A systematic review and meta-analysis of treatment and natural history of popliteal artery aneurysms

Brad Beuschel, BS,[a] Tarek Nayfeh, MD,[a] Ahmad Kunbaz, MD,[a] Abdullah Haddad, MD,[a] Muayad Alzuabi, MD,[a] Shravani Vindhyal, MD,[a] Alik Farber, MD, MBA, FACS,[b] *and* M. Hassan Murad, MD, MPH,[a] *Rochester, Minn; and Boston, Mass*

ABSTRACT

Objective: To summarize the best available evidence comparing open vs endovascular popliteal artery aneurysm (PAA) repair. We also summarized the natural history of PAAs to support of the Society for Vascular Surgery guidelines.

Methods: We searched MEDLINE, EMBASE, Cochrane databases, and Scopus for studies of patients with PAAs treated with an open vs an endovascular approach. We also included studies of natural history of untreated patients. Studies were selected and appraised by pairs of independent reviewers. A meta-analysis was performed when appropriate.

Results: We identified 32 original studies and 4 systematic reviews from 2191 candidate references. Meta-analysis showed that compared with the endovascular approach, open surgical repair was associated with higher primary patency at 1 year (odds ratio [OR], 2.10; 95% confidence interval [CI], 1.41-3.12), lower occlusion rate at 30 days (OR, 0.41; 95% CI, 0.24-0.68) and fewer reinterventions (OR, 0.28; 95% CI, 0.17-0.45), but a longer hospital stay (standardized mean difference, 2.16; 95% CI, 1.23-3.09) and more wound complications (OR, 5.18; 95% CI, 2.19-12.26). There was no statistically significant difference in primary patency at 3 years (OR, 1.38; 95% CI, 0.97-1.97), secondary patency (OR, 1.59; 95% CI, 0.84-3.03), mortality at the longest follow-up (OR, 0.49; 95% CI, 0.21-1.17), mortality at 30 days (OR, 0.28; 95% CI, 0.06-1.36), or amputation (incidence rate ratio, 0.85; 95% CI, 0.56-1.31). The certainty in these estimates was, in general, low. Studies of PAA natural history suggest that thromboembolic complications and amputation develop at a mean observation time of 18 months and they are frequent. One study showed that at 5 years, approximately one-half of the patients had complications.

Conclusions: This systematic review provides event rates for outcomes important to patients with PAAs. Despite the low certainty of the evidence, these rates along with surgical expertise and anatomic feasibility can help patients and surgeons to engage in shared decision-making. (J Vasc Surg 2022;75:121S-5S.)

Keywords: Meta-analysis; Guideline; Popliteal; Aneurysm

Although peripheral artery aneurysms are rare, popliteal artery aneurysms (PAAs) are the most common type of peripheral arterial aneurysm with a reported prevalence rate of 0.007% in men, and 0.001% in women. Patients with PAAs are at increased risk of concomitant abdominal aortic aneurysms (33%) and contralateral PAA disease (50%).[1,2] Given the anatomic location of the popliteal artery, untreated aneurysmal disease of this artery can lead to complications, including limb loss.

Treatments of PAAs can be performed using endovascular aneurysm repair (EVAR) or open aneurysm repair (OAR). OAR typically involves bypass around the aneurysm, aneurysm ligation or aneurysmorhaphy. EVAR involves placing a stent graft across the aneurysm. Thrombolysis is an adjunct treatment used with both therapeutic strategies if acute limb ischemia is present. Although endovascular repair is less invasive than surgical bypass, its durability has been questioned. Therefore, empirical evidence comparing the long-term outcomes of OAR with EVAR remains unclear. Consequently, there is equipoise and a lack of consensus about the comparative effectiveness of either approach in managing PAAs.

The Society for Vascular Surgery has convened a committee of experts to develop clinical practice guidelines on the management of PAAs.[3] To support these guidelines, we conducted a systematic review and meta-analysis to summarize the best available evidence comparing the efficacy of OAR with EVAR in the treatment of PAAs, as well as the natural history of PAAs.

METHODS

This systematic review follows a protocol established a priori by a committee from the Society for Vascular Surgery. This report is consistent with the PRISMA statement.[4]

From the Evidence-based Practice Center, Mayo Clinic Rochester, Rochester[a]; and the Division of Vascular and Endovascular Surgery, Boston Medical Center, Boston University School of Medicine, Boston.[b]

Partially funded by the Society for Vascular Surgery.

Author conflict of interest: none.

Additional material for this article may be found online at www.jvascsurg.org.

Correspondence: M. Hassan Murad, MD, MPH, Mayo Clinic, 200 1st Street SW, Rochester, MN 55905 (e-mail: murad.mohammad@mayo.edu).

The editors and reviewers of this article have no relevant financial relationships to disclose per the JVS policy that requires reviewers to decline review of any manuscript for which they may have a conflict of interest.

0741-5214

https://doi.org/10.1016/j.jvs.2021.05.023

Study eligibility data sources and search strategies. We included studies with 10 patients or more that reported outcomes of patients with PAAs treated with open or endovascular approaches. Studies had to be comparative with longitudinal follow up and evaluate an outcome of interest (mortality, amputation, need of reintervention, thromboembolic events, patency, length of hospital stay or surgical complications). Traumatic and iatrogenic aneurysms were excluded. We also included studies that reported the rate of complications without treatment (ie, natural history studies). Because some studies reported results per aneurysms and not per patients and to present evidence on all outcomes, we summarized data from several selected existing systematic reviews. Supplementary Table I (online only) includes details of the two clinical questions in the patients, intervention, comparison, outcomes (PICO) format.

A comprehensive search of several databases from database inception to June 15th, 2018 was conducted without language restrictions. The databases included MEDLINE Epub Ahead of Print, Medline In-Process & Other Non-Indexed Citations, MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, and Scopus. The search strategy was designed and conducted by a medical reference librarian with input from the investigators. Controlled vocabulary supplemented with keywords was used to search for studies of open or endovascular repair of PAAs. The actual strategy is available in the Appendix (online only).

Study selection, data extraction, and methodologic quality assessment. Studies were selected and data were extracted by pairs of independent reviewers. Data extracted included patient and setting description, procedure description, risk of bias indicators and outcome data. Because the studies were nonrandomized, we used the Newcastle Ottawa tool[5] to assess the risk of bias. This tool evaluates three main domains: cohort selection, comparability, and outcome assessment. We did not calculate a score; rather, we made a global judgment about the risk of bias in each study.[6]

Statistical analysis and certainty in evidence. We calculated the odds ratio (OR) with 95% confidence interval (CI) for primary and secondary outcomes, as well as determined an incidence rate ratio for amputations across the studies. Thus, the OR of a bad outcome (amputation) in which the intervention reduces the outcome would be less than one and for a beneficial intervention (patency) would be greater than one. Because of anticipated heterogeneity, the DerSimonian and Laird random effects model[7] was used to pool estimates from the included studies. The I^2 statistic was used to estimate heterogeneity. Analysis was done using R Statistical Computing software version 4.0.0 (The R Foundation, Vienna, Austria). Data were insufficient to conduct preplanned subgroup analyses (aneurysm size, extension to superficial femoral artery, and concomitant aneurysms).

