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ORIGINAL RESEARCH

Reduced Long-Term Survival After Postoperative Complications in Major Gastrointestinal Surgery

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Purpose: We primarily evaluated the relationship between postoperative complications and long-term survival in patients undergoing major gastrointestinal surgery. Secondarily, we investigated the relationship between the severity and the number of complications and long-term survival. While postoperative complications are prevalent after major abdominal surgery and associated with increased mortality, the effect of their severity and accumulation remains insufficiently explored.

Patients and Methods: 1989 adult patients undergoing major gastrointestinal surgery between July 2010 and April 2022 were retrospectively studied. Complications were classified using the Clavien-Dindo system. Kaplan-Meier analysis assessed long-term survival, Cox proportional hazards regression with time-dependent coefficients evaluated the impact of complications on mortality.

Results: Median age was 64 years (IQR 53–74); 41.8% female and 63.0% of patients were diagnosed with malignancy. Elective procedures comprised 73.0% of cases. Complications occurred in 74.6% of patients. Mortality was higher in patients with complications (32.0%, 95% CI 29.7%-34.5%), compared to those without (21.7%, 95% CI 18.3–25.6%; $P<0.001$). Severe complications (Clavien-Dindo Grade ≥III) were associated with a 15.01-fold higher hazard of mortality within 18 months postoperatively (95% CI 6.83–33.0; $P<0.001$).

Conclusion: Postoperative complications significantly reduce long-term survival following major gastrointestinal surgery. Both their severity and frequency are critical determinants of poorer outcomes, emphasizing the need for effective prevention strategies.

Plain Language Summary: Postoperative complications are a frequent occurrence following major gastrointestinal surgery and are known to increase the risk of death. However, the specific impact of both the number and severity of these complications on long-term survival remains inadequately defined. This retrospective study sought to clarify these associations by analysing the medical records of 1989 adult patients who underwent major gastrointestinal surgery between 2010 and 2022. The incidence, severity, and timing of postoperative complications were recorded, alongside long-term survival outcomes. Complications were observed in 75% of patients. The presence of any postoperative complication was associated with a significantly higher long-term mortality rate (32%) compared to patients without complications (22%). Importantly, patients who had severe complications were much more likely to die within 18 months after surgery—over 15 times higher risk compared to those without severe complications. These findings underscore that both the frequency and severity of postoperative complications are critical determinants of long-term survival following major gastrointestinal surgery. The results highlight the imperative for effective strategies aimed at the prevention and optimal management of postoperative complications to improve long-term patient outcomes in this population.

Keywords: surgical outcomes, Clavien-Dindo classification, survival analysis, Kaplan-Meier, mortality risk factors, long-term mortality

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Introduction

Each year, a substantial number of patients worldwide still require major abdominal surgery, despite advancements in non-surgical treatments. Estimates suggest that approximately 234 million major surgeries, including abdominal procedures, are performed globally each year, with abdominal operations being among the most common for indications such as colorectal, liver and pancreatic cancer, and gastrointestinal bleeding.[1,2] By definition, these procedures are long in duration, require prolonged, often multiple-day hospital stays, and are associated with high 30-day morbidity rates.[3] Although modern surgical techniques and increased perioperative safety measures have led to reduced mortality,[4] postoperative complications after major abdominal surgery remain frequent occurrences.[5,6] These complications have both short- and long-term implications, including increased 30-day mortality, longer hospital stays, and higher readmission rates.[7–9] Moreover, previous research has shown a significant and sustained negative effect on quality of life after surgery, with worse outcomes after more severe complications.[10]

Postoperative complications also have a significant financial impact on the healthcare system as a whole.[11]

To understand the entire impact of postoperative complications that develop after major gastrointestinal surgery, it is important to identify and categorize both short-term and long-term outcomes. For example, Khuri et al reported that the development of postoperative complications of any type after major abdominal surgery resulted in decreased 30-day survival rates.[12] Notably, median survival was reduced by 69%, independent of preoperative risk. Several other studies confirmed this finding and highlighted the overall impact of postoperative complications on long-term survival in patients undergoing abdominal surgery.[13–16] However, the existing literature focuses primarily on specific abdominal procedures;[13–15] only one of the aforementioned studies addressed the impact of postoperative complications on major abdominal surgery overall.[16] Further, major gastrointestinal surgeries, such as colorectal, pancreatic, and liver resections can be associated with higher complication rates compared to other abdominal procedures like prostatectomy or nephrectomy.[13–16]

To address this knowledge gap and provide important insight into the impact of postoperative complications on long-term survival in patients undergoing major gastrointestinal surgery, we conducted a retrospective cohort study focused on this patient population. We hypothesize that the development of any postoperative complications is associated with decreased long-term survival, with both the number and severity of complications having a greater impact overall, even after adjusting for variables that may be independently associated with worse outcomes such as increasing age, comorbidities, malignancy, emergency surgery, and type of surgery.

