Renal Insufficiency and Use of Revascularization among a National Cohort of Men with Advanced Lower Extremity Peripheral Arterial Disease

Ann M. O'Hare,*‡§ Daniel Bertenthal,‡ Anton N. Sidawy,** Michael G. Shlipak,*‡§¶ Saunak Sen,‡¶ and Mary-Margaret Chren†‡‖

*Departments of Medicine and †Dermatology, and the ‡Health Services Research Enhancement Award Program to Improve Care for Older Veterans, VA Medical Center, San Francisco, California; §Departments of Medicine, ‖Dermatology, and ¶Epidemiology and Biostatistics, University of California, San Francisco, California; **Surgical Services, VA Medical Center, Department of Surgery, George Washington University Medical Center, Washington, DC

Although peripheral arterial disease is prevalent in patients with renal insufficiency, little is known about how the disease is managed in this patient group. The management of advanced limb ischemia was examined in a large cohort of male veterans (n = 6227). Patients were classified according to whether they underwent lower extremity revascularization, amputation, or no procedure within the first 6 mo after their first diagnosis of critical limb ischemia, defined as ischemic rest pain, ulceration, or gangrene. The association of renal insufficiency with revascularization and the association of management strategy with mortality within 1 yr of cohort entry were measured. Within 6 mo of initial diagnosis of critical limb ischemia, 39% of patients underwent lower extremity revascularization, 27% underwent major amputation, and 34% did not undergo either procedure. Patients with an estimated GFR 30 to 59 (adjusted odds ratio [OR] 0.84; 95% confidence interval [CI] 0.72 to 0.96), 15 to 29 ml/min per 1.73 m^2 (OR 0.47; 95% CI 0.35 to 0.65), <15 ml/min per 1.73 m^2 not on dialysis (OR 0.32; 95% CI 0.16 to 0.62), and dialysis patients (OR 0.62; 95% CI 0.47 to 0.84) were less likely to undergo revascularization than those with an estimated GFR ≥60 ml/min per 1.73 m^2. At all levels of renal function, mortality risk was lowest for patients who underwent revascularization. Patients with critical limb ischemia and concomitant renal insufficiency are less likely to be treated with revascularization. However, among patients with renal insufficiency, mortality is lowest for patients who receive a revascularization. Further studies are needed to determine the optimal care for this high-risk patient group.

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Patients with renal insufficiency have a high prevalence of subclinical and clinically overt peripheral arterial disease (PAD) (1–3). Among patients with PAD, renal insufficiency is common and seems to be a risk factor for death and for adverse surgical outcomes (4–6). However, it is not known whether the presence of renal insufficiency affects the clinical management of PAD. To address this question, we examined the clinical management of critical lower limb ischemia, defined as rest pain, ischemic ulceration, or gangrene, by level of renal function in a large national cohort of male veterans. Our primary goal was to compare the clinical management of critical limb ischemia in patients with different levels of renal function. Our secondary goal was to compare mortality across different clinical management strategies.

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Address correspondence to: Dr. Ann M. O'Hare, VA Medical Center, San Francisco, Box 111J, Nephrology, 4150 Clement Street, San Francisco, CA 94121. Phone: 415-221-4810 ext. 4953; Fax: 415-750-6949; E-mail: ann.o'hare@med.va.gov

Materials and Methods

Data Sources

We constructed a cohort of male veterans with an initial diagnosis of critical limb ischemia using the following strategy. We identified all patients who had an *International Classification of Diseases, Ninth Revision* (ICD-9) code for critical limb ischemia recorded in the Department of Veterans Affairs' (VA's) National Patient Care Database (NPCD) between January 1, 2000, and June 1, 2002. The NPCD is a comprehensive data source that includes encounter information for all inpatient and outpatient VA care (7). The NPCD has excellent specificity and moderate sensitivity for a variety of different comorbid conditions (including PAD) (8). To maximize specificity, we required that each patient have at least one subsequent critical limb ischemia diagnostic code entry within 1 yr of their initial code entry. The date of the first diagnostic code entry for critical limb ischemia was taken as the point of cohort entry for each patient.

