Peripheral Artery Disease Surgery: Systematic Review with ☸SAIMSARA.

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Abstract: To systematically review the current evidence on peripheral artery disease surgery, focusing on outcomes, risk factors, treatment comparisons, and emerging trends, to inform clinical practice and future research. The review utilises 1342 studies with 3092231 total participants (naïve ΣN). Bypass surgery for peripheral artery disease (PAD) was associated with a significantly lower re-intervention rate (median 20%, range 17.0–20%) compared to endovascular revascularization (median 25%, range 25.2–35.1%), with no significant difference in major amputation or mortality. These findings apply to a broad population of patients with PAD, often with multiple comorbidities, undergoing various revascularization procedures. The heterogeneity in study designs and outcome reporting across the literature remains the most significant limitation, affecting the certainty of direct comparisons. Moving forward, clinicians should prioritize individualized treatment plans based on patient risk factors and lesion characteristics, while researchers focus on standardized, long-term comparative effectiveness studies to refine treatment guidelines.

Keywords: Peripheral Artery Disease; Vascular Surgery; Surgical Revascularization; Lower Extremity Bypass; Postoperative Outcomes; Critical Limb Ischemia; Amputation; Endovascular Therapy; Arterial Disease; Limb Salvage

Review Stats

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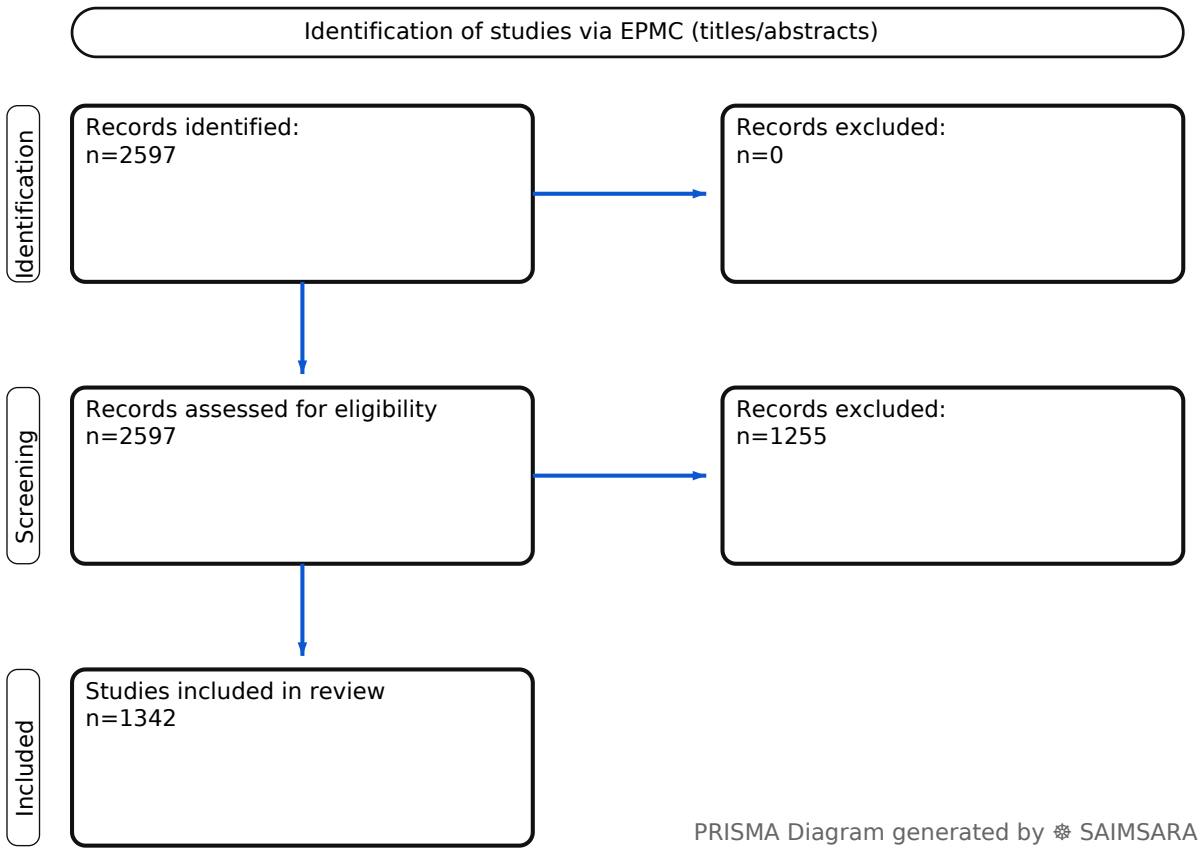
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Studies included in review
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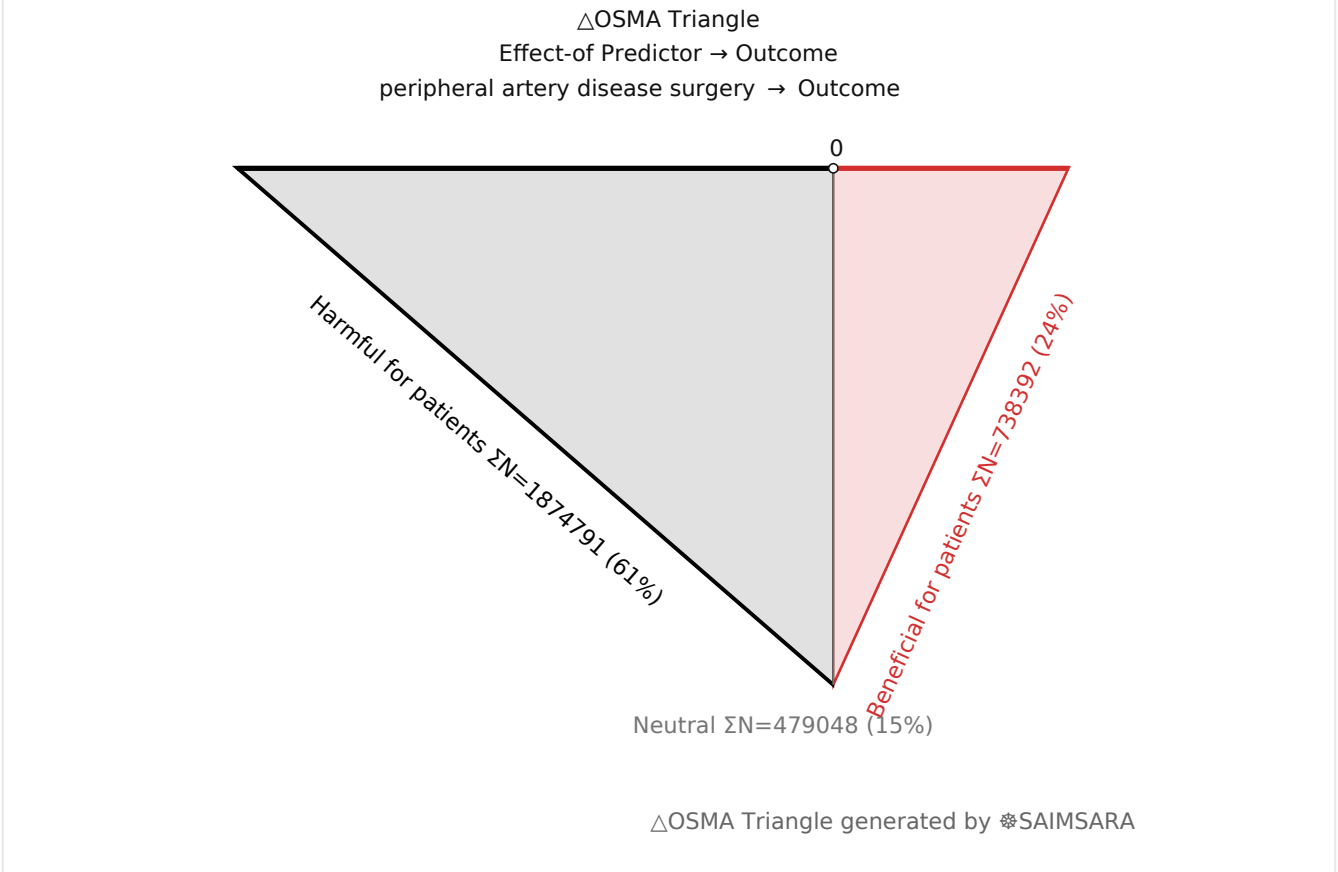
PRISMA Diagram generated by ☸ SAIMSARA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Effect-of Predictor → Outcome
peripheral artery disease surgery → Outcome
0
Harmful for patients ΣN=1874791 (61%)
Beneficial for patients ΣN=738392 (24%)
Neutral ΣN=479048 (15%)
△OSMA Triangle generated by ☸SAIMSARA

