Original Article



Outcomes of Patients Undergoing Elective Pancreatic Surgery During COVID-19 Pandemic: A Multicenter, Prospective Cohort Study



Ning Pu^{1#}, Siyao Liu^{1#}, Xuewei Bai^{2#}, Jiali Yang³, Tao Qian⁴, Zixian Wei², Tao Ma^{4*}[®], Lei Cai^{3*}[®] and Wenchuan Wu^{1*}[®]

¹Department of Pancreatic Surgery, Zhongshan Hospital, Fudan University, Shanghai, China; ²Department of Hepatobiliary and Pancreatic Surgery, Qunli Branch, the First Affiliated Hospital of Harbin Medical University, Harbin, Heilongjiang, China; ³Institute of Hepatopancreatobiliary Surgery, Chongqing General Hospital, University of Chinese Academy of Sciences, Chongqing, China; ⁴Department of Hepatobiliary and Pancreatic Surgery, The First Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou, Zhejiang, China

Received: July 09, 2023 | Revised: September 29, 2023 | Accepted: October 17, 2023 | Published online: November 30, 2023

Abstract

Background and objectives: The coronavirus disease 2019 (COVID-19) pandemic continues to affect global health, and the emergence of new variants has added a layer of uncertainty to medical practice. Although elective surgeries are recommended to be postponed for at least 7 weeks after severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection to be considered safe, the safety and optimal timing for pancreatic surgery after this infection remains unknown.

Methods: Conducted in four high-volume pancreas centers in China, this prospective, multicenter clinical trial aimed to provide a realistic representation of the key perioperative parameters for pancreatic surgery after SARS-CoV-2 infection. The primary outcome was 30-day perioperative survival, and the secondary outcomes included major complications, pulmonary complications, and surgical complications.

Results: Our results revealed that elective pancreatic surgery within 4 weeks of SARS-CoV-2 infection may be correlated with a prolonged hospital stay. Specifically, patients who underwent surgery within 0–2 weeks (24.7 days average) or 3–4 weeks (21.8 days average) after infection had obviously longer hospital stays compared to those without prior infection (15.5 days average) or those who underwent surgery more than 4 weeks after infection. However, there was no apparent increase in the total post-

#Contributed equally to this work.

operative complications classified as Clavien-Dindo grade \geq 3, even among patients who underwent surgery within 2 weeks after SARS-CoV-2 infection.

Conclusions: No significant increase in major complications is observed among patients undergoing pancreatic surgery following a diagnosis of SARS-CoV-2. However, it would be safer to perform pancreatic surgery at least 4 weeks after SARS-CoV-2 infection.

Introduction

Since the emergence of coronavirus disease 2019 (COVID-19), it has rapidly disseminated across the globe. By the end of 2022, there were over 630 million confirmed cases and 6.6 million deaths worldwide. In the first half of 2023, over 760 million confirmed cases and 6.9 million deaths had been reported to the World Health Organization (WHO).¹ The data indicate that the pandemic

© 2023 The Author(s). This article has been published under the terms of Creative Commons Attribution-Noncommercial 4.0 International License (CC BY-NC 4.0), which permits noncommercial unrestricted use, distribution, and reproduction in any medium, provided that the following statement is provided. "This article has been published in *Cancer Screening and Prevention* at https://doi.org/10.14218/CSP.2023.00001S and can also be viewed on the Journal's website at https://www.xiahepublishing.com/journal/csp".

Keywords: SARS-CoV-2; Pancreatic surgery; Postoperative outcome; Surgical timing; Safety.

Abbreviations: ASA, American Association of Anesthesiologists; COVID-19, coronavirus disease 2019; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; STROBE, Strengthening the Reporting of Observational Studies in Epidemiology; WHO, World Health Organization.

^{*}Correspondence to: Wenchuan Wu, Department of Pancreatic Surgery, Zhongshan Hospital, Fudan University, 180 Fenglin Road, Shanghai 200032, China. ORCID: https://orcid.org/0000-0002-8408-885X. Tel/Fax: +86-10-6404-1990, E-mail: wu wenchuan@zs-hospital.sh.cn; Lei Cai, Institute of Hepatopancreatobiliary Surgery, Chongqing General Hospital, University of Chinese Academy of Sciences, 118 Star Avenue, Chongqing 400722, China. ORCID: https://orcid.org/0000-0002-3489-4386. Tel: +86-23-6339-0596, Fax: +86-23-6339-0955, E-mail: cailei@rocketmail.com; Tao Ma, Department of Hepatobiliary and Pancreatic Surgery, The First Affiliated Hospital, Zhejiang University School of Medicine, 79 Qingchun Road, Hangzhou, Zhejiang 310003, China. ORCID: https://orcid.org/0009-0006-0990-8172. Tel/Fax: +86-571-8723-6621, E-mail: zjumatao@zju.edu.cn

How to cite this article: Pu N, Liu S, Bai X, Yang J, Qian T, Wei Z, *et al.* Outcomes of Patients Undergoing Elective Pancreatic Surgery During COVID-19 Pandemic: A Multicenter, Prospective Cohort Study. *Cancer Screen Prev* 2023;2(4):229–237. doi: 10.14218/CSP.2023.00001S.

may persist, and with the recent emergence of a new highly transmissible variant, Omicron, the potential for prolonged impact and the likelihood of continuous reinfection caused by the emerging variants remains.² Hence, it is imperative to investigate the influence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) on the perioperative period.