We eliminated all patients who had a previous diagnosis of critical limb ischemia or had undergone a previous lower extremity amputation or revascularization procedure before this time by searching the NPCD, VA Fee Basis files, and Medicare claims. VA Fee Basis files record episodes of care that occur outside the VA under VA contract. Medicare claims were searched as far back as January 1, 1999, and VA files were searched as far back as October 1, 1996.

The aforementioned Medicare and VA data sources were also used to define demographic characteristics and comorbid conditions that were

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present before or at the time of initial diagnosis of critical limb ischemia as well as major amputation and revascularization procedures that occurred within 6 mo of the initial diagnosis of critical limb ischemia. We also used these data sources to identify major amputation procedures that occurred within 1 yr after lower extremity revascularization. Mortality follow-up was ascertained using the Beneficiary Identifier and Locator Subsystem (BIRLS). Recent studies suggest sensitivity rates >94% for BIRLS (9–11).

We identified prevalent dialysis and transplant patients using data from the United States Renal Data System (USRDS), a national registry of patients with ESRD (www.usrds.org). The VA decision support system laboratory results database was used to obtain the most recent serum creatinine level obtained at the time of or within 3 mo before the diagnosis of critical limb ischemia (http://www.virec.research.med.va.gov/insights/WEBPAGENO.2NOV99.PDF). We also used this file to obtain most recent serum glucose measurement within 3 mo of cohort entry.

The patient's residence zip code at the time of cohort entry was ascertained from the NPCD and then linked to geographic information on census region and distance to the closest VA Medical center. This was obtained from the VA Planning Systems Support Group web site (http://vaww.pssg.med.va.gov).

Patients

Eligible cohort patients included all male veterans who had their first diagnostic code entry for critical limb ischemia during the study period and had not undergone a previous amputation or revascularization procedure. We also excluded patients who did not have a serum creatinine measurement within 3 mo before cohort entry. We also excluded a small number of patients who had undergone an episode of dialysis within the VA before cohort entry but were not identified as patients with ESRD by USRDS, because of the difficulty of knowing with certainty whether these were chronic or acute dialysis patients. Because only a very small number of cohort patients had undergone renal transplantation ($n = 37$), we also excluded these patients.

We identified 7889 male veterans who received their first diagnosis of critical limb ischemia between January 1, 2000, and June 1, 2002, and had at least one subsequent diagnostic code entry for critical limb ischemia within 1 yr of cohort entry. Excluded were 1599 patients who did not have a serum creatinine measurement recorded within 3 mo of cohort entry, 37 patients who had undergone renal transplantation, and 26 patients who had undergone at least one previous episode of dialysis but were not identified in the USRDS database. The study sample thus consisted of 6227 patients.

Predictor Variables. The primary predictor variable for this analysis was the most recent level of renal function within 3 mo before diagnosis of critical limb ischemia. We used the abbreviated Modification of Diet in Renal Disease (MDRD) formula to estimate GFR using serum creatinine, age, and race among cohort patients (12). Patients were classified by level of renal function according to Kidney Disease Outcomes Quality Initiative guidelines: Estimated GFR (eGFR) ≥60 ml/min per 1.73 m^2 (normal or mildly reduced renal function), eGFR 30 to 59 ml/min per 1.73 m^2 (moderate renal insufficiency), and eGFR 15 to 29 ml/min per 1.73 m^2 (severe renal insufficiency); renal failure defined as an eGFR <15 ml/min per 1.73 m^2 or on dialysis (13). We examined separately outcomes among patients who had renal failure and were and were not on dialysis.

Secondary Predictor Variables. Multivariate analyses were adjusted for demographic and clinical characteristics at the time of cohort entry, including age; race (black *versus* nonblack); and previous diagnoses of diabetes, coronary artery disease, congestive heart failure, cerebrovascular disease, chronic obstructive pulmonary disease, and hypertension. Patients without a previous diagnosis of diabetes were considered to have diabetes when their most recent serum glucose measurement within 3 mo before the diagnosis of critical limb ischemia was ≥200 mg/dl.

