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Identifying Risk Factors for Renal Failure and Myocardial Infarction Following Colorectal Surgery

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Background. **The development of acute renal failure and myocardial infarction (MI) following colectomy prolongs recovery and is associated with worse outcomes. The purpose of this study is to identify perioperative factors that predispose patients to an adverse cardiac or renal complication.**

Materials and Methods. **We conducted a retrospective review of colectomies from 2001 to 2009. Patients were evaluated based upon the electronic inpatient record and followed to determine the incidence of acute renal failure (creatinine elevation over 50% of baseline) and myocardial injury.**

Results. **A total of 339 inpatient records were reviewed, of which 134 were female (40%) and 205 male (60%). The mean age was 61.96 ± 16.2 years with 39.5% right hemicolectomies, 22.7% sigmoidectomy, 13.9% Left hemicolectomy, 11.5% total abdominal colectomy, and 6.2% for ileocectomy and transverse colectomy. Within the cohort, 13.9% had baseline renal insufficiency (Cr > 1.4), 7.1% sustained anastomotic leak, 23.9% required postoperative intubation, 15% sustained postoperative sepsis, 11.2% postoperative MI, and 5% clinically significant acidosis. Excluding patients with an anastomotic leak, postoperative intubation, and sepsis, we found that the need for blood product transfusion was associated with postoperative acute renal failure (OR = 7.15 [2.4–20.7]). Preoperative creatinine > 1.5, limited functional capacity, and preoperative systolic blood pressure < 90 mm Hg were all associated with increased MI rates (OR = 15.7 [3.6–66.8], 9.5 [2.1–42.2], 12.0 [5.523–26.072], and 40.6 [1.7–968], respectively).**

Conclusion. **This study demonstrates that several potentially modifiable preoperative and intraoperative factors exist that predispose patients to postoperative cardiac and renal dysfunction in the absence of major surgical complications.** © 2011 Elsevier Inc. All rights reserved.

Key Words: **renal failure; myocardial infarction; complications; colectomy.**

INTRODUCTION

In this era of evidence-based medicine where outcomes following all types of surgeries, including colectomy, are increasingly scrutinized, perioperative management often requires significant emphasis on optimizing patient comorbidities. It is well known that increasing preoperative comorbidities present a higher risk of untoward outcomes. Yet, viewed in the other direction, the onset of major postoperative complications such as anastomotic leak or sepsis also has a dramatic impact on the secondary occurrence of problems with other organ systems, exponentially increasing the overall morbidity and mortality. Two of the more common organs affected are the heart and kidneys, with the development of acute renal failure and/or myocardial injury leading to a more prolonged length of recovery and increased morbidity and mortality [1]. By analyzing the factors associated with successful postoperative recovery, surgeons are able to more clearly determine the optimal clinical management strategy for each individual patient and counsel patients better, allowing patients to make more informed decisions about their health care. Careful preoperative planning and risk factor analysis with modification, where possible, leads to improved perioperative care [2–4]. The purpose of this study was to identify perioperative factors associated

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with the development of acute renal failure and myocardial injury in an uncomplicated recovery, detect differences when associated with a major complication, and to understand who develops acute renal failure and myocardial infarction when divided based upon having a major surgical complication.

