

Outcomes following Revascularisation for Acute Lower Limb Ischaemia Using Contemporary Endovascular, Hybrid, or Open Surgical Techniques in a Multicentre, Retrospective Cohort: The Acute Lower Limb Ischaemia Vascular Outcomes Evaluation (ALIVE) Registry

Nikolaos Konstantinou ^{a,*,†}, Dimitrios Vlastos ^{b,‡}, Athanasios Saratzis ^b, Nicola Troisi ^c, Mario D'Oria ^d, Luca Bertoglio ^e, Walter Dorigo ^f, Gladiol Zenunaj ^g, Angeliki Argyriou ^{h,‡}, Lukla Biasi ^j, Michael Czihal ^k, Georgios A. Pitoulis ^l, Teresa Martín González ^m, Manar Khashram ^{n,o}, Pablo Del Canto Peruyera ^p, João Ferreira Pires ^q, Konstantinos Stavroulakis ^{a,r}, on behalf of the ALIVE Registry collaborators [†]

^a Department of Vascular Surgery, University Hospital, LMU Munich, Munich, Germany

^b National Institute for Health and Care Research, Leicester Biomedical Research Centre, University of Leicester, Leicester, UK

^c Vascular Surgery Unit, Department of Translational Research and New Technologies in Medicine and Surgery, University of Pisa, Pisa, Italy

^d Division of Vascular and Endovascular Surgery, Cardiovascular Department, University Hospital of Trieste, Trieste, Italy

^e Division of Vascular Surgery, Department of Surgical and Clinical Sciences, University and ASST Spedali Civili Hospital of Brescia, Brescia, Italy

^f Vascular Surgery, Careggi University Teaching Hospital, University of Florence School of Medicine, Florence, Italy

^g Unit of Vascular and Endovascular Surgery, University Hospital of Ferrara, Ferrara, Italy

^h Department of Vascular Surgery, St Franziskus Hospital GmbH, Münster, Germany

ⁱ Department of Vascular Surgery, Klinikum Dortmund GmbH, Dortmund, Germany

^j Guy's and St Thomas' NHS Foundation Trust, King's Health Partners and Cleveland Clinic London, London, UK

^k Division of Angiology, University Hospital, LMU Munich, Munich, Germany

^l Division of Vascular Surgery, Second Department of Surgery, Faculty of Medicine, School of Health Sciences, G. Gennimatas Thessaloniki Hospital, Aristotle University of Thessaloniki, Thessaloniki, Greece

^m Department of Vascular Surgery, Villeneuve d'Ascq Private Hospital, Villeneuve d'Ascq, France

ⁿ Department of Surgery, Faculty of Medicine and Health Sciences, University of Auckland, Auckland, New Zealand

^o Department of Vascular and Endovascular Surgery, Waikato Hospital, Waikato, Hamilton, New Zealand

^p Vascular and Endovascular Surgery Department, Cabueñes University Hospital, Gijón, Gijón, Spain

^q Vascular Surgery Department, Hospital de Santa Maria, Faculty of Medicine of the University of Lisbon, Centro Cardiovascular da Universidade de Lisboa, Lisbon, Portugal

^r Vascular and Endovascular Surgery Unit, Mathias Spital Rheine, Rheine, Germany

WHAT THIS PAPER ADDS

This large, multicentre study provides contemporary data on outcomes after open, endovascular, and hybrid revascularisation for acute lower limb ischaemia (ALLI). The findings demonstrate differences in both early and long term outcomes between treatment strategies, with endovascular approaches associated with a lower risk of amputation and similar survival compared with open surgery. By reporting standardised outcomes beyond the early post-operative period and over an extensive follow up of up to three years, this analysis contributes valuable evidence to inform clinical decision making, patient counselling, and future guideline development in the management of ALLI.

Objective: To report peri-operative and midterm outcomes following open surgical, endovascular, and hybrid revascularisation for acute lower limb ischaemia (ALLI) using contemporary techniques and to provide adjusted comparative analyses accounting for key baseline differences.

Methods: This was a multicentre, retrospective study including patients treated for ALLI (January 2016 – November 2024) across 20 international vascular centres. Patients underwent open surgery (55.8%), endovascular treatment (20.2%), or hybrid procedures (24%). Primary outcome was major amputation and/or death at the latest follow up. Secondary outcomes included peri-operative death, amputation, acute kidney injury, and re-intervention. Multivariable Cox regression analyses adjusted for age, sex, Rutherford stage, and chronic kidney disease were performed. A Fine–Gray competing risk model accounted for death as a competing event for major amputation.

[†] A list of the authors in the ALIVE Registry collaborators group is included in [Appendix A](#).

[‡] Nikolaos Konstantinou and Dimitrios Vlastos contributed equally to this work.

* Corresponding author. Department of Vascular Surgery, University Hospital, LMU Munich, Marchioninistraße 15, 81377 Munich, Germany.

E-mail address: ni.konstantinou@outlook.com

www.linkedin.com/in/nikolaos-konstantinou-57363535a

1078-5884/© 2026 The Author(s). Published by Elsevier B.V. on behalf of European Society for Vascular Surgery. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).

