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Randomized multicenter trial on percutaneous versus open access in endovascular aneurysm repair (PiERO)

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ABSTRACT

Background: In endovascular valve and aortic repair, vascular access through a percutaneous approach has become the competing technique to an open surgical approach. The effect on postoperative complications and surgical site infections (SSIs) has been investigated, but randomized evidence is lacking. The objective was to investigate whether percutaneous access of the common femoral artery (CFA) with a percutaneous closure device would decrease the number of SSIs compared with open surgical access of the CFA in endovascular aneurysm repair (EVAR).

Methods: Patients with an abdominal aortic aneurysm suitable for EVAR were randomized to open or percutaneous access of the main device (MD) through the CFA. Through the contralateral side, access was obtained with the other technique than the one for which the MD was randomized. The primary outcome was number of SSIs. Secondary outcomes were wound complications, visual analog scale for pain scores, and standardized wound assessment scores during follow-up. Preoperative screening culture and groin biopsy specimens were obtained from all patients.

Results: Both groups contained 137 groins. SSI rate was 1.5% in the open group vs 0% in the percutaneous group. For MDs only, SSI rate was 3.1% (odds ratio, 3.3; 95% confidence interval, 0.31-347; $P = .34$). Wound complications were comparable in both groups. Neither nasal nor groin *Staphylococcus aureus* carriage had a significant effect on SSIs, Southampton Wound Assessment score, or visual analog scale score. Adjusted pain score was 0.69 lower, in favor of percutaneous access. Wound assessment was better after 2 weeks (odds ratio, 3.57; 95% confidence interval, 1.02-12.44; $P = .046$), also in favor of percutaneous access.

Conclusions: Percutaneous access of the CFA does not reduce the number of SSIs. It does, however, reduce pain and improve wound healing with less inflammation 1 day and 2 weeks after EVAR, respectively. (J Vasc Surg 2019;69:1429-36.)

Keywords: Vascular access devices; Percutaneous; Abdominal aortic aneurysm; Surgical wound infection

Endovascular aneurysm repair (EVAR) of an abdominal aortic aneurysm has decreased postoperative morbidity and mortality compared with open repair.[1] The endovascular technique has further developed toward percutaneous common femoral artery (CFA) access with a vascular closure device (VCD), which enables closure of the arterial defect without direct visualization.

In previous studies, the use of closure devices was found to be technically feasible and to reduce both duration of surgery (DOS) and hospital length of stay.[2-4] However, other studies including a recent meta-analysis[5] were unable to confirm this reduction.[6-8] High-quality evidence is lacking. Most reports are based on cohort studies at different times.[5]

Both open and percutaneous access techniques have disadvantages. The open surgical technique requires a larger incision that may cause more surgical site infections (SSIs), and *Staphylococcus aureus* (SA) carriage may be of importance.[9] Percutaneous access allows a smaller incision, but lack of control may cause access-related vascular injury (ARVI), such as stenosis or pseudoaneurysm. Failure of the device resulting in conversion may lead to additional blood loss and emergency surgery.

In performing EVAR, two CFA access sites are necessary. As such, the effects of two different approaches in terms of the patient's comfort and postoperative complications can be compared in one patient. This would be the first

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Clinical trial registration: NTR4257.

Author conflict of interest: none.

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comparison of both techniques with optimal control of confounding risk factors such as diabetes mellitus (DM), smoking, obesity, and vessel calcification in one patient. Differences in postoperative complications can be ascribed only to the access technique used, and patients themselves will be able to compare results of the two techniques.

A randomized clinical trial named Percutaneous access in Endovascular Repair vs Open (PiERO) was designed to assess the relationship between type of CFA access and the occurrence of wound complications, particularly SSI.

ARTICLE HIGHLIGHTS

- **Type of Research:** Multicenter single-blind randomized controlled trial
- **Key Findings:** Percutaneous access was compared with open surgical access of the common femoral artery in 137 patients undergoing endovascular aneurysm repair with respect to surgical site infections, wound complications, pain scores, and wound assessment scores. No difference in surgical site infections or wound complications was found, but a reduction of pain and wound inflammation was observed.
- **Take Home Message:** This study suggests that percutaneous access of the common femoral artery is safe and reduces pain and inflammation.

