Eur J Vasc Endovasc Surg (2021) 61, 383—394

Editor's Choice – Percutaneous Access Does Not Confer Superior Clinical Outcomes Over Cutdown Access for Endovascular Aneurysm Repair: Meta-Analysis and Trial Sequential Analysis of Randomised Controlled Trials

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WHAT THIS PAPER ADDS

A meta-analysis was conducted of the most up to date, randomised clinical trial data of percutaneous *vs.* cutdown endovascular aneurysm repair (EVAR). The risk of bias was assessed with the updated Cochrane methodology, and the evidence was appraised with the GRADE system (Grades of Recommendation, Assessment, Development and Evaluation). Percutaneous EVAR was not found to have superior clinical outcomes to cutdown EVAR. The studies were judged to be high risk of bias or have some concerns, and the level of evidence was graded as low or very low for all investigated outcomes. The study highlights the need for high quality evidence on the potential advantages of percutaneous over cutdown EVAR.

Objective: To investigate whether a percutaneous approach has better clinical outcomes than surgical access for standard endovascular repair of abdominal aortic aneurysms.

Data sources: MEDLINE and Embase were searched using the Healthcare Databases Advanced Search interface developed by the National Institute for Health and Care Excellence.

Review methods: Randomised controlled trials (RCTs) that compared percutaneous and cutdown endovascular aneurysm repair (EVAR) were considered. Pooled effect estimates were calculated using the odds ratio (OR), risk difference, or mean difference (MD) and 95% confidence interval (CI). The Mantel—Haenszel or inverse variance statistical method was used as appropriate. Trial sequential analysis was performed to quantify the available evidence and control for the risk of type 1 and type 2 error. Risk of bias was assessed with the revised tool developed by Cochrane and the quality of evidence was graded using the GRADE system (Grades of Recommendation, Assessment, Development and Evaluation).

Results: Four RCTs were identified, reporting a total of 368 patients and 530 access sites. Meta-analysis showed no difference in access site complications or infection, post-operative bleeding/haematoma, access related arterial injury, femoral artery occlusion, pseudo-aneurysm, or peri-operative mortality between percutaneous and cutdown EVAR. Seroma/lymphorrhoea was significantly less frequent after percutaneous EVAR (0%) compared with cutdown EVAR (3%; OR 0.18 [95% CI 0.04—0.83]) and the procedure time was significantly shorter (MD −11.53 minutes; 95% CI −15.71—7.34), but hospital length of stay was not different between treatments. Neither the O'Brien—Fleming boundaries nor the futility boundaries were crossed by the cumulative Z curve, and the required information size was not reached for any of the outcomes. All trials were judged to be high risk of bias or have some concerns, and the level of the body of evidence was low or very low for all outcomes.

Conclusion: The evidence is very uncertain about the effect of percutaneous EVAR on clinically important outcomes.

Keywords: Aortic aneurysm, Endovascular aneurysm repair, EVAR, Percutaneous
Article history: Received 7 June 2020, Accepted 4 November 2020, Available online 10 December 2020

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https://doi.org/10.1016/j.ejvs.2020.11.008

INTRODUCTION

With the advent of minimally invasive techniques for the treatment of vascular disease over the past two decades,

the vascular community has witnessed a transition from traditional vascular surgery to modern, innovative endovascular intervention. Such a paradigm shift in endovascular practice is illustrated in percutaneous endovascular aneurysm repair (EVAR). The endovascular technique for abdominal aortic aneurysm (AAA) repair has evolved to allow percutaneous arterial access and remote closure of the arterial defect with a vascular closure device without direct visualisation of the access artery.

Percutaneous EVAR has potential advantages over EVAR performed with conventional surgical access to the femoral arteries, such as reduction in surgical site infection and/or lymphorrhoea and seroma formation.[1] Another potential benefit of percutaneous EVAR is the optimisation of resource utilisation, such as reduced procedure time and hospital length of stay, which may have substantial implications for stakeholders and healthcare policymakers.[1] However, concerns have been raised about the risks of percutaneous EVAR, especially in high risk patients for percutaneous arterial access, such as those with calcified femoral arteries and obese patients, including arterial injury and pseudo-aneurysm formation.[2,3] In light of the uncertainty around the risk/benefit balance of percutaneous EVAR, a comprehensive review of the literature was conducted, the most up to date, highest level evidence on the comparative effectiveness of percutaneous and cutdown EVAR was identified, and data were compiled in a meta-analysis.

Objective

The objective was to investigate whether percutaneous access has better or worse clinical outcomes than surgical access for standard endovascular AAA repair.

MATERIALS AND METHODS

Review design

The review objectives and methodology were prespecified in a protocol. The review was developed in line with the principles described in the Cochrane Handbook for Systematic Reviews of Interventions, which is the official guide detailing the process of preparing and maintaining Cochrane systematic reviews on the effects of healthcare interventions.[4] The review was reported in accordance with the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) standards.[5]

Study selection and criteria for consideration of studies

Two independent review authors conducted the prespecified literature searches and selected studies against the eligibility criteria listed below. Discrepancies and/or disagreements were resolved by discussion.

Types of studies. Randomised controlled trials (RCTs) comparing outcomes of percutaneous EVAR with those of femoral artery surgical cutdown EVAR were considered.

Types of participants. Male or female patients of any age who underwent standard EVAR in an elective setting were considered. Patients treated for symptomatic or ruptured AAA were excluded. Cases of complex endovascular aortic procedures, for example, fenestrated EVAR, and cases of endovascular treatment of the thoracic aorta were also excluded.

Types of interventions. The intervention of interest was EVAR performed with percutaneous access to the femoral arteries in the groin. Percutaneous EVAR could have been performed with any commercially available percutaneous closure device. The comparator intervention was EVAR performed with surgical exposure of the access femoral arteries in the groin via a vertical or oblique skin incision.

Types of outcome measure. The primary outcomes were (1) access site infection; (2) post-operative bleeding/haematoma; (3) pseudo-aneurysm of the access artery; (4) access site lymphorrhoea/seroma; and (5) peri-operative mortality.

Following interrogation of the selected studies, additional outcome measures were identified, reported by more than one study, as follows: (1) access site complications; (2) access related arterial injury; and (3) femoral artery occlusion. Because of their clinical importance, these outcomes were defined as additional primary outcomes.

Secondary outcomes were (1) procedure time; (2) hospital length of stay; and (3) patient quality of life.

Search methods for the identification of studies

The literature search strategy was developed by one of the review authors with experience in outreach, knowledge, and evidence search.

Electronic searches. The Healthcare Databases Advanced Search interface developed by the National Institute for Health and Care Excellence was used to interrogate electronic bibliographic sources. MEDLINE and Embase were searched. Relevant terms were selected to identify eligible reports. Thesaurus headings, search operators, and limits in each of the above databases were adapted accordingly. The electronic literature search was run on 9 April 2020. No language constraints were applied. The literature search strategy is presented in Appendix 1 (see Supplementary Material).

Searching other resources. The bibliographic lists of articles that met the review inclusion criteria were screened for additional studies.

Data extraction and management

One review author extracted data from the selected studies and a second review author cross checked the extracted data. Discrepancies were resolved by consensus. The following information was extracted from the studies and included in the qualitative and quantitative synthesis:

- Study related data: journal and year of publication; country of the corresponding author; single or multicentre study; inclusion and exclusion criteria for patient enrolment in the individual trials; and intention to treat (ITT) or per protocol analysis.

