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Effect of Preoperative Renal Insufficiency on Postoperative Outcomes after Pancreatic Resection: A Single Institution Experience of 1,061 Consecutive Patients

Malcolm H Squires III, MD, MS, Vishes V Mehta, BA, Sarah B Fisher, MD, Neha L Lad, MD, David A Kooby, MD, FACS, Juan M Sarmiento, MD, FACS, Kenneth Cardona, MD, Maria C Russell, MD, Charles A Staley III, MD, FACS, and Shishir K Maithel, MD, FACS

Department of Surgery, Division of Surgical Oncology, Winship Cancer Institute (Squires, Mehta, Fisher, Lad, Kooby, Cardona, Russell, Staley, Maithel) and the Division of General and GI Surgery (Sarmiento), Emory University, Atlanta, GA

Abstract

BACKGROUND—Chronic kidney disease (CKD) is known to adversely affect cardiac and vascular surgery outcomes. We examined the effect of preoperative renal insufficiency on postoperative outcomes after pancreatic resection.

STUDY DESIGN—All patients who underwent pancreatic resection between January 2005 and July 2012 were identified. Glomerular filtration rate (eGFR) was estimated by the Modification of Diet in Renal Disease formula. Severe CKD (stages 4–5) was defined as eGFR < 30 mL/min/1.73m². Renal function also was analyzed using serum creatinine (sCr) dichotomized at 1.8 mg/dL. Primary outcomes were any complication, major complications, and respiratory failure. Multivariate models for each endpoint were constructed by including all variables with p value 0.10 on univariate analysis.

RESULTS—There were 1,061 patients identified; 709 underwent pancreaticoduodenectomy, 307 distal pancreatectomy, and 45 central or total pancreatectomy. Median sCr value was 0.86 mg/dL (range 0.30 to 14.1 mg/dL). Eighteen patients (1.7%) had severe CKD and 31 (2.9%) had sCr 1.8 mg/dL. Complications occurred in 622 patients (58.6%), major complications in 198 (18.7%), and respiratory failure in 48 (4.5%). Both severe CKD and sCr 1.8 mg/dL were associated with any complication, major complications, and respiratory failure on univariate analysis. On multivariate analysis, severe CKD was associated with increased complications (odds ratio [OR] 5.5; 95% CI 1.3 to 25.5; p = 0.02) and respiratory failure (OR 6.1; 95% CI 1.8 to 20.5; p = 0.03),

Correspondence address: Shishir K Maithel, MD, FACS, Winship Cancer Institute, Division of Surgical Oncology, 1365C Clifton Rd NE, 2nd Floor, Atlanta, GA 30322. smaithe@emory.edu.

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Author Contributions

Study conception and design: Squires, Kooby, Sarmiento, Cardona, Staley, Maithel

Acquisition of data: Squires, Mehta, Lad

Analysis and interpretation of data: Squires, Fisher, Kooby, Cardona, Russell, Maithel

Drafting of manuscript: Squires, Fisher, Maithel

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but not major complications. Using sCr ≥ 1.8 mg/dL as a surrogate marker for renal insufficiency, patients with sCr ≥ 1.8 mg/dL had increased risk of any complication (OR 3.5; 95% CI 1.3 to 9.3; $p = 0.01$), major complications (OR 2.2; 95% CI 1.04 to 4.8; $p = 0.04$), and respiratory failure (OR 4.7; 95% CI 1.8 to 12.6; $p = 0.002$).

CONCLUSIONS—Few patients with significant renal insufficiency are candidates for pancreatic resection. Severe CKD (stages 4–5) is associated with increased risk of complication and respiratory failure. Serum creatinine ≥ 1.8 mg/dL may serve as a useful marker of renal insufficiency and identifies patients at significantly increased risk of any complication, major complication, and respiratory failure after pancreatic resection.

Preoperative renal insufficiency is a well-known risk factor associated with adverse outcomes after cardiac surgery and vascular surgery procedures. Patients with reduced renal function undergoing cardiac surgery are at increased risk of postoperative complications and mortality.^{1–3} Both short-term and long-term outcomes of patients undergoing cardiac surgery are negatively affected by preoperative renal insufficiency.^{4,5} In patients undergoing lower extremity vascular bypass procedures, preoperative renal insufficiency, whether determined by estimated creatinine clearance or glomerular filtration rate, has similarly been shown to be a significant independent risk factor for postoperative mortality and cardiopulmonary complications.^{6,7} Multiple studies assessing patients undergoing carotid endarterectomy have also demonstrated increased risk of postoperative complications and mortality associated with the presence of chronic renal insufficiency.^{8–10}

Less is known regarding the specific postoperative risks of patients with renal insufficiency undergoing general surgery procedures. Two recent large analyses using the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) database investigated the risk of postoperative complications after nonemergent general surgery procedures in patients on long-term dialysis¹¹ or patients with chronic renal insufficiency.¹² Patients on long-term dialysis were shown to be at increased risk of postoperative complications, especially respiratory complications, and at increased risk of death after general surgical procedures.¹¹ Similarly, chronic kidney disease was found to be an independent risk factor for 30-day mortality and major postoperative complications after general and vascular surgery procedures.¹² Although the strength of these analyses lies in the sheer number of patients included in the analysis, the applicability of results generalized across all general surgery procedures to a single procedure or organ site remains unknown.