Analyses were also adjusted for clinical presentation of critical limb ischemia on the basis of ICD-9 code at cohort entry (rest pain [440.22], ischemic ulceration [440.23], or gangrene [440.24]), census division of residence, distance from the patient's residence to the closest VA medical center, and whether the patient had Medicare coverage. Because Medicare claims for Medicare health maintenance organization (HMO) patients do not appear in the Medicare data that were used for this study, we also distinguished between Medicare HMO and non-HMO patients. Finally, analyses were also adjusted for year of cohort entry to account for the fact that information on previous diagnoses and procedures was obtained over a longer period for those who entered the cohort during later years.

Outcome Variables. The major outcome variable was the performance of a revascularization procedure (*versus* either no intervention or major amputation) within 6 mo of the diagnosis of critical limb ischemia. Lower extremity revascularizations included both surgical and percutaneous procedures. All lower extremity amputations at the ankle joint and above were considered major amputations. We did not include minor amputations (below the ankle joint) because these amputations can be performed along with a lower extremity revascularization as part of a limb salvage procedure. When patients underwent a revascularization procedure on the same day as a major amputation, they were classified as undergoing an amputation as the first procedure for critical limb ischemia ($n = 187$).

We also measured the association of management strategy with mortality within 1 yr of initial diagnosis with critical limb ischemia after adjustment for level of renal function and other potential confounders. Among patients who underwent a revascularization procedure as the initial procedure within 6 mo of diagnosis with critical limb ischemia, we examined the association of level of renal function with need for subsequent major amputation during the year after revascularization.

Statistical Analyses

We compared patient characteristics and clinical presentation across management strategies (revascularization, amputation, and no intervention within 6 mo) using a t test for continuous variables (as these were normally distributed) and a χ^2 test for categorical variables. Patients who received a revascularization procedure served as the referent category for this analysis.

We used a logistic regression model adjusted for a fixed effect for center to examine the association of renal insufficiency with receipt of a revascularization procedure *versus* other management (amputation or no procedure). To address the possibility that the data sources examined did not capture all episodes of care for cohort patients, we conducted a sensitivity analysis among a group of patients for whom these data were most likely to capture all episodes of care: Those who were 65 yr and older and had non-HMO Medicare Part B coverage. We also used logistic regression adjusted for a fixed effect for center to measure the association of management strategy (revascularization, amputation, or no procedure) with death within 1 yr of critical limb ischemia.

Among patients who underwent revascularization within 6 mo of their initial diagnosis with critical limb ischemia, we used the same analytic approach to examine the association between level of renal function with this outcome. All statistical analyses were conducted using STATA statistical software (College Station, TX).

Results

During the first 6 mo after diagnosis, 39% of patients underwent lower extremity revascularization, 27% underwent major amputation, and 34% did not undergo either procedure. Only 3% of these procedures were performed under Medicare; the remaining procedures were performed in the VA or under VA contract. Compared with patients who underwent revascularization, those who underwent either amputation or no procedure were older, included a higher percentage of black patients, and had a higher prevalence of most comorbidities, including renal insufficiency (Table 1). The most common presenting complaints were, respectively, rest pain among those who underwent revascularization, gangrene among those who underwent amputation, and ischemic ulceration among those who did not undergo either procedure. Patients with renal insufficiency were more likely than those with normal renal function to present with gangrene and less likely to present with rest pain (Figure 1). This tendency was most pronounced in patients who had an eGFR <15 ml/min per 1.73 m^2 and were not on dialysis compared with all other groups (even dialysis patients).

Among cohort patients, 28% ($n = 1759$) had an eGFR 30 to 59 ml/min per 1.73 m^2, 5% ($n = 326$) had an eGFR 15 to 29 ml/min per 1.73 m^2, 1% ($n = 82$) had an eGFR <15 ml/min per 1.73 m^2 and were not on dialysis, and 6% ($n = 371$) were on dialysis. With declining renal function, the percentage of patients who underwent revascularization within 6 mo of initial diagnosis of critical limb ischemia decreased, with a larger percentage undergoing either major amputation or neither major amputation nor revascularization (Figure 2). Results were similar when we excluded patients who died within 6 mo of the initial diagnosis of critical limb ischemia.

