The American Journal of Surgery (2014) 208, 41-44

The American Journal of Surgery

Clinical Science

Unique risks for mortality in patients with end-stage renal disease undergoing nonemergent colorectal surgery

James J. Liu, B.A., Adrian Y. Kohut, B.S., David E. Stein, M.D., Richard Sensenig, M.S., M.S.E.E., Juan L. Poggio, M.D.*

Department of Surgery, Division of Colorectal Surgery, Drexel University College of Medicine, 245 North 15th Street, Suite 7150 NCB, Philadelphia, PA 19102, USA

KEYWORDS:
American College of Surgeons National Surgical Quality Improvement Program;
End-stage renal disease;
Colorectal surgery;
Mortality;
Serum creatinine

Abstract

BACKGROUND: The aim of this study was to identify unique risk factors for mortality in patients with end-stage renal disease undergoing nonemergent colorectal surgery.

METHODS: A multivariate logistic regression model predicting 30-day mortality was constructed for patients with end-stage renal disease undergoing nonemergent colorectal procedures. Data were obtained from the National Surgical Quality Improvement Program (2005–2010).

RESULTS: Among the 394 patients analyzed, those with serum creatinine levels >7.5 mg/dL had .07 times the adjusted mortality risk of those with levels <3.5 mg/dL. For colorectal surgery patients, the average serum creatinine level was 5.52 ± 2.6 mg/dL, and mortality was 13% (n = 50).

CONCLUSIONS: High serum creatinine was associated with a lower risk for mortality in patients with end-stage renal disease, even though creatinine is often considered a risk factor for surgery. These results show how variables from a patient-centered subpopulation can differ in meaning from the general population.

Patients with end-stage renal disease (ESRD) on dialysis make up a significant portion of our patient population: 209,094 and counting according to the United States Renal Data System.[1] Studies have shown that patients with ESRD undergoing colorectal surgery have poorer outcomes than the general population.[2] Yet information has been limited on what preoperative risks, especially laboratory values, influence postoperative outcomes in patients with ESRD. Investigators in the past have either struggled with sample size[3] or could not incorporate laboratory values into their analyses.[2]

For this reason, we chose to use the American College of Surgeons National Surgical Quality Improvement Program (NSQIP) database, which has tracked >200,000 surgical procedures since its inception.[4] This database is a tool that records perioperative risk factors for addressing surgical morbidity and mortality. Our objective was to use the NSQIP data to create a multivariate model to identify unique risk factors predicting mortality in patients with ESRD undergoing nonemergent colorectal procedures.

The American College of Surgeons National Surgical Quality Improvement Program and its participating hospitals are the sources of the data used herein; they have not verified and are not responsible for the statistical validity of the data analysis or the conclusions derived by the authors.

The authors declare no conflicts of interest.

* Corresponding author. Tel.: +1-215-762-175; fax: +1-215-762-8389.
E-mail address: jpoggio@msn.com

Manuscript received April 24, 2013; revised manuscript July 16, 2013

http://dx.doi.org/10.1016/j.amjsurg.2013.08.034

Methods

Patient selection

We performed a query of the NSQIP database and obtained patient information recorded between 2005 and 2010 from the NSQIP Participant Use Data File. Colorectal cases were identified using Current Procedural Terminology codes (Table 1). All emergent cases (patients who required intervention within 12 hours of either symptom onset or admission) were excluded from the study. Then we selected for patients who were on dialysis. This was defined in the NSQIP database as a patient with acute or chronic renal failure requiring dialysis within 2 weeks of surgery. From these dialysis patients, we excluded those with acute renal failure (those with increasing azotemia and creatinine >3 mg/dL as defined by the NSQIP). This remaining pool of patients formed our study population: nonemergent cases of colorectal surgery patients requiring long-term renal dialysis (patients with ESRD). This study was reviewed by the Drexel University College of Medicine institutional review board and was deemed appropriate for exemption from institutional review board oversight because no personal identifiers were used.

Predictor and postoperative variables

Within the NSQIP database, we selected 35 perioperative candidate variables of interest on the basis of previous clinical experience. The variables included demographic information such as age, sex, race, and body mass index (divided into categories of underweight, normal, overweight, and obese classes 1–3). Preoperative patient risks included peripheral vascular disease, transient ischemic attacks, cerebral vascular accidents, chronic obstructive pulmonary disease, smoking, hypertension, and corticosteroid use. Additional presurgical variables included functional status (totally dependent), ascites, and dyspnea (at rest or during moderate exertion).