Pancreatic resections are procedures associated with significant risk for morbidity and mortality, and little is known regarding the influence of preoperative renal function on surgical outcomes. Only 1 small study to date has specifically examined preoperative renal function in patients who underwent pancreaticoduodenectomy, and the only outcome assessed was postoperative renal dysfunction.¹³ Given the significant perioperative fluid shifts occurring in patients undergoing pancreatic resection, pre-existing renal insufficiency may place patients at increased risk of numerous postoperative complications, beyond just renal dysfunction. We sought to examine the role of preoperative renal insufficiency on postoperative outcomes in a large single-institution series of consecutive patients undergoing pancreatic resection.

METHODS

All patients undergoing pancreatectomy at a single academic institution between January 1, 2005 and July 1, 2012 were identified from a prospectively maintained institutional database. Patients undergoing pancreaticoduodenectomy (Whipple), distal pancreatectomy, central pancreatectomy, or total pancreatectomy were included; those undergoing enucleation or pancreatic debridement procedures were excluded. Permission from the Institutional Review Board was obtained and all research activities were conducted in compliance with the Health Insurance Portability and Accountability Act of 1996.

A comprehensive review of the medical record was conducted to identify patient demographics, medical comorbidities, and preoperative laboratory values. Renal function was evaluated on the basis of the last preoperative serum creatinine (sCr) value and the estimated glomerular filtration rate (eGFR), calculated from the Modification of Diet in Renal Disease (MDRD) formula: $\text{eGFR (mL/min/1.73 m}^2\text{)} = 175 \times (\text{sCr})^{-1.154} \times (\text{Age})^{-0.203} \times (0.742 \text{ if female}) \times (1.212 \text{ if African-American})$.¹⁴ Preoperative medical records for all patients were thoroughly reviewed to confirm that elevated preoperative sCr or diminished preoperative eGFR values were in fact representative of chronic renal insufficiency and did not reflect an acute change. Preoperative sCr was analyzed both as a continuous variable and as a dichotomous variable, with 1.8 mg/dL serving as the cutoff value. The cutoff value of 1.8 mg/dL was selected because it represented the upper limit of 1 standard deviation from the mean sCr value for the entire cohort ($0.97 \text{ mg/dL} \pm 0.78 \text{ mg/dL}$). Severity of renal dysfunction was classified by chronic kidney disease (CKD) stage, with severe renal dysfunction classified as CKD stage 4 and 5 ($\text{eGFR} < 30 \text{ mL/min/1.73 m}^2$).¹⁵

Operative details were also collected, including the need for intraoperative transfusion and, when available and applicable, the pancreatic duct diameter. Postoperative complications, defined as any complications occurring within 30 days of the operative date or within the same hospitalization, were determined from the surgical discharge summary and subsequent follow-up notes in the medical record and were graded in severity based on the Clavien-Dindo scoring system.¹⁶ Primary postoperative outcomes measures included any complication, major complications (Clavien grade III–V), and respiratory failure, defined as need for reintubation. Additional endpoints examined included 30-day and 90-day mortality, any pancreatic fistula, grade B/C pancreatic fistulas as defined by the International Study Group on Pancreatic Fistula,¹⁷ and acute renal failure requiring new-onset postoperative hemodialysis, from which any patients on hemodialysis preoperatively were excluded.

Statistical analysis

Univariate and multivariate logistic regression analyses were performed with relevant perioperative variables for each of the previously described postoperative endpoints. Variables with a p value ≤ 0.10 on univariate analysis were included into the multivariate model for each endpoint. Preoperative renal dysfunction was analyzed based on 2 distinct variables: sCr $\geq 1.8 \text{ mg/dL}$, and CKD stage 4–5. If sCr $\geq 1.8 \text{ mg/dL}$ and CKD stage 4–5 were both significant on univariate regression analysis for a given endpoint, separate multivariate models were constructed to examine the value of each renal function variable independently. Statistical significance on multivariate analysis was defined as a p value

0.05. Analyses were performed on all pancreatectomy patients as well as on procedure-specific subsets for patients undergoing pancreaticoduodenectomy or distal pancreatectomy. All statistical analyses were performed with Statistical Package for the Social Sciences 19.0 software (IBM, Inc).

RESULTS

During the study period, a total of 1,061 consecutive patients underwent pancreatic resection at Emory University Hospital. Of these, 709 patients (66.8%) underwent pancreaticoduodenectomy (Whipple), 307 patients (28.9%) underwent distal pancreatectomy, and 45 patients (4.2%) underwent central or total pancreatectomy. Demographics, comorbidities, and preoperative laboratory values are summarized in Table 1. The median sCr level was 0.86 mg/dL, with a range of 0.3 to 14.1 mg/dL. Thirty-one patients (2.9%) had a preoperative sCr $\geq$ 1.8 mg/dL. Estimated GFR calculations by the MDRD formula yielded a median eGFR of 82.6 mL/min/1.73m², with a range of 4.4 to 237.5 mL/min/1.73m². One hundred sixty-eight patients (15.8%) had moderate CKD (stage 3), defined as an eGFR of 30 to 59 mL/min/1.73m². Only 18 patients (1.6%) had severe CKD (stage 4 or 5), defined as eGFR $<$ 30 mL/min/1.73m² or dialysis dependence. Eight of these patients, all classified as CKD stage 5, were dialysis dependent preoperatively and were maintained on scheduled hemodialysis postoperatively. These reported values of sCr and eGFR for patients with preoperative renal dysfunction all reflect states of chronic renal insufficiency rather than an acute kidney injury.