In both unadjusted and adjusted analyses, patients with moderate and severe renal insufficiency and renal failure were significantly less likely than those with normal renal function to receive a revascularization procedure within 6 mo of diagnosis with critical limb ischemia (Table 2). Patients who had renal failure and were not on dialysis were less likely than those who were on dialysis to receive a revascularization procedure. The

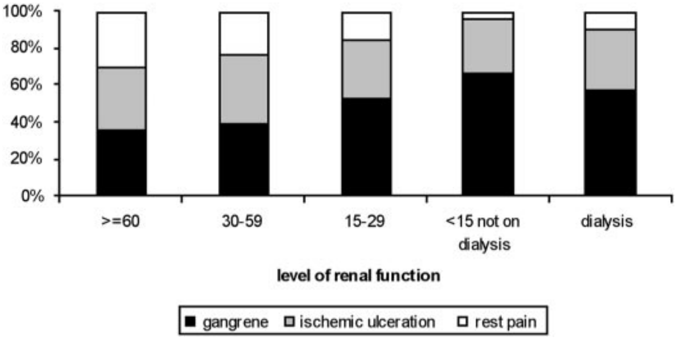

Figure 1. Presentation at time of initial diagnosis of critical limb ischemia by level of renal function.

Table 1. Baseline patient characteristics by management strategy[a]

	Revascularization ($n = 2326$)	Amputation ($n = 1495$)	No Intervention ($n = 1978$)
eGFR ml/min per 1.73 m^2 (%)			
≥60	68	53	54
30 to 59	25	29	32
15 to 29	3	7	7
<15 not on dialysis	0.5	2	2
dialysis	4	9	6
Mean age ± SD (yr)	67 ± 10	71 ± 10[c]	70 ± 11[c]
Black (%)	18	29[d]	20
Diabetes (%)	53	71[d]	67[d]
Hypertension (%)	81	85[c]	87[d]
Coronary artery disease (%)	56	59	62[d]
Congestive heart failure (%)	26	42[d]	40[d]
Cerebrovascular disease (%)	23	37[d]	29[d]
Chronic obstructive pulmonary disease	39	38	42[e]
Initial presentation[b]			
Rest pain	42	6	22
Ischemic ulceration	32	22	49
Gangrene	26	72	29

[a]All comparisons are with the referent category with a GFR ≥60 ml/min per 1.73 m^2. Column totals may not sum to 100% because of rounding. eGFR, estimated GFR.
[b]Overall χ^2 test for presentation $P < 0.001$.
[c]$P < 0.01$.
[d]$P < 0.001$.
[e]$P < 0.05$.

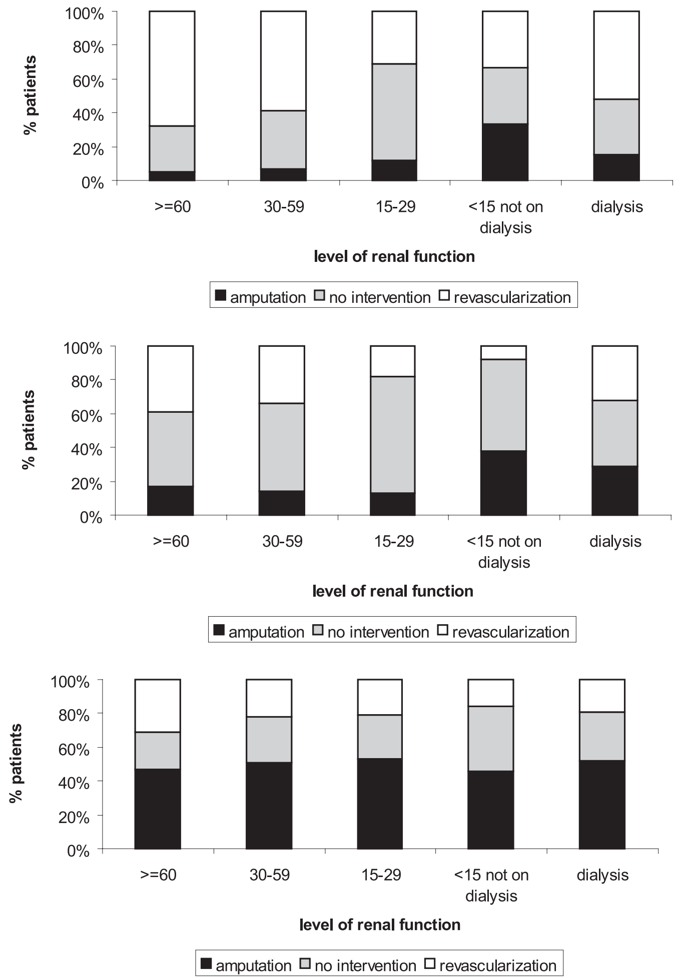

Figure 2. Clinical management of critical limb ischemia by presentation and level of renal function: Rest pain, ischemic ulceration, and gangrene.

pattern was similar regardless of the specific presentation of critical limb ischemia.

