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CLINICAL RESEARCH
Cardiac and vascular surgery

Long-term outcomes following endovascular and surgical revascularization for peripheral artery disease: a propensity score-matched analysis

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Aims

Peripheral artery disease (PAD) revascularization can be performed by either endovascular or open surgical approach. Despite increasing use of endovascular revascularization, it is still uncertain which strategy yields better long-term outcomes.

Methods and results

This retrospective cohort study evaluated patients hospitalized with PAD in Australia and New Zealand who underwent either endovascular or surgical revascularization between 2008 and 2015, and compared procedures using a propensity score-matched analysis. Hybrid interventions were excluded. The primary endpoint was mortality or major adverse limb events (MALE), defined as a composite endpoint of acute limb ischaemia, urgent surgical or endovascular reintervention, or major amputation, up to 8 years post-hospitalization using time-to-event analyses 75 189 patients fulfilled eligibility (15 239 surgery and 59 950 endovascular), from whom 14 339 matched pairs (mean ± SD age 71 ± 12 years, 73% male) with good covariate balance were identified. Endovascular revascularization was associated with an increase in combined MALE or mortality [hazard ratio (HR) 1.13, 95% confidence interval (CI): 1.09–1.17, $P < 0.001$]. There was a similar risk of MALE (HR 1.04, 95% CI: 0.99–1.10, $P = 0.15$), and all-cause urgent rehospitalizations (HR 1.01, 95% CI: 0.98–1.04, $P = 0.57$), but higher mortality (HR 1.16, 95% CI: 1.11–1.21, $P < 0.001$) when endovascular repair was compared to surgery. In subgroup analysis, these findings were consistent for both claudication and chronic limb-threatening ischaemia presentations.

Conclusion

Although the long-term risk of MALE was comparable for both approaches, enduring advantages of surgical revascularization included lower long-term mortality. This is at odds with some prior PAD studies and highlights contention in this space.

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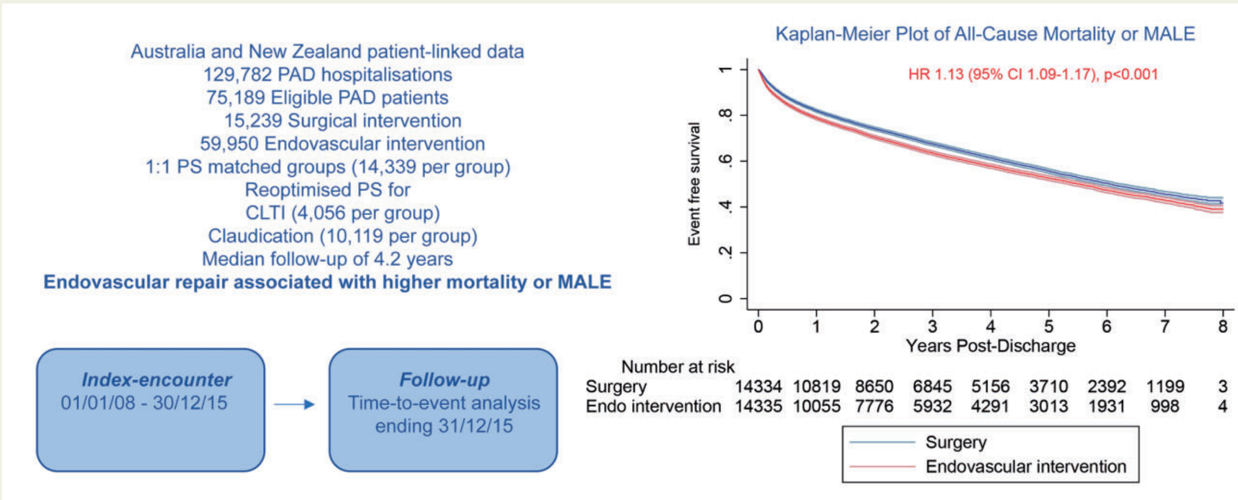
Graphical Abstract



Keywords Peripheral artery disease • Revascularization • Mortality

Introduction

In Western countries, peripheral artery disease (PAD) becomes more prevalent with increasing age and affects more than 14% of people above the age of 70. The disease burden is expected to increase due to ageing demographics and the rise in metabolic risk factors.[1] Peripheral artery disease exists as a spectrum spanning asymptomatic subclinical disease, stable claudication, and chronic limb-threatening ischaemia (CLTI), which is associated with ulceration, gangrene, and amputation.[2,3] Peripheral artery revascularization may be performed to improve symptoms, walking distance, wound healing, or limb salvage. Traditionally, revascularization was achieved with open surgical repair, where lower extremity atherosclerotic plaques are removed by endarterectomy or bypassed using an autogenous vein or prosthetic graft.[4] Endovascular repair, consisting of balloon angioplasty with or without stent insertion, has evolved and has rapidly gained dominance as the more commonly used approach to revascularization.[5]

The popularity of endovascular repair stems from the less-invasive nature of these procedures, shorter length of hospital stay, and a perceived reduction in periprocedural complications compared with open surgery.[6,7] However, persisting debate exists as to whether surgical repair leads to more durable vascularization, and therefore is associated with less reintervention, lower long-term risk of major adverse limb events (MALE), and possibly differences in long-term survival. Current evidence favouring either strategy is limited, with few randomized trials directly comparing endovascular or surgical repair.[8] Existing clinical trials have also been restricted by small sample size, open-label, and non-comparative designs, limiting the strength of their conclusions.[9] So, despite the widespread use of revascularization for PAD treatment, the optimal strategy for durable outcomes has not been determined.

