# Impact of Renal Insufficiency on Short-Term Morbidity and Mortality after Lower Extremity Revascularization: Data from the Department of Veterans Affairs' National Surgical Quality Improvement Program

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*Abstract*. Few data are available on the impact of renal insufficiency on short-term operative outcomes after lower extremity surgical revascularization. We used prospectively collected data from the Department of Veterans Affairs' National Surgical Quality Improvement Program (NSQIP) to explore the association with renal dysfunction of adverse outcomes occurring within 30 d of lower extremity surgical revascularization in a cohort of all patients undergoing at least one lower extremity surgical revascularization from 1/1/94 to 9/30/01 ($n$ = 18,217). Even moderate renal insufficiency (estimated GFR 30-59cc/min/1.73m$^2$) was associated with an increased incidence of postoperative death (adjusted odds ratio (OR) 1.44, 95% confidence interval (CI), 1.17 to 1.77, $P = 0.001$), cardiac arrest (OR 1.43, CI 1.09 to 1.88, $P = 0.011$), myocardial infarction (OR 1.68, 1.39 to 2.16, $P < 0.001$), unplanned intubation (OR 1.69, CI 1.39 to 2.07, $P < 0.001$) and prolonged intubation (OR 1.57, CI 1.28 to 1.94, $P < 0.001$) within 30 d of lower extremity revascularization. However, the incidence of wound infection and graft failure requiring return to the operating room did not appear to be substantially higher in this group. Our data also show that patients with renal insufficiency undergoing revascularization were more likely to require distal procedures and to present with limb-threatening infection compared to those with normal renal function. Efforts to improve pre-and post-operative care in patients with renal insufficiency undergoing lower extremity revascularization should take into account the increased incidence of postoperative death and cardiopulmonary complications in this group in addition to more traditional concerns about operative site complications. Further studies are needed to explore reasons for the higher rate of limb-threatening infection in patients with renal insufficiency undergoing revascularization.

Peripheral vascular disease requiring operative intervention (*i.e.* amputation or revascularization) is more prevalent among patients with renal insufficiency than in those with normal renal function (1–3). High serum creatinine is associated with poor long-term outcomes after lower extremity revascularization (4) and numerous small retrospective surgical series of revascularization in patients with advanced renal insufficiency have now shown that these patients are at increased risk for short- and long-term post-operative mortality and graft failure compared to patients with normal renal function (5–23).

However, few data are available to patients, families and health care providers regarding the association of specific adverse outcomes for patients with renal insufficiency after lower extremity revascularization surgery. Large variations in patient characteristics (such as inclusion of patients not yet requiring dialysis or renal transplant patients), indications for surgery and nature of surgery performed exist between retrospective surgical series. Therefore, it has proven difficult to

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determine from single center case series whether adverse outcomes in patients with renal insufficiency simply reflect differences in patient disease burden, quality of pre-operative care, and/or type of revascularization procedure performed or whether renal insufficiency is independently associated with poor outcomes (24). Furthermore, the association of these outcomes with advancing degrees of renal dysfunction is unknown both because most studies have only included patients with advanced renal insufficiency and because level of renal function has not been carefully defined.

In the present analysis, we use prospectively collected data from the Department of Veterans Affairs' (VA) National Surgical Quality Improvement Program (NSQIP) to explore differences in a range of short-term (within 30 d post-operatively) surgical outcomes after lower extremity revascularization among patients with different levels of renal function. NSQIP has collected detailed data on most lower extremity revascularization surgeries occurring in the VA since 1994 and provides a unique opportunity to examine complications and mortality after revascularization, stratified for level of renal function, in a large group of patients. Our goal was to measure the association of complications, including graft failure and death occurring within 30 d post-operatively, with increasing degrees of renal insufficiency adjusted for key patient and operative characteristics.

## Materials and Methods

### *Database*

The VA NSQIP is an ongoing quality management initiative for surgical care. Since its inception on January 1, 1994, NSQIP has prospectively collected data on most major surgeries occurring at VA medical centers (VAMCs) across the country. A detailed account of NSQIP study design is provided elsewhere (25). At present, a total of 123 VAMCs participate in NSQIP. Patients are enrolled in NSQIP at the time of surgery. At this time, data on baseline clinical and demographic characteristics are obtained from the medical record, patient interview or from the surgeon caring for the patient. Pre-operative laboratory values are transmitted electronically from the VA's decentralized hospital computer system (VistA) to the coordinating center at the Denver VA Medical Center and the University of Colorado Health Outcomes Program. Patients are then followed prospectively into surgery and for 30 d after surgery by surgical clinical nurse reviewers. Data on the surgery itself and on post-surgical complications occurring within 30 d are ascertained by these nurse reviewers using the medical record, surgeon interview and by patient follow-up (by letter or telephone call requesting follow-up data). All deaths occurring within 30 d post-operatively are verified against the VA Beneficiary Identification and Records Locator System (BIRLS) death records (26,27). Patients are eligible for inclusion in NSQIP if their procedure is performed under general, spinal or epidural anesthesia.