Also associated with a lower odds of revascularization were black race (odds ratio [OR] 0.83; 95% confidence interval [CI] 0.70 to 0.99), older age (OR 0.82 per 10-yr increase; 95% CI 0.77 to 0.88), cerebrovascular disease (OR 0.80; 95% CI 0.70 to 0.92), congestive heart failure (OR 0.69; 95% CI 0.60 to 0.81), diabetes (OR 0.76; 95% CI 0.66 to 0.86), and ischemic ulceration (OR 0.38; 95% CI 0.32 to 0.44) or gangrene (OR 0.28; 95% CI 0.24 to 0.33) *versus* rest pain. Odds of receiving a revascularization were similarly decreased for patients with renal insufficiency when we restricted our analysis to the 2864 patients who were aged 65 yr and older and had non-HMO Medicare and Medicare Part B (OR for GFR 30 to 59: 0.85, 95% CI 0.69 to 1.05; OR for GFR 15 to 29: 0.55, 95% CI 0.36 to 0.85; OR for eGFR <15 ml/min per 1.73 m^2 and not on dialysis: 0.26, 95% 0.09 to 0.79; OR for dialysis patients: 0.82, 95% 0.53 to 1.28).

Across renal function categories, mortality rates at 1 yr after cohort entry were highest for those who underwent amputation and lowest for those who underwent revascularization (Figure 3). Odds of death were increased both for those who received an amputation and for those who did not receive any procedure relative to those who underwent revascularization (Table 3), and this did not differ by level of renal function ($P = 0.22$ for interaction of renal function with management strategy). After adjustment for management strategy and other potential confounders, odds of death at 1 yr increased with decreasing renal function (eGFR 30 to 59 ml/min per 1.73 m^2: OR 1.24, 95% CI 0.99 to 1.56; eGFR 15 to 29 ml/min per 1.73 m^2: OR 1.80, 95% CI 1.16 to 2.78; eGFR <15 ml/min per 1.73 m^2 not on dialysis: OR 2.62, 95% CI 1.25 to 5.50; and dialysis: OR 3.49, 95% CI 1.72 to 7.10).

Among the 2437 patients who underwent a revascularization procedure within the first 6 mo after diagnosis with critical limb ischemia, 330 (14%) underwent a subsequent major amputation during the following year. From the data sources available, it is not possible to determine whether the subsequent amputation occurred in the revascularized leg. One-year amputation rates among patients who underwent revascularization ranged from 11% among those with an eGFR ≥60 to 44% among those who were on dialysis (Figure 4). Dialysis patients and those who had an eGFR <15 ml/min per 1.73 m^2 and were not on dialysis had a statistically significantly increased odds of amputation after revascularization even after adjustment for potential confounders (Table 4).

Discussion

In a large national cohort of male veterans, patients with even moderate renal insufficiency were less likely to receive a revascularization procedure for critical lower extremity ischemia than those with normal renal function. Although renal insufficiency was a risk factor for death and for amputation after revascularization, risk for death was lower among patients who underwent revascularization than among those who underwent amputation or no intervention, even in patients with renal insufficiency.