Outcome-Sentiment Meta-Analysis (OSMA): *(LLM-only)*

Frame: Effect-of Predictor → Outcome • *Source*: Europe PMC

Outcome: Outcome Typical timepoints: peri/post-op, 30-day. Reported metrics: %, CI, p.

Common endpoints: Common endpoints: mortality, complications, survival.

Predictor: peripheral artery disease surgery — exposure/predictor. Doses/units seen: 10mg, 8 g, 150 mg. Routes seen: oral, intravenous, iv, intramuscular…. Typical comparator: primary bypass surgery, endovascular interventions, patients with severe obesity, control….

- **1) Beneficial for patients** — Outcome with peripheral artery disease surgery — [5], [11], [12], [13], [15], [20], [44], [57], [58], [66], [72], [85], [91], [93], [94], [128], [137], [139], [141], [149], [154], [155], [159], [165], [174], [177], [182], [184], [189], [194], [209], [212], [217], [223], [229], [233], [238], [259], [262], [263], [265], [268], [275], [279], [286], [289], [291], [296], [302], [306], [307], [308], [314], [315], [317], [320], [326], [328], [339], [358], [361], [364], [369], [372], [373], [377], [383], [384], [387], [398], [400], [403], [406], [416], [418], [424], [425], [428], [432], [435], [437], [441], [444], [446], [449], [451], [452], [458], [471], [475], [477], [479], [481], [487], [488], [491], [497], [501], [503], [506], [516], [527], [556], [557], [563], [571], [572], [576], [582], [588], [589], [591], [597], [616], [617], [620], [625], [632], [643], [644], [655], [663], [687], [689], [691], [717], [721], [724], [726], [736], [742], [745], [748], [750], [755], [759], [760], [766], [771], [779], [782], [794], [797], [798], [806], [807], [816], [820], [839], [840], [845], [847], [849], [856], [864], [870], [875], [880], [883], [887], [891], [897], [902], [909], [911], [915], [919], [932], [938], [971], [976], [979], [1003], [1007], [1011], [1012], [1013], [1016], [1023], [1029], [1033], [1041], [1045], [1052], [1053], [1055], [1060], [1062], [1063], [1065], [1066], [1070], [1071], [1072], [1076], [1077], [1078], [1085], [1101], [1103], [1106], [1110], [1132], [1152], [1156], [1157], [1158], [1166], [1172], [1186], [1205], [1207], [1213], [1216], [1217], [1224], [1225], [1229], [1230], [1237], [1245], [1268], [1273], [1274], [1311], [1318], [1319], [1320], [1322], [1334], [1335], [1340] — ΣN=738392
- **2) Harmful for patients** — Outcome with peripheral artery disease surgery — [2], [8], [9], [18], [19], [23], [24], [26], [32], [33], [34], [37], [38], [41], [46], [47], [48], [56], [59], [62], [63], [64], [65], [77], [78], [81], [83], [86], [87], [95], [99], [100], [101], [102], [103], [104], [108], [109], [113], [114], [121], [124], [130], [131], [133], [135], [138], [143], [146], [148], [156], [157], [163], [167], [173], [188], [191], [195], [198], [201], [204], [205], [206], [210], [225], [227], [230], [231], [234], [235], [241], [244], [246], [247], [248], [252], [256], [260], [267], [272], [273], [274], [278], [281], [282], [285], [287], [288], [292], [294], [295], [297], [298], [301], [303], [305], [310], [311], [312], [313], [318], [321], [322], [325], [327], [333], [335], [336], [338], [340],

