No changes in clinical presentation, treatment strategies and survival of pancreatic cancer cases during the SARS-COV-2 outbreak: A retrospective multicenter cohort study on real-world data

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No changes in clinical presentation, treatment strategies and survival of pancreatic cancer cases during the SARS-COV-2 outbreak: A retrospective multicenter cohort study on real-world data

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Abstract

The SARS-COV-2 pandemic disrupted healthcare systems. We assessed its impact on the presentation, care trajectories and outcomes of new pancreatic cancers (PCs) in the Paris area. We performed a retrospective multicenter cohort study on the data warehouse of Greater Paris University Hospitals (AP-HP). We identified all patients newly referred with a PC between January 1, 2019, and June 30, 2021, and excluded endocrine tumors. Using claims data and health records, we analyzed the timeline of

Abbreviations: aHR, adjusted hazard ratio; AP HP, Assistance Publique Hôpitaux de Paris; CCAM, Common Classification of Medical Procedures; CI, confidence interval; COVID, Coronavirus disease; HR, hazard ratio; IRB, Institutional Review Board; MDM, multidisciplinary meeting; OS, overall survival; PC, pancreatic cancer; TNM, tumor, node, metastasis; WHO, World Health Organization.

care trajectories, the initial tumor stage, the treatment categories: pancreatectomy, exclusive systemic therapy or exclusive best supportive care (BSC). We calculated patients' 1-year overall survival (OS) and compared indicators in 2019 and 2020 to 2021. We included 2335 patients. Referral fell by 29% during the first lockdown. The median time from biopsy and from first MDM to treatment were 25 days (16-50) and 21 days (11-40), respectively. Between 2019 and 2020 to 2021, the rate of metastatic tumors (36% vs 33%, $P = .39$), the pTNM distribution of the 464 cases with upfront tumor resection ($P = .80$), and the proportion of treatment categories did not vary: tumor resection (32% vs 33%), exclusive systemic therapy (49% vs 49%), exclusive BSC (19% vs 19%). The 1-year OS rates in 2019 vs 2020 to 2021 were 92% vs 89% (aHR = 1.42; 95% CI, 0.82-2.48), 52% vs 56% (aHR = 0.88; 95% CI, 0.73-1.08), 13% vs 10% (aHR = 1.00; 95% CI, 0.78-1.25), in the treatment categories, respectively. Despite an initial decrease in the number of new PCs, we did not observe any stage shift. OS did not vary significantly.

KEYWORDS
COVID-19, delivery of healthcare, early detection of cancer, health services research, incidence, pancreatic neoplasms, quality of healthcare, routinely collected health data

What's new?

Healthcare systems were heavily impacted during the beginning of the COVID-19 pandemic, and whether the clinical prognosis of aggressive tumors was impaired as a result remains unclear. This retrospective multicenter cohort study conducted in the Paris area shows that, despite an initial decrease of 29% in the number of newly diagnosed pancreatic cancers during the first lockdown, there was no tumor stage shift or impairment in the treatment intent (curative vs palliative) in 2020 to 2021 compared to 2019. The delays in initial care management and the patients' overall survival did not vary significantly.

1 | INTRODUCTION

In the beginning of the SARS-COV-2 pandemic, healthcare systems were heavily impacted by the inflow of contaminated patients. Many governments instated lockdowns and social distancing policies, which also affected health services. These disruptions may have impaired the care trajectories of cancer patients worldwide.[1]

Pancreatic cancer (PC) is a very aggressive disease, with rising incidence and poor clinical outcomes, despite recent innovations in diagnostic and treatment.[2-4] Shorter diagnostic delays have been associated with better clinical outcomes, so treatment must be initiated as quickly as possible.[5]

Even though international guidelines classified some newly diagnosed PC cases as "high priorities" of care during the SARS-COV-2 pandemic, other patient categories, such as elderly patients, were considered "medium priorities."[6] The number of newly referred cancer patients dropped during the first waves, with no subsequent catching up.[7] Because of potential delays in diagnosis and treatment, modelers have anticipated an increase in PC-specific mortality in the coming years.[8-10] Nonetheless, empirical evaluations of the impact of the outbreak on care trajectories and outcomes of new PC cases remain rare, especially when it comes to studying survival, where only small-scale single-center studies are available.[11]

The aim of our study was to assess the impact of the SARS-COV-2 pandemic on tumor stage at diagnosis, anticancer upfront treatments and 1-year overall survival (OS) of newly referred PC cases, in the Greater Paris area, before, during and after the outbreak of the SARS-COV-2 pandemic in early 2020.

2 | METHODS

We performed a retrospective multicenter cohort study on the Clinical Data Warehouse (CDW) of Greater Paris University Hospitals (Assistance Publique-Hôpitaux de Paris, AP-HP), which contains routinely collected medical and administrative data for 11.4 million patients, following the REporting of studies Conducted using Observational Routinely collected Data (RECORD) extension of the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.[7] To identify patients and events, we used the claims database of the CDW, which contains two types of structured information: diagnoses coded with the International Classification of Diseases

(ICD, 10th edition), and medical procedures coded with the French Common Classification of Medical Procedures (CCAM, 11th edition).