We used the GRADE approach to evaluate certainty in the evidence (also called quality of evidence).[8] In this approach, randomized trials start at high level of certainty and observational studies start at low level of certainty. Certainty can be graded down owing to study limitations, imprecision, indirectness, inconsistency, or publication bias. Certainty can also be increased, for example, for a large effect size.[9]

ARTICLE HIGHLIGHTS

- **Type of Research:** Systematic review and meta-analysis to support Society for Vascular Surgery guideline.
- **Key Findings:** This meta-analysis provides event rates for patient important outcomes after treatment of popliteal artery aneurysms.
- **Take Home Message:** The open approach for treating popliteal artery aneurysms is associated with higher primary patency and lower short-term occlusion, but longer hospital stay and more wound complications. There was no significant difference in mortality or amputation rate between open and endovascular approaches.

RESULTS

Included studies. We identified 32 original studies in 33 publications[10-42] and 4 systematic reviews[1,43-45] from 2191 candidate references. The Fig depicts the process of study selection. Thirty original studies in 31 publications[10-20,22-34,36-42] were included in the quantitative synthesis comparing OAR and EVAR. These studies included 5381 patients with mean age range of 63 to 68 years; 91.6% of patients were male (descriptive data are from studies that reported outcomes per patient, not per aneurysm). All studies were nonrandomized,[11-20,22-34,36-42] except for one randomized trial.[10] Supplementary Table II (online only) includes the characteristics of original included studies. Supplementary Table III (online only) includes the evaluation of the risk of bias of these studies. We also identified three systematic reviews that reported the outcomes of reintervention rate, wound complications, and hospital length of stay.[43-45] These analyses were deemed adequate and the most recent dataset[43] was used to extract these outcomes (14 studies, 4880 aneurysms). In terms of natural history outcomes, we identified an existing systematic review of 13 surgical case series (437 aneurysms)[1] and 2 additional series with additional 399 aneurysms.[21,35]

Comparison of open vs endovascular approaches. A meta-analysis showed that, compared with EVAR, OAR was associated with higher primary patency at 1 year (OR,

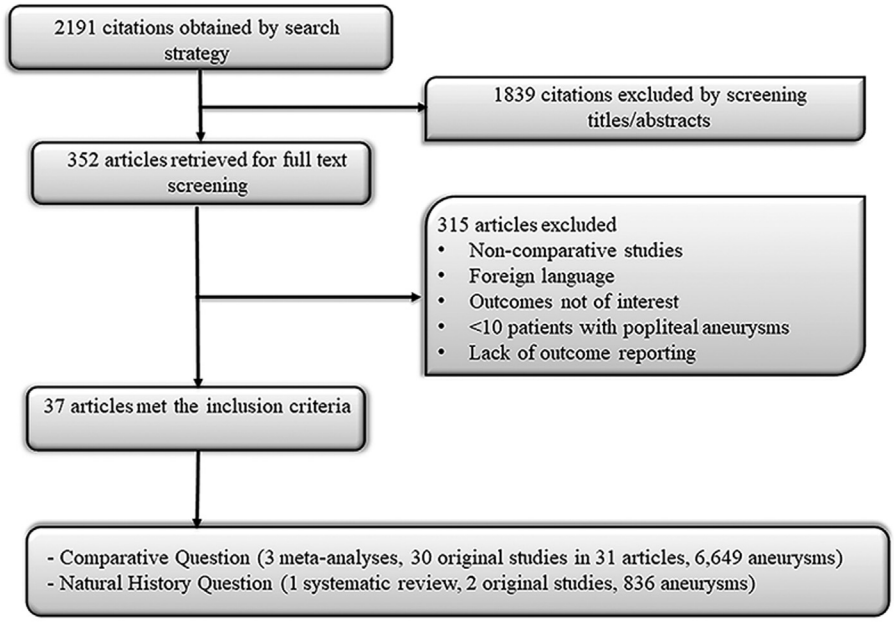


Fig. The study selection process.

2.10; 95% CI, 1.41-3.12). There was no statistically significant difference in primary patency at 3 years, secondary patency, mortality, or the amputation rate. The open approach was associated with lower embolic and thrombotic occlusions at 30 days (OR, 0.41; 95% CI, 0.24, 0.68). Forest plots are in Supplementary Figs 1 and 2 (online only).

Data from the systematic reviews identified in the search have shown that OAR was associated with lower reintervention rate (OR, 0.28; 95% CI, 0.17-0.45) more wound complications (OR, 5.18; 95% CI, 2.19-12.26), and longer length of stay, standardized mean difference of 2.16 (95% CI, 1.23-3.09).[43]

Studies of natural history. Studies of natural history suggested that complications of popliteal aneurysms develop at a mean observation time of 18 months.[1] The incidence of thromboembolic complications ranged from 8% TO 100% across series and that in patients with complications, amputation rate was 25%.[1] In one series with a longer follow-up, only 53% of patients treated conservatively were free of complications at 5 years.[35] In a second case series, 36% of asymptomatic patients had complications at 26 months.[21]

Certainty in estimates and publication bias. The risk of bias was in general high across studies owing to a lack of adjustment for prognostic risk factors. The certainty in the comparative estimates was low owing to the observational nature of the studies and the small sample sizes. Although we were unable to evaluate statistically for publication bias, this type of bias is likely present in a body of evidence that consists of smaller series that do not require registration. It is plausible that published results are more favorable than unpublished ones.

DISCUSSION

Main findings. We conducted a systematic review and meta-analysis to support the Society for Vascular Surgery guideline on the management of PAAs. A meta-analysis showed that, compared with the endovascular approach, the open surgical approach was associated with higher primary patency at 1 year, lower embolic and thrombotic occlusions at 30 days, and lower reintervention rates, but more wound complications and longer lengths of stay. There was no statistically significant difference in secondary patency, mortality, or amputation rate. Our findings were comparable with previous literature.[43] However, in contrast with Leake et al,[43] our results do not favor OAR over EVAR in terms of primary patency at 3 years because no statistically significant difference between the two modalities was found. Our review of the natural history of PAAS is consistent with the existing literature in demonstrating sparse data and low certainty. Studies of PAAs natural history suggested that thromboembolic complications and amputation develop at a mean observation time of 18 months and they are frequent. At 5 years, approximately one-half of the patients had complications.

Implications. These findings suggest that open PAA repair may be more durable than endovascular repair, albeit with a higher risk of complications and resource use. These data need to be taken in context, because they have not been validated by a well-powered randomized trial comparing these two treatment strategies. As such, depending on patient comorbidities and anatomic factors such as the presence of an optimal conduit, both OAR and EVAR remain important tools in

the management of patients with PAAs. A systematic review of the natural history data of asymptomatic PAAs suggests that PAAs present a significant risk of thromboembolic complications that may lead to limb loss. Therefore, consideration of an appropriately timed intervention to treat such aneurysms is an important strategy.