These findings underline the complexity of decision making in patients with critical limb ischemia and concomitant renal insufficiency. Although revascularization is generally regarded as the optimal management strategy for critical limb ischemia, this may not always be the case; these procedures can be associated with intra- and postoperative complications that may prohibit surgery in higher risk patients or in situations in which ischemic wounds are likely to heal without revascularization. Thus, low rates of revascularization in patients with renal insufficiency may reflect in part the increased risk for death and for other complications after lower extremity revascularization such as amputation in this patient group (4,5,14). In addition, not all cases of critical limb ischemia are amenable to revascularization, and this may be particularly true in patients with renal insufficiency. In support of this possibility, several previous studies have shown that patients who have renal insufficiency and undergo revascularization have more distal disease than their counterparts with normal renal function (4,5,15). In addition, revascularization may be of limited utility in cases of advanced tissue damage and infection related to PAD. This may also be a consideration in patients with renal insufficiency. Dialysis patients who undergo revascularization

Table 2. Association of level of renal function with revascularization within 6 mo of diagnosis with critical limb ischemia

Level of Renal Function	Unadjusted	Adjusted[a]
All patients		
eGFR ≥60	1.00 (referent)	1.00 (referent)
eGFR 30 to 59	0.66 (0.59 to 0.74)	0.84 (0.72 to 0.96)
eGFR 15 to 29	0.34 (0.26 to 0.45)	0.47 (0.35 to 0.65)
eGFR <15 not on dialysis	0.21 (0.12 to 0.39)	0.32 (0.16 to 0.62)
dialysis	0.45 (0.35 to 0.57)	0.62 (0.47 to 0.84)
Rest pain		
eGFR ≥60	1.00 (referent)	1.00 (referent)
eGFR 30 to 59	0.66 (0.52 to 0.83)	0.86 (0.64 to 1.15)
eGFR 15 to 29	0.21 (0.11 to 0.38)	0.30 (0.15 to 0.62)
eGFR <15 not on dialysis	0.23 (0.02 to 2.56)	0.32 (0.02 to 5.25)
dialysis	0.49 (0.25 to 0.99)	0.65 (0.27 to 1.54)
Ischemic ulceration		
eGFR ≥60	1.00 (referent)	1.00 (referent)
eGFR 30 to 59	0.81 (0.66 to 0.98)	0.89 (0.70 to 1.12)
eGFR 15 to 29	0.35 (0.21 to 0.58)	0.41 (0.23 to 0.74)
eGFR <15 not on dialysis	0.14 (0.03 to 0.61)	0.20 (0.04 to 0.91)
dialysis	0.74 (0.50 to 1.09)	0.79 (0.50 to 1.26)
Gangrene		
eGFR ≥60	1.00 (referent)	1.00 (referent)
eGFR 30 to 59	0.62 (0.50 to 0.77)	0.79 (0.61 to 10.3)
eGFR 15 to 29	0.60 (0.41 to 0.88)	0.60 (0.38 to 0.95)
eGFR <15 not on dialysis	0.44 (0.22 to 0.91)	0.32 (0.14 to 0.74)
dialysis	0.54 (0.38 to 0.77)	0.47 (0.30 to 0.75)

[a]Adjusted for age; black race; diabetes; random serum glucose; history of coronary artery disease, congestive heart failure, hypertension, stroke, and chronic obstructive pulmonary disease (COPD); clinical presentation (rest pain, ischemic ulceration, or gangrene); distance from nearest veterans affairs (VA) medical center; census division of residence; Medicare coverage (non-Medicare, Medicare health maintenance organization [HMO], Medicare non-HMO); year of cohort entry; and VA medical center.

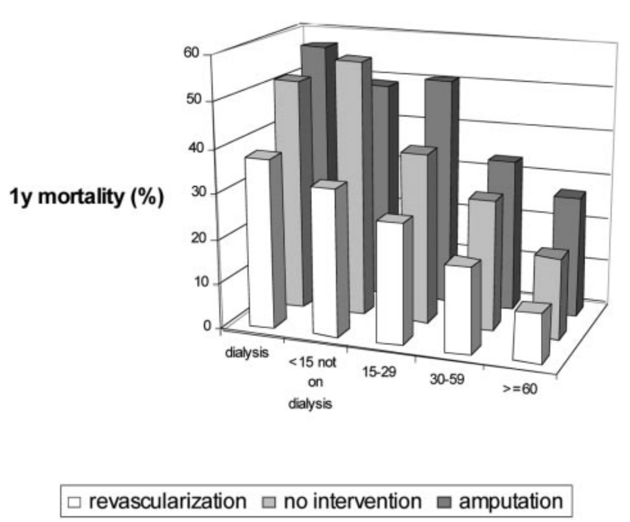

Figure 3. One-year mortality by management strategy and level of renal function.

for PAD seem to be more likely than others to have extensive tissue damage or signs of limb-threatening infection (5,15). Other considerations that may complicate the treatment of patients with renal insufficiency and advanced PAD include concern for contrast nephropathy as a result of both diagnostic angiography and the revascularization procedure itself. Finally, it is also possible that revascularization rates in patients with renal insufficiency are inappropriately low despite the aforementioned considerations. Such an argument has been made for coronary angiography in patients with renal insufficiency (16).