We considered patients newly referred to one of the 28 AP-HP teaching hospitals between January 1, 2019, and June 30, 2021, for whom clinical data were available since January 2017. Patients were included if an ICD-10 C25x code was registered as principal or related diagnosis, without having been coded in the previous 2 years. Patients with codes for another type of cancer were excluded, as well as patients diagnosed with endocrine tumors (ICD-10 code C254).

We classified cancer treatments into four mutually exclusive categories: pancreatectomy (using CCAM codes in Annex 1 and regardless of potential perioperative cancer treatments), exclusive systemic anticancer therapy (chemotherapy ICD-10 Z511, regardless of radiation therapy), exclusive best supportive care (ICD-10 Z515) or no cancer-related treatment (a 10% sample of the charts were reviewed manually). We calculated the 3-month moving average (average of the values of the current month, the previous month and the following month) of the percentage of patients who received each type of treatment. We compared the proportions of patients who received neo-adjuvant chemoradiation therapy (ICD-10 code Z5101) or systemic neo-adjuvant chemotherapy (ICD-10 Z511) in 2019 and 2020 to 2021. We considered elderly patients as those over the age of 70 years and compared their pancreatectomy rates during lockdown periods with those outside of lockdown.

Among patients with a cancer diagnosis made inside AP-HP teaching hospitals, we calculated the median delay between the pathology report prior to cancer treatment and the occurrence of the first treatment. We calculated the time from a patient's first multidisciplinary team meeting (MDM) to the start of their treatment (with negative delays in cases when the treatment preceded the MDM). The MDM data were available in the structured information associated with each MDM report and the treatment date was obtained from claims data. For patients who were treated at AP-HP, we classified the first hospitalization according to the entry mode specified in the structured data associated with the hospital visit.

We used rule-based natural language processing algorithms for (i) identifying the initial tumor stage using both baseline CT-scan reports (ie, those recorded between 90 days before and 45 days after the date of the first encounter with an ICD-10 PC code) and the first postoperative pathology report for resected tumors and (ii) determining the metastatic tumor stage from baseline CT-scan reports (details on the development and validation of these algorithms are provided as Supporting Information S1). For resected tumors with no preoperative anticancer treatment, we classified the pTNM tumor stage (eighth WHO TNM classification) as low-risk for $pTxN_0$ and high-risk for $pTxN_{1\text{-}2}$. Patients with nonmetastatic tumors and without any cancer resection were considered to have locally advanced tumors.

The AP-HP's CDW has been linked with the National Death Registry kept up to date by the French National Institute of Statistics and Economic Studies (INSEE), which allows us to analyze the survival of our patients. Overall patient survival was defined as the time between the date of the first occurrence of an ICD-10 PC code and the patient's death. Living patients were censored at the date of the last National Death Registry update in the CDW (June 2022). We used the Kaplan-Meier method to plot survival curves and to estimate the 1-year survival probability and the Cox proportional hazard model to obtain hazard ratios (HR) adjusted for age and sex with their 95% confidence intervals (CIs), for comparing patients referred in 2019 to those referred in 2020 to 2021, overall and per treatment category. We compared survival for patients who attended the ICU postoperatively in 2019 and 2020 to 2021 by fitting a Cox regression for operated patients who were alive after a postoperative period of 30 days. Finally, we analyzed the effect of SARS-COV-2 infection defined by a positive PCR, or a positive serological test, or the presence of one of the U071x ICD-10 codes in the year after the date of cancer diagnosis. The effect of the SARS-COV-2 infection among patients with a tumor resection or exclusive chemotherapy was tested in a Cox model where SARS-COV-2 infection was considered as a time-varying exposure.

Other collected variables for 2019 and 2020 to 2021 were compared using a χ^2 test (categorical variables) or a *t*-test (continuous variables), with a focus on the French lockdowns (March 17 to May 11, 2020, and October 29 to December 15, 2020). Statistical significance was set at $P < .05$. Final data extraction was performed on December 5, 2022. Analysis was conducted using Python 3.7 (https://www.python.org).

3 | RESULTS

3.1 | Patient characteristics and treatments received

Among the 2531 patients with an ICD-10 PC code hospitalized between January 1, 2019, and June 30, 2021, we excluded 196 patients with an endocrine tumor and ultimately included 2335 patients newly referred for a PC to AP-HP (945 in 2019, 1390 in 2020-2021). Demographic characteristics and treatment strategies are shown in Table 1. After manual review of a random sample of charts, we determined that patients with no treatment coded at AP-HP were patients seeking second opinions. During the first national lockdown (March 17-May 11, 2020), the number of hospitalizations for PC fell by 29% compared to the same period in 2019 (147 vs 206), with no catch-up afterward (Figure 1). The distribution of patients between treatment categories was similar during the two periods (Figure 2). The proportion of patients who underwent a neo-adjuvant treatment did not differ between 2019 and 2020 to 2021 ($P = .68$, Supp Figure 1).

Among the whole population, 4 (11%) of the 37 elderly patients referred during the first lockdown received surgical treatment, compared to 218 (20%) of the 1113 elderly patients referred either before or after the first lockdown ($P = .26$). The repartition of patients according to treatment and age categories is summarized in Table S1.