METHODS

We received study approval from our local institutional human study review board. We collected retrospective data on all consecutive colectomies performed at a single institution from January 2001 through December 2009. Inclusion criteria included all patients > 18-y-old who underwent emergent and elective colectomies. Those patients with rectal operations were excluded. We reviewed perioperative records, looking specifically for antecedent co-morbidities, laboratory test results including perioperative trends, and the postoperative incidence of a "major surgical complication" defined as prolonged mechanical ventilation requirement, re-intubation, sepsis, sustained acidosis, and anastomotic leak. Preoperative evaluations, including an examination by primary care providers and clinical perioperative monitoring, were based on standard clinical practice guidelines. Intraoperative anesthetic monitoring (i.e., lines, echocardiography, and anesthetic type) was performed according to individual routine clinical practice as determined by the anesthesia provider. Postoperatively, patients were monitored either in the intensive care unit, cardiac care ward, or surgical ward, depending, in part, on their risk profile assessment and perioperative stability. The postoperative course was reviewed from the electronic medical record to determine those patients sustaining our primary outcomes of interest: postoperative in-hospital myocardial infarction and/or acute renal failure. Myocardial injury was defined as a troponin elevation above our laboratory's upper limit of normal, while myocardial infarction (MI) was defined as a rise in cardiac biomarkers (typically troponin measurement) above the 99th percentile of the upper reference limit, with corresponding changes in the EKG. In each instance, cardiology consultation and assessment was performed to confirm our findings. Acute renal failure was defined as a creatinine elevation greater than 50% of baseline. Baseline renal insufficiency was defined as a serum creatinine > 1.4. We defined an uncomplicated recovery was defined as one without the development of sepsis, anastomotic leak, acidosis, or cardiopulmonary failure [i.e., (re)-intubation, congestive heart failure, new onset symptomatic arrhythmia] to attempt to separate those patients developing an MI or acute renal failure independent of and not secondary to a major surgical complication.

Statistical Analysis

The primary endpoint was the development of a postoperative myocardial injury and/or acute renal failure, as defined above. Secondary endpoints included mortality, the development of other complications (i.e., wound infection, urinary tract infection, pneumonia), and hospital length of stay. Statistical analysis was performed using PASW 18.0 (SPSS Inc.; Chicago, IL). Descriptive statistics were used to describe the study population and continuous variables are shown as mean ± standard deviation. Dichotomous variables are presented as a rate. The data were then analyzed using Student's t-tests for continuous variables and χ^2 tests for categorical variables, where appropriate. Multivariate logistic regression analysis was performed, including all related preoperative factors with $P < 0.1$ on univariate analysis such as alcohol and tobacco use, urgency of the case, and operative variables (i.e., blood loss, transfusion requirements, physiologic variables including vital signs and laboratory analysis). For all statistical analysis, final $P < 0.05$ was considered statistically significant. A predicted probabilities curve was developed to analyze the impact of preoperative continuous variables on the probability of sustaining a postoperative complication.

RESULTS

During the study interval, 339 patients met inclusion criteria. The mean age was 61.9 ± 16.2 y, with 205 patients (60.5%) being male. For the entire cohort, ASA class was categorized as 3.2% class I, 62.4% class II, and 29.9% class III. Comorbidities within the entire population demonstrated 45% with hypertension, 24% with hyperlipidemia, 21% with diabetes, 17% with chronic obstructive pulmonary disease (COPD), 11% with baseline coronary artery disease, and 6.8% with pre-existing renal insufficiency. Overall, 13.4% of cases were performed on an emergent basis, with less emergency cases occurring in those who did not have a major complication (9.8% *versus* 21.6%, $P = 0.003$, Table 1). The procedures performed were right hemicolectomy (39.5%), sigmoidectomy (22.7%), left hemicolectomy (13.9 %), total abdominal colectomy (11.5%), and ileocectomy and transverse colectomies (6.2%). Procedure type did not have an impact on incidence of developing a major surgical complication (Table 1).

Overall, 11.8% of all patients sustained acute renal failure and 11.2% sustained myocardial infarction. Overall, 59 patients (17.4%) received blood transfusions (12.2% without and 29.4% with a major surgical complication, $P < 0.001$). The overall in-hospital mortality within the cohort was 5.9% (1.4% without a major complication, 16.7% with a major complication, $P < 0.001$). Furthermore, in the absence of a major surgical complication, the mortality rate of those who sustained acute renal failure or an MI was not significantly different to those who did not develop either of these conditions (6.3% *versus* 0.9%, $P = 0.065$ and 0% *versus* 1.3%, $P = 0.729$; respectively). Conversely, of those who sustained a major surgical complication, the mortality rate of those who developed acute renal failure or an MI was increased or equivalent to those who did not develop either of these conditions (30.4% *versus* 12.7%, $P = 0.044$ and 34.5% *versus* 9.6%, $P = 0.002$, respectively).