In this study, we compared the long-term incidence of combined mortality or MALE following either surgery or endovascular revascularization using national data from Australia and New Zealand. We also evaluated other secondary outcomes and performed a subgroup analysis, according to clinical presentation with CLTI and intermittent claudication.

Methods

Study design

We used a retrospective cohort study design using hospital administrative data and death data linked at an individual patient level from Australia and New Zealand and followed the STROBE guidelines for reporting of observational studies.[10]

Data source

Hospitalization data were obtained from the Admitted Patient Collection from each Australian State and Territory and the equivalent New Zealand National Minimum Dataset (Hospital Events) from 1 January 2008 to 31 December 2015. These datasets record all inpatient and day-only admissions from all public and most (80%) private sector hospitals and day procedure centres. For each contact, procedural data are collected using a standard set of variables including patient characteristics, primary and secondary diagnoses, all procedures performed, and the patient status at discharge. In Australia and New Zealand, diagnoses are coded according to the International Classification of Diseases, 10th Revision-Australian Modification (ICD-10-AM), and all procedures are coded according to the Australian Classification of Health Interventions (ACHI). Prior studies in the Australian setting have shown >85% coding accuracy with cardiovascular diagnoses and procedures, and lower-limb amputations being particularly well coded.[11,12]

In Australia, the patients' hospitalization was linked to subsequent events in any hospital and each region's Registry of Deaths to assess long-term outcomes. Linkages of all health records were performed using probabilistic matching techniques based on multiple patient identifiers by designated data-linkage units within each region. This approach has been shown to have a low likelihood of linkage errors.[13] In New Zealand, hospital encounters are linked nationally using a unique National Health Index number, and all deaths are recorded in the National Health Index sociodemographic profile.

The Human Research Ethics Committees of all respective Australian states and territories provided ethics approval to undertake the study with a waiver of informed consent to use de-identified patient data. Data from New Zealand are obtained under a data user agreement with the New Zealand Ministry of Health.

Study population

We included patients aged ≥18 years who were hospitalized with a primary diagnosis of PAD (or equivalent) and had procedure code indicating surgical or endovascular peripheral artery revascularization during their admission. Diabetes with lower extremity complications, lower-limb osteomyelitis, or a procedure for lower extremity osteomyelitis were considered as PAD-equivalent diagnoses in the context of revascularization. This mirrored previously published methods.[14,15] ICD-10-AM diagnoses and ACHI procedure codes were used to define these encounters (Supplementary material online, *Table S1*). We excluded patients with hybrid interventions where surgery and an endovascular intervention were coded during the same admission. We also excluded patients who discharged against medical advice. For patients with multiple admissions in the study period, the first hospitalization was considered the index encounter to prevent double counting of patients and to ensure included patients were unique. Subsequent hospitalizations for these patients were considered as outcomes if they met the outcome definition(s). Presentations with rest pain, osteomyelitis, ulceration, or gangrene were classified as CLTI, whereas all others were considered to be intermittent claudication.

Study outcomes

The primary outcome was the incidence of a combined endpoint of all-cause mortality and MALE, which was defined as a primary diagnosis of acute limb ischaemia, urgent endovascular reintervention or embolectomy, urgent surgical reintervention, or major amputation (defined as occurring at or above the ankle). Secondary endpoints were individual components of the primary outcome, major bleeding, all-cause urgent rehospitalization, and less-severe adverse limb events, including elective surgical or endovascular reintervention, and minor amputation (defined as occurring below the ankle). Urgent reinterventions and urgent rehospitalizations were defined as clinical conditions requiring admission within 24 h consistent with the definition of emergency hospitalization,[16] with all other hospitalizations defined as an elective (scheduled or planned) encounter. The diagnosis and procedure codes used to identify these events are available in the Supplementary material online, *Table S2*.

Statistical analysis

Data are summarized as frequencies and percentages for categorical variables. For continuous variables, we assessed the normality of the data by assessing the distribution of data points. Continuous variables are presented as mean and standard deviation for normally distributed variables or median and interquartile range (IQR) for non-normally distributed variables. The χ^2 test, Fisher's exact test, and Student's *t*-test were used to compare endovascular and surgical intervention as appropriate.