[343], [345], [347], [348], [349], [350], [351], [353], [354], [357], [359], [362], [366], [367], [371], [375], [376], [380], [381], [382], [385], [386], [388], [389], [392], [393], [395], [404], [405], [409], [411], [412], [413], [419], [429], [436], [438], [439], [442], [443], [453], [457], [460], [461], [465], [466], [467], [468], [469], [472], [473], [484], [486], [493], [496], [499], [500], [505], [507], [513], [514], [517], [520], [522], [524], [526], [528], [534], [535], [538], [539], [541], [543], [544], [546], [548], [550], [551], [558], [562], [565], [569], [573], [577], [578], [580], [581], [583], [584], [586], [587], [593], [598], [599], [600], [602], [604], [605], [608], [611], [612], [619], [622], [624], [626], [627], [628], [630], [634], [635], [636], [639], [641], [645], [648], [650], [653], [658], [661], [664], [665], [668], [669], [670], [672], [675], [676], [682], [683], [684], [690], [693], [694], [695], [696], [707], [712], [723], [725], [729], [731], [733], [735], [737], [739], [740], [746], [752], [757], [768], [772], [773], [774], [775], [781], [784], [785], [787], [796], [799], [802], [804], [805], [808], [810], [811], [814], [815], [818], [819], [821], [822], [823], [827], [828], [832], [834], [835], [836], [838], [841], [843], [846], [848], [851], [858], [859], [860], [861], [862], [863], [867], [871], [873], [877], [881], [888], [890], [893], [894], [895], [896], [900], [908], [912], [916], [920], [921], [923], [925], [936], [939], [940], [943], [944], [945], [947], [948], [949], [951], [953], [961], [963], [965], [972], [973], [982], [983], [984], [986], [988], [990], [991], [992], [993], [994], [995], [998], [999], [1000], [1002], [1004], [1008], [1017], [1021], [1026], [1031], [1035], [1038], [1044], [1047], [1050], [1054], [1056], [1059], [1068], [1069], [1073], [1074], [1075], [1080], [1081], [1082], [1083], [1084], [1087], [1088], [1090], [1091], [1093], [1096], [1097], [1098], [1099], [1102], [1107], [1108], [1111], [1112], [1113], [1115], [1117], [1119], [1120], [1123], [1124], [1125], [1127], [1128], [1137], [1138], [1141], [1142], [1144], [1146], [1150], [1154], [1155], [1164], [1165], [1167], [1170], [1171], [1174], [1175], [1179], [1181], [1182], [1184], [1198], [1203], [1204], [1208], [1210], [1211], [1218], [1222], [1223], [1231], [1232], [1233], [1235], [1236], [1238], [1241], [1242], [1246], [1249], [1250], [1255], [1258], [1259], [1261], [1262], [1267], [1271], [1284], [1301], [1302], [1304], [1306], [1307], [1313], [1314], [1317], [1325], [1326], [1331], [1332], [1337], [1338] — ΣN=1874791

- **3) No clear effect** — Outcome with peripheral artery disease surgery — [1], [3], [4], [6], [7], [10], [14], [16], [17], [21], [22], [25], [27], [28], [29], [30], [31], [35], [36], [39], [40], [42], [43], [45], [49], [50], [51], [52], [53], [54], [55], [60], [61], [67], [68], [69], [70], [71], [73], [74], [75], [76], [79], [80], [82], [84], [88], [89], [90], [92], [96], [97], [98], [105], [106], [107], [110], [111], [112], [115], [116], [117], [118], [119], [120], [122], [123], [125], [126], [127], [129], [132], [134], [136], [140], [142], [144], [145], [147], [150], [151], [152], [153], [158], [160], [161], [162], [164], [166], [168], [169], [170], [171], [172], [175], [176], [178], [179], [180], [181], [183], [185], [186], [187], [190], [192], [193], [196], [197], [199], [200], [202], [203], [207], [208], [211],

