensity of end-of-life (EOL) care in France.

Design: A retrospective study of patients registered in the French Nationwide database who were hospitalized in France for pancreatic adenocarcinoma from January 1, 2014 to December 31, 2019, and subsequently died during the follow-up period.

Methods: Data on patient demographics, clinical characteristics, hospitalization details, and palliative care were collected. The primary outcome measure was the evaluation of HI-EOL care, defined by indicators such as death in an intensive care unit (ICU), multiple hospitalizations, and chemotherapy administration within the last 30 days of life. Secondary outcomes included indicators of most-intensive EOL (MI-EOL) care and invasive procedures (IP). Univariate and multivariate logistic regression analyses were conducted to identify factors associated with each outcome measure.

Results: A total of 42,696 patients who died from pancreatic adenocarcinoma were included. Among them, 41.1% experienced HI-EOL, with the most common indicators being multiple hospitalizations and death in an ICU, emergency room, or acute care unit. A smaller proportion (2.8%) received MI-EOL care, while 28.1% underwent IPs in the last 30 days of life. The multivariate analysis revealed that male gender and follow-up in non-cancer specialized care facilities were associated with a higher risk of HI-EOL. Conversely, palliative care involvement and older age at death were identified as protective factors. Male gender, older age at death, and palliative care involvement were associated with lower rates of MI-EOL care and IPs.

Conclusion: These results underscore the importance of palliative care integration and individualized approaches in improving the EOL quality of care and patient outcomes for individuals with advanced pancreatic cancer.

Keywords: outcomes research, palliative care, pancreatic cancer, quality of life, surgery

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Correspondence to:

Ugo Marchese
Department of Digestive,
HPB and Endocrine
Surgery, Hôpital Cochin,
AP-HP Centre, 27 rue du
Faubourg St Jacques,
Paris 75014, France

Université de Paris Cité, 15
rue de l'école de médecine
75006 Paris, France
ugo.marchese@aphp.fr

Vanessa Pauly
Veronica Orleans
Laurent Boyer
Département
d'Information Médicale,
Hôpital de la Timone, 264
Rue Saint-Pierre, 13005
Marseille, France

Université d'Aix-Marseille,
Jardin du Pharo, 58
Boulevard Charles Livon,
13007 Marseille, France

Anna Pellat
Department of
Gastroenterology and
Digestive Oncology, Hôpital
Cochin, AP-HP Centre,
27 rue du Faubourg St
Jacques, 75014 Paris,
France

Université de Paris Cité, 15
rue de l'école de médecine
75006 Paris, France

Yasmina Richa
School of Medicine,
University College Cork,
Cork, Ireland

Guillaume Fond
Department of University
Psychiatry, Sainte
Marguerite University
Hospital, Assistance
Publique des Hôpitaux
de Marseille, Marseille,
France

Assistance Publique des
Hôpitaux de Marseille,
Aix-Marseille University,
UR3279: Health Service
Research and Quality of
Life Center - CEReSS,
Marseille, France

Stylios Tzedakis
Martin Gaillard

Department of Digestive,
HPB and Endocrine
Surgery, Hôpital Cochin,
AP-HP Centre, 27 rue du
Faubourg St Jacques,
75014 Paris, France

Université de Paris Cité, 15
rue de l'école de médecine
75006 Paris, France

Basile Fuchs

Département
d'Information Médicale,
Hôpital de Brest, 2 avenue
Foch, 29200 Brest, France

David Fuks

Department of Digestive
Surgery, Centre
Hospitalier Universitaire
Vaudois, 1011 Lausanne,
Switzerland

Mehdi El Amrani

Department of
Digestive Surgery and
Transplantation, CHRU de
Lille, 2 Av. Oscar Lambret,
59000 Lille, France