3.2 | Location of diagnostic procedures and initial care pathways

Among the 1824 patients with any type of anticancer treatment at AP-HP, 805 (44%) had a cancer diagnosis performed within AP-HP teaching hospitals with a median delay of 25 days (IQR: 16-40)

TABLE 1 Initial characteristics of patients newly referred with a pancreatic cancer to AP-HP

	January 2019 to December 2019	January 2020 to June 2021	*P*-value
Number of patients	945	1390	
Women, n (%)	444 (47)	678 (49)	.42
Age, median (IQR)	69 (60-77)	69 (60-77)	.54
Treatment categories, n (%)			
Tumor resection	233 (25)	355 (26)	.94
Exclusive systemic anticancer therapy	362 (38)	533 (38)	
Exclusive best supportive care	142 (15)	199 (14)	
No treatment code	208 (22)	303 (22)	
Neo-adjuvant treatment, n (%)			
Surgery without neo-adjuvant treatment	188 (81)	276 (78)	.68
Neo-adjuvant chemoradiation therapy	3 (1)	6 (2)	
Systemic neo-adjuvant anticancer therapy	42 (18)	73 (21)	
Patients' referral to ED before hospitalization for patients with anticancer treatment at AP-HP, n (%)	132/737 (18)	187/1087 (17)	.74

Abbreviation: ED, emergency department.

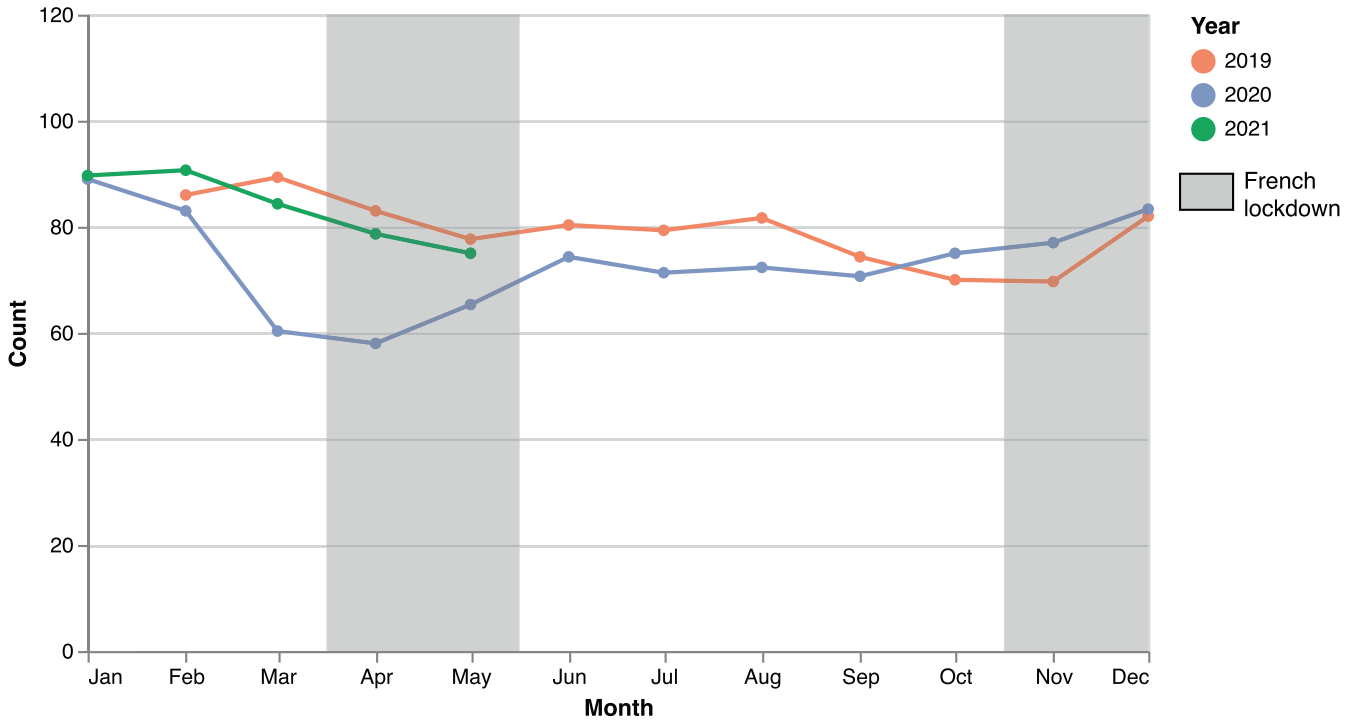

FIGURE 1 Monthly (3-month moving average) number of pancreatic cancer cases newly referred to Assistance Publique-Hôpitaux de Paris (AP-HP) hospitals between January 2019 and June 2021 [Color figure can be viewed at wileyonlinelibrary.com]

between the pathology report prior to cancer treatment and the initiation of the first treatment. The percentage of patients with a pathology report prior to cancer treatment did not vary over time in the general population (Figures S2 and S3).