- Study population clinical data: type of percutaneous closure device; configuration of surgical groin incision (vertical or oblique); number of patients and access sites in each group; baseline demographics (age, sex and body mass index [BMI]); American Society of Anaesthesiologists (ASA) classification; proportion of patients with diabetes mellitus; type of anaesthesia (general, local, or regional); and sheath size for introducing the endovascular device.
- Data pertaining to the risk of bias assessment.
- Outcome data.

Assessment of risk of bias in included studies

The revised Cochrane risk of bias tool for RCTs was used. It provides a framework for considering the risk of bias in the RCT findings and is specific to a single trial result.[6] The tool is structured into five domains: (1) bias arising from the randomisation process; (2) bias due to deviations from intended interventions; (3) bias due to missing outcome data; (4) bias in measurement of the outcome; and (5) bias in selection of the reported result.

The template for randomised parallel group trials was used. Possible responses to signalling questions in each domain were "yes", "probably yes", "probably no", "no", and "no information", and the possible risk of bias judgements were "low risk of bias", "some concerns", and "high risk of bias". The tool's algorithms that map responses to signalling questions were used, but the proposed judgements were verified by the review authors and were changed if it was felt it was appropriate. The effect of assignment to intervention was estimated by the ITT principle, which includes all randomised participants.

A summary of findings table was also generated. The quality of evidence was graded using the system developed by the GRADE (Grades of Recommendation, Assessment, Development and Evaluation) working group applying an online platform (https://gdt.gradepro.org/app/).[7]

Statistical synthesis

Measures of treatment effect. Pooled estimates of dichotomous outcomes were calculated using odds ratio (OR) and 95% confidence interval (CI) using the Mantel—Haenszel statistical method. If one or more trials recorded zero events in both intervention arms, the risk difference (and 95% CI) was calculated instead. For continuous data, the pooled mean difference (MD; and 95% CI) was calculated with the inverse variance statistical method.

Unit of analysis issues. The unit of analysis was the individual patient or the access site in the groin depending on the outcome of interest; for example, for peri-operative mortality, the unit of analysis was the patient, whereas for access site infection, the unit of analysis was the access site in the groin.

Dealing with missing data. No attempt was made to contact trial authors about missing data.

Assessment of heterogeneity. Between study heterogeneity was examined with the Cochrane's Q (chi square) test. Inconsistency was quantified by calculating I^2 and interpreted using the following guide: 0%—40% might not be important; 30%—60% may represent moderate heterogeneity; 50%—90% may represent substantial heterogeneity; and 75%—100% may represent considerable heterogeneity.[8]

Assessment of reporting biases. Publication bias was assessed visually by evaluating the symmetry of the funnel plot for each individual outcome, if $>$ 10 studies were available.

Data synthesis. The summary outcome estimates were calculated using the fixed effect model, unless there was evidence of conceptual or statistical heterogeneity, in which case the random effects method of DerSimonian and Laird was applied. Significant statistical heterogeneity was defined as $I^2 > 75\%$ and Cochrane's Q (chi square) test p value $< .05$. A forest plot was created for each treatment effect.

Subgroup analysis and investigation of heterogeneity. Subgroup analysis was performed for the type of percutaneous closure device and the configuration of skin incision in the groin.

Sensitivity analysis. Sensitivity analysis was performed excluding studies that were judged to be high risk of bias or to have some concerns using the revised Cochrane risk of bias tool, to discern differences in calculated summary effect estimates.

Trial sequential analysis

Trial sequential analysis controls the risks for type 1 and type 2 errors, helps to clarify whether additional trials are needed, and provides important information regarding the required sample size for clinical trials.[9,10] In order to control the risk of type 1 error, the thresholds for the z values were adjusted using the O'Brien—Fleming α-spending function, allowing the type 1 error risk to be restored to the desired maximum risk. Crossing the O'Brien—Fleming α-spending boundaries by a z curve indicates statistical significance. Moreover, the z values were penalised according to the strength of the available evidence and the number of repeated significance tests as defined by the law of the iterated logarithm.

The risk of type 2 error was controlled using the β-spending function and futility boundaries. Adjusted thresholds for non-superiority and non-inferiority (or no difference) were constructed. Together, adjusted non-superiority and non-inferiority boundaries make up what is referred to as futility boundaries or inner wedge boundaries. Crossing the futility boundaries by a z curve indicates that the two interventions do not differ more than the anticipated intervention effect.

The information size for the analyses was estimated based on 80% power and 5% type 1 error. The incidence in

Table 1. Characteristics of randomised controlled trials comparing endovascular aneurysm repair (EVAR) performed by a cutdown (cEVAR) or percutaneous (pEVAR) approach

First author (country)	Journal (year of publication)	Recruitment period	Single/ multi-centre	Intention to treat	Percutaneous closure device	Surgical incision in the cEVAR	Patients/ wounds in pEVAR – *n*	Patients/ wounds in cEVAR – *n*
Vierhout (the Netherlands)[11]	*J Vasc Surg* (2019)	February 2014 – March 2016	Multi	Yes	Prostar XL* or ProGlide device*	Vertical	73/137	64/137
Uhlmann (Austria)[12]	*J Vasc Surg* (2018)	July 2016 – February 2017	Single	Yes	ProGlide device*	Transverse	50/50	50/50
Nelson (USA)[13]	*J Vasc Surg* (2014)	July 2010 – February 2012	Multi	Yes	Prostar XL* or ProGlide device*	Transverse	101/101	50/50
Torsello (Germany)[14]	*J Vasc Surg* (2003)	January 2002 – July 2002	Single	Not stated	Prostar XL*	Transverse	15/25	15/30

* Abbott Vascular (Temecula, CA, USA).

the intervention and control arm was calculated by pooling the incidence rates of complications reported in the included trials in a proportion meta-analysis (the pooled proportion was calculated as the back transformation of the weighted mean of the transformed proportions).

Statistical software

The following software applications were used for statistical analyses: RevMan version 5.4 (The Cochrane Collaboration, Copenhagen, Denmark); CMA (Biostat, Englewood, NJ, USA); and Trial Sequential Analysis Software 0.9.5.5 Beta (Copenhagen Trial Unit, Copenhagen, Denmark).

RESULTS

Search results

The literature search identified four RCTs that met the review inclusion criteria and these were included in the qualitative and quantitative synthesis.[11–14] A published study protocol was found for two of them.[15,16] The PRISMA study selection flow diagram is presented in Fig. S1 (Supplementary Material).