We used propensity score matching to account for differences in baseline characteristics arising from the non-random assignment of surgical or endovascular intervention. We first developed a propensity score, indicating the conditional probability that any individual patient would undergo endovascular intervention using a logistic regression model. Variables included patient age, gender, geographic region, PAD history, cardiovascular history, and other comorbidities. Cardiac history and comorbidities were derived using the Condition Categories classification,[17,18] which groups ICD-10-AM codes into clinically meaningful comorbidities using secondary diagnosis codes from the index hospitalization, as well as the principal and secondary diagnosis codes from all hospitalizations in the preceding 12 months (see Supplementary material online, *Table S3*, which outlines the Condition Categories used to define comorbidities). Patients undergoing endovascular intervention were then matched 1:1 without replacement to patients who underwent surgery based on the propensity score using a calliper width of 0.01 to derive a propensity score-matched cohort.[19] Covariate balance post-matching was assessed by estimating the mean absolute standardized difference between the treatment groups.[20] Due to the potential heterogeneity among patients, we conducted analyses of outcomes in patients with CLTI and intermittent claudication separately, reoptimizing the propensity score and matching 1:1 within each group.

Unadjusted event-free survival curves in the propensity score-matched cohort were generated using Kaplan–Meier estimates and compared using the log-rank test. All time-to-event outcomes were reported as hazard ratios (HRs) and 95% confidence intervals (CIs) with patients treated with surgery as the reference group. The significance levels were two-sided with a $P < 0.05$. No correction for multiple hypothesis testing was applied. The analyses were conducted using SAS 9.4 (SAS Institute Inc., Cary, NC, USA).

Results

Study population

We identified 75 189 eligible patients, including 15 239 (20.3%) initially undergoing surgery and 59 950 (79.7%) treated endovascularly (see Supplementary material online, *Figure S1*). The baseline characteristics of these unmatched groups are displayed in the Supplementary material online, *Table S4*. A propensity score model with a good discriminatory capacity (c statistic 0.742) was derived using 141 measured baseline variables. Patients undergoing endovascular and surgical intervention were then matched 1:1 to create a final cohort consisting of 28 678 patients with 14 339 patients per group. These two groups had comparable baseline characteristics distribution of propensity scores post-matching (*Table 1* and Supplementary material online, *Table S4* and *Figure S2*). Post-matching, all variables had a standardized difference of <10%, indicating minimal residual covariate imbalance (Supplementary material online, *Figure S3*).[20,21] A subgroup analysis was also performed with reoptimized 1:1 matching of endovascular and surgical patients presenting with CLTI ($n = 4056$ per group) and intermittent claudication ($n = 10\,119$ per group). The baseline characteristics of the matched CLTI and intermittent claudication cohorts remained similar (Supplementary material online, *Table S5*). The maximum duration of follow-up was 8 years, with a median follow-up duration of 4.2 years (IQR 2.1, 6.2 years) (*Graphical abstract*).

Table 1 Baseline characteristics[a] in the propensity score-matched cohorts

	Propensity score-matched cohorts		Standardized difference (%)
	Surgical (n = 14 339) n (%)	Endovascular (n = 14 339) n (%)	
Demographics			
Age, years (mean ± SD)	71.0 ± 11.5	70.9 ± 12.2	1.1
Age group			
18–54	1225 (8.5)	1525 (10.6)	7.1
55–64	2689 (18.8)	2650 (18.4)	1.0
65–74	4615 (32.2)	4236 (29.5)	5.8
75–84	4320 (30.1)	4115 (28.7)	3.1
≥85	1490 (10.4)	1813 (12.6)	6.9
Male sex	10 453 (72.9)	10 314 (71.9)	2.1
Presentation			
Elective	11 379 (79.4)	10 916 (76.1)	8.0
CLTI	4093 (28.5)	4462 (31.1)	5.7
Private hospital	4291 (29.9)	3750 (26.2)	8.0
Region			
NSW/ACT	3264 (22.8)	3627 (25.3)	5.9
VIC	3742 (26.1)	3324 (23.2)	6.7
QLD	2952 (20.6)	2747 (19.2)	3.5
SA/NT	915 (6.4)	948 (6.6)	0.8
TAS	132 (0.9)	145 (1.0)	1.0
WA	826 (5.8)	687 (4.8)	4.5
NZ	2508 (17.5)	2861 (20.0)	6.4
Limb history			
Prior vascular disease[b]	6296 (43.9)	6897 (48.1)	9.1
Prior vascular intervention[b]	934 (6.5)	1096 (7.6)	4.8
Prior limb amputation	655 (4.6)	794 (5.5)	4.6
Cardiovascular history			
Prior coronary angiogram	1000 (7.0)	1122 (7.8)	3.4
Prior PCI	290 (2.0)	333 (2.3)	2.0
Prior CABG	210 (1.5)	235 (1.6)	1.5
ACS	665 (4.6)	793 (5.5)	4.1
Ischaemic heart disease	1640 (11.4)	1859 (13.0)	4.9
Hypertension	4812 (33.6)	5293 (36.9)	7.2
Heart failure	1063 (7.4)	1204 (8.4)	3.7
Valvular heart disease	361 (2.5)	407 (2.8)	2.1
Arrhythmia or conduction disorder	1100 (7.7)	1261 (8.8)	4.1
Cerebrovascular diseases	464 (3.2)	521 (3.6)	2.3
Other comorbidities			
Diabetes mellitus	3932 (27.4)	4260 (29.7)	5.0
Chronic lung disease	804 (5.6)	904 (6.3)	3.2
Renal failure	1217 (8.5)	1425 (9.9)	4.9