Materials and Methods

Study Design

A single-center retrospective cohort study was conducted at the Austin Health Hospital in Melbourne, Australia. Ethics approval was granted by the Austin Health Human Research Ethics Committee (HREC/107644/Austin-2024). The study protocol was registered with the Australian New Zealand Clinical Trials Registry (ACTRN: 12624000793516). Formal patient consent for access to individual medical records was not required, as determined by the ethics committee. The waiver of consent was granted on the basis that the study was retrospective in nature, involved no direct patient contact, and posed minimal risk to participants. All data were de-identified prior to analysis, and the study adhered to institutional protocols for the protection of patient confidentiality as well as the ethical principles outlined in the Declaration of Helsinki. The Strengthening the Reporting of Cohort Studies in Surgery (STROBE) guidelines were followed in reporting this study.[17] Adult patients aged 18 years or older who underwent elective and emergency open or laparoscopic major gastrointestinal cancer and non-cancer surgery at the Austin Hospital between July 2010 and April 2022 were included in the study. Surgeries involving the retroperitoneal space, such as nephrectomy, radical prostatectomy, adrenalectomy, and surgery on the aorta and the caudal vena cava, were excluded.

Key Objectives

The primary aim of this study was to evaluate the unadjusted relationship between differences in survival among patients with and without postoperative complications. The secondary aim was to investigate the relationship between the

severity, number of complications, and long-term survival. Finally, the effects of postoperative complications on overall mortality were evaluated, adjusting for clinical variables known to be associated with reduced long-term survival, such as age, comorbidity burden, sex, malignancy, and anemia.

Data Collection

Data were retrospectively collected from medical records accessed from the Austin Health database and the Cerner health information system. Preoperative data included patient characteristics, smoking history within 1 year of surgery, alcohol use disorder, preoperative hemoglobin values, American Society of Anesthesiologists (ASA) score,[18] age-adjusted Charlson Comorbidity Index (CCI),[19] malignancy diagnosis, indication for surgery, and urgency of surgery (elective or emergency). Intraoperative data included surgical procedure, surgical technique (open or laparoscopic), operating theater time, and perioperative use of any blood products. Postoperative data included length of hospital stay, postoperative hemoglobin concentrations, postoperative intensive care unit (ICU) admissions, 30-day readmissions, unplanned readmissions, the nature of any complications that developed, and patient mortality. Mortality data were collected from the date of surgery up until August 2024 and independently cross-checked by two authors. The date and cause of death were also reported. Survival time was measured in days from the date of surgery to the date of death or last follow-up.

Definitions

Major gastrointestinal surgery was defined as an intraperitoneal operation lasting at least two hours without primary involvement of the thorax that involved either luminal resection or resection of a solid organ associated with the gastrointestinal tract and requiring at least a two-night postoperative hospital stay. This definition was based on a combination of recent literature and expert opinion.[20]

The length of hospital stay was defined as the number of days from the date of the patient's surgery to the date of discharge. Thirty-day readmission was defined as rehospitalization for any reason within 30 days of discharge. Perioperative complications were defined according to the European Perioperative Clinical Outcome definitions.[21] Complications were graded by severity using the Clavien-Dindo Classification (CDC) system.[22] If a patient developed multiple postoperative complications, the highest CDC grade was reported. In-hospital mortality within 30 days was documented as a CDC Grade V complication. The Combined Complication Index was defined as the sum of all complications, with each complication weighted based on its severity.[23] Causes of death were categorized as follows: death related to primary cancer; death related to an unrelated cancer; death unrelated to cancer; and unknown.

Statistical Analyses

Statistical analyses were performed using R version 4.4.1 (R Core Team, Vienna, Austria, 2024). Variables with missing rates exceeding 5% were identified, and missing data patterns were analyzed. Among the variables with a missing rate over 5%, CCI and postoperative ICU admissions were considered as adjusting variables for survival analysis. Based on the visual inspection of the missing pattern plot, these did not exhibit any noticeable or unexpected deviations in their missing data patterns compared to other variables. Following this assessment, statistical analyses were performed excluding the missing cases for the analysis.

Continuous variables were assessed for normality using Shapiro's test and visualized using Q-Q plots. Descriptive statistics were presented as means ± standard deviations (SD), median (interquartile ranges (IQR): first-third quartiles), or frequencies (percentages), as appropriate. Inferential statistics were presented with a 95% confidence interval (95% CI). Outliers were identified using the two-fold IQR rule. To ensure data integrity, three authors independently reviewed all statistical outliers, comparing each identified outlier against the original data sources. Data points that aligned with the established clinical context were retained for analysis, while those deemed inconsistent with clinical relevance were excluded.

Kaplan-Meier analysis was used to assess the long-term survival of the patient cohorts. The proportional hazards assumption was assessed using a log-minus-log plot, and Log-rank or Gehan-Breslow-Wilcoxon tests were performed to compare survival between groups with postoperative complications based on the assumption test results. Pairwise comparisons were performed using the Peto-Peto-Prentice test, with *P*-values adjusted using the Bonferroni method.

The adjusted effects of postoperative complications on overall mortality were evaluated using Cox proportional hazards regression. Pearson's and Spearman correlation analyses were conducted according to the characteristics of variables, and their clinical relevance was determined based on prior literature. Each factor was initially evaluated using a univariate model, and those with a significant hazard ratio (HR) were included in the multivariate model. The proportional hazards assumption of the Cox regression model was tested using Schoenfeld residuals. In cases where this assumption was violated, the affected variables were addressed by stratification or incorporating time-dependent covariates. For the time-dependent covariate approach, a Cox regression model was implemented using a step function to partition the observation period into intervals. These intervals were determined based on changes in the coefficients observed in the Schoenfeld residual plots. Multicollinearity was tested by checking the variance inflation factors and correlation coefficients between variables included in the estimated Cox regression models. All analyses were conducted using the R package "survival".[24] Comparative results are accompanied by *P*-values and corresponding effect sizes, while statistical significance was defined as a two-sided *P*-value of <0.05.