Previous research has indicated that patients suffering from chronic diseases such as cancers, who are undergoing various treatments such as adjuvant therapy and surgical treatment, are at a significantly higher risk of contracting the SARS-CoV-2 virus.³ Moreover, patients with cancer, particularly those with highly aggressive cancers, such as pancreatic cancer, may face a greater risk of mortality during the pandemic.⁴ As such, researchers have been exploring ways to balance the necessity of diagnosis and treatment and the implementation of epidemic prevention measures.⁵ During the early stages, surgical centers focused on careful patient screening and evaluation to ensure their suitability for surgery owing to safety concerns, consequently reducing their weekly procedures.^{6,7} The current focus has shifted from patient screening to identifying the optimal timing for surgery in a diverse population and investigating the perioperative impacts of COVID-19.

In the past 3 years, as surgeons and researchers have gained a deeper understanding of the COVID-19 epidemic, in addition to the gradual recovery of surgical volumes, an international consensus on optimal surgical timing during the pandemic has been reached and published. The consensus recommends that patients should avoid elective surgery within 7 weeks after SARS-CoV-2 infection and undergo a comprehensive multidisciplinary evaluation before the procedure.8 However, there is still a lack of relevant research in pancreatic surgery. Compared to other surgical procedures, pancreatic surgery is associated with higher mortality and increased incidences of complications owing to the unique anatomical structure and technical demands of the pancreas,9 although there is a trend toward minimally invasive pancreatic surgery.¹⁰ The mortality rate for Whipple surgery, which is the most classic pancreatic surgery performed in high-volume centers, is nearly 2%, but it remains significantly higher compared to other surgical procedures.¹¹ Also, complications following pancreatic surgery are significantly higher, with certain studies indicating an overall incidence rate as high as 40%. The most common and severe complication following pancreatectomy is the occurrence of a postoperative pancreatic fistula, which can result in life-threatening complications, including serious infection and bleeding.¹² Multiple high-quality studies have confirmed that the overall incidence of clinically relevant postoperative pancreatic fistula is more than 20%.^{13,14} Owing to these complications, the perioperative period following pancreatic surgery tends to be prolonged, resulting in an average hospital stay exceeding 14 days.^{15,16}

Given the popularity and gradual decline in the virulence of the new variant,² whether the current guidelines can be optimized remains unclear. In the context of the prevalence of the new variant, there is no expert consensus or surgical timing guidelines specifically tailored to pancreatic surgery. Given the potential of Omicron to cause reinfection in individuals previously infected with other strains of SARS-CoV-2, this study was deemed necessary.¹⁷ Meanwhile, whether Omicron infection results in an increased viral load is debatable. Therefore, the perioperative effects of Omicron infection from an immunological perspective remain unknown, although most infected individuals are asymptomatic.¹⁸

Therefore, we initiated this study to prospectively investigate the perioperative effects of SARS-CoV-2 infection, with a focus on the newly emerged variant, on patients undergoing elective panPu N. et al: Elective pancreatic surgery during COVID-19

creatic surgery and to guide the optimal timing of surgery after infection in China. This study was designed to serve as an ideal representation for exploring the impact of these new variants of SARS-CoV-2 on the perioperative period and the timing of pancreatic surgical intervention in infected patients.

Methods

Study design

This multicenter, observational, prospective study enrolled patients who underwent elective pancreatic surgery with curative intent during the COVID-19 pandemic in China. A total of four hospitals participated in this study, namely Zhongshan Hospital, Fudan University, the First Affiliated Hospital of Harbin Medical University, the First Affiliated Hospital of Zhejiang University School of Medicine, and Chongqing Hospital, University of Chinese Academy of Sciences. The study protocol of this design followed the Strengthening the Reporting of Observational Studies in Epidemiology, commonly referred to as STROBE statement.

Patient eligibility criteria

Consecutive patients aged 18 years and above who underwent elective pancreatic surgery (including distal pancreatectomy, pancreaticoduodenectomy, total pancreatectomy, and segmental pancreatectomy) from January 8, 2023 to March 4, 2023 at each center and who are followed up for 30 days postoperatively were eligible for inclusion. Patients lacking data on follow-ups or SARS-CoV-2 infection were excluded.

Outcome measures

The primary outcome was the 30-day perioperative survival, defined as death due to any cause within 30 days from the date of surgery. The secondary outcomes included pulmonary complications, surgical complications, and major complications (Clavien-Dindo grade III, including death). Pulmonary complications included pneumonia, and surgical complications included pancreas-specific surgical complications (including pancreatic fistula, bile leak, and stomal leak), deep vein thrombosis, and hemorrhage. We defined postoperative bile leak according to the International Study Group of Liver Surgery criteria and postoperative pancreatic fistula according to the International Study Group on Pancreatic Surgery criteria.

Diagnosis of SARS-CoV-2 infection

SARS-CoV-2 infection was defined based on clinical, radiological, or laboratory criteria. The clinical diagnosis was established by a senior clinician documenting signs and symptoms consistent with SARS-CoV-2 infection, in line with the WHO COVID-19 case definition, which included fever, cough, and myalgia. Radiological diagnosis involved computed tomography of the thorax, with reports adhering to local protocols. Laboratory diagnosis was confirmed by quantitative reverse transcription polymerase chain reaction testing or antigen detection for SARS-CoV-2.