Strengths and limitations. The current systematic review followed a rigorous approach, including searching multiple databases, reviewing the literature by independent pairs of reviewers, and collaboration with content experts from the Society for Vascular Surgery.

A clear limitation in this body of evidence is the small sample size of series of a rare condition.

The lack of anatomic variables to allow patient selection for the endovascular approach is another major limitation. A planned subgroup analyses were not feasible owing to the lack of available information. Particularly, we were unable to stratify the analysis comparing emergent from elective cases as this distinction was not explicitly made in many of the published series. Similarly, data on other patient important outcomes such as acute limb ischemia, late conversion from endovascular to open repair, and quality of life were insufficient to estimate a treatment effect. Randomized trials of treatments of PAAS are challenging. Future research efforts could focus on establishing rigorous multicenter registries that document the clinical and anatomic presentations, treatment choices and outcomes of PAAs.

AUTHOR CONTRIBUTIONS

Conception and design: BB, TN, AF, MM
Analysis and interpretation: BB, TN, MM
Data collection: BB, TN, AK, AH, MA, SV
Writing the article: BB, TN, MM
Critical revision of the article: BB, TN, AK, AH, MA, SV, AF, MM
Final approval of the article: BB, TN, AK, AH, MA, SV, AF, MM
Statistical analysis: BB, TN
Obtained funding: MM
Overall responsibility: MM

REFERENCES

1. Dawson I, Sie RB, van Bockel JH. Atherosclerotic popliteal aneurysm. Br J Surg 1997;84:293-9.
2. Henke PK. Popliteal artery aneurysms: tried, true, and new approaches to therapy. Semin Vasc Surg 2005;18:224-30.
3. Farber A, Angle N, Avgerinos E, Dubois L, Eslami M, Geraghty P, et al. The Society for Vascular Surgery clinical practice guidelines on popliteal artery aneurysms. J Vasc Surg 2021 May 20. [E-pub ahead of print].
4. Moher D, Liberati A, Tetzlaff J, Altman DG, Group P. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. J Clin Epidemiol 2009;62:1006-12.
5. Wells GA, Shea B, O'Connell D, Peterson J, Welch V, Losos M, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. Available from: http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp. Accessed June 24, 2021.
6. Viswanathan M, Patnode CD, Berkman ND, Bass EB, Chang S, Hartling L, et al. Recommendations for assessing the risk of bias in systematic reviews of health-care interventions. J Clin Epidemiol 2018;97:26-34.
7. DerSimonian R, Laird N. Meta-analysis in clinical trials Control. Clin Trials 1986;7:177-88.
8. Hultcrantz M, Rind D, Akl EA, Treweek S, Mustafa RA, Iorio A, et al. The GRADE Working Group clarifies the construct of certainty of evidence. J Clin Epidemiol 2017;87:4-13.
9. Murad MH. Clinical practice guidelines: a primer on development and dissemination. Mayo Clin Proc 2017;92:423-33.
10. Antonello M, Frigatti P, Battocchio P, Lepidi S, Cognolato D, Dall'Antonia A, et al. Open repair versus endovascular treatment for asymptomatic popliteal artery aneurysm: results of a prospective randomized study. J Vasc Surg 2005;42:185-93.
11. Antonello M; Frigatti PBPLSDAADGPGF. Endovascular treatment of asymptomatic popliteal aneurysms: 8-year concurrent comparison with open repair. J Cardiovasc Surg 2007;48:267.
12. Braga AFF, Catto RC, Ribeiro MS, Piccinato CE, Joviliano EE. Open versus endovascular surgery for treatment of popliteal artery aneurysms: 5 years' experience at the HCRP-FMRP-USP. J Vasc Bras 2015;14:297-304.
13. Buethe JY, Soriano S, Jean-Claude J, Pinault G, Kang P. Endovascular versus open surgical popliteal artery aneurysm repair: a single-center experience. J Vasc Interv Radiol 2016;27:e3.
14. Cervin A, Tjarnstrom J, Ravn H, Acosta S, Hultgren R, Welander M, et al. Treatment of popliteal aneurysm by open and endovascular surgery: a contemporary study of 592 procedures in Sweden. Eur J Vasc Endovasc Surg 2015;50:342-50.
15. Curi MA, Geraghty PJ, Merino OA, Veeraswamy RK, Rubin BG, Sanchez LA, et al. Mid-term outcomes of endovascular popliteal artery aneurysm repair. J Vasc Surg 2007;45:505-10.
16. Deglise S, Van Ouwenaller F, Briner L, Dubuis C, Saucy F, Corpataux JM. Five years single-center experience of consecutive open repair and endovascular treatment of popliteal artery aneurysm. Vasa 2015;44(Suppl. 89):19.
17. Del Tatto B, Lejay A, Meteyer V, Roussin M, Georg Y, Thaveau F, et al. Open and endovascular repair of popliteal artery aneurysms. Ann Vasc Surg 2018;50:119-27.
18. Dorigo W, Fargion A, Masciello F, Piffaretti G, Pratesi G, Giacomelli E, et al. A matched case-control study on open and endovascular treatment of popliteal artery aneurysms. Scand J Surg 2018;107:236-43.
19. Dorigo W, Pulli R, Pratesi C. Results of open or endovascular management of thrombosed popliteal artery aneurysms following successful intra-arterial thrombolysis in a multicentric registry. J Vasc Surg 2016;63(6 Suppl. 1):17S-8S.
20. Eslami MH, Rybin D, Doros G, Farber A. Open repair of asymptomatic popliteal artery aneurysm is associated with better outcomes than endovascular repair. J Vasc Surg 2015;61:663-9.
21. Farina C, Cavallaro A, Schultz RD, Feldhaus RJ, di Marzo L. Popliteal aneurysms. Surg Gynecol Obstet 1989;169:7-13.
22. Galiñanes EL, Dombrovskiy VY, Graham AM, Vogel TR. Endovascular versus open repair of popliteal artery aneurysms: outcomes in the US Medicare population. Vasc Endovasc Surg 2013;47:267-73.
23. Gladiol Z, Traina L, Acciarri P, Mascoli F. Endovascular versus open repair for popliteal artery aneurysm. A single center experience. It J Vasc Endovasc Surg 2016;23:10-6.
24. Hoehn MR, McEnaney RM, Yuo TH, Chaer RA, Rhee RY, Makaroun MS, et al. Comparative analysis of endovascular and open popliteal artery aneurysm repair: midterm results. J Vasc Surg 2012;55:619.
25. Huang Y, Gloviczki P, Oderich GS, Duncan AA, Kalra M, Fleming MD, et al. Outcomes of endovascular and contemporary open surgical repairs of popliteal artery aneurysm. J Vasc Surg 2014;60:631-8.e2.
26. Kim BJ, Garg K, Rockman C, Jaco- bowitz GR, Maldonado T, Lamparello P, et al. Comparison of endovascular and open popliteal artery aneurysm repair. J Vasc Surg 2010;51(6 Suppl. 1):60S-1S.
27. Leake AE, Avgerinos ED, Chaer RA, Singh MJ, Makaroun MS, Marone LK. Contemporary outcomes of open and endovascular popliteal artery aneurysm repair. J Vasc Surg 2016;63:70-6.
28. Monaca V, Turiano SA, Tringale R, Vinciguerra D, Catalfamo S, Guzzo G, et al. Outcome assessment of open repair versus