Previous studies have shown that renal insufficiency is a risk factor for adverse outcomes after lower extremity revascularization (4,5,14). However, these studies have provided little information on the risks associated with alternative management strategies for critical limb ischemia among patients with renal insufficiency. In an elegant propensity score analysis among dialysis patients who underwent amputation or revascularization for PAD, Logar *et al.* (17) recently demonstrated that lower extremity revascularization was associated with lower mortality than amputation among dialysis patients with a low propensity for amputation. In our analysis, mortality was lowest among patients who received a lower extremity revascularization procedure regardless of their level of renal function. Although lower mortality rates among patients who undergo revascularization may be explained by selection bias,

Table 3. Association of management strategy with 1-yr mortality after first diagnosis of critical limb ischemia

	Odds of Death (95% CI)		
	Revascularization	Amputation	No procedure
Unadjusted	1.00 (referent)	2.91 (2.50 to 3.39)	2.05 (1.76 to 2.38)
Adjusted[a]	1.00 (referent)	1.68 (1.38 to 2.04)	1.58 (1.32 to 1.89)

[a]Adjusted for level of renal function; age; black race; diabetes; random serum glucose; history of coronary artery disease, congestive heart failure, hypertension, stroke, and COPD; clinical presentation (rest pain, ischemic ulceration, or gangrene); distance from nearest VA medical center; census division of residence; Medicare coverage (non-Medicare, Medicare HMO, Medicare non-HMO); and year of cohort entry. CI, confidence interval.

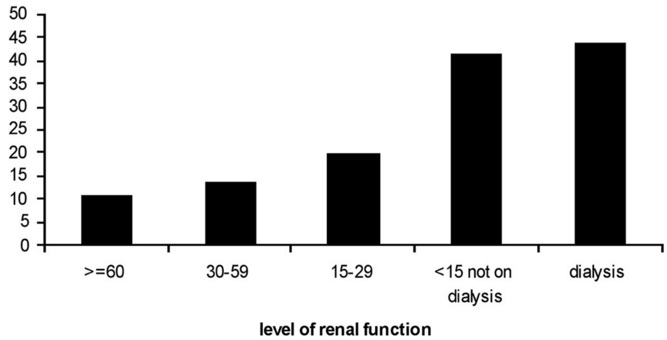

Figure 4. Percentage of patients who underwent revascularization and underwent major amputation during the subsequent year.

rather than the management strategy itself, the findings presented here clearly indicate a need for further studies to understand in detail why patients with chronic kidney disease are less likely than others to receive a revascularization. Such studies should help to determine how clinical decision-making can be optimized for this high-risk patient group.

Although previous studies have shown that dialysis patients are more likely than others to receive an amputation rather than a revascularization procedure (18,19), the impact of non–dialysis-dependent chronic kidney disease on procedure choice has not been examined. Our analysis suggests that even patients with moderate renal insufficiency are less likely to undergo a revascularization procedure than those with normal renal function. It is interesting that patients who had an eGFR <15 ml/min per 1.73 m^2 and were not on dialysis at diagnosis were less likely than dialysis patients to undergo a revascularization procedure. This could reflect a greater severity of limb ischemia (*e.g.*, more extensive gangrene) and other comorbid conditions in this group not captured in this analysis. It may also reflect differences in perceived and real risk associated with contrast administration and surgery for lower extremity ischemia in patients who have marginal renal function and are not yet on dialysis compared with those who are already on dialysis and those with milder levels of renal insufficiency.