Data recording and explanatory variables

Data were recorded by clinicians based on a prespecified protocol and uploaded to the Sense Data platform (a secure online database, edc.zs-hospital.sh.cn). The explanatory variables accounting for the risk of SARS-CoV-2 and perioperative risk included patient demographics (age, sex, American Association of Anesthesiologists grade, existing comorbidities, revised cardiac risk index,

vaccination, smoking), operative characteristics (tumor type, surgical procedure, surgical approach), postoperative complications (Clavien-Dindo classification, ICU admission, unscheduled reoperation, leakage, pneumonia, deep vein thrombosis, hemorrhage, mortality).

Statistical analysis

Categorical data were presented using frequencies and percentages, whereas continuous data were described using means and standard deviations. The date of surgery was considered as day 0 when calculating the time to death. To evaluate the risk of death and complications in patients with/without SARS-CoV-2 infection during the COVID-19 pandemic, the χ^2 test or Fisher's exact test was used to help surgeons decide the safest timing for elective pancreatic surgery. All data were analyzed using SPSS 21.0 software (IBM Corporation, Armonk, NY, USA). A two-tailed analysis with a *p*-value < 0.05 was used to determine statistical significance.

Results

During the study period, 102 patients who underwent elective pancreatic surgery across four hospitals in China were enrolled. Six patients lacking information on SARS-CoV-2 and one patient without survival outcome data were excluded. Thus, a total of 95 patients who underwent elective pancreatic surgery during the COVID-19 pandemic were included in this study. The baseline characteristic data, surgical characteristics, and postoperative complications are shown in Table 1. In total, 82 (86.3%) patients were diagnosed with SARS-CoV-2 before surgery. The time interval between the SARS-CoV-2 diagnosis and surgery was 0-2 weeks in 9 (9.5%) patients, 3-4 weeks in 11 (11.6%) patients, 5-6 weeks in 16 (16.8%) patients (Table 1). At the time of surgery, most patients were asymptomatic, with symptoms either having resolved or never having presented at all.

Patients with preoperative SARS-CoV-2 infection were more likely to have concomitant preoperative pneumonia when compared to patients without SARS-CoV-2 infection (p < 0.001). However, no significant association was found between preoperative SARS-CoV-2 infection and other general clinicopathological features and postoperative complications (Table 2). Overall, within 30 days, 13.7% (13/95) of patients experienced complications that were grade III or higher on the Clavien-Dindo classification. Postoperative ICU admissions were noted in 17.9% (17/95) of patients, and 12.6% (12/95) underwent unscheduled reoperations. The total incidence rates of postoperative leakage, pneumonia, deep vein thrombosis, and hemorrhage were 17.9% (17/95), 9.5% (9/95), 1.1% (1/95), and 7.4% (7/95), respectively. The overall 30-day postoperative mortality rate was 1.1% (1/95).

The 30-day postoperative mortality rates, stratified by the time interval from SARS-CoV-2 diagnosis to surgery, were as follows: 11.1% (1/9) for 0–2 weeks; 0% (0/11) for 3–4 weeks; 0% (0/16) for 5–6 weeks; 0% (0/30) for 7–8 weeks; and 0% (0/16) for \geq 8 weeks. Concomitantly, the 30-day mortality rate in patients without preoperative SARS-CoV-2 infection was 0% (0/13). In the overall analysis for elective pancreatic surgery, patients undergoing surgery within 0–2 weeks (24.7 days) and 3–4 weeks (21.8 days) after SARS-CoV-2 infection had obviously longer hospital stays compared to patients with no SARS-CoV-2 infection (15.5 days) and those who underwent surgery 4–5 weeks (17.1 days), 6–7 weeks (15.7 days), or \geq 8 weeks (15.3 days) after infection. Thus, patients undergoing surgery \geq 6 weeks after SARS-CoV-2 infection may

have a length of hospital stay comparable to patients without infection, and patients operated within 4 weeks after SARS-CoV-2 infection may have higher postoperative mortality, ICU admission, leakage, and hemorrhage. The total postoperative complications that were grade III or higher in the Clavien-Dindo classification did not obviously increase after SARS-CoV-2 infection, even in patients who underwent surgery within 2 weeks.

Discussion

In this randomized, prospective clinical study, we assessed the duration from SARS-CoV-2 infection diagnosis to surgery, postoperative mortality and complications, as well as duration of hospitalization length, all of which are crucial perioperative indicators. Our data reveal intriguing findings, presenting novel insights into the influence of SARS-CoV-2 infection on pancreatic surgery and shedding new light on the optimal timing for the surgery.

With regard to the comprehensive data on postoperative complications in infected patients, the findings of this study aligned with many previous researches. No significant increase was observed in the 30-day mortality (1.2%), unscheduled reoperation (7.7%), and major postoperative complications (13.4%) in patients infected with SARS-CoV-2 compared to the uninfected ones.¹⁹ However, early studies often involved rigorous patient screening for safety reasons. For example, Quero et al.7 reported similar rates of ICU admission and postoperative mortality between infected and uninfected surgical patients, with reductions of 45.4% and 61.9% in laparoscopic and robot-assisted surgeries, respectively. It is noteworthy that during the initial wave of the COVID-19 pandemic, which significantly disrupted surgical center operations and the provision of surgical oncology, the majority of studies conducted were retrospective, observational studies rather than prospective clinical trials,²⁰ thus potentially limiting their generalizability and persuasiveness.