Postoperative outcomes and complications are presented in Table 1. Among all patients undergoing pancreatic resection, 622 patients (58.6%) experienced a complication, with similar rates among patients undergoing the Whipple procedure (59.0%) and distal pancreatectomy (54.7%). Of these 622 patients, 198 (18.7%) experienced a major complication, defined as a Clavien grade $\geq$ 3. Forty-eight patients (4.5%) developed postoperative respiratory failure, with more frequent occurrence after Whipple resection (5.5%) vs distal pancreatectomy (2.0%). Two hundred twenty-seven patients (21.4%) developed a pancreatic fistula, with 130 patients (12.3%) developing clinically significant grade B or C pancreatic fistulae. Excluding the 8 patients with CKD stage 5 on dialysis preoperatively, 12 patients (1.1%), all of whom underwent Whipple resection, experienced acute renal failure requiring unplanned postoperative hemodialysis. The overall 30-day and 90-day mortality rates were 2.2% and 4.4%, respectively.

Risk factors for any complication

On univariate analysis of all patients undergoing pancreatic resection (n = 1,061), significant risk factors for any complication included both sCr $\geq$ 1.8 mg/dL and CKD stage 4–5 (Table 2). The most common types of complications associated with preoperative renal insufficiency included pancreatic fistula, respiratory failure, gastrointestinal bleeding, intra-abdominal abscess, and anemia requiring transfusion. Factors examined that were not associated with risk of any complication on univariate analysis included body mass index (BMI), smoking history, chronic obstructive pulmonary disease (COPD), diabetes, alcohol abuse, hypoalbuminemia (serum albumin $<$ 3.0 g/dL), pancreatic duct size, a diagnosis of

pancreatic ductal adenocarcinoma (PDAC), and a diagnosis of pancreatitis. On multivariate analysis using sCr ≥ 1.8 mg/dL as a marker of renal dysfunction, male sex, increasing age, preoperative stent placement, intraoperative drain placement, and sCr ≥ 1.8 mg/dL (odds ratio [OR] 3.46; 95% CI 1.30 to 9.28; $p = 0.01$) remained significant risk factors for any postoperative complication (Table 2). A similar multivariable model using CKD stage 4–5 as a marker of renal dysfunction demonstrated that CKD stage 4–5 was independently associated with a 5-fold increased risk of any complication (OR 5.54; 95% CI 1.25 to 25.54; $p = 0.02$; Table 2).

Among patients undergoing Whipple resection ($n = 709$), significant risk factors for any complication on univariate analysis included sCr ≥ 1.8 mg/dL and CKD stage 4–5 (Table 2). On multivariate analysis using sCr, male sex, increasing age, intraoperative drain placement, and sCr ≥ 1.8 mg/dL (OR 3.65; 95% CI 1.03 to 12.91; $p = 0.045$) remained significant risk factors (Table 2). On the multivariable model using CKD, CKD stage 4–5 demonstrated a trend toward increased risk of any complication (OR 5.73; 95% CI 0.70 to 47.00; $p = 0.10$; Table 2).

Among patients undergoing distal pancreatectomy ($n = 307$), multivariate analysis demonstrated a trend toward association of sCr ≥ 1.8 mg/dL with increased risk of any complication (OR 6.78; 95% CI 0.84 to 54.58; $p = 0.07$; Table 2). The multivariate model using CKD stage also demonstrated a trend toward association of CKD stage 4–5 with increased risk of any complication (OR 4.77; 95% CI 0.57 to 4.03; $p = 0.15$; Table 2).

Risk factors for major (Clavien grade III–V) complications

Factors significant on univariate analysis for increased risk of major (Clavien grade III–V) complications among all patients undergoing pancreatic resection included age, hypertension, intraoperative transfusion, and sCr ≥ 1.8 mg/dL (Table 3). Nonsignificant factors included sex, body mass index, smoking, COPD, diabetes, alcohol abuse, serum albumin <3.0 g/dL, pancreatic duct size, intraoperative drain placement, a diagnosis of PDAC, and a diagnosis of pancreatitis. Chronic kidney disease stage 4–5 was associated with a slight trend toward increased risk of major complications among all patients ($p = 0.12$). The multivariate model for major complications among all pancreatic resections demonstrated that among the other significant risk factors of increasing age, hypertension, and intraoperative transfusion, sCr ≥ 1.8 mg/dL retained the strongest predictive association (OR 2.24; 95% CI 1.04 to 4.80; $p = 0.04$; Table 3).

