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ORIGINAL ARTICLE

Impact of the COVID-19 pandemic on short-term outcomes after pancreaticoduodenectomy for pancreatic cancer: A retrospective study from the Japanese National Clinical Database, 2018–2021

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Abstract

Aim: The coronavirus disease 2019 (COVID-19) pandemic greatly impacted medical resources such as cancer screening, diagnosis, and treatment given to people for various diseases. We surveyed the impacts of the pandemic on the incidence of complications and mortality following pancreaticoduodenectomy for pancreatic cancer in Japan.

Methods: Data on patients who underwent pancreaticoduodenectomy for pancreatic cancer were extracted from the Japanese National Clinical Database (NCD) between 2018 and 2021. The number of the pancreaticoduodenectomy for pancreatic cancer were obtained and then the morbidity and mortality rates were evaluated using a standardized morbidity/mortality ratio (SMR), which is the ratio of the observed number of incidences to the expected number of incidences calculated by the risk calculator previously developed by the NCD.

Results: This study included 22 255 cases. The number of pancreaticoduodenectomies exhibited an increasing trend even during the COVID-19 pandemic. The mean observed incidence rates of Grade C pancreatic fistula and Clavien–Dindo grade ≥4 complications, and the 30-day mortality and surgical mortality rates were 0.8%, 1.8%, 0.8% and 0.9%, respectively. The standardized morbidity ratios did not increase during the COVID-19 pandemic. The standardized mortality ratios remained within the range of variations observed before the COVID-19 pandemic.

Conclusion: The increasing trend in the number of pancreaticoduodenectomies and favorable short-term outcomes even in the COVID-19 pandemic suggest the medical care for pancreatic cancer in Japan functioned well during the pandemic.

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KEYWORDS
COVID-19, pancreatic cancer, pancreaticoduodenectomy, postoperative complication, short-term outcome

1 | INTRODUCTION

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2, was first detected in Wuhan, China in December 2019, and rapidly spread across the globe in 2020.[1] The COVID-19 pandemic has changed daily lifestyle, and infection prevention required the mandatory use of face masks and staying at home even for work, which had a significant impact on overall healthcare. Importantly, the COVID-19 pandemic also had an impact on cancer screening, diagnosis, and treatment.[2–4] Globally, 81.7% of benign surgery and 37.7% of cancer surgery had been canceled or postponed during a 12-week period in the very early phase of the COVID-19 pandemic.[5] In Japan, to maintain sufficient medical resources for treating and preventing in-hospital COVID-19 outbreaks, in April 2020, the Japanese Surgical Society recommended surgical triage according to disease severity.[6] Surgeries for patients with benign or nonurgent diseases were recommended to be postponed. This recommendation and healthcare change led to a decreased number of surgeries, including an approximately 15% reduction in gastrointestinal surgeries, during the COVID-19 pandemic according to an analysis of nationwide data in Japan.[7]

Pancreatic cancer is the fourth leading cause of death in Japan and has the worst prognosis among all cancers.[8,9] Despite recent improvements in surgical techniques and perioperative management, pancreaticoduodenectomy for pancreatic cancer remains a highly invasive procedure associated with high rates of postoperative mortality and morbidities, including pancreatic fistula. Although the short-term outcomes have improved in recent years, previous nationwide web-based database studies in Japan revealed a 90-day mortality rate of 2.8% in patients undergoing pancreaticoduodenectomy and reported that 4.8% and 4.4% of patients developed Grade C pancreatic fistula[10] and severe complications greater than Clavien–Dindo Grade IV, respectively, after pancreaticoduodenectomy.[11,12]

The COVID-19 pandemic has led to shortages in medical resources, such as medical staff, hospital space, and equipment, and might have increased the failure to rescue the cases who suffer life-threatening morbidity after pancreaticoduodenectomy. In fact, our research group previously investigated morbidity and mortality after gastrointestinal surgery during the pandemic and reported that there were no increasing mortality and morbidity rates in upper and lower gastrointestinal surgery even in 2021, when the number of severe infected cases reached highest.[13–15] However, as for pancreaticoduodenectomy, another previous study showed a slight increase in the mortality rate in patients undergoing pancreaticoduodenectomy for pancreatic cancer in the early phase of the COVID-19 pandemic in 2020.[3] However, it focused on changes in crude mortality rates and did not adjust for preoperative confounding factors such as clinical stage and age. It also remains unclear whether the rates of complications were impacted by the COVID-19 pandemic and whether mortality rates continued to be impacted in 2021, considered as the late phase of the COVID-19 pandemic. Therefore, in the present study, we aimed to evaluate the frequencies of postoperative complications and mortality in patients undergoing surgery for pancreatic cancer in Japan during the COVID-19 pandemic with comparison to the prepandemic period by risk adjustment based on patient background characteristics.