ACS, acute coronary syndrome; CABG, coronary artery bypass grafting; CLTI, chronic limb-threatening ischaemia; PCI, percutaneous coronary intervention; SD, standard deviation.
[a]A more comprehensive list of baseline characteristics of the matched cohorts is available in Supplementary material online, *Table S1*.
[b]Refers broadly to any prior peripheral vascular disease or peripheral vascular intervention.

Outcomes

Following propensity score matching, endovascular repair was associated with higher rates of MALE or all-cause mortality compared with surgery (41.2% vs. 40.1%, HR 1.13, 95% CI 1.09–1.17, $P < 0.001$; *Table 2* and *Figure 1A*). When secondary outcomes were considered, the endovascular and surgical groups had similar rates, respectively, of MALE (17.4% vs. 17.6%, HR 1.04, 95% CI 0.99–1.10, $P = 0.15$), major bleeding (9.0% vs. 9.3%, HR 1.03, 95% CI 0.95–1.11, $P = 0.46$), and all-cause urgent rehospitalizations (53.5% vs. 55.9%, HR 1.01, 95% CI 0.98–1.04, $P = 0.57$) (*Figure 1B*), but higher rates of all-cause

Table 2 Outcomes of endovascular vs. surgical revascularization for the propensity score-matched patients

Outcomes	Cumulative incidence for surgery (n = 14 339)	Cumulative incidence for endovascular intervention (n = 14 339)	HR (95% CI)	*P*-value
MALE or mortality	5745 (40.1%)	5904 (41.2%)	1.13 (1.09–1.17)	<0.001
MALE	2529 (17.6%)	2493 (17.4%)	1.04 (0.99–1.10)	0.153
Mortality	4170 (29.1%)	4396 (30.7%)	1.16 (1.11–1.21)	<0.001
MALE subcategories				
Urgent surgical reintervention	760 (5.3%)	528 (3.7%)	0.72 (0.65–0.81)	<0.001
Urgent endovascular reintervention	1105 (7.7%)	1249 (8.7%)	1.20 (1.11–1.30)	<0.001
Major amputation	966 (6.7%)	950 (6.6%)	1.03 (0.94–1.13)	0.480
Thrombolysis	278 (1.9%)	256 (1.8%)	0.97 (0.82–1.15)	0.742
Arterial emboli/thrombus	1054 (7.4%)	829 (5.8%)	0.82 (0.75–0.90)	<0.001
Less-severe limb events	10 411 (72.6%)	10 756 (75.0%)	1.14 (1.11–1.17)	<0.001
Less-severe limb events subcategories				
Elective surgical reintervention	2286 (15.9%)	1496 (10.4%)	0.67 (0.63–0.71)	<0.001
Elective endovascular reintervention	2935 (20.5%)	3930 (27.4%)	1.50 (1.43–1.57)	<0.001
Minor amputation	912 (6.4%)	1209 (8.4%)	1.40 (1.28–1.52)	<0.001
PAD-related readmission not meeting MALE criteria	6586 (45.9%)	6281 (43.8%)	1.02 (0.98–1.05)	0.388
Major bleeding	1336 (9.3%)	1287 (9.0%)	1.03 (0.95–1.11)	0.463
All-cause urgent rehospitalizations	8016 (55.9%)	7667 (53.5%)	1.01 (0.98–1.04)	0.565

HR expressed with surgical intervention as the reference group.
CI, confidence interval; HR, hazard ratio; MALE, major adverse limb events; PAD, peripheral artery disease.