### *Sample Selection*

We searched the NSQIP database for the first occurrence of a lower-extremity surgical revascularization procedure for individual patients–as coded by Current Procedural Terminology (CPT) – from January 1, 1994 to September 30, 2001 (CPT lower extremity revascularization codes used in procedure code search: 35286, 35372, 35521, 35533, 35541, 35546, 35548, 35549, 35551, 35556, 35558, 35563, 35565, 35566, 35571, 35582, 35583, 35585, 35587, 35621, 35623, 35641, 35646, 35651, 35654, 35656, 35661, 35663, 35665, 35666, 35671). We included only the chronologically first procedure for each patient occurring during the study period to analyze all data at the individual patient level and to exclude as many secondary procedures as possible. Patients were included in the study if a CPT code for lower extremity revascularization appeared in the principal procedure code field listed in NSQIP. In this manner, we identified all patients who underwent at least one lower extremity revascularization between January 1, 1994 and September 30, 2001 recorded as a principal procedure in NSQIP.

### *Ascertainment of Postoperative Outcomes*

Operative outcomes examined in this analysis were death and several other adverse clinical outcomes occurring within 30 d of the procedure. These included operative site complications (wound infection [superficial and deep], wound dehiscence, and graft failure requiring return to the operating room), cardiac complications (cardiac arrest requiring CPR, myocardial infarction), pulmonary complications (unplanned post-operative intubation for respiratory or cardiac failure and failure to wean from the ventilator after 48 h), infectious complications (sepsis, pneumonia) and other complications (stroke, coma >24 h, post-operative bleeding requiring >4 units of packed red blood cells or whole blood within the first 72 h after surgery, and acute renal failure requiring dialysis in a patient not previously on dialysis).

### *Determination of Renal Function*

A single pre-operative serum creatinine measurement was available for most patients in the NSQIP database. In addition, nurse reviewers (who have access to the medical record) also recorded whether patients experienced pre-operative acute renal failure (defined as rapidly rising creatinine above 3mg/dl and oliguria). For the primary analysis, GFR was calculated for each patient using the abbreviated Modification of Diet in Renal Disease (MDRD) formula (28) which predicts GFR based on serum creatinine, albumin, age and race. This equation probably estimates GFR more accurately than serum creatinine alone because it takes into account racial and gender differences in creatinine production (28).

Patients were grouped according to the level of renal function as follows: normal or mildly reduced renal function (estimated GFR≥60 cc/min/1.73m$^2$), moderate renal insufficiency (estimated GFR 30 to 59 cc/min/1.73m$^2$), severe renal insufficiency (estimated GFR <30cc/min/1.73m$^2$) and dialysis-dependent renal failure. This classification is similar to the definition recommended by the National Kidney Foundation's Dialysis Outcome Quality Initiative (NKF-DOQI) guidelines for chronic kidney disease (29) with one exception: To draw comparisons between dialysis patients and non-dialysis patients (a clinically relevant distinction), the small number of patients with an estimated GFR<15cc/min/1.73m$^2$ but not on dialysis were included in the severe renal insufficiency group (estimated GFR <30cc/min/1.73m$^2$) and not included with dialysis patients in a "kidney failure" category as suggested by NKF-DOQI guidelines. We excluded from the analysis all patients who had pre-operative acute renal failure to include only patients likely to have chronic renal insufficiency. Because the MDRD formula has not been validated in a veteran population, as a sensitivity analysis we also measured the association of operative outcomes with level of renal function defined purely by serum creatinine levels. For this purpose we adopted the following creatinine cutoffs to correspond respectively with a GFR of <60cc/min/1.73m$^2$ and <30cc/min/1.73m$^2$ as reported by Couchoud *et al.*

(30): 1.57 mg/dl and 2.19 mg/dl for men and 1.17 mg/dl and 1.77 mg/dl for women. As for the primary analysis, dialysis patients were included as a separate category.

### *Ascertainment of Patient Baseline Characteristics, Preoperative Condition, and Operative Characteristics*

Patient characteristics included age, white race (*versus* non-white), sex, co-morbid conditions at the time of the procedure (history of diabetes, insulin use, chronic obstructive pulmonary disease (COPD), history of congestive heart failure (CHF) during the month before surgery, history of transient ischemic attack, history of stroke with neurologic deficit, current smoking, current alcohol use). To develop a complete picture of disease burden, we also included whether the patient had a do-not-resuscitate (DNR) order in the chart signed by an attending in the 30 d before surgery, history of >10% unintentional weight loss during the preceding 6 mo, and presence of dyspnea at rest.