2 | MATERIALS AND METHODS

2.1 | Data collection from the National Clinical Database

In this retrospective study, data between January 1, 2018, and December 31, 2021, were extracted from the Japanese National Clinical Database (NCD), a nationwide web-based surgical patient registration system that enables the collection of data on all surgical procedures performed in Japan, in addition to perioperative factors. Approximately 5000 hospitals have registered more than 14 340 000 procedures, accounting for more than 90% of all surgeries performed in Japan.[16,17] The NCD has constructed software for an internet-based data collection system, and data managers in participating hospitals are responsible for forwarding their data to the NCD office.[16] To determine the impact of COVID-19 on postoperative outcomes after pancreaticoduodenectomy for pancreatic cancer, the registered data on patients who underwent pancreaticoduodenectomy during the study period were initially extracted to investigate monthly changes in the following outcomes: number of surgeries, use of intensive care unit (ICU), incidence of pancreatic fistula, Clavien–Dindo grade ≥4 complications, 30-day mortality, and surgical mortality (death during hospitalization within 90 days). ICUs were defined as wards/units that could provide the most intensive medical care in the hospital. Patients fulfilling the following criteria were excluded from the final analysis: patients with benign tumors, other malignant diseases, or T0 (Tis) pancreatic cancer; those without tumors; those younger than 18 years; those undergoing emergency surgery; and those with missing data. Pathologic stage was determined according to the Union for International Cancer Control TNM stage classification, 8th edition.[18] Next, the number of patients with severe COVID-19 were obtained from the homepage of Ministry of Health, Labor, and Welfare in Japan.[2] Severe cases were defined as those who required ventilator, extracorporeal membrane oxygenation, or critical care in the ICU.

Our study protocol was reviewed and adopted by the Japanese Society of Gastrointestinal Surgery Committee and approved by the Institutional Review Board of Kochi Medical School (Approval No. ID: 2022-75) and it conforms to the provisions of the Declaration of Helsinki.

2.2 | Definitions of COVID-19 epidemic areas and waves

The cumulative number of infected people per population at the end of 2020 for each prefecture was used as the index for degree of infection.[19] Based on this value, the following 12 prefectures were defined as COVID-19 epidemic areas: Aichi, Chiba, Fukuoka, Hokkaido, Hyogo, Kanagawa, Kyoto, Nara, Okinawa, Osaka, Saitama, and Tokyo. All data were compared among all prefectures and among the epidemic areas to assess the relationship between the level of infection and short-term outcomes. The waves of COVID-19 pandemic in Japan were defined according to the number of severe COVID-19 cases/day as follows: first wave (March 2020–June 2020), second wave (July 2020–October 2020), third wave (November 2020–February 2021), fourth wave (March 2021–June 2021), and fifth wave (July 2021–December 2021; end of the study period).[20,21]

2.3 | Standardized morbidity and mortality ratios

Standardized morbidity and mortality ratios (SMR) were calculated to accurately evaluate mortality or morbidity by considering the risk of postoperative complications. Standardized morbidity and mortality ratios were defined as the ratio of the observed number of patients with the morbidity or mortality outcome to the expected number of patients with the same morbidity or mortality outcome and were used to investigate trends in risk-adjusted outcomes. The expected morbidity and mortality rates for each month were calculated using a previously established risk calculator based on the NCD data.[11,12] Briefly, nine variables, including age, male sex, emergency surgery, chronic obstructive pulmonary disease, bleeding disorders, weight loss >10%, body mass index >25 kg/m^2, prothrombin time/international normalized ratio >1.1, and serum urea nitrogen level <8.0 mg/dL, were included as independent variables in the risk model for 30-day mortality.[11] Thirteen significant risk factors, including age, respiratory distress, activities of daily living within 30 days before surgery, angina, weight loss >10%, American Society of Anesthesiologists physical status class >3, Brinkman index >400, body mass index >25 kg/m^2, white blood cell count >11 000 cells/μL, platelet count <120 000 cells/μL, prothrombin time/international normalized ratio >1.1, activated partial thromboplastin time >40 s, and serum creatinine level >3.0 mg/dL, were included in the risk model for surgical mortality.[11] The models for pancreatic fistula Grade C according to the International Study Group of Pancreatic Fistula and Clavien–Dindo grade ≥4 complications were also constructed using approaches similar to that reported in a previous study.[12]

2.4 | Statistical analysis

Categorical data were presented as numbers and percentages. Data on standardized morbidity and mortality ratios were categorized as follows: the ratio >1, observed number of patients exceeded expectations calculated with the risk calculator; the ratio <1, observed number of patients was lower than the expectations calculated with the risk calculator; and the ratio = 1, observed number of patients was equal to the expectations calculated with the risk calculator. A significant difference between the observed number of patients and the expected number of patients was considered if the 95% confidence interval did not include 1.0. All statistical data were analyzed using R, version 4.1.2 (R Foundation for Statistical Computing, Vienna, Austria).

3 | RESULTS

3.1 | Changes in the number of pancreaticoduodenectomies for pancreatic cancer

Figure 1 shows the study flow chart. Briefly, the final study population included a total of 22 255 cases, including 13 336 (59.9%) cases in the COVID-19 epidemic areas. The variability in the monthly number of pancreaticoduodenectomies was within the range observed before the COVID-19 pandemic, with no marked decrease observed during the study period (Figure 2). There was a trend of increase in the annual number of patients undergoing pancreaticoduodenectomy for pancreatic cancer during the COVID-19 pandemic compared to the prepandemic level (Table 1). The overall trend in the number of pancreaticoduodenectomies was similar between the epidemic and nonepidemic areas.

The degree of cancer progression and the proportion of age were not different between the prepandemic (2018 and 2019) and pandemic (2020 and 2021) periods (Table 2). Similar findings were also found in all prefectures and epidemic areas.