Moreover, McKay *et al.*²¹ designed a prospective study and found that the incidence of postoperative complications, including postoperative bleeding and grade B/C pancreatic fistula, in patients infected with SARS-CoV-2 was higher compared to those without infection. Although they reported a significant difference in major complications (29.1% vs. 13.2%) and perioperative mortality (9.4% vs. 2.6%) between infected and uninfected patients, in our study, we found no obvious difference in both mortality (1.2% vs. 0%) and major complications (13.4% vs. 15.4%). This discrepancy could be attributable to the fact that nearly all patients with COVID-19 in this study were infected with the Omicron variant, which is comparatively less virulent. Considering that the current circulating strain is Omicron, the findings from our study may hold greater applicability at present.

In our study, approximately 40% (37/95) of patients had borderline or malignant tumors. Given the highly malignant nature of pancreatic malignancies, it is imperative to investigate the influence of COVID-19 infection on patients with pancreatic cancer. We further observed that SARS-CoV-2 infection did not significantly impede postoperative recovery in patients who had undergone resection of malignant cancers (26 cases, 31.7%), owing to the absence of significant differences in the length of hospital stay and incidence of complications between patients with COVID-19 having malignant tumors and patients without COVID-19. As previously suggested, although the infection does not affect adjuvant treatment options and drug dosages for patients with unresectable pancreatic cancer, its impact on progression-free survival or overall survival remains controversial.^{22,23} Brugel *et al.*²⁴ pointed

Pu N. et al: Elective pancreatic surgery during COVID-19

Table 1. Baseline characteristics and outcomes for patients undergoing pancreatic surgery stratified by time from diagnosis of SARS-CoV-2 infection

Variables	No preopera- tive SARS-CoV-2 infection, <i>n</i> = 13	Preoperative SARS-CoV-2 infection (by tim- ing of diagnosis before surgery)				
variables		0–2 weeks, n = 9	3–4 weeks, n = 11	5–6 weeks, n =16	7–8 weeks, n = 30	≥ 8 weeks, <i>n</i> = 16
Range of age in years						
30–49	2 (15.4%)	1 (11.1%)	3 (27.3%)	2 (12.5%)	7 (23.3%)	4 (25.0%)
50–69	9 (69.2%)	7 (77.8%)	8 (72.7%)	9 (56.3%)	12 (40.0%)	9 (56.3%)
≥07	2 (15.4%)	1 (11.1%)	0 (0%)	5 (31.2%)	11 (36.7%)	3 (18.7%)
Sex						
Female	6 (46.2%)	2 (22.2%)	8 (72.8%)	6 (37.5%)	17 (56.7%)	6 (37.5%)
Male	7 (53.8%)	7 (77.8%)	3 (27.2%)	10 (62.5%)	13 (43.3%)	10 (62.5%)
ASA physical status						
1	3 (23.1%)	2 (22.2%)	2 (18.2%)	2 (12.5%)	8 (26.7%)	3 (18.7%)
2	6 (46.2%)	5 (55.6%)	9 (81.8%)	12 (75.0%)	20 (66.7%)	11 (68.8%)
3	4 (30,7%)	2 (22.2%)	0 (0%)	2 (12.5%)	2 (6.6%)	2 (12.5%)
Revised cardiac risk index						
0	10 (76.9%)	5 (55.5%)	11 (100.0%)	15 (93.8%)	25 (83.3%)	13 (81.3%)
1	3 (23.1%)	4 (45.5%)	0 (0%)	1 (6.2%)	5 (16.7%)	3 (18.7%)
Vaccination						
0	2 (15.4%)	1 (11.1%)	0 (0%)	4 (25.0%)	3 (10.0%)	5 (31.3%)
1	0 (0%)	1 (11.1%)	0 (0%)	1 (6.2%)	0 (0%)	0 (0%)
≥2	11 (84.6%)	7 (77.8%)	11 (100%)	11 (68.8%)	27 (90.0%)	11 (68.7%)
Smoking						
Never	11 (84.6%)	7 (77.8%)	10 (90.9%)	14 (87.5%)	21 (70.0%)	14 (87.5%)
Quit within 6 weeks	1 (7.7%)	0 (0%)	0	0 (0%)	1 (3.3%)	1 (6.3%)
Quit before 6 weeks	0 (0%)	1 (11.1%)	1 (9.1%)	1 (6.2%)	2 (6.7%)	1 (6.3%)
Yes	1 (7.7%)	1 (11.1%)	0	1 (6.2%)	6 (20.0%)	0 (0%)
Respiratory comorbidities						
Yes	0 (0%)	2 (22.2%)	1 (9.1%)	2 (12.4%)	0 (0%)	1 (6.3%)
COVID-19 symptoms						
Asymptomatic	Na	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Symptomatic – resolved	Na	4 (44.4%)	11 (100%)	16 (100%)	30 (100%)	16 (100%)
Symptomatic – ongoing	Na	5 (55.6%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Tumor type						
Benign	8 (61.5%)	8 (88.9%)	6 (54.5%)	11 (68.7%)	16 (53.3%)	9 (56.2%)
Borderline	0 (0%)	0 (0%)	0 (0%)	0 (0%)	4 (13.4%)	2 (12.5%)
Malignant	5 (38.5%)	1 (11.1%)	5 (45.5%)	5 (31.3%)	10 (33.3%)	5 (31.3%)
Surgical procedure						
Total pancreatectomy	0 (0%)	0 (0%)	0 (0%)	2 (12.5%)	0 (0%)	0 (0%)
Pancreaticoduodenectomy	5 (38.5%)	6 (66.7%)	9 (81.8%)	9 (56.2%)	18 (60.0%)	11 (68.7%)
Distal pancreatectomy	7 (53.8%)	2 (22.2%)	1 (9.1%)	4 (25.0%)	10 (33.3%)	5 (31.3%)
Segmental pancreatectomy	1 (7.7%)	1 (11.1%)	1 (9.1%)	1 (6.3%)	2 (6.7%)	0 (0%)