METHODS

Study design. The PiERO trial is a multicenter phase 4, randomized single-blind controlled trial evaluating the difference in wound complications between percutaneous CFA access in one groin and open surgical CFA access in the other groin in patients undergoing EVAR. The study was conducted between February 2014 and April 2016 at six Dutch hospitals. All participating vascular surgeons and interventional radiologists had performed at least 20 open CFA access and percutaneous procedures. In addition, percutaneous access technique was reviewed and certified by the company supplying the closure device (Abbott Vascular, Redwood City, Calif) before patients were entered in the study. The study was completed and reported according to the revised Consolidated Standards of Reporting Trials statement.[10] The study protocol of this trial was registered (www.trialregister.nl; NTR4257) and previously published.[11]

The Institutional Review Board approved the study (NL44578.042.13). The study was conducted in accordance with the Declaration of Helsinki and Good Clinical Practices.[12] All patients provided written informed consent. Data were analyzed anonymously.

Eligibility criteria. Patients scheduled for an elective EVAR who met the following eligibility criteria were screened for enrollment in the study: age older than 18 years, physically and mentally capable of giving consent, aneurysm of the abdominal aorta exceeding 5.5 cm in diameter, and growth of at least 5 mm within 6 months. Exclusion criteria were CFA access sites with >50% circumferential calcification based on the multidisciplinary discussion and the radiologists' report,[3,7] previous CFA surgery, documented infection at time of operation, and fewer or more than two access sites (additional brachial or carotid), fenestrated or branched EVAR. Vessel size of the CFA was not an exclusion criterion.

Interventions. In the percutaneous group, access of the main device (MD) was obtained through ultrasound-guided puncture of the CFA, followed by positioning of one or more Prostar XL or ProGlide devices (Abbott Vascular) through an incision of approximately 1 cm. The technical aspects of the devices have been described before with similar results.[13] In the open group, access of the MD was obtained through a 3- to 4-cm craniocaudal incision and puncture of the CFA under direct vision.

Prophylactic antibiotics were administered 15 to 60 minutes before surgery. Before disinfection, nasal and groin culture specimens were obtained from each patient for detection of SA carriage. After disinfection, two punch biopsy specimens were taken from the right groin. One biopsy specimen was stored in a culture medium (thioglycollate medium USP; Mediaproducts, Groningen, The Netherlands), enabling microbiologic culture analysis; another was stored in formalin (2MC Medical Logistics, Huizen, The Netherlands) for histologic analysis.

During the procedure, 5000 units of heparin were administered intravenously. Deployment of the endovascular stent graft was performed according to protocol. After completion angiography and removal of the sheaths, hemostasis was performed in the percutaneous group, with gentle manual pressure to the proximal CFA and advancement of the preformed knot of the closure device with a knot pusher. In the open access group, hemostasis was obtained with a running, interrupted, or crossing polypropylene suture.

Outcomes. The primary end point of the study was the number of SSIs in each group. This end point was chosen because of its clear definition and expected difference as found in earlier research.[5] Secondary end points were wound complications, Southampton Wound Assessment (SWA) score,[14] and visual analog scale (VAS) score. Vascular injuries due to the access technique were clustered as ARVI. Serious adverse events were defined as any undesirable experience associated with the trial intervention and reported to the Medical Research Ethics Committee within 2 weeks.

Sample size. Assuming 6.8% SSIs to occur in the open CFA access groin with a craniocaudal incision compared with a 0.1% SSI rate in the percutaneous groin,[11] a sample

of 120 patients (α of .05 and 80% power) would be sufficient to detect a significant difference in SSI rate between the two access techniques.[6,15-18]

Randomization. Because of its larger size, the introduction technique of the MD was randomized. The performing surgeon decided which side would be used for access of the MD on the basis of the patient's anatomy. The surgeon could not be blinded. The study was therefore single blinded, as both the introduction side (right or left) and the introduction technique of the MD of the endoprosthesis (percutaneous or open) were concealed to patients, the physicians doing follow-up, data collectors, and data analysts. The smaller contralateral device (CLD) was introduced by the other technique than the one for which the MD was randomized; for instance, when the MD was introduced percutaneously, the CLD was introduced through surgical access of the CFA. Patients were randomly assigned in a 1:1 ratio to the percutaneous or the open CFA access group. Randomization was performed before surgery using blinded envelopes. These envelopes were produced outside the centers and delivered in a 1:1 ratio and an amount of 20 envelopes per batch. Envelopes contained the study forms, a punch for biopsy, and culture media in accordance with the previously published protocol.[11]