3.2 | Proportion of ICU admissions after surgery

Figure 3 shows the changes in the proportion of patients admitted to the ICU during the study period. The analysis of all prefectures revealed that the proportions of patients who were admitted to the ICU in all prefectures were 69.3%, 72.6%, 71.0%, and 71.3% in 2018, 2019, 2020, and 2021, respectively. Additionally, the proportions of patients who were admitted to the ICU for more than 2 days in all prefectures were 34.8%, 35.0%. 35.6%, and 34.4% in 2018, 2019, 2020, and 2021, respectively. The proportions of patients admitted to the ICU for at least 1 day and more than 2 days

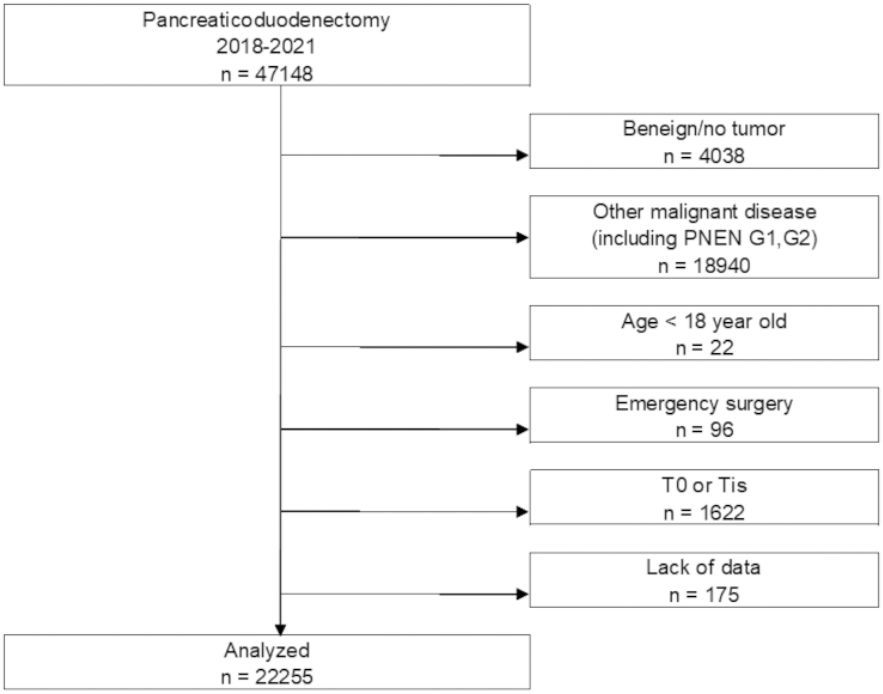

FIGURE 1 Schema of the study.

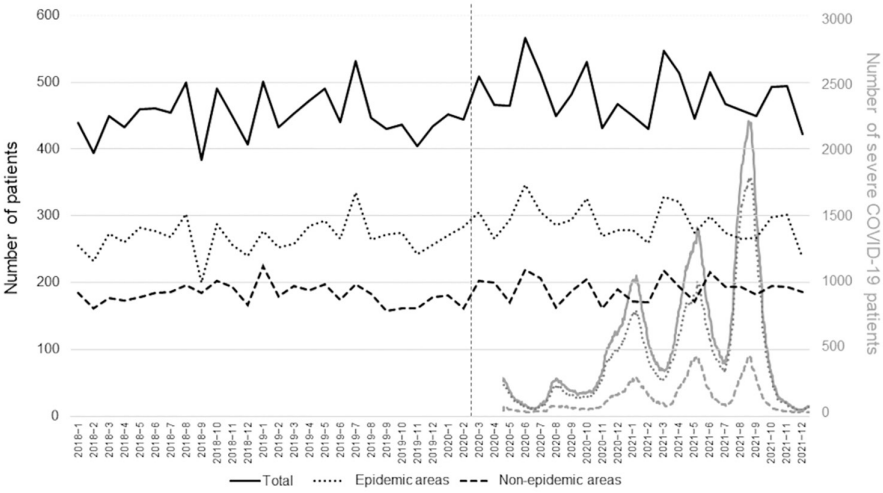

FIGURE 2 Changes in the numbers of patients undergoing pancreaticoduodenectomy and those with severe COVID-19. Changes in the numbers of patients undergoing pancreaticoduodenectomy (black line) and those with severe COVID-19 (gray line) are shown. Solid lines indicate patients who underwent pancreaticoduodenectomy in all prefectures, dotted lines indicate those who underwent pancreaticoduodenectomy in epidemic areas, and dashed lines indicate those who underwent pancreaticoduodenectomy in nonepidemic areas.

remained unchanged throughout the study period. A similar trend was observed in the COVID-19 epidemic areas.

3.3 | Postoperative morbidity and mortality after pancreaticoduodenectomy

Next, we examined the changes in the incidence rates of postoperative complications during the study period. The observed incidence rates of Grade C pancreatic fistula and Clavien–Dindo grade ≥4 complications were 0.8% and 1.8%, respectively, during the study period. The annual incidence rates of Grade C pancreatic fistula were 0.9%, 0.8%, 0.7%, and 0.7% in 2018, 2019, 2020, and 2021, respectively. Moreover, the annual incidence rates of Clavien–Dindo grade ≥4 complications were 1.3%, 1.3%, 1.6%, and 1.0% in 2018, 2019, 2020, and 2021, respectively. As shown in Figure 4, the monthly trends in the expected morbidity rate and standardized morbidity ratios for Grade C pancreatic fistula and Clavien–Dindo grade ≥4 complications did not change mostly throughout the study period.