endovascular treatment for popliteal artery aneurysm. Italian Journal of Vascular and Endovascular Surgery 2015;22:203-8.
29. Pulli R, Dorigo W, Castelli P, Dorrucci V, Ferilli F, De Blasis G, et al. A multicentric experience with open surgical repair and endovascular exclusion of popliteal artery aneurysms. Eur J Vasc Endovasc Surg 2013;45:357-63.
30. Pulli R, Drigo W, Fargion A, Pratesi G, Innocenti AA, Angiletta D, et al. Comparison of early and midterm results of open and endovascular treatment of popliteal artery aneurysms. Ann Vasc Surg 2012;26:809-18.
31. Ravn H, Wanhainen A, Björck M. Surgical technique and long-term results after popliteal artery aneurysm repair: results from 717 legs. J Vasc Surg 2007;46:236-43.
32. Ronchey S, Pecoraro F, Alberti V, Serrao E, Orrico M, Lachat M, et al. Popliteal artery aneurysm repair in the endovascular era: fourteen-years single center experience. Medicine 2015;94:e1130.
33. Rosenthal D, Matsuura JH, Clark MD, Kirby LB, Knoepp LF. Popliteal artery aneurysms: is endovascular reconstruction durable? J Endovasc Ther 2000;7:394-8.
34. Scarcello E, Morrone F, Conti A, Mazzei M, Piro P, Tarsitano S, et al. Surgical and endovascular treatment of popliteal artery aneurysms: single centre experience. Italian Journal of Vascular and Endovascular Surgery 2010;17:79-82.
35. Schroder A, Gohlke J, Gross-Fengels W, Horstmann R. [Popliteal aneurysms–surgical management versus conservative procedure]. Langenbecks Arch Chir Suppl Kongressbd 1996;113:857-63.
36. Serrano Hernando FJ, Martínez López I, Hernández Mateo MM, Hernando Rydings M, Sánchez Hervás L, Rial Horcajo R, et al. Comparison of popliteal artery aneurysm therapies. J Vasc Surg 2015;61:655-61.
37. Spina I, Paperetti L, Fargion A, Pulli R, Dorigo W, Pratesi C. Early and one-year comparison between open and endovascular treatment of popliteal artery aneurysms. Eur Surg Res 2010;45:260-1.
38. Stone PA, Armstrong PA, Bandyk DF, Keeling WB, Flaherty SK, Shames ML, et al. The value of duplex surveillance after open and endovascular popliteal aneurysm repair. J Vasc Surg 2005;41:936-41.
39. Stone PA, Jagannath P, Thompson SN, Campbell JE, Mousa AY, Knackstedt K, et al. Evolving treatment of popliteal artery aneurysms. J Vasc Surg 2013;57:1306-10.
40. Taurino M, Filippi F, Ficarelli R, Fantozzi C, Dito R, Brancadoro D, et al. Different approaches in popliteal artery aneurysm management. Eur Surg 2013;45:221-6.
41. Wooster M, Back M, Gaeto H, Shames M. Late longitudinal comparison of endovascular and open popliteal aneurysm repairs. Ann Vasc Surg 2016;30:253-7.
42. Wrede A, Wiberg F, Acosta S. Increasing the elective endovascular to open repair ratio of popliteal artery aneurysm. Vasc Endovasc Surg 2018;52:115-23.
43. Leake AE, Segal MA, Chaer RA, Eslami MH, Al-Khoury G, Makaroun MS, et al. Meta-analysis of open and endovascular repair of popliteal artery aneurysms. J Vasc Surg 2017;65:246-56.e2.
44. Shahin Y, Barakat H, Shrivastava V. Endovascular versus open repair of asymptomatic popliteal artery aneurysms: a systematic review and meta-Analysis. J Vasc Interv Radiol 2016;27:715-22.
45. von Stumm M, Teufelsbauer H, Reichenspurner H, Debus ES. Two decades of endovascular repair of popliteal artery aneurysm–a meta-analysis. Eur J Vasc Endovasc Surg 2015;50:351-9.

Submitted Feb 9, 2021; accepted May 17, 2021.

Additional material for this article may be found online at www.jvascsurg.org.

APPENDIX (online only).

Data sources and search strategies

A comprehensive search of several databases from 1946 to June 15, 2018, in all languages was conducted. The databases of Ovid Embase, Ovid MEDLINE 1946 to Present and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Ovid MEDLINE Daily, Ovid Cochrane Central Register of Controlled Trials, Ovid Cochrane Database of Systematic Reviews, and Scopus. A complete list of search terms and how they are combined is available in the Appendix.

Question 1: Endovascular approach/Open approach
Scopus

(((TITLE-ABS-KEY ("popliteal arter*")) AND (TITLE-ABS-KEY (aneurysm*))) OR (TITLE-ABS-KEY ("popliteal artery aneurysm*"))) AND ((TITLE-ABS-KEY (endovascular OR intravascular OR angioplasty OR angioscopy)) OR (TITLE-ABS-KEY (catheteriz* W/3 (central OR peripheral))) OR (TITLE-ABS-KEY ("percutaneous coronary" W/3 (interven* OR technique* OR procedure*))))

Natural history search

SCOPUS

((TITLE-ABS-KEY (("brain w/3 bleed*") OR (acute W/3 limb* W/3 ischemi*) OR (compress* W/3 ruptur*) OR (chronic W/3 ischemi*))) OR (TITLE-ABS-KEY (mortality OR morbidity OR amputat* OR thromb* OR ali OR "chronic ischemia" OR stroke OR "cerebrovascular accident" OR "brain vascular accident*" OR cvas OR cva OR "cerebral stroke*" OR "cerebrovascular stroke")) OR (TITLE-ABS-KEY ("cerebrovascular apoplexy" OR "heart attack*" OR "cardiovascular stroke*" OR "intracranial hemorrhage*" OR "intracranial haemorrhag*" OR ich OR "heart failure" OR "myocardial infarct*"))) AND ((TITLE-ABS-KEY ("popliteal arter*" AND aneurysm*)) OR (TITLE-ABS-KEY ("popliteal artery aneurysm*")))

AND NOT

((TITLE-ABS-KEY ("popliteal arter*" AND aneurysm*)) OR (TITLE-ABS-KEY ("popliteal artery aneurysm*"))) AND (TITLE-ABS-KEY ((endovascular OR intravascular OR angioplasty OR angioscopy) OR (catheteriz* W/3 (central OR peripheral)) OR ("percutaneous coronary" W/3 (interven* OR technique* OR procedure*))))

Supplementary Table I (online only). Patients, intervention, comparison, outcomes (*PICOs*)

PICO 1. Which is more effective, open or endovascular repair of PAAs?			
Population	**Intervention**	**Comparison**	**Outcomes**
PAAs[a]	Open approach	Endovascular approach	Mortality Amputation Thromboembolic events Patency Length of hospital stay Surgical complications
PICO2. What is the natural history of untreated PAAs?			
PAAs[a]	None	None	Mortality Amputation Thromboembolic events Patency Length of hospital stay Surgical complications

PAA, Popliteal artery aneurysm.
[a]Traumatic and iatrogenic aneurysms were excluded.

