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Early hospital readmission for gastrointestinal-related complications predicts long-term mortality after pancreatectomy

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Abstract

BACKGROUND—The purpose of this study was to investigate the prognostic significance of early (30-day) hospital readmission (EHR) on mortality after pancreatectomy.

METHODS—Using a prospectively collected institutional database linked with a statewide dataset, we evaluated the association between EHR and overall mortality in all patients undergoing pancreatectomy at our tertiary institution (2005 to 2010).

RESULTS—Of 595 pancreatectomy patients, EHR occurred in 21.5%. Overall mortality was 29.4% (median follow-up 22.7 months). Patients with EHR had decreased survival compared with those who were not readmitted ($P = .011$). On multivariate analysis adjusting for baseline group differences, EHR for gastrointestinal-related complications was a significant independent predictor of mortality (hazard ratio 2.30, $P = .001$).

CONCLUSIONS—In addition to known risk factors, 30-day readmission for gastrointestinal-related complications following pancreatectomy independently predicts increased mortality. Additional studies are necessary to identify surgical, medical, and social factors contributing to EHR, as well as interventions aimed at decreasing postpancreatectomy morbidity and mortality.

Keywords

Pancreatectomy; Readmission; Mortality; Outcomes

In the current era of healthcare reform, hospital readmissions have come under intense scrutiny, and readmission rates are increasingly used as a metric of quality of patient care.¹ The Center for Medicare and Medicaid Services currently mandates the reporting of early (30-day) hospital readmission (EHR) rates for certain medical conditions, and it is expected that these requirements will expand to include surgical procedures in the near future.² Furthermore, with implementation of the Patient Protection and Affordable Care Act,

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Supplementary data

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hospitals with EHR rates above expected levels may be subject to reduced reimbursement.³ This proposed financial penalty has prompted a number of authors to investigate current EHR rates associated with certain procedures, as well as factors predictive of readmission, in an attempt to identify high-risk patients in the preoperative setting.⁴

Recent single-institution and population-based studies of patients undergoing pancreatectomy have demonstrated readmission rates of 12% to 21% within 30 days of initial discharge.^{1,5–8} While previous studies have sought to identify factors associated with readmission after pancreatectomy, the impact of readmission on subsequent patient outcomes remains poorly understood. Specifically, there are limited data exploring the potential role of early readmission as an independent marker of long-term survival. In addition to the incidence and causative factors, identifying the consequences of early rehospitalization following surgery may allow for greater understanding of its impact on overall patient welfare. The purpose of this study is to further elucidate patient, operative, and postoperative factors associated with mortality after pancreatectomy, and to investigate the prognostic significance of early readmission on long-term outcomes.

Methods

Study design

We analyzed records from the Johns Hopkins Pancreatic Resection Database (PRD) of all patients who underwent pancreatectomy at the Johns Hopkins Hospital from 2005 to 2010. Patients who died during their initial hospitalization or within 30 days of surgery (ie, perioperative deaths; n = 13) and those who underwent planned readmission (ie, to rehabilitation institutions; n = 15) were excluded from subsequent analysis^{5,9,10} to allow specifically for the study of long-term outcomes. Given the low incidence of minimally invasive pancreatectomy at our institution during the study period, we also excluded subjects who underwent laparoscopic and/or robotic surgery to reduce the potential for confounding. To identify readmissions to other institutions, the PRD was supplemented by the Maryland Non-Confidential Inpatient Discharge dataset. Because non-Maryland residents are more likely to present for readmission at an institution outside the state, this study was limited to Maryland residents to capture all readmissions. Additional details regarding the data and methodology used herein have been published previously.⁵ This study was approved by the Institutional Review Board at the Johns Hopkins Medical Institutions.

EHR was defined as hospital readmission within 30 days of discharge from the initial operative admission. The primary outcome was overall mortality, which was obtained via the National Social Security Death Index.¹¹ Surgical pathology was obtained from the PRD and the primary diagnosis was categorized as malignant or nonmalignant. Additional patient diagnoses were obtained using International Classification of Diseases, Ninth Revision (ICD-9) codes as previously described.⁵ As per previous investigations, the principal diagnosis code was considered the reason for readmission and grouped into clinically relevant categories.^{10,12} Specific ICD-9 codes for gastrointestinal-related and other readmission diagnoses are listed in Supplementary Table 1.