Figure 5 shows the monthly trends in the expected mortality rate and standardized mortality ratios for 30-day mortality and surgical mortality, respectively. Briefly, the expected 30-day mortality did not vary throughout the study period, except for a few months during the first and second waves of COVID-19 pandemic. The standardized mortality ratio of 30-day mortality throughout the study period also remained within the range of variation observed before the COVID-19 pandemic, although it appears to be slightly higher in the second half of 2020 without statistical significance. The expected surgical mortality and standardized mortality ratios

TABLE 1 Number of patients undergoing pancreaticoduodenectomy for pancreatic cancer.

		Month											
Year	Total	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec
All prefectures													
2018	5320	439	394	450	433	460	461	454	499	384	490	449	407
2019	5474	501	433	453	473	490	440	532	447	430	437	404	434
2020	5774	452	444	508	466	465	566	512	449	481	531	432	468
2021	5687	450	430	547	514	446	515	468	458	449	493	494	423
Epidemic areas													
2018	3133	255	232	273	260	282	277	268	303	200	287	256	240
2019	3275	277	253	258	285	292	266	335	264	272	275	242	256
2020	3526	271	283	305	266	294	347	306	286	294	326	270	278
2021	3402	278	259	329	321	274	299	274	265	267	298	301	237

Note: Epidemic areas where there is a high cumulative number of infections per population: Aichi, Chiba, Fukuoka, Hokkaido, Hyogo, Kanagawa, Kyoto, Nara, Okinawa, Osaka, Saitama, and Tokyo.

after the COVID-19 pandemic also remained within the range of variation observed before the COVID-19 pandemic, although the standardized mortality ratio of surgical mortality was slightly higher in the epidemic areas in the second half of 2020 without statistical significance.

4 | DISCUSSION

Our analysis of the Japanese NCD from 2018 to 2021 revealed an increasing trend in the number of pancreaticoduodenectomies performed for pancreatic cancer even during the COVID-19 pandemic while the proportion of patients requiring ICU admission did not change during the same period. Furthermore, the examination of morbidity and mortality rates revealed that the standardized morbidity and mortality ratios and expected morbidity and mortality rates did not exhibit significant changes throughout most of the study period.

Pancreatic cancer is characterized by low resectability rates, with only 15%–20% of all cases considered resectable. Hence, early detection is required.[22] The annual incidence of pancreatic cancer in Japan has been increasing (40 000 in 2018, 40 600 in 2019, 42 800 in 2020, and 43 900 in 2021).[23] Thus, the number of pancreaticoduodenectomy procedures could have been high if there were no missed opportunities for diagnosis. The current study showed that the nationwide healthcare system was relatively well preserved during the COVID-19 pandemic. Several reports have shown that the COVID-19 pandemic negatively affected cancer treatment in Japan. A study using NCD data revealed that the number of surgical procedures decreased in 2020 due to the COVID-19 pandemic.[7] Another study found that the COVID-19 pandemic resulted in an increased number of patients diagnosed with advanced-stage cancer due to the reduced screening rates for various cancer types.[3] However, the number of patients with COVID-19 in Japan was lower than that in other countries worldwide. Furthermore, surgical services in Japan may have been maintained compared with those in other countries where the infection rate was significantly higher. The COVIDSurg study group previously reported that the cancellation rate of cancer surgeries worldwide within a 12-week period during the COVID-19 pandemic was 38%. Meanwhile, the cancellation rate in Japan was relatively low at 30%.[5] In April 2020, the Japan Surgical Society, which includes 10 major surgical societies in Japan, stated that surgeries for malignant diseases should be prioritized even during a pandemic.[6] These conditions might have contributed in preventing the true medical collapse in the domestic clinical practice for the management of pancreatic cancer, which is known as the poorest malignant disease, even in the very early phase of the pandemic. Then, the Japan Surgical Society also issued another statement for the recovery of the surgical care during the COVID-19 pandemic in May 2020.[24] To maintain the surgical functions in hospitals, patients without COVID-19 based on routine nasal swab testing should be selected,[25] and vaccination must be prioritized.[26] These measures can then promote a COVID-19-free elective surgery pathway.[27] Consequently, these programs could have been established earlier and functioned well in Japan. We further considered the detection of pancreatic cancer during the pandemic. A report on medical checkups in Japan during the COVID-19 pandemic revealed that the rate of medical checkups in 2020 decreased by approximately 10%.[28] However, pancreatic cancer screening has not yet been established in Japan, and the number of cases detected via screening may be limited. We predicted that patients with pancreatic cancer symptoms, such as jaundice, would receive appropriate medical treatment. Hence, the pandemic did not impact the incidence of pancreatic cancer and the increasing trend in the number of pancreaticoduodenectomy procedures performed even during the pandemic. In fact, we previously reported that the number of pancreaticoduodenectomies was maintained both in 2020 and 2021 compared to the prepandemic era.[7,29] Moreover, surgical resection is the only curative treatment for pancreatic cancer and preoperative chemotherapy, which has become a standard of care in recent

TABLE 2 Clinical characteristics of patients undergoing pancreaticoduodenectomy for pancreatic cancer in all prefectures and epidemic areas.