Previous studies that reported less frequent revascularization *versus* amputation among dialysis patients with PAD were restricted to patients who underwent a procedure for limb ischemia and excluded the group that was not treated surgically (18,19). In our cohort, more than one third of all patients and almost half of those with an eGFR 15 to 29 ml/min per 1.73 m^2 did not undergo surgery within 6 mo of the diagnosis of critical limb ischemia. The group that did not undergo surgery is likely to be a heterogeneous group that consists of some patients who are deemed too sick to undergo either amputation or revascularization and others who have relatively mild manifestations of critical limb ischemia and in whom a procedure is not believed to be necessary. Striking, mortality rates at 1 yr after diagnosis were almost as high for this group as for those who underwent amputation. This study thus also underlines the need for more detailed studies of this patient group to understand better why they are not referred for surgery and how they are treated.

Consistent with previous studies in dialysis patients (5,14,20), our study demonstrates that patients who have advanced renal insufficiency and undergo revascularization for critical limb ischemia are at risk for requiring a subsequent major amputation. Unfortunately, our data do not indicate whether subsequent amputations occurred in the same or opposite leg as the revascularization procedure. Nonetheless, this finding suggests that decision-making in patients with advanced renal insufficiency and critical limb ischemia should take into account future risk for amputation.

The major limitation of our study is that we relied on ICD-9 diagnostic codes for critical limb ischemia to define the study cohort and adjust for clinical presentation of PAD. ICD-9 codes for PAD in the VA system are only moderately sensitive (8). Furthermore, we required two critical limb ischemia codes within 1 yr of cohort entry to maximize specificity at the cost of sensitivity. For these reasons, our cohort may not be representative of all veterans with critical limb ischemia and probably represents a group with more severe critical limb ischemia. Although this bias should not have an impact on the association of renal function with management strategy, the proportion of patients who are treated by amputation or revascularization *versus* no intervention reported here cannot be extrapolated to the larger population of all veterans with critical limb ischemia. Second, our results may not be generalizable to nonveteran populations and specifically to women. It is certainly possible that renal insufficiency may have an impact on practice patterns differently across health care systems and in women compared with men; thus, further studies outside the VA are needed to investigate these possibilities.

Table 4. Odds of amputation within 1 yr of lower extremity revascularization by level of renal function

Level of Renal Function, All Patients	Odds of Amputation (95% CI)	
	Unadjusted	Adjusted[a]
eGFR ≥60	1.00 (referent)	1.00 (referent)
eGFR 30 to 59	1.2 (1.09 to 3.66)	1.05 (0.75 to 1.48)
eGFR 15 to 29	2.00 (1.09 to 3.66)	1.72 (0.86 to 3.47)
eGFR <15 not on dialysis	5.71 (1.79 to 18.17)	4.72 (1.23 to 18.0)
Dialysis	6.25 (4.08 to 9.59)	4.23 (2.39 to 7.50)

[a]Adjusted for level of renal function; age; black race; diabetes; random serum glucose; history of coronary artery disease, congestive heart failure, hypertension, stroke, and COPD; clinical presentation (rest pain, ischemic ulceration, or gangrene); distance from nearest VA medical center; census division of residence; Medicare coverage (non-Medicare, Medicare HMO, Medicare non-HMO); and year of cohort entry.

The absence of directly measured renal function is also a limitation of this study. The abbreviated MDRD equation has not been validated in our cohort, and creatinine measurements for cohort patients are not calibrated to the MDRD reference laboratory (12). Nevertheless, use of eGFR is preferable to the use of either serum creatinine alone or diagnostic codes for renal insufficiency. Finally, the data sources that are available to us do not provide information on smoking history, an important risk factor for PAD. However, it is unlikely that our analyses are confounded by smoking history because in other cohorts with PAD, rates of past and present smoking seem to be lower among patients with renal insufficiency than those with normal renal function (4,5).

Conclusion

Patients with critical limb ischemia and concomitant renal insufficiency are less likely to be treated with revascularization than those with normal renal function. Renal insufficiency is a strong predictor of mortality in patients with critical limb ischemia independent of management strategy and of subsequent amputation among patients who undergo revascularization. However, even among patients with renal insufficiency, mortality is lowest for patients who have critical limb ischemia and receive revascularization. These findings underline the need for studies to determine the optimal care for patients with renal insufficiency and critical limb ischemia.

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