Université de Lille, 42 Rue
Paul Duez, 59000 Lille,
France

Introduction

Pancreatic cancer, predominantly represented by pancreatic adenocarcinoma, is the 6th leading cause of cancer-related death worldwide.^{1,2} Its impact is particularly pronounced in Western countries, and it is anticipated to become the second most prevalent cause of cancer-related deaths by 2030.^{3,4} While surgery is the only curative treatment, it is only possible for about 15% of patients.^{5,6} Overall, pancreatic cancer is often a lethal disease, frequently presenting with severe symptoms such as pain, bowel obstruction, diabetes, or jaundice, especially in advanced stages, including locally advanced and metastatic disease. The substantial symptom burden of pancreatic cancer often leads to high-intensity medical interventions, raising concerns about the impact on patients' quality of life and end-of-life (EOL) experiences.⁷ In France, patients are referred by physicians to palliative care services. A study showed that 57% of patients had access to inpatient palliative care varying between short stays, homecare units, and rehabilitation care units.⁸ Previous research suggests that aggressive care during this period can negatively affect patients' quality of life.^{9,10} Furthermore, studies have demonstrated that early engagement with palliative care can not only improve patients' well-being but also extend survival, as observed in cases of lung cancer.¹¹ In this context, the management of pancreatic cancer patients in high-intensity care settings, particularly near the EOL, is a critical but currently underexplored area of research. The objectives of this study are as follows: (i) to describe the intensity of EOL care among adult patients with pancreatic cancer who died between 2014 and 2019 in France and (ii) to identify the factors impacting the intensity of EOL care.

Patients and methods

Study design and data sources

We conducted a population-based, retrospective cohort study of patients who died of pancreatic adenocarcinoma in France between January 1, 2014, and December 31, 2019. Data were collected from the French national health data system (Système National des Données de Santé (SNDS)), a comprehensive national medico-administrative database covering about 99% of the French population. The SNDS database contains individual, anonymous, and comprehensive data on all health expenditure reimbursements of the French National Health Insurance

Information System (Système national d'information Inter-Régime de l'Assurance Maladie), along with patient demographic data (sex, age, comorbidities, etc.). The data include both outpatient and inpatient medical health expenditures, as it is integrated with the French Hospital Discharge database (Programme de Médicalisation des Systèmes d'Information (PMSI)). In the PMSI, diagnoses and interventions are collected and summarized according to the International Classification of Diseases, 10th edition (ICD-10)¹² and the Classification Commune des Actes Médicaux (CCAM),¹³ respectively. The coding process involves a combination of manual and artificial intelligence coding techniques, ensuring comprehensive and accurate data representation.¹⁴ The PMSI database is frequently and thoroughly verified by both its producer and payers due to possible financial and legal consequences as it is used to determine financial resources.¹⁵ This study complied with the French National Health Guidelines on Research involving Human Subjects and the manuscript follows the REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) statement¹⁶ and was approved by an ethical committee (registration number 4266138 Bis). This study followed the STROBE guidelines for reports of cohort studies. Data were anonymized according to French law and informed consent was not required.¹⁷

Population

All adults hospitalized in France for pancreatic adenocarcinoma between January 1, 2014 and December 31, 2019 and who died during the follow-up period (until the end of 2020) were included in the analysis. For the patient cohort, we selected patients using the ICD-10 codes corresponding to a related or primary diagnosis for admission in the acute care unit (ACU): C25*, C24*, C17, C240, C241, and C249. For the analysis, we selected only patients who had a diagnosis of pancreatic adenocarcinoma. To analyze only incident cases, we excluded patients who had an ICD-10 code related to pancreatic adenocarcinoma diagnosis within the past 2 years. To exclude mortality related to surgical complications, we excluded patients who died in the postoperative period, 90 days after surgery with curative intent. Patients who died within 30 days following diagnosis were excluded because analysis of the primary outcome was not possible in this subgroup (indicators of care during the last

30 days of life). Moreover, we excluded patients who stayed in hospitals with no available data on the number of conventional beds, patients transferred within 48 h, and those hospitalized in non-metropolitan areas because of substantial differences in healthcare infrastructure, resources, and access to specialized care.¹⁸