Statistical analysis

Baseline patient demographics were tabulated for the overall cohort. Continuous variables are presented using median value and intraquartile range (IQR), and categorical variables are expressed as the number and proportion of patients effected. Bivariate analysis was performed using Cox proportional hazards models to identify patient-level factors associated with mortality. Forward and backward stepwise multivariate regressions were performed including covariates found to be significantly associated with mortality on bivariate analysis. All variables were evaluated for collinearity, and variables with 10% missing data were excluded from multivariate analysis. Kaplan–Meier analysis was used to calculate cumulative mortality in those who did and did not experience readmission, and subanalysis was performed after stratification by readmission diagnosis and malignancy. Survival was compared using the log-rank test. All statistical tests were two-sided, and the level of significance was set as .05. Statistical analysis was performed using Intercooled STATA, version 13.0 (Stata Corp., College Station, TX).

Results

Patient demographics

During the study period, 595 patients meeting inclusion criteria underwent pancreatectomy at our institution. The baseline demographic data, procedure type, and hospital course characteristics are shown in Table 1. The mean age of the study population was 61.9 ± 14.2 years. Approximately half (51%) the cohort was female, and the majority (84.7%) of patients were of white race. On average, patients lived 27.2 miles from our institution where the pancreatectomy was performed. Pancreaticoduodenectomy was the most common procedure and was performed in 61.9% of patients, while 34.1% and 4.0% underwent distal pancreatectomy and total pancreatectomy, respectively.

The median length of postoperative hospital stay was 8 days (IQR 6 to 13 days). Readmission to any hospital in Maryland within 30 days of discharge occurred in 21.5% of patients. One hundred seventy-five deaths (29.4%) occurred during median follow-up of 22.7 months (IQR 11.2 to 43.8, range 1.0 to 73.4 months).

Patient-level factors associated with mortality after pancreatectomy

The associations between long-term mortality following pancreatectomy and various preoperative factors are shown in Table 2. Increasing age ($P < .001$), the presence of symptoms at diagnosis ($P = .001$), and pre-existing cardiac disease ($P < .001$) were all associated with a significantly increased risk of mortality. Mortality was also associated with lower albumin, higher white blood cell count, and higher hematocrit on preoperative laboratory studies (all $P < .011$). The presence of diabetes, hypertension, and preoperative liver disease were not associated with increased risk of death.

Operative and postoperative factors associated with mortality after pancreatectomy

The bivariate associations between various clinical factors and mortality following pancreatectomy are shown in Table 3. Patients who underwent distal pancreatectomy had a lower risk of death than those who underwent classic pancreaticoduodenectomy or total

pancreatectomy ($P < .001$). The need for intraoperative blood transfusion, but not operative time, was associated with increased risk of mortality ($P < .001$). Malignant disease, positive lymph nodes, and a positive surgical margin were also significantly associated with increased mortality (all $P < .001$).

In the postoperative setting, patients who experienced complications had an increased risk of mortality, although this did not reach statistical significance (hazard ratio [HR] 1.29, 95% confidence interval [CI] .96 to 1.74, $P = .088$). Evaluation of specific complications demonstrated that wound complications, delayed gastric emptying, and pancreatic fistulae were not significantly associated with mortality ($P =$ nonsignificant; Table 3). In contrast, patients diagnosed with an intra-abdominal abscess or anastomotic leak during initial hospitalization had an increased hazard of subsequent mortality ($P = .033$). Notably, EHR within 30 days of pancreatectomy was significantly associated with mortality (HR 1.52, 95% CI 1.10 to 2.11, $P = .012$). Specifically, patients readmitted for GI-related diagnoses demonstrated a hazard ratio of 1.80 (95% CI 1.15 to 2.82, $P = .010$) for mortality.

On Kaplan–Meier analysis, patients with EHR had a decreased survival compared with those who were not readmitted (log-rank test, $P = .011$; Fig. 1A). Furthermore, subgroup analysis including only those patients who underwent resection of a malignant lesion demonstrated a persistent association between EHR and mortality. In the 409 patients who underwent pancreatectomy for a malignant indication, EHR was associated with significantly decreased survival (log-rank test, $P = .025$; Fig. 1B). After stratification by GI vs non-GI causes for EHR, patients who were readmitted for GI-related diagnoses had decreased survival compared with those readmitted for other diagnoses and those who were not readmitted ($P = .014$; Fig. 1C).