Conditions that can lead to excessive bleeding requiring hospitalization (eg, hemophilia, thrombocytopenia, nondiscontinued chronic anticoagulation therapy) were defined as bleeding disorders. Operative variables included laparoscopic versus open, wound class (contaminated or dirty/infected), operative time, ventilator dependence, and relative value unit. Preoperative laboratory values, including sodium, hematocrit, white blood cell count, and platelet count, were made categorical on the basis of previous studies.[5] We categorized creatinine levels into quartiles. Our primary outcome of interest was 30-day mortality regardless of discharge or transfer status.

Table 1 Procedure types for colorectal surgery

Current Procedural Terminology code	Type	Description
44205	Laparoscopic	Ileocolic resection
44204	Laparoscopic	Partial colectomy
44206	Laparoscopic	Hartmann's procedure
44207, 44208	Laparoscopic	Low pelvic anastomosis
44210	Laparoscopic	Total abdominal colectomy
44160	Open	Ileocolic resection
44140	Open	Partial colectomy
44143	Open	Hartmann's procedure
44145, 44146	Open	Low pelvic anastomosis
44150	Open	Total abdominal colectomy
44155	Open	Total proctocolectomy/ end ileostomy

Statistical analysis

To identify preoperative predictors of mortality and postoperative complications, we created multivariate logistic regression models for each of the outcomes. Each multivariate model began with 35 candidate variables selected a priori from the NSQIP database. Using univariate analysis, we ran these variables against each of the outcomes. We then selected univariately significant variables ($P < .10$) to create the full model. The full model was then reduced by stepwise selection on the basis of the Akaike information criterion and clinical judgment.[6] We used variables that remained after model reduction for the final, adjusted multivariate model that we report in this study. Model discrimination was evaluated using the C-statistic, obtained from the receiver operating characteristic curve. The C-statistic describes a model's accuracy in differentiating those with and those without an outcome. Calibration with the Hosmer-Lemeshow test determined the agreement between the observed and expected outcomes. All analysis was conducted using R version 2.15.0 (R Foundation for Statistical Computing, Vienna, Austria).

We removed missing variables by listwise deletion. We excluded any variable with >10% missing data from the univariate analysis. Variables not considered because of excessive missing data were preoperative albumin, prothrombin time, international normalized ratio, alkaline phosphate, and aspartate aminotransferase.

Results

A total of 459 patients met the inclusion criteria. Of those, 394 (86%) remained in the final models after listwise deletion of missing data during univariate selection. The average age was 64 years, with a near equal distribution of men and women (Table 2). Open partial colectomy (n = 144), ileocolic resection (n = 53), and open low pelvic anastomoses (n = 44) were the most common operations.

The mortality rate was 13% (n = 50). In the final multivariate model predicting surgical mortality, functional status (odds ratio, 3.46; 95% confidence interval, 1.49–8.05),

Table 2 Characteristics of patients with end-stage renal disease on dialysis in the American College of Surgeons National Surgical Quality Improvement Program, 2005 to 2010 (n = 394)

Variable	Value
Age (y)*	64.25 ± 13.47
<55	92 (23%)
55–65	96 (24%)
65–75	107 (27%)
>75	99 (25%)
Men	198 (50%)
BMI (kg/m^2)	28.23 ± 7.67
Normal	128 (32%)
Underweight	17 (4%)
Overweight	121 (31%)
Obese class 1	62 (16%)
Obese class 2	39 (10%)
Obese class 3	27 (7%)
Peripheral vascular disease	43 (11%)
Transient ischemic attack	27 (7%)
Cerebral vascular accident	66 (17%)
Steroid use	32 (8%)
Ascites	20 (5%)
Dyspnea, presurgical	82 (21%)
Bleeding disorder	65 (16%)
Operation time (min)	155.8 ± 82.88
Open (vs laparoscopic)†	303 (80%)
Hematocrit (%)	34.09 ± 6.1
Normal (35–45)	159 (40%)
Mild low (30–35)	123 (31%)
Severely low (<30)	99 (25%)
Mild/severely high (>45)	13 (3.3%)
WBC count (×1,000/mm^3)	8.64 ± 4.85
Normal (4–10)	252 (63%)
Mild/severely low (<4)	31 (7.9%)
Mild high (10–15)	71 (18%)
Severely high (>15)	40 (10%)
Creatinine (mg/dL)	5.52 ± 2.6
<3.5	97 (25%)
3.5–5.3	99 (25%)
5.3–7.2	99 (25%)
>7.2	99 (25%)

Data are expressed as mean ± SD or number (percentage).
BMI = body mass index; WBC = white blood cell.
*Age >90 years was recorded as 90 years.
†Three hundred three patients (80%) underwent open surgeries; the remaining procedures were laparoscopic.

dyspnea (odds ratio, 2.51; 95% confidence interval, 1.22–5.16), and bleeding disorders (odds ratio, 2.56; 95% confidence interval, 1.19–5.52) were all significant predictors of 30-day mortality (Table 3).