<https://doi.org/10.1016/j.ejvs.2025.12.060>

Results: From 19 European centres and one centre in New Zealand, 1 259 patients (55.4% men; mean age 72 ± 14 years; no popliteal aneurysms) were included. At 30 days, the peri-operative mortality rate was 11.2% (open 12.3%, endovascular 3.1%, hybrid 7.4%; $p = .042$), and major amputation occurred in 9% (open 10.1%, endovascular 8.3%, hybrid 7.2%; $p = .41$). Median follow up was 36 months (range 8 – 49 months). At three years, the estimated mortality rate was 22.9% (standard error [SE] 1.5%) after open, 11.5% (SE 1.9%) after endovascular, and 19.6% (SE 2.2%) after hybrid procedures. Adjusted analyses demonstrated that endovascular treatment was associated with a lower risk of the composite outcome of major amputation and or death compared with open surgery (hazard ratio 0.69, 95% confidence interval [CI] 0.53 – 0.89; $p = .005$). For major amputation, the Fine–Gray competing risk analysis showed a reduced subdistribution hazard with endovascular treatment (subdistribution hazard ratio 0.71, 95% CI 0.33 – 0.99; $p = .006$).

Conclusion: Endovascular ALLI intervention was associated with lower long term amputation risk compared with open surgery, with comparable survival. These findings support endovascular treatment as a safe alternative in patients with ALLI.

Keywords: Acute lower limb ischaemia, Amputation, Endovascular, Peripheral arterial disease

Article history: Received 16 July 2025, Accepted 30 December 2025, Available online 20 January 2026

© 2026 The Author(s). Published by Elsevier B.V. on behalf of European Society for Vascular Surgery. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>).

INTRODUCTION

Acute lower limb ischaemia (ALLI) represents a vascular emergency associated with devastating patient outcomes.^{1–7} Despite advances in vascular care, ALLI continues to result in high rates of major amputation and death, particularly in patients with multiple long term conditions (co-occurrence of at least two chronic conditions in the same individual), frail individuals, or delayed presentation. Historical data suggest that up to 30% of patients may not survive beyond the first year following an episode of ALLI, while major amputation rates in survivors remain substantial.^{1,2,8,9} The clinical and economic burden of ALLI is therefore considerable, with significant implications for both patients and healthcare systems.

Management of ALLI has evolved considerably over recent decades. While open surgical revascularisation has traditionally been regarded as the standard of care, advances in endovascular technologies and hybrid techniques (combining endovascular and open surgery) have expanded the available therapeutic options. These contemporary approaches offer the potential for reduced peri-operative morbidity, shorter hospital stays, and comparable efficacy in selected patients. However, the evidence base supporting the use of these modern techniques in ALLI is limited. Since the large, randomised trials comparing open surgery with catheter directed lysis in the 1990s,^{10,11} there has been a striking paucity of randomised data in this clinical setting. Most existing studies represent either single centre series, contain modest sample sizes, focus predominantly on peri-operative outcomes within the first 90 days, and do not provide an ischaemia adjusted analysis. Furthermore, reporting standards are variable, limiting the ability to draw meaningful comparisons or to inform evidence based practice across different healthcare settings.

Importantly, data describing longer term outcomes after ALLI treated with modern endovascular or hybrid interventions remain scarce and focus on single centre outcomes. The lack of multicentre, real world evidence

capturing outcomes beyond the initial post-operative period hampers efforts to optimise care pathways, refine patient selection, and develop robust clinical guidelines. There is therefore an urgent need to provide high quality data on the outcomes of ALLI treatment using contemporary techniques to support modern clinical decision making.

To address these gaps in the current literature, the Acute lower Limb Ischaemia Vascular Outcomes Evaluation (ALIVE) registry was established: a large, multicentre observational study involving multiple international vascular referral centres. The aim of this study was to report outcomes following open surgical, endovascular, or hybrid revascularisation for ALLI, focusing not only on early peri-operative results but also on longer term rates of amputation, death, and re-intervention. By providing comprehensive and standardised outcome data, this study sought to inform contemporary clinical care and to guide future research in the management of ALLI.

MATERIALS AND METHODS

Study design

This was a retrospective, multicentre study across 20 vascular centres (hospitals), conducted according to the STrengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for reporting in retrospective studies.¹² All participating hospitals were regional referral centres for arterial disease, which routinely offer open, endovascular, and hybrid (combination of open and endovascular techniques) revascularisation for people presenting with acute limb ischaemia. All patients treated by endovascular, hybrid, or open surgery for symptomatic ALLI between January 2016 and November 2024 were identified at each participating centre (sites and number of participants per site are listed in [Appendix A](#)), and eligible patients (see below) were only included in this report.

Inclusion criteria were any adult (> 18 years of age) who presented with acute (within a maximum of 14 days since