	All prefectures				Epidemic areas			
	2018	2019	2020	2021	2018	2019	2020	2021
	N (%)	*N* (%)	*N* (%)	*N* (%)	*N* (%)	*N* (%)	*N* (%)	*N* (%)
Patient characteristics								
Sex								
Female	2380 (44.7)	2395 (43.8)	2539 (44.0)	2587 (45.5)	1400 (44.7)	1424 (43.5)	1591 (45.1)	1559 (45.8)
Male	2940 (55.3)	3079 (56.2)	3235 (56.0)	3100 (54.5)	1733 (55.3)	1851 (56.5)	1935 (54.9)	1843 (54.2)
Age								
18–59	695 (13.1)	677 (12.4)	722 (12.5)	702 (12.3)	443 (14.1)	409 (12.5)	439 (12.5)	454 (13.3)
60–69	1490 (28.0)	1478 (27.0)	1413 (24.5)	1341 (23.6)	831 (26.5)	844 (25.8)	826 (23.4)	763 (22.4)
70–79	2349 (44.2)	2478 (45.3)	2718 (47.1)	2765 (48.6)	1419 (45.3)	1533 (46.8)	1708 (48.4)	1630 (47.9)
≥80	786 (14.8)	841 (15.4)	921 (16.0)	879 (15.5)	440 (14.0)	489 (14.9)	553 (15.7)	555 (16.3)
T factor								
T1	894 (16.8)	1082 (19.8)	1254 (21.7)	1310 (23.0)	511 (16.3)	636 (19.4)	726 (20.6)	781 (23.0)
T2	2117 (39.8)	2168 (39.6)	2236 (38.7)	2252 (39.6)	1189 (38.0)	1254 (38.3)	1355 (38.4)	1292 (38.0)
T3	2169 (40.8)	2105 (38.5)	2170 (37.6)	2021 (35.5)	1344 (42.9)	1315 (40.2)	1384 (39.3)	1267 (37.2)
T4	140 (2.6)	119 (2.2)	114 (2.0)	104 (1.8)	89 (2.8)	70 (2.1)	61 (1.7)	62 (1.8)
N factor								
N positive	2746 (51.6)	2670 (48.8)	2758 (47.8)	2599 (45.7)	1645 (52.5)	1590 (48.5)	1726 (49.0)	1561 (45.9)
N negative	2574 (48.4)	2804 (51.2)	3016 (52.2)	3088 (54.3)	1488 (47.5)	1685 (51.5)	1800 (51.0)	1841 (54.1)
M factor								
M positive	153 (2.9)	156 (2.8)	135 (2.3)	134 (2.4)	99 (3.2)	84 (2.6)	95 (2.7)	71 (2.1)
M negative	5167 (97.1)	5318 (97.2)	5639 (97.7)	5553 (97.6)	3034 (96.8)	3191 (97.4)	3431 (97.3)	3331 (97.9)
Morbidities								
Pancreatic fistula	46 (0.86)	46 (0.84)	38 (0.66)	40 (0.70)	26 (0.83)	24 (0.73)	22 (0.62)	17 (0.50)
Clavien–Dindo ≥4	98 (1.84)	96 (1.75)	117 (2.03)	91 (1.60)	46 (1.47)	60 (1.83)	79 (2.24)	53 (1.56)
Mortalities								
30-day mortality	37 (0.70)	42 (0.77)	62 (1.07)	41 (0.72)	19 (0.61)	28 (0.85)	45 (1.28)	24 (0.71)
Surgical mortality	68 (1.28)	71 (1.30)	91 (1.58)	59 (1.04)	39 (1.24)	43 (1.31)	61 (1.73)	33 (0.97)

Note: Epidemic areas where there is a high cumulative number of infections per population: Aichi, Chiba, Fukuoka, Hokkaido, Hyogo, Kanagawa, Kyoto, Nara, Okinawa, Osaka, Saitama, and Tokyo.

years, might have made it possible to keep the chance of surgery even during the COVID-19 pandemic.[30]

Pancreaticoduodenectomy is one of the most complex surgical procedures, with a non-negligible rate of major postoperative complications. Postoperative pancreatic fistula represents the most common and feared complication in pancreatic surgery as it can lead to other lethal complications, such as bleeding and infections. Whether the COVID-19 pandemic had an adverse effect on surgical safety is unclear. Therefore, we investigated the relationship between the COVID-19 pandemic and short-term outcomes using standardized morbidity and mortality ratios that are an objective, risk-adjusted metrics. The patient background characteristics might vary during the COVID-19 pandemic; therefore, we evaluated mortality and morbidity rates using the risk-adjusted metrics. First, our analysis showed that there was no impact on severe pancreatic fistula although pancreatic head cancer often induced impairment of