Multivariate analysis of survival after pancreatectomy

On multivariate analysis, increasing patient age, surgery earlier in the study period, pre-existing cardiac disease, malnutrition, malignancy, positive lymph nodes and/or positive margins on pathology, and early readmission for GI-related complications were all independent predictors of mortality (all $P < .05$; Table 4). EHR for non-GI-related reasons demonstrated a trend toward increased mortality, but this was not statistically significant (HR 1.45, 95% CI .95 to 2.20, $P = .082$).

Comments

Recent policy changes in healthcare reimbursement have resulted in an increased focus on hospital readmission rates, both as a means of reducing costs and as a surrogate measure of hospital quality of care. We have previously demonstrated a 30-day readmission rate of 21.5% following pancreatectomy at our tertiary high-volume center, and we identified patient-level factors predictive of readmissions, including increasing age, pre-existing liver disease, and postoperative drain placement.⁵ In this study, we evaluated patient-level, operative, and postoperative factors associated with mortality after pancreatectomy. Specifically, we aimed to explore whether readmissions soon after the initial hospitalization may be indicative of a poorer long-term prognosis.

Our findings indicate that early readmission after pancreatectomy is significantly associated with decreased overall survival, independent of patient- and disease-level factors. While Zhu et al¹³ and Yermilov et al¹⁴ have previously reported lower median survival times (21 vs 46 months, and 12.3 vs 22 months, respectively) among patients requiring readmission within 1 year of pancreatectomy, the majority of these readmissions were secondary to cancer progression and were thus necessarily associated with greater mortality. Our study is unique in that we have investigated readmissions in the early postoperative period, during which time very few readmissions occur secondary to cancer progression.⁵ Interestingly, we demonstrate consistently shorter survival among patients readmitted during the early postoperative period following pancreatectomy compared with those who were not readmitted (20.3 vs 23.1 months). Furthermore, this relationship is significant even after adjustment for malignancy, raising the possibility that EHR is indicative of an overall poorer health state that predicts survival independent of the primary disease.

In contrast to our findings, Ahmad et al¹⁵ recently observed no significant difference in survival for readmitted vs nonreadmitted patients at 90 days following pancreatectomy (19.5 vs 20.3 months), suggesting no differences in outcomes among patients with acute and subacute postoperative complications. The disparities in these findings may be reflective of improved readmission definitions and capturing via use of a statewide-linked database in our study, differences in overall follow-up times, or the populations assessed. No matter the explanation, the correlation between readmission and survival is important. If early readmission can be reliably shown to predict earlier mortality, it may be possible to identify high-risk patients based on readmissions data.¹⁶ Likewise, this correlation suggests that the use of hospital readmission rates as a surrogate measure of hospital quality of care may not be appropriate without implementation of adequate risk-adjustment measures.

Of note, we also uniquely demonstrate that patients readmitted within 30 days for GI-related diagnoses had decreased survival following pancreatectomy compared with those readmitted within 30 days for other diagnoses and those who were not readmitted. Gastrointestinal-related EHRs were consistently predictive of mortality even after adjusting for malignancy and other previously well-defined mortality risk factors, including calendar year of surgery.^{17–20} Gastrointestinal complications are the most common risk factors for 30-day hospital readmission among general surgery patients,¹² and a well-recognized complication of pancreatectomy that can be associated with high risk of death.^{5,21} In our study, GI-related readmissions increased risk of death by 2.3 times, making it the second strongest predictor of mortality behind malignancy-related measures. The precise manner by which GI-related admissions increase risk of death is currently unknown, but may relate to the postoperative complication severity or possibly overall patient state of health. There have recently been a number of studies documenting an association between patient frailty and postoperative complications, especially among the older population¹² and among cancer patients.²³ There are currently no studies evaluating a global assessment of frailty on pancreatectomy outcomes, but this measure deserves further investigation, as it may provide insight into specific strategies to identify and intervene on high-risk clinical presentations before surgery.