symptom onset) lower limb ischaemia at baseline, and underwent revascularisation (of any type). Patients treated by conservative therapy or primary amputation were excluded. Vascular trauma and other non-occlusive causes of ALLI were additional exclusion criteria. Patients with ALLI in the setting of a popliteal artery aneurysm were identified but excluded, as this represents a distinct clinical entity with different therapeutic strategies and outcomes, introducing heterogeneity into the analysis. Patients with aortoiliac ALLI were included, as treatment goals and techniques are comparable to infra-inguinal ALLI, and their exclusion could introduce selection bias. In patients presenting with bilateral ALLI, the limb with the more severe clinical presentation, determined according to the Rutherford classification, was defined as the index limb and used for limb specific analyses. Mortality was analysed at the patient level. Patient data were collected retrospectively using a purpose built electronic case report form via a secure data exchange system through each participating site and managed centrally. Patients were identified once the lower limb revascularisation procedure had already taken place at each study site, to ensure all treatments offered were pragmatic. A local lead or collaborator was responsible for data quality and data control at each participating site (member of the Research Collaborative for Peripheral Arterial Disease [RCPAD]—<https://www.rcpad.org/>; an international independent collaborative including sites that treat people with vascular diseases across Europe). Anatomical, clinical, and demographic data were reported based on medical notes and clinical letters, accessed by each site collaborator, and verified at each site level, by at least two independent practitioners. Data queries were resolved via correspondence with each local investigator by A.S., N.K., and K.S. The site investigator was also responsible for local or regional approvals (Appendix A). A.S., N.K., and K.S. collated data and assessed for accuracy and missing information. For missing data (< 1% of the dataset in this instance) relating to baseline characteristics and the key outcomes of interest during follow up, the sites' investigators or collaborators were contacted and the missing data were obtained accordingly, in all cases. No imputation was necessary for this report. Adjudication of data and missing data queries were addressed locally at each participating site by the main RCPAD investigators and an additional collaborator at each site (who also verified the accuracy of data at site level). A.S. and K.S. managed data centrally and checked for consistency and erroneous figures with the aid of an independent statistician at the National Institute for Health and Care Research (NIHR) Leicester Biomedical Research Centre and D.V. (both A.S. and D.V. have formal statistics training; D.V. acted as an independent external dataset adjudicator before final analyses). No further external sources were involved in data collection or adjudication.

Definitions and reporting

Diagnoses and all clinical and procedural events were defined as per the American Heart Association guidance¹³

and the reporting standards of the Society for Vascular Surgery for peripheral arterial disease.¹⁴ Technical success was defined as completion of a procedure as planned with no additional intraprocedural intervention, with at least one artery patent to the foot. Acute kidney injury incidence was defined using serum creatinine measurements within 48 hours of the index procedure per the Kidney Disease Improving Global Outcomes (KDIGO) criteria.¹⁵ Only major amputations (above the ankle joint) were included in analyses. Pre-, intra-, and post-procedural information was collected using a purpose built data collection form. Data collected from endovascular and or hybrid interventions were reported and collected using principles of the EndoSTAR framework.¹⁶

Outcomes of interest

The primary outcome of interest was the composite of amputation and or death from the time of hospital presentation until three years after the procedure. Secondary outcomes of interest included: clinical characteristics of patients when presenting for revascularisation due to ALLI, and amputation, re-intervention, and mortality rates over the first 30 days after the index procedure or during the initial hospital admission, as well as during follow up. All causes of death were verified against electronic patient records at each site before data lock.

Statistical analysis and sample size

Statistical support was formally provided by the NIHR Leicester Biomedical Research Centre by the in house Bioinformatics Hub; this support was independently funded via the NIHR, including contributions by A.S. and D.V.; A.S. and D.V. had drawn a pre-specified statistical analysis plan before finalising the dataset for subsequent analyses. A minimum three year amputation and death incidence of 50% (conservative assumption) was assumed with a 10% standard deviation. To be able to precisely report the true amputation and death rate at 90% power within a 95% confidence interval (CI), a minimum of 566 patients should have been included. The pre-drawn statistical analysis plan was finalised following consultation with an independent qualified statistician. All analyses were performed using IBM SPSS Statistics Version 24.0 (IBM Corp., Armonk, NY, USA) and the R package version 4.2.3 (Windows). Normality of distributions was assessed using histograms, skewness, and kurtosis, as well as the Kolmogorov–Smirnov test. Results are reported as mean $\pm$ standard deviation for normally distributed variables and median with range for non-normally distributed values. Absolute values and proportions (%) are reported for categorical variables; of note, all clinical and demographic variables at baseline and those included in the regression analyses were normally distributed. Events were reported per type of procedure (open, endovascular, and hybrid) performed for each acutely ischaemic lower limb, with open revascularisation being the index reference mode of intervention gold standard compared with both

Table 1. Baseline characteristics of consecutive patients (*n* = 1 259) who underwent treatment for acute lower limb ischaemia included in the study.

