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Editor's Choice — Comparison of Outcomes After Open Surgical and Endovascular Lower Extremity Revascularisation Among End Stage Renal Disease Patients on Dialysis

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WHAT THIS PAPER ADDS

End stage renal disease (ESRD) patients with peripheral arterial disease are at high risk of complications following open surgical (OSR) or endovascular revascularisation (ER). In this retrospective analysis of a large administrative database, ESRD patients suffer from high mortality and amputation rates following both ER and OSR. Compared with OSR, ER is associated with lower mortality at all time points with equivalent long-term limb salvage. These findings suggest that an endovascular first approach in ESRD patients may be warranted, although a realistic appraisal of the patient's overall medical status and risk of competing mortality is important prior to attempting revascularisation.

Objectives: End stage renal disease (ESRD) patients with peripheral arterial disease (PAD) are at high risk of complications following open surgical revascularisation (OSR). Endovascular revascularisation (ER) is an option, but its role is unclear. This study sought to characterise the outcomes of ER and OSR in ESRD patients treated for claudication or critical limb ischaemia (CLI).
Methods: The United States Renal Data System was used to investigate outcomes after lower extremity ER and OSR from 2005 to 2011. Primary outcomes were mortality, amputation, and peri-procedural myocardial infarction (MI). Kaplan-Meier (K-M) estimates were generated for mortality and amputation, logistic regression models for 30 day predictors, and proportional hazards models for long-term predictors.
Results: A total of 20,347 patients underwent OSR and ER (20.3% OSR, 79.7% ER). CLI was the indication in 80.8% of ER and 88.4% of OSR. The unadjusted major amputation rate at 30 days was higher after ER compared with OSR (8.8% vs. 6.4%, $p < .001$). Conversely, the unadjusted mortality rate at 30 days was lower after ER compared with OSR (8.0% vs. 10.5%, $p < .001$). Multivariable logistic regression models adjusting for medical covariables and CLI versus claudication status demonstrated increased 30 day mortality risk with OSR compared with ER (OR 2.00, 95% CI 1.43—1.79, $p < .001$), MI (OR 1.38, 1.23—1.54, $p < .001$), and the combined endpoint of mortality and major amputation (OR 1.57, 1.16—2.12, $p = .004$), but lower odds of 30 day major amputation alone (OR 0.67, 0.58—0.77, $p < .001$). Proportional hazards models demonstrated increased long-term mortality risk with OSR compared with ER (HR 1.05, 1.00—1.09, $p = .037$), without a difference in major amputation (HR 0.99, 0.93—1.05, $p =$ NS).
Conclusions: In this retrospective analysis of an administrative database, ESRD patients suffer from high mortality and amputation rates following lower extremity revascularisation. Compared with ER, OSR is associated with higher mortality. OSR has better 30 day limb salvage, although long-term outcomes are similar.

Keywords: End stage renal disease, Endovascular revascularisation, Lower extremity, Open surgical revascularisation, Peripheral arterial disease, Renal failure
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INTRODUCTION

Patients with end stage renal disease (ESRD) have a high incidence of peripheral arterial disease (PAD); cross sectional studies suggest a prevalence of 27.5% in the United States with about 13% having a diagnosis of critical limb ischaemia (CLI).[1] Further, as the overall population

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ages and the rate of diabetes mellitus increases, more revascularisation and amputation procedures in this population are being performed.[2] Management of ESRD patients with PAD can be challenging, with low rates of graft patency and limb salvage with open surgical revascularisation (OSR).[3–8] Endovascular revascularisation (ER) may offer lower peri-procedural complication risk, but long-term patency and limb salvage are not well established.[2] Another important predictor is the effect of indication: claudication versus CLI, with claudicants in general having lower risks of peri-procedural complications than patients with CLI.[9] In patients without ESRD, the BASIL trial compared ER and OSR; one of the key conclusions suggested that patients with life expectancy greater than 2 years would probably be better served by OSR, with the converse being true in patients with life expectancy less than 2 years.[10,11]

This concept of tailoring treatment options based on life expectancy is particularly important in patients with ESRD, given their well known high background mortality rate.[12] Previous investigators have presented disappointing results with open surgical techniques in the ESRD population and have concluded that a selective approach to revascularisation is necessary.[13–17]

Most studies of ESRD patients undergoing ER or OSR are based on small series or subgroup analyses without significant longitudinal follow up. Therefore, this study sought to characterise contemporary peri-operative and long-term outcomes after lower extremity revascularisation in patients on dialysis in the United States. Using a large administrative database, the goal was to compare clinically relevant outcomes after OSR and ER in ESRD patients to determine the impact of indication for revascularisation on outcomes and whether ER or OSR may be superior in terms of survival and avoidance of amputation.