Further supporting the hypothesis that GI-related EHRs and mortality are related to poor preoperative state of health, we also found that low preoperative serum albumin levels were associated with increased long-term mortality. These findings are consistent with prior studies demonstrating that hypoalbuminemia is an independent predictor of postoperative morbidity, surgical site infection, hospital stay, and hospital readmission following pancreatectomy.^{24,25} As such, measures aimed at optimizing preoperative nutritional status, including careful preoperative screening of nutritional status using measures such as albumin, prealbumin, and transferrin levels, subjective global assessment, and bioelectrical impedance analysis, may have significant effects on lowering hospital readmission rates and on improving postoperative survival.²⁶

One of the limitations of this study is that it is a retrospective review of a prospectively maintained database, and therefore vulnerable to errors in the medical data record. We sought to more fully and accurately capture EHRs by using a statewide database in conjunction with our institutional database, thus allowing us to include readmissions to both index and nonindex institutions. Although we have previously shown improved readmission capture using this technique compared to other studies on this topic,⁵ our methodology does fail to capture out of state readmissions. Another shortcoming of the study is that, although we can make associations between risk factors and mortality, we do not have data regarding the cause of death of these individuals, which may allow insight into strategies for risk modification. In addition, we categorized complication diagnoses using ICD-9 codes based on a grouping scheme determined a priori. We believe our categorization to be highly accurate as it was determined by clinical assessment and agreement of 3 authors (C.W.H., J.J.T., C.L.W.), but it is possible that other clinicians may have assigned some diagnoses differently. We have listed each specific diagnosis for review in Supplementary Table 1. Finally, although prior studies have reported on the association between overall hospital readmissions and mortality, we focused on the 30-day time period specifically in an effort to uniquely capture any potential correlation between acute postoperative complications and long-term mortality. We chose to study the association between early (30 day) readmission and mortality because this is the time interval during which hospitals will be held financially accountable for readmissions as detailed in the Patient Protection and Affordable Care Act.^{2,3}

In summary, following a complex procedure such as pancreatectomy, EHR is a common phenomenon.⁵ In the current era of healthcare policy reform, increased scrutiny of healthcare outcomes and costs has brought proposals for financial penalization of hospitals with high readmission rates. However, the repercussions of early admission after surgery remain poorly understood. Here we have delineated patient, operative, and postoperative factors contributing to long-term mortality following pancreatectomy, and investigated the consequences of EHR in this context. EHR, and specifically early readmission for GI-related complications, significantly reduces survival following pancreatectomy. Future studies delineating the use of preoperative risk stratification strategies are essential for the early identification of high-risk patients, and to provide insights into specific interventions that could be implemented to decrease postpancreatectomy morbidity and mortality.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.

Kaplan–Meier survival curves. Patients who were admitted within 30 days of pancreatectomy had decreased survival compared with those who were not readmitted (log-rank test, $P = .011$; panel A). Subgroup analysis demonstrated that early hospital readmission was also associated with significantly decreased survival among those patients who underwent resection of a malignant lesion (log-rank test, $P = .025$; panel B). In addition, patients who were readmitted for GI-related diagnoses had decreased survival compared with those readmitted for other diagnoses and those who were not readmitted ($P = .014$; panel C).

Table 1

Baseline patient demographics

	Number (n = 595)	Percent
Median age (IQR, years)	62.8 (53.7–72.8)	
Female sex	303	50.9
White race	504	84.7
Married	381	64.0
Median distance from JHH (IQR, miles)	25.1 (12.7–34.0)	
Comorbid conditions		
Hypertension	290	48.7
Diabetes mellitus	157	26.4
Hyperlipidemia	148	24.9
Obesity	75	12.6
Ischemic heart disease	70	11.8
Liver disease	55	9.2
Albumin 2.5 g/dL	97	16.3
Creatinine 1.3 mg/dL	42	7.1
Procedure		
Pancreaticoduodenectomy	368	61.9
Distal pancreatectomy	203	34.1
Total pancreatectomy	24	4.0
Malignancy	409	68.7
Adenocarcinoma	290	48.7
Endocrine carcinoma	67	11.3
Solid pseudopapillary neoplasm	11	1.85
Sarcoma	8	1.34
Metastasis	8	1.34
Adenosquamous carcinoma	6	1.01
Other	19	3.19
Postoperative complication	279	46.9
Median length of stay (range, days)	8.0 (6.0–13.0)	

IQR = intraquartile range; JHH = Johns Hopkins hospital.