(continued)

Variables	No preopera-	Preoperative SARS-CoV-2 infection (by tim- ing of diagnosis before surgery)				
Variables	infection, $n = 13$	0–2 weeks, n = 9	3–4 weeks, n = 11	5–6 weeks, n =16	7–8 weeks, n = 30	≥ 8 weeks, n = 16
Approach						
Laparoscope	7 (53.8%)	2 (22.2%)	5 (45.5%)	5 (31.2%)	10 (33.3%)	4 (25.0%)
Robotic	1 (7.7%)	2 (22.2%)	0 (0%)	0 (0%)	0 (0%)	3 (18.7%)
Open	5 (38.5%)	5 (55.6%)	6 (54.5%)	11 (68.8%)	20 (66.7%)	9 (56.3%)
Clavien-Dindo classification						
<3	11 (84.6%)	8 (88.9%)	9 (81.8%)	14 (87.5%)	27 (90.0%)	13 (81.3%)
≥3	2 (15.4%)	1 (11.1%)	2 (18.2%)	2 (12.5%)	3 (10.0%)	3 (18.7%)
Postoperative ICU admission						
Yes	2 (15.4%)	2(22.2%)	5 (45.5%)	4 (25.0%)	3 (10.0%)	1 (6.3%)
Postoperative unscheduled reoperation						
Yes	1 (7.7%)	1 (11.1%)	2 (18.2%)	2 (12.5%)	3 (10.0%)	3 (18.7%)
Postoperative leakage						
Yes	2 (15.4%)	2 (22.2%)	3 (27.3%)	2 (12.5%)	5 (16.7%)	3 (18.7%)
Postoperative pneumonia						
Yes	1 (7.7%)	2 (22.2%)	0 (0%)	1 (6.3%)	2 (6.7%)	3 (18.7%)
Deep vein thrombosis						
Yes	0 (0%)	1 (11.1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Postoperative hemorrhage						
Yes	0 (0%)	1 (11.1%)	1 (11.1%)	0 (0%)	2 (6.7%)	3 (18.7%)
30-day postoperative mortality						
Yes	0 (0%)	1 (11.1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Average length of stay in days	15.5	24.7	21.8	17.1	15.7	15.3

Table 1. (continued)

Values are number (proportion). ASA, American Association of Anesthesiologists; COVID-19, coronavirus disease 2019; ICU, intensive care unit; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

out that COVID-19 may result in missed diagnoses of pancreatic cancer and disease progression, particularly from resectable to unresectable pancreatic cancer, during the treatment gap. Based on expert consensus and our study findings, it can be concluded that delays in surgical treatment due to SARS-CoV-2 infection are unwarranted, because SARS-CoV-2 infection, particularly the new variants, may not significantly affect surgical complications in patients with pancreatic cancer. Additionally, neoadjuvant therapy can be administered to control tumor progression during this treatment interval before surgery.⁵ The impact of SARS-CoV-2 infection on the overall outcome of pancreatic surgery remains debatable; however, there is increasing clarity regarding the management of pancreatectomy in patients with the infection.

Current consensus recommends a 7-week delay for elective surgery after SARS-CoV-2 infection,⁸ however, there is no such authoritative statement or guideline for pancreatic surgery. Previous surgical studies have indicated that pancreatic surgery should be considered carefully for some special groups of patients with COVID-19, particularly those with positive symptoms, ensuring appropriate hospitalization duration.²⁵ Kędzierska-Kapuza *et al.*²⁵ revealed an average postoperative hospitalization of 15.8 days,

whereas our study showed longer average hospital stays of 24.7 days and 21.8 days for surgeries performed within 0-2 weeks and 2-4 weeks after infection, respectively. Therefore, our findings suggest a potential correlation between the time interval from infection to surgery and the length of hospital stay in patients infected with SARS-CoV-2. Moreover, the length of hospitalization for patients who underwent surgery after 6 weeks of SARS-CoV-2 infection was comparable to that of patients without SARS-CoV-2 infection (15.7/15.3 days vs. 15.5 days). Those who underwent surgery within 4 weeks of SARS-CoV-2 infection showed a higher incidence of major postoperative complications, such as ICU admission, postoperative pancreatic fistula, postoperative hemorrhage, postoperative leakage, and death. Specifically, patients who underwent surgery 0-2 weeks and 3-4 weeks after infection required longer stays (24.7 and 21.8 days, respectively) compared to those who were not infected or infected after more than 4 weeks. Therefore, the recommended optimal interval for pancreatic surgery after infection in our study is 4 weeks, different from the recent consensus, which suggests a recommended timing of 7 weeks,⁸ based on a baseline validated risk assessment tool.²⁶