MATERIALS AND METHODS

The United States Renal Data System (USRDS) database was used to investigate outcomes in dialysis patients undergoing lower extremity revascularisation in the United States between 2005 and 2011. Using USRDS standard analytic files, diagnoses and procedures were identified by ICD-9 and CPT codes respectively. This database is a prospectively maintained national registry that includes all ESRD patients in the United States and is designed specifically for health outcome analyses in this patient population.[18] The University of Pittsburgh Institutional Review Board approved this study. Explicit patient consent was not obtained, pursuant to Centres for Medicare and Medicaid Services rules allowing for release of limited data sets with a data use agreement executed with the USRDS Coordinating Centre.[19]

Data abstraction

The CMS-2728 form was used to identify dialysis patients. Then, CPT procedure codes were used to identify those who underwent an index ER or OSR. Patients who underwent both ER and OSR were analysed based on the first procedure identified in the database. Major amputation was defined as amputation at the above or below knee level as defined by subsequent CPT codes that indicated performance of those operations. Amputation free survival was defined as the complement of a composite endpoint that treated both major amputation and mortality as equivalent. Clinical indication for the procedure was determined by ICD-9 diagnosis codes. Changes in coding over time were accounted for in the selection of codes for this analysis (Table S1).

Statistical analyses

Primary outcomes were peri-operative and long-term mortality, amputation, a combined endpoint of amputation and mortality, and peri-procedural myocardial infarction (MI). Bivariable associations were tested using the chi-square test. Kaplan-Meier (K-M) estimates were generated for mortality and the combined endpoint of mortality and major amputation. Logistic regression models were created for 30 day predictors, while long-term predictors were identified using Cox regression models. Fig. 1 outlines how the analysis sample was selected from the full USRDS Physician-Supplier data set for 2005–2011. Patients with missing comorbidity data were dropped from the regression models; patients that did not reach the mortality endpoint were censored at the last known date alive based on available billing records.

Cox regression models were constructed for long-term mortality and the composite endpoint of mortality and amputation. For amputation, proportional hazards regressions were generated treating mortality as a competing risk. For each outcome, the interaction effect was tested, then omitted from the final model if it was non-significant. For all models, predictors were selected with a significant bivariable association (at $p < .2$) and included in a stepwise regression, with backward entry and $p > .1$ for variable removal. Procedure, indication for the procedure (i.e., claudication versus CLI), and age were included in all regressions for clinical relevance.

RESULTS

Patient characteristics

A total of 20,347 incident dialysis patients underwent OSR and ER (20.3% OSR, 79.7% ER). CLI was the indication in 80.8% of ER, and 88.4% of OSR. Patients who underwent OSR on average had lower BMI, were more likely to be male and active smokers, had fewer months on dialysis, and were slightly older. Compared with CLI patients, claudicants had lower BMI, were less likely to require assistance with daily activities, and were more likely to be smokers. Supplemental Table 2 outlines all available patient characteristics and comorbidities, while Table 1 compares procedure groups nested within limb diagnosis groups.

Thirty day (Peri-procedural) results

Within 30 days of the lower extremity revascularisation procedure, outcomes were generally worse for CLI patients,

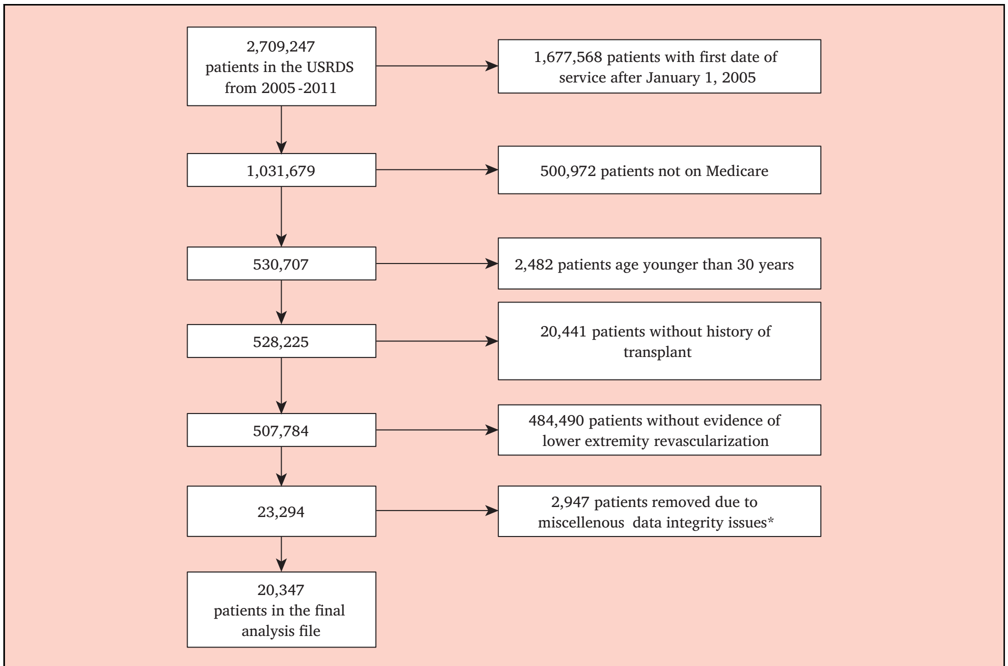

Figure 1. Patient flow chart. Excluded patients exhibited data issues primarily included inconsistent date of service and lack of ICD-9 diagnosis codes consistent with lower extremity ischemia. USRDS = United States Renal Data System. ICD-9 = Interntional Classification of Diseases, Ninth Revision.

compared with claudicants (Table 2). Specifically, major amputation was more frequent (CLI 9.4% vs. claudicants 3.2%, $p < .001$). Mortality was also higher among CLI patients (CLI 9.0% vs. claudicants 6.2%, $p < .001$). The rate of myocardial infarction was not significantly different between the two groups (CLI 8.8% vs. claudicants 9.3%, $p =$ NS).