Description of studies

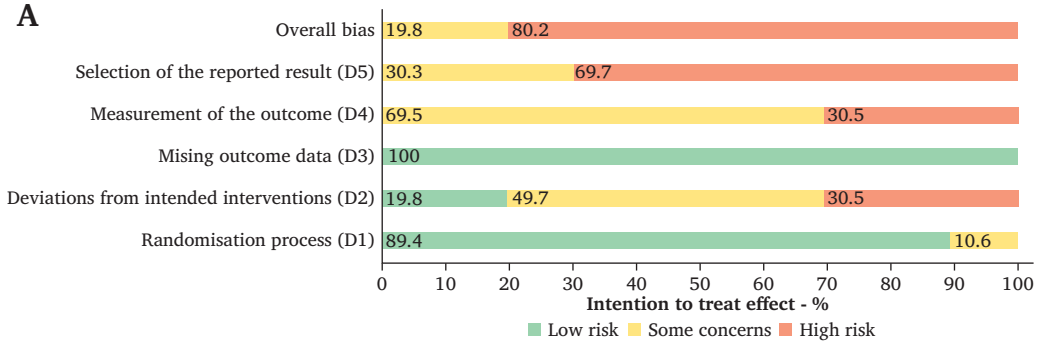
The four RCTs reported a total of 368 patients and 530 groin access sites. The oldest trial was published in 2003[14] and the most recent in 2019.[11] The patient recruitment period spanned from 2002 to 2017. Three RCTs were conducted in Europe (the Netherlands,[11] Austria,[12] and Germany[14]) and the fourth in the USA.[13] Two were multicentre studies,[11,13] and two were single centre studies.[12,14]

Vierhout *et al.*[11] assigned cases to open or percutaneous access of the main device; access on the contralateral side was achieved with the opposite technique. In the RCT by Uhlmann *et al.*,[12] the assignment to percutaneous access and cutdown was balanced to 25 left sided and 25 right sided percutaneous approaches. In the study by Nelson *et al.*,[13] randomisation was done for the ipsilateral site (the site of introduction of the main body of the aortic device), whereas access to the contralateral site varied. Torsello *et al.*[14] randomised 15 patients (27 access sites) to percutaneous EVAR and another 15 patients (28 access sites) to cutdown EVAR.[14]

The ITT principle was applied in three trials;[11–13] in the fourth trial, it was not stated whether an ITT or per protocol analysis was performed.[14] The inclusion and exclusion criteria for patient enrolment in the individual studies are listed in Table S1 (Supplementary Material). The Prostar XL or ProGlide device (Abbott Vascular, Temecula, CA, USA) was used in all studies for percutaneous access. Vierhout *et al.*[11] used a vertical groin incision in the surgical arm, whereas in the remaining studies, a transverse/oblique skin incision was used.[12–14] The study characteristics are summarised in Table 1. Patient demographics (age, sex, and BMI), clinical data (diabetes mellitus and ASA classification), and information on the type of anaesthesia and sheath size are presented in Table S2 (Supplementary Material).

Risk of bias in included studies

The overall risk of bias was judged to be high in three trials,[11,12,14] and some concerns were identified in the fourth trial.[13] In general, no flaws were identified in the randomisation process, with an appropriate process of allocation sequence generation and allocation sequence concealment being described in all trials. Some concerns were recorded in the "Deviations from intended interventions" domain; in two studies, an appropriate analysis was not used to estimate the effect of assignment to intervention.[11,12] Data for the assessed outcomes were available in all, or nearly all, participants randomised, resulting in a low risk of bias in the "Missing outcome data" domain. In the "Measurement of the outcome" domain, some concerns were related to insufficient information on whether the outcome assessors were aware of the intervention received by study participants. In the study by Vierhout *et al.*,[11] the methods of statistical analysis stated in the protocol were different from those stated in the main article, and multiple eligible analyses were noted in two studies,[11,12] resulting in a judgement of high risk of bias in the "Selection of the reported result" domain. The risk of bias graph and summary are presented in Fig. 1, and a detailed description of support for



B

Study	Experimental	Comparator	Outcome	Weight	D1	D2	D3	D4	D5	Overall
Vierhout[8]	pEVAR	cEVAR	Access site complicatior	0.438	+	?	+	?	−	−
Uhlmann[9]	pEVAR	cEVAR	Access site complicatior	0.341	+	−	+	−	−	−
Nelson[10]	pEVAR	cEVAR	Access site complicatior	0.221	+	+	+	?	?	?
Torsello[11]	pEVAR	cEVAR	Surgical site infection	0.118	?	?	+	?	?	−

Figure 1. (A) Risk of bias graph and (B) summary of the four randomised controlled trials comparing percutaneous and cutdown access for endovascular aneurysm repair based on the review authors' judgements about each risk of bias item presented as percentages across all included studies. The numbers in (A) represent the proportion of "low risk", "some concerns", and "high risk" of bias in the included four studies multiplied by the weight of each study in each risk of bias domain. (+) = low risk; (?) = some concerns; (−) = high risk.

judgements in the individual domains of the tool for each study is presented in Appendix S2 (Supplementary Material).

The overall certainty of evidence was judged to be low or very low for all primary outcomes (Table 2). The main factors that decreased (downgraded) the quality level of the body of evidence were limitations in the design and implementation of the studies, suggesting a high likelihood of bias and imprecision of results, which was reflected in the wide CIs noted for several outcomes.

Effects of interventions

Primary outcomes. Access site complications were recorded in three trials reporting a total of 525 access sites (288 in the percutaneous EVAR arm and 237 in the cutdown EVAR arm).[11–13] The definitions of access site complications are presented in Table S3 (see Supplementary Material). Patients receiving percutaneous EVAR had lower odds of access site complications than those receiving cutdown EVAR, but the difference was not statistically significant (OR 0.61, 95% CI 0.34–1.11; $p = .11$). The statistical between study heterogeneity was negligible ($I^2 = 9\%$; $p = .33$) (Fig. 2A).

Access site infection was reported in three trials, with a total of 480 access sites (263 in the percutaneous EVAR arm and 217 in the cutdown EVAR arm).[11,13,14] No significant risk difference was found between percutaneous and cutdown EVAR (risk difference −0.01, 95% CI −0.03 − 0.01; $p = .37$). There was no statistical evidence of between study heterogeneity ($I^2 = 0\%$; $p = .74$) (Fig. 2B).

Post-operative bleeding/haematoma was reported in three trials, with a total of 525 access sites (288 in the percutaneous EVAR arm and 237 in the cutdown EVAR arm).[11–13] The difference in the odds of developing post-operative bleeding/haematoma was not significant between the treatment arms (OR 0.80, 95% CI 0.36–1.78; p = .58). The statistical heterogeneity was insignificant ($I^2 = 0\%$; $p = .62$) (Fig. 2c).

Data on access related arterial injury were reported in two trials, with a total of 425 access sites (238 in the percutaneous EVAR group and 187 in the cutdown EVAR group).[11,13] The odds of developing such an injury were not significantly different between the groups (OR 2.30, 95% CI 0.37–14.30; $p = .37$). There was no statistical evidence of between study heterogeneity ($I^2 = 0\%$; $p = .84$) (Fig. 2D).

Data on femoral artery occlusion (resulting from arterial access) were reported in all four studies (580 access sites; 313 in the percutaneous EVAR group and 267 in the cutdown EVAR group).[11–14] The odds of femoral artery occlusion were not significantly different between interventions (OR 0.73, 95% CI 0.23–2.29; $p = .59$), with an insignificant statistical heterogeneity ($I^2 = 0\%$; $p = .71$) (Fig. 2E).

The occurrence of pseudoaneurysm as an outcome was reported in two studies with a total of 329 access sites (162 in the percutaneous EVAR group and 167 in the cutdown EVAR group).[11,14] The risk difference between interventions was insignificant (risk difference 0.01, 95% CI −0.01 − 0.04; $p = .31$), and the between study heterogeneity was low ($I^2 = 0\%$; $p = .69$) (Fig. 2F).