Our conclusions are derived from a prospective observational

Table 2.	Correlations between	clinicopathological	characteristics and	status of SARS	-CoV-2 infection
----------	-----------------------------	---------------------	---------------------	----------------	------------------

Variables	No preoperative SARS- CoV-2 infection, n = 13	Preoperative SARS- CoV-2 infection, n = 82	p-value
Range of age in years			0.719
30–49	2 (15.4%)	17 (20.7%)	
50–69	9 (69.2%)	45 (54.9%)	
≥07	2 (15.4%)	20 (24.4%)	
Sex			0.925
Female	6 (46.2%)	39 (47.6%)	
Male	7 (53.8%)	43 (52.4%)	
ASA physical status			0.096
1	3 (23.1%)	17 (20.7%)	
2	6 (46.2%)	57 (69.5%)	
3	4 (30,7%)	8 (9.8%)	
Revised cardiac risk index			0.804
0	10 (76.9%)	69 (84.1%)	
1	3 (23.1%)	13 (15.9%)	
Vaccination			0.867
0	2 (15.4%)	13 (15.9%)	
1	0 (0%)	2 (2.4%)	
≥2	11 (84.6%)	67 (81.7%)	
Smoking			0.549
Never	11 (84.6%)	66 (80.5%)	
Quit within 6 weeks	1 (7.7%)	2 (2.4%)	
Quit before 6 weeks	0 (0%)	6 (7.3%)	
Yes	1 (7.7%)	8 (9.8%)	
Respiratory comorbidities			0.592
Yes	0 (0%)	6 (7.3%)	
No	13 (100%)	76 (92.7%)	
Preoperative pneumonia			<0.001
No	13 (100%)	39 (47.6%)	
Yes, <25%	0 (0%)	42 (51.2%)	
Yes, 25–50%	0 (0%)	1 (1.2%)	
Tumor type			0.8
Benign	8 (61.5%)	50 (61.0%)	
Borderline	0 (0%)	6 (7.3%)	
Malignant	5 (38.5%)	26 (31.7%)	
Surgical procedure			0.197
Total Pancreatectomy	0 (0%)	2 (2.4%)	
Pancreaticoduodenectomy	5 (38.5%)	53 (64.6%)	
Distal Pancreatectomy	7 (53.8%)	22 (26.8%)	
Segmental pancreatectomy	1 (7.7%)	5 (6.1%)	
Approach			0.179

(continued)

Variables	No preoperative SARS- CoV-2 infection, n = 13	Preoperative SARS- CoV-2 infection, n = 82	p-value
Laparoscope	7 (53.8%)	26 (31.7%)	
Robotic	1 (7.7%)	5 (6.1%)	
Open	5 (38.5%)	51 (62.2%)	
Clavien-Dindo classification			1
<3	11 (84.6%)	71 (86.6%)	
≥3	2 (15.4%)	11 (13.4%)	
Postoperative ICU admission			0.576
Yes	2 (15.4%)	15 (18.3%)	
No	11 (84.6%)	67 (81.7%)	
Postoperative unscheduled reoperation			0.898
Yes	1 (7.7%)	11 (13.4%)	
No	12 (92.3%)	71 (86.6%)	
Postoperative leakage			1
Yes	2 (15.4%)	15 (18.3%)	
No	11 (84.6%)	67 (81.7%)	
Postoperative pneumonia			1
Yes	1 (7.7%)	8 (9.8%)	
No	12 (92.3%)	74 (90.2%)	
Deep vein thrombosis			1
Yes	0 (0%)	1 (1.2%)	
No	13 (100%)	81 (98.8%)	
Postoperative hemorrhage			0.588
Yes	0 (0%)	7 (8.5%)	
No	13 (100%)	75 (91.5%)	
30-day postoperative mortality			0.441
Yes	0 (0%)	1 (1.2%)	
No	13 (100%)	81 (98.8%)	

Table 2. (continued)

Values are number (proportion). ASA, American Association of Anesthesiologists; ICU, intensive care unit; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

cohort study focusing on pancreatic surgery rather than overall surgery. In addition, our study was conducted during a different phase of the pandemic, when most of the enrolled patients may have been infected with a less toxic variant of Omicron and thus, had milder symptoms. Moreover, our study does not draw conclusions from an epidemiological point of view, but only studies the timing of surgery from a surgical outcome standpoint. The goal is to provide surgeons with valuable data to decide the optimal timing of surgery by gauging the postoperative condition of the patients.

Limitations

Despite our efforts to mitigate potential issues that may arise, there are still certain limitations to this study that must be acknowledged. First, this study was not conducted as a double-blind clinical trial, and all surgeons and investigators were fully informed of each patient's condition throughout the study. Second, the limited number of enrolled cases may constrain the statistical power of our analyses and contribute to potential bias in the results. Third, we did not assess the specific variants of infection; hence, we can only speculate many of the results based on the characteristics and popularity of the new variants. Therefore, a larger multicenter, prospective, and double-blind clinical trial is required to further confirm our findings.