We also compared the acute pre-operative condition of patients in each renal insufficiency group. Variables indicating patient condition at the time of procedure included pre-operative albumin, hematocrit and white blood cell count, whether the patient was admitted from home (*versus* transferred from nursing home, acute care hospital or other setting), the presence of wound infection, pre-operative sepsis, and length of pre-operative hospital stay.

Finally, we compared operative characteristics between patients with different levels of renal function. Revascularization procedures were classified as inflow procedures if they provided a blood supply from vessels above the inguinal ligament to the inguinal vessels (common femoral, superficial femoral or profunda femoral arteries) and outflow procedures if they provided a blood supply to or beyond the popliteal artery (CPT codes were used to categorize revascularization procedures in this way). Other operative characteristics included were type of graft material (prosthetic or composite *versus* autogenous vein), whether a lower extremity amputation was performed during the same operating session, whether the procedure was an emergency, wound classification (contaminated *versus* clean), operation time and type of anesthesia (general *versus* other).

### *Statistical Analysis*

We compared patient characteristics, acute pre-operative condition and operative outcomes in each reduced renal function category to the reference category of patients with normal or mildly reduced renal function using a $\chi^2$ test. For simplicity, continuous variables were presented and analyzed as categorical variables dichotomized either at the mean value for normally distributed variables (age), median value for non-normally distributed variables (pre-operative hospital stay and operation time) or at clinically meaningful cutoffs (*e.g.* albumin ≤3g/dl, hematocrit ≤30%, white blood cell count >12,000 cells/microliter) in descriptive analysis. We measured the association of level of renal function with each operative outcome using logistic regression analysis adjusted for the three groups of variables identified above (baseline characteristics, pre-operative condition and operative characteristics). To accommodate the potentially correlated nature of procedure data from individual surgical centers, all multivariable models were adjusted for a random center effect (31). For logistic regression analysis, continuous variables were not dichotomized as for descriptive analysis above. Primary analyses were conducted using estimated GFR categories as defined by the abbreviated MDRD equation. A sensitivity analysis was conducted using categories of renal function defined by serum creatinine cutoffs as described above.

Some variables were missing data. For most of these variables less than 1% of values were missing (race, history of TIA, dyspnea at rest (<2%), alcohol use, pre-operative hematocrit, history of weight loss, DNR order, pre-operative wound infection, white blood count, pre-operative hospital stay (<3%), and operation time). Several variables were missing larger amounts of data (*i.e.* pre-operative albumin (37%), setting from which patient was admitted (home *versus* other) (23%) and pre-operative sepsis (23%)). For continuous variables, a mean value was imputed for missing values with an additional variable (missing indicator variable) included in the model that was equal to one if the variable was originally missing and equal to zero otherwise. This allowed all observations to be used in estimating the effects of variables that were not missing, but including the missing indicator variable ensured that the particular values imputed (in this case the overall means), had no influence on the variables' estimated effects. Missing values for categorical variables were included as a separate "missing" category. All analyses were completed using Stata Statistical Software (College Station, TX).

## Results

### *Study Population*

A total of 18,939 patients underwent at least one lower extremity revascularization that was listed as a principal procedure in NSQIP during the study period. Of these, 110 had pre-operative acute renal failure and were excluded from the analysis. Of the remaining 18,829 eligible patients, 612 patients were excluded because they lacked data on renal function (in the form of either a pre-operative serum creatinine or an indication that they were on dialysis at the time of surgery). Our study population consisted of the 18,217 remaining patients who underwent at least one revascularization during the study period, had data on renal function, and did not have acute renal failure during the pre-operative period. In this group, 73% of patients had normal or mildly reduced renal function (mean creatinine 1.0 ± 0.2mg/dl), 23% had moderate renal insufficiency (mean creatinine 1.5 ± 0.3 mg/dl), 2% had severe renal insufficiency but were not on dialysis (mean creatinine 3.2 ± 1.4mg/dl) and 2% were dialysis dependent.