Development of lymphorrhoea or seroma was reported in all four studies (580 access sites; 313 in the percutaneous EVAR group and 267 in the cutdown EVAR group).[11–14] The odds of developing lymphorrhoea/seroma were significantly lower in patients who received percutaneous EVAR (OR

Table 2. Summary of findings and GRADE (Grades of Recommendation, Assessment, Development and Evaluation) assessment of randomised controlled trials (RCTs) on endovascular aneurysm repair (EVAR) performed by cutdown (cEVAR) or percutaneouly (pEVAR)

Certainty assessment							Summary of findings				
Outcome and participants (studies) − *n*	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Overall certainty of evidence	Study event rates − *n* (%)		Relative effect (95% CI)	Anticipated absolute effects	
							With cEVAR	With pEVAR		Risk with cEVAR	Risk difference with pEVAR
Access site complications											
525 (3 RCTs)	Very serious*	Not serious	Not serious	Not serious	None	⊕⊕◯◯ LOW	28/237 (11.8)	22/288 (7.6)	OR 0.61 (0.34 −1.11)	118/ 1 000	43 fewer per 1 000 (from 75 fewer to 11 more)
Access site infection											
480 (3 RCTs)	Very serious*	Not serious	Not serious	Serious†	None	⊕◯◯◯ VERY LOW	2/217 (0.9)	0/263 (0.0)	RD −0.01 (0.03 −0.01)	9/1 000	10 more per 1 000 (from 10 fewer to 30 more)
Post-operative bleeding/haematoma											
525 (3 RCTs)	Very serious*	Not serious	Not serious	Not serious	None	⊕⊕◯◯ LOW	13/237 (5.5)	13/288 (4.5)	OR 0.80 (0.36 −1.78)	55 per 1 000	10 fewer per 1 000 (from 34 fewer to 39 more)
Access related arterial injury											
425 (2 RCTs)	Very serious*	Not serious	Not serious	Very serious‡	Strong association	⊕◯◯◯ VERY LOW	1/187 (0.5)	5/238 (2.1)	OR 2.30 (0.37 −14.30)	5/1 000	7 more per 1 000 (from 3 fewer to 66 more)
Femoral artery occlusion											
580 (4 RCTs)	Very serious*	Not serious	Not serious	Serious‡	None	⊕◯◯◯ VERY LOW	5/267 (1.9)	5/313 (1.6)	OR 0.73 (0.23 −2.29)	19/1 000	5 fewer per 1 000 (from 14 fewer to 23 more)
Pseudoaneurysm											
329 (2 RCTs)	Very serious*	Not serious	Not serious	Serious†	None	⊕◯◯◯ VERY LOW	0/167 (0.0)	2/162 (1.2)	RD 0.01 (−0.01 −0.04)	0 per 1 000	10 fewer per 1 000 (from 40 fewer to 10 more)
Lymphorrhoea/seroma											
580 (4 RCTs)	Very serious*	Not serious	Not serious	Serious†	None	⊕◯◯◯ VERY LOW	8/267 (3.0)	0/313 (0.0)	OR 0.18 (0.04 −0.83)	30 per 1 000	24 fewer per 1 000 (from 29 fewer to 5 fewer)
Peri-operative mortality											
151 (1 RCT)	Serious§	Not serious	Not serious	Very serious‡	None	⊕◯◯◯ VERY LOW	0/50 (0.0)	1/101 (1.0)	OR 1.51 (0.06 −37.67)	0 per 1 000	0 fewer per 1 000 (from 0 fewer to 0 fewer)

CI = confidence interval; OR = odds ratio; RD = risk difference.
* The overall risk of bias was judged to be high or have some concerns for all of the studies.
† Few events.
‡ Wide CIs.
§ Some concerns were identified in the risk of bias assessment.

0.18, 95% CI 0.04—0.83; $p = .03$), with negligible statistical heterogeneity ($I^2 = 0\%$; $p = 0.98$) (Fig. 2G).

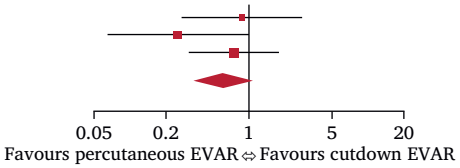
Peri-operative mortality, which was reported in one study only with a total of 151 patients (101 treated with percutaneous EVAR and 50 treated with cutdown EVAR),[13] was not different between interventions, but the event rate was very low, resulting in a wide CI (OR 1.51, 95% CI 0.06—37.67; $p = .80$) (Fig. 2H).

Secondary outcomes. Data on the overall duration of the procedure were reported in three studies.[11,13,14] Uhlmann *et al.*[12] reported access and closure time instead of duration of the entire EVAR procedure. The study by Vierhout *et al.*[11] was not included in this analysis, as patients in both the intervention and control arms had percutaneous access in one groin. Meta-analysis of the three remaining trials showed that the procedure time was statistically

A

Study or Subgroup	Percutaneous EVAR Events	Total	Cutdown EVAR Events	Total	Odds Ratio M-H, Fixed, 95% CI	Weight
Nelson 2014[10]	9	101	5	50	0.88 [0.28, 2.78]	22.1%
Uhlmann 2018[9]	3	50	10	50	0.26 [0.07, 0.99]	34.1%
Vierhout 2019[8]	10	137	13	137	0.75 [0.32, 1.78]	43.8%
Total	**22**	**288**	**28**	**237**	**0.61 [0.34, 1.11]**	**100.0%**

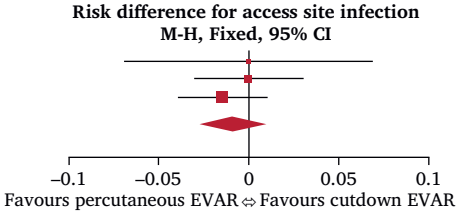
Heterogeneity: Chi^2 = 2.20, df = 2 (p = .33); I^2 = 9%
Test for overall effect: Z = 1.62 (p = .11)



B

Study or Subgroup	Percutaneous EVAR Events	Total	Cutdown EVAR Events	Total	Risk Difference M-H, Fixed, 95% CI	Weight
Torsello 2003[11]	0	25	0	30	0.00 [–0.07, 0.07]	11.8%
Nelson 2014[10]	0	101	0	50	0.00 [–0.03, 0.03]	28.9%
Vierhout 2019[8]	0	137	2	137	–0.01 [–0.04, 0.01]	59.3%
Total	**0**	**263**	**2**	**217**	**–0.01 [–0.03, 0.01]**	**100.0%**

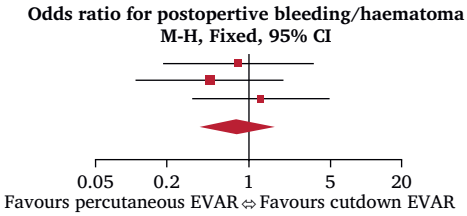
Heterogeneity: Chi^2 = 0.60, df = 2 (p = .74); I^2 = 0%
Test for overall effect: Z = 0.89 (p = .37)



C

Study or Subgroup	Percutaneous EVAR Events	Total	Cutdown EVAR Events	Total	Odds Ratio M-H, Fixed, 95% CI	Weight
Nelson 2014[10]	5	101	3	50	0.82 [0.19, 3.56]	28.7%
Uhlmann 2018[9]	3	50	6	50	0.47 [0.11, 1.99]	42.4%
Vierhout 2019[8]	5	137	4	137	1.26 [0.33, 4.79]	29.0%
Total	**13**	**288**	**13**	**237**	**0.80 [0.36, 1.78]**	**100.0%**

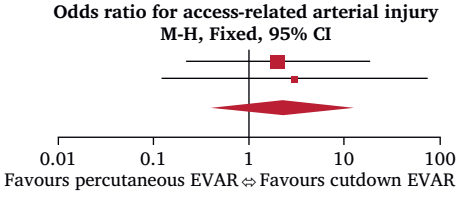
Heterogeneity: Chi^2 = 0.97, df = 2 (p = .62); I^2 = 0%
Test for overall effect: Z = 0.55 (p = .58)