[213], [214], [215], [216], [218], [219], [220], [221], [222], [224], [226], [228], [232], [236], [237], [239], [240], [242], [243], [245], [249], [250], [251], [253], [254], [255], [257], [258], [261], [264], [266], [269], [270], [271], [276], [277], [280], [283], [284], [290], [293], [299], [300], [304], [309], [316], [319], [323], [324], [329], [330], [331], [332], [334], [337], [341], [342], [344], [346], [352], [355], [356], [360], [363], [365], [368], [370], [374], [378], [379], [390], [391], [394], [396], [397], [399], [401], [402], [407], [408], [410], [414], [415], [417], [420], [421], [422], [423], [426], [427], [430], [431], [433], [434], [440], [445], [447], [448], [450], [454], [455], [456], [459], [462], [463], [464], [470], [474], [476], [478], [480], [482], [483], [485], [489], [490], [492], [494], [495], [498], [502], [504], [508], [509], [510], [511], [512], [515], [518], [519], [521], [523], [525], [529], [530], [531], [532], [533], [536], [537], [540], [542], [545], [547], [549], [552], [553], [554], [555], [559], [560], [561], [564], [566], [567], [568], [570], [574], [575], [579], [585], [590], [592], [594], [595], [596], [601], [603], [606], [607], [609], [610], [613], [614], [615], [618], [621], [623], [629], [631], [633], [637], [638], [640], [642], [646], [647], [649], [651], [652], [654], [656], [657], [659], [660], [662], [666], [667], [671], [673], [674], [677], [678], [679], [680], [681], [685], [686], [688], [692], [697], [698], [699], [700], [701], [702], [703], [704], [705], [706], [708], [709], [710], [711], [713], [714], [715], [716], [718], [719], [720], [722], [727], [728], [730], [732], [734], [738], [741], [743], [744], [747], [749], [751], [753], [754], [756], [758], [761], [762], [763], [764], [765], [767], [769], [770], [776], [777], [778], [780], [783], [786], [788], [789], [790], [791], [792], [793], [795], [800], [801], [803], [809], [812], [813], [817], [824], [825], [826], [829], [830], [831], [833], [837], [842], [844], [850], [852], [853], [854], [855], [857], [865], [866], [868], [869], [872], [874], [876], [878], [879], [882], [884], [885], [886], [889], [892], [898], [899], [901], [903], [904], [905], [906], [907], [910], [913], [914], [917], [918], [922], [924], [926], [927], [928], [929], [930], [931], [933], [934], [935], [937], [941], [942], [946], [950], [952], [954], [955], [956], [957], [958], [959], [960], [962], [964], [966], [967], [968], [969], [970], [974], [975], [977], [978], [980], [981], [985], [987], [989], [996], [997], [1001], [1005], [1006], [1009], [1010], [1014], [1015], [1018], [1019], [1020], [1022], [1024], [1025], [1027], [1028], [1030], [1032], [1034], [1036], [1037], [1039], [1040], [1042], [1043], [1046], [1048], [1049], [1051], [1057], [1058], [1061], [1064], [1067], [1079], [1086], [1089], [1092], [1094], [1095], [1100], [1104], [1105], [1109], [1114], [1116], [1118], [1121], [1122], [1126], [1129], [1130], [1131], [1133], [1134], [1135], [1136], [1139], [1140], [1143], [1145], [1147], [1148], [1149], [1151], [1153], [1159], [1160], [1161], [1162], [1163], [1168], [1169], [1173], [1176], [1177], [1178], [1180], [1183], [1185], [1187], [1188], [1189], [1190], [1191], [1192], [1193], [1194], [1195], [1196], [1197], [1199], [1200], [1201], [1202], [1206], [1209], [1212], [1214], [1215], [1219], [1220], [1221], [1226], [1227], [1228], [1234], [1239], [1240], [1243], [1244], [1247],

[1248], [1251], [1252], [1253], [1254], [1256], [1257], [1260], [1263], [1264], [1265], [1266], [1269], [1270], [1272], [1275], [1276], [1277], [1278], [1279], [1280], [1281], [1282], [1283], [1285], [1286], [1287], [1288], [1289], [1290], [1291], [1292], [1293], [1294], [1295], [1296], [1297], [1298], [1299], [1300], [1303], [1305], [1308], [1309], [1310], [1312], [1315], [1316], [1321], [1323], [1324], [1327], [1328], [1329], [1330], [1333], [1336], [1339], [1341], [1342] — ΣN=479048

1) Introduction

Peripheral artery disease (PAD) represents a significant global health burden, characterized by atherosclerotic obstruction of arteries supplying the limbs, most commonly the lower extremities. Surgical interventions, encompassing a range of open and endovascular procedures, are critical for managing symptomatic PAD, particularly in cases of lifestyle-limiting claudication and chronic limb-threatening ischemia (CLTI) [2, 9, 116]. The landscape of PAD management is evolving, with ongoing research into patient risk stratification, optimal treatment modalities, perioperative care, and long-term outcomes [3, 15, 74]. This paper synthesizes current findings to delineate the efficacy, safety, and associated factors of surgical approaches for PAD.

2) Aim

To systematically review the current evidence on peripheral artery disease surgery, focusing on outcomes, risk factors, treatment comparisons, and emerging trends, to inform clinical practice and future research.

3) Methods

Systematic review with multilayer AI research agent: keyword normalization, retrieval & structuring, and paper synthesis (see SAIMSARA About section for details).

- **Bias:** Qualitatively inferred from study design fields. Retrospective designs are common, introducing potential selection and recall bias [1, 2, 6]. Cross-sectional studies provide snapshots but cannot establish causality [1, 20]. Unspecified study designs or directionality in some reports limit the ability to assess methodological rigor [3, 7, 10]. Small sample sizes in some experimental or case series studies restrict generalizability [13, 17, 41]. Heterogeneity in patient populations, interventions, and follow-up periods across studies further complicates direct comparisons.

4) Results

4.1 Study characteristics

The review encompassed a variety of study designs, including retrospective cohort studies [1, 2, 6, 12, 18, 22, 25, 27, 28, 33, 34, 35, 38], cross-sectional analyses [1, 20, 36, 203], randomized controlled trials (RCTs) [9, 127, 171, 187, 199, 274, 276, 320, 435], and prospective cohort studies [18, 33, 35, 154, 155, 156, 206, 361, 394]. Patient populations ranged from vascular surgery inpatients [1] and those undergoing lower extremity bypass (LEB) [2] to specific cohorts such as diabetic foot ulcer patients [23, 154], critical limb ischemia (CLTI) patients [20, 161], and those with concomitant cardiac conditions undergoing coronary artery bypass grafting (CABG) [19, 24, 27]. Follow-up periods varied widely, from immediate perioperative outcomes [35, 38, 409] and 30-day assessments [9, 133] to short-term (6 months, 1 year) [6, 22, 155] and long-term (3, 5, 10 years, or unspecified long-term) evaluations [3, 6, 26, 34, 193].

4.2 Main numerical result aligned to the query

Bypass surgery for peripheral artery disease (PAD) was associated with a significantly lower re-intervention rate (median 20%, range 17.0–20% [217, 332]) compared to endovascular revascularization (median 25%, range 25.2–35.1% [81, 217, 332]), with no significant difference in major amputation or mortality [21].