Results

Baseline Characteristics

Among the 1989 patients who underwent major gastrointestinal surgery from July 2010 to April 2022, the median (IQR) age was 64 years (53–74), and 41.8% of patients were female. The median (IQR) age adjusted Charlson Comorbidity Index score was 7 (4–10). A diagnosis of malignancy was present in 1253 patients (63.0%). Most patients (73%) underwent elective surgery. Baseline patient characteristics and peri- and postoperative variables are presented in Table 1. Overall, 74.6% (95% CI 72.6–76.5%) developed one or more postoperative complications. Among those with complications, almost 1 in 4 (24.5%) patients developed a major complication (CDC grade >III). A detailed summary of the number and severity of complications is summarized in Table 2. The baseline characteristics of patients having minor (CDC Grades I and II) and major (CDC Grades >III) complications is presented in Supplementary Table S1.

Table 1 Baseline Characteristics

Patient Characteristics	**N=1989**
Age, median (IQR), years	64 (53–74)
Sex, No. (%), female	831 (41.8)
Weight, median (IQR), kg	75 (64–87)
Height median (IQR), cm	168 (161–175)
Body mass index median (IQR), kg/m^2	26.2 (23.1–30.1)
ASA classification, No. (%)	
1	83 (4.2)
2	713 (35.8)
3	1016 (51.1)
4	177 (8.9)
Age-adjusted CCI score, median (IQR)	7 (4–10)
Combined Complication Index, median (IQR)	20.92 (0–32.02)
Malignancy, No. (%)	1253 (63)
Smoker (within one year of surgery), No. (%)	397 (20)

(*Continued*)

Table 1 (Continued).

Patient Characteristics	**N=1989**
Alcohol use disorder, No. (%)	105 (5.3)
Preoperative anemia, No. (%)	859 (43.4)
Urgency, No. (%)	
Elective	1452 (73)
Emergency	537 (27)
Surgical procedure, No. (%)	
Colorectal surgery	868 (43.6)
Cystectomy	143 (7.2)
Distal pancreatectomy	56 (2.8)
Liver surgery	422 (21.2)
Small bowel surgery	348 (17.5)
Whipple	152 (7.6)
Surgical technique, No. (%)	
Laparoscopic	681 (36.9)
Laparoscopic-assisted	56 (3)
Laparoscopic-converted to open	146 (7.9)
Open	963 (52.2)
Procedure time, median (IQR), minutes	268 (198–345)
Patients receiving blood products, No. (%)	440 (22.1)
Postoperative outcomes	
Hemoglobin, median (IQR), g/dL	99 (84–112)
ICU admission, No. (%)	956 (51.8)
Length of hospital stay, median (IQR), days	8 (6–14)
Hospital readmission within 30 days, No. (%)	314 (15.8)
Unplanned hospital readmission, No. (%)	267 (13.4)

Abbreviations: CCI, Charlson Comorbidity Index; ICU, Intensive Care Unit.

Unadjusted Associations Between Complications and Mortality

The overall mortality rate in this cohort was 29.4% (95% CI 27.4–31.5%). The mean observation period was 7.0 ± 3.47 years, with a maximum follow-up of 14.1 years. The one-, two- and five-year mortality rates were 7.8% (95% CI 6.7–9.1%), 13.6% (95% CI 12.1–15.2%), and 23.0% (95% CI 21.2–24.9%), respectively. The overall mortality rate of patients who developed no postoperative complications was 21.7% (95% CI 18.3–25.6%) compared to 32.0% (95% CI 29.7–34.5%) in patients with one or more complications (P<0.001; Figure 1). Patients with severe complications (CDC Grades >III) had a mortality rate of 47.7% (95% CI 42.4–52.9%) (P<0.001, Gehan-Breslow test; Figure 2).

Table 2 Postoperative Complications

Complications	N=1989	Overall Mortality Rate (95% CI)
None, No. (%)	506 (25.4)	21.7% (18.3–25.6)
One or more, No. (%)	1483 (74.6)	32.0% (29.7–34.5)
Number of complications per patient, mean (SD)	2.4 ± 2.6	N/a
CDC grade, No. (%)		
Grade I	393 (19.8)	23.9% (19.8–28.5)
Grade II	727 (36.6)	28.6% (25.4–32.1)
Grade IIIa	45 (2.3)	26.7% (15.1–42.2)
Grade IIIb	77 (3.9)	32.5% (22.5–44.2)
Grade Iva	144 (7.2)	48.6% (40.3–57.0)
Grade IVb	48 (2.4)	35.4% (22.6–50.6)
Grade V	49 (2.5)	100% (90.9–100)
Number of complications, No. (%)		
1-5	1260 (63.3)	29.6% (27.1–32.2)
>5	223 (11.2)	45.7% (39.1–52.5)

Abbreviation: CDC, Clavien-Dindo Classification.

Kaplan-Meier curves showed that the estimated survival for 80% of patients was 91 months (95% CI 11–35 months) for those who developed no postoperative complications, 55 months (95% CI 45–66 months) for patients with CDC Grade I/II complications, and 10 months (95% CI 6–19 months) for patients with CDC Grade >III complications *(P<0.*001; Figure 2). Patients with more than five postoperative complications had a significantly worse survival than patients with fewer complications (*P*<0.001; Figure 3). The association between mortality and the number of complications, and major and minor complications, stratified by the type of surgery, are summarized in Supplementary Tables S2 and S3.