Among patients undergoing a Whipple procedure, the multivariate model using sCr demonstrated a trend toward association of sCr ≥ 1.8 mg/dL with increased risk of major complications (OR 2.27; 95% CI 0.86 to 6.02; $p = 0.10$; Table 4). Other significant risk factors for major complications on multivariate analysis included increasing age, intraoperative drain placement, and a diagnosis of PDAC. Using CKD stage in the multivariate model, CKD stage 4–5 was not associated with increased risk of major complication ($p = 0.24$; Table 4).

Among patients undergoing distal pancreatectomy, neither sCr ≥ 1.8 mg/dL nor CKD stage 4–5 were associated with major complications on univariate analysis (Table 5). The only

significant risk factor for major complications on multivariate analysis was diabetes mellitus (OR 2.04; 95% CI 1.05 to 3.97; $p = 0.04$; Table 5).

Risk factors for respiratory failure

Among all patients undergoing pancreatic resection, significant risk factors for respiratory failure on univariate analysis included both sCr ≥ 1.8 mg/dL and CKD stage 4–5, as well as increasing age, COPD, hypertension, albumin <3 g/dL, and intraoperative transfusion (Table 6). Factors not associated with respiratory failure included sex, body mass index, smoking, diabetes, alcohol abuse, preoperative stent placement, pancreatic duct size, intraoperative drain placement, a diagnosis of PDAC, and a diagnosis of pancreatitis. On multivariate analysis using sCr, COPD, preoperative albumin <3 g/dL, and sCr ≥ 1.8 mg/dL (OR 4.71; 95% CI 1.76 to 12.60; $p = 0.002$) remained significant risk factors for respiratory failure, with sCr ≥ 1.8 mg/dL associated with a nearly 5-fold increased risk (Table 6). Using CKD in the alternate multivariate model, CKD stage 4–5 similarly remained the single strongest risk factor for respiratory failure (OR 6.12; 95% CI 1.83 to 20.46; $p = 0.003$; Table 6).

Among patients undergoing Whipple procedures, significant risk factors for respiratory failure on univariate analysis again included both sCr ≥ 1.8 mg/dL and CKD stage 4–5, as well as age, COPD, hypertension, and albumin <3 g/dL (Table 6). On multivariate analysis using sCr, preoperative albumin <3 g/dL and sCr ≥ 1.8 mg/dL (OR 3.87; 95% CI 1.17 to 12.79; $p = 0.03$) remained significant risk factors for respiratory failure (Table 6). Using CKD stage in the alternate multivariate model, CKD stage 4–5 demonstrated a trend toward association with increased risk of respiratory failure (OR 4.21; 95% CI 0.81 to 21.94; $p = 0.09$; Table 6).

Among the distal pancreatectomy group, both sCr ≥ 1.8 mg/dL and CKD stage 4–5 were significant risk factors for respiratory failure on univariate analysis (Table 7). Multivariate analysis was not performed due to the limited number of events ($n = 6$) in this cohort. Of 12 patients with sCr ≥ 1.8 mg/dL, 2 patients (16.7%) experienced respiratory failure, compared with only 4 patients among the 291 patients with sCr < 1.8 mg/dL (1.4%), a greater than 10-fold increased incidence. Similarly, patients with CKD stage 4–5 demonstrated a rate of respiratory failure (2 of 7 patients, 22.2%) significantly greater than those with minimal or no renal dysfunction (4 of 294 patients, 1.3%). Neither smoking nor COPD was associated with increased risk of respiratory failure among this cohort. The prognostic value of sCr ≥ 1.8 mg/dL and CKD stage 4–5 for each of the 3 primary postoperative outcomes, stratified by procedure type, is summarized in Table 8.

Risk factors for 30-day and 90-day mortality

Among all patients undergoing pancreatic resection, neither sCr ≥ 1.8 mg/dL nor CKD stage 4–5 was significantly associated with 30-day or 90-day mortality on univariate analysis. Only increasing age remained a significant risk factor for 30-day mortality on multivariate analysis (OR 1.06; 95% CI 1.02 to 1.10; $p = 0.002$). Among those undergoing a Whipple procedure, neither sCr ≥ 1.8 mg/dL nor CKD stage 4–5 was associated with 30 or 90-day mortality. Similarly, neither sCr ≥ 1.8 mg/dL nor CKD stage 4–5 was associated with 30- or 90-day mortality in patients undergoing distal pancreatectomy.

Risk factors for pancreatic fistula

Preoperative renal insufficiency, whether defined by sCr ≥ 1.8 mg/dL or CKD stage 4–5, was not associated with increased risk for any postoperative pancreatic fistula or grade B/C pancreatic fistula on multivariate analysis of risk factors among all patients undergoing pancreatic resections, those undergoing Whipple resection, or those undergoing distal pancreatectomy.