### *Patient Characteristics*

Table 1 shows that most baseline characteristics differed substantially by level of renal function. Most notably, the percentage of patients with diabetes increased with advancing degrees of renal insufficiency. Table 2 shows that there were also differences in acute pre-operative condition across groups, with patients with renal insufficiency being less likely to be admitted from home and more likely to present with pre-operative wound infection, pre-operative sepsis, elevated white blood cell count, and to have longer pre-operative hospital stays compared to patients with normal or mildly reduced renal function. Table 3 shows that the types of procedures differed between groups. Patients with renal insufficiency were less likely to undergo inflow procedures and were also less likely to have a prosthetic (*versus* autogenous vein) graft than patients with normal renal function. Lower extremity amputation performed under the same anesthetic as the principal revascularization procedure was a more frequent occurrence in patients with severe or dialysis dependent renal insufficiency than in

*Table 1.* Baseline patient characteristics by level of renal function[a]

| Characteristic | GFR ≥ 60 (*n* = 13,292) | GFR 30 to 59 (*n* = 4118) | GFR < 30 (*n* = 424) | Dialysis (*n* = 383) |
|---|---|---|---|---|
| Age > 65 yr | 44% | 70%[d] | 71%[d] | 55%[d] |
| Male | 99% | 99% | 97%[d] | 99% |
| White | 79% | 84%[d] | 85%[d] | 57%[d] |
| Diabetic patients | 31% | 42%[d] | 56%[d] | 61%[d] |
| Diabetic patients on insulin | 16% | 25%[d] | 39%[d] | 47%[d] |
| COPD | 19% | 21%[b] | 22%[b] | 14%[c] |
| History of CHF | 3% | 7%[d] | 13%[d] | 10%[d] |
| History of TIA | 4% | 7%[d] | 6% | 4% |
| History of stroke | 9% | 12%[d] | 13%[c] | 13%[b] |
| Dyspneic at rest | 1% | 2% | 5%[d] | 2% |
| Current smokers | 63% | 43%[d] | 38%[d] | 27%[d] |
| Alcohol users | 16% | 8%[d] | 7%[d] | 2%[d] |
| Weight loss | 3% | 3% | 4% | 6%[d] |
| DNR order | 0.7% | 1.0%[b] | 1.7%[b] | 2.6%[d] |

[a] GFR estimated glomerular filtration rate in cc/min/1.73 $m^2$; COPD chronic obstructive pulmonary disease; CHF congestive heart failure during the month prior to surgery, TIA history of transient ischemic attack; DNR do not resuscitate.
[b] $P \leq 0.05$; [c] $P \leq 0.1$; [d] $P \leq 0.001$. $P$ values are for pair-wise $\chi^2$ tests (patients with a GFR ≥ 60 cc/min per 1.73 $m^2$ used as reference category for each comparison). $P \leq 0.002$ for overall $\chi^2$ tests across all groups for all variables where pair-wise tests show a statistically significant difference between the reference category and one or more groups.

*Table 2.* Acute preoperative condition by level of renal function[a]

| Characteristic | GFR ≥ 60 (*n* = 13,292) | GFR 30 to 59 (*n* = 4118) | GFR < 30 (*n* = 424) | Dialysis (*n* = 383) |
|---|---|---|---|---|
| Preop albumin ≤ 3 g/dl | 12% | 15%[d] | 32%[d] | 39%[d] |
| Hematocrit ≤ 30% | 6% | 10%[d] | 27%[d] | 38%[d] |
| Admitted from home | 94% | 93% | 91%[b] | 87%[d] |
| Preoperative wound infection | 28% | 33%[d] | 42%[d] | 64%[d] |
| Preoperative sepsis | 0.7% | 0.8% | 1.9%[d] | 2.9%[d] |
| WBC > 12,000 cells/ml | 10% | 11% | 19%[d] | 25%[d] |
| Preoperative hospital stay > 2 d | 46% | 49%[c] | 59%[d] | 66%[d] |

[a] GFR, estimated glomerular filtration rate in cc/min per 1.73 $m^2$ WBC, white blood cell count.
[b] $P \leq 0.05$, [c] $P \leq 0.1$, [d] $P \leq 0.001$. $P$ values are for pair-wise $\chi^2$ tests (patients with a GFR > 60 cc/min per 1.73 $m^2$ used as reference category for each comparison). $P \leq 0.001$ for overall $\chi^2$ tests across all groups for all variables where pair-wise tests show a statistically significant difference between the reference category and one or more groups.

those with normal renal function or milder degrees of renal insufficiency. Patients with renal insufficiency were also more likely to undergo emergency procedures, more likely to have contaminated wounds, and less likely to undergo general anesthesia than patients with normal renal function.

### *Postoperative Complications*

Table 4 shows the incidence of 30-d post-operative complications by degree of renal insufficiency. Death within 30 d, cardiac arrest, unplanned intubation, systemic sepsis, coma, and post-operative bleeding were more common in patients with renal insufficiency (even those with moderate renal dysfunction). In contrast, patients with renal insufficiency did not appear to have a higher rate of operative site complications such as wound infection, wound dehiscence, and graft failure requiring return to the operating room than those with normal renal function.

The incidence of most of the aforementioned complications was similar to or higher in patients with severe renal insufficiency than patients on dialysis. In addition, patients with moderate or severe renal insufficiency had a higher incidence of myocardial infarction, prolonged intubation and (by definition) post-operative acute renal failure requiring dialysis compared to patients on dialysis.