Postoperative major surgical complications occurred in 92 patients (27%), encompassing postoperative anastomotic leak (7.1%), respiratory failure (23.9%), sepsis (15%), and clinically significant acidosis (5%). A major surgical complication increased the overall time to hospital discharge by 16.9 d (24.7 ± 20.5 *versus* 7.8 ± 5.7 d, $P < 0.0001$). Acute renal failure increased time to hospital discharge by 5.1 d (7.8 ± 5.8 *versus* 12.9 ± 8.8 d, $P < 0.001$) in patients who had an uncomplicated recovery ($n = 247$) and increased hospital stay by 13 days (24.7 ± 20.5 *versus* 37.7 ± 26.4, $P = 0.039$) in patients with a major surgical complication. Additionally, in the

TABLE 1

Demographics and Outcomes Within the Study Population

Preoperative comorbidities	Overall ($n = 339$)	Without major complication ($n = 247$, 73%)	Major complication* ($n = 92$, 27%)	P value
Cardiovascular ($n = 203$)	59.9%	58.2%	63.7%	0.34
Pulmonary ($n = 109$)	32.2%	27.0%	44.1%	0.002
Limited functional capacity ($n = 49$)	14.5%	12.2%	19.6%	0.077
Renal Insufficiency ($n = 39$)	11.5%	6.3%	23.5%	<0.001
ETOH use ($n = 150$)	44.2%	47.3%	37.3%	0.089
Tobacco Use ($n = 152$)	44.8%	45.1%	44.1%	0.861
Demographic variable				
Age (y)	61.96 ± 0.94	16.5 ± 1.1	15.015 ± 1.6	0.004
Case duration (min)	228.2 ± 10.5	164.1 ± 12.1	191.8 ± 20.1	0.324
Blood products total (mL)	127.1 ± 23.5	71.0 ± 20.5	257.5 ± 60.1	0.004
Intravenous crystalloids (mL)	3832.8 ± 160.9	2114.6 ± 175.0	2734.6 ± 347.3	0.207
Blood loss (mL)	383.2 ± 36.9	399.7 ± 28.8	913.6 ± 100.3	0.161
Preoperative hemoglobin (g/dL)	12.706 ± 0.1281	2.3 ± 0.15	2.4 ± 0.24	0.124
Preoperative creatinine (g/dL)	1.099 ± 0.0418	0.68 ± 0.0448	0.89 ± 0.09	0.004
Emergency	N= 45, 13.3%	N= 24, 9.8%	N= 19, 21.6%	0.003
Surgical procedures				
Right hemicolectomy ($n = 134$)	39.5%	42.6%	32.4%	0.541
Left hemicolectomy ($n = 47$)	13.9%	12.7%	16.7%	
Sigmoidectomy ($n = 77$)	22.7%	22.4%	23.5%	
Total abdominal colectomy ($n = 39$)	11.5%	10.5%	13.7%	
Ileocectomy ($n = 21$)	6.2%	5.5%	7.8%	
Transverse colectomy ($n = 21$)	6.2%	6.3%	5.9%	
Postoperative outcomes				
Acute renal failure ($n = 40$)	11.8%	7.0%	22.8%	<0.001
Myocardial injury ($n = 38$)	11.2%	3.8%	28.4%	<0.001
Mortality ($n = 20$)	5.9%	1.3%	16.7%	<0.001
Hospital length of stay (overall, d)	12.0 ± 13.6	7.8 ± 5.8	24.7 ± 20.5	<0.001
Acute renal failure	22.6 ± 21.3	12.9 ± 8.8	37.7 ± 26.4	0.023
Myocardial injury	24.3 ± 21.2	10.0 ± 5.2	31.0 ± 22.6	0.003

ARF = acute renal failure; MI = myocardial infarction; ETOH = alcohol.