The proportion of patients who came from an emergency department at the time of their first hospitalization did not vary between 2019 and 2020 to 2021 (Figure 3). Subgroup analyses by type of anticancer treatment yielded similar results (Figure S4).

Among the 1483 patients undergoing active anticancer treatment, 91% had an MDM report available. The median time between the first MDM and the first therapeutic procedure did not vary over time, particularly during the lockdown periods (Figure 4).

3.3 | Initial tumor stage

Five hundred eighty-eight patients received surgical treatment. Among the 464 patients who underwent upfront tumor resection, 456 (98%) had available pathology reports following tumor

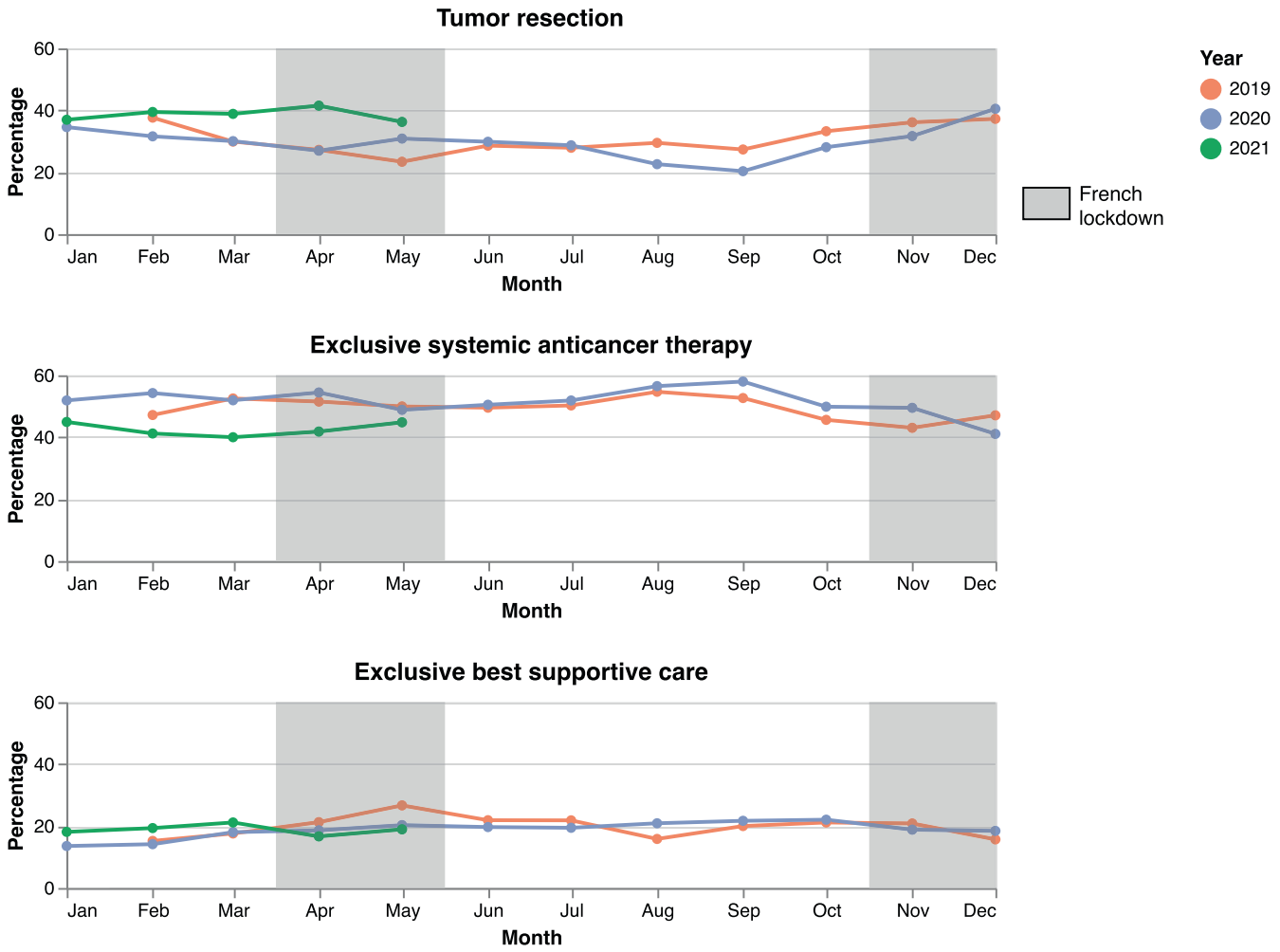

FIGURE 2 Repartition (3-month moving average) of initial upfront treatment strategies for pancreatic cancer cases newly referred to AP-HP hospitals between January 2019 and June 2021. In gray, the national lockdown periods of 2020 [Color figure can be viewed at wileyonlinelibrary.com]