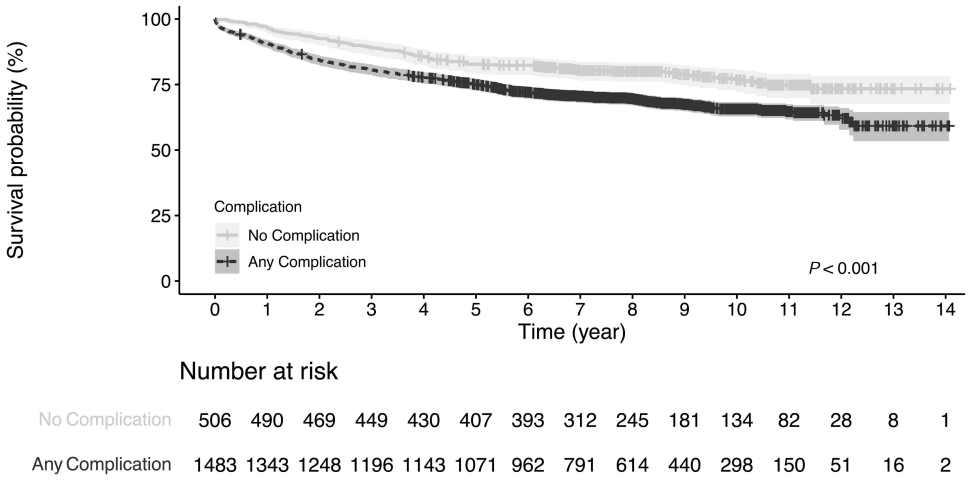


Figure 1 Kaplan-Meier Curves Documenting Survival, Patients Grouped by Complication.
Note: *P*<0.001, Log Rank test.

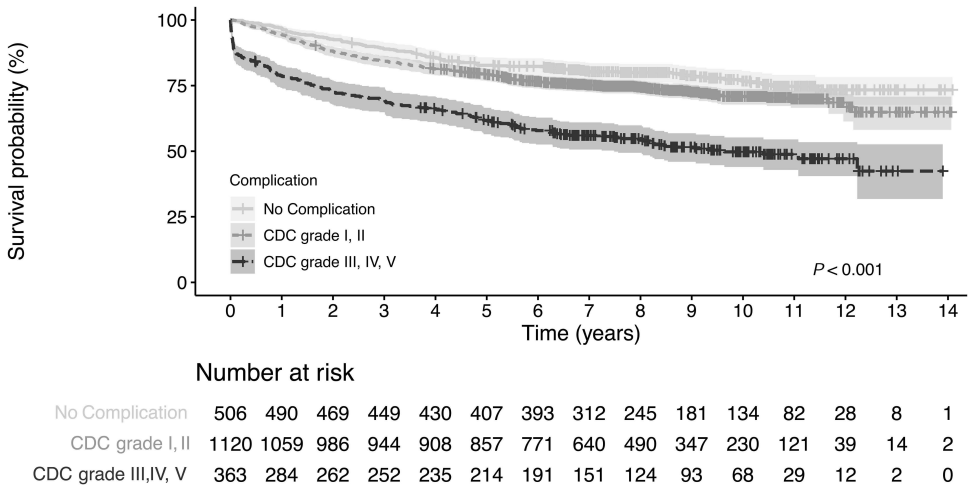


Figure 2 Kaplan-Meier Curves Documenting Survival, Patients Grouped by Clavien-Dindo Grade (CDC).
Note: *P*<0.001, Gehan-Breslow test.

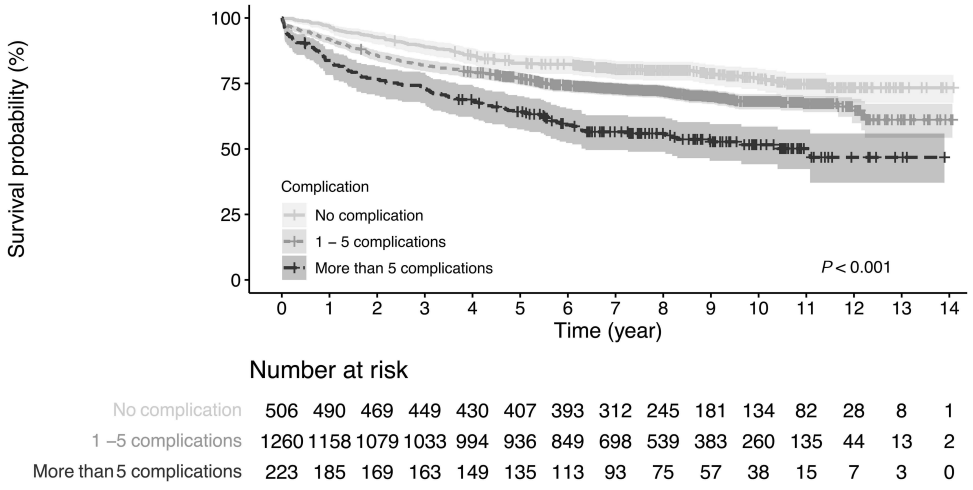


Figure 3 Kaplan-Meier Curves Documenting Survival, Patients Grouped by Number of Complications.
Note: *P*<0.001, Gehan-Breslow test.