4.3 Topic synthesis

- **Patient Risk Factors and Comorbidities:** Peripheral artery disease (PAD) is strongly associated with various comorbidities that impact surgical outcomes. The triglyceride-glucose index (TyGI) is positively associated with PAD, with gender-specific differences [1]. Preoperative gabapentinoid use is linked to longer postoperative length of stay in lower extremity bypass (LEB) patients [2]. Chronic kidney disease (CKD) and hemodialysis significantly predict worse outcomes, including lower amputation-free survival and higher mortality after bypass surgery [34, 148, 273, 354, 739]. Diabetes mellitus (DM) is a pervasive comorbidity, influencing surgical site infections (SSIs) [18, 95], free flap failure [23], exercise capacity [31], saphenous vein graft (SVG) occlusion [32], and outcomes after infrainguinal bypass [102]. Frailty in PAD patients undergoing major vascular surgery is associated with functional decline and changes in living situation [113]. Older age, male sex, smoking, and other cardiovascular diseases (coronary artery disease (CAD), abdominal aortic aneurysm (AAA), carotid artery stenosis (CAS)) are consistently identified as risk factors for adverse events and mortality across various vascular and cardiac surgeries [24, 26, 27, 30, 32, 38, 48, 63, 72, 77, 78, 86, 95, 104, 133, 143, 173, 201, 206, 210, 241, 244, 247, 248, 250, 256, 257, 260, 270, 271, 292, 297, 298, 305, 311, 322, 333, 335, 338, 340, 345, 346, 351, 362, 366, 388, 393, 395, 404, 411, 413, 419, 461, 463, 469, 472, 496, 499,

513, 520, 538, 539, 562, 565, 587, 602, 608, 611, 612, 619, 627, 639, 641, 645, 648, 650, 680, 682, 693, 694, 752, 757, 768, 772, 781, 783, 796, 816, 819, 823, 835, 838, 839, 843, 851, 852, 863, 873, 874, 877, 881, 884, 887, 889, 892, 894, 908, 920, 939, 943, 949, 950, 952, 953, 956, 962, 965, 978, 982, 983, 984, 985, 986, 987, 990, 997, 999, 1000, 1008, 1009, 1021, 1030, 1081, 1083, 1084, 1085, 1086, 1090, 1091, 1096, 1097, 1098, 1115, 1117, 1119, 1128, 1141, 1142, 1144, 1158, 1173, 1181, 1203, 1204, 1211, 1226, 1231, 1284, 1285, 1306, 1313, 1314, 1337]. Chronic obstructive pulmonary disease (COPD) is also a significant risk factor for complications and mortality [62, 78, 130, 163, 863].

- **Surgical Outcomes and Complications:** Survival rates after PAD surgery vary by procedure and patient characteristics, with machine learning models predicting 1-, 3-, and 5-year survival AUCs of 0.86, 0.84, and 0.80, respectively [3]. Postoperative length of stay can be prolonged by factors like preoperative gabapentinoid use [2] or surgical complexity [59]. Major adverse limb events (MALE) and amputation rates are key outcomes, with bypass surgery showing comparable major amputation and mortality rates to endovascular revascularization, but lower re-intervention rates [21]. Patency of the profunda femoris artery (PFA) and common iliac artery are strong predictors of successful below-knee amputation stump healing [12]. Surgical site infections (SSIs) are a concern, with C-reactive protein (CRP) and hyperglycemia identified as predictive factors [18, 409]. Postoperative delirium (POD) is common after infrainguinal bypass and is associated with increased resource utilization, major amputation, myocardial infarction (MI), and mortality [281].
- **Treatment Modalities and Comparisons:** National trends show an increase in total vascular operative volume among graduating chief residents, with peripheral cases being the most frequent and demonstrating the greatest annual growth [4]. Lifestyle modifications can significantly decrease PAD severity and operation rates, leading to reduced amputations and increased pain-free patients [5]. Bypass surgery after endovascular treatment for PAD shows comparable perioperative, short-term, or mid-term clinical outcomes to primary bypass [6]. Bypass surgery demonstrates higher technical success and 1-year primary patency for PAD but is associated with increased 30-day morbidity, mortality, and 1-year major amputation rates compared to endovascular interventions [9]. Atherectomy followed by balloon angioplasty for infrainguinal PAD shows high technical success rates (95.83–100%) with acceptable restenosis and complication rates [14]. Endovascular treatment of the common femoral artery (CFA) is associated with higher reintervention rates compared to open treatment [81]. Percutaneous deep vein arterialization (pDVA) achieved 100% procedural success and 75% limb salvage in end-stage PAD patients [182].
- **Diagnostic and Predictive Tools:** Machine learning tools can predict survival after PAD surgery [3, 302]. A novel ultrasound platform prototype demonstrated accurate flow velocity measurements for remote surveillance [7]. Lower resistance index (RI) of distal-leg arteries correlates with higher rates of plantar arch patency in critical limb ischemia (CLI) patients

[20]. Subtraction computed tomography angiography (CTA) with volume position matching achieves higher diagnostic accuracy than conventional CTA in patients with severe calcific sclerosis [50]. Near-infrared (NIR) fluorescence imaging with indocyanine green (ICG) is a promising modality for diagnosing PAD and predicting postoperative skin necrosis after amputation [370, 408]. Deep learning models can accurately segment the vascular system and measure vascular calcification in femoral endarterectomy patients [168].