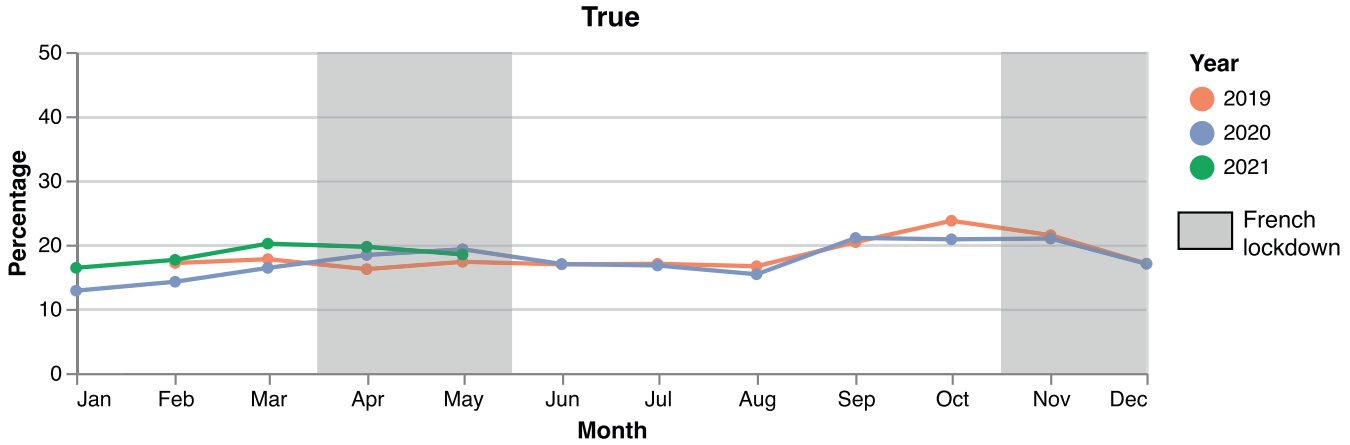

FIGURE 3 Repartition (3-month moving average) of emergency initial care pathways for pancreatic cancer cases newly referred to AP-HP teaching hospitals between January 2019 and June 2021 [Color figure can be viewed at wileyonlinelibrary.com]

resection without preoperative cancer treatment and 385 (83%) patients had a pTNM score identifiable in their report. The repartition of the pTNM risk groups did not vary between periods: 50% vs 52% for the low-risk category, 50% vs 48% for the high-risk category in 2019 and 2020 to 2021, respectively ($P = .80$).

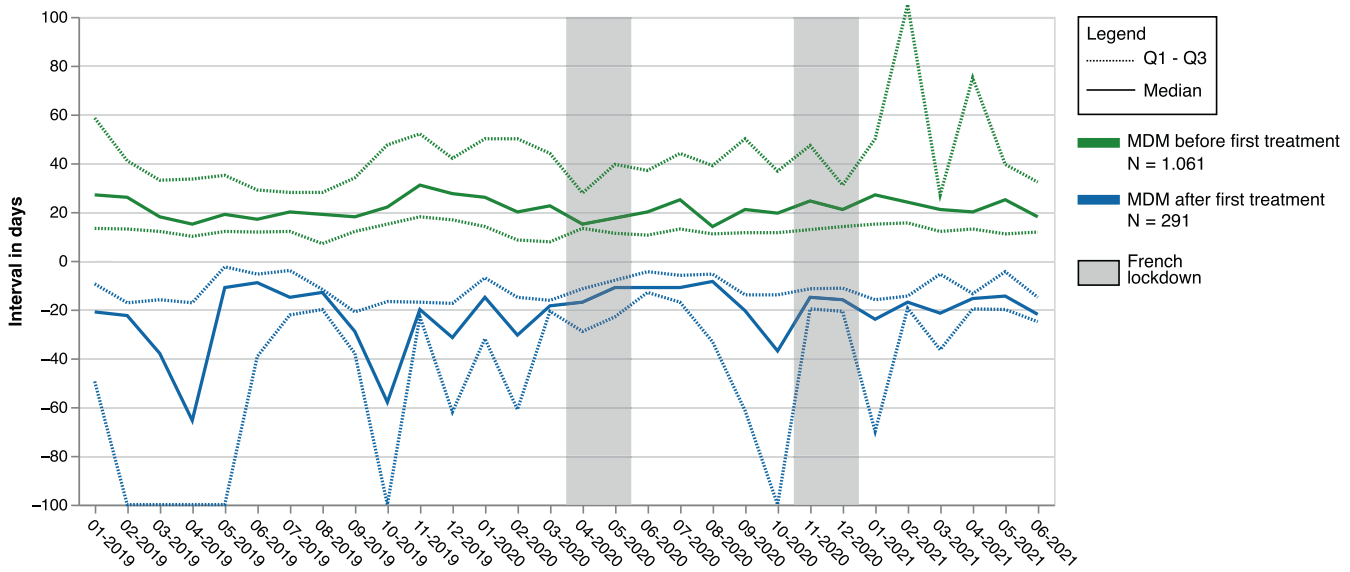

FIGURE 4 Time interval in days (median, interquartile rate as dotted lines) between the first multidisciplinary meeting (MDM) report and the first occurrence of the active anticancer treatment for pancreatic cancer cases newly referred to AP-HP hospitals between January 2019 and June 2021. When the MDM happened after the first treatment, a negative delay was counted. Grayed areas represent lockdown periods in France [Color figure can be viewed at wileyonlinelibrary.com]

Among the 124 patients with neo-adjuvant treatment, 117 (94%) had available pathology reports following tumor resection and 111 (89%) patients had an ypTNM identifiable in their report. The repartition of the ypTNM risk groups did not vary between periods: 59% vs 70% for the low-risk category and 41% vs 30% for the high-risk category in 2019 and 2020 to 2021, respectively ($P = .30$).