D

Study or Subgroup	Percutaneous EVAR Events	Total	Cutdown EVAR Events	Total	Odds Ratio M-H, Fixed, 95% CI	Weight
Nelson 2014[10]	4	101	1	50	2.02 [0.22, 18.57]	72.2%
Vierhout 2019[8]	1	137	0	137	3.02 [0.12, 74.83]	27.8%
Total	**5**	**238**	**1**	**187**	**2.30 [0.37, 14.30]**	**100.0%**

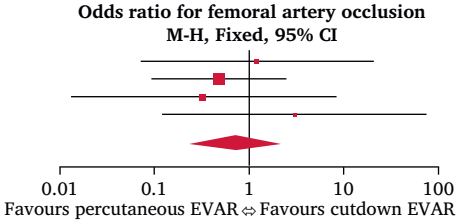
Heterogeneity: Chi^2 = 0.04, df = 1 (p = .84); I^2 = 0%
Test for overall effect: Z = 0.89 (p = .37)



E

Study or Subgroup	Percutaneous EVAR Events	Total	Cutdown EVAR Events	Total	Odds Ratio M-H, Fixed, 95% CI	Weight
Torsello 2003[11]	1	25	1	30	1.21 [0.07, 20.35]	12.9%
Nelson 2014[10]	3	101	3	50	0.48 [0.09, 2.47]	57.7%
Uhlmann 2018[9]	0	50	1	50	0.33 [0.01, 8.21]	22.0%
Vierhout 2019[8]	1	137	0	137	3.02 [0.12, 74.83]	7.3%
Total	**5**	**313**	**5**	**267**	**0.73 [0.23, 2.29]**	**100.0%**

Heterogeneity: Chi^2 = 1.37, df = 3 (p = .71); I^2 = 0%
Test for overall effect: Z = 0.54 (p = .59)



F

Study or Subgroup	Percutaneous EVAR Events	Total	Cutdown EVAR Events	Total	Risk Difference M-H, Fixed, 95% CI	Weight
Torsello 2003[11]	0	25	0	30	0.00 [–0.07, 0.07]	16.6%
Vierhout 2019[8]	2	137	0	137	0.01 [–0.01, 0.04]	83.4%
Total	**2**	**162**	**0**	**167**	**0.01 [–0.01, 0.04]**	**100.0%**

Heterogeneity: Chi^2 = 0.16, df = 1 (p = .69); I^2 = 0%
Test for overall effect: Z = 1.01 (p = .31)

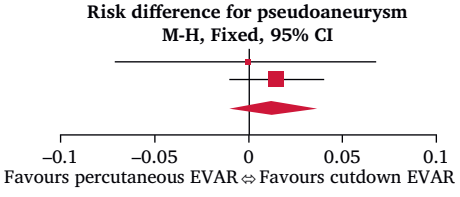


Figure 2. Forest plots of comparison of primary outcomes of percutaneous *vs.* cutdown endovascular aneurysm repair (EVAR) in randomised controlled trials for (A) access site complications, (B) access site infection, (C) post-operative bleeding/haematoma, (D) access related arterial injury, (E) femoral artery occlusion, (F) pseudo-aneurysm, (G) lymphorrhoea/seroma, and (H) peri-operative mortality. The solid squares denote the odds ratios or risk differences, the horizontal lines represent the 95% confidence intervals (CIs), and the diamonds denote the pooled odds ratios or risk differences. M-H = Mantel–Haenszel.

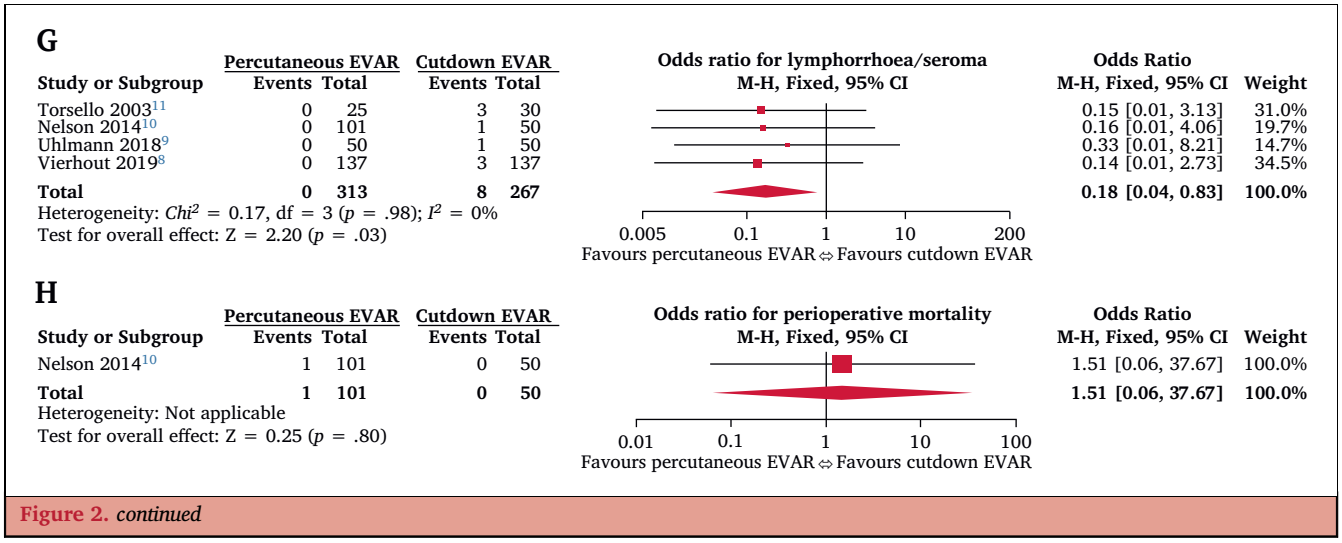


Figure 2. *continued*

significantly reduced in percutaneous EVAR compared with cutdown EVAR (MD −11.53 minutes, 95% CI −15.71 − −7.34; $p < .001$), with a low statistical heterogeneity ($I^2 = 53\%$; $p = .12$) (Fig. 3A).

Length of hospital stay, which was reported by Nelson *et al.*[13] only with 50 patients in each group, was similar between percutaneous and cutdown EVAR (MD −0.10 days, 95% CI −0.42 − 0.22; $p = .54$) (Fig. 3B).

Reporting bias. Reporting bias was not performed, as a small number of studies were included in this review.

Subgroup analysis. Data were not available to conduct the subgroup analyses specified in the "Methods" section.

Sensitivity analysis. All studies were judged to be high risk of bias or to have some concerns; hence, no such sensitivity analysis was undertaken. Removing one study at a time did not change the effect estimate for any of the outcomes except for lymphorrhoea/seroma, when removing the study of Vierhout *et al.*[11] and Torsello *et al.*[14] resulted in a non-significant difference between percutaneous and cutdown EVAR.

Trial sequential analysis

All components of trial sequential analysis for each primary outcome, that is, the required information size, two sided significance testing boundaries, non-superiority futility boundaries, and non-inferiority futility boundaries, are presented in Fig. 4. For the outcomes of access site complications, access site infection, post-operative bleeding/haematoma, access related arterial injury, and femoral artery occlusion, the cumulative *z* curve crosses neither the conventional boundary, nor the O'Brien—Fleming boundaries or the non-superiority/non-inferiority futility boundaries, and the required information size, is not reached, indicating that the meta-analyses for those outcomes are inconclusive. For the outcome of lymphorrhoea/seroma, the cumulative *z* score leads to a conclusion of statistical significance using the conventional single test threshold. However, using the O'Brien—Fleming boundaries, a greater *z* value is required (at this information size) in order to conclude statistical significance. The boundaries are not crossed and the meta-analysis is therefore inconclusive. No data are available to make any inferences regarding the outcome of pseudoaneurysm.