Data collection

The following data were collected: (1) socio-demographic information, including age, sex, year of death, and ecological deprivation score based on patients' residence (deprivation index (FDep99 index) derived from multidimensional sources and validated on French data)¹⁹; (2) clinical information, including date of diagnosis, chronic comorbidities according to the Charlson comorbidities index (ChCI)²⁰; and (3) hospital data, including location of the last admission before death (from home, from another hospital, or from another unit in the same hospital), hospital type for last hospitalization before death (specialty center (university hospital or cancer center) vs non-specialty center), place of death (acute care, rehabilitation facilities, post-acute care, home, or home-based hospitalization), in-hospital palliative care during the preceding month (authorization of palliative unit or bed care or the presence of Z515 ICD-10 code implying involvement of palliative care, diagnostic-related groups 2303A01, 2303B1, 2303C1 for rehabilitation units; or type of care 04 for home-based hospitalization)), and travel time from the patient's home to the place of death (≤ 30 , 30–60, or > 60 min).

Outcome measures

The primary outcome was the intensity of EOL care according to the “high-intensive end-of-life” (HI-EOL) criteria by Earle *et al.*,⁹ as defined by the occurrence of at least one of the following indicators: death in an intensive care unit (ICU) or emergency room (ER) or ACU; ≥ 1 hospitalization in an ICU in the last 30 days of life; > 1 ER admission in the last 30 days of life; or > 1 hospitalization in an ACU in the last 30 days of life; ≥ 1 session of intrahospital intravenous chemotherapy < 14 days from death.²¹ The secondary outcomes included indicators of Most Invasive End-of-Life (MI-EOL) care or Invasive Procedures (IP) as defined by Earle *et al.*⁹ and Mullins *et al.*¹⁰ MI-EOL was defined as the occurrence of at least one of the following indicators: intubation, mechanical ventilation, cardiopulmonary resuscitation, and hemodialysis in the

last 30 days of life. The HI-EOL criteria by Earle *et al.* and the MI-EOL indicators by Earle and Mullins *et al.* have been developed using population-based studies of adult patients with cancer to allow for comparisons of care between countries. IP was defined as the occurrence of at least one of the following indicators in the last 30 days of life: arterial line placement, central line placement, surgery requiring general anesthesia, radiological interventional procedures, radiotherapy, artificial feeding, digestive endoscopy, and biliary tract interventional endoscopy.¹⁰ Table S1 lists all the specific codes (ICD-10 codes or procedure codes) as referenced by the French Classification of Medical Acts (CCAM).

Statistical analysis

Descriptive analyses for socio-demographic, clinical, and hospital data were presented as frequencies and percentages for qualitative variables and as mean \pm standard deviation with median (interquartile range, IQR) for quantitative variables. The percentages of patients who experienced HI-EOL, MI-EOL, and IP care were determined. Univariate and multivariate analyses using logistic models were employed to determine the socio-demographic, clinical, and hospital factors associated with the different outcomes. Each outcome was used as a separate dependent variable in the univariate and multivariable models. Variables relevant to the models were selected based on a threshold p value ≤ 0.2 in the univariate analysis (either in the HI-EOL or the MI-EOL model) and were included in the multivariable logistic models to calculate the odds of experiencing each outcome. Adjusted odds ratios (OR) were expressed with 95% confidence intervals.

We conducted a sensitivity analysis to evaluate the reliability of our primary multivariate analysis. The analysis included patients who did not undergo surgical resection for cancer within the last 90 days of their life.

Statistical significance was defined as $p < 0.05$. The statistical analysis was performed with SAS 9.4 (SAS Institute Inc., Cary, NC, USAS).

Results

Study population

During the study period, 42,696 patients died of pancreatic adenocarcinoma (flow chart—Figure 1).