Table 5 and Figure 1 show adjusted associations of degree of renal insufficiency with post-operative complications. While we tested the association of all outcomes presented in Table 4 with level of renal function, only those associations that were statistically significantly associated with the outcome are presented. Even after adjustment for differences in

*Table 3.* Operative characteristics by level of renal function[a]

| Operative Characteristics | GFR ≥ 60 ($n$ = 13,292) | GFR 30 to 59 ($n$ = 4118) | GFR < 30 ($n$ = 424) | Dialysis ($n$ = 383) |
|---|---|---|---|---|
| Procedure type | | | | |
| inflow only | 45% | 36%[d] | 31%[d] | 13%[d] |
| outflow only | 54% | 63%[d] | 68%[d] | 87%[d] |
| inflow and outflow | 1% | 1% | 1% | <1% |
| Artificial (*versus* vein) grafts | 53% | 48% | 43%[d] | 31%[d] |
| Amputation performed | 4% | 5%[b] | 7%[c] | 13%[d] |
| Emergency cases | 4.7% | 5.4% | 9.9%[c] | 4.7% |
| Contaminated wounds | 8% | 9% | 13%[d] | 16%[d] |
| Operation time > 4 h | 58% | 60%[b] | 59% | 71%[d] |
| General anesthesia | 72% | 68%[d] | 69% | 62%[d] |

[a] GFR estimated glomerular filtration rate in cc/min per 1.73 $m^2$.
[b] $P \leq 0.05$, [c] $P \leq 0.1$, [d] $P \leq 0.001$. $P$ values are for pair-wise $\chi^2$ tests (patients with a GFR > 60 cc/min per 1.73 $m^2$ used as reference category for each comparison). $P \leq 0.001$ for overall $\chi^2$ tests across all groups for all variables where pair-wise tests show a statistically significant difference between the reference category and one or more groups.

*Table 4.* Incidence of 30-d postoperative complications by level of renal function

| Complication | Level of Renal Insufficiency | | | |
|---|---|---|---|---|
| | GFR > 60 ($n$ = 13,292) | GFR 30 to 59 ($n$ = 4118) | GFR < 30 ($n$ = 424) | Dialysis ($n$ = 383) |
| Death within 30 d | 290 (2%) | 175 (4%)[c] | 42 (10%)[c] | 40 (10%)[c] |
| Operative site complications | | | | |
| superficial wound infection | 863 (7%) | 289 (7%) | 36 (9%) | 16 (4%) |
| deep wound infection | 404 (3%) | 119 (3%) | 13 (3%) | 18 (5%) |
| wound dehiscence | 227 (2%) | 79 (2%) | 8 (2%) | 6 (2%) |
| graft failure requiring return to the operating room | 541 (4%) | 169 (4%) | 15 (4%) | 18 (5%) |
| Cardiopulmonary complications | | | | |
| cardiac arrest | 162 (1%) | 92 (2%)[c] | 21 (5%)[c] | 18 (5%)[c] |
| myocardial infarction | 167 (1%) | 116 (3%)[c] | 15 (4%)[c] | 8 (2%) |
| unplanned intubation | 309 (2%) | 187 (5%)[c] | 27 (6%)[c] | 15 (4%)[b] |
| intubated > 48 h | 326 (3%) | 165 (4%)[c] | 32 (8%)[c] | 13 (3%) |
| Infectious complications | | | | |
| systemic sepsis | 163 (1%) | 68 (2%)[b] | 14 (3%)[c] | 14 (4%)[c] |
| pneumonia | 446 (3%) | 170 (4%)[b] | 32 (8%)[c] | 16 (4%) |
| Other complications | | | | |
| stroke | 69 (<1%) | 25 (<1%) | 5 (1%) | 2 (<1%) |
| coma > 24 h | 15 (0.11%) | 11 (0.27%)[b] | 2 (0.47%)[b] | 4 (1.04%)[c] |
| bleeding | 189 (1%) | 94 (2%)[c] | 13 (3%)[c] | 11 (3%)[b] |
| acute renal failure | 71 (<1%) | 60 (2%)[c] | 24 (6%)[c] | Not included |

[a] GFR, estimated glomerular filtration rate in cc/min per 1.73 $m^2$.
[b] $P < 0.05$, [c] $P < 0.001$. $P$ values are for $\chi^2$ test (patients with a GFR > 60 cc/min per 1.73 $m^2$ used as reference category for each comparison). $P \leq 0.001$ for overall $\chi^2$ tests across all groups for all variables where pair-wise tests show a statistically significant difference between the reference category and one or more groups.