Comparing outcomes after ER versus OSR within 30 days of the lower extremity revascularisation procedure, death, MI, and the combined endpoint of death, major

Table 1. **Patient characteristics and comorbidities: by procedure within limb diagnosis**

	Claudicant (N = 3,590)			CLI (N = 16,757)		
	ER	OSR	*p*	ER	OSR	*p*
N	3112 (87%)	478 (13%)		13,114 (78%)	3643 (22%)	
Age, years	69.2	69.3	.939	69.4	70.4	< .001
BMI, kg/m^2	28.5	26.8	< .001	29.4	28	< .001
Months on dialysis	18.3	15.7	< .001	17.9	15.2	< .001
Male	55.9%	62.3%	.009	57.3%	60.4%	.001
White race	69.4%	74.9%	.014	69.4%	69.7%	.694
Hispanic ethnicity	7.0%	5.2%	.150	8.1%	6.2%	< .001
Atherosclerotic heart disease	35.0%	36.4%	.558	33.5%	36.9%	< .001
Congestive heart failure	41.7%	40.0%	.477	46.8%	45.7%	.241
Other cardiac comorbidities	22.6%	24.5%	.352	22.7%	22.7%	.975
Cancer	5.9%	5.2%	.553	5.5%	5.9%	.372
Hypertension	87.6%	86.8%	.633	87.6%	86.2%	.023
Stroke or transient ischaemic attack	13.6%	15.7%	.224	14.4%	15.7%	.044
Diabetes	65.2%	50.6%	< .001	76.5%	70.9%	< .001
Peritoneal dialysis	6.1%	6.3%	.874	4.5%	4.7%	.519
Unable to ambulate	5.0%	5.2%	.864	9.5%	8.0%	.004
Unable to transfer	2.2%	2.3%	.943	4.2%	3.3%	.016
Institutionalised	4.8%	5.0%	.825	9.8%	8.0%	.002
Needs assistance with daily activities	9.6%	7.7%	.185	14.6%	12.6%	.003
Congenital abnormality	0.0%	0.2%	.133	0.1%	0.0%	.221
Tobacco use (current smoker)	8.4%	13.8%	< .001	5.5%	7.4%	< .001
Drug dependence	0.4%	0.4%	.688	0.3%	0.3%	.703
Alcohol dependence	0.9%	0.4%	.422	0.8%	0.7%	.573
Toxic nephropathy	0.1%	0.2%	.511	0.3%	0.3%	.583

BMI = body mass index; CLI = critical limb ischaemia; ER = endovascular revascularisation; OSR = open surgical revascularisation.

Table 2. **Unadjusted 30 day outcome rates.**

	Claudicants (N = 3,590)	CLI (N = 16,757)	*p*
Death	6.2%	9.0%	< .001
MI	9.3%	8.8%	.427
Major amputation	3.2%	9.4%	< .001
Death/major amputation	8.7%	17.4%	< .001
Death/MI/major amputation	16.5%	23.8%	< .001
	OSR (N = 4,130)	**ER (N = 16,217)**	***p***
Death	10.5%	8.0%	< .001
MI	11.1%	8.3%	< .001
Major amputation	6.4%	8.8%	< .001
Death/major amputation	16.0%	15.8%	.788
Death/MI/major amputation	24.5%	22.0%	< .001

CLI = critical limb ischaemia; ER = endovascular revascularisation; MI = myocardial infarction; OSR = open surgical revascularisation.

amputation, and MI were more common after OSR than ER (Table 2). The mortality rate at 30 days for CLI patients was 9.0% (8.6% ER, 10.5% OSR, $p < .001$), and for claudicants was 6.2% (5.6% ER, 10.7% OSR, $p =$ NS). Major amputation was less frequent after OSR (OSR 6.4% vs. ER 8.8%, $p < .001$). A comparison of vein grafts and prosthetic grafts was also performed. Of the 4121 OSR procedures, 2083 were performed with vein and 2038 were performed with a prosthetic graft. Thirty day amputation rates were approximately equal between the vein and prosthetic groups (6.1% vs. 6.7%, $p =$ NS).

Thirty day outcomes after ER versus OSR stratified by indication (CLI vs. claudication) are shown in Table 3. Among CLI patients, ER was associated with lower rates of death, MI, and the combined endpoint of death, MI, and major amputation, compared with OSR. The combined endpoint of death and amputation without MI was equally frequent after OSR and ER. The only outcome where OSR was superior to ER was the rate of major amputation (ER 10.1% vs. OSR 6.9%, $p < .001$). Meanwhile, among claudicants, ER was associated with significantly lower rates of death (ER 5.6% vs. OSR 10.7%, $p < .001$) compared with OSR, with no significant difference in the rate of major amputation.