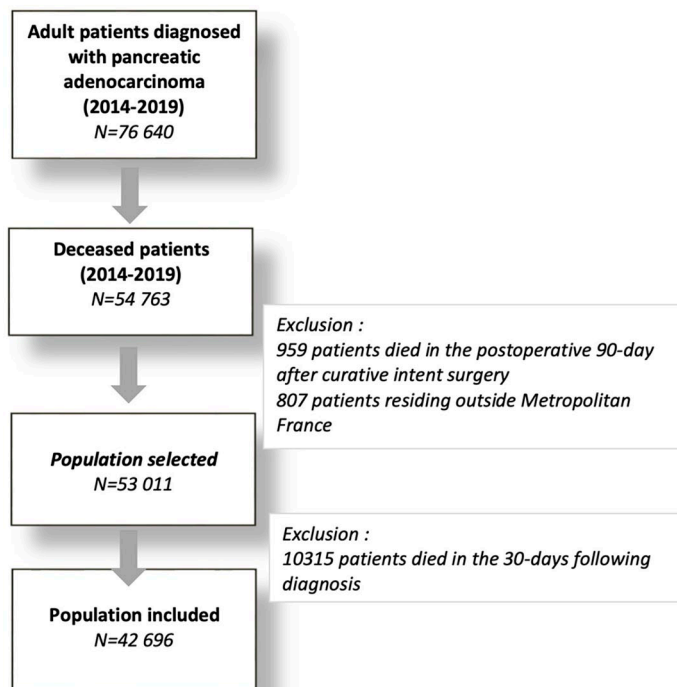


Figure 1. Flow chart.

As detailed in Table 1, the study population included 21,783 (51%) males. The median (SD) age at death for all patients was 72 years (11, 65). Of the selected common comorbidities at the time of death, 61.8% had a ChCI score higher than or equal to 3. Regarding the main type of center involved in patient care, 9348 (21.9%) and 2284 (5.4%) were managed in academic and cancer centers, respectively. The proportion of patients who received at least one cycle of chemotherapy was 66.9% and the median (IQR) number of cycles completed was 10 (4–20). During the observation period, 75.6% of patients received palliative care. Regarding the place of death, 13,939 patients (67.6%) died in an ACU and 9870 patients (23.1%) died at home, including 6232 patients who died without a hospital-based home service.

Primary outcomes

The primary outcome measures are presented in Table 2. A total of 41.1% patients experienced HI-EOL. The most frequent indicators of HI-EOL were hospitalization in an ACU more than once in the last 30 days of life (32.8%) and death in an ICU, ER, or ACU (32.8%). Among these patients, 3.7% died in an ICU or ER.

Secondary outcomes

Secondary outcomes are also presented in Table 2. A total of 2.8% of patients experienced MI-EOL care of whom 2.3% underwent mechanical ventilation. 28.1% experienced IP care, with the most frequent indicators being arterial or central line placement (9.8%), digestive endoscopy (7.7%), surgery requiring anesthesia, and biliary tract interventional endoscopy (5.7%).

Factors associated with HI-EOL, MI-EOL, and PI care

Univariable analysis results are presented in Table 2. Based on the multivariable analysis (Table 3), the factors associated with a higher risk of HI-EOL were as follows: male gender (OR=1.313; $p < 0.0001$), follow-up in a non-cancer specialized care facility (OR=1.093; $p = 0.0009$), and a greater home-place of death distance (OR=1.155; $p < 0.0001$). The presence of identified palliative care involvement (OR=0.088; $p < 0.0001$) and older age at death (OR=0.465; $p < 0.0001$ for ≥ 80 vs ≤ 65) were identified as highly protective factors. Male gender, age at death, home-place of death distance, and palliative care implication were the only variables associated with lower odds of MI-EOL and

Table 1. Demographic and clinical characteristics of the study population during the observation period ($n=42,696$).

Characteristics	N	%
Gender		
Men	21,783	51.0
Age at death		
≤65	11,085	26.0
66–75	12,844	30.1
76–80	6677	15.6
>80	12,090	28.3
Socially deprived (1067 missing)		
Socially disadvantaged area	23,740	55.6
Living in urban area (672 missing)		
Urban/suburban	33,069	77.5
Charlson score of comorbidities at diagnosis		
1–2	16,302	38.28
≥3	26,394	61.8
Curative surgery	5343	12.51
Chemotherapy (at least one cycle)	28,574	66.9
Metastatic disease	32,833	76.9
Palliative care	32,217	75.6
Main hospital type		
Speciality center	11,632	27.24
Non-speciality center	31,064	72.76
Year of death		
2014	3055	7.1
2015	6231	14.6
2016	7477	17.5
2017	8107	19.0
2018	8754	20.5
2019	9072	21.3