DISCUSSION

Summary of main results

Meta-analysis of four RCTs reporting a total of 530 groin access sites in 368 patients showed no significant difference between percutaneous and cutdown EVAR regarding access site complications, access site infection, post-operative bleeding/haematoma, access related arterial injury, femoral artery occlusion, pseudoaneurysm formation, and peri-operative mortality. A significant reduction in the odds of developing lymphorrhoea/seroma was found with percutaneous EVAR. Furthermore, percutaneous EVAR was found to have a significantly shorter procedure time, whereas the hospital length of stay, reported by only one study, was not different in the treatment arms. Trial sequential analysis showed that the obtained information size is currently below the required information size, and that the existing evidence is inconclusive, with neither the O'Brien-Fleming nor the futility boundaries being crossed by the cumulative *z* curve.

Overall completeness, applicability, and quality of evidence

A limited amount of randomised clinical trial data was identified to answer the review question. The review population size for all investigated outcomes was well below the required information size for a conclusive and reliable meta-analysis.

Nelson *et al.*[13] narrowed down their eligibility criteria to patients who were anatomically suitable for the Endologix device, but the remaining trial authors applied a wide spectrum of criteria for patient enrolment, reflecting a

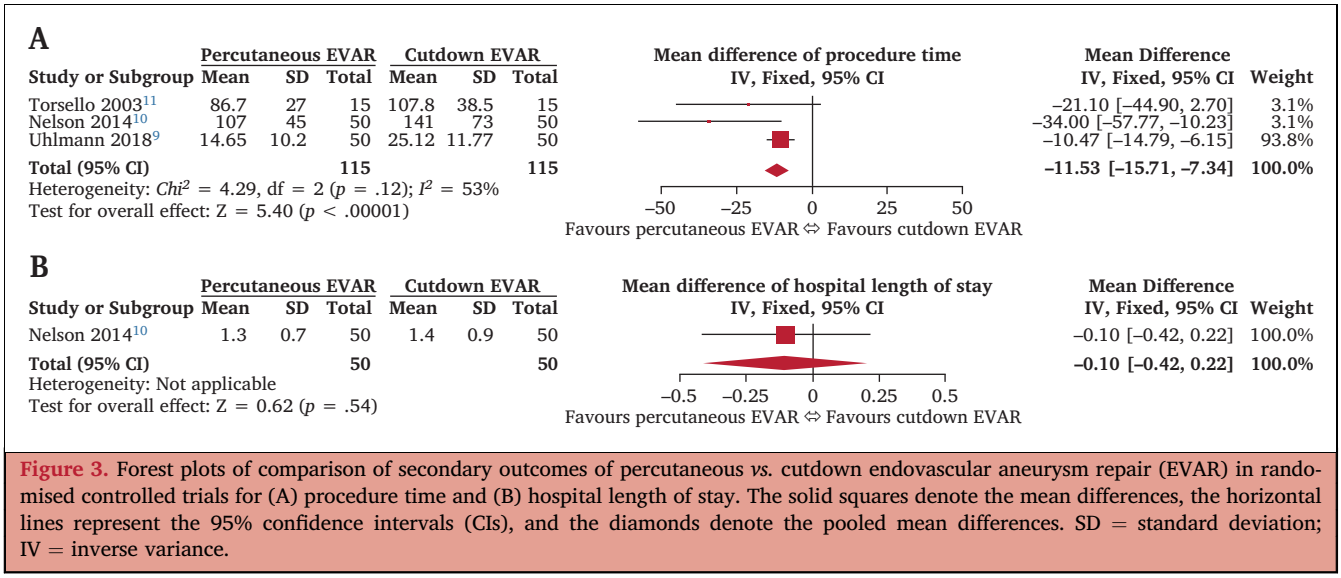


Figure 3. Forest plots of comparison of secondary outcomes of percutaneous *vs.* cutdown endovascular aneurysm repair (EVAR) in randomised controlled trials for (A) procedure time and (B) hospital length of stay. The solid squares denote the mean differences, the horizontal lines represent the 95% confidence intervals (CIs), and the diamonds denote the pooled mean differences. SD = standard deviation; IV = inverse variance.

sufficient external validity of the review. Notwithstanding, patient selection appears to be an important determinant of successful outcome, as most investigators considered severe femoral artery calcification or small diameter access arteries and previous arterial reconstructive surgery in the groin as contraindications to percutaneous EVAR.

Most studies were judged to suffer from major limitations that are likely to result in a biased assessment of the intervention effect. The main methodological issues concerned measurement of outcome and selection of the reported results, with multiple eligible outcome measurements and analyses having been carried out. Furthermore, issues were identified with the precision of results, as several studies included few participants/access sites with a small number of events and thus have wide CIs. As a result, the level of the body of evidence was downgraded, with the overall certainty of evidence being graded as low or very low for all primary outcomes.

Although pain assessments were conducted by some authors, mainly in the form of a visual analogue scale (VAS), solid data on quality of life reflecting patient experience are lacking. Vierhout *et al.*[11] found an adjusted pain score in favour of percutaneous access. Similarly, in the study by Uhlmann *et al.*,[12] significantly lower VAS scores were demonstrated after percutaneous EVAR.

The previous experience of participating investigators should be taken into account when interpreting the results of this meta-analysis. Nelson *et al.*[13] explicitly stated that an advanced level of familiarity with the percutaneous closure device was required for specialists to be able to enrol cases in the trial, as indicated by evidence of training and experience in the use of closure devices for small hole closure and being certified for more than 20 percutaneous EVAR cases. Vierhout *et al.*[11] stated that all participating vascular surgeons and interventional radiologists should have performed at least 20 open femoral access and percutaneous procedures, but the other authors did not specify the experience of participating investigators. It is possible that the learning curve may be a crucial factor of technical success and complication risk.

Potential biases in the review process

This review was conducted to a high standard applying a transparent, prespecified methodology. Limitations in the review process were failure to search the grey literature for unpublished material and to source missing outcome data from trial investigators. It has previously been demonstrated that confirmation of data accuracy and supplementation of missing data were provided by a small proportion of RCT authors (7.8%).[17]

Agreements and disagreements with other studies or reviews

A multitude of observational studies have been published in recent years comparing outcomes of percutaneous access with those of surgical exposure of the femoral arteries for endovascular repair of abdominal, thoracic, and/or thoracoabdominal aortic aneurysms. Previous meta-analysis of such studies by an evidence synthesis research group showed a reduced risk of access site infection and lymphocoele formation, and a shorter procedure time and hospital stay with percutaneous EVAR, but no difference in incidence rates of groin haematoma or pseudo-aneurysm.[1] On this basis, the European Society for Vascular Surgery clinical practice guidelines recommended that an ultrasound guided percutaneous approach should be considered in EVAR.[18] Although the findings of this meta-analysis support such a recommendation, trial sequential analysis demonstrated that the evidence is currently insufficient to allow a robust conclusion about the superiority of percutaneous over cutdown EVAR.