Supplementary Table II (online only). Study characteristics

Author, year	Study design	Demographics	Open patients	Endovascular patients	Open aneurysms	Endovascular aneurysms	Mean follow-up, months
Del Tatto et al,[17] 2018	Retrospective observational	126 patients Open: 69.4 years, 48-89. 4.6% female Endovascular: 70.4 years, 53-86 7.7% female	87	39	103	50	46.9
Dorigo et al,[18] 2018	Retrospective observational	112 patients Open: 68.6 ± 9.7 years 5.5% female Endovascular: 74.5 ± 7.8.0.0% female	n/a	n/a	250	59	38.0
Wrede et al,[42] 2018	Retrospective observational	Open: 66 years, 48-81 0.0% female Endovascular: 69 years, 56-87 7.4% female	n/a	n/a	39	27	31.5
Leake et al,[27] 2016	Retrospective observational	Open: 70.5 years 4.2% female Endovascular: 72.7 years 3.3% female	n/a	n/a	110	76	32.0
Wooster et al,[41] 2016	Retrospective observational	66 patients Open: 69.9 years, 51-74 2.0% female Endovascular: 82 years, 66-98 0.0% female	46	20	52	25	38.3
Ronchey et al,[32] 2015	Retrospective observational	67 patients, 49-97 years, 17.9% female Open: 67 years, Endovascular: 71 years	42	25	n/a	n/a	35.0
Cervin et al,[14] 2015	Retrospective observational	499 patients Open: 68 years, 42-102 3.8% female Endovascular: 74 years, 46-89 6.3% female	n/a	n/a	473	95	12.0
Eslami et al,[20] 2015	Retrospective observational	390 patients Open: 68.4 ± 10.6 years 4.5% female Endovascular: 73.5 ± 9.8 years 1.8% female	221	169	221	169	12.0
Huang et al,[25] 2014	Retrospective observational	120 patients Open: 71 years, 45-92.1.1% female Endovascular: 81 years, 64-91	91	35	107	42	41.8

Supplementary Table II (online only). Continued.

Author, year	Study design	Demographics	Open patients	Endovascular patients	Open aneurysms	Endovascular aneurysms	Mean follow-up, months
Pulli et al,[29] 2013	Retrospective observational	312 patients Open: 70 years ±8.9 92.5% female Endovascular: 74.9 years ±7.9 90.5% female	178	134	n/a	n/a	30.4
Stone et al,[39] 2013	Retrospective observational	72 patients Open: 66.0 years, 32-85 0.0% female Endovascular: 76 years, 50-92 5.0% female	52	20	64	24	40.5
Pulli et al,[30] 2012	Prospective observational	Open: 73.4 years. 4.5% female Endovascular: 74 years 0.0% female	n/a	n/a	43	21	22.5
Curi et al,[15] 2007	Retrospective observational	43 patients Open: 68 years ±2.4 7.0% female Endovascular: 75 years ±1.6 7.0% female	30	13	41	15	16.1
Stone et al,[38] 2005	Retrospective observational	46 patients, 72 years, 42-92 0.0% female	n/a	n/a	55 total	55 total	20.0
Rosenthal et al,[30] 2000	Retrospective observational	22 patients, 61 years, 44-81 0.0% female	12	10	n/a	n/a	13.6
Monaca et al,[28] 2015	Retrospective observational	56 patients Open: 66.7 years, 39-87 0.0% female Endovascular: 65.3 years, 47-86 0.0% female	30	26	n/a	n/a	44.3
Buethe et al,[13] 2016	Retrospective observational	18 patients	n/a	n/a	13	9	31.0
Gladiol et al,[23] 2016	Retrospective observational	41 patients Open: 67 years, 54-85 11.0% female Endovascular: 77 years, 64-91 20.0% female	n/a	n/a	30	16	18.5
Dorigo et al,[19] 2016	Retrospective observational	31 patients	18	13	n/a	n/a	42.0
Braga et al,[12] 2015	Retrospective observational	27 patients Open: 71.0 years 0.0% female Endovascular: 67.6 years 0.0% female	18	9	21	10	12.0

(Continued on next page)

Supplementary Table II (online only). Continued.