Tables 4 and 5 present multivariable logistic models for individual and composite 30 day outcomes. Where a procedure by indication interaction is significant, post-hoc tests of procedure within indication are provided at the bottom of the table, with Bonferroni adjusted *p* values. Interpreting only the statistically significant coefficients, OSR (compared with ER) and CLI (compared with claudicants) were found to be strongly associated with most post-operative adverse outcomes, except for major amputation. For that endpoint, OSR was associated with lower risk of 30 day amputation (OR 0.67, 95% CI 0.58—0.77, $p < .001$). Further analysis was performed investigating the effect of conduit type on OSR outcomes, while adjusting for CLI status in multivariable logistic regression. ER is associated with a higher 30 day amputation risk compared with OSR with prosthetic (OR 1.36, 95% CI 1.13—1.64, $p < .001$). Compared with OSR with prosthetic, OSR with vein conduit had lower risk of 30 day amputation, but this was not statistically significant (OR 0.81, 95% CI 0.62—1.04, $p =$ NS).

Compared with ER, OSR was associated with increased 30 day mortality risk (OR 2.00, 95% CI 1.43—2.79, $p < .001$), MI (OR 1.38, 95% CI 1.23—1.54, $p < .001$), and the composite endpoints of mortality and major amputation (OR 1.57, 95% CI 1.16—2.12, $p = .004$) and mortality, major amputation, and myocardial infarction (OR 1.38, 95% CI 1.08—1.76, $p = .009$). Among claudicants, using a Bonferroni correction, OSR was associated with higher 30 day mortality odds (OR 2.00, 95% CI 1.43—2.79, $p < .001$) and the composite endpoints of mortality or amputation (OR 1.57, 95% CI 1.16—2.12, $p = .008$) and mortality, amputation, or MI (OR 1.38, 95% CI 1.08—1.76, $p = .019$) compared with ER. Among CLI patients, again using a Bonferroni correction, OSR was associated with higher mortality risk (OR 1.21, 95% CI 1.07—1.37, $p = .006$).

Table 3. **Unadjusted 30 day outcome rates, condition, and procedure crosstabulation**

	ER	OSR	*p*
Claudication			
Death	5.6%	10.7%	< .001
MI	9.1%	10.3%	.416
Major amputation	3.3%	2.5%	.373
Death/major amputation	8.2%	12.1%	.004
Death/MI/major amputation	15.8%	20.5%	.011
CLI			
Death	8.6%	10.5%	< .001
MI	8.2%	11.3%	< .001
Major amputation	10.1%	6.9%	< .001
Death/major amputation	17.6%	16.5%	.108
Death/MI/major amputation	23.4%	25.0%	.044

CLI = critical limb ischaemia; ER = endovascular revascularisation; MI = myocardial infarction; OSR = open surgical revascularisation.

Medium and long-term results

By Kaplan-Meier (K-M) analysis at one year, 87% of claudicants (87% ER, 85% OSR) and 67% of CLI patients (67% ER, 66% OSR) were major amputation free. Log rank test demonstrates that the difference in freedom from amputation for the entire curve between claudicants and CLI patients is significant at $p < .001$. However, the difference between ER and OSR is not significant. This is also true after stratifying by indication (CLI and claudication) (Supplemental Table 3). Fig. 2 displays K-M survival curves for relevant outcomes, truncated at 60 months because of a diminishing number of patients available for follow up.

With regards to mortality, 67% of claudicants (68% ER, 63% OSR) and 54% of CLI patients (54% ER, 53% OSR) were alive at one year. Log rank test demonstrates that claudicants have better survival than CLI patients. Further, patients who underwent ER have better survival than OSR

Table 4. Logistic models, 30-day outcomes.

	Death		MI		Major amputation	
	OR (95% CI)	*p*	OR (95% CI)	*p*	OR (95% CI)	*p*
Open Surgical Repair (OSR)	2.00 (1.43–2.79)	<0.001	1.38 (1.23–1.54)	<0.001	0.67 (0.58–0.77)	<0.001
Critical Limb Ischemia (CLI)	1.61 (1.36–1.91)	<0.001	0.93 (0.82–1.05)	0.237	3.20 (2.63–3.89)	<0.001
Open X CLI		0.006				
OSR within Claudication[a]	2.00 (1.43–2.79)	<0.001				
OSR within CLI[a]	1.21 (1.07–1.37)	0.006				
Age (per year)	1.03 (1.03–1.04)	*<0.001*	0.99 (0.99–1.00)	0.325	0.99 (0.98–0.99)	<0.001
BMI (per kg/m^2)	0.99 (0.98–1.00)	0.014				
Years on dialysis (per year)	1.07 (1.03–1.11)	0.001			0.96 (0.92–0.99)	0.024
Male gender	0.90 (0.81–1.00)	0.042			1.12 (1.01–1.24)	0.039
White race	1.45 (1.28–1.64)	<0.001	1.24 (1.11–1.38)	<0.001	0.71 (0.64–0.79)	<0.001
Hispanic ethnicity	0.70 (0.56–0.87)	0.001				
Atherosclerotic heart disease	1.10 (0.99–1.23)	0.08	1.20 (1.08–1.32)	<0.001		
Congestive heart failure	1.27 (1.14–1.41)	<0.001				
Other cardiac comorbidities	1.19 (1.06–1.33)	0.003				
Hypertension						
Diabetes	0.83 (0.74–0.93)	0.001			1.32 (1.16–1.50)	<0.001
Peritoneal dialysis	1.34 (1.08–1.67)	0.009			1.43 (1.16–1.77)	0.001
Unable to ambulate	1.17 (0.97–1.41)	0.096				
Institutionalized	1.16 (0.97–1.39)	0.098				
Drug dependence					1.81 (0.95–3.42)	0.069
Alcohol dependence	1.58 (0.93–2.68)	0.091				