Similarly, another more recent meta-analysis of 13 observational studies and four RCTs of percutaneous *vs.* surgical access for a wide range of endovascular aortic and aortic valve procedures found a significantly lower risk of access site infection and seroma formation after

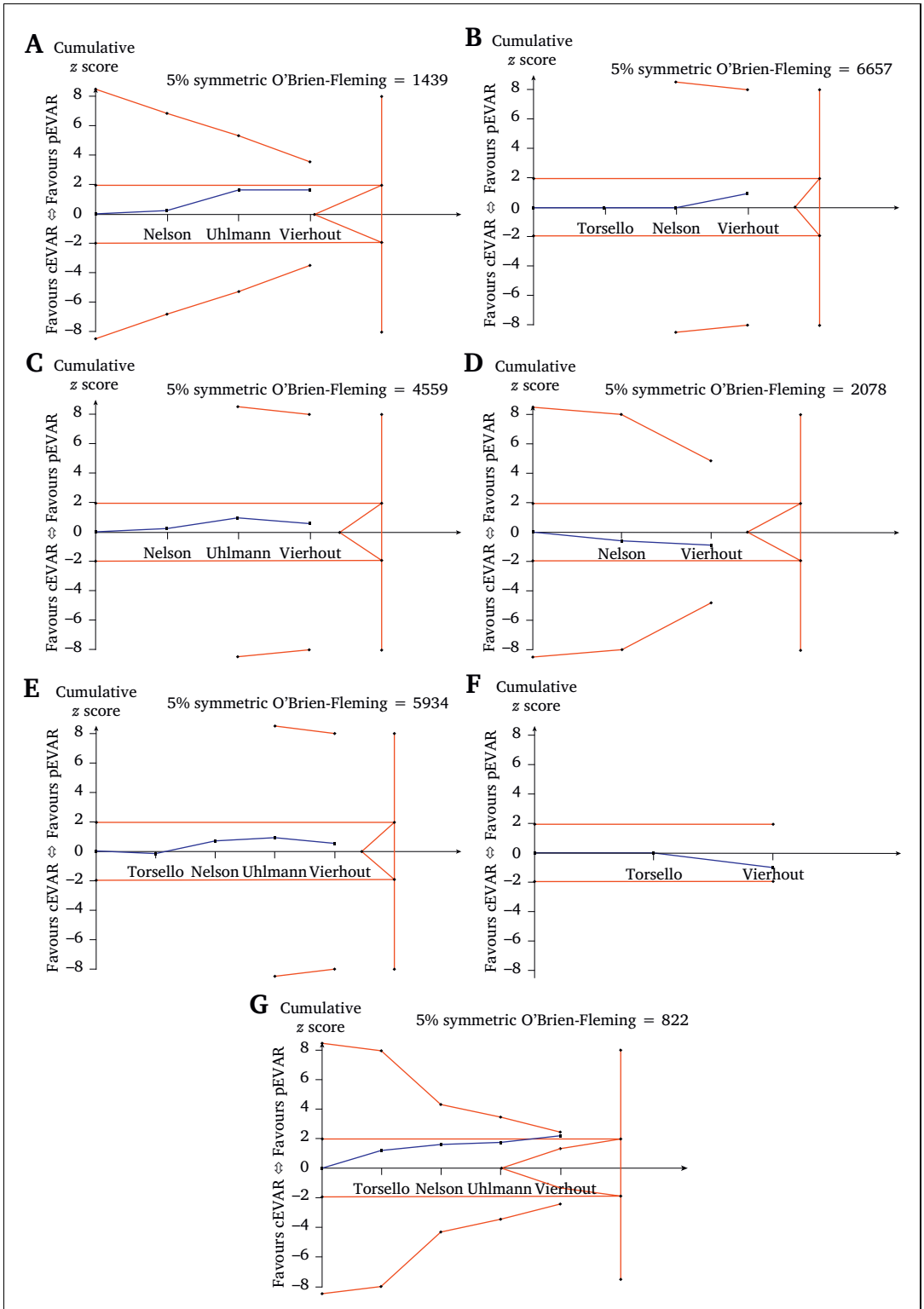


Figure 4. Trial sequential analysis diagrams for (A) access site complications, (B) access site infection, (C) post-operative bleeding/haematoma, (D) access related arterial injury, (E) femoral artery occlusion, (F) pseudoaneurysm, and (G) lymphorrhoea/seroma in randomised controlled trials (Table 1) comparing percutaneous (pEVAR) and cutdown (cEVAR) access for endovascular aneurysm repair (EVAR), including both repeated non-superiority/non-inferiority and two sided significance testing, showing no significant benefit for any of the outcomes of pEVAR compared with cEVAR (the cumulative *z* score [blue] does not reach significance by either crossing both the conventional boundary or the O'Brian–Fleming boundaries [red]). For the outcome pseudoaneurysm, boundary 5% symmetric O'Brien–Fleming was ignored by the software due to little information use (4.5%).

percutaneous treatment but a higher frequency of pseudoaneurysm formation at the puncture site.[19] This meta-analysis is limited by heterogeneity in treated pathologies, which ranged from infrarenal aortic aneurysm and thoracic aortic pathologies to aortic valve disease. It is also limited by the combination of randomised and observational data, a practice that organisations, such as the Cochrane Collaboration, have strongly recommended to refrain from. Furthermore, this meta-analysis inappropriately included a RCT comparing the fascia suture technique with a suture mediated closure device for femoral arterial closure after endovascular aortic repair.

Endovascular treatment is a dynamic treatment that changes over time with improved learning curves, technical skills, and continuous improvement in manufactured materials. This meta-analysis contains the most up to date evidence, including an additional two RCTs. Only high level data from RCTs have been included in quantitative synthesis, obviating the risk of selection bias. Furthermore, the analysis focused on a homogenous population of patients with AAA treated by standard EVAR to help define the risks and benefits of percutaneous access for EVAR across consistent clinical settings. An advanced statistical framework applying the trial sequential analysis methodology was used to quantify the available evidence, adjust thresholds for statistical significance according to the quantified strength of evidence and the impact of multiplicity, and construct thresholds for futility, which will help guide future research on the area of percutaneous EVAR. Complementing advanced meta-analytical techniques for synthesis of evidence data, the GRADE methodology was applied for appraising the evidence and the most recent version of the Cochrane risk of bias tool was used.

Conclusion

Implications for practice. Percutaneous EVAR appears to be safe and effective having comparable clinical outcomes with conventional EVAR performed by surgical exposure of the femoral arteries. The duration of the procedure is shorter than cutdown EVAR, and it can be considered in patients in whom local anaesthesia is deemed a better anaesthetic option. Furthermore, a percutaneous approach may be a suitable option for patients undergoing ambulatory EVAR, who have reduced requirements for analgesia and monitoring of surgical sites for seroma or infection.[20]

Implications for research

The available high level evidence is insufficient. A well powered RCT could shed light on potential advantages of percutaneous EVAR. Patient experience and quality of life should be an area of future research. As with almost every aspect of vascular and endovascular intervention, patient selection appears to be key in attaining the desired result, and further research needs to investigate which patients would benefit most from percutaneous EVAR, for example, unfit patients undergoing EVAR under local anaesthesia, and identify anatomical and clinical factors that may increase the complication risk, for example, femoral artery calcification, diabetes mellitus, and obesity.

CONFLICTS OF INTEREST

None.

FUNDING

None.

APPENDIX A. SUPPLEMENTARY DATA

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejvs.2020.11.008.