Table 2

Bivariate analysis of preoperative factors associated with mortality after pancreatectomy

	HR (95% CI)	P value
Demographics		
Female sex	.80 (.60–1.08)	.145
Age (per year)	1.03 (1.02–1.04)	<.001
Married	1.14 (.83–1.55)	.428
Calendar year (per year)	.84 (.76–.94)	.002
Presenting symptoms		
Symptomatic	3.07 (1.56–6.06)	.001
Weight loss	1.84 (1.30–2.61)	.001
Jaundice	2.75 (1.93–3.90)	<.001
Pruritus	1.75 (1.08–2.85)	.024
Abdominal pain	.79 (.55–1.12)	.186
Bleeding	1.44 (.67–3.10)	.348
Comorbidities		
Hypertension	1.14 (.84–1.53)	.399
Diabetes mellitus	1.23 (.89–1.70)	.214
Hyperlipidemia	.90 (.63–1.29)	.574
Liver disease	1.11 (.68–1.81)	.665
Cardiac disease	1.72 (1.27–2.34)	<.001
Laboratory values		
Albumin	.58 (.48–.70)	<.001
Creatinine	1.06 (.78–1.44)	.721
Blood urea nitrogen	.99 (.97–1.02)	.532
White blood cell count *	1.03 (1.01–1.06)	.011
Hematocrit	.96 (.94–.99)	.003

CI = confidence interval; HR = hazard ratio.

* Per 1,000 cell/dL increase.

Table 3**Bivariate analysis of operative factors and mortality**

	HR (95% CI)	P value
Operative details		
Procedure		
Pancreaticoduodenectomy	1.00 (Reference)	-
Distal pancreatectomy	.46 (.32–.67)	<.001
Total pancreatectomy	1.27 (.69–2.36)	.443
Operative time (per 1 hour)	1.04 (.95–1.14)	.396
Transfusion	2.64 (1.93–3.62)	<.001
Pathology		
Malignancy	7.32 (4.15–12.91)	<.001
Tumor size (cm)	1.02 (.99–1.01)	.250
Positive margin	3.72 (2.59–5.35)	<.001
Positive nodes	6.40 (4.53–9.06)	<.001
Postoperative complications		
Any complication	1.29 (.96–1.74)	.088
Delayed gastric emptying	1.33 (.93–1.09)	.121
Wound complication	1.01 (.64–1.59)	.956
Pancreatic fistula	.62 (.36–1.07)	.087
Abdominal abscess	1.78 (1.05–3.02)	.033
Anastomotic leak	2.59 (1.63–4.13)	<.001
Other*	1.78 (1.20–2.65)	.005
Any readmission	1.52 (1.10–2.11)	.012
GI related	1.80 (1.15–2.82)	.010
Non-GI related	1.23 (.82–1.84)	.313

CI = confidence interval; GI = gastrointestinal related (Supplementary Table 1); HR = hazard ratio.

Operative time (n = 424) and transfusion (n = 513) calculated from smaller sample size because of missing data.

* Bleed, cardiac event, pneumonia, sepsis, venous thromboembolic event, pancreatitis.

Table 4

Multivariate analysis for predictors of mortality after pancreatectomy

Predictive factor	HR (95% CI)	P value
Age (per year)	1.02 (1.01–1.03)	.002
Calendar year (per year)	.87 (.77–.97)	.015
Cardiac disease	1.41 (1.02–1.96)	.038
Albumin (per 1 g/dL)	.80 (.65–.98)	.034
Malignant indication	2.97 (1.58–5.57)	.001
Positive lymph nodes	3.62 (2.44–5.37)	<.001
Positive margin	1.81 (1.24–2.64)	.002
GI-related readmission (30-day)	2.30 (1.43–3.69)	.001
Non-GI-related readmission (30-day)	1.45 (.95–2.20)	.082

CI = confidence interval; GI = gastrointestinal related (Supplementary Table 1); HR = hazard ratio.