High serum creatinine levels were inversely associated with postoperative mortality compared with patients in the reference group (<3.5 mg/dL). After controlling for potential confounding factors accounted for in the model, the risk for mortality in patients with serum creatinine values between 5.3 and 7.2 mg/dL was almost one quarter (odds ratio, .22; 95% confidence interval, .09–.54) the risk

Table 3 Odds ratios, 95% confidence intervals, and *P* values for variables predicting mortality in patients with end-stage renal disease (n = 394)

Predictor	Adjusted odds ratio (95% confidence interval)	*P*	Case mortality (% of all mortality)
Creatinine (mg/dL)			
<3.5	1	—	31 (62%)
3.5–5.3	.23 (.09–.54)	<.001	9 (18%)
5.3–7.2	.22 (.09–.54)	.001	8 (16%)
>7.2	.07 (.02–.34)	<.001	2 (4%)
Functional status (totally dependent)	3.46 (1.49–8.05)	.004	16 (32%)
Bleeding disorders	2.56 (1.19–5.52)	.016	17 (34%)
Dyspnea	2.51 (1.22–5.16)	.013	22 (44%)
Age (y)			
55	1	—	5 (10%)
55–65	1.84 (.54–6.32)	.332	10 (20%)
65–75	2.76 (.87–8.77)	.086	16 (32%)
>75	2.55 (.81–8.07)	.111	19 (38%)

Hosmer-Lemeshow statistic = 8.017 (P = .432, df = 8); C-statistic = .822.

in the reference group. The risk for mortality in patients with serum creatinine values >7.2 mg/dL was .07 times (95% confidence interval, .02–.34) that of the reference group (Table 3).

Multivariate model calibration and discrimination were tested with training samples. The Hosmer-Lemeshow test for calibration describes how well the expected probabilities fit with the observed probabilities. Hosmer-Lemeshow results were insignificant ($P > .05$), suggesting that the predicted probabilities did not deviate from the expected results. The C-statistics for all the models also demonstrated that the model was significant in differentiating the positive and negative outcomes of interest, including mortality (Table 3).

Comments

We identified patients with ESRD on dialysis undergoing nonemergent colorectal surgery to create a multivariate logistic regression model that predicted 30-day mortality. Our adjusted model shows an association between high serum creatinine level and lowered risk for mortality. In the general population, high serum creatinine values are associated with greater risk for mortality.[5,7,8]

One explanation for this difference is the role of serum creatinine in ESRD as a surrogate marker for nutritional status. Ordinarily, serum creatinine level is used to estimate glomerular filtration rate when assessing kidney function.[9] Reduced kidney function, therefore, is associated with increased risk in surgery.[5,7,8,10] However, in patients with advanced kidney disease, serum creatinine no longer becomes informative of glomerular filtration rate.[11] Serum creatinine level in this case may be used as an estimate of muscle mass[12–14] and indirectly as a surrogate marker for nutritional status. (In patients on long-term hemodialysis, high serum creatinine levels are inversely related to 5-year mortality.[14]) Thus, we would expect patients with ESRD undergoing colorectal surgery who have greater muscle mass to be better nourished and to better withstand the physiologic demands of surgery.

The population of patients with ESRD is unique given the extent of their comorbidities and the physiologic impact of dialysis. For this reason, variables (eg, creatinine) from the general population can convey different meaning in the context of a subpopulation. If we neglect analysis of patient-specific cohorts, such as patients with ESRD, we may overlook risk factors that may be significant in determining critical surgical decisions.

The NSQIP database does not track the timing of dialysis in relation to surgery, so it is conceivable that the timing of dialysis may have affected some of our data. However, as with all database studies, there are some limitations inherent to the data analyzed. On the basis of the size of the cohort studied, we do not believe this single factor significantly affects our data.