REFERENCES

1 Hajibandeh S, Hajibandeh S, Antoniou SA, Child E, Torella F, Antoniou GA. Percutaneous access for endovascular aortic aneurysm repair: a systematic review and meta-analysis. *Vascular* 2016;**24**:638–48.
2 Mousa AY, Campbell JE, Broce M, Abu-Halimah S, Stone PA, Hass SM, et al. Predictors of percutaneous access failure requiring open femoral surgical conversion during endovascular aortic aneurysm repair. *J Vasc Surg* 2013;**58**:1213–9.
3 Rijkée MP, Statius van Eps RG, Wever JJ, van Overhagen H, van Dijk LC, Knippenberg B. Predictors of failure of closure in percutaneous EVAR using the Prostar XL percutaneous vascular surgery device. *Eur J Vasc Endovasc Surg* 2015;**49**:45–9.
4 Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, et al., editors. *Cochrane Handbook for systematic reviews of interventions version 6.0*; 2019. Available at: https://training.cochrane.org/cochrane-handbook-systematic-reviews-interventions. [Accessed 4 November 2019].
5 Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JP, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. *BMJ* 2009;**339**:b2700.
6 Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ* 2019;**366**:l4898.
7 Antoniou SA, Antoniou GA. The GRADE approach to appraising the evidence or how to increase the credibility of your research. *Am J Surg* 2020;**220**:290–3.
8 Deek JJ, Higgins JPT, Altman DG. On Behalf of the Cochrane Statistical Methods Group. Analysing Data and Undertaking Meta-Analyses. Available at: https://training.cochrane.org/handbook/current/chapter-10. [Accessed 4 November 2020].
9 Wetterslev J, Thorlund K, Brok J, Gluud C. Trial sequential analysis may establish when firm evidence is reached in cumulative meta-analysis. *J Clin Epidemiol* 2008;**61**:64–75.
10 Thorlund K, Engstrøm J, Wetterslev J, Brok J, Imberger G, Gluud C. User manual for trial sequential analysis (TSA). Available at: www.ctu.dk/tsa. [Accessed 4 November 2020].
11 Vierhout BP, Pol RA, Ott MA, Pierie MEN, van Andringa de Kempenaer TMG, Hissink RJ, et al. Randomized multicenter trial on percutaneous versus open access in endovascular aneurysm repair (PiERO). *J Vasc Surg* 2019;**69**:1429–36.
12 Uhlmann ME, Walter C, Taher F, Plimon M, Falkensammer J, Assadian A. Successful percutaneous access for endovascular aneurysm repair is significantly cheaper than femoral cutdown in a prospective randomized trial. *J Vasc Surg* 2018;**68**:384–91.
13 Nelson PR, Kracjer Z, Kansal N, Rao V, Bianchi C, Hashemi H, et al. A multicenter, randomized, controlled trial of totally percutaneous access versus open femoral exposure for endovascular aortic aneurysm repair (the PEVAR trial). *J Vasc Surg* 2014;**59**:1181–93.

14 Torsello GB, Kasprzak B, Klenk E, Tessarek J, Osada N, Torsello GF. Endovascular suture versus cutdown for endovascular aneurysm repair: a prospective randomized pilot study. *J Vasc Surg* 2003;**38**:78–82.
15 Vierhout BP, Saleem BR, Ott A, van Dijl JM, van Andringa de Kempenaer TD, Pierie MEN, et al. A comparison of percutaneous femoral access in endovascular repair versus open femoral access (PiERO): study protocol for a randomized controlled trial. *Trials* 2015;**16**:408.
16 Krajcer Z, Nelson PR, Bianchi C, Rao V, Morasch MD, Bacharach JM. Percutaneous endovascular abdominal aortic aneurysm repair: methods and initial outcomes from the first prospective, multicenter trial. *J Cardiovasc Surg (Torino)* 2011;**52**:651–9.
17 Tsokani S, Mavridis D, Hajibandeh S, Hajibandeh S, Antoniou GA, Andreou A, et al. An observational study of missing data inquiry from randomized trial authors showed a poor response. *J Clin Epidemiol* 2020;**119**:19–25.
18 Wanhainen A, Verzini F, Van Herzeele I, Allaire E, Bown M, Cohnert T, et al. Editor's choice – European society for vascular surgery (ESVS) 2019 clinical practice guidelines on the management of abdominal aorto-iliac artery aneurysms. *Eur J Vasc Endovasc Surg* 2019;**57**:8–93.
19 Vierhout BP, Pol RA, El Moumni M, Zeebregts CJ. Editor's choice – arteriotomy closure devices in EVAR, TEVAR, and TAVR: a systematic review and meta-analysis of randomised clinical trials and cohort studies. *Eur J Vasc Endovasc Surg* 2017;**54**:104–15.
20 El Bakbachi O, Antoniou GA, Breakton C, Torella F, Neequaye S. Can standard endovascular abdominal aortic aneurysm repair be performed as a day case in selected patients? *Int Angiol* 2016;**35**:108–10.

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COUP D'OEIL

An Aortic Band

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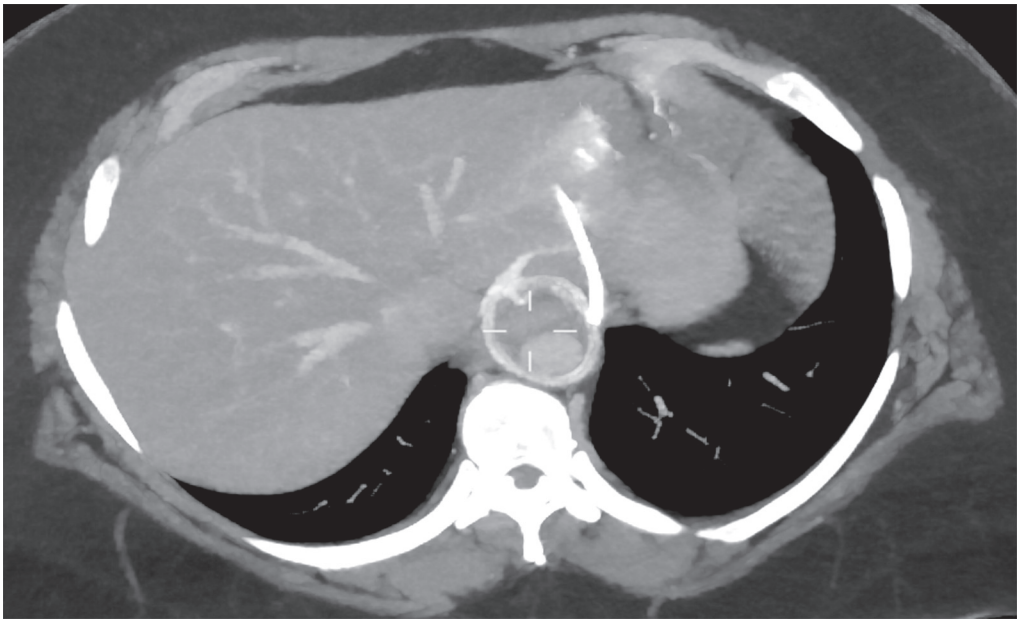

A 50 year old female presented to the general surgery department with dysphagia and a non-progressive food bolus. She had a past medical history of placement of a gastric band performed privately 10 years ago, as well as hypothyroidism and asthma. Computed tomography scans of the abdomen and pelvis revealed the gastric band to be encompassing both the oesophagus and aorta at the level of the diaphragmatic hiatus. There were no clinical features attributable to the band encompassing the aorta.

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https://doi.org/10.1016/j.ejvs.2020.10.013