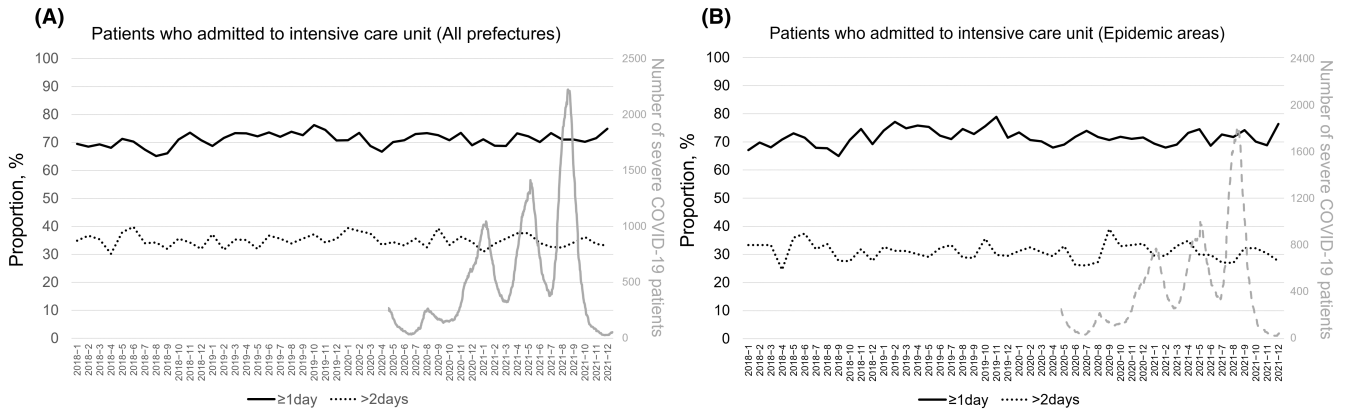

FIGURE 3 Changes in the proportion of patients admitted to ICU. Solid lines indicate patients who were admitted to the intensive care unit (ICU) for at least 1 day and dotted lines indicate those who were admitted to the ICU for more than 2 days in all prefectures (A) and in epidemic areas (B). ICU, intensive care unit.

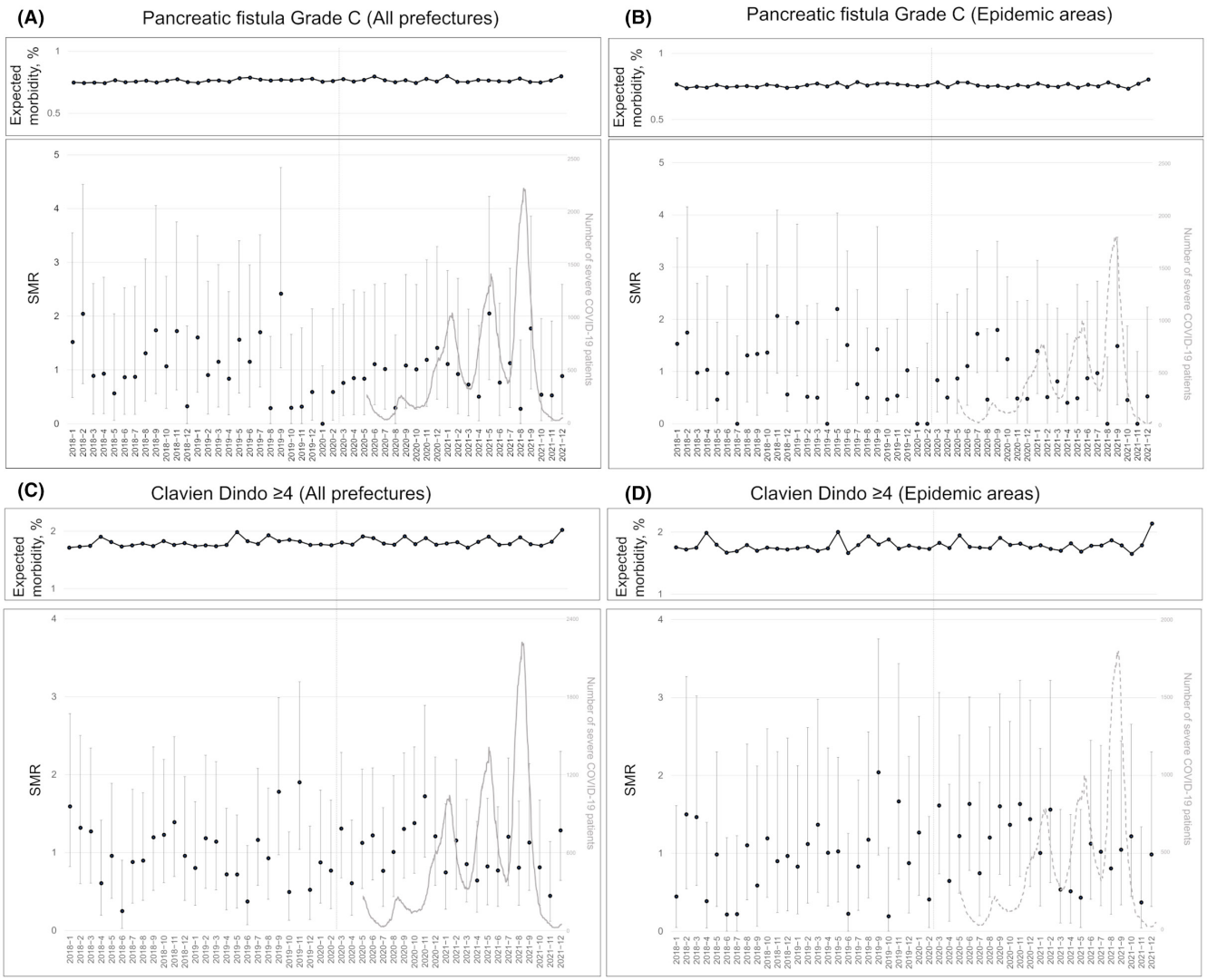

FIGURE 4 Monthly standardized morbidity ratios and expected morbidity rates for Grade C pancreatic fistula (A, B) and Clavien–Dindo grade ≥4 complications (C, D). Data in all prefectures (A, C) and in epidemic areas (B, D). Vertical lines indicate standardized morbidity ratios with 95% confidence intervals, and gray lines indicate the number of patients with severe COVID-19 in all prefectures (solid line) and epidemic areas (dot line). SMR, standardized morbidity ratio.