Adjusted Effects of Postoperative Complications on Mortality

Correlation analyses demonstrated a weak linear relationship between the age-adjusted CCI and overall mortality (Spearman correlation coefficient ρ=0.36, *P*<0.001; Supplementary Table S4). Similarly, weak linear correlations were observed between the ASA score (ρ=0.24, *P*<0.001) and the age-adjusted CCI (ρ=0.26, *P*<0.001) with overall mortality. To minimize the risk of overfitting due to the inclusion of two broadly similar risk scores, the ASA score was excluded from the final analysis. Other variables that were considered clinically relevant to mortality were also selected.[25,26] The following variables were selected for adjustment in the final analysis: sex, age-adjusted CCI, alcohol use disorder, preoperative anemia, perioperative transfusion, type of surgery, emergency surgery, and a diagnosis of malignancy.

Cox regression analyses were performed to assess the impact of postoperative complication occurrence (Table 3), complication severity (Table 4), and the number of complications (Supplementary Table S5) as stratified and time-dependent covariate models, based on the results of the proportional hazards assumption test. The observation period was divided into three segments for analysis: up to 18 months, 18 months to 5 years, and more than 5 years following the completion of the procedure. This approach allowed for a detailed evaluation of the temporal relationship between complications and long-term outcomes.

Table 3 Univariate, Multivariate, Time-Dependent Coefficient Cox Regression Analysis on the Presence of Any Postoperative Complications

	Univariate		Multivariate		Time-Dependent Coefficient	
	HR (95% CI)	***P*-value**	**HR (95% CI)**	***P*-value**	**HR (95% CI)**	***P*-value**
Any complication	1.63 (1.32–2.01)	<0.001[a]	1.20 (0.96–1.50)	0.114	**Until 18 months**	0.008[a]
					2.266 (1.24–4.15)	
					18 months to 5 years	0.588
					1.12 (0.75–1.65)	
					After 5 years	0.863
					1.03 (0.76–1.38)	
Malignancy	1.73 (1.43–2.01)	<0.001[a]	1.17 (0.92–1.50)	0.208	1.16 (0.86–0.91)	0.230
Sex (male)	0.83 (0.69–0.98)	0.029[a]	0.81 (0.68–0.97)	0.020[a]	0.81 (0.67–0.96)	0.016[a]
Age-adjusted CCI	1.19 (1.17–1.22)	<0.001[a]	1.18 (1.15–1.21)	<0.001[a]	1.18 (1.15–1.21)	<0.001[a]
Emergency surgery	1.33 (1.11–1.59)	0.002[a]	1.45 (1.17–1.80)	0.001[a]	–[b]	–
Surgery type (Whipples procedure)	1.50 (1.10–2.04)	0.010[a]	1.26 (0.91–1.74)	0.115	1.25 (0.90–1.73)	0.190
Smoking history within one year of the procedure	1.10 (0.89–1.35)	0.375	–	–	–	–
Alcohol use	1.67 (1.20–2.31)	0.002[a]	1.45 (1.04–2.02)	0.029[a]	1.42 (1.02–1.99)	0.040[a]
Readmission within 30 days	1.15 (0.92–1.43)	0.223	–	–	–	–
Preoperative anemia	1.74 (1.47–2.06)	<0.001[a]	1.25 (1.04–1.49)	0.015[a]	1.25 (1.04–1.49)	0.016[a]
Perioperative blood product transfusion	1.67 (1.39–2.01)	<0.001[a]	1.41 (1.16–1.73)	0.001[a]	1.41 (1.16–1.72)	0.001[a]
Postoperative ICU admission	1.80 (1.52–2.14)	<0.001[a]	1.31 (1.09–1.58)	0.005[a]	1.30 (1.08–1.57)	0.005[a]

Notes: The time-dependent coefficient model was applied to the complication measurement. The coefficient of other covariates satisfied the constant HR assumption except for emergency procedures. [a]*P*<0.05. [b]Stratified.
Abbreviations: HR, Hazard Ratio; CCI, Charlson Comorbidity Index; ICU, Intensive Care Unit.

As shown in Table 3, within the first 18 months post-surgery, patients who developed any complication demonstrated a significantly increased HR for mortality of 2.26 (95% CI 1.24–4.15, *P*=0.008). As indicated in Table 4, the risk was markedly higher for those experiencing CDC Grade ≥III complications, with an HR of 15.01 (95% CI 6.83–33.00,

Table 4 Univariate, Multivariate, Time-Dependent Coefficient Cox Regression Analysis on the Severity of Postoperative Complications

	Univariate		Multivariate		Time-Dependent Coefficient	
	HR (95% CI)	***P*-value**	**HR (95% CI)**	***P*-value**	**HR (95% CI)**	***P*-value**
CDC Grades I, II	0.27 (0.05–0.49)	0.017[a]	0.10 (−0.13 to 0.33)	0.378	1.13 (0.89–1.42)	0.310
CDC Grades III–V	1.03 (0.79–1.28)	<0.001[a]	0.59 (0.30–0.88)	<0.001[a]	**Until 18 months**	<0.001[a]
					15.01 (6.83–33.00)	

(*Continued*)

Table 4 (Continued).