One limitation of this study was that we could not validate the model given the sample size of the population. Ideally, a portion of the population that was not used to build the model is set aside to test, or validate, the model.[2,5,7] Such validation studies can be conducted in the near future as the size of the NSQIP database continues to grow. Additionally, the variables and outcomes in our model are limited by what the NSQIP database tracks. For example, NSQIP does not record operative mortality beyond the standard 30-day window, which has been suggested to underreport mortality.[15] Also, we elected not to use the International Classification of Diseases, Ninth Revision, to further homogenize our sample population. Billing codes are not the perfect replacement for a clinical diagnosis and we did not want to misrepresent the indications for surgery with a surrogate for operative diagnosis. Ideally, we would review each case individually on the basis of clinical data. However, this is not within the scope of the NSQIP database.

Despite these limitations, we have identified the predictive nature of serum creatinine values in patients with ESRD undergoing colorectal surgery (n = 394 vs 28).[3] Additionally, the sample size allowed us to create a multivariate model to adjust for comorbid risk factors common in patients with ESRD.

Conclusions

Our results concerning creatinine level and its association with lowered mortality risk suggest that the same variables from the general population can convey different meaning in the context of ESRD. Variables used to construct risk models are important clinically because they influence surgical decisions. NSQIP and other quality improvement databases offer an immense amount of surgical information. In cases in which sample size is sufficient, it may be worthwhile to supplement or even revisit known risk factors[5,7] with patient-centered subpopulations.[16]

References

1. United States Renal Data System. USRDS 2012 annual data report: atlas of chronic kidney disease and end-stage renal disease in the United States. Available at: http://www.usrds.org/2012/slides/indiv/v2index.html. Accessed June 18, 2013.
2. Drolet S, Maclean AR, Myers RP, et al. Morbidity and mortality following colorectal surgery in patients with end-stage renal failure: a population-based study. Dis Colon Rectum 2010;53:1508–16.
3. Yasuda K, Tahara K, Kume M, et al. Risk factors for morbidity and mortality following abdominal surgery in patients on maintenance hemodialysis. Hepatogastroenterology 2007;54:2282–4.
4. Henderson WG, Daley J. Design and statistical methodology of the National Surgical Quality Improvement Program: why is it what it is? Am J Surg 2009;198(suppl):S19–27.
5. O'Brien MM, Gonzales R, Shroyer AL, et al. Modest serum creatinine elevation affects adverse outcome after general surgery. Kidney Int 2002;62:585–92.
6. Austin PC, Tu JV. Automated variable selection methods for logistic regression produced unstable models for predicting acute myocardial infarction mortality. J Clin Epidemiol 2004;57:1138–46.
7. Cohen ME, Bilimoria KY, Ko CY, et al. Development of an American College of Surgeons National Surgery Quality Improvement Program: morbidity and mortality risk calculator for colorectal surgery. J Am Coll Surg 2009;208:1009–16.
8. Dehne MG, Junger A, Hartmann B, et al. Serum creatinine and perioperative outcome–a matched-pairs approach using computerised anaesthesia records. Eur J Anaesthesiol 2005;22:89–95.
9. Stevens LA, Coresh J, Greene T, et al. Assessing kidney function–measured and estimated glomerular filtration rate. N Engl J Med 2006;354:2473–83.
10. Mathew A, Devereaux PJ, O'Hare A, et al. Chronic kidney disease and postoperative mortality: a systematic review and meta-analysis. Kidney Int 2008;73:1069–81.
11. Beddhu S, Samore MH, Roberts MS, et al. Creatinine production, nutrition, and glomerular filtration rate estimation. J Am Soc Nephrol 2003;14:1000–5.
12. Keshaviah PR, Nolph KD, Moore HL, et al. Lean body mass estimation by creatinine kinetics. J Am Soc Nephrol 1994;4:1475–85.
13. Schutte JE, Longhurst JC, Gaffney FA, et al. Total plasma creatinine: an accurate measure of total striated muscle mass. J Appl Physiol 1981;51:762–6.
14. Kalantar-Zadeh K, Streja E, Kovesdy CP, et al. The obesity paradox and mortality associated with surrogates of body size and muscle mass in patients receiving hemodialysis. Mayo Clin Proc 2010;85:991–1001.
15. Visser BC, Keegan H, Martin M, et al. Death after colectomy: it's later than we think. Arch Surg 2009;144:1021–7.
16. Kwok AC, Lipsitz SR, Bader AM, et al. Are targeted preoperative risk prediction tools more powerful? A test of models for emergency colon surgery in the very elderly. J Am Coll Surg 2011;213:220–5.