*(Continued)***Table 1.** (Continued)

Characteristics	N	%
Place of death		
Acute care unit	13,937	32.6
Palliative care unit	14,942	35
Rehabilitation facilities	3942	9.2
Home (with or without home-hospitalization)	9870	23.1
With	3638	8.5
Without	6232	14.6
Distance (km) between place of death and home categorized (10,286 missing)		
≤30 km	25,204	59.0
>30 km	4939	11.6
>60 km	2267	5.3

IP. We also observed a significantly decreased incidence of both HI-EOL and IP during the follow-up period (OR=0.800; $p < 0.0001$ and OR=0.687; $p < 0.0001$, respectively).

Discussion

Our results demonstrate that 41.1% of patients who died from pancreatic adenocarcinoma in France between 2014 and 2019 experienced HI-EOL. Moreover, palliative care intervention during follow-up for this population is associated with improved EOL quality of care, reducing the risk of HI-EOL, MI-EOL, and IP. To the best of our knowledge, this series is the first to comprehensively evaluate the EOL care of patients who died from pancreatic adenocarcinoma in France. These findings suggest that palliative care intervention at any stage of treatment can be considered as an independent protective factor enhancing EOL care. Given that cancer-related deaths affect over 90% of patients with pancreatic adenocarcinoma,²² patients should receive palliative care widely and early. Patients with incurable cancers often experience variable and high symptom burden, especially in pancreatic adenocarcinoma²³ underlying the importance of

Table 2. Intensity of EOL treatment and care in the last 30 days of life.

Intense and invasive care	n (%)
HI-EOL care	17,577 (41.1)
Death in ICU or ER or ACU	13,971 (32.8)
In ICU	772 (1.8)
In ER	821 (1.9)
In ACU	13,937 (32.6)
≥1 hospitalization in an ICU in the last 30 days of life	1743 (4.1)
>1 ER visit in the last 30 days of life	2009 (4.7)
>1 hospitalization in an ACU in the last 30 days of life	14,002 (32.8)
Last intra-hospital chemotherapy <14 days from death	5042 (11.8)
MI-EOL care	1186 (2.8)
Intubation	286 (0.6)
Mechanical ventilation	963 (2.3)
Cardiopulmonary resuscitation	77 (0.2)
Hemodialysis	331 (0.8)
Invasive procedures	11,960 (28.1)
Arterial/central line placement	4199 (9.8)
Surgery requiring general anesthesia	2991 (7.0)
Radiological interventional procedures	2081 (4.9)
Radiotherapy	976 (2.3)
Artificial feeding	2425 (5.7)
Digestive endoscopy	3272 (7.7)
Biliary tract interventional endoscopy	2435 (5.7)

ACU, acute care unit; ER, emergency room; HI-EOL, high-intensity end of life; ICU, intensive care unit; MI-EOL, most invasive end of life.

early identification of palliative care situations and the need for transversal collaboration.²⁴

In our series, younger male patients were more likely to be treated with HI-EOL care in the last month before death. This finding could be explained by a probable trend for more aggressive treatment and a higher probability of maintaining a good performance status over time for young compared to older patients.²⁵ Moreover, patients with a higher comorbidity index received HI-EOL and MI-EOL more often which may be due to the fact that these patients are more fragile and more likely to be hospitalized as their conditions are more difficult to manage in home-based care.

Limited information exists regarding the HI-EOL care experiences for individuals with pancreatic cancer. In a study conducted in Ontario between 2005 and 2010, intensive exposure to palliative care for patients with pancreatic adenocarcinoma was associated with a proportional reduction in the aggressiveness of EOL care.²⁶ However, the impact of expert center involvement and distance from home to place of death were not investigated. The application of these results in the French healthcare system is limited due to differences in infrastructures between both countries and the evolution of healthcare over the past 15 years. Indeed, in France, the philosophy of palliative care emphasizes the importance of maintaining patients in their familiar environments as long as possible, to improve their quality of life.²⁷ In this series, only one in four patients died at home, underlying the complexity in management of pancreatic cancer, due to both the high symptom burden and the need for multidisciplinary team involvement which is challenging in home-based palliative care settings. Earlier involvement of palliative care teams and a higher rate of home-based EOL care could increase the ratio of patients dying in their home.²⁸

In this study, patients living far from the hospital receive HI-EOL more frequently. To address this, efforts should be made to improve the standardization of palliative care practices and to ensure equitable access regardless of geographic location. In France, 2/3 of patients desire to die at home, although only 37% do.²⁹ Thus, it is important to increase access to and quality of home-based palliative care, particularly for patients who reside far from the hospitals and who may not have easy access to inpatient palliative services.

