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INPLASY

Prosthetic versus autologous great saphenous vein bypass to below-knee targets: a systematic review and meta-analysis of patency and limb salvage

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ADMINISTRATIVE INFORMATION

Support - No support.

Review stage at the time of initial registration - Data analysis.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 9 November 2026 and was last updated on 9 November 2026.

INTRODUCTION

Review question / Objective O compare graft patency and limb outcomes after below-knee bypass with prosthetic grafts versus autologous great saphenous vein (GSV) in patients with peripheral arterial disease. Primary outcomes were loss of primary patency at 1 year and at 3–5 years and major amputation at 1 year and at 3–5 years; secondary outcomes were loss of secondary patency at 3–5 years and adjusted hazard ratios for major amputation, amputation or death, and loss of primary patency. A secondary objective was to assess whether distal target (below-knee popliteal versus tibial), prosthetic graft type (heparin-bonded ePTFE versus standard prosthetic) and publication era modify these associationsPubMed/MEDLINE, Embase and Cochrane CENTRAL were searched on 9 November 2026 without date limits. Search strings combined terms for peripheral arterial disease or limb ischaemia, BK or infrapopliteal targets, bypass, prosthetic grafts (including ePTFE, Dacron and heparin-bonded grafts) and saphenous vein; animal-only studies were excluded (Supplementary Table S1). Reviews, case reports, comments, editorials and letters were removed after retrieval. Reference lists of included studies and prior reviews, together with web searching, were screened for additional reports. Only English-language reports were included.

Rationale Autologous great saphenous vein (GSV) is the recommended conduit for below-knee bypass, yet prosthetic grafts, including heparin-bonded expanded polytetrafluoroethylene (HB-ePTFE), remain widely used when vein is unavailable and sometimes for expediency. The only randomised comparison was conducted between 1978 and 1985 using standard ePTFE, and the Cochrane review of graft type was dominated by above-knee reconstructions. Recent reviews have been restricted to HB-ePTFE and pooled small unadjusted retrospective cohorts, reporting no difference from vein, whereas large registries and the BEST-CLI trial suggest worse limb outcomes with prosthetic conduits. No synthesis has pooled all direct prosthetic-versus-

GSV comparisons restricted to below-knee targets, separated graft patency from major amputation, incorporated adjusted estimates, or examined whether distal target level or heparin bonding modifies these associations. This review aims to address these gaps to inform conduit choice for below-knee bypass.

Condition being studied Peripheral arterial disease (PAD) of the lower limb, particularly chronic limb-threatening ischaemia (CLTI), the most advanced form of PAD, defined by ischaemic rest pain, non-healing ulcers or gangrene. CLTI carries a high risk of major amputation and death. Patients with extensive occlusive disease below the knee often require surgical bypass from the femoral or popliteal artery to the below-knee popliteal, tibial or peroneal arteries. The durability of the bypass, and therefore limb salvage, depends largely on the conduit used, either autologous great saphenous vein or a prosthetic graft such as expanded polytetrafluoroethylene (ePTFE), heparin-bonded ePTFE or Dacron. This review also includes patients undergoing below-knee bypass for disabling intermittent claudication.

METHODS

Search strategy PubMed/MEDLINE, Embase (Embase.com) and the Cochrane Central Register of Controlled Trials (CENTRAL) were searched from inception to 9 November 2026 without date restrictions. The search combined terms for (1) peripheral arterial disease or limb ischaemia, (2) below-knee, infrapopliteal, tibial, crural or femorodistal targets, (3) bypass or graft, (4) prosthetic grafts (PTFE, ePTFE, Dacron, heparin-bonded grafts, Propaten) and (5) saphenous or autologous vein, using both controlled vocabulary (MeSH/Emtree) and free-text terms. Animal-only studies were excluded. Reviews, case reports, editorials, comments and letters were excluded after retrieval. Only English-language reports were included. Reference lists of included studies and previous reviews were hand-searched.