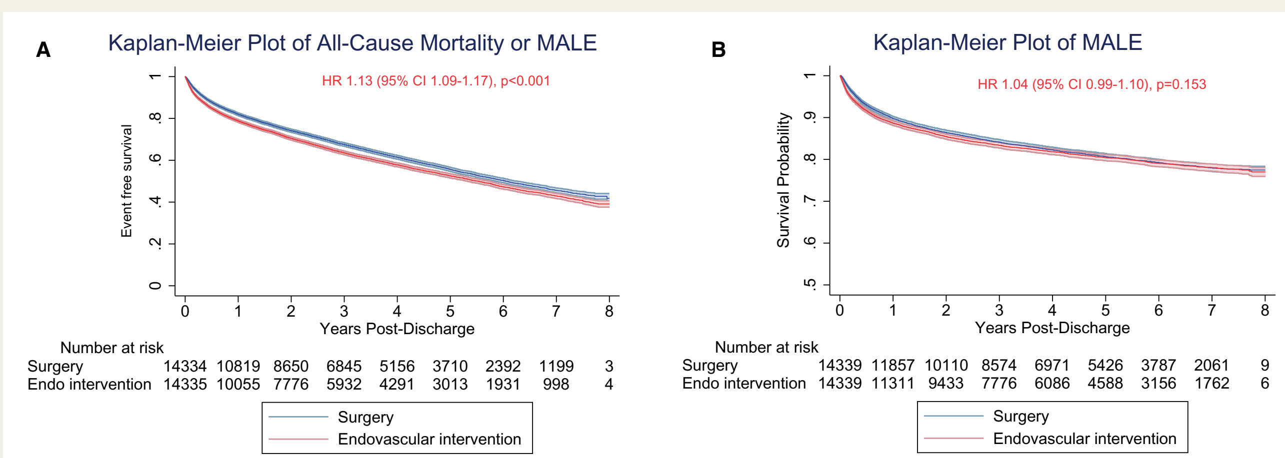


Figure 1 Kaplan–Meier survival curve in propensity score-matched individuals receiving endovascular and surgical revascularization. Kaplan–Meier curves for (*A*) all-cause mortality or major adverse limb events and (*B*) major adverse limb events.

mortality (30.7% vs. 29.1%, HR 1.16, 95% CI 1.11–1.21, $P < 0.001$) and the composite of less-severe limb events (75.0% vs. 72.6%, HR 1.14, 95% CI 1.11–1.17, $P < 0.001$). These outcome differences were similar at 6 months, 1, and 5 years (Supplementary material online, *Table S6*). When we repeated the analysis with a Cox regression model to adjust for variables with a post-matching standardised difference ≥5%, endovascular revascularisation was still significantly associated with the primary outcome (Supplemental material online, Table S7).

Of the MALE subcategories, endovascular patients were less likely to require urgent surgical reintervention (3.7% vs. 5.3%, HR 0.72, 95% CI 0.65–0.81, $P < 0.001$), or experience arterial embolus/thrombus (5.8% vs. 7.4%, HR 0.82, 95% CI 0.75–0.90, $P < 0.001$), but at the expense of higher rates of urgent endovascular reintervention (8.7% vs. 7.7%, HR 1.20, 95% CI 1.11–1.30, $P < 0.001$). Examining less-severe limb events that were not categorized as MALE, the endovascular patients had a higher rate of elective endovascular intervention (27.4% vs. 20.5%, HR 1.50, 95% CI

Table 3 Outcomes of endovascular vs. surgical revascularization for propensity score-matched individuals presenting with chronic limb-threatening ischaemia

Outcomes	Chronic limb-threatening ischaemia			
	Cumulative incidence for surgery ($n = 4056$)	Cumulative incidence for endovascular intervention ($n = 4056$)	HR (95% CI)	*P*-value
MALE or mortality	2432 (60.0%)	2385 (58.8%)	1.09 (1.03–1.16)	0.002
MALE	1043 (25.7%)	1029 (25.4%)	1.05 (0.96–1.14)	0.266
Mortality	1895 (46.7%)	1827 (45.8%)	1.09 (1.02–1.16)	0.008
MALE subcategories				
Urgent surgical reintervention	284 (7.0%)	193 (4.8%)	0.71 (0.59–0.85)	<0.001
Urgent endovascular reintervention	443 (10.9%)	533 (13.1%)	1.30 (1.15–1.47)	<0.001
Major amputation	561 (13.8%)	539 (13.3%)	1.02 (0.90–1.14)	0.800
Thrombolysis	82 (2.0%)	68 (1.7%)	0.87 (0.63–1.20)	0.401
Arterial emboli/thrombus	275 (6.8%)	180 (4.4%)	0.69 (0.57–0.83)	<0.001
Less-severe limb events	3058 (75.4%)	3158 (77.9%)	1.16 (1.11–1.22)	<0.001
Less-severe limb events subcategories				
Elective surgical reintervention	538 (13.3%)	310 (7.6%)	0.59 (0.52–0.68)	<0.001
Elective endovascular reintervention	812 (20.0%)	1029 (25.4%)	1.40 (1.28–1.54)	<0.001
Minor amputation	608 (15.0%)	772 (19.0%)	1.37 (1.23–1.52)	<0.001
PAD-related readmission not meeting MALE criteria	1912 (47.1%)	1845 (45.5%)	1.06 (0.99–1.13)	0.079
Major bleeding	454 (11.2%)	436 (10.8%)	1.03 (0.90–1.17)	0.702
All-cause urgent rehospitalizations	2578 (63.6%)	2476 (61.1%)	1.04 (0.98–1.09)	0.213

CI, confidence interval; HR, hazard ratio; MALE, major adverse limb events; PAD, peripheral artery disease.