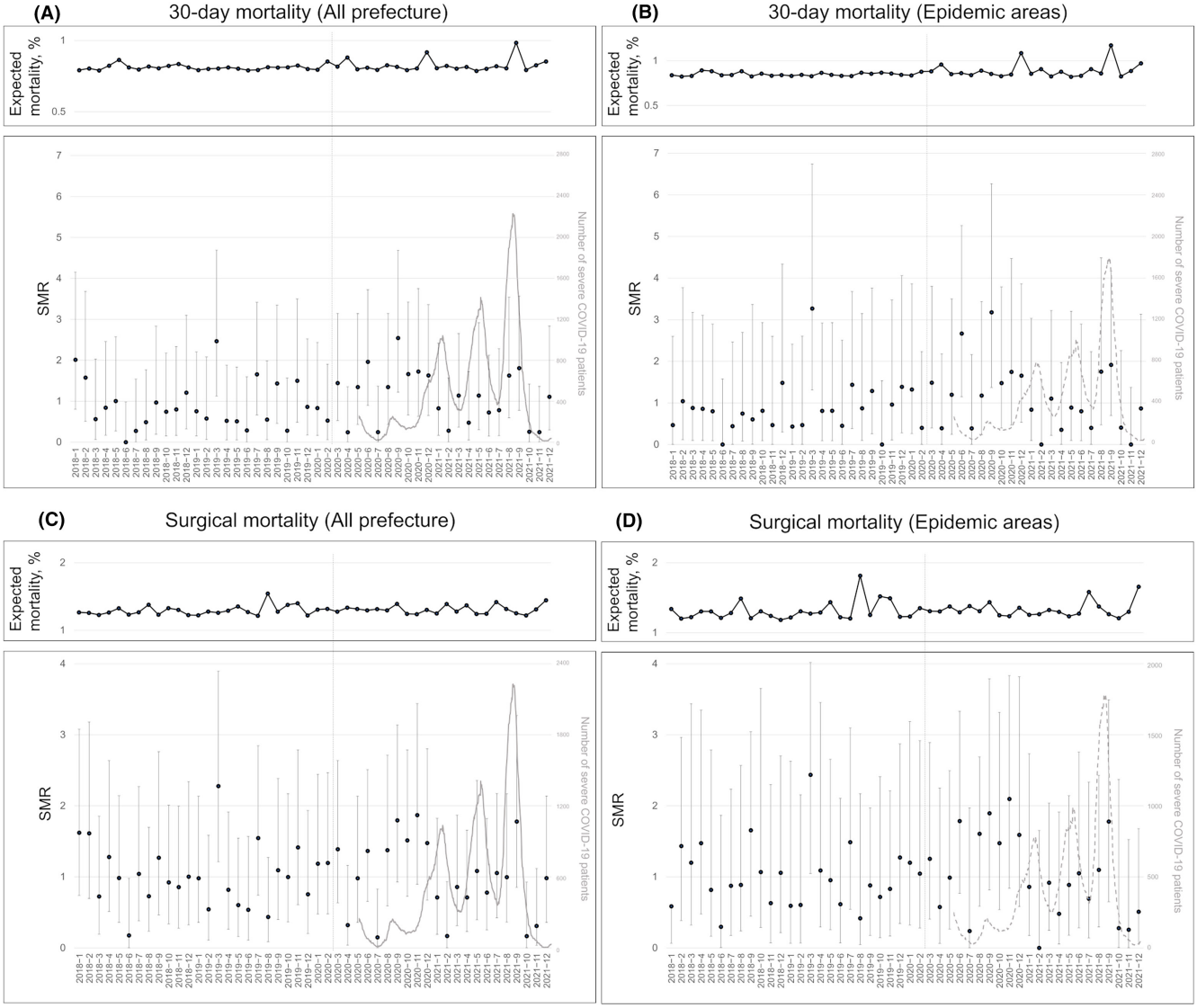

FIGURE 5 Monthly standardized mortality ratios and expected mortality rates for 30-day mortality (A, B) and surgical mortality (C, D). Data in all prefectures (A, C) and in epidemic areas (B, D). Vertical lines indicate standardized mortality ratios with 95% confidential intervals, and gray lines indicate the number of patients with severe COVID-19 in all prefectures (solid line) and epidemic areas (dot line). SMR, standardized mortality ratio.

exocrine pancreatic function; additionally, the likelihood of grade C pancreatic fistula seemed to be originally low. We also evaluated the standardized morbidity and mortality ratios of Clavien–Dindo grade ≥4 complications, surgical mortality, and 30-day mortality, and found that the trends were similar to those observed for pancreatic fistula. Importantly, the standardized mortality ratios of surgical mortality and 30-day mortality were slightly higher in 2020, without statistically significant difference. However, the 30-day and surgical mortality rates in 2020 were even lower than those observed in 2011–2012 based on the NCD data (30-day mortality, 1.1% in 2020 vs. 1.3% in 2011–2012; surgical mortality, 1.6% in 2020 vs. 2.9% in 2011–2012), which seem to be within a safe range.[31] In Japan, postoperative outcomes have improved following the introduction of high-level training institutions and the training surgeon system.[32,33] Moreover, we found that the proportion of ICU admissions did not significantly change during the pandemic compared to the prepandemic period. As early detection and early intensive treatment are critical to reduce mortality,[34] ICU availability after surgery reflects medical resources. Therefore, these results suggest that the Japanese surgeons and medical staff could maintain the level of clinical quality during the pandemic and that adequate medical resources were available despite the pandemic. Of course, our analyses could not determine whether appropriate ICU care was fully provided to the most severely ill patients, which should be assessed in more detail in future studies.