Characteristic	Open surgery (<i>n</i> = 703)	Endovascular (<i>n</i> = 254)	Hybrid (<i>n</i> = 302)	<i>p</i> value
Age – y	75 ± 14	71 ± 13	70 ± 14	<.001
Sex				.001
Men	359 (51)	155 (61)	184 (61)	
Women	344 (49)	99 (39)	118 (39)	
Rutherford stage				<.001
I	121 (17.2)	64 (25.2)	32 (10.6)	
IIa	241 (34.3)	107 (42.1)	127 (42.1)	
IIb	270 (38.4)	64 (25.2)	109 (36.1)	
III	71 (10.1)	19 (7.5)	34 (11.2)	
Acute on chronic thrombosis	220 (31.4)	132 (52)	130 (43)	<.001
Embolisation	300 (42.8)	56 (22)	75 (24.8)	<.001
Compartment syndrome and fasciotomy	28 (4)	13 (5.1)	15 (5)	.44
Coronary artery disease	211 (30)	79 (31.1)	88 (29.1)	.092
Peripheral arterial disease	112 (15.9)	38 (15)	48 (15.9)	<.001
Past atrial fibrillation	274 (39)	56 (22)	72 (23.8)	<.001
New atrial fibrillation	63 (9)	10 (3.9)	21 (7)	.015
Chronic kidney disease	162 (23)	76 (29.9)	79 (26.2)	.003
Hypertension	513 (73)	193 (76)	208 (68.9)	.10
Diabetes	190 (27)	76 (29.9)	92 (30.5)	.48
Dyslipidaemia	373 (53.1)	163 (64.2)	157 (52)	.003
Malignancy	112 (15.9)	38 (15)	57 (18.9)	.21
Smoking history	309 (44)	152 (59.8)	193 (63.9)	<.001
Angiotensin enzyme inhibitor	211 (30)	66 (26)	94 (31.1)	.55
β blocker	288 (41)	94 (37)	106 (35.1)	.35
Calcium channel blocker	167 (23.8)	56 (22)	69 (22.8)	.79
Aspirin	285 (40.5)	152 (59.8)	133 (44)	<.001
Clopidogrel	84 (11.9)	51 (20.1)	42 (13.9)	.014
Vitamin K antagonist	77 (11)	33 (13)	24 (7.9)	.27
Other oral anticoagulant	120 (17.1)	30 (11.8)	45 (14.9)	.34
Statin	361 (51.4)	155 (61)	157 (52)	.043

Data are presented as mean ± standard deviation or *n* (%). Percentages are column percentages within each treatment group.

endovascular and hybrid revascularisation in non-adjusted and adjusted (Cox regression including time to event analysis) regression(s). Adjustments in each Cox model were performed using key pre-selected variables that differed at baseline, and which are known to influence outcome(s) after lower limb vascular intervention (age, sex, Rutherford stage, and presence of chronic kidney disease were all forced into the adjusted time to event Cox regression model); age was entered as a continuous variable and Rutherford class was treated as an ordinal variable. Hazard ratios (HRs) with 95% CIs are reported in each instance (with each regression), and a *p* value < .050 was considered statistically significant in each case. Cumulative incidences of key clinical outcomes were estimated using Kaplan–Meier survival curves, with corresponding standard errors (SEs) calculated for each time point. Additionally, a competing risks analysis was performed using the Fine–Gray subdistribution hazard model, with death considered as a competing event. This approach allowed estimation of the cumulative incidence of major amputation while appropriately accounting for the risk of death as a non-negligible competing outcome. Subdistribution hazard ratios with 95% CIs are reported, providing effect estimates that reflect the real world likelihood of amputation in the presence of death as a

competing risk. This approach is reported for the incidence of the composite outcome of death and or amputation.

RESULTS

Data from 1 259 consecutive patients were analysed (55.4% men; mean age 72 ± 14 years, details per group or intervention type listed in Table 1 and Supplementary Table S1). All patients were treated for symptomatic ALLI (at least one lower limb affected), with all presenting within a maximum of seven days of symptom onset to the treating centre (mean 2 ± 0.5 days). Only 41 patients (3.3%) had bilateral lower limb ischaemia on presentation, for whom the more symptomatic limb was considered the index limb. A total of 232 patients had a history of at least one malignancy (18.4%), with only 61 having received cancer treatment in the three months before presentation. Rutherford stages are presented in Table 1; there were statistically significant differences in terms of Rutherford stage, with more advanced ischaemia present in those treated with open surgery as the first line index procedure (Table 1), and those who underwent open surgery also had a higher prevalence of other long term conditions and cardiovascular disease, hence multivariable analyses are reported. All participants had infrainguinal procedures, with 72

Table 2. Multivariable binary logistic regression for peri-operative death (within 30 days of the index procedure).

Parameter of interest	HR (95%CI)	p value
<i>Type of surgery</i>		
Open	1.0 (ref.)	—
Endovascular	0.25 (0.12–0.54)	<.001
Hybrid	1.00 (0.63–1.57)	.99
Age per one year increment, continuous	1.01 (1.00–1.03)	.12
Sex, men	0.76 (0.51–1.13)	.18
<i>Rutherford stage</i>		
I	1.0 (ref.)	—
Ila	5.25 (1.85–14.95)	.002
Ilb	5.83 (2.06–16.46)	.001
III	16.10 (5.48–47.29)	<.001
Chronic kidney disease	2.77 (1.86–4.12)	<.001
Smoking	0.85 (0.56–1.27)	.42

HR = hazard ratio; CI = confidence interval.

(5.7%) requiring an aorto-iliac procedure, which was endovascular in all cases (covered stenting); no participant underwent an iliac or aortic bypass. Of all participants, 703 (55.8%) were treated with open surgery alone, 254 (20.2%) with endovascular percutaneous techniques alone, and 302 (24.0%) with hybrid procedures (combination of open and endovascular procedure).

Early outcomes

During the early post-operative period (30 days), the overall mortality rate was 11.2%, with peri-operative death occurring in 12.3% of patients undergoing open surgery, 3.1% of those undergoing endovascular treatment, and 7.4% in the hybrid group ($p = .042$). All peri-operative deaths were due to cardiovascular causes or sepsis. Major amputation within 30 days was observed in 9% of the cohort overall, comprising 10.1% of open surgery patients, 8.3% of endovascular patients, and 7.2% of those treated with hybrid procedures ($p = .41$). The composite outcome of amputation or death within 30 days occurred in 16.8% of all patients; a more granular breakdown by treatment group is provided for the follow up period. In adjusted regression analyses, endovascular surgery was associated with a lower chance of peri-operative death (Table 2) and acute kidney injury (Table 3) (adjusted for key clinical variables that differed at baseline and Rutherford stage on presentation).