Risk factors for acute renal failure requiring hemodialysis

On univariate analysis of all patients undergoing pancreatic resection, both sCr ≥ 1.8 mg/dL and CKD stage 4–5 were significant risk factors for postoperative acute renal failure requiring new-onset hemodialysis; this was observed in 12 patients, all of whom underwent Whipple resection. Using sCr on multivariate analysis, sCr ≥ 1.8 mg/dL remained an independent risk factor for postoperative acute renal failure (OR 14.0; 95% CI 3.45 to 57.17; $p < 0.001$). Stage 4–5 CKD also remained a significant risk factor for postoperative acute renal failure on multivariate analysis (OR 12.9; 95% CI 2.22 to 75.00; $p = 0.004$).

DISCUSSION

This study presents a single-institution analysis of the effect of preoperative renal insufficiency on postoperative outcomes in 1,061 consecutive patients undergoing pancreatic resection over a 7-year period. To the best of the authors' knowledge, this represents the largest such series in the literature. This study demonstrated that preoperative renal insufficiency is a significant risk factor for adverse postoperative outcomes, independent of typical risk factors. Among all pancreatic resections, on multivariate analysis, preoperative sCr ≥ 1.8 mg/dL remained the most significant risk factor associated with any complication, major complications, and respiratory failure. Stage 4–5 CKD was also significantly associated with increased risk of any complication and respiratory failure, but was not associated with major complications.

A recent large analysis with the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) database evaluated the association of renal dysfunction with the risk of postoperative complications after nonemergent general surgery procedures.¹² This NSQIP analysis demonstrated that CKD was a substantial independent risk factor for 30-day postoperative mortality and major complications after general and vascular surgery procedures, but the applicability of these generalized results to procedure-specific outcomes is not known. Although preoperative renal insufficiency is a well-known risk factor for adverse outcomes and mortality after cardiac surgery or vascular surgery procedures, little is known regarding the effect of renal dysfunction on outcomes after pancreatic resection, a procedure associated with significant morbidity and mortality at baseline.

This study analyzed the associated risks of preoperative renal insufficiency for postoperative outcomes within a large series of patients undergoing pancreatic resection. The observed frequencies of any complications (59%) and major complications (19%) among the study population correspond to comparable rates from similar large series.^{18,19} This study

evaluated the risk of any complication, major complications (Clavien class III–V), and respiratory failure associated with preoperative renal insufficiency. Other endpoints examined included 30-day and 90-day mortality and risk of pancreatic fistula. Preoperative renal insufficiency was evaluated on the basis of both sCr value and the eGFR, as calculated by the MDRD equation.

Renal dysfunction analyzed by sCr ≥ 1.8 mg/dL was associated with significantly increased risk of any postoperative complications, major complications, and respiratory failure; this, however, was not associated with an increased 30-day or 90-day mortality. Renal dysfunction also was not associated with increased risk of postoperative pancreatic fistula formation.

On subset analysis of patients undergoing Whipple procedures, sCr ≥ 1.8 mg/dL remained a significant independent risk factor for any complication on multivariate analysis, and was associated with a trend toward increased risk of major complications. Serum sCr ≥ 1.8 mg/dL was also the most significant risk factor for respiratory failure among the Whipple cohort, associated with a nearly 4-fold increased risk. On subset analysis of the distal pancreatectomy group, sCr ≥ 1.8 mg/dL was associated with a trend toward increased risk of any complication; neither sCr nor CKD stage 4–5 was associated with major complications after distal pancreatectomy. Among patients undergoing distal pancreatectomy, sCr ≥ 1.8 mg/dL and CKD stage 4–5 were associated with substantially increased risk of respiratory failure.

The results of this study demonstrate that patients undergoing pancreatic resection are inherently well selected. Only 31 patients had a preoperative sCr ≥ 1.8 mg/dL, and only 18 patients were classified as having severe (stage 4–5) CKD, defined as eGFR < 30 mL/min/1.73m². Given the physiologic stress of a substantial abdominal operative procedure, few patients with severe underlying renal dysfunction are suitable operative candidates to undergo pancreatic resection. Due to the retrospective nature of this study, it is not possible to quantify the number of patients who may have been excluded from a pancreatic resection due to the severity of their renal insufficiency.

The significantly increased risk of respiratory failure among patients with preoperative renal insufficiency, even when accounting for COPD and smoking history, may be due to the complexities of managing perioperative fluid status in these patients. A recent analysis of intraoperative fluid management in patients undergoing pancreatectomy at Memorial Sloan-Kettering failed to demonstrate a meaningful association between intraoperative fluids administered and postoperative complications, although the authors did not comment on patients' preoperative renal function nor did they assess postoperative fluid administration.²⁰ Although this study did not assess fluid resuscitation, preoperative renal insufficiency was associated with a 4-fold increased risk of respiratory failure, regardless of the extent of pancreatic resection.

Serum Cr ≥ 1.8 mg/dL was a significant risk factor for any complication and respiratory failure among Whipple procedure patients; severe CKD was not a significant risk factor but was associated with a trend toward increased risk of any complication ($p = 0.10$) and

respiratory failure ($p = 0.09$). This difference in significance between the 2 renal insufficiency variables could be a function of statistical power because more patients undergoing Whipple procedures had $\text{sCr} \geq 1.8 \text{ mg/dL}$ ($n = 19$) vs patients with severe CKD ($n = 9$). This difference could also partially reflect that patients within the severe CKD cohort included a greater proportion of patients with stage 5 CKD who were dialysis dependent preoperatively and were maintained on scheduled hemodialysis postoperatively. Although difficult to prove in a retrospective fashion, the overall fluid balance of these patients may have been better controlled as a result of early scheduled hemodialysis on postoperative day 1 or 2, potentially leading to less of an association with complications or respiratory failure.