The present study has several limitations. First, in studies investigating a healthcare system during a pandemic, it is challenging to consider changes in medical resources based on the NCD as only

data on ICU use was available for analysis. Second, the total number of pancreatic cancer diagnoses, the distribution of cancer stages including unresectable stage, long-term outcomes, and patients with pancreatic tail cancer, which is difficult to detect in early stage, were not considered in the present study. They should be evaluated in the future analyses.

Our study showed that the efforts to maintain surgical care in Japan were sufficient to preserve the domestic clinical practice for the management of pancreatic cancer during the COVID-19 pandemic. If the COVID-19 pandemic or a similar one occurs again in the future, the following efforts made by Japan should be practiced: (1) attempt to establish as many components of the COVID-19-free pathway as possible, which include collaboration with neighboring hospitals[27]; (2) prioritize cancer and emergent surgeries; (3) perform routine tests on patients before elective surgery with a single RT-PCR nasal swab test within 3 days before hospital admission[25]; (4) prioritize vaccination in patients who will undergo elective surgery[26]; and (5) if possible, surgery should be delayed for at least 7 weeks in patients who acquired SARS-CoV-2 infection.[35]

In conclusion, the present study revealed the increasing number of patients with pancreatic cancer and improved short-term outcomes even during the COVID-19 pandemic. Surgical safety for pancreaticoduodenectomy could be maintained during the COVID-19 pandemic through the systematic endeavor of all surgical departments and hospitals in Japan. These findings should provide a clearer understanding of the surgical landscape in Japan during the COVID-19 pandemic and should be helpful in ensuring that adequate staffing and facility resources are in place for future outbreaks.

AUTHOR CONTRIBUTIONS

H. Maeda, H. Endo, T. Hibi, Y. Nakano, R. Seishima, M. Takeuchi, H. Yamamoto, and K. Hanazaki. contributed to the study conception and design. T. Hibi, H. Yamamoto, H. Maeda, A. Taketomi, Y. Kakeji, Y. Seto, H. Ueno, M. Mori, and Y. Kitagawa managed this study. H. Endo collected and analyzed data. Y. Takemura, Y. Nakano, and T. Hibi. interpreted the results. Y. Takemura and T. Hibi drafted the article. All authors reviewed and approved the final version of the manuscript.

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CONFLICT OF INTEREST STATEMENT

Y. Kitagawa is Editor in Chief of *Annals of Gastroenterological Surgery*. M. Mori is Emeritus Editor in Chief of *Annals of Gastroenterological Surgery*. H. Ueno is currently Associate Editor of *Annals of Gastroenterological Surgery*. Y. Kakeji is an editorial board member of *Annals of Gastroenterological Surgery*. Y. Kitagawa reports Honoraria from Asahi Kasei Pharma Corporation, AstraZeneca K.K., Ethicon Inc., Ono Pharmaceutical Co., Ltd., Otsuka Pharmaceutical Factory, Inc., Olympus Corporation, Cardinal Health K.K., Shionogi & Co., Ltd., Taiho Pharmaceutical Co., Ltd., Chugai Pharmaceutical Co., Ltd., Bristol-Myers Squibb K.K., MSD K.K., Smith & Nephew KK, Kaken Pharmaceutical Co., Ltd., ASKA Pharmaceutical Co., Ltd., Miyarisan Pharmaceutical Co., Ltd., Toray Industries, Inc., Daiichi Sankyo Company Ltd., Chugai Foundation for Innovative Drug Discovery Science, Nippon Kayaku Co., Ltd. EA Pharma Co., Ltd., Intuitive Surgical G.K., Takeda Pharmaceutical Company Limited, Sysmex Corporation, and Tsumura & Co. Y. Kitagawa also receive research funding from Asahi Kasei Pharma Corporation, Ono Pharmaceutical Co., Ltd., Otsuka Pharmaceutical Factory Inc., Nippon Covidien Inc., Taiho Pharmaceutical Co., Ltd., Chugai Pharmaceutical Co., Ltd., Kaken Pharmaceutical Co., Ltd., EA Pharma Co., Ltd., Yakult Honsha Co. Ltd., Otsuka Pharmaceutical Co., Ltd., Tsumura & Co. Sumitomo Pharma Co., Ltd., Eisai Co., Ltd., Kyowa Kirin Co., Ltd., Takeda Pharmaceutical Co., Ltd., Teijin Pharma Ltd., Cardinal Health., and Kowa Company, Ltd. Y. Kitagawa received the other fees from Sysmex Corporation and Medicaroid Corporation outside the submitted work. E. Hideki and Y. Hiroyuki are affiliated with the Department of Healthcare Quality Assessment at the University of Tokyo. The department is a social collaboration department supported by grants from the National Clinical Database, Intuitive Surgical Sarl, Johnson & Johnson K.K., and Nipro Co.

DATA AVAILABILITY STATEMENT

The datasets used in this study are available from the corresponding author on reasonable request.

ETHICS STATEMENT

Approval of the research protocol: Our study protocol was reviewed and adopted by the Japanese Society of Gastrointestinal Surgery Committee and approved by the Institutional Review Board of Kochi Medical School (Approval No. ID: 2022-75) and it conforms to the provisions of the Declaration of Helsinki.
Informed Consent: N/A.
Registry and the Registration No. of the study/trial: N/A.
Animal Studies: N/A.

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