Outcomes during follow up

At a median follow up of 36 months (range 8 – 49 months), complete clinical follow up was available for all patients at discharge, at 30 days, and at their latest recorded visit, including information on death, major amputation, re-interventions, and cardiovascular events. Based on the Kaplan–Meier estimates at 3 years, the overall mortality

Table 3. Multivariable binary logistic regression for peri-operative acute kidney injury, defined using the Kidney Disease Improving Global Outcomes criteria¹⁵ using 48 hour serum creatinine measurements.

Parameter of interest	HR (95% CI)	p value
<i>Type of surgery</i>		
Open	1.0 (ref.)	—
Endovascular	0.43 (0.22–0.85)	.016
Hybrid	1.37 (0.87–2.18)	.18
Age per 1 year increment, continuous	1.00 (1.00–1.02)	.81
Sex, men	0.76 (0.50–1.15)	.20
<i>Rutherford stage</i>		
I	1.0 (ref.)	—
Ila	1.41 (0.70–2.87)	.34
Ilb	1.74 (0.87–3.48)	.12
III	3.26 (1.5–7.08)	.003
Chronic kidney disease	3.32 (2.19–5.03)	<.001
Smoking	1.00 (0.65–1.52)	.98

HR = hazard ratio; CI = confidence interval.

rate was 22.9% (SE 1.5%) after open surgery, 11.5% (SE 1.9%) following endovascular treatment, and 19.6% (SE 2.2%) after hybrid repair. Major amputation rates at 3 years were estimated at 9.2% (SE 1.0%) after open surgery, 25.7% (SE 2.5%) after endovascular therapy, and 13.7% (SE 1.9%) after hybrid repair. The 3 year re-intervention rates were estimated at 7.8% (SE 0.9%) for open, 18.6% (SE 2.3%) for endovascular, and 16.4% (SE 2.0%) for hybrid procedures. Table 4 describes the absolute proportions of re-interventions, amputations, and death during follow up. The respective Kaplan–Meier estimation curves can be found in Supplementary Figures S1 – S4.

Multivariable analyses, adjusted for key clinical variables that differed at baseline, demonstrated that, compared with open surgery, endovascular treatment was associated with a statistically significantly lower risk of amputation at 3 years (HR 0.69, 95% CI 0.48 – 0.97; $p = .035$) and of the composite endpoint of amputation and or death (HR 0.69, 95% CI 0.53 – 0.89; $p = .005$). Regarding major amputation, the subdistribution hazard ratio based on the competing risk analysis (for death) was 0.71 (95% CI 0.33 – 0.99; $p = .006$). There was no statistically significant difference in mortality risk at 3 years between groups (endovascular HR 0.84, 95% CI 0.57 – 1.24, $p = .38$; hybrid HR 0.98, 95% CI 0.71 – 1.35, $p = .89$). All adjusted analyses across follow up relating to incidence of amputation, death, and amputation or death (combined) are reported in Tables 5 – 7. A Cox regression analysis was performed with the same parameters included in the reported regressions, forcing presence of aortic or iliac thrombus in the model, to explore the potential interaction of the presence of aortic or iliac disease. The presence of aorto-iliac disease did not impact any of the outcomes in this forced model (including major amputation, death, and amputation free survival).

Table 4. Absolute frequencies of key clinical events at one, two, and three years after the index procedure.

Parameter of interest	Open	Endovascular	Hybrid
Re-intervention at one year	46/610 (7.5)	51/268 (19.0)	46/287 (16.0)
Re-intervention at two year	68/610 (11.1)	59/268 (22.0)	52/287 (18.1)
Re-intervention at three year	71/610 (11.6)	59/268 (22.0)	55/287 (19.2)
Amputation at one year	63/650 (9.7)	53/262 (20.2)	35/300 (11.7)
Amputation at two year	74/650 (11.4)	66/262 (25.2)	43/300 (14.3)
Amputation at three year	78/650 (12.0)	76/262 (29.0)	43/300 (14.3)
Death at one year	162/701 (23.1)	27/254 (10.6)	55/302 (18.2)
Death at two year	183/701 (26.1)	31/254 (12.2)	58/302 (19.2)
Death at three year	185/701 (26.4)	34/254 (13.4)	62/302 (20.5)

Data are presented as *n/N* (%).

DISCUSSION

The ALIVE registry represents a multicentre, real world series comparing peri-operative and three year outcomes following open surgical, endovascular, and hybrid revascularisation for ALLI, incorporating adjusted analyses for key baseline differences, including Rutherford stage, age, sex, and chronic kidney disease. This study offers contemporary data on the management of ALLI, addressing a long standing evidence gap in the field.