- **Perioperative Management and Optimization:** Preoperative use of gabapentinoids is associated with longer postoperative length of stay [2]. Rivaroxaban reduced the primary composite endpoint in PAD patients undergoing surgical bypass, with consistent benefits regardless of conduit type, despite increased bleeding risk [15, 29]. Dual antiplatelet therapy (DAPT) remains common after endovascular treatment, but dual pathway inhibition (DPI) with low-dose rivaroxaban plus aspirin may require caution in nearly 50% of CLTI patients due to high bleeding risk [99, 112]. Direct oral anticoagulants (DOACs) show no significant difference in bypass patency compared to warfarin for below-the-knee autologous vein bypasses [22]. A multidisciplinary delirium prevention bundle significantly reduced postoperative delirium in cardiac surgery patients, with PAD identified as an independent risk factor [138].
- **Health Disparities and Healthcare System Factors:** Patients residing furthest from tertiary hospitals present with more severe PAD and have higher rates of PAD surgery [28]. Peripheral artery disease (PAD) and aortic disease are the most studied conditions using the Vascular Quality Initiative (VQI) database for health disparities research, with sex being the most commonly studied variable [10]. Regional variations in revascularization rates for PAD are observed in Japan, influenced by medical resources and training facilities [166]. Medical centers with vascular surgery training programs are more likely to perform preoperative vein mapping and utilize autologous vein conduits for infrainguinal bypass [57]. Unconscious pro-White bias among vascular surgeons has implications for health disparities in PAD care [200].
- **Emerging Therapies and Research Models:** Inhibition of SRPK1 enhances collateralization in mouse models and in vitro human monocyte models of PAD by altering VEGF splicing [55, 196, 202]. Revascularization surgery significantly improved knee range of motion (ROM) and gait regularity in PAD patients [13]. Mesenchymal stem cells overexpressing microRNA-126 show promise for critical limb ischemia (CLI) treatment [421]. Photobiomodulation therapy (PBMT) can induce therapeutic angiogenesis and may be a novel treatment for PAD [425].

5) Discussion

5.1 Principal finding

Bypass surgery for peripheral artery disease (PAD) was associated with a significantly lower re-intervention rate (median 20%, range 17.0–20% [217, 332]) compared to endovascular revascularization (median 25%, range 25.2–35.1% [81, 217, 332]), with no significant difference in major amputation or mortality [21].

5.2 Clinical implications

- **Personalized Treatment Selection:** Given comparable major amputation and mortality rates, the choice between bypass surgery and endovascular revascularization should consider the patient's risk profile, lesion characteristics (e.g., common femoral artery lesions may have higher reintervention with endovascular approaches [81]), and the lower re-intervention rate associated with bypass surgery [21].
- **Enhanced Preoperative Optimization:** Preoperative screening for comorbidities like chronic kidney disease [148], diabetes [102], and frailty [113] is crucial for risk stratification. Addressing factors like hyperglycemia [409] and anemia [376] can significantly reduce postoperative complications.
- **Improved Postoperative Care:** Strategies for reducing postoperative delirium, such as multidisciplinary bundles, should be implemented, especially in high-risk patients [138, 281]. Careful consideration of antithrombotic regimens, balancing patency and bleeding risk, is essential [15, 99].
- **Importance of Lifestyle and Exercise:** Lifestyle modifications and structured exercise programs should be strongly encouraged as they can decrease PAD severity and reduce the need for surgery, improving patient outcomes [5, 144, 361].
- **Addressing Health Disparities:** Clinicians should be aware of and actively work to mitigate health disparities in PAD care, including those related to socioeconomic status, geographic access, and unconscious bias [28, 200, 269].

5.3 Research implications / key gaps

- **Standardized Outcome Reporting:** Heterogeneity in outcome definitions (e.g., patency, MALE, mortality timeframes) hinders direct comparison and meta-analysis [9, 21].
- **Long-Term Comparative Effectiveness:** More long-term (e.g., >5 years) randomized controlled trials are needed to compare open surgical and endovascular interventions across diverse PAD phenotypes, particularly for complex lesions [187, 199].
- **Biomarker-Guided Therapy:** Further research is needed to validate and integrate novel biomarkers (e.g., TyGI [1], H2S [278], microRNAs [47, 315]) into clinical decision-making for risk prediction and treatment response.

- **Impact of Socioeconomic Factors:** Studies are needed to quantify the precise impact of socioeconomic status and geographic remoteness on access to specialized PAD care and long-term surgical outcomes [28, 248, 269].
- **Optimizing Antithrombotic Strategies:** Further RCTs are required to define optimal antithrombotic regimens (e.g., DAPT vs. DPI) for various PAD surgical and endovascular procedures, considering individual bleeding and thrombotic risks [29, 99, 112].

5.4 Limitations

- **Retrospective Study Designs** — Many studies were retrospective, limiting causal inference and increasing susceptibility to confounding.
- **Heterogeneous Patient Populations** — Wide variation in PAD severity, comorbidities, and indications for surgery affects generalizability.
- **Varied Follow-up Durations** — Inconsistent follow-up periods make it challenging to compare long-term outcomes across studies.
- **Lack of Standardized Metrics** — Different definitions and reporting of key outcomes (e.g., patency, reintervention) limit direct quantitative synthesis.
- **Qualitative Bias Assessment** — Bias was inferred qualitatively, lacking a formal, quantitative assessment across all studies.

5.5 Future directions

- **Conduct Prospective RCTs** — Compare surgical and endovascular therapies for specific PAD anatomies.
- **Develop Predictive Models** — Integrate clinical, imaging, and biomarker data for personalized risk assessment.
- **Standardize Outcome Measures** — Facilitate robust comparisons across future PAD studies.
- **Investigate Novel Therapies** — Explore gene and cell therapies to enhance revascularization and limb salvage.
- **Implement Health Equity** — Design interventions to address disparities in PAD care access and outcomes.

6) Conclusion

Bypass surgery for peripheral artery disease (PAD) was associated with a significantly lower re-

intervention rate (median 20%, range 17.0–20% [217, 332]) compared to endovascular revascularization (median 25%, range 25.2–35.1% [81, 217, 332]), with no significant difference in major amputation or mortality [21]. These findings apply to a broad population of patients with PAD, often with multiple comorbidities, undergoing various revascularization procedures. The heterogeneity in study designs and outcome reporting across the literature remains the most significant limitation, affecting the certainty of direct comparisons. Moving forward, clinicians should prioritize individualized treatment plans based on patient risk factors and lesion characteristics, while researchers focus on standardized, long-term comparative effectiveness studies to refine treatment guidelines.