Table 4 Outcomes of endovascular vs. surgical revascularization for propensity score-matched individuals presenting with intermittent claudication

Outcomes	Intermittent claudication			
	Cumulative incidence for surgery ($n = 10\,119$)	Cumulative incidence for endovascular intervention ($n = 10\,119$)	HR (95% CI)	*P*-value
MALE or mortality	3243 (32.1%)	3319 (32.8%)	1.11 (1.06–1.16)	<0.001
MALE	1460 (14.4%)	1401 (13.9%)	1.01 (0.93–1.08)	0.887
Mortality	2231 (22.1%)	2356 (23.3%)	1.16 (1.09–1.23)	<0.001
MALE subcategories				
Urgent surgical reintervention	472 (4.7%)	344 (3.4%)	0.76 (0.66–0.87)	<0.001
Urgent endovascular reintervention	663 (6.6%)	668 (6.6%)	1.06 (0.96–1.18)	0.261
Major amputation	398 (3.9%)	342 (3.4%)	0.90 (0.78–1.04)	0.170
Thrombolysis	190 (1.9%)	212 (2.1%)	1.18 (0.97–1.43)	0.106
Arterial emboli/thrombus	768 (7.6%)	696 (6.9%)	0.95 (0.85–1.05)	0.290
Less-severe limb events	7255 (71.7%)	7516 (74.3%)	1.14 (1.10–1.18)	<0.001
Less-severe limb events subcategories				
Elective surgical reintervention	1745 (17.2%)	1205 (11.9%)	0.70 (0.66–0.76)	<0.001
Elective endovascular reintervention	2092 (20.7%)	3024 (29.9%)	1.64 (1.55–1.74)	<0.001
Minor amputation	287 (2.8%)	385 (3.8%)	1.52 (1.22–1.65)	<0.001
PAD-related readmission not meeting MALE criteria	4594 (45.4%)	4279 (42.3%)	0.98 (0.94–1.02)	0.335
Major bleeding	866 (8.6%)	778 (7.7%)	0.96 (0.87–1.05)	0.354
All-cause urgent rehospitalizations	5349 (52.9%)	10 119 (49.1%)	0.97 (0.93–1.01)	0.142

CI, confidence interval; HR, hazard ratio; MALE, major adverse limb events; PAD, peripheral artery disease.

1.43–1.57, $P < 0.001$) and minor amputation (8.4% vs. 6.4%, HR 1.40, 95% CI 1.28–1.52, $P < 0.001$), but less elective surgical reintervention (10.4% vs. 15.9%, HR 0.67, 95% CI 0.63–0.71, $P < 0.001$).

Subgroup analysis

In subgroup analyses of Australia and New Zealand, men and women, individuals of age <75 and those of age ≥75 years, endovascular revascularization was consistently associated with significantly higher rates of composite MALE or mortality, while the rates of MALE alone were comparable to surgery, all of which were consistent with the findings of the overall analysis (Supplementary material online, *Table S8*).

For the subgroup analyses of the presentations with CLTI and claudication, endovascular repair was still associated with higher hazard rates for the composite of MALE or mortality (CLTI, 58.8% vs. 60.0%, HR 1.09, 95% CI 1.03–1.16, $P = 0.002$; claudication, 32.8% vs. 32.1%, HR 1.11, 95% CI 1.06–1.16, $P < 0.001$) and mortality alone (CLTI, 45.8% vs. 46.7%, HR 1.09, 95% CI 1.02–1.16, $P = 0.008$; claudication, 23.3% vs. 22.1%, HR 1.16, 95% CI 1.09–1.23, $P < 0.001$), but with no significant difference in MALE (CLTI, 25.4% vs. 25.7%, HR 1.05, 95% CI 0.96–1.14, $P = 0.27$; claudication, 13.9% vs. 14.4% HR 1.01, 95% CI 0.93–1.08, $P = 0.89$) (*Tables 3 and 4*, and Supplementary material online, *Figures S4* and *S5*).

Endovascular revascularization was associated with a greater number of less-severe limb events (CLTI, 77.9% vs. 75.4%, HR 1.16, 95% CI 1.11–1.22, $P < 0.001$; claudication, 74.3% vs. 71.7%, HR 1.14, 95% CI 1.10–1.18, $P < 0.001$), with no significant differences in major bleeding (10.8% vs. 11.2%, HR 1.03, 95% CI 0.90–1.17, $P = 0.70$; 7.7% vs. 8.6%, HR 0.96, 95% CI 0.87–1.05, $P = 0.35$) or all-cause urgent rehospitalization (61.1% vs. 63.6%, HR 1.04, 95% CI 0.98–1.09, $P = 0.21$; 49.1% vs. 52.9%, HR 0.97, 95% CI 0.93–1.01, $P = 0.14$) for CLTI and claudication presentations.