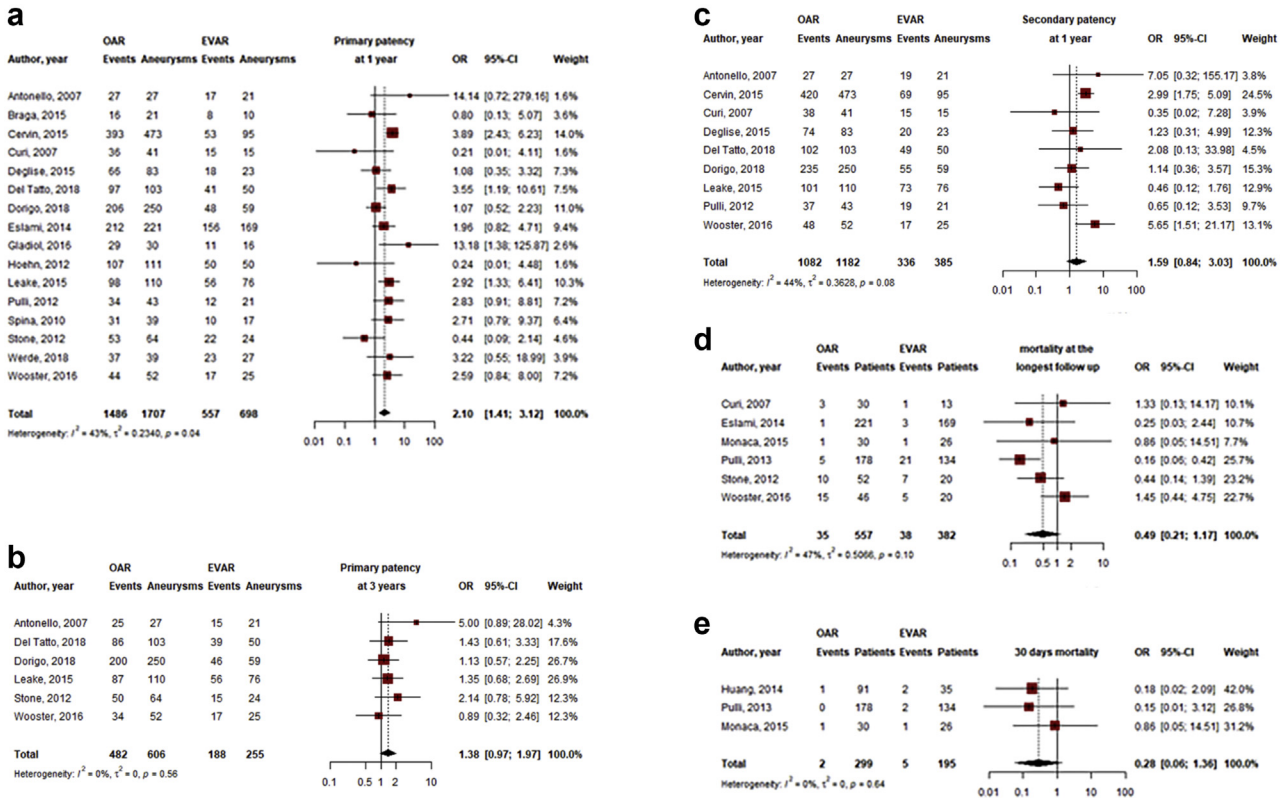
Author, year	Study design	Demographics	Open patients	Endovascular patients	Open aneurysms	Endovascular aneurysms	Mean follow-up, months
Deglise et al,[16] 2015	Retrospective observational	–	n/a	n/a	83	23	24.0
Taurino et al,[40] 2013	Prospective observational	36 patients, 59-80 years 5.5% female	n/a	n/a	33	6	27.0
Hoehn et al,[24] 2012	Retrospective observational	70.6 years 4.0% female	n/a	n/a	111	50	29.7
Scarcello et al,[34] 2010	Retrospective observational	73 years, 46-95 4.8% female	n/a	n/a	11	9	27.1
Spina et al,[37] 2010	Retrospective observational	50 patients	n/a	n/a	39	17	12.0
Kim et al,[26] 2010	Retrospective observational	45 patients Open: 71 ± 11 years Endovascular: 74 ± 9 years	n/a	n/a	29	24	28.0
Serrano Hernando et al,[36] 2015	Retrospective observational	171 patients Open: 68.7 years, 40-87 0.0% female Endovascular: 74.3 years, 56-88 0.0% female	139	32	171 total	171 total	49.0
Galiñanes et al,[22] 2013	Retrospective observational	2962 patients Open: 76.3 ± 6.2 years 5.0% female Endovascular: 77.9 ± 7.0 9.1% female	2413	549	n/a	n/a	3.0
Ravn et al,[31] 2007	Retrospective observational	5.3% female	n/a	n/a	681	26	12.0
Antonello et al,[11] 2007[a]	Prospective observational	42 patients Open: 62.8 years, 51-83 8.7% female Endovascular: 65.7 years, 51-85 19% female	n/a	n/a	27	21	97.0

n/a, Not applicable.
[a]Antonello, 2007 is a prospective nonrandomized long follow-up of Antonello et al,[10] 2005.

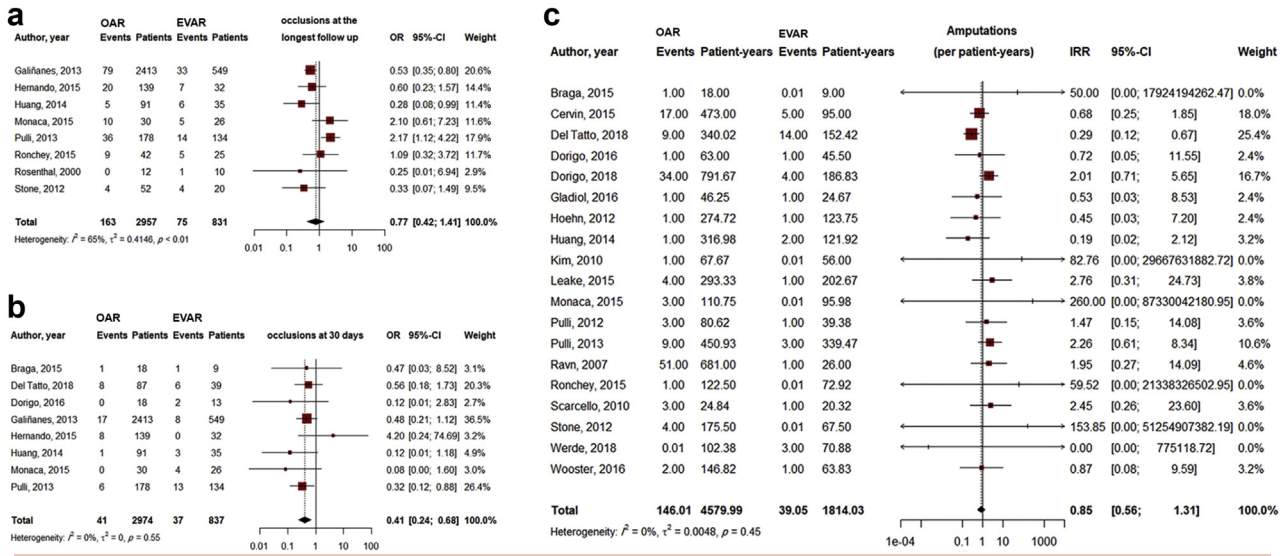
Supplementary Table III (online only). Study risk of bias evaluation

Author, year	Cohort selection	Comparability	Outcome assessment	Overall risk of bias
Del Tatto et al,[17] 2018	High risk	High risk	Low risk	High
Dorigo et al,[18] 2018	High risk	High risk	Low risk	High
Wrede et al,[42] 2018	Low risk	Low risk	Low risk	Low
Leake et al,[27] 2016	Low risk	High risk	Low risk	High
Wooster et al,[41] 2016	High risk	Unclear	Unclear	High
Ronchey et al,[32] 2015	High risk	High risk	Low risk	High
Cervin et al,[14] 2015	Low risk	High risk	Low risk	High
Eslami et al,[20] 2015	Low risk	Low risk	Low risk	Low
Huang et al,[25] 2014	Low risk	Low risk	Low risk	Low
Pulli et al,[29] 2013	Low risk	Low risk	Low risk	Low
Stone et al,[39] 2013	Low risk	High risk	Low risk	High
Pulli et al,[30] 2012	Low risk	Low risk	Low risk	Low
Curi et al,[15] 2007	Low risk	Low risk	Low risk	Low
Stone et al,[38] 2005	Unclear	Unclear	Unclear	High
Rosenthal et al,[30] 2000	High risk	High risk	Low risk	High
Monaca et al,[28] 2015	High risk	High risk	Low risk	High
Buethe et al,[13] 2016	Low risk	Unclear	Unclear	High
Gladiol et al,[23] 2016	Low risk	Low risk	Low risk	Low
Dorigo et al,[19] 2016	Unclear	High risk	Low risk	High
Braga et al,[12] 2015	Low risk	Low risk	Low risk	Low
Deglise et al,[16] 2015	Low risk	Unclear	Low risk	Moderate
Taurino et al,[40] 2013	Low risk	Unclear	Low risk	Moderate
Hoehn et al,[24] 2012	High risk	Unclear	Low risk	High
Scarcello et al,[34] 2010	Low risk	High risk	Low risk	High
Spina et al,[37] 2010	Unclear	High risk	Low risk	High
Kim et al,[26] 2010	High risk	High risk	Low risk	High
Serrano Hernando et al,[36] 2015	High risk	High risk	Low risk	High
Galiñanes et al,[22] 2013	High risk	High risk	Low risk	High
Ravn et al,[31] 2007	Low risk	Unclear	Low risk	Moderate
Antonello et al,[11] 2007[a]	Low risk	Low risk	Low risk	Low

[a]Antonello, 2007 is a prospective nonrandomized long follow-up of Antonello et al,[10] 2005.