For OSR, the reference is endovascular revascularization. For CLI, the reference is claudication. For male gender, the reference is female. For white race, the reference is non-white. For Hispanic ethnicity, the reference is non-Hispanic. For peritoneal dialysis, the reference is hemodialysis. For all other dichotomous variables, the reference is the absence of the covariate. Where no values are presented for the covariates in question, these were not significant at P less than 0.1 and are intentionally omitted.
BMI = Body Mass Index, MI = Myocardial Infarction, OSR = Open Surgical Revascularisation, OR = Odds ratio, CI = Confidence interval.
[a] Open X CLI interaction is significant and the Bonferroni-adjusted *p*-values for significance testing (P < .025) are presented.

patients, as a group and also when stratified by indication (CLI vs. claudication). Similar results were seen with amputation free survival (AFS) (Supplemental Table 3).

The results of multivariable proportional hazards modelling are presented in Table 6. This demonstrated increased long-term risk of mortality with OSR compared with ER (HR 1.05, 95% CI 1.00—1.09, $p = .037$), although there was no difference in major amputation (HR 0.99, 95% CI 0.93—1.05, $p =$ NS) and the combined endpoint of mortality and major amputation (HR 0.97, 95% CI 0.94—1.01, $p =$ NS). CLI was independently associated with greater risk in terms of mortality (HR 1.45, 95% CI 1.38—1.53, $p < .001$), major amputation (HR 2.34, 95% CI 2.13—2.57, $p < .001$), and the combined endpoint of mortality and major amputation (HR 1.53, 95% CI 1.47—1.60, $p < .001$). In none of those models was the diagnosis by procedure interaction significant, suggesting that the effect of the procedure does not vary between the two diagnoses.

The majority of patients did not receive any re-interventions after initial lower extremity revascularisation in this data set, and those that did receive a re-intervention tended to stay with the initial modality. After ER, 77.6% did not undergo any subsequent lower extremity interventions. Only 4.2% changed revascularisation modality and underwent subsequent OSR; 16.7% underwent repeat ER, and 1.5% underwent both ER and OSR. Similarly, after initial OSR, 80.0% did not undergo any subsequent lower extremity interventions. Only 7.0% changed modality and underwent ER; 10.7% underwent repeat OSR, and 2.3% underwent both ER and OSR. While the absolute difference in repeat procedures between initial ER and OSR was small, this was statistically significant (ER 77.6%, OSR 80.0%; $p < .001$).

DISCUSSION

The present analysis, which used a large contemporary administrative database from the United States, suggests challenging short and long-term mortality rates after both OSR and ER for ESRD patients. These results echo other recent analyses studying smaller populations with ESRD.[20,21] Patients with ESRD on dialysis have higher rates of limb loss and mortality compared with patients with normal renal function or milder degrees of renal insufficiency.[22,23] The majority of ESRD patients in this series were treated for CLI,[20] and in general, CLI patients have worse outcomes than claudicants.[9,24]

In line with this literature, patients with CLI had poorer outcomes compared with claudicants, with much higher mortality rates and lower limb salvage rates. Further, increasing age, increasing time on dialysis, lower BMI, and white race were also associated with worse outcomes, as in previous studies of ESRD patients; survival rates in this cohort also appear to be worse than the overall ESRD population.[12] The present findings, however, differed in certain respects. Most importantly, it was found that OSR was associated with significantly increased risk of both peri-

Table 5. Logistic models, 30-day outcomes.

	Death or amputation		Death, MI or amputation	
	OR (95% CI)	*p*	OR (95% CI)	*p*
Open Surgical Repair (OSR)	1.57 (1.16–2.12)	0.004	1.38 (1.08–1.76)	0.009
Critical Limb Ischemia (CLI)	2.42 (2.11–2.78)	<0.001	1.63 (1.47–1.81)	<0.001
Open X CLI	0.57	0.001	0.77	0.048
OSR within Claudication[a]	1.57 (1.16–2.12)	0.008	1.38 (1.08–1.76)	0.019
OSR within CLI[a]	0.89 (0.81–0.99)	0.057	1.06 (0.98–1.16)	0.311
Age (per year)	1.01 (1.00–1.01)	<0.001	1.00 (1.00–1.01)	0.016
BMI (per kg/m^2)	0.99 (0.99–1.00)	0.054	0.99 (0.99–1.00)	0.02
Years on dialysis (per year)				
Male gender				
White race				
Hispanic ethnicity	0.87 (0.75–1.02)	0.079		
Atherosclerotic heart disease	1.09 (1.01–1.19)	0.037	1.12 (1.04–1.21)	0.002
Congestive heart failure	1.15 (1.06–1.24)	0.001	1.12 (1.04–1.20)	0.002
Other cardiac comorbidities	1.11 (1.01–1.21)	0.024	1.11 (1.02–1.20)	0.011
Hypertension			0.90 (0.82–0.99)	0.039
Diabetes				
Peritoneal dialysis	1.41 (1.19–1.66)	<0.001	1.18 (1.01–1.37)	0.036
Unable to ambulate	1.19 (1.04–1.35)	0.010		
Institutionalized				
Drug dependence	1.71 (0.96–3.06)	0.071		
Alcohol dependence				