*Major complication is defined as having a postoperative leak, intubation, or sepsis.

absence of a major surgical complication ($n = 247$), 56.3% of those developing acute renal failure also developed an infectious complication (pneumonia, urinary tract infection, wound infection, etc.), compared with 30.3% in those not sustaining acute renal failure ($P = 0.032$). In patients without major surgical complications who sustained acute renal failure, multivariate analysis demonstrated that the risk increased 7.1-fold (95% CI [2.4–20.7], $P = 0.004$) when blood product transfusions were needed intraoperatively. Factors that trended toward significance for the development of renal failure were the transduction of central venous pressure monitoring or arterial blood pressure monitoring by the anesthesiologist ($P = 0.053$ and $P = 0.057$, respectively).

In a similar analysis, myocardial injury was associated with a 12.3-d increase in hospital length of stay (12.0 ± 13.6 versus 24.3 ± 21.2 d, $P < 0.001$) for the overall cohort, 2.2 d (7.8 versus 10 d, $P = 0.31$) for those with an uncomplicated recovery, and by 6 d (24.7 versus 31 d, $P = 0.173$) when associated with a major surgical complication (Table 1). Multivariate analysis demonstrated that, in patients without significant complications, a preoperative creatinine ≥ 1.5 was associated with an increased risk (OR = 15.7 [3.6– 66.8], $P = 0.001$), a preoperative SBP < 90 (OR = 12.0 [5.52–26.07], $P = 0.041$), and limited functional capacity (OR = 9.5 [2.1–42.2], $P = 0.002$) were associated with an increased rate of postoperative myocardial injury (Table 2). A predicted probabilities curve also demonstrated an increased risk of myocardial injury with increasing preoperative creatinine levels, and this held true even for patients who sustained a major postoperative complication (Fig. 1). The only factor that demonstrated a trend toward significance in the development of myocardial infarction was an intraoperative blood product transfusion (OR = 3.885 [0.9–16.5], $P = 0.066$).

DISCUSSION

While the development of acute renal failure and myocardial infarction secondary to major postoperative complications is often uncontrollable and has a tremendous negative impact on overall outcomes, isolating potential causes of these complications independent of the

TABLE 2

Multivariate Analysis of Perioperative Variables in Patients not Sustaining a Major Complication

Variable	Acute renal failure		Myocardial injury	
	Hazard ratio [95% confidence interval]	*P* value	Hazard ratio [95% confidence interval]	*P* value
Gender	1.1 [0.3–3.7]	0.801	2.5 [0.2–25.]	0.416
Pulmonary disease	2.8 [0.9–9.0]	0.07	2.1 [0.2–18.1]	0.466
Cardiovascular disease	2.3 [0.6–8.9]	0.203	N/A	N/A
Renal disease*	2.0 [0.3–11.9]	0.426	15.7 [3.6–66.8]	0.001
Functional limitations	1.1 [0.2–5.6]	0.821	9.5 [2.1–42.2]	0.002
Alcohol use	0.7 [0.2–2.3]	0.573	1.9 [0.2–14.]	0.503
Tobacco use	0.7 [0.2–2.3]	0.578	1.0 [0.1–9.5]	0.986
Transfusion	7.5 [1.9–28.6]	0.003	4.2 [0.4–43.]	0.224
SBP < 90 on preoperative examination	2.4 [0.7–9.5]	0.18	12.0 [5.523–26.072]	0.041
Elective *versus* emergent indication	0.8 [0.1–5.2]	0.884	0.1 [0.0–3.6]	0.269

*Determined by baseline creatinine.

more drastic outcomes may be overlooked. As such, it may be more important to analyze the impact of acute renal failure and myocardial injury incidence and results in the context of defining potentially modifiable factors associated with prolonged recovery and poor outcomes. By identifying these physiologic factors associated with a new onset of acute renal failure and cardiac complications, individual risk assessment and appropriate intervention can take place.