The study's findings demonstrate that both modern endovascular and hybrid approaches are associated with favourable outcomes overall. Notably, after adjusting for key confounders, endovascular treatment was linked to a significantly reduced risk of major amputation and the composite endpoint of amputation or death at three years, compared with open surgery. These data suggest that contemporary endovascular strategies can offer effective limb salvage while maintaining comparable survival, even in a high risk population presenting with a vascular

emergency. Importantly, while peri-operative mortality remained higher in patients who underwent open surgery, probably reflecting greater baseline disease severity, there were no significant differences in adjusted mortality risk at three years between the three treatment modalities.

A unique feature of this report is the rigorous adjustment for baseline clinical differences, particularly Rutherford stage, which is a major determinant of outcome in ALLI but is often inadequately accounted for in previous studies.¹⁷ This study's large sample size, inclusion of multiple high volume centres, and long term follow up further strengthen the validity and generalisability of these findings. Unlike previous reports, which have been limited by single centre designs, small cohorts, or focus on short term outcomes, this work provides robust data on both early and late outcomes that can inform patient counselling, shared decision making, and guideline development.

Previous retrospective registries have reported variable outcomes regarding the acute and long term results of endovascular, open, and hybrid treatments. A propensity matched analysis of the National Inpatient Sample suggested a short term benefit of endovascular therapy,¹⁸ and a two centre German study observed significantly higher amputation free survival rates after endovascular therapy

Table 5. Multivariable Cox regression for major amputation of the index limb at the end of follow up (median three years).

Parameter of interest	HR (95% CI)	<i>p</i> value
<i>Type of surgery</i>		
Open	1.0 (ref.)	—
Endovascular	0.69 (0.48–0.97)	.035
Hybrid	0.86 (0.57–1.28)	.46
Age per one year increment, continuous	1.01 (0.99–1.02)	.30
Sex, men	0.99 (0.86–1.15)	.92
<i>Rutherford stage</i>		
I	1.0 (ref.)	—
IIa	1.11 (0.64–1.90)	.72
IIb	0.97 (0.57–1.67)	.92
III	3.05 (1.46–6.36)	.003
Chronic kidney disease	1.12 (0.95–1.30)	.17
Smoking	1.03 (0.75–1.42)	.84

HR = hazard ratio; CI = confidence interval.

In the Fine–Gray competing risk analysis with death as the competing event, endovascular treatment likewise showed a reduced subdistribution hazard of major amputation compared with open surgery (subdistribution hazard ratio 0.71, 95% confidence interval 0.33 – 0.99; *p* = .006).

Table 6. Multivariable Cox regression for death at the end of follow up (median three years).

Parameter of interest	HR (95% CI)	<i>p</i> value
<i>Type of surgery</i>		
Open	1.0 (ref.)	—
Endovascular	0.84 (0.57–1.24)	.38
Hybrid	0.98 (0.71–1.35)	.89
Age per one year increment, continuous	1.00 (0.99–1.01)	.81
Sex, men	1.07 (0.95–1.22)	.28
<i>Rutherford stage</i>		
I	1.0 (ref.)	—
IIa	1.24 (0.74–2.10)	.41
IIb	1.46 (0.88–2.43)	.14
III	1.48 (0.86–2.56)	.16
Chronic kidney disease	0.92 (0.81–1.04)	.19
Smoking	1.08 (0.83–1.40)	.58

HR = hazard ratio; CI = confidence interval.

Table 7. Multivariable Cox regression for amputation and or death at the end of follow up (median 3 years).

Parameter of interest	Hazard ratio (95% confidence interval)	<i>p</i> value
<i>Type of surgery</i>		
Open	1.0 (ref.)	—
Endovascular	0.69 (0.53–0.89)	.005
Hybrid	0.86 (0.67–1.11)	.24
Age per one year increment, continuous	1.01 (1.00–1.01)	.26
Sex, men	1.01 (0.92–1.11)	.85
<i>Rutherford stage</i>		
I	1.0 (ref.)	—
Ila	0.88 (0.52–1.51)	.65
Ilb	0.97 (0.58–1.63)	.91
III	1.09 (0.61–1.93)	.78
Chronic kidney disease	0.98 (0.89–1.09)	.75
Smoking	1.02 (0.74–1.39)	.93

HR = hazard ratio; CI = confidence interval.

over the follow up.¹⁹ A large, prospective Swedish registry similarly found higher amputation free survival rates and lower mortality rates over the early post-operative period as well as over follow up in a propensity matched cohort after primary endovascular treatment for ALLI compared with open surgery.²⁰ On the contrary, the PROMOTE-ALI registry did not find any difference between patients treated by open or endovascular repair.²¹ A French registry based on insurance data demonstrated a significant benefit of endovascular treatment, whereas a Japanese registry observed a significant clinical benefit from open repair.^{17,22} However, neither study^{17,22} provided data on the severity of ischaemia, making a meaningful comparison between the treatment groups impossible. Given that the last randomised controlled trials (RCTs) were conducted in the 1990s and compared only the effectiveness of catheter directed thrombolysis with surgical repair, it remains questionable whether their results reflect current clinical practice.^{23,24}

Despite these strengths, this study's findings also highlight the limitations of current evidence and the urgent need for a large, effectiveness driven RCT. Treatment allocation in this registry was not randomised and was probably influenced by local expertise, anatomical considerations, and patient comorbidities, introducing potential selection bias despite statistical adjustment. Moreover, while these data suggest a limb salvage benefit with endovascular treatment, causality cannot be established in the absence of randomisation. A well designed RCT would enable definitive assessment of the comparative clinical and cost effectiveness of these strategies, ensure balanced baseline characteristics, and provide the high level evidence needed to guide practice globally.