References

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Figure 1. Publication-year distribution of included originals

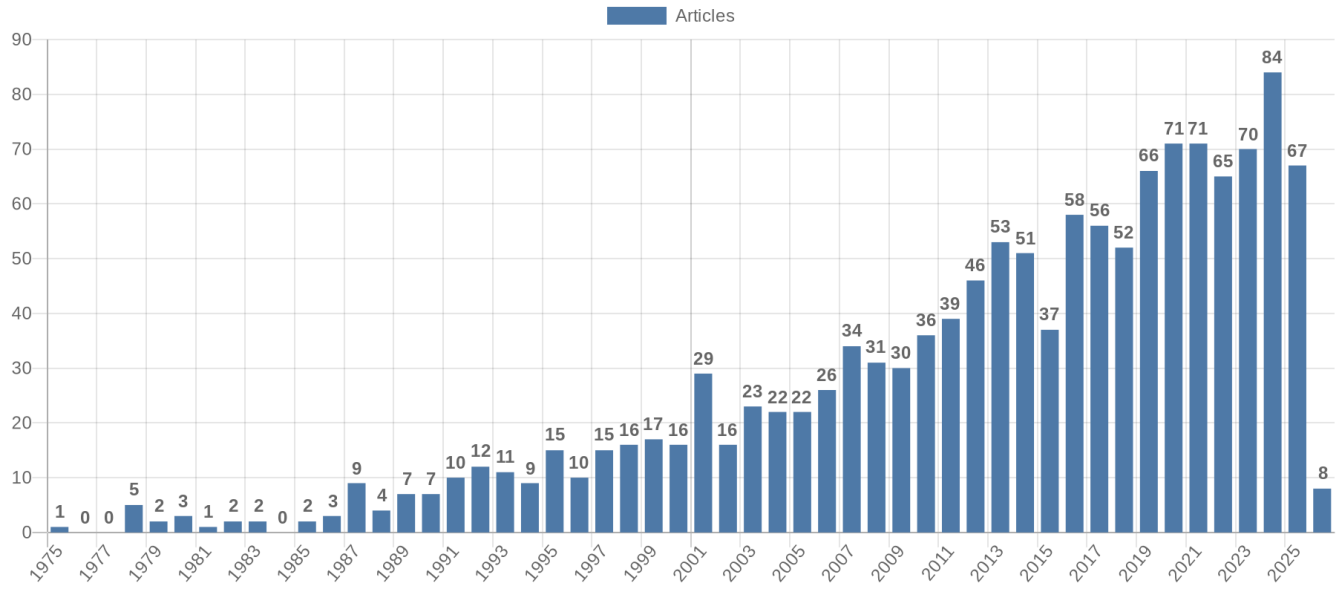

Figure 2. Study-design distribution of included originals

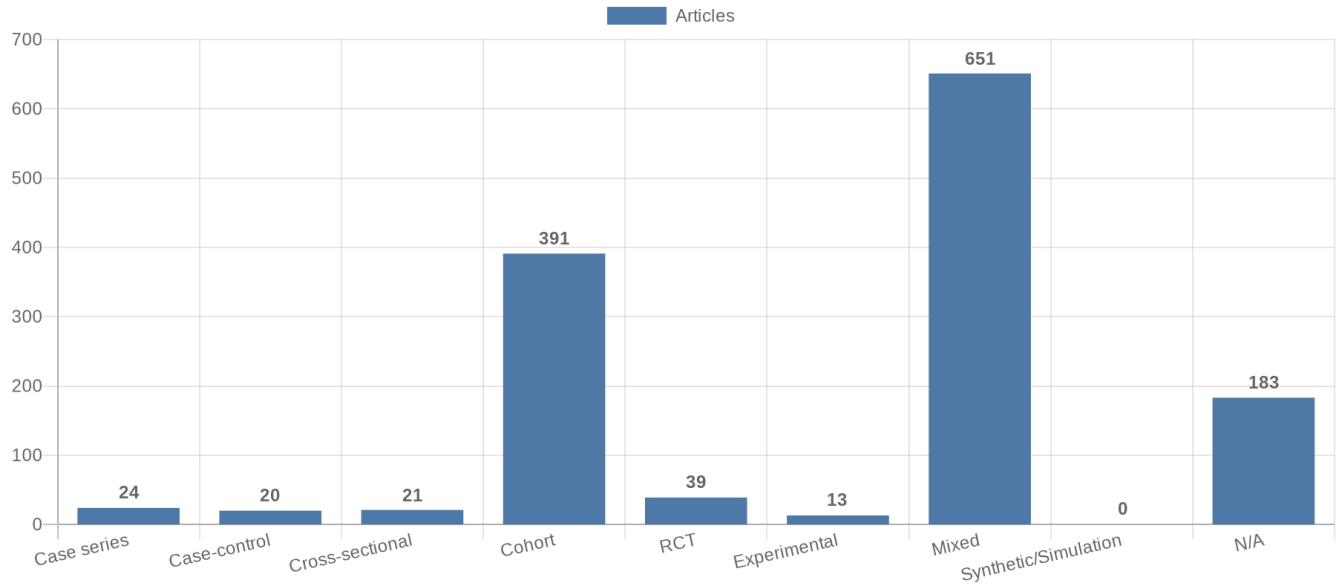