PubMed search string:
("Peripheral Arterial Disease"[Mesh] OR "Chronic Limb-Threatening Ischemia"[Mesh] OR "Ischemia"[Mesh] OR "Lower Extremity"[Mesh] OR "peripheral arter*"[tiab] OR "limb ischemia"[tiab] OR "limb ischaemia"[tiab] OR CLTI[tiab] OR CLI[tiab] OR "limb salvage"[tiab]) AND ("below-knee"[tiab] OR "below knee"[tiab] OR "below-the-knee"[tiab] OR infrapopliteal[tiab] OR infragenicular[tiab] OR infrageniculate[tiab] OR tibial[tiab] OR crural[tiab] OR femorocrural[tiab] OR femorodistal[tiab] OR "femoro-distal"[tiab] OR "femoral-distal"[tiab] OR femoropopliteal[tiab] OR "femoro-popliteal"[tiab] OR "femoral-popliteal"[tiab] OR infrainguinal[tiab]) AND ("Vascular Grafting"[Mesh] OR "Blood Vessel Prosthesis"[Mesh] OR bypass[tiab] OR graft*[tiab] OR conduit*[tiab]) AND ("Polytetrafluoroethylene"[Mesh] OR PTFE[tiab] OR ePTFE[tiab] OR polytetrafluoroethylene[tiab] OR prosthe*[tiab] OR synthetic[tiab] OR Dacron[tiab] OR "heparin-bonded"[tiab] OR "heparin bonded"[tiab] OR Propaten[tiab]) AND ("Saphenous Vein"[Mesh] OR saphenous[tiab] OR "autologous vein"[tiab] OR "autogenous vein"[tiab] OR "vein graft*"[tiab] OR GSV[tiab] OR "venous graft*"[tiab]) NOT ("Animals"[Mesh] NOT "Humans"[Mesh])

The strategy was adapted for Embase (Emtree terms, :ti,ab field tags) and CENTRAL.

Participant or population Adults with lower-limb peripheral arterial disease undergoing bypass with a distal anastomosis below the knee (below-knee popliteal, tibial, peroneal or other infrapopliteal artery), for chronic limb-threatening ischaemia (rest pain, ulceration or gangrene) or disabling intermittent claudication. Studies were eligible only if outcomes for below-knee reconstructions could be separated from those for above-knee reconstructions. Studies of bypass for aneurysm, trauma, infection or acute limb ischaemia were excluded.

Intervention Below-knee bypass using a prosthetic conduit, including standard expanded polytetrafluoroethylene (ePTFE), heparin-bonded ePTFE (e.g. Propaten), pre-cuffed ePTFE, PTFE with distal vein cuff or patch, and Dacron grafts. Studies in which the prosthetic arm consisted of, or was pooled with, human umbilical vein or other biological grafts, or composite prosthetic-vein grafts that could not be separated, were excluded.

Comparator Below-knee bypass using autologous great saphenous vein (ipsilateral or contralateral; reversed, non-reversed or in situ). Studies whose vein arm included a minority of other autologous veins (arm vein, small saphenous vein or spliced vein) were eligible but were excluded in a sensitivity analysis. Studies in which the comparator was a "disadvantaged" or alternative autologous vein, rather than great saphenous vein, were excluded.

Study designs to be included Randomised controlled trials, post hoc or as-treated analyses of randomised trials, prospective and retrospective cohort studies, and registry-based analyses that directly compared prosthetic with great saphenous

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vein conduits for below-knee bypass and reported patency or limb outcomes separately for each conduit. Single-arm series, case reports, case series without a vein comparator, reviews, editorials, letters and conference abstracts without extractable comparative data were excluded.

Eligibility criteria Inclusion criteria: (1) adults with lower-limb peripheral arterial disease undergoing bypass to a below-knee popliteal, tibial, peroneal or other infrapopliteal target; (2) direct comparison of a prosthetic graft (ePTFE, heparin-bonded ePTFE, pre-cuffed or cuffed ePTFE, or Dacron) with autologous great saphenous vein; (3) patency (primary or secondary), limb salvage or major amputation, or amputation-free survival reported for each conduit separately at a stated time point, or as an adjusted hazard ratio; (4) randomised trials, as-treated analyses of randomised trials, registry analyses or cohort studies; (5) English language; no restriction on publication date.

Exclusion criteria: (1) above-knee and below-knee reconstructions not separable; (2) prosthetic arm consisting of, or pooled with, human umbilical vein or other biological grafts; (3) comparator not great saphenous vein (e.g. "disadvantaged" or alternative autologous vein only); (4) outcomes reported only after graft occlusion; (5) bypass for aneurysm, trauma, infection or acute limb ischaemia; (6) single-arm studies, case reports, reviews, editorials and letters; (7) overlapping cohorts — when multiple reports came from the same cohort, they were not pooled within the same analysis.

Information sources Electronic databases: PubMed/MEDLINE, Embase (Embase.com) and the Cochrane Central Register of Controlled Trials (CENTRAL), each searched from inception to 9 November 2026. Additional sources: ClinicalTrials.gov (via CENTRAL and Embase trial records) for registered trials and posted results; reference lists of included studies and of previous systematic reviews and meta-analyses; and web searching for reports not indexed in the above databases. Authors of included studies were not contacted.