baseline characteristics, death within 30-d, cardiac arrest, myocardial infarction, unplanned or prolonged intubation, and acute renal failure requiring dialysis were strongly associated with level of renal function. Dialysis patients had a higher incidence of death, cardiac arrest, sepsis and coma but not of other complications listed above than for patients with lesser degrees of renal insufficiency. In addition, we found no statistically significant adjusted (or unadjusted) associations for operative site complications such as wound infection or graft failure with renal insufficiency. The results of multivariate analysis using categories of renal function defined by serum creatinine alone did not differ sub-

*Table 5.* Postoperative complications associated with renal insufficiency adjusted for baseline characteristics, preoperative condition, and operative characteristics

| | Odds ratio (95% confidence interval)[a] | | |
|---|---|---|---|
| | GFR 30 to 59 (*n* = 4118) | GFR < 30 (*n* = 424) | Dialysis (*n* = 383) |
| Death | 1.44 (1.17 to 1.77)[e] | 2.58 (1.76 to 3.79)[e] | 4.37 (2.95 to 6.48)[e] |
| Superficial wound infection | 1.00 (0.86 to 1.16) | 1.23 (0.85 to 1.77) | 0.57 (0.34 to 0.96)[c] |
| Cardiac arrest | 1.43 (1.09 to 1.88)[c] | 2.72 (1.66 to 4.48)[e] | 3.48 (2.03 to 5.98)[e] |
| Myocardial infarction | 1.68 (1.39 to 2.16)[e] | 2.13 (1.22 to 3.73)[d] | 1.60 (0.76 to 3.37) |
| Unplanned intubation | 1.69 (1.39 to 2.07)[e] | 2.01 (1.30 to 3.10)[d] | 1.76 (1.01 to 3.09)[c] |
| Intubated > 48 h | 1.57 (1.28 to 1.94)[e] | 2.70 (1.77 to 4.13)[e] | 1.98 (1.08 to 3.64)[c] |
| Systemic sepsis | 1.11 (0.82 to 1.51) | 1.53 (0.84 to 2.78) | 2.18 (1.18 to 3.99)[c] |
| Pneumonia | 1.11 (0.92 to 1.36) | 1.85 (1.23 to 2.79)[d] | 1.64 (0.95 to 2.83) |
| Coma > 24 h | 1.73 (0.72 to 4.14) | 3.19 (0.62 to 16.32) | 9.95 (2.47 to 40.09)[d] |
| Postoperative bleeding > 4 units | 1.34 (1.02 to 1.76)[c] | 1.53 (0.83 to 2.84) | 1.74 (0.90 to 3.39) |
| Acute renal failure requiring dialysis | 2.51 (1.73 to 3.65)[e] | 7.54 (4.41 to 12.89)[e] | Not included |

[a] All odds ratios are relative to a value of 1.00 for the referent category with GFR > 60 cc/min per 1.73 $m^2$ (*n* = 13,292).
[b] Adjusted for baseline characteristics, preoperative condition, and operative characteristics.
[c] $P \leq 0.05$, [d] $P \leq 0.01$, [e] $P \leq 0.001$ using logistic regression analysis with random center effect.

stantially from the results presented for the primary analysis using estimated GFR.

## Discussion

A high percentage (27%) of patients undergoing a first lower extremity revascularization recorded in NSQIP during the study period had at least moderate renal insufficiency probably reflecting the older age and disease profile (*i.e.* high prevalence of diabetes and vascular disease) of the patient population studied. This finding alone underlines the importance of both understanding the association of renal insufficiency with outcomes after lower extremity revascularization and of efforts to improve outcomes after revascularization for this patient group.

Prior retrospective case series of revascularization in patients with renal insufficiency have suggested that this group is more likely to experience short- and long-term graft failure and limb loss. In the present analysis of prospectively collected data for a large multi-center sample of patients, we found no statistically significant differences by level of renal function in the incidence of short-term graft failure requiring return to the operating room or in post-operative soft tissue infections. However, patients with even a moderate degree of renal insufficiency undergoing lower extremity revascularization were more likely to die and to experience serious post-operative cardiopulmonary complications within 30 d of the procedure.

These findings are consistent with the wider literature identifying renal insufficiency as a risk factor for cardiovascular complications and death after cardiac (32,33) and non-cardiac (34,35) surgery. The present analysis suggests that decision-making before lower extremity revascularization in this patient group should take into account the increased incidence of cardiac complications in addition to more traditional concerns about risk of graft failure and subsequent limb loss. Our findings also raise the question of whether improvements in the prevention and management of postoperative cardiac complications could improve outcomes in this group.