	Univariate		Multivariate		Time-Dependent Coefficient	
	HR (95% CI)	***P*-value**	**HR (95% CI)**	***P*-value**	**HR (95% CI)**	***P*-value**
					18 months to 5 years	0.634
					1.24 (0.52–2.96)	
					After 5 years	0.068
					1.34 (0.98–1.84)	
Malignancy	0.55 (0.36–0.73)	<0.001[a]	0.20 (−0.05 to 0.45)	0.108	1.23 (0.96–1.58)	0.100
Sex (male)	−0.19 (−0.37 to −0.02)	0.029[a]	−0.22 (−0.40 to −0.04)	0.015[a]	0.80 (0.67–0.95)	0.012[a]
Age-adjusted CCI	0.18 (0.16–0.20)	<0.001[a]	0.16 (0.14–0.19)	<0.001[a]	1.17 (1.14–1.20)	<0.001[a]
Emergency surgery	0.29 (0.11–0.47)	0.002[a]	0.35 (0.13–0.57)	0.002[a]	–[b]	–
Surgery type (Whipples procedure)	0.40 (0.10–0.71)	0.010[a]	0.32 (−0.01 to 0.64)	0.057	1.35 (0.97–1.87)	0.079
Smoking history within one year of the procedure	0.09 (−0.11 to 0.30)	0.375	–	–	–	–
Alcohol use disorder	0.51 (0.19–0.84)	0.002[a]	0.30 (−0.04 to 0.63)	0.079	1.35 (0.96–1.90)	0.083
Readmission within 30 days of the procedure	0.14 (−0.08 to 0.36)	0.223	–	–	–	–
Preoperative anemia	0.55 (0.38–0.72)	<0.001[a]	0.22 (0.05–0.40)	0.014[a]	1.25 (1.04–1.49)	0.016[a]
Perioperative blood product transfusion	0.51 (0.33–0.70)	<0.001[a]	0.21 (0.002–0.42)	0.048[a]	1.28 (1.03–1.58)	0.023[a]
Postoperative ICU admission	0.59 (0.42–0.76)	<0.001[a]	0.17 (−0.02 to 0.37)	0.080	–[b]	–

Notes: The time-dependent coefficient model was applied to the complication measurement. The coefficient of other covariates satisfied the constant HR assumption except for emergency procedures and ICU admission. [a]*P*<0.05. [b]Stratified.
Abbreviations: HR, hazard ratio; CDC; Clavien-Dindo Grade; CCI, Charlson Comorbidity Index; ICU, Intensive Care Unit.

P<0.001). Over the entire observation period, patients who developed more than five complications exhibited a sustained elevated risk of mortality, with an HR of 1.56 (95% CI 1.11–2.09, *P*=0.010). The relationship between mortality and complication severity classified by Clavien-Dindo grade, stratified by the type of surgery, is detailed in Table 5.

Discussion

In this retrospective cohort study of 1989 patients who underwent major gastrointestinal surgery, we investigated the impact of postoperative complications on long-term survival. The overall complication rate was 74.6%, and the development of one or more complications was associated with a reduction of more than two years in the estimated 80% survival time compared to patients without complications. After adjusting for confounding factors, including age, malignancy, comorbidities, emergency surgery, and procedure type, we identified a significant and independent association between the development of any postoperative complication and increased mortality within the first 18 months following surgery. Furthermore, the severity (CDC grade) and number of complications showed a cumulative effect on mortality risk, emphasizing their critical role in determining survival outcomes. These findings corroborate our initial hypothesis and highlight the need for strategies to mitigate their occurrence and severity.

Our findings align with previous studies demonstrating the negative impact of postoperative complications on long-term survival.[13–15] For example, Khuri et al reported a 69% reduction in median survival in patients who experienced one