For OSR, the reference is endovascular revascularization. For CLI, the reference is claudication. For male gender, the reference is female. For white race, the reference is non-white. For Hispanic ethnicity, the reference is non-Hispanic. For peritoneal dialysis, the reference is hemodialysis. For all other dichotomous variables, the reference is the absence of the covariate. Where no values are presented for the covariates in question, these were not significant at P less than 0.1 and are intentionally omitted.
BMI = Body Mass Index, MI = Myocardial Infarction, OR = Odds ratio, CI = Confidence interval.
[a] Open X CLI interaction is significant and the Bonferroni-adjusted *p*-values for significance testing ($P < .025$) are presented.

operative and long-term mortality, compared with ER. The high 30 day peri-operative mortality rates found after OSR (10.5%) are on par with those reported in another recent United States observational database (7.8%).[23] While there is a lower risk of 30 day amputation with OSR, this initial advantage was not durable, and both univariable and proportional hazards multivariable models demonstrated equivalent long-term outcomes.

Recently, Fallon et al. queried the Vascular Study Group of New England (VSGNE) database. They reported that the only statistically significant difference between the ER and OSR groups was improved patency in the ER group. They did not report a difference in major adverse limb events, overall survival, nor amputation free survival.[20] The difference between the present results and those reported by Fallon et al. may in part be related to the larger sample size afforded by the USRDS, with more than 20,000 patients available for analysis.

The data from this study demonstrate that amputation was less frequent than mortality, with two thirds of patients free from amputation at one year in both the ER and OSR groups. These limb salvage rates compare favourably with smaller studies.[4,20] Further, the present data show that ER is associated with superior survival and AFS rates with equivalent long-term amputation rates in both claudicants and CLI patients, compared with OSR. These findings suggest that an "endovascular first" approach may be appropriate for ESRD patients with CLI, especially as the median survival of CLI patients was a little over one year in this analysis. Similarly, the BASIL trialists suggested that ER be offered to patients whose life expectancy is less than 2 years, given the peri-operative morbidity and higher first year resource expenditures associated with OSR.[10,11]

Some authors have advocated the aggressive management of critical limb ischaemia in ESRD patients, based on the observation that patients who undergo amputation are at high risk of subsequent death.[25] More recently, other authors have recommended reserving revascularisation for patients with favourable survival potential and offering palliative options or primary amputation to the remainder.[20] As limb loss is clearly associated with loss of independence and the need for institutional care, with significant implications for quality of life and cost of care,[25] an aggressive limb salvage effort in this population can be justified, with ER and OSR having important roles.

Consensus regarding the optimal management of CLI has not yet emerged. Revascularisation distal to the zone of arterial stenosis or occlusion is usually necessary to improve limb perfusion. The decision to employ OSR or ER varies among providers. This is probably related to disease pattern, the availability of great saphenous vein for conduit, the clinical specialty and training of the clinician, the surgical and endovascular skills of the practitioners, and access to suitable facilities.[26] In practice, a diagnostic arteriogram is useful for nearly all ESRD patients with CLI who can tolerate the procedure. If the