Among the 855 patients (overall population) with a baseline CT-scan report available, the proportion of locally advanced cancers did not differ between periods [40% in 2019 vs 42% in 2020-2021 ($P = .55$)], as well as the proportion of metastatic cancers [36% in 2019 vs 33% in 2020-2021 ($P = .39$)].

3.4 | Clinical outcomes and overall survival

The 1-year patient OS rate across treatment categories was 59% in 2019 vs 59% from 2020 to 2021 (aHR = 0.99; 95% CI 0.87-1.13; Figure 5A). For patients undergoing tumor resection, 92% vs 89% (aHR = 1.42; 95% CI, 0.82-2.48; Figure 5B). For exclusive systemic anticancer therapy, 52% in 2019 vs 56% in 2020 to 2021 (aHR = 0.88; 95% CI, 0.73-1.08l Figure 5C). For best supportive care, 13% in 2019 vs 10% in 2020 to 2021 (aHR = 0.99; 95% CI, 0.78-1.25; Figure 5D).

Among the 588 patients undergoing a tumor resection, 565 were still alive 30 days after the surgery. Of those, 322 had been admitted to an intensive care unit (ICU) within the 30 days following surgery (Figure S5). The survival of these patients was not different in 2019 and 2020 to 2021 (aHR = 0.7; 95% CI, 0.38-1.28; Figure S6).

3.5 | SARS-COV-2 infection

Among patients undergoing a tumor resection, a confirmed SARS-COV-2 infection was diagnosed in 8/233 (3%) vs 35/355 (10%) in 2019 and 2020 to 2021, respectively. Among these 43 SARS-COV-2 infections, 27 (63%) happened within the 30 days following surgery, and 8 (18.6%) led to the patients' death. Among patients who received systemic anticancer therapy, 17/362 (5%) had a confirmed SARS-COV-2 infection in 2019, vs 61/533 (11%) in 2020 to 2021. For best supportive care, the figures were 1/142 (1%) vs 18/199 (9%). For patients diagnosed in 2020 to 2021 who underwent surgical treatment, confirmed SARS-COV-2 infection significantly decreased with a worse survival in a time-varying exposure Cox model (aHR = 3.48; 95% CI, 1.56-7.75). The same was true for patients who underwent exclusive anticancer systemic therapy (aHR = 4.26:95% CI, 3.06-5.92).

4 | DISCUSSION

In this multicentric cohort study of 2235 cases, we observed a significant decrease in the number of patients newly referred for a PC to AP-HP hospitals during the first national COVID-19 lockdown, with no catch-up afterward. The initial hospital delays of management, the tumor stages, the cases distribution across treatment categories and the 1-year patients' OS rates did not vary between 2019 and 2020 to 2021.

Such a decrease in newly referred cases during the first lockdown is consistent with the published data in France and in other countries.[12-14] No decrease, as already reported for other tumors,[15] but