Table 3. Multivariable analysis of factors associated with HI-EOL, MI-EOL, and IPs (adjusted OR and p values issued from multivariable logistic regressions).

Variable	Comparison Group	HI-EOL (41.2%)		MI-EOL (2.8%)		IP (28%)	
		AOR	p Value	AOR	p Value	AOR	p Value
Gender	Men vs women	1.313 (1.254–1.374)	<0.0001	1.454 (1.282–1.648)	<0.0001	1.255 (1.201–1.312)	<0.0001
Social deprivation	Deprived vs non-deprived	1.096 (1.043–1.151)	0.0003	0.942 (0.826–1.075)	0.375	0.947 (0.903–0.933)	0.025
Urban status	Urban vs rural	0.957 (0.903–1.015)	0.147	1.062 (0.903–1.247)	0.467	0.946 (0.894–1.002)	0.057
Year of death			0.0003		0.682		<0.0001
	2015 vs 2014	0.822 (0.742–0.910)	0.0002	0.806 (0.619–1.050)	0.111	0.748 (0.679–0.823)	<0.0001
	2016 vs 2014	0.872 (0.790–0.963)	0.0069	0.838 (0.649–1.082)	0.175	0.706 (0.643–0.775)	<0.0001
	2017 vs 2014	0.832 (0.754–0.918)	0.0003	0.842 (0.653–1.085)	0.184	0.674 (0.614–0.739)	<0.0001
	2018 vs 2014	0.837 (0.759–0.923)	0.0003	0.812 (0.631–1.044)	0.105	0.687 (0.627–0.753)	<0.0001
	2019 vs 2014	0.800 (0.726–0.881)	<0.0001	0.852 (0.663–1.094)	0.210	0.687 (0.627–0.753)	<0.0001
Patient benefiting from curative surgery during follow-up	Yes vs No	0.988 (0.922–1.059)	0.742	1.635 (1.399–1.911)	<0.0001	0.794 (0.742–0.850)	<0.0001
Patient with metastasis during follow-up	Yes vs No	1.087 (1.023–1.154)	0.007	0.359 (0.313–0.411)	<0.0001	1.058 (0.998–1.121)	0.057
Palliative care during follow-up	Yes vs No	0.088 (0.082–0.094)	<0.0001	0.216 (0.191–0.244)	<0.0001	0.707 (0.672–0.745)	<0.0001
Type of primary care facility during follow-up	Non-cancer specialized vs cancer specialized	1.093 (1.037–1.151)	0.0009	0.777 (0.682–1.885)	0.0001	0.903 (0.859–0.950)	0.0008
Charlson's score of comorbidity	3 + vs 1/2	1.062 (1.013–1.114)	0.013	1.298 (1.142–1.474)	<0.0001	0.983 (0.938–1.029)	0.4565
Age at death			<0.0001		<0.0001		<0.0001
	From 66 to 74 vs ≤65	0.832 (0.785–0.882)	<0.0001	0.880 (0.763–1.014)	0.0774	0.826 (0.781–0.873)	<0.0001
	From 75 to 79 vs ≤65	0.657 (0.612–0.706)	<0.0001	0.656 (0.543–0.792)	<0.0001	0.682 (0.636–0.731)	<0.0001
	≥80 vs ≤65	0.465 (0.435–0.497)	<0.0001	0.353 (0.289–0.430)	<0.0001	0.505 (0.473–0.539)	<0.0001
Distance home-place of death			<0.0001		<0.0001		<0.0001
	From 31 to 60 vs ≤30km	1.155 (1.077–1.238)	<0.0001	1.215 (1.021–1.446)	0.0280	1.213 (1.134–1.298)	<0.0001
	≥60 vs ≤30 km	1.027 (0.932–1.132)	0.591	1.695 (1.386–2.073)	<0.0001	1.574 (1.437–1.724)	<0.0001