An inherent limitation of this study is its retrospective design, which prevents any definitive conclusions regarding the causative effect of renal insufficiency on postoperative outcomes. An additional limitation of analysis was the small number of patients with significant renal insufficiency. This likely reflects the fact that most patients with severe preoperative renal dysfunction are not selected for pancreatectomy, given the association with adverse outcomes after other procedure types.

CONCLUSIONS

The results of this study demonstrate that significant preoperative renal dysfunction is associated with increased risk of adverse outcomes after pancreatectomy and should be included among the usual risk factors assessed for patients being considered for pancreatic surgery. Severe CKD (stages 4–5) is associated with increased risk of complications and respiratory failure, but may be of limited clinical utility due to an inherent selection bias that often excludes these patients from surgery. Serum creatinine $\geq 1.8 \text{ mg/dL}$ may serve as a useful surrogate marker of renal insufficiency and identifies patients at significantly increased risk of any complication, major complication, and respiratory failure after pancreatic resection. These findings selectively persist when stratifying by operation type, specifically, Whipple procedure vs distal pancreatectomy. The results of this study may help guide physicians and counsel patients regarding the risk associated with preoperative renal insufficiency in patients being considered for pancreatic resection.

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Abbreviations and Acronyms

CKD	chronic kidney disease
eGFR	estimated glomerular filtration rate
MDRD	Diet in Renal Disease
OR	odds ratio

PDAC	pancreatic ductal adenocarcinoma
sCr	serum creatinine

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Table 1

Demographic and Clinicopathologic Characteristics

Variable	All patients (n = 1,061)	Whipple (n = 709)	Distal (n = 307)
Sex, male, n (%)	477 (45.0)	352 (49.6)	111 (36.2)
Race, n (%)			
White	752 (70.9)	497 (70.1)	220 (71.7)
Black	240 (22.6)	159 (22.4)	74 (24.1)
Other	69 (6.5)	53 (7.5)	13 (4.2)
Age, y, median (range)	60.3 (15.4-89.1)	62.4 (15.4-89.1)	57.2 (18.3-88.6)
Diabetes mellitus, n (%)	312 (29.4)	222 (31.3)	77 (25.1)
Hypertension, n (%)	540 (53.7)	381 (53.7)	142 (46.3)
COPD, n (%)	92 (8.7)	72 (10.2)	20 (6.5)
Smoking history, >10 pack-y, n (%)	445 (41.9)	325 (45.8)	104 (33.9)
Alcohol abuse, n (%)	146 (13.8)	105 (14.8)	38 (12.4)
Perioperative characteristics			
Any preoperative stenting, n (%)	386 (36.4)	371 (52.3)	10 (3.2)
Endoscopic	328 (30.9)	314 (44.3)	9 (2.9)
Percutaneous	58 (5.5)	57 (8.0)	1 (0.3)
Albumin < 3.0 g/dL, n (%)	237 (22.3)	204 (28.8)	28 (9.1)
Total bilirubin, mg/dL, median (range)	0.8 (0.1-39.9)	1.0 (0.1-39.9)	0.6 (0.1-10.2)
Serum creatinine, mg/dL, median (range)	0.86 (0.3-14.1)	0.87 (0.3-11.7)	0.86 (0.4-14.1)
Serum creatinine > 1.8 mg/dL, n (%)	31 (2.9)	19 (2.7)	12 (3.9)
eGFR by MDRD, mL/min/1.73m ² , median (range)	82.6 (4.4-237.5)	82.6 (4.8-237.5)	81.4 (4.4-192.7)
CKD stage, n (%)			
Stage 1: GFR ≥ 90 mL/min/1.73m ²	377 (35.5)	258 (36.4)	98 (31.9)
Stage 2: GFR 60-89 mL/min/1.73m ²	498 (46.9)	325 (45.8)	153 (49.8)
Stage 3: GFR 30-59 mL/min/1.73m ²	168 (15.8)	117 (16.5)	47 (15.3)
Stage 4: GFR 15-29 mL/min/1.73m ²	9 (0.8)	6 (0.8)	3 (1.0)
Stage 5: GFR < 15 mL/min/1.73m ² (or dialysis)	9 (0.8)	3 (0.4)	6 (2.0)
Intraoperative transfusion, n (%)	112 (10.6)	96 (13.6)	16 (5.2)
Pancreatic duct size, mm, median (range)	2.0 (1.0-30.0)	2.0 (1.0-30.0)	-
Pathology, n (%)			
Adenocarcinoma	508 (47.9)	451 (63.6)	53 (17.3)
Pancreatitis	166 (15.6)	88 (12.4)	58 (18.9)
Postoperative outcomes, n (%)			
30-d mortality	23 (2.2)	18 (2.5)	3 (1.0)
90-d mortality	47 (4.4)	37 (5.2)	4 (1.3)
Any complication	622 (58.6)	418 (59.0)	168 (54.7)
Clavien grade I	203 (19.1)	112 (15.8)	80 (26.1)