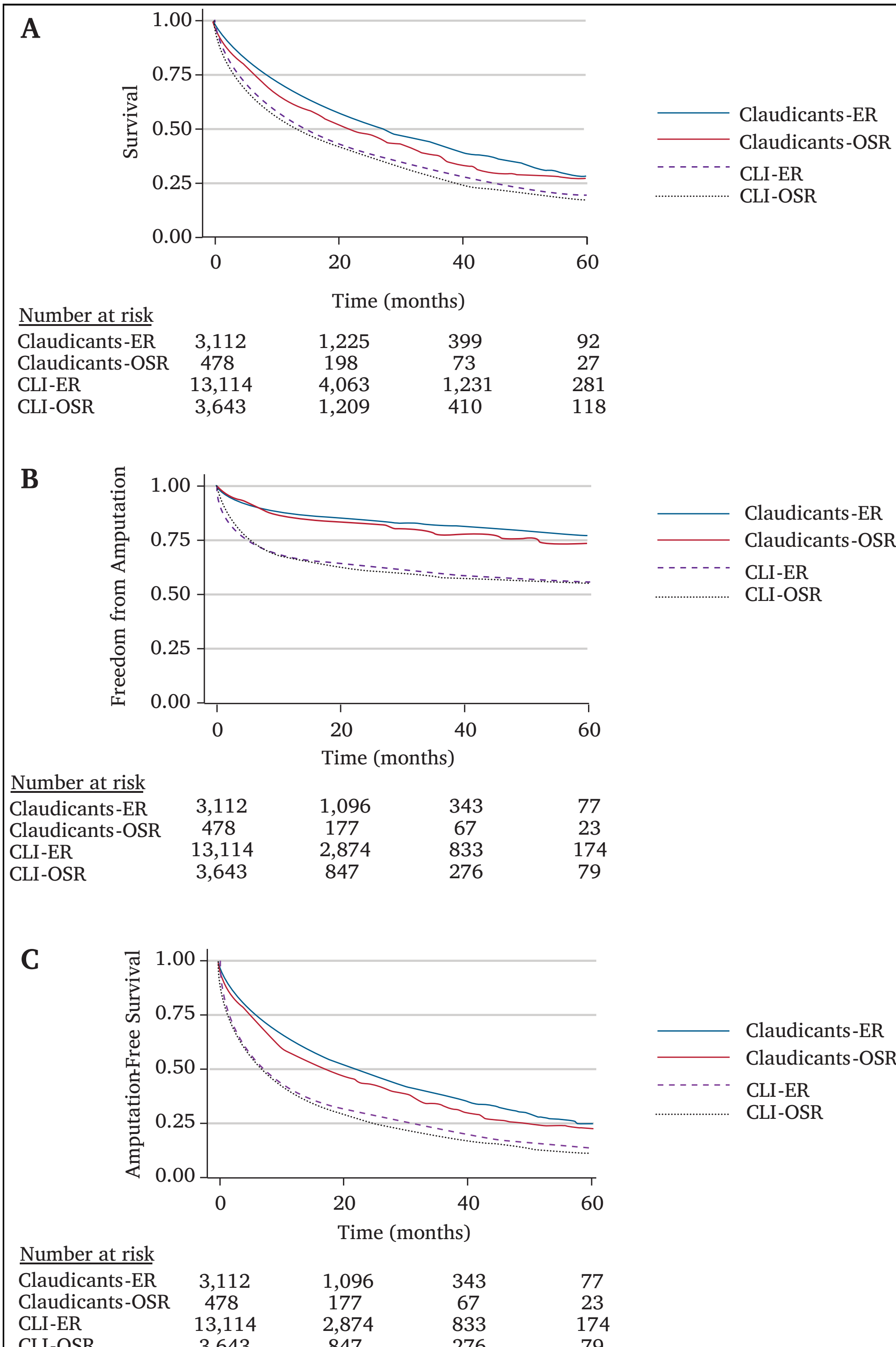

Figure 2. Kaplan-Meier survival estimates after lower extremity revascularisation: survival (A), freedom from amputation (B), and amputation free survival (C). Standard error less than 10% at all time points. CLI = Critical Limb Ischemia, ER = Endovascular Revascularisation, OSR = Open Surgical Revascularisation.

patient has anatomy suitable for endovascular treatment, intervention can be offered. Setting expectations for the patient and the family is critical, ensuring that they understand that even if the limb is salvaged, mortality rates are still high. OR can also be offered if the patient's anatomy and physiology are appropriate. In certain situations where limb salvage is unlikely or inappropriate because of non-ambulatory status, extensive tissue loss,

Table 6. Multivariate long-term proportional-hazards regression models.

	Death		Major amputation		Death or Major amputation	
	HR (95% CI)	*p*	HR (95% CI)	*p*	HR (95% CI)	*p*
Open Surgical Repair (OSR)	1.05 (1.00–1.09)	0.037	0.99 (0.93–1.05)	0.729	0.97 (0.94–1.01)	0.152
Critical Limb Ischemia (CLI)	1.45 (1.38–1.53)	<0.001	2.34 (2.13–2.57)	<0.001	1.53 (1.47–1.60)	<0.001
Age, per year	1.02 (1.02–1.02)	<0.001	0.98 (0.98–0.99)	<0.001	1.01 (1.01–1.01)	<0.001
BMI, per kg/m2	0.99 (0.99–0.99)	<0.001			0.99 (0.99–1.00)	<0.001
Years on dialysis			0.93 (0.91–0.95)	<0.001	1.06 (1.05–1.08)	<0.001
Male gender			1.24 (1.17–1.31)	<0.001	1.09 (1.05–1.12)	<0.001
White race	1.33 (1.28–1.39)	<0.001	0.65 (0.61–0.69)	<0.001	1.11 (1.07–1.15)	<0.001
Hispanic ethnicity	0.81 (0.75–0.87)	<0.001	1.21 (1.10–1.33)	<0.001	0.89 (0.84–0.94)	<0.001
Atherosclerotic heart disease			1.07 (1.01–1.14)	0.020		
Congestive heart failure	1.18 (1.13–1.22)	<0.001			1.12 (1.09–1.15)	<0.001
Other cardiac comorbidities	1.13 (1.09–1.18)	<0.001			1.11 (1.07–1.15)	<0.001
Cancer	1.10 (1.02–1.18)	0.013	0.90 (0.79–1.02)	0.099		
Hypertension	0.91 (0.86–0.96)	<0.001			0.92 (0.88–0.96)	<0.001
Peripheral vascular disease	0.95 (0.92–0.99)	0.016	1.07 (1.00–1.13)	0.035		
Diabetes			1.42 (1.33–1.53)	<0.001	1.08 (1.05–1.12)	<0.001
Peritoneal dialysis	1.26 (1.16–1.36)	<0.001	1.24 (1.10–1.40)	<0.001	1.23 (1.15–1.32)	<0.001
Unable to ambulate	1.09 (1.01–1.18)	0.029			1.12 (1.06–1.19)	<0.001
Unable to transfer	1.10 (0.98–1.22)	0.097				
Institutionalized	1.07 (1.00–1.15)	0.04			1.11 (1.05–1.18)	<0.001
Needs assistance with daily activities			1.07 (0.99–1.16)	0.083		
Tobacco use (current smoker)	1.09 (1.01–1.18)	0.019	0.85 (0.75–0.95)	0.004	1.08 (1.02–1.15)	0.015
Toxic nephropathy	0.67 (0.46–0.99)	0.045				