Supplementary Fig 1 (online only). Forest plots for the comparison of open aneurysm repair (*OAR*) versus endovascular aneurysm repair (*EVAR*) in terms of **(a)** primary patency at 1 year, **(b)** primary patency at 3 years, **(c)** secondary patency at 1 year, **(d)** mortality at the longest follow-up, and **(e)** 30-day mortality.



Supplementary Fig 2 (online only). Forest plots for the comparison of open aneurysm repair (*OAR*) versus endovascular aneurysm repair (*EVAR*) in terms of **(a)** occlusion at the longest follow-up, **(b)** occlusion at 30 days, and **(c)** amputations.

Question 1: Endovascular approach/Open approach
Ovid MEDLINE(R) 1946 to Present and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) Daily

#	Searches	Results	Type
1	exp Popliteal Artery/or "popliteal arter*".mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	10,442	Advanced
2	exp ANEURYSM/or aneurysm*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	146,943	Advanced
3	1 and 2	1961	Advanced
4	"popliteal artery aneurysm*".mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	412	Advanced
5	3 or 4	1961	Advanced
6	endovascular.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	45,273	Advanced
7	exp endovascular procedures/	106,278	Advanced
8	("endovascular procedure*" or "endovascular technique*" or "intravascular procedure*" or "intravascular technique*" or angioplasty or angioscopy).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	90,625	Advanced
9	(catheteriz* adj3 (central or peripheral)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	21,739	Advanced
10	("percutaneous coronary" adj3 (interven* or technique* or procedure*)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	32,946	Advanced
11	6 or 7 or 8 or 9 or 10	157,603	Advanced
12	5 and 11	339	Advanced
13	5 and open.ti.	37	Advanced
14	13 not 12	6	Advanced

Question 1: Endovascular approach/Open approach
Embase <1988 to 2018 Week 24>

#	Searches	Results	Type
1	exp Popliteal Artery/ or "popliteal arter*".mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]	7850	Advanced
2	exp ANEURYSM/ or aneurysm*.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]	155,744	Advanced
3	1 and 2	1805	Advanced
4	"popliteal artery aneurysm*".mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]	701	Advanced
5	3 or 4	1805	Advanced
6	endovascular.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]	69,835	Advanced
7	exp endovascular procedures/	30,561	Advanced
8	("endovascular procedure*" or "endovascular technique*" or "intravascular procedure*" or "intravascular technique*" or angioplasty or angioscopy).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]	95,488	Advanced
9	(catheteriz* adj3 (central or peripheral)).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]	9324	Advanced
10	("percutaneous coronary" adj3 (interven* or technique* or procedure*)).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]	71,177	Advanced
11	6 or 7 or 8 or 9 or 10	216,435	Advanced
12	5 and 11	619	Advanced
13	5 and open.ti.	58	Advanced
14	13 not 12	7	Advanced

Question 1: Endovascular approach/Open approach
Ovid Cochrane Central Register of Controlled Trials, Ovid Cochrane Database of Systematic Reviews

#	Searches	Results	Type
1	exp Popliteal Artery/ or "popliteal arter*".mp. [mp=ti, ot, ab, sh, hw, kw, tx, ct]	490	Advanced
2	exp ANEURYSM/ or aneurysm*.mp. [mp=ti, ot, ab, sh, hw, kw, tx, ct]	3790	Advanced
3	1 and 2	29	Advanced
4	"popliteal artery aneurysm*".mp. [mp=ti, ot, ab, sh, hw, kw, tx, ct]	8	Advanced
5	3 or 4	29	Advanced
6	endovascular.mp. [mp=ti, ot, ab, sh, hw, kw, tx, ct]	2576	Advanced
7	exp endovascular procedures/	7387	Advanced
8	("endovascular procedure*" or "endovascular technique*" or "intravascular procedure*" or "intravascular technique*" or angioplasty or angioscopy).mp. [mp=ti, ot, ab, sh, hw, kw, tx, ct]	7627	Advanced
9	(catheteriz* adj3 (central or peripheral)).mp. [mp=ti, ot, ab, sh, hw, kw, tx, ct]	1610	Advanced
10	("percutaneous coronary" adj3 (interven* or technique* or procedure*)).mp. [mp=ti, ot, ab, sh, hw, kw, tx, ct]	7223	Advanced
11	6 or 7 or 8 or 9 or 10	16,218	Advanced
12	5 and 11	23	Advanced
13	5 and open.ti.	4	Advanced
14	13 not 12	0	Advanced

Natural history search
Ovid MEDLINE(R) 1946 to Present and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) Daily

#	Searches	Results	Type
1	exp Popliteal Artery/or "popliteal arter*".mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	10,445	Advanced
2	exp ANEURYSM/or aneurysm*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	146,991	Advanced
3	1 and 2	1961	Advanced
4	"popliteal artery aneurysm*".mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	412	Advanced
5	3 or 4	1961	Advanced
6	endovascular.mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	45,310	Advanced
7	exp endovascular procedures/	106,310	Advanced
8	("endovascular procedure*" or "endovascular technique*" or "intravascular procedure*" or "intravascular technique*" or angioplasty or angioscopy).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	90650	Advanced
9	(catheteriz* adj3 (central or peripheral)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	21,743	Advanced
10	("percutaneous coronary" adj3 (interven* or technique* or procedure*)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	32,969	Advanced
11	6 or 7 or 8 or 9 or 10	157,678	Advanced
12	5 and 11	339	Advanced
13	(mortality or morbidity or amputat* or thromb* or ali or "chronic ischemia" or stroke or "cerebrovascular accident" or "brain vascular accident*" or cvas or cva or "cerebral stroke*" or "cerebrovascular stroke" or "cerebrovascular apoplexy" or "heart attack*" or "cardiovascular stroke*" or "intracranial hemorrhage*" or "intracranial haemorrhag*" or ICH or "heart failure" or "myocardial infarct*").mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	2,037,869	Advanced
14	mortality.fx.	517,821	Advanced
15	amputation/or exp stroke/or exp "intracranial Hemorrhages"/or exp "heart failure"/or exp "myocardial infarction"/	446,608	Advanced
16	("brain adj3 bleed*" or (acute adj3 limb* adj3 ischemi*) or (compress* adj3 ruptur*)).mp. or (chronic disease/and ischemi*.mp.) [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	6957	Advanced

(Continued on next page)

Continued.