Variable	All patients (n = 1,061)	Whipple (n = 709)	Distal (n = 307)
Grade II	221 (20.9)	170 (24.0)	40 (13.0)
Grade III	98 (9.2)	57 (8.0)	31 (10.1)
Grade IV	71 (6.7)	57 (8.0)	13 (4.2)
Grade V	29 (2.7)	23 (3.2)	4 (1.3)
Infectious complications	291 (27.4)	216 (30.5)	60 (19.5)
Respiratory failure	48 (4.5)	39 (5.5)	6 (2.0)
Pancreatic fistula, any grade	227 (21.4)	109 (15.4)	101 (32.9)
Pancreatic fistula, B/C grade	130 (12.3)	76 (10.7)	42 (13.7)
Acute renal failure requiring HD	12 (1.1)	12 (1.7)	0

CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; HD, hemodialysis; MDRD, Modified Diet in Renal Disease.

Table 2

Univariate and Multivariate Analyses of Risk Factors for All Complications

Variable	Univariate		Multivariate with Cr 1.8 mg/dL		Multivariate with CKD 4-5		
	p Value	OR	95% CI	p Value	OR	95% CI	p Value
All patients (n = 1,061)							
Male sex	0.001 *	1.44 *	1.12-1.86 *	0.01 *	1.47 *	1.14-1.90 *	0.003 *
Increasing age, y	0.002 *	1.01 *	1.00-1.02 *	0.04 *	1.01 *	1.00-1.02 *	0.03 *
Hypertension	0.02 *	1.12	0.86-1.47	0.41	1.13	0.86-1.48	0.38
Any preoperative stent	0.02 *	1.44 *	1.09-1.90 *	0.01 *	1.42 *	1.08-1.87 *	0.01 *
Intraoperative blood transfusion	0.02 *	1.82	0.97-3.44	0.06	1.83	0.97-3.45	0.06
Intraoperative drain placement	0.03 *	1.49 *	1.14-1.94 *	0.003 *	1.48 *	1.14-1.93 *	0.003 *
Cr 1.8 mg/dL	0.01 *	3.46 *	1.30-9.28 *	0.01 *	-	-	-
Severe CKD (stages 4-5)	0.02 *	-	-	-	5.54 *	1.25-25.54 *	0.02 *
Whipple patients (n = 709)							
Male sex	0.01 *	1.42 *	1.04-1.94 *	0.03 *	1.45 *	1.07-1.98 *	0.02 *
Increasing age, y	<0.001 *	1.02 *	1.01-1.04 *	<0.001 *	1.02 *	1.01-1.04 *	<0.001 *
Any preoperative stent	0.05 *	1.35	0.99-1.84	0.06	1.32	0.97-1.80	0.08
Intraoperative drain placement	<0.001 *	1.95 *	1.40-2.73 *	<0.001 *	1.96 *	1.40-2.73 *	<0.001 *
Cr 1.8 mg/dL	0.03 *	3.65 *	1.03-12.91 *	0.045 *	-	-	-
Severe CKD (stages 4-5)	0.10 *	-	-	-	5.73	0.70-47.00	0.10
Distal pancreatectomy patients (n = 307)							
Male sex	0.03 *	1.47	0.90-2.40	0.13	1.55	0.95-2.53	0.08
Hypertension	0.03 *	1.35	0.84-2.16	0.22	1.42	0.89-2.27	0.15
Albumin < 3.0 g/dL	0.07 *	1.59	0.65-3.89	0.31	1.58	0.65-3.88	0.32
Intraoperative blood transfusion	0.04 *	3.37	0.92-12.33	0.07	3.38	0.92-12.36	0.07
Cr 1.8 mg/dL	0.06 *	6.78	0.84-54.58	0.07	-	-	-

Variable	Univariate		Multivariate with Cr		1.8 mg/dL		Multivariate with CKD 4–5	
	p Value	OR	95% CI	p Value	OR	95% CI	p Value	
Severe CKD (stages 4–5)	0.07 *	–	–	–	4.77	0.57–4.03	0.15	

* Statistically significant.

Cr, creatinine; CKD, chronic kidney disease; OR, odds ratio.

Table 3

Univariate and Multivariate Analyses of Risk Factors for Major Complications among All Patients (n = 1,061)

Variable	Univariate	Multivariate w/Cr 1.8 mg/dL		
	p Value	OR	95% CI	p Value
Increasing age, y	0.02 *	1.01	0.99-1.02	0.10
Hypertension	0.02 *	1.27	0.90-1.78	0.17
Intraoperative blood transfusion	0.02 *	1.77	0.96-3.25	0.07
Cr 1.8 mg/dL	0.01 *	2.24 *	1.04-4.80 *	0.04 *

* Statistically significant.

Cr, creatinine; OR, odds ratio.