Main outcome(s) Primary outcomes: (1) loss of primary patency at 1 year and at 3–5 years; (2) major amputation (above the ankle; 1 – limb salvage) at 1 year and at 3–5 years. Outcomes were extracted as Kaplan–Meier estimates at the stated time points; for the 3–5-year window, the latest estimate reported between 36 and 60 months was used. Effect measure: risk ratio of failure (prosthetic versus great saphenous vein), with events reconstructed as N × (1 – Kaplan–Meier estimate).

Additional outcome(s) 1) Loss of secondary patency at 3–5 years (risk ratio, as above); (2) adjusted hazard ratios (prosthetic versus great saphenous vein) for major amputation, amputation or death, and loss of primary patency, pooled on the log scale by generic inverse variance; (3) 30-day mortality and early (30-day) graft occlusion, where reported (descriptive).

Data management Records retrieved from each database were exported and deduplicated by normalised title matching, with residual duplicates removed manually. Titles and abstracts were screened, followed by full-text assessment against the eligibility criteria; reasons for full-text exclusion were recorded. Data were extracted into a standardised structured form capturing study characteristics (country, period, design, distal target, prosthetic type, indication, follow-up), group sizes and outcome data (Kaplan–Meier estimates at stated time points and adjusted hazard ratios with 95% confidence intervals). For every extracted value, the source page and a verbatim quotation were recorded to allow verification. Overlapping cohorts were identified by centre, registry and enrolment period. 【Screening and extraction were performed by [reviewer 1] and independently verified by [reviewer 2]; disagreements were resolved by consensus or a third reviewer.】 The extraction dataset and analysis code are retained and available on request.

Quality assessment / Risk of bias analysis Risk of bias was assessed at the comparison level. Randomised comparisons were assessed with the revised Cochrane risk-of-bias tool (RoB 2; five domains). Non-randomised comparisons, including as-treated analyses of randomised trials, were assessed with ROBINS-I across seven domains: confounding, selection of participants, classification of interventions, deviations from intended interventions, missing data, measurement of outcomes and selection of the reported result. Key confounders prespecified for this question were indication (CLTI versus claudication), tissue loss, prior failed revascularisation, dialysis or end-stage renal disease, diabetes, distal target level and run-off; because conduit choice is driven by vein availability, unadjusted comparisons were judged at least at serious risk of confounding, and propensity-matched or multivariable-adjusted comparisons could be judged moderate. Overall judgement followed the worst domain. Results were displayed as a traffic-light plot, and a

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sensitivity analysis was restricted to studies at moderate risk of bias. 【Assessments were performed by [reviewer 1] and checked by [reviewer 2].】 Certainty of evidence for each outcome was rated with GRADE.

Strategy of data synthesis Or time-point outcomes, the number of failures in each arm was reconstructed as N × (1 − Kaplan–Meier estimate), and risk ratios (RR) of failure (prosthetic versus great saphenous vein) were calculated. Adjusted hazard ratios (HR) were pooled on the log scale by generic inverse variance. All analyses used random-effects models with the DerSimonian–Laird estimator of between-study variance and Hartung–Knapp–Sidik–Jonkman confidence intervals. When a study reported below-knee popliteal and tibial strata separately, each stratum was entered as an independent comparison. Reports from overlapping cohorts were never pooled within the same analysis; one report per cohort was selected for each outcome. Heterogeneity was quantified with I^2 and τ^2, and 95% prediction intervals were calculated. Small-study effects were assessed with funnel plots and Egger's regression test when at least 10 comparisons were available. Certainty of evidence was rated with GRADE, and absolute effects were calculated from the median vein-arm risk. Analyses were performed in Python (NumPy, SciPy). A two-sided $P < 0.05$ was considered statistically significant.

Subgroup analysis Prespecified subgroup analyses examined: (1) distal target (below-knee popliteal versus tibial/infrapopliteal versus mixed below-knee); (2) prosthetic graft type (heparin-bonded ePTFE versus standard or other prosthetic grafts); and (3) publication era (before 2000 versus 2000 onwards). Differences between subgroups were tested with the between-subgroup Cochran Q statistic. Subgroups with fewer than three comparisons were reported for completeness only and not interpreted.

Sensitivity analysis Sensitivity analyses: (1) exclusion of comparisons whose vein arm included non-great saphenous autologous veins; (2) exclusion of studies with mixed or claudication-only indications (CLTI-predominant studies only); (3) restriction to studies at moderate (rather than serious or high) risk of bias; (4) leave-one-out analysis omitting each comparison in turn;.

Language restriction English.

Country(ies) involved Taiwan.

Keywords below-knee bypass; prosthetic graft; polytetrafluoroethylene; heparin-bonded ePTFE; great saphenous vein; chronic limb-threatening ischaemia; graft patency; major amputation; meta-analysis.

Contributions of each author

Author 1 - Ying-Sheng Li - drafted the manuscript and data analysis
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