This study had three specific goals: to identify perioperative factors associated with the development of acute renal failure and myocardial injury in an uncomplicated recovery, to determine differences when associated with a major complication, and to analyze the impact, if any, of preoperative creatinine levels on the development of postoperative myocardial injury. As shown in the current study, acute renal failure and myocardial injury are significant events in postoperative recovery whether or not a major complication occurs. In the absence of a major complication, acute renal failure development was associated with a 5-d increase in hospital length of stay and was nearly double the rate of other infectious complications (56% *versus* 30%). As it is difficult to determine the inciting event, the immediate implication is that patients with postoperative acute renal failure should undergo a prompt and very thorough workup to identify secondary potential infectious complications when none are immediately obvious. However, as or more important, this also highlights the need for precise measures to be in place to minimize or prevent infectious complications, such as ensuring appropriate SCIP guidelines regarding proper antibiotic timing and length of therapy are followed, pathways regarding early ambulation and pulmonary toilet are in place, no delays in removal of catheters and lines, and avoiding breaks of sterile condition or

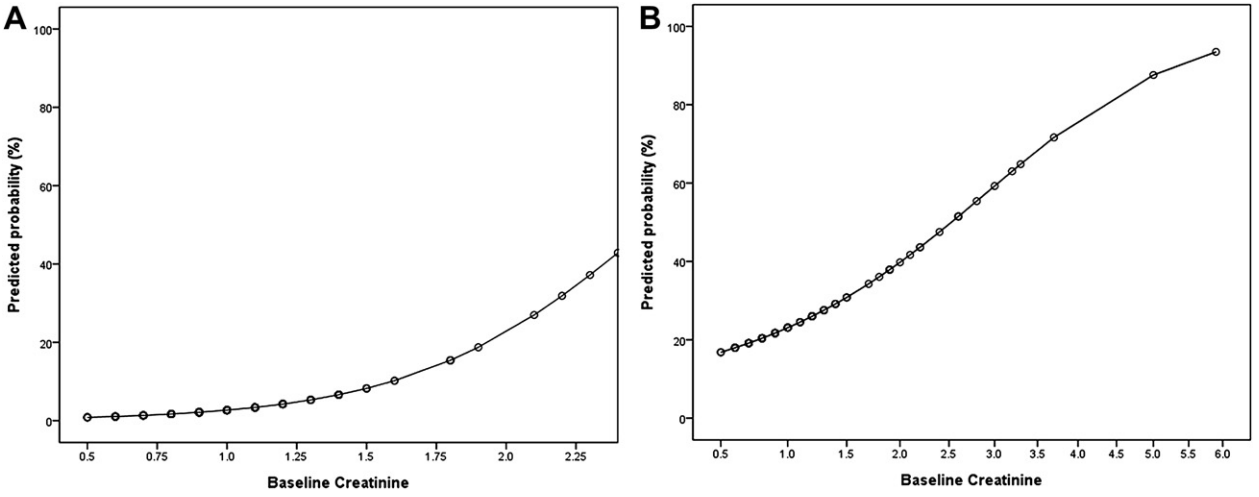

FIG. 1. Predicted probabilities curves demonstrating the association between preoperative creatinine levels and postoperative myocardial injury, (A) without a major complications, (B) with a major complication.

intraoperative spillage at all costs. While not surprising, this is particularly important as mortality was nearly 13-fold higher with a major complication (Table 1). Even more concerning, though, in the absence of major complications, 6.3% of patients with acute renal failure died, compared with only 0.9% ($P = 0.065$) without the development of acute renal failure. Though not statistically significant, likely due to small numbers of overall mortality, it underscores the need to have measures in place to avoid or rapidly correct this complication.

We also determined that there is an independent and direct impact of preoperative creatinine levels on the incidence of postoperative myocardial injury. Though this may seem inherently intuitive, this study links the estimated rise in incidence of postoperative myocardial infarction to the preoperative baseline creatinine in colorectal surgery. Once again, this highlights a need to identify these patients prior to surgery, even those with mild elevations in creatinine, for a possible referral to their primary care providers or a specialist for medication review, further testing, or even evaluation for occult cardiac disease. Not surprisingly, subsequent myocardial injury, even in the absence of a major complication, almost doubled the overall hospital length of stay (and inferred costs), primarily from required testing, intervention, and recovery (Table 1). By linking the preoperative variables and postoperative outcomes, the physiologic role of renal function is highly significant in determining the overall physiologic tolerance to major colorectal surgery. This study allows a unique comparison between patients with major complications and those without major complications through a direct analysis of the two different predicted probabilities myocardial injury curves (Fig. 1) The predicted probabilities curve for major complications (Fig. 1B) demonstrates an almost linear association in comparison to those without major complications (Fig. 1A), where there is an exponential relationship. This likely signifies that renal function is highly integral to the tolerance of major surgery and that at a certain level and inflection point, such as creatinine > 1.5, the physiologic reserve required to successfully recover from surgery is less in some patients, and as the added stress of a major complication completely drains this compensatory buffer.