For OSR, the reference is endovascular revascularization. For CLI, the reference is claudication. For male gender, the reference is female. For white race, the reference is non-white. For Hispanic ethnicity, the reference is non-Hispanic. For peritoneal dialysis, the reference is hemodialysis. For all other dichotomous variables, the reference is the absence of the covariate. Where no values are presented for the covariates in question, these were not significant at P less than 0.1 and are intentionally omitted.
BMI = Body Mass Index; HR = Hazard ratios or sub-Hazard Ratios from Cox regression or competing-risks regression; CI = Confidence interval.

or infection, primary amputation may be the patient's best option.

The findings from this study also touch on management strategies for ESRD patients with claudication. Claudicants typically have a relatively benign natural history compared with patients with CLI.[9,26] In that context, the observation that about one third of claudicants had died one year after the index procedure, regardless of modality, is significant. This high risk of mortality needs to be weighed carefully against any possible improvement in quality of life. Non-invasive therapy, maximizing medical management, should be the preferred treatment for ESRD patients with claudication. In the rare circumstances where revascularisation is pursued, ER may be the preferred option.

The present findings can also be placed in the context of the latest European Society of Cardiology Guidelines on the diagnosis and treatment of peripheral arterial disease.[27] This consensus document offers a balanced view of both ER and OSR being employed in the management of lower extremity arterial disease, depending on medical and anatomical characteristics. In patients who are considered high surgical risk, endovascular therapy can be a first line therapy. The present findings suggest that many ESRD patients are at high risk of surgery; as such, first line treatment with ER may be reasonable, in patients with appropriate anatomy.

Limitations

The USRDS has been used previously to analyse outcomes in ESRD patients in the United States and has known weaknesses.[28,29] As with other observational studies using administrative databases, the present analysis rests on the accuracy of the coding of procedures, outcomes, and diagnoses. Further, the analysis did not benefit from information including degree of stenosis, length of occlusions, or runoff vessels, which are not available in the database. Inevitably, the choice of ER versus OSR will be affected by these anatomical details, the patient's clinical presentation and surgical history, and the biases and training of the clinicians treating the patients. None of this is available in the USRDS, although attempts were made to use available ICD-9 codes and clinical data to adjust for medical diagnoses where possible. Other issues include lack of information on laterality, and an apparent dearth of patients who underwent simultaneous OSR and ER at the time of the index procedure, which was found in less than 1% of the study population; this may be an underestimate. It is recognised that unmeasured confounders are still present, leading to residual selection bias. The effects on the study results are difficult to predict. It is unclear whether ER patients are differentially coded compared with OSR patients, reducing the possible impact on the comparison between the two revascularisation modalities. The possibility of subsequent procedures was also investigated, and while the majority of subjects did not undergo subsequent procedures, there was some minor crossover. Finally, caution should be used in extrapolating these results to justify ER in situations that have not conventionally been managed by ER, as this analysis is unable to ascertain outcomes after interventions where a surgical bypass would traditionally be considered the only option.

Despite these limitations, the large sample size analysed in this study allows reporting on the clinically relevant and well defined endpoints of amputation and survival, and also provides considerable power to detect differences in these outcomes. Future analyses investigating subgroups and the impact of different conduit types for bypass or endovascular revascularisation techniques may be possible based on procedure codes.

CONCLUSIONS

Patients with ESRD who undergo lower extremity revascularisation are fragile and suffer from high rates of peri-procedural and long-term mortality after both ER and OSR. As OSR is associated with higher rates of peri-operative and long-term mortality but similar rates of long-term amputation, ER may be the preferred initial modality. However, randomised studies are needed in this population before drawing firm conclusions. Finally, a realistic appraisal of the patient's overall medical status and risk of competing mortality is important when determining whether even an attempt at revascularisation is appropriate.

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APPENDIX A. SUPPLEMENTARY DATA

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejvs.2018.09.008.

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CONFLICT OF INTEREST

None.

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