Conclusions

The incidence of major complications did not significantly increase in patients who underwent pancreatic surgery following SARS-CoV-2 diagnosis. However, it may be much safer if pancreatic surgery is performed 4 or more weeks after SARS-CoV-2 infection.

Acknowledgments

None.

Funding

This study was funded by the National Natural Science Foundation of China (82103409), China Postdoctoral Science Foundation (2021M690037), Shanghai Sailing Program (21YF1407100), and Youth Fund of Zhongshan Hospital Fudan University (LCB-SHZX003).

Conflict of interest

Dr. Ning Pu has been an editorial board member of *Cancer Screening and Prevention* since November 2021. The authors have no other conflicts of interest.

Author contributions

Funding acquisition, study design, data acquisition, data analysis, statistical analysis, manuscript writing, manuscript review (NP); data acquisition, data analysis, statistical analysis, manuscript writing, manuscript review (SL); data acquisition, manuscript review (XB, JY, TQ, ZW, TM, LC); and study design, data acquisition, manuscript review, guarantor (WW).

Ethical statement

The study protocol was approved by the Ethics Committee of Zhongshan Hospital, Fudan University (No. B2020-255R). All subjects provided written informed consent in accordance with the Declaration of Helsinki.

Data sharing statement

The data that support the findings of this study are available on request from the corresponding author.

References

- Allan M, Lièvre M, Laurenson-Schafer H, de Barros S, Jinnai Y, Andrews S, *et al.* The World Health Organization COVID-19 surveillance database. Int J Equity Health 2022;21(Suppl 3):167. doi:10.1186/ s12939-022-01767-5, PMID:36419127.
- [2] Fan Y, Li X, Zhang L, Wan S, Zhang L, Zhou F. SARS-CoV-2 Omicron variant: recent progress and future perspectives. Signal Transduct Target Ther 2022;7(1):141. doi:10.1038/s41392-022-00997-x, PMID: 35484110.
- [3] Lee KA, Ma W, Sikavi DR, Drew DA, Nguyen LH, Bowyer RCE, et al. Cancer and Risk of COVID-19 Through a General Community Survey. Oncologist 2021;26(1):e182–e185. doi:10.1634/theoncologist. 2020-0572, PMID:32845538.
- [4] Kutikov A, Weinberg DS, Edelman MJ, Horwitz EM, Uzzo RG, Fisher RI. A War on Two Fronts: Cancer Care in the Time of COVID-19. Ann Intern Med 2020;172(11):756–758. doi:10.7326/M20-1133, PMID:32219410.
- [5] Oba A, Stoop TF, Löhr M, Hackert T, Zyromski N, Nealon WH, et al. Global Survey on Pancreatic Surgery During the COVID-19 Pandemic. Ann Surg 2020;272(2):e87–e93. doi:10.1097/SLA.000000000004006, PMID:32675507.
- [6] Campi R, Amparore D, Capitanio U, Checcucci E, Salonia A, Fiori C, et al. Reply to Vincenzo Ficarra, Giuseppe Mucciardi, and Gianluca Giannarini's Letter to the Editor re: Riccardo Campi, Daniele Amparore,

Pu N. et al: Elective pancreatic surgery during COVID-19

Umberto Capitanio, *et al.* Assessing the Burden of Nondeferrable Major Uro-oncologic Surgery to Guide Prioritisation Strategies During the COVID-19 Pandemic: Insights from Three Italian High-volume Referral Centres. Eur Urol2020;78:11-15. Eur Urol 2020;78(4):e169–e170. doi:10.1016/j.eururo.2020.05.017, PMID:32475746.