The current study also found that in the absence of major complications, the only factor associated with increased postoperative acute renal failure was intraoperative blood transfusions. Consistent with past studies that have also demonstrated increased complication rates with transfusions, our findings may represent an activation of the immune system with homologous blood administration and cytokine release systemically [5–7]. It does not appear to be a result of intraoperative hypotension treated with blood, as hypotension was not found to have an association with renal failure, only myocardial infarction. Additionally, it does not appear to be a result of transfusion reaction, as we did not have any cases, or correlate with the amount of products transfused (data not shown). This association needs further study to fully understand the exact relationship. Additionally, myocardial infarction was higher postoperatively in patients with chronic renal insufficiency (creatinine > 1.5), limited functional capacity, and preoperative hypotension [4]. Previous studies, especially following vascular surgery, have similarly found an increase in secondary cardiovascular events in patients with underlying chronic renal disease, including a greater than 2-fold risk of cardiovascular death [8, 9]. Interestingly, one series following carotid surgery found that even in those patients with moderate renal failure (eGFR 30–59), 38% had received ACE-inhibitors, 74% were on statins, and only 34% had seen a nephrologists [8]. Although the exact link between myocardial dysfunction and renal failure is likely multi-factorial, this again highlights the need to identify these patients and intervene wherever possible prior to undergoing elective and semi-elective surgery. These, even subtle, abnormalities in perioperative physiologic variables may be critically important in fully identifying the overall risk associated with colorectal surgery and optimizing outcomes [4].

We have attempted to quantify the risk of MI and acute renal failure in patients who develop significant postoperative complications (leak, respiratory failure, sepsis), finding a 9-fold increased rate of myocardial infarction and a 2.75-fold increased rate of acute renal failure [10]. This is not surprising, considering that the physiologic impact of life-threatening complications is profound, and dramatically increases the stress on vital end organs, yet early identification of these complications allows the opportunity to implement changes, embarking on early medical intervention, and a more rapid return to the operating room when needed, to potentially mitigate the overall negative impact. This likely requires more intensive postoperative care through higher acuity monitoring, measurement of physiologic parameters, and physician monitoring that may extend beyond the intraoperative environment [11]. It may be this patient cohort that benefits from clearly defined postoperative multidisciplinary team management, including the trend of clinical pathways to maximize overall care [2, 4]. Clearly, patients with respiratory failure and sepsis will have more aggressive care needs, as these patients are typically being cared for in an intensive care setting; however, identification of patients preoperatively with more subtle changes such as a creatinine $>$ 1.5 that may not raise an issue at first would not only herald a mandatory preoperative evaluation, but invoke a “red-flag” for closer observation perioperatively.

The limitations of this study are the inherent limitations with retrospective studies. The chart review is limited to the accuracy of the documentation and overall assessment made by the physicians at the time of the initial surgery. Also this represents a single center study with inherent biases involving the systems of postoperative care, and any systematic problem intrinsic to the institution may not necessarily be applicable to other centers. This is partially mitigated by the longer study interval with rotating staff. Additionally, the ability to determine the exact values of all variables and to associate that with outcomes and 100% follow-up are often not possible when using a large population database, allowing more comprehensive data collection and analysis of multiple highly relevant variables.

CONCLUSION

The current study analyzed variables specifically related to the development of acute renal failure and myocardial infarction, and ultimately worse patient outcomes, following colorectal surgery. In quantifying these risks to include perioperative transfusion and identifying preoperative high-risk findings (creatinine > 1.5), physicians can more readily recognize those patients at risk, intervene as soon as possible, counsel patients appropriately, and hopefully minimize the risks of undergoing major abdominal surgery.

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