Most retrospective analyses of lower extremity revascularization have focused solely on post-operative outcomes in patients with *advanced* renal insufficiency. Hence little is known about the association of milder degrees of renal insufficiency with outcomes after lower extremity revascularization. The present analysis demonstrates that (as has been shown for both cardiac (32) and general (35) surgery) the incidence of death and postoperative cardiac complications is increased even among patients with moderate renal insufficiency. This finding is particularly important because 23% of the study sample had moderate renal insufficiency.

A further point is that in the present analysis, most cardiopulmonary complications were more common for patients with severe renal insufficiency not on dialysis than for those already on dialysis, identifying this group as having a particularly high incidence of postoperative death and cardiopulmonary complications after lower extremity revascularization. This might reflect the impact of selection bias among dialysis patients leading to more careful pre-operative screening and heightened clinician awareness of their increased operative risk compared to patients with severe renal insufficiency not on dialysis. This possibility is supported by the fact that patients selected for revascularization in the severe renal insufficiency category were older with a higher prevalence of most co-morbid conditions compared to dialysis patients. The high incidence of postoperative acute renal failure requiring dialysis in this group also raises the question of whether interventions to prevent and/or improve management of acute renal failure could potentially lead to lower rates of cardiopulmonary complications for these patients.

Current American Heart Guidelines for pre-operative risk

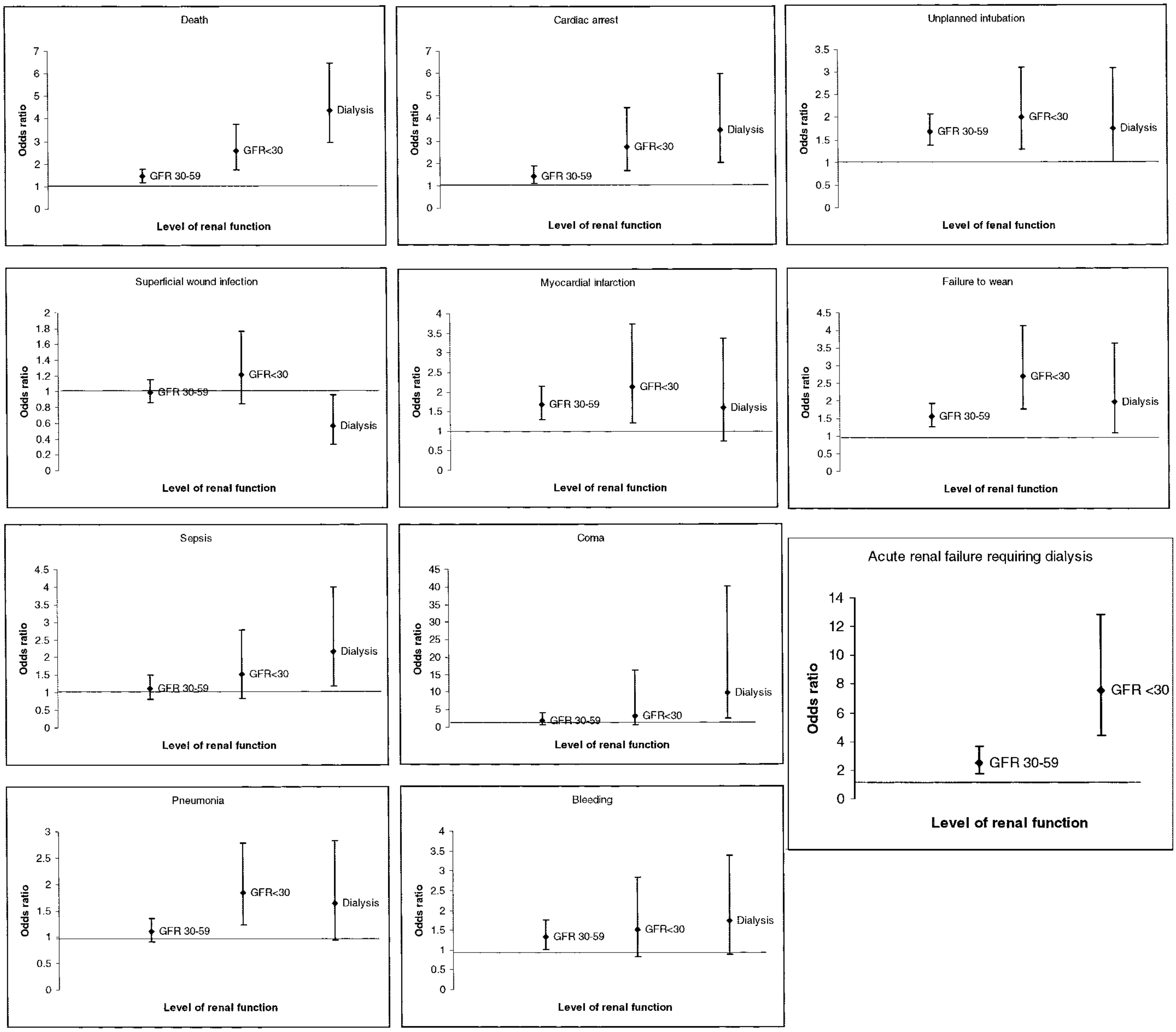


*Figure 1.* Odds ratio plots for association of level of renal function with post-operative complications. All complications for which there was a statistically significant association with at least one renal insufficiency group are presented. The reference category for all plots is patients with a GFR >60 cc/min/1.73m$^2$.