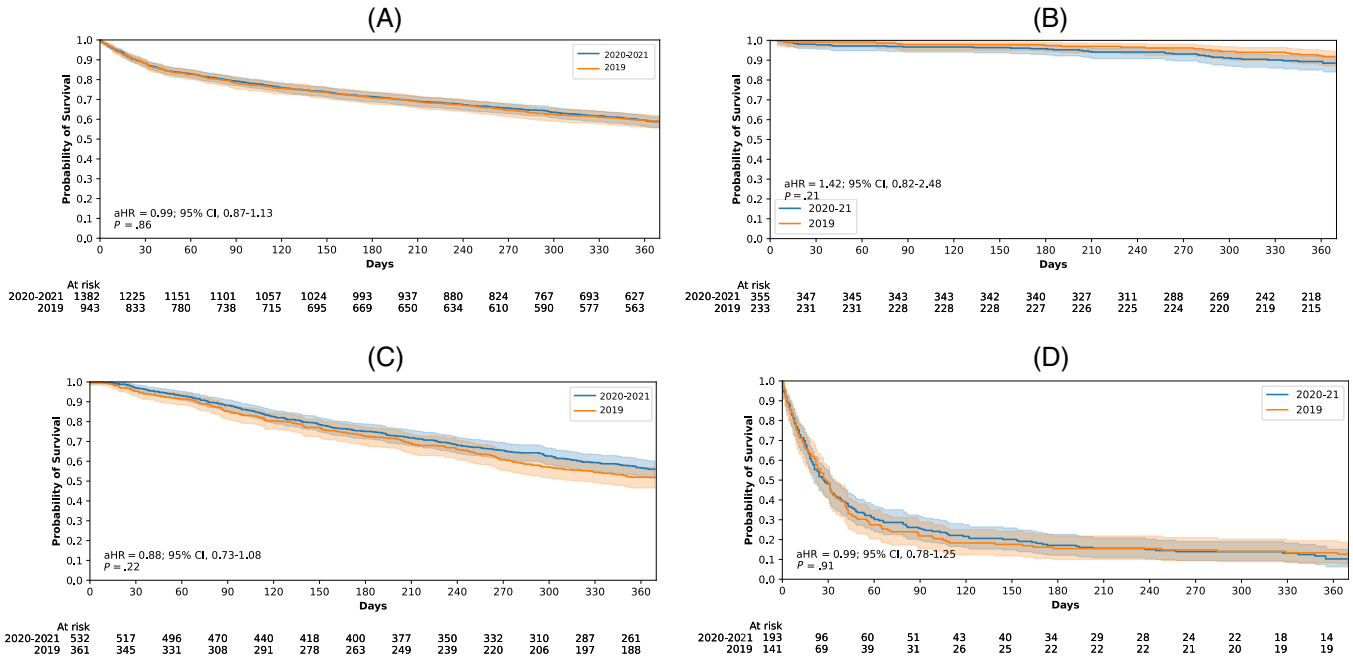

FIGURE 5 One-year overall survival rates of newly referred pancreatic cancer patients for all patients (A), and for patients undergoing upfront tumor resection (B), exclusive anticancer systemic therapy (C) or best supportive care (D) in 2019 and 2020 to 21, at AP-HP teaching hospitals. aHR, adjusted hazard ratio [Color figure can be viewed at wileyonlinelibrary.com]

neither did we observe compensation for cases that were expected but had not been diagnosed. The initial hospital delays between diagnostic procedure, first MDM and first administration of cancer treatment did not vary over time, suggesting that French practitioners managed to maintain PC care during the initial waves of the pandemic for patients who seeked care.[12] This is an important finding, as a timely surgical procedure is a milestone in the therapeutic strategy of resectable PC.[16] In the future, centralized diagnostic processes might reduce the initial delays of nonmetastatic PC anticancer treatment.[17]

We did not identify impairments in the initial clinical presentation nor in the intent of anticancer therapeutic strategies of patients diagnosed during and after the SARS-COV-2 outbreak, including the surgical option, suggesting that patients did not exhibit higher tumor burden because of diagnosis or surgery delays.[15] This is despite the clear potential for lead time bias, generated by missed diagnoses during the first wave: some cancers may have been diagnosed later than they would have under normal circumstances, potentially leading to conclude that an independent factor affected their outcomes. Even if this bias cannot be excluded, it did not yield a significant difference in outcomes.

Other studies obtained contrasted results on this point. A French retrospective multicentric study on 833 patients diagnosed with PC between September 2019 and October 2020 showed a tumor stage shift, with more advanced tumors and less borderline tumors ($P = .046$) after the first national lockdown.[12] A Japanese study on 379 nonresectable PC cases showed that the access to systemic therapies and the chemotherapy regimens did not vary during the pandemic, while home death increased significantly.[18] An American study compared 923 to 796 patients diagnosed with a new metastatic PC in 2019 and 2020, respectively. It showed that the rate of *de novo* stage IV tumors was higher in 2020 than in 2019 (70% vs 62%) and that the median OS was shorter in patients diagnosed in 2020 compared to 2019 (8.4 vs 6.1 months, $P < .001$).[14] In our study, the mortality rate did not impair in 2020, compared to 2019, even in the subgroup of patients with a SARS-COV-2 infection.[19,20]

In our study, 25% of PC patients underwent neoadjuvant systemic therapy with no tumor stage shift in the ypTNM. A British survey showed that one-third of 29 PC centers shifted from upfront surgery to neoadjuvant chemotherapy for the treatment of resectable PCs during the first pandemic wave, which is an accepted therapeutic option in resectable PCs.[12] Nevertheless, the level of evidence remains low and this therapeutic strategy remains the standard of borderline PC management.[21]

The British survey also showed that elderly patients were less likely to access anticancer treatment during the pandemic,[12] which was not found in our study with constant rates of pancreatectomy in patients aged >70 years.[22] An international prospective study was performed on 958 PC patients undergoing elective cancer surgery during the pandemic. The 30-day OS reached 4% and was around four times higher in the subgroup of patients with a perioperative SARS-COV-2 infection (n = 78, 8%).[23] Our study shows, like others, that PC resection during SARS-COV-2 pandemic waves was a reasonable therapeutic option when ICU access was guaranteed.[11]

We studied a large cohort of PC patients in a French region severely hit by the SARS-COV-2 pandemic, with extensive EHR data on their care and outcomes. We relied on claims data to identify patients and treatment strategies. Although claims data are not always as precise as registry data for identifying cancer cases, in France

evidence suggests that they are reliable. Quality of coding may improve over time, but it is unlikely to have affected our results over such a short period of time. We cannot be as categoric regarding the SARS-COV-2 infection status data we used, since tests were not always systematic (eg, tests were not available at the beginning of the pandemic, when healthcare systems were most severely hit).