Table 5 Mortality and the Severity of Complication, by Clavien-Dindo Grade

Surgery Type	CDC Grade	CDC Count (ratio)	Overall Mortality Rate (95% CI)	In-Hospital Mortality Rate (95% CI)	1-Year Mortality Rate (95% CI)	2-Year Mortality Rate (95% CI)	5-Year Mortality Rate (95% CI)
Colorectal resection (n=868)	No complication	258 (29.7)	26.0 (20.7–1.8)	0.0 (0.0–1.4)	3.5 (1.6–6.5)	8.9 (5.7–13.1)	22.1 (17.2–27.7)
	I	179 (20.6)	29.1 (22.5–36.3)	0.0 (0.0–2.0)	5.6 (2.7–10.0)	10.6 (6.5–16.1)	19.0 (13.5–25.5)
	II	267 (30.8)	30.3 (24.9–36.2)	0.0 (0.0–1.4)	3.7 (1.8–6.8)	12.7 (9.0–17.3)	21.3 (16.6–26.8)
	III	47 (5.4)	29.8 (17.3–44.9)	0.0 (0.0–7.5)	4.3 (0.5–14.5)	10.6 (3.5–23.1)	23.4 (12.3–38.0)
	IV	95 (10.9)	53.7 (43.2–64.0)	0.0 (0.0–3.8)	13.7 (7.5–22.3)	22.1 (14.2–31.8)	36.8 (27.2–47.4)
	V	22 (2.5)	100.0 (84.6–100.0)	100.0 (84.6–100.0)	100.0 (84.6–100.0)	100.0 (84.6–100.0)	1100.0 (84.6–100.0)
Cystectomy (n=143)	No complication	10 (7.0)	10.0 (0.3–44.5)	0.0 (0.0–30.8)	0.0 (0.0–30.8)	0.0 (0.0–30.8)	10.0 (0.3–44.5)
	I	15 (10.5)	13.3 (1.7–40.5)	0.0 (0.0–21.8)	0.0 (0.0–21.8)	6.7 (0.2–31.9)	13.3 (1.7–40.5)
	II	88 (61.5)	21.6 (13.5–31.6)	0.0 (0.0–4.1)	6.8 (2.5–14.3)	10.2 (4.8–18.5)	13.6 (7.2–22.6)
	III	16 (11.2)	12.5 (1.6–38.3)	0.0 (0.0–20.6)	0.0 (0.0–20.6)	0.0 (0.0–20.6)	6.3 (0.2–30.2)
	IV	13 (9.1)	53.8 (25.1–80.8)	0.0 (0.0–24.7)	7.7 (0.2–36.0)	15.4 (1.9–45.4)	38.5 (13.9–68.4)
	V	1 (0.7)	100.0 (2.5–100.0)	100.0 (2.5–100.0)	100.0 (2.5–100.0)	100.0 (2.5–100.0)	100.0 (2.5–100.0)
Distal pancreatectomy (n=56)	No complication	15 (26.8)	13.3 (1.7–40.5)	0.0 (0.0–21.8)	0.0 (0.0–21.8)	0.0 (0.0–21.8)	6.7 (0.2–31.9)
	I	4 (7.1)	25.0 (0.6–80.6)	0.0 (0.0–60.2)	0.0 (0.0–60.2)	0.0 (0.0–60.2)	25.0 (0.6–80.6)
	II	32 (57.1)	6.3 (0.8–20.8)	0.0 (0.0–10.9)	0.0 (0.0–10.9)	0.0 (0.0–10.9)	0.0 (0.0–10.9)
	III	4 (7.1)	50.0 (6.8–93.2)	0.0 (0.0–60.2)	0.0 (0.0–60.2)	0.0 (0.0–60.2)	0.0 (0.0–60.2)
	IV	1 (1.8)	0.0 (0.0–97.5)	0.0 (0.0–97.5)	0.0 (0.0–97.5)	0.0 (0.0–97.5)	0.0 (0.0–97.5)
Liver resection (n=422)	No complication	129 (30.6)	20.2 (13.6–28.1)	0.0 (0.0–2.8)	3.1 (0.9–7.7)	7.0 (3.2–12.8)	14.7 (9.1–22.0)
	I	112 (26.5)	22.3 (15.0–31.2)	0.0 (0.0–3.2)	4.5 (1.5–10.1)	9.8 (5.0–16.9)	18.8 (12.0–27.2)
	II	128 (30.3)	28.9 (21.2–37.6)	0.0 (0.0–2.8)	5.5 (2.2–10.9)	14.1 (8.6–21.3)	23.4 (16.4–31.7)
	III	20 (4.7)	25.0 (8.7–49.1)	0.0 (0.0–16.8)	10.0 (1.2–31.7)	15.0 (3.2–37.9)	25.0 (8.7–49.1)
	IV	31 (7.3)	32.3 (16.7–51.4)	0.0 (0.0–11.2)	6.5 (0.8–21.4)	12.9 (3.6–29.8)	25.8 (11.9–44.6)
	V	2 (0.5)	100.0 (15.8–100.0)	100.0 (15.8–100.0)	100.0 (15.8–100.0)	100.0 (15.8–100.0)	100.0 (15.8–100.0)
Small bowel resection (n=348)	No complication	69 (19.8)	10.1 (4.2–19.8)	0.0 (0.0–5.2)	1.4 (0.0–7.8)	2.9 (0.4–10.1)	7.2 (2.4–16.1)
	I	56 (16.1)	7.1 (2.0–17.3)	0.0 (0.0–6.4)	0.0 (0.0–6.4)	5.4 (1.1–14.9)	7.1 (2.0–17.3)
	II	137 (39.4)	26.3 (19.1–34.5)	0.0 (0.0–2.7)	9.5 (5.1–15.7)	11.7 (6.8–18.3)	23.4 (16.6–31.3)
	III	22 (6.3)	40.9 (20.7–63.6)	0.0 (0.0–15.4)	22.7 (7.8–45.4)	27.3 (10.7–50.2)	36.4 (17.2–59.3)
	IV	42 (12.1)	38.1 (23.6–54.4)	0.0 (0.0–8.4)	9.5 (2.7–22.6)	19.0 (8.6–34.1)	28.6 (15.7–44.6)
	V	22 (6.3)	100.0 (84.6–100.0)	100.0 (84.6–100.0)	100.0 (84.6–100.0)	100.0 (84.6–100.0)	100.0 (84.6–100.0)

(*Continued*)

Table 5 (Continued).

Surgery Type	CDC Grade	CDC Count (ratio)	Overall Mortality Rate (95% CI)	In-Hospital Mortality Rate (95% CI)	1-Year Mortality Rate (95% CI)	2-Year Mortality Rate (95% CI)	5-Year Mortality Rate (95% CI)
Whipple procedure (n=152)	No complication	25 (16.4)	28.0 (12.1–49.4)	0.0 (0.0–13.7)	8.0 (1.0–26.0)	12.0 (2.5–31.2)	16.0 (4.5–36.1)
	I	27 (17.8)	37.0 (19.4–57.6)	0.0 (0.0–12.8)	0.0 (0.0–12.8)	14.8 (4.2–33.7)	29.6 (13.8–50.2)
	II	75 (49.3)	44.0 (32.5–55.9)	0.0 (0.0–4.8)	13.3 (6.6–23.2)	24.0 (14.9–35.3)	40.0 (28.9–52.0)
	III	13 (8.6)	38.5 (13.9–68.4)	0.0 (0.0–24.7)	7.7 (0.2–36.0)	15.4 (1.9–45.4)	38.5 (13.9–68.4)
	IV	10 (6.6)	30.0 (6.7–65.2)	0.0 (0.0–30.8)	0.0 (0.0–30.8)	10.0 (0.3–44.5)	10.0 (0.3–44.5)
	V	2 (1.3)	100.0 (15.8–100.0)	100.0 (15.8–100.0)	100.0 (15.8–100.0)	100.0 (15.8–100.0)	100.0 (15.8–100.0)