- [7] Quero G, Pecorelli N, Paiella S, Fiorillo C, Petrone MC, Rosa F, et al. Quantitative assessment of the impact of COVID-19 pandemic on pancreatic surgery: an Italian multicenter analysis of 1423 cases from 10 tertiary referral centers. Updates Surg 2022;74(1):255–266. doi:10.1007/s13304-021-01171-8, PMID:34817837.
- [8] El-Boghdadly K, Cook TM, Goodacre T, Kua J, Denmark S, McNally S, et al. Timing of elective surgery and risk assessment after SARS-CoV-2 infection: an update: A multidisciplinary consensus statement on behalf of the Association of Anaesthetists, Centre for Perioperative Care, Federation of Surgical Specialty Associations, Royal College of Anaesthetists, Royal College of Surgeons of England. Anaesthesia 2022;77(5):580–587. doi:10.1111/anae.15699, PMID:35194788.
- [9] Kawaida H, Kono H, Hosomura N, Amemiya H, Itakura J, Fujii H, et al. Surgical techniques and postoperative management to prevent postoperative pancreatic fistula after pancreatic surgery. World J Gastroenterol 2019;25(28):3722–3737. doi:10.3748/wjg.v25.i28.3722, PMID:31391768.
- [10] de Rooij T, Klompmaker S, Abu Hilal M, Kendrick ML, Busch OR, Besselink MG. Laparoscopic pancreatic surgery for benign and malignant disease. Nat Rev Gastroenterol Hepatol 2016;13(4):227–238. doi:10.1038/nrgastro.2016.17, PMID:26882881.
- [11] Bliss LA, Witkowski ER, Yang CJ, Tseng JF. Outcomes in operative management of pancreatic cancer. J Surg Oncol 2014;110(5):592–598. doi:10.1002/jso.23744, PMID:25111970.
- [12] Hartwig W, Werner J, Jäger D, Debus J, Büchler MW. Improvement of surgical results for pancreatic cancer. Lancet Oncol 2013;14(11):e476– e485. doi:10.1016/S1470-2045(13)70172-4, PMID:24079875.
- [13] Cheng Y, Briarava M, Lai M, Wang X, Tu B, Cheng N, et al. Pancreaticojejunostomy versus pancreaticogastrostomy reconstruction for the prevention of postoperative pancreatic fistula following pancreaticoduodenectomy. Cochrane Database Syst Rev 2017;9(9):CD012257. doi:10.1002/14651858.CD012257.pub2, PMID:28898386.
- [14] Topal B, Fieuws S, Aerts R, Weerts J, Feryn T, Roeyen G, et al. Pancreaticojejunostomy versus pancreaticogastrostomy reconstruction after pancreaticoduodenectomy for pancreatic or periampullary tumours: a multicentre randomised trial. Lancet Oncol 2013;14(7):655–662. doi:10.1016/S1470-2045(13)70126-8, PMID:23643139.
- [15] Nakamura M, Wakabayashi G, Miyasaka Y, Tanaka M, Morikawa T, Unno M, et al. Multicenter comparative study of laparoscopic and open distal pancreatectomy using propensity score-matching. J Hepatobiliary Pancreat Sci 2015;22(10):731–736. doi:10.1002/jhbp. 268, PMID:26087943.
- [16] Khaled YS, Malde DJ, Packer J, De Liguori Carino N, Deshpande R, O'Reilly DA, et al. A Case-matched Comparative Study of Laparoscopic Versus Open Distal Pancreatectomy. Surg Laparosc Endosc Percutan Tech 2015;25(4):363–367. doi:10.1097/SLE.000000000000179, PMID:26121539.
- [17] Zhang X, Wu S, Wu B, Yang Q, Chen A, Li Y, et al. SARS-CoV-2 Omicron strain exhibits potent capabilities for immune evasion and viral entrance. Signal Transduct Target Ther 2021;6(1):430. doi:10.1038/ s41392-021-00852-5, PMID:34921135.
- [18] Migueres M, Dimeglio C, Trémeaux P, Abravanel F, Raymond S, Lhomme S, et al. Influence of immune escape and nasopharyngeal virus load on the spread of SARS-CoV-2 Omicron variant. J Infect 2022;84(4):e7–e9. doi:10.1016/j.jinf.2022.01.036, PMID:35143815.
- [19] Hansen CP, Storkholm JH, Sillesen MH, Krohn PS, Burgdorf SK, Hillingsø JG. Pancreatic surgery during the COVID-19 pandemic 2020-2021: an observational cohort study from a third level referral center. BMC Surg 2022;22(1):200. doi:10.1186/s12893-022-01651-7, PMID:35597984.
- [20] Marchegiani G, Perri G, Bianchi B, Esposito A, Landoni L, Casetti L, et al. Pancreatic surgery during COVID-19 pandemic: major activity disruption of a third-level referral center during 2020. Updates Surg 2022;74(3):953–961. doi:10.1007/s13304-021-01197-y, PMID: 34689316.

- [21] McKay SC, COVIDSurg Collaborative. Outcomes of patients undergoing elective liver and pancreas cancer surgery during the SARS-CoV-2 pandemic: an international, multicentre, prospective cohort study. HPB (Oxford) 2022;24(10):1668–1678. doi:10.1016/j. hpb.2022.03.002, PMID:35562256.
- [22] Kasuga A, Nojima M, Okamoto T, Ishitsuka T, Yamada M, Nakagawa H, et al. Impact of the COVID-19 Pandemic on the Management and End-of-life Care of Unresectable Pancreatic Cancer. Intern Med 2022;61(24):3641–3649. doi:10.2169/internalmedicine.0492-22, PMID:36198597.
- [23] Paluri R, Laursen A, Gaeta J, Wang S, Surinach A, Cockrum P. Impact of the COVID-19 Pandemic on Management of Patients with Metastatic Pancreatic Ductal Adenocarcinoma in the United States. Oncologist 2022;27(6):e518–e523. doi:10.1093/oncolo/oyac029, PMID: 35285490.
- [24] Brugel M, Letrillart L, Evrard C, Thierry A, Tougeron D, El Amrani M, et al. Impact of the COVID-19 pandemic on disease stage and treatment for patients with pancreatic adenocarcinoma: A French comprehensive multicentre ambispective observational cohort study (CAPANCOVID). Eur J Cancer 2022;166:8–20. doi:10.1016/j. ejca.2022.01.040, PMID:35259629.
- [25] Kędzierska-Kapuza K, Witkowski G, Baumgart-Gryn K, Szylińska A, Durlik M. Impact of COVID-19 on pancreatic cancer surgery: A highvolume Polish center experience. Adv Clin Exp Med 2022;31(4):389– 398. doi:10.17219/acem/144134, PMID:35106977.
- [26] Karamolegkou AP, Fergadi MP, Magouliotis DE, Samara AA, Tatsios E, Xanthopoulos A, *et al.* Validation of the Surgical Outcome Risk Tool (SORT) and SORT v2 for Predicting Postoperative Mortality in Patients with Pancreatic Cancer Undergoing Surgery. J Clin Med 2023;12(6):2327. doi:10.3390/jcm12062327, PMID:36983326.