#	Searches	Results	Type
17	"natural history".mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	44,966	Advanced
18	exp Disease Progression/	156,132	Advanced
19	(untreated or "disease progression").mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	341,189	Advanced
20	13 or 14 or 15 or 16 or 17 or 18 or 19	2,427,068	Advanced
21	5 and 20	879	Advanced
22	21 not 12	671	Advanced
23	(trauma* or iatrogenic).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	406,208	Advanced
24	22 not 23	615	Advanced
25	limit 24 to (addresses or autobiography or bibliography or biography or dictionary or directory or interactive tutorial or interview or news or newspaper article or patient education handout or personal narratives or portraits or video-audio media or webcasts)	1	Advanced
26	24 not 25	614	Advanced

Natural history search
Embase <1988 to 2018 Week 25>

#	Searches	Results	Type
1	exp Popliteal Artery/or "popliteal arter*".mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]	7855	Advanced
2	exp ANEURYSM/or aneurysm*.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]	156,043	Advanced
3	1 and 2	1806	Advanced
4	"popliteal artery aneurysm*".mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]	701	Advanced
5	3 or 4	1806	Advanced
6	endovascular.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]	70,185	Advanced
7	exp endovascular procedures/	30,631	Advanced
8	("endovascular procedure*" or "endovascular technique*" or "intravascular procedure*" or "intravascular technique*" or angioplasty or angioscopy).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]	95,568	Advanced
9	(catheteriz* adj3 (central or peripheral)).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]	9333	Advanced
10	("percutaneous coronary" adj3 (interven* or technique* or procedure*)).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]	71,307	Advanced
11	6 or 7 or 8 or 9 or 10	216,957	Advanced
12	5 and 11	620	Advanced
13	(mortality or morbidity or amputat* or thromb* or ali or "chronic ischemia" or stroke or "cerebrovascular accident" or "brain vascular accident*" or cvas or cva or "cerebral stroke*" or "cerebrovascular stroke" or "cerebrovascular apoplexy" or "heart attack*" or "cardiovascular stroke*" or "intracranial hemorrhage*" or "intracranial haemorrhag*" or ICH or "heart failure" or "myocardial infarct*").mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]	2,711,327	Advanced
14	mortality.fx.	0	Advanced
15	amputation/or exp stroke/or exp "intracranial Hemorrhages"/or exp "heart failure"/or exp "myocardial infarction"/	864,221	Advanced
16	("brain adj3 bleed*" or (acute adj3 limb* adj3 ischemi*) or (compress* adj3 ruptur*)).mp. or (chronic disease/and ischemi*.mp.) [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]	6613	Advanced
17	"natural history".mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]	54,565	Advanced
18	exp Disease Progression/	2,783,610	Advanced
19	(untreated or "disease progression").mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]	288997	Advanced
20	13 or 14 or 15 or 16 or 17 or 18 or 19	5,127,007	Advanced
21	5 and 20	1072	Advanced
22	21 not 12	622	Advanced

(Continued on next page)

Continued.

#	Searches	Results	Type
23	(trauma* or iatrogenic).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]	433,620	Advanced
24	22 not 23	542	Advanced
25	limit 24 to (addresses or autobiography or bibliography or biography or dictionary or directory or interactive tutorial or interview or news or newspaper article or patient education handout or personal narratives or portraits or video-audio media or webcasts) [Limit not valid in Embase; records were retained]	542	Advanced
26	24 not 25	0	Advanced

Natural history search
Ovid Cochrane Central Register of Controlled Trials, Ovid Cochrane Database of Systematic Reviews

#	Searches	Results	Type
1	exp Popliteal Artery/or "popliteal arter*".mp. [mp=ti, ot, ab, sh, hw, kw, tx, ct]	490	Advanced
2	exp ANEURYSM/or aneurysm*.mp. [mp=ti, ot, ab, sh, hw, kw, tx, ct]	3790	Advanced
3	1 and 2	29	Advanced
4	"popliteal artery aneurysm*".mp. [mp=ti, ot, ab, sh, hw, kw, tx, ct]	8	Advanced
5	3 or 4	29	Advanced
6	endovascular.mp. [mp=ti, ot, ab, sh, hw, kw, tx, ct]	2576	Advanced
7	exp endovascular procedures/	7387	Advanced
8	("endovascular procedure*" or "endovascular technique*" or "intravascular procedure*" or "intravascular technique*" or angioplasty or angioscopy).mp. [mp=ti, ot, ab, sh, hw, kw, tx, ct]	7627	Advanced
9	(catheteriz* adj3 (central or peripheral)).mp. [mp=ti, ot, ab, sh, hw, kw, tx, ct]	1610	Advanced
10	("percutaneous coronary" adj3 (interven* or technique* or procedure*)).mp. [mp=ti, ot, ab, sh, hw, kw, tx, ct]	7223	Advanced
11	6 or 7 or 8 or 9 or 10	16,218	Advanced
12	5 and 11	23	Advanced
13	(mortality or morbidity or amputat* or thromb* or ali or "chronic ischemia" or stroke or "cerebrovascular accident" or "brain vascular accident*" or cvas or cva or "cerebral stroke*" or "cerebrovascular stroke" or "cerebrovascular apoplexy" or "heart attack*" or "cardiovascular stroke*" or "intracranial hemorrhage*" or "intracranial haemorrhag*" or ICH or "heart failure" or "myocardial infarct*").mp. [mp=ti, ot, ab, sh, hw, kw, tx, ct]	156,944	Advanced
14	mortality.fx.	0	Advanced
15	amputation/or exp stroke/or exp "intracranial Hemorrhages"/or exp "heart failure"/or exp "myocardial infarction"/	25,091	Advanced
16	("brain adj3 bleed*" or (acute adj3 limb* adj3 ischemi*) or (compress* adj3 ruptur*)).mp. or (chronic disease/and ischemi*.mp.) [mp=ti, ot, ab, sh, hw, kw, tx, ct]	410	Advanced
17	"natural history".mp. [mp=ti, ot, ab, sh, hw, kw, tx, ct]	2076	Advanced
18	exp Disease Progression/	6381	Advanced
19	(untreated or "disease progression").mp. [mp=ti, ot, ab, sh, hw, kw, tx, ct]	27,274	Advanced
20	13 or 14 or 15 or 16 or 17 or 18 or 19	181,376	Advanced
21	5 and 20	20	Advanced
22	21 not 12	2	Advanced
23	(trauma* or iatrogenic).mp. [mp=ti, ot, ab, sh, hw, kw, tx, ct]	19,379	Advanced
24	22 not 23	2	Advanced
25	limit 24 to (addresses or autobiography or bibliography or biography or dictionary or directory or interactive tutorial or interview or news or newspaper article or patient education handout or personal narratives or portraits or video-audio media or webcasts) [Limit not valid in CCTR,CDSR; records were retained]	0	Advanced
26	24 not 25	2	Advanced