Figure 3. Study-type (directionality) distribution of included originals

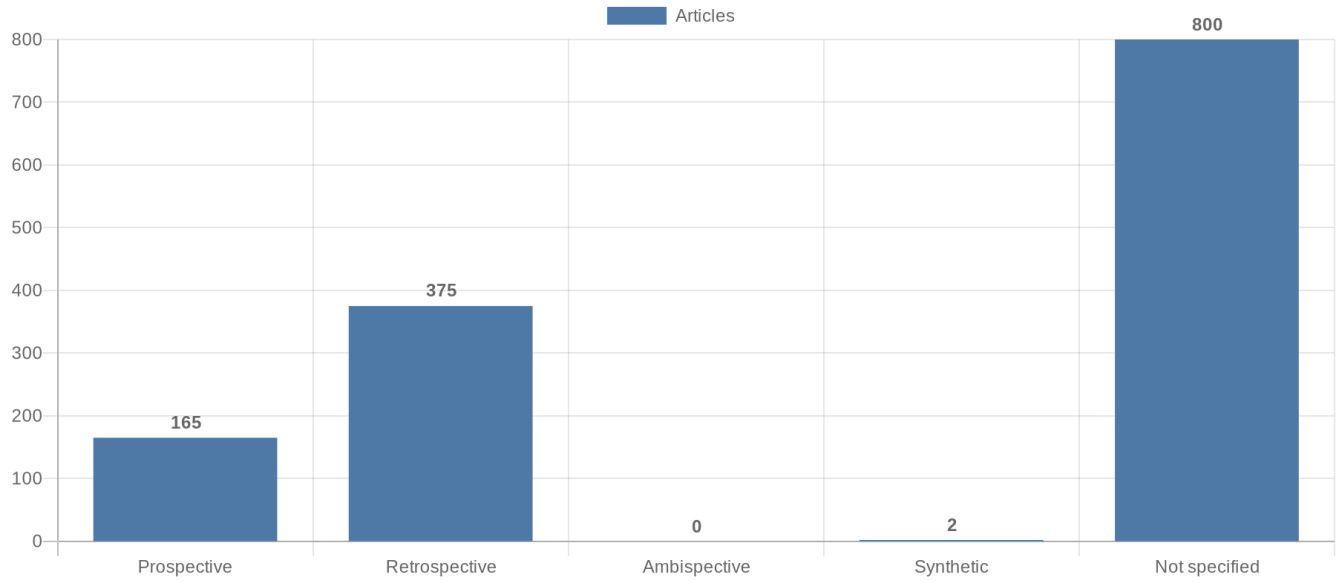

Figure 4. Main extracted research topics

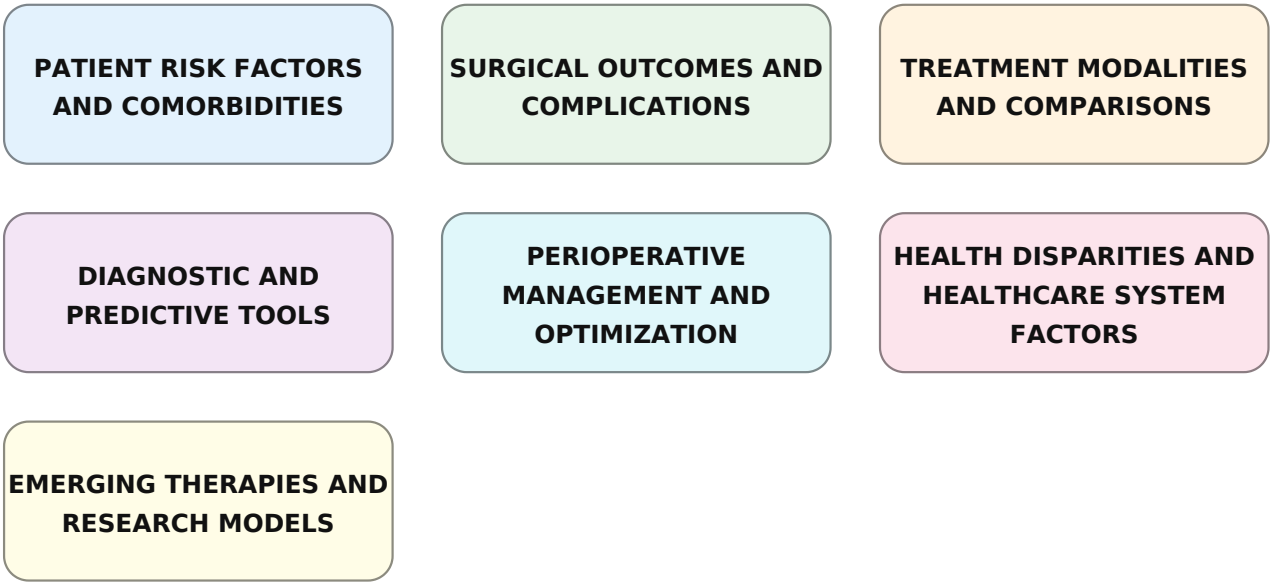

Figure 5. Limitations of current studies (topics)

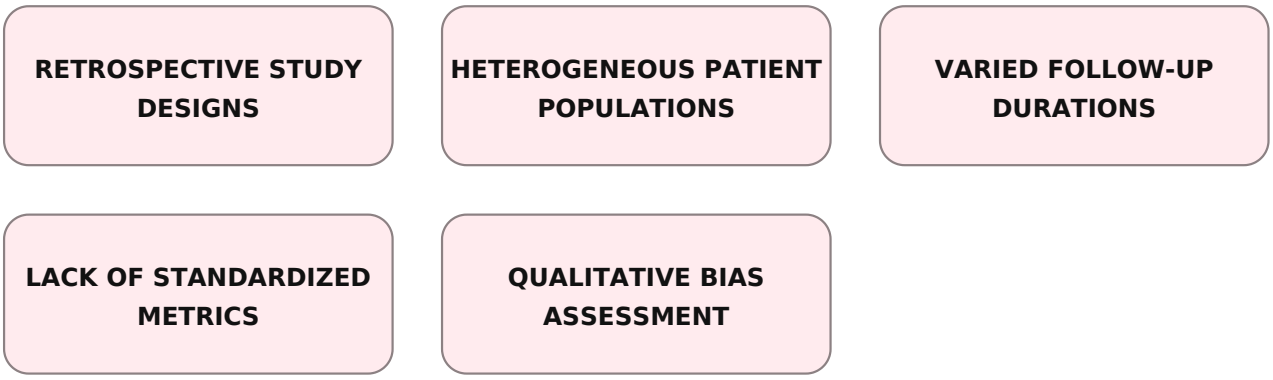

Figure 6. Future research directions (topics)