Finally, future research should also explore the role of novel endovascular devices, adjunctive pharmacotherapies,²⁵ and care pathways in improving outcomes after ALLI, as well as patient centred outcomes such as functional status and quality of life, areas that remain under reported in the existing literature.²⁶ Given the substantial

morbidity, mortality, and health system costs associated with ALLI, investment in such high quality trials should be prioritised to enable optimal care for this complex and vulnerable patient population.²⁷

Limitations

This study has several limitations. Firstly, although data were collected across multiple high volume vascular centres, the observational design introduces the potential for selection bias, as treatment choice was not randomised and may have been influenced by local practice patterns, operator expertise, or patient comorbidities. Secondly, while data collection was standardised using a purpose built case report form, variations in reporting or documentation across sites cannot be excluded. In addition, information on ethnicity was not collected as part of the pre-defined dataset, which could represent a potential confounder. Thirdly, although follow up was robust, the study relied on retrospective data collection, and loss to follow up or under reporting of late events remains possible. Finally, although definitions of anatomical assessments and procedure categories were pre-specified in the study protocol and agreed upon during investigator meetings before data collection, the absence of central core laboratory adjudication may still have introduced variability between centres.

Conclusions

This international, multicentre study reports contemporary outcomes following open, endovascular, and hybrid revascularisation for ALLI. The findings demonstrate that modern endovascular and hybrid techniques are associated with at least comparable outcomes compared with open surgery. These results provide important real world data to inform current clinical practice and guide patient counselling. However, given the observational nature of this study and the potential for selection bias, prospective RCTs are urgently needed to robustly assess the clinical and cost effectiveness of different revascularisation strategies in ALLI.

ETHICAL STATEMENT

Each site sought ethical approval as per institutional and national guidance. No identifiable patient data were exchanged or recorded. Raw data were not available to external partners or shared between collaborators. For the UK, the East Midlands Central Ethics Committee advised that no National Health Service (NHS) ethical approval or individual consenting was necessary in order to analyse anonymised data for this report. This study was not registered prospectively, given that no individual patient consent was deemed necessary by any of the sites included as per their local regulations.

CONFLICTS OF INTEREST

Konstantinos Stavroulakis consults for Phillips, Shockwave, Terumo, and Boston Scientific; has received honoraria from Medtronic, Abbott, Cook, Bentley, and Biotronic; and has received research grants from Boston Scientific. Athanasios Saratzis has received honoraria and lecture fees/consulting

from Shockwave, Abbott, and Cook; has received educational grant support from Cook; and has received research funding from Shockwave, Abbott, Boston Scientific, and Angiodroid. Nikolaos Konstantinou has received honoraria and lecture fees from Cook Medical, AstraZeneca, Bentley Innomed, and Boston Scientific. The remaining authors declare no conflicts of interest.

FUNDING

This study was not funded by any external sources.

APPENDIX A. SUPPLEMENTARY DATA

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ejvs.2025.12.060>.