Discussion

This study evaluated the long-term outcomes of lower extremity revascularization in an Australian and New Zealand population. After propensity score matching, patients undergoing endovascular repair had similar rates of MALE throughout follow-up compared with those having surgery. Nevertheless, the endovascular approach was associated with a 16% higher risk of mortality, 13% higher risk of the combination of MALE or mortality, 40% higher risk of minor amputation, and 50% greater need for elective endovascular reintervention. However, it should be noted that differences in the cumulative incidence of adverse events at the end of follow-up were modest. There were no significant differences in major bleeding or all-cause urgent rehospitalization. These trends were evident for both claudication and CLTI presentations. The durable benefits of surgical revascularization were different from some prior observations, and they underscore a need for further debate and research on the optimal revascularization strategy for patients with PAD.

Few randomized studies have compared endovascular and surgical revascularization outcomes. The BASIL trial featured 452 patients presenting with CLTI randomized to initial bypass surgery or balloon angioplasty. No significant differences in amputation-free survival were apparent during the first 2 years, although beyond that time, open surgery was associated with higher amputation-free survival.[8,22] Our findings are consistent with the BASIL trial's long-term outcomes, with the matched surgery patients demonstrating a lower long-term risk of mortality, in addition to major amputation. The BASIL trial had caveats that would limit generalizability to current practice. The study investigated a modest number of patients and only CLTI presentations. Participant recruitment began 20 years ago, in an era before modern endovascular techniques, such as stenting. A high proportion (25%) of surgical patients received a prosthetic graft, which is less durable than the saphenous vein graft[4,7] and is now less commonly used.[22,23] In our cohort, encounters from 2008 onwards were chosen to reflect current vascular practice, thus incorporating more advanced endovascular interventions and progress in surgical planning. The endovascular approach was preferred, as evidenced by an approximate 4:1 ratio of endovascular to surgery cases in the unmatched groups, consistent with other recent observational studies.[24,25] It can also be argued that the results of earlier studies have become less applicable, with the evolution of medical therapy, public health messages regarding smoking, clinical guidelines, and the familiarity that specialists have with newer procedures.[26–28] These trends necessitate a comparative analysis in a more contemporary setting than with the BASIL study.

We assessed two national populations, which should provide broader generalizability of our results than previous small and single-centre studies.[29–31] Data from a specific institution have more potential for unique influences relating to procedural experience, patient selection, and local clinical practices.[26] From the small number of larger observational studies that compared outcomes of different PAD interventions, endovascular revascularization has typically been followed by more favourable outcomes. Wiseman *et al.*[14] found the endovascular approach to be associated with a lower adjusted risk of death or major amputation (HR 0.84, 95% CI 0.79–0.89) after up to 4 years, compared with surgery. This study drew from a narrow (5%) sample of all US Medicare hospitalizations between 2006 and 2009, once again representing a more historical cohort. These patients were older, as all individuals were above 65, and they had more cardiovascular comorbidities and CLTI presentations than our study. The 4-year incidence of death and major amputation was 48.6% for endovascular and 54.0% for surgery patients ($P < 0.001$), compared with 37.3% and 35.8%, respectively, in the current study with a median follow-up of 4.2 years. Hence, we examined a lower-risk clinical setting. Lin *et al.*[15] found open surgery to be associated with worse amputation-free survival (HR 1.16, 95% CI 1.13–1.20), without a mortality difference (HR 0.94, 95% CI 0.89–1.11). They assessed PAD revascularizations performed for CLTI within a Californian state-wide dataset. Fewer covariates were used for the propensity score-matched analysis, and therefore, there was less emphasis on baseline PAD and cardiovascular history. Meanwhile, Tsai *et al.*[32] performed a smaller study comparing 883 patients who underwent endovascular repair with 975 who had PAD surgery. There were no differences in amputation rates, but endovascular revascularization was again associated with lower mortality than surgery. From these aforementioned studies, much less information was available about outcomes in patients with intermittent claudication than CLTI. Intermittent claudication is a lower-risk disease than CLTI.[2]

However, it is important to note that our subgroup analysis showed a mortality benefit for surgery with both clinical presentations.