Models are also adjusted on the region of residence but are not presented here. AOR, adjusted odds ratio; HI-EOL, high-intensity end of life; IP, invasive procedures; MI-EOL, most invasive end of life. Bold entries in the table represent statistically significant comparisons $p < 0.05$.

The observed heterogeneity in healthcare trajectories among patients with pancreatic adenocarcinoma highlights the complex nature of this disease and its impact on the provision of care. While our study aimed to focus on the last month before death, confounding factors such as variations in treatment protocols, patient preferences, and healthcare accessibility, likely contributed to the inconsistent reliability of secondary and tertiary outcome measures. Future studies should consider these confounders and employ more refined methodologies as analysis based on the subtypes of patients' healthcare trajectories to mitigate their effects.

In addition, we excluded individuals who died within 1 month after diagnosis. This specific group likely represents a distinct population characterized by late-stage diagnosis, poor performance status, or particularly aggressive disease at the time of diagnosis.³⁰ Excluding this group of patients allowed for a sufficient follow-up period to analyze the quality of EOL care.

Limitations

This study presents limitations similar to other series that rely on administrative databases, as they can be prone to miscoding and over-coding due to potential financial incentives,³¹ particularly in France.³² While the PMSI database's main advantage lies in its comprehensive nature, our study had certain limitations. Important factors such as resection rates, tumor characteristics, histopathological data, intraoperative complications, and the extent of resection, were not included in our analysis as these variables are inconsistently documented in the discharge database. Moreover, socioeconomic and cultural factors that may impact the intensity of EOL care could not be analyzed as data are not available. In addition, although coding errors can occur, their impact is mitigated by the large population size involved.³³ Future studies should overcome the inherent limitations of administrative databases and aim to capture a more comprehensive picture of the complex, multi-dimensional aspects of palliative care.

Conclusion

In France, a significant proportion of patients with pancreatic adenocarcinoma die without clear palliative care intervention, far from home, and experience HI-EOL care. This inequity in care

calls for immediate attention and action to ensure that patients with pancreatic cancer receive adequate and equitable EOL support and treatment, and to define the standard for EOL quality of care.

Declarations

Ethics approval and consent to participate

This study complied with the French National Health Guidelines on Research Involving Human Subjects and the manuscript follows the REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) Statement and was approved by an ethical committee (registration number 4266138 Bis). All the data were anonymized according to French law, an informed consent was not necessary.

Consent for publication

Not applicable.

Author contributions

Ugo Marchese: Conceptualization; Formal analysis; Methodology; Writing – original draft; Writing – review & editing.

Vanessa Pauly: Conceptualization; Formal analysis; Methodology; Writing – original draft; Writing – review & editing.

Anna Pellat: Conceptualization; Formal analysis; Methodology; Writing – original draft; Writing – review & editing.

Yasmina Richa: Investigation; Writing – original draft; Writing – review & editing.

Guillaume Fond: Conceptualization; Investigation; Writing – review & editing.

Stylios Tzedakis: Investigation; Writing – review & editing.

Martin Gaillard: Investigation; Writing – review & editing.

Basile Fuchs: Methodology; Writing – review & editing.

Veronica Orleans: Formal analysis; Writing – review & editing.

David Fuks: Methodology; Writing – original draft; Writing – review & editing.

Mehdi El Amrani: Conceptualization; Methodology; Writing – original draft.

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Competing interests

The authors declare that there is no conflict of interest.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

ORCID iDs

Yasmina Richa  <https://orcid.org/0009-0008-9036-8891>

Stylianos Tzedakis  <https://orcid.org/0000-0002-5934-0320>

Laurent Boyer  <https://orcid.org/0000-0003-1229-6622>

Supplemental material

Supplemental material for this article is available online.

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