REFERENCES

- Juneja A, Garuthara M, Talathi S, Rao A, Landis G, Etkin Y. Predictors of poor outcomes after lower extremity revascularization for acute limb ischemia. *Vascular* 2024;**32**:632–9.
- Galyfos G, Chamzin A, Intzes N, Matthaiou G, Spiliotopoulos S, Sotirakis D, et al. Acute limb ischemia. *J Cardiovasc Surg (Torino)* 2023;**64**:396–405.
- Xiao X, Feng R, Wang M, Sun H, Jing T, Su L, et al. Comparisons of outcomes of open surgery versus endovascular intervention for thrombotic popliteal artery aneurysm with acute lower limb ischemia: a systematic review. *BMC Surg* 2022;**22**:398.
- Apichartpiyakul P, Shinlapawittayatorn K, Rerkasem K, Chattipakorn SC, Chattipakorn N. Mechanisms and interventions on acute lower limb ischemia/reperfusion injury: a review and insights from cell to clinical investigations. *Ann Vasc Surg* 2022;**86**:452–81.
- Beckman JA, Schneider PA, Conte MS. Advances in revascularization for peripheral artery disease: revascularization in PAD. *Circ Res* 2021;**128**:1885–912.
- Loffroy R, Falvo N, Galland C, Frécher L, Ledan F, Midulla M, et al. Percutaneous rotational mechanical atherectomy plus thrombectomy using Rotarex S device in patients with acute and subacute lower limb ischemia: a review of safety, efficacy, and outcomes. *Front Cardiovasc Med* 2020;**7**:557420.
- Theodoridis PG, Davos CH, Dodos I, Iatrou N, Potouridis A, Pappas GM, et al. Thrombolysis in acute lower limb ischemia: review of the current literature. *Ann Vasc Surg* 2018;**52**:255–62.
- Argyriou A, Kafetzakis A, Saratzis A, Huasen B, Coscas R, Renard R, et al. Revascularization outcomes in patients with acute limb ischemia and active neoplastic disease. *J Endovasc Ther* 2021;**28**:100–6.
- Calderbank T, Karim A, Wall M, Syed A, Davies RSM, Saratzis A. The effect of malignancy on outcomes following revascularization for critical limb ischemia: a case–control study. *Vasc Endovascular Surg* 2018;**52**:325–9.
- Ouriel K, Veith FJ, Sasahara AA, Thrombolysis or peripheral arterial surgery: phase I results. TOPAS Investigators. *J Vasc Surg* 1996;**23**:64–73; discussion 74–5.
- Weaver FA, Comerota AJ, Youngblood M, Froehlich J, Hosking JD, Papanicolaou G, Surgical revascularization versus thrombolysis for nonembolic lower extremity native artery occlusions: results of a prospective randomized trial. The STILE Investigators. Surgery versus Thrombolysis for Ischemia of the Lower Extremity. *J Vasc Surg* 1996;**24**:513–21; discussion 521–3.
- von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, STROBE Initiative, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Lancet* 2007;**370**:1453–7.
- Hicks KA, Tcheng JE, Bozkurt B, Chaitman BR, Cutlip DE, Farb A, et al. 2014 ACC/AHA key data elements and definitions for cardiovascular endpoint events in clinical trials: a report of the American College of Cardiology/American Heart Association Task Force on clinical data standards (Writing committee to develop cardiovascular endpoints data standards). *J Am Coll Cardiol* 2015;**66**:403–69.
- Stoner MC, Calligaro KD, Chaer RA, Dietzek AM, Farber A, Guzman RJ, et al. Reporting standards of the Society for Vascular Surgery for endovascular treatment of chronic lower extremity peripheral artery disease. *J Vasc Surg* 2016;**64**:e1–21.
- Johansen KL, Garimella PS, Hicks CW, Kalra PA, Kelly DM, Martens S, et al. Central and peripheral arterial diseases in chronic kidney disease: conclusions from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference. *Kidney Int* 2021;**100**:35–48.
- Zywicka EM, Moore AJ, Twine C, Behrendt CA, Bosiers M, Brodmann M, et al. Endovascular treatment of peripheral arterial disease: Endo-STAR framework for the design, conduct, and reporting of trials. *Br J Surg* 2025;**112**:znaf020s.
- Ozawa T, Yanishi K, Fujioka A, Seki T, Zen K, Matoba S. Editor's Choice – Comparison of clinical outcomes in patients with acute lower limb ischaemia undergoing endovascular therapy and open surgical revascularisation: a large scale analysis in Japan. *Eur J Vasc Endovasc Surg* 2024;**68**:748–56.
- Kolte D, Kennedy KF, Shishehbor MH, Mamdani ST, Stangenberg L, Hyder ON, et al. Endovascular versus surgical revascularization for acute limb ischemia: a propensity-score matched analysis. *Circ Cardiovasc Interv* 2020;**13**:e008150.
- Konstantinou N, Argyriou A, Dammer F, Bisdas T, Chlouverakis G, Torsello G, et al. Outcomes after open surgical, hybrid, and endovascular revascularization for acute limb ischemia. *J Endovasc Ther* 2025;**32**:1499–507.
- Grip O, Wanhainen A, Michaëlsson K, Lindhagen L, Björck M. Open or endovascular revascularization in the treatment of acute lower limb ischaemia. *Br J Surg* 2018;**105**:1598–606.
- Gratl A, Busch A, Caradu C, Doukas P, Noronen K, European Vascular Research Collaborative (EVRC), et al. Prospective multicentre observational study evaluating acute lower limb ischaemia (PROMOTE-ALI). *Br J Surg* 2024;**11**:znae230.
- Espitia O, Del Giudice C, Hartung O, Herquelot E, Schmidt A, Sapoval M, et al. Editor's Choice – Survival, limb salvage, and management of patients with lower limb acute ischaemia: a French national retrospective observational study. *Eur J Vasc Endovasc Surg* 2024;**67**:631–42.
- Björck M, Earnshaw JJ, Acosta S, Bastos Gonçalves F, Cochenne F, ESVS Guidelines Committee, et al. Editor's Choice – European Society for Vascular Surgery (ESVS) 2020 clinical practice guidelines on the management of acute limb ischaemia. *Eur J Vasc Endovasc Surg* 2020;**59**:173–218.
- Jongkind V, Earnshaw JJ, Bastos Gonçalves F, Cochenne F, Debus ES, Hinchliffe R, et al. Editor's Choice – Update of the European Society for Vascular Surgery (ESVS) 2020 clinical practice guidelines on the management of acute limb ischaemia in light of the COVID-19 pandemic, based on a scoping review of the literature. *Eur J Vasc Endovasc Surg* 2022;**63**:80–9.
- Twine CP, Kakkos SK, Aboyans V, Baumgartner I, Behrendt CA, ESVS Guidelines Committee, et al. Editor's Choice – European Society for Vascular Surgery (ESVS) 2023 clinical practice guidelines on antithrombotic therapy for vascular diseases. *Eur J Vasc Endovasc Surg* 2023;**65**:627–89.
- Hoitz N, Kraima A, Fioole B, Mees B, de Borst GJ, Ünlü Ç. Surveillance after surgical and endovascular treatment for peripheral artery disease: a Dutch survey. *Eur J Vasc Endovasc Surg* 2024;**67**:980–6.
- Kulezic A, Acosta S. Epidemiology and prognostic factors in acute lower limb ischaemia: a population based study. *Eur J Vasc Endovasc Surg* 2022;**63**:296–303.