assessment for non-cardiac surgery probably represent the best clinical reference for pre-operative cardiac evaluation in patients undergoing lower extremity revascularization at the current time (36). However, these guidelines rank serum creatinine >2mg/dl as an “intermediate” cardiac risk factor. Our findings show that patients with serum creatinine below this level can also have an increased incidence of cardiovascular complications and also that the incidence of cardiovascular complications may not increase linearly as level of renal insufficiency increases. Hence future studies should assess the applicability of these guidelines to patients with renal insufficiency undergoing lower extremity revascularization.

In the present analysis, patients with renal insufficiency were more likely to undergo distal (outflow) procedures and (consistent with this) were less likely to require prosthetic grafts compared to patients with normal renal function. These findings suggest that patients with renal insufficiency are more likely to present with a more distal pattern of atherosclerosis (even after controlling for diabetes) than patients with normal renal function. While this may reflect a different disease process in this group, it could also reflect late presentation with advanced atherosclerosis. It was also much more common for patients with renal insufficiency to undergo a concurrent amputation at the same time as the revascularization procedure (limb salvage procedure), suggesting the more frequent occurrence of limb-threatening infection and/or advanced ischemia in this group. Patients with renal insufficiency were also more likely to present with pre-operative wound infection, sepsis, elevated white blood cell count and contaminated wounds and they were more likely to require emergency procedures than patients with normal renal function. Compared to patients with normal renal function, they also faced longer pre-operative hospital stays and were more likely to have been admitted from another facility (*versus* home) before the procedure. More studies are needed to determine whether patients with renal insufficiency receive different care than patients with normal renal function that might account for their more frequent presentation with advanced atherosclerosis and limb-threatening infection or whether this reflects more rapid (or different) progression of peripheral vascular disease in this group.

The present analysis offers several advantages over prior surgical case series of lower extremity revascularization in patients with renal insufficiency. These include the large size of the cohort studied, the multi-center study design, prospective rather than retrospective data collection and the fact that the study population included patients with diverse levels of renal function. However, the study does have a number of limitations. First, our results are based on an observational study and not a randomized controlled trial of revascularization outcomes among patients with different levels of renal insufficiency. Therefore we cannot imply causality for associations identified here because reported results may reflect some element of selection bias. Second, there were relatively few dialysis patients and patients with advanced renal insufficiency in the cohort, thus confidence intervals for some associations were relatively wide yielding inaccurate point estimates. Our imperfect measure of limb preservation is a third limitation. Since NSQIP only contains information about whether the patient had graft failure requiring return to the operating room, patients who had graft failure but were not taken back to the operating room within 30 d of the original procedure would not be captured. Fourthly, our conclusions may not be generalizeable to non-veteran populations because veterans represent a unique patient group that is predominantly male. Fifthly, chronic kidney disease is traditionally defined as GFR$<$60 cc/min/1.73m$^2$ for $\geq$3 mo (29). However, the duration of pre-operative renal insufficiency was unknown for study patients since only one pre-operative creatinine was reported for each patient. This may limit the generalizability of these study findings to patients with chronic kidney disease. Finally, it is uncertain whether the abbreviated MDRD equation represents the optimal method for GFR estimation in this population (particularly in the setting of uncalibrated serum creatinine measurements) (28,30,37–39) (30). However, sensitivity analysis using level of renal function defined by serum creatinine measurements alone provides some reassurance that the associations of renal dysfunction with post-operative complications after revascularization reported here are robust.

In conclusion, while to date, operative complications such as wound infection and graft failure have been a primary concern guiding decisions about revascularization in patients with renal insufficiency. This analysis suggests that efforts to improve short-term pre-and post-operative management of patients with renal insufficiency undergoing lower extremity revascularization should focus primarily on the increased incidence of death and cardiopulmonary complications in this group (even among patients with moderate renal insufficiency and particularly among patients with severe renal insufficiency). A second finding is that patients with renal insufficiency were more likely to undergo outflow (*versus* inflow) procedures and were more likely to present pre-operatively with limb threatening infection compared to patients with normal renal function. Future studies should focus on whether these differences reflect systematic differences in the care received by patients with renal insufficiency leading to later presentation for surgery or whether they simply reflect a different disease course in this group.

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