Table 4
Univariate and Multivariate Analyses of Risk Factors for Major Complications among Whipple Patients

Whipple patients (n = 709)	Univariate		Multivariate w/Cr		1.8 mg/dL		Multivariate w/CKD 4–5	
	p Value	OR	95% CI	p Value	OR	95% CI	p Value	
Male sex	0.09 *	1.24	0.84–1.83	0.27	1.27	0.86–1.87	0.22	
Increasing age, y	0.004 *	1.03 *	1.01–1.05 *	0.004 *	1.03 *	1.01 – 1.05 *	0.004 *	
Hypertension	0.004 *	1.52	0.99–2.32	0.05	1.55 *	1.02–2.36 *	0.04 *	
Intraoperative blood transfusion	0.05 *	1.78	0.81–3.91	0.15	1.81	0.83–3.96	0.14	
Intraoperative drain placement	0.01 *	1.77 *	1.77–2.19 *	0.01 *	1.77 *	1.19–2.65 *	0.01 *	
PDAC vs all other diagnoses	0.08 *	1.88 *	1.24–2.84 *	0.003 *	1.87 *	1.24–2.83 *	0.003 *	
Cr 1.8 mg/dL	0.02 *	2.27	0.86–6.02	0.10	–	–	–	
Severe CKD (stages 4–5)	0.07 *	–	–	–	2.33	0.57–9.45	0.24	

* Statistically significant.

CKD, chronic kidney disease; Cr, creatinine; OR, odds ratio; PDAC, pancreatic ductal adenocarcinoma.

Table 5

Univariate and Multivariate Analysis of Risk Factors for Major Complications among Distal Pancreatectomy Patients (n = 307)

Variable	Univariate	Multivariate		
	p Value	Odds ratio	95% CI	p Value
COPD	0.03 *	2.25	0.79-6.38	0.13
Diabetes mellitus	0.03 *	2.04 *	1.05-3.97 *	0.04 *
Intraoperative blood transfusion	0.04 *	2.62	0.85-8.09	0.10

* Statistically significant.

Table 6

Univariate and Multivariate Analysis of Risk Factors for Respiratory Failure

Variable	Univariate		Multivariate w/Cr 1.8 mg/dL		Multivariate w/CKD 4-5		
	p Value	OR	95% CI	p Value	OR	95% CI	p Value
All patients (n = 1,061)							
Increasing age, y	0.03 *	1.02	0.99-1.05	0.17	1.02	0.99-1.05	0.15
COPD	0.05 *	2.35 *	1.03-5.33 *	0.04 *	2.47 *	1.09-5.59 *	0.03 *
Hypertension	0.03 *	1.37	0.70-2.68	0.35	1.39	0.72-2.71	0.33
Albumin < 3.0 g/dL	0.004 *	2.12 *	1.15-3.91 *	0.02 *	2.14 *	1.16-3.94 *	0.02 *
Intraoperative blood transfusion	0.10 *	2.20	0.81-5.95	0.12	2.23	0.82-6.03	0.11
Cr 1.8 mg/dL	<0.001 *	4.71 *	1.76-12.60 *	0.002 *	-	-	-
Severe CKD (stages 4-5)	0.001 *	-	-	-	6.12 *	1.83-20.46 *	0.003 *
Whipple patients							
Increasing age, y	0.05 *	1.02	0.99-1.05	0.28	1.02	0.99-1.05	0.28
COPD	0.10 *	2.12	0.88-5.13	0.10	2.15	0.89-5.17	0.09
Hypertension	0.01 *	2.03	0.93-4.45	0.08	2.08	0.95-4.54	0.07
Albumin < 3.0 g/dL	0.02 *	2.16 *	1.11-4.20 *	0.03 *	2.22 *	1.14-4.30 *	0.02 *
Cr 1.8 mg/dL	0.01 *	3.87 *	1.17-12.79 *	0.03 *	-	-	-
Severe CKD (stages 4-5)	0.05 *	-	-	-	4.21	0.81-21.94	0.09

* Statistically significant.

CKD, chronic kidney disease; Cr, creatinine; OR, odds ratio; PDAC, pancreatic ductal adenocarcinoma.

Table 7

Univariate Analyses of Risk Factors for Respiratory Failure among Distal Pancreatectomy Patients (n = 307)

Variable	Univariate
	p Value
Cr > 1.8 mg/dL	0.004 *
Severe CKD (stages 4-5)	0.001 *

* Statistically significant.

CKD, chronic kidney disease; Cr, creatinine.

Table 8

Summary of Significant Associations of Preoperative Renal Insufficiency Variables on Multivariate Analysis of Risk Factors for Any Complication, Major Complications, and Respiratory Failure

Complication	All pancreatic resection patients (n = 1,061)	Whipple patients (n = 709)	Distal pancreatectomy patients (n = 307)
Any complication	Cr 1.8 mg/dL Severe CKD (stages 4—5)	Cr 1.8 mg/dL	
Major complications	Cr 1.8 mg/dL		
Respiratory failure	Cr 1.8 mg/dL Severe CKD (stages 4—5)	Cr 1.8 mg/dL	Cr 1.8 mg/dL Severe CKD (stages 4—5)

CKD, chronic kidney disease; Cr, creatinine.