Several potential mechanisms could explain the excess mortality associated with endovascular therapy. Some literature points to excess mortality associated with paclitaxel-coated balloons and stents. Deployment of these devices for the endovascular treatment of femoropopliteal artery disease has been linked to increased all-cause patient mortality in clinical trials.[33] However, these findings are contentious as this association was not confirmed in other studies.[34,35] Secondly, all patients receiving PAD interventions are expected to have serial clinical evaluation and imaging surveillance.[36] The rationale for post-procedural surveillance is to detect restenoses early, so this can be treated electively and with a less complicated procedure than if this were to advance. Any variations in the surveillance programmes and approaches to surgically and endovascularly treated patients could drive a discrepancy in the urgency or frequency of reintervention and mortality. Similarly, we did not account for medication use and cardiovascular risk factor control, which could have important associations with myocardial infarction, stroke, MALE, and mortality. The optimal medical management of PAD can include prescription of antiplatelets, statins, angiotensin-converting enzyme inhibitors (or angiotensin II receptor blockers), as well as smoking abstinence and control of hypertension, dyslipidaemia, and diabetes mellitus.[37] Possible medical management discrepancies among surgically and endovascularly treated patients, which we could not account for, might cause residual confounding and explain the mortality differences. Lastly, unmeasured confounders could influence patient selection for a revascularization approach, especially as endovascular repair was more popular than surgery. In particular, we did not have access to reliable information about anatomical or lesion characteristics that may have meant that patients were not amenable to surgery, and therefore, could only be intervened upon endovascularly. Patient selection can be dictated by the type of lesion, the segment of disease, and the suitability of the saphenous vein for grafting.[2,3] Tsai *et al.*[32] attempted to adjust for some of these variables, albeit with fewer patients. The extent to which these factors could have influenced our results is not clear. Still, it does not seem intuitive that patient selection of surgical PAD patients would be associated with less atherosclerotic burden to explain the lower mortality. Rather, it might be expected that surgical revascularization would be reserved for cases of more severe atherosclerotic disease, but it is difficult to firmly conclude about these selection practices.

Our findings should also be interpreted in the context of our longer follow-up period. Shorter PAD studies have reported higher rates of perioperative bleeding and urgent rehospitalization for individuals receiving open surgery than endovascular intervention.[30,32] The long-term rates for these adverse events were similar in our surgery and endovascular groups, which may have been impacted by unmeasured factors in the years following these procedures, such as the type and duration of antithrombotic therapy. Open surgery would be expected to have a higher incidence of perioperative bleeding. Limited studies suggest dual antiplatelet therapy is potentially associated with improved surgical bypass graft[38] and stent patency,[39] at the expense of a higher bleeding rate. There is no consensus regarding the duration, or indeed the efficacy of dual antiplatelet therapy following PAD revascularization.[7] It remains to be seen whether the evidence for dual antiplatelet therapy after drug-eluting stent insertion for coronary disease[40] extends to the PAD setting. Therefore, a wide range of clinical practices is possible. The prolonged prescription of dual antiplatelet therapy after endovascular revascularization, where drug-coated technology is increasingly utilized,[5] could increase the risk of bleeding over time and offset a lower likelihood of perioperative complications than surgery. Likewise, these medical treatment differences would influence the primary outcome by way of fatal bleeding, major adverse cardiovascular events, and MALE.[37]

Our study has some caveats worth noting. This was a retrospective evaluation of administrative data, which has the potential for coding and data entry inaccuracies. While propensity score matching was performed, the possibility of unmeasured confounders cannot be excluded. As described, clinical information on lower-limb disease relating to anatomical and lesion characteristics, smoking, and medication use was unavailable. Additionally, while we matched for prior peripheral vascular disease and intervention, we may not fully account for the frequency or extent of prior peripheral artery revascularizations. It is uncertain how these factors affected patient selection, where the endovascular approach was overwhelmingly preferred. In addition to patient selection, our study did not evaluate the deployment rates of paclitaxel-coated devices to conclude about these. Despite these limitations, there is evidence that broader details of demographics and medical comorbidities can correlate with patterns of vascular disease.[14,41] Also, the goals and strategies for treating intermittent claudication and CLTI differ,[36] and so the subgroup analyses of these presentations help further distinguish between the types of PAD. Given the limited information regarding anatomical and lesion characteristics, or the revascularization side, adverse events might not have occurred at the same index lesion site. However, we anticipate that these matched endovascular and surgery groups would experience similar lower-limb morbidity, including MALE, at sites unrelated to the initial revascularization. The literature suggests management of PAD, including the use of surgical and endovascular intervention, may vary among countries and limit the generalizability of our results to other populations.[42] This study compared revascularization outcomes by focusing on MALE, mortality, and other less-severe adverse events. Some results, including quality of life and walking impairment, were not captured. There are upcoming randomized clinical trials that will compare endovascular and surgical revascularization by evaluating various clinical endpoints, and these will be less affected by confounding.[43,44] Nevertheless, our data's strength is in the heterogeneity of the study population, as this is likely to reflect current real-world practice better than clinical trials where participation is subject to recruitment and eligibility.

Conclusion

Although endovascular and surgical revascularization had comparable long-term risks of MALE, surgery was associated with a lower combined rate of MALE and mortality, which is at odds with prior observations and highlights ongoing contention in this field. There is a need for carefully conducted, randomized clinical trials to clarify the relative merits of these two strategies.

Supplementary material

Supplementary material is available at *European Heart Journal* online.

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Data availability

The data underlying this article will be shared on reasonable request to the corresponding author.

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