Our study is limited to one regional healthcare provider. The disruptions generated by the pandemic may have modified hospital recruitment patterns, which could only be detected in a population-based study. Claims data may suffer from misclassification biases regarding the distinction between incident and prevalent cancer cases, impacting both sensitivity and specificity of our methods of patients' identification. The suboptimal sensitivity of the CT staging scan algorithm might add uncertainty to our results. Longer follow-up will also be necessary to detect the potential consequences of the drop in incidence during the first months of the pandemic. Finally, despite our efforts in development and validation, natural language processing algorithms on free text to identify tumor dissemination may suffer misclassification.

5 | CONCLUSION

Despite a large decrease in the number of patients newly referred for a PC during the first pandemic wave, the initial hospital delays of management, the tumor stages, the cases distribution across treatment categories and the 1-year patients' OS rates did not vary between 2019 and 2020 to 2021.

AUTHOR CONTRIBUTIONS

The work reported in the paper has been performed by the authors, unless clearly specified in the text. **Emmanuelle Kempf, Sonia Priou, Guillaume Lamé, Alexis Laurent, Stylianos Tzedakis, David Fuks, Gilles Chatellier, Christophe Tournigand:** conceptualization; **Emmanuelle Kempf, Sonia Priou, Guillaume Lamé, Alexis Laurent, Etienne Guével, Stylianos Tzedakis, Romain Bey, David Fuks, Gilles Chatellier, Xavier Tannier, Gilles Galula, Rémi Flicoteaux, Christel Daniel, Christophe Tournigand:** methodology; **Emmanuelle Kempf, Sonia Priou, Etienne Guével, Romain Bey, Xavier Tannier, Christel Daniel:** software; **Emmanuelle Kempf, Sonia Priou, Guillaume Lamé, Romain Bey, Gilles Chatellier:** validation; **Emmanuelle Kempf, Sonia Priou, Guillaume Lamé, Alexis Laurent, Etienne Guével, Stylianos Tzedakis, Romain Bey, David Fuks, Gilles Chatellier, Xavier Tannier, Gilles Galula, Rémi Flicoteaux, Christel Daniel, Christophe Tournigand:** formal analysis; **Emmanuelle Kempf, Sonia Priou, Guillaume Lamé, Alexis Laurent, Etienne Guével, Stylianos Tzedakis, Romain Bey, David Fuks, Gilles Chatellier, Xavier Tannier, Gilles Galula, Rémi Flicoteaux, Christel Daniel, Christophe Tournigand:** investigation; **Emmanuelle Kempf, Guillaume Lamé, Romain Bey, Xavier Tannier, Christel Daniel, Christophe Tournigand:** resources; **Emmanuelle Kempf, Sonia Priou, Etienne Guével, Romain Bey, Xavier Tannier, Rémi Flicoteaux:** data curation; **Emmanuelle Kempf, Sonia Priou, Guillaume Lamé, Gilles Chatellier, Romain Bey:** writing – original draft; **Emmanuelle Kempf, Sonia Priou, Guillaume Lamé, Alexis Laurent, Etienne Guével, Stylianos Tzedakis, Romain Bey, David Fuks, Gilles Chatellier, Xavier Tannier, Gilles Galula, Rémi Flicoteaux, Christel Daniel, Christophe Tournigand:** writing – review and editing; **Emmanuelle Kempf, Sonia Priou, Guillaume Lamé, Alexis Laurent, Etienne Guével, Stylianos Tzedakis, Romain Bey, David Fuks, Gilles Chatellier, Xavier Tannier, Gilles Galula, Rémi Flicoteaux, Christel Daniel, Christophe Tournigand:** visualization; **Emmanuelle Kempf, Guillaume Lamé, Alexis Laurent, Romain Bey, Gilles Chatellier, Xavier Tannier, Rémi Flicoteaux, Christel Daniel, Christophe Tournigand:** supervision; **Emmanuelle Kempf, Romain Bey, Christel Daniel, Christophe Tournigand:** project administration; **Emmanuelle Kempf, Guillaume Lamé, Romain Bey, Christel Daniel, Christophe Tournigand:** funding acquisition.

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CONFLICT OF INTEREST STATEMENT

The authors have no conflict of interest to disclose.

DATA AVAILABILITY STATEMENT

All source code is publicly available on GitHub (https://github.com/aphp/edsteva). The process to access the raw data of the clinical data warehouse is described on its website eds.aphp.fr. Other data that support the findings of our study are available from the corresponding author upon request.

ETHICS STATEMENT

The French Data Protection Agency (CNIL, Commission Nationale de l'Informatique et des Libertés) authorized the constitution of the APHP Clinical Data Warehouse (CDW) on January 19, 2017 (approval no. 19800120). AP-HP declared to the CNIL a single commitment to comply with the national reference methodology MR-004 (https://www.legifrance.gouv.fr/jorf/id/JORFTEXT000037187498) governing the processing of personal data for research projects of a public interest nature that do not involve the human person, in particular studies that reuses already collected data. Our study was approved by the APHP's Scientific and Ethics Committee (IRB00011591; approval CSE 20-0055_COVONCO-AP) on May 15, 2020. Only data strictly necessary and relevant to the research objectives were used for this project.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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