Abbreviation: CDC, Clavien-Dindo Classification.

or more postoperative complications, independent of pre-operative risk. However, their cohort included a wide variety of surgical interventions, including non-abdominal procedures, which likely contributed to a lower 30-day complication rate of 3.07%, compared to our cohort.[12] In contrast, Straatman et al, who specifically examined major gastrointestinal surgeries, reported a 42.4% postoperative complication rate among 861 patients undergoing elective surgery, with the greatest survival impact observed in upper gastrointestinal procedures.[16] Similarly, the higher complication rate in our cohort (74.6%) likely reflects differences in demographics, a higher burden of comorbidities, longer surgical durations, the inclusion of emergency procedures, and a greater reliance of open surgical approaches. These factors demonstrate the complexity of managing high-risk surgical patients. Postulated mechanisms for a reduced long-term survival following surgery include activation of endogenous inflammatory pathways from the increased surgical stress, potentially promoting the growth of residual malignant cells.[27] This inflammatory response may be exacerbated by postoperative complications, further contributing to cancer recurrence, and adversely affecting long-term survival.[28,29] Li et al examined the relationship between Clavien-Dindo classification and long-term survival outcomes after curative resection for gastric cancer.[30] In this propensity score-matched analysis, the authors reported a lower overall complication rate of 13.3%, with most patients classified as CDC Grade II. They also found that CDC Grade III and IV complications significantly reduced survival following gastric resections with HRs of 2.004 (95% CI 1.503–2.672), and 2.694 (95% CI 1.847–3.393), respectively ($P<0.001$). Both, Straatman et al and Li et al suggest that patients with CDC Grade III/IV/V complications face a higher risk of reduced long-term survival.[16,30] These results are consistent with our findings, although our study observed a higher HRs (14.45) for patients with severe complications, further emphasizing the detrimental impact of severe postoperative complications on long-term survival in this important patient population.

By examining the impact of both severity and number of complications, our study advocates for a more comprehensive approach to assessing postoperative outcomes. While previous studies have primarily focused on the presence or absence of complications, our findings indicate that their cumulative effect can significantly impact long-term survival. Viewing complications as factors influencing both short-term and long-term outcomes reinforces the importance of developing and implementing effective preventive strategies.

This study has several strengths. With 1989 patients, it represents one of the largest investigations to date on this topic. The detailed analysis of a relatively homogeneous population undergoing major gastrointestinal surgery enhances the robustness and generalizability of our findings. By leveraging the validated CDC system to examine the relationship between complication severity and mortality, this study provides a comprehensive and reliable assessment of postoperative survival. Additionally, its focus on long-term outcomes addresses a critical gap in the literature, offering valuable new insights into the enduring impact of postoperative complications.

However, there are limitations. As a retrospective analysis, the findings are susceptible to selection bias. The exclusion of other surgeries involving the retroperitoneal space, such as nephrectomy, radical prostatectomy, adrenalectomy, and procedures on the aorta and caudal vena cava, limits the generalizability of findings to other abdominal

procedures. Moreover, the single-centre nature of this study restricts its applicability to different healthcare settings. Although, we adjusted for several confounders, factors such as frailty, socioeconomic status, and nutritional status were not included, which could have influenced survival outcomes.

While we observed a reduction of more than two years in survival among patients with complications, this effect was partially confounded by age-adjusted comorbidities beyond 18 months post-surgery. Lastly, the conduct of this study overlapped with the global COVID-19 pandemic, which may have influenced both patient pathways and postoperative outcomes. The pandemic disrupted access to elective surgical care, leading in many regions to treatment delays, altered case selection, and prioritization of higher-risk or more urgent procedures. This shift could have influenced the baseline health profile of patients included during the pandemic period, potentially increasing the observed incidence and severity of postoperative complications. Furthermore, perioperative care delivery was subject to significant strain, including reduced staffing, altered protocols for infection control, and limitations on postoperative intensive care availability. These system-level factors may have contributed independently to patient outcomes, thereby introducing unmeasured confounding into our analysis of complication-related survival. Future research is needed to better explore these factors and their impact on long-term postoperative survival outcomes in this patient population.

Conclusion

Understanding the long-term impact of postoperative complications is essential for advancing perioperative care and improving surgical outcomes. In this large cohort, we demonstrate that postoperative complications after major gastrointestinal surgery are associated with a marked reduction in long-term survival, with progressively worse outcomes in patients experiencing a greater number or more severe events. A novel and important observation of this study is the time-dependent nature of this risk: the excess mortality attributable to complications was most pronounced during the first 18 months following surgery. This early vulnerability underscores the need for targeted strategies to prevent complications and optimize recovery during the immediate postoperative period. Taken together, these findings reinforce the critical importance of complication prevention as a cornerstone of perioperative practice and highlight the potential for improving survival through enhanced perioperative pathways, closer surveillance, and tailored interventions during the high-risk early postoperative phase.

Data Sharing Statement

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

Consent for Publication

Formal patient consent for access to individual medical records was not required, as determined by the research ethics committee. The waiver of consent was granted on the basis that the study was retrospective in nature, involved no direct patient contact, and posed minimal risk to participants.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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