Data collection. The number of conversions from percutaneous access to open access because of VCD failure was recorded. An independent researcher, different per location, was blinded for access site of the MD and assessed postoperative complications at fixed intervals using the SWA score. In short, the SWA grading ranges from 0 to IV, with 0 representing normal wound healing; I, mild bruising or erythema; II, erythema plus other signs of inflammation; III, clear or serosanguineous discharge; and IV, pus evacuation. During data analysis, SWA scores were dichotomized into clean or bruised (score 0-I) and inflamed or infected (scores II-IV). A VAS score was used to evaluate patients' wound complaints 1 day and 2 weeks after surgery. This unidimensional continuous 10-cm-long scale was anchored by two descriptors: "no pain" and "a lot of pain." No intermediate points were added to this scale.

Statistical analysis. Baseline characteristics were described as mean (standard deviation) for continuous variables and as percentages for categorical variables. Logistic regression was used to analyze the relationship between type of access (percutaneous or open) and primary and secondary outcomes. With multivariable analysis, we adjusted for age, sex, body mass index (BMI), smoking status, DM, DOS, blood loss, and positive SA cultures of nose or groin. Using maximum likelihood estimation in logistic regression to estimate odds ratios (ORs) resulted in substantial upward bias when a response variable was separated by a single or a combination of covariates, known as sparse data bias.[19] To overcome sparse data bias, we used penalized likelihood for logistic regression (Firth's bias reduction method) as implemented in the R[20] package logistf.[21] Confidence intervals (CIs) were computed by penalized profile likelihood.

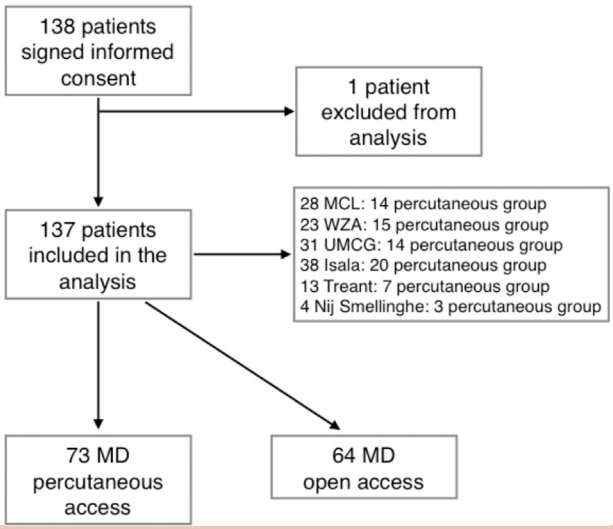

Fig 1. Flow chart of inclusion and collaborating hospitals in the Percutaneous access in Endovascular Repair vs Open (PiERO) study. The contralateral device (CLD) was introduced with the other technique (not shown). *MCL,* Medical Center Leeuwarden; *MD,* main device; *UMCG,* University Medical Center Groningen; *WZA,* Wilhelmina Ziekenhuis Assen.

Univariable generalized estimating equations (GEEs) with an exchangeable correlation structure were used to evaluate the relationship between type of access and both VAS and SWA scores. GEE takes into account the dependency of repeated observations within an individual. For the estimates, differences in VAS and ORs for SWA were reported with the corresponding 95% CI. Using multivariable GEE models, the analyses were then adjusted for age, sex, BMI, smoking status, DM, DOS, blood loss, and positive SA cultures of groin or nares. The GEE analyses were conducted in R[20] using the GEE package.[22] Baseline characteristics were compared with the Statistical Package for the Social Sciences, version 22 (IBM Corp, Armonk, NY). All regression coefficients with a *P* value $<.05$ were considered statistically significant.

RESULTS

A total of 138 patients were enrolled. One patient was excluded because of protocol deviation; the treating vascular surgeon chose to change sides after randomization because of calcifications in the percutaneous leg. The study population thus consisted of 137 patients, 73 of whom were assigned to the percutaneous group and 64 to the open group (Fig 1).

Baseline data. The majority of the patients were male (90%), with a mean age of 72 years (range, 56-93 years) and a mean BMI of 27 kg/m^2 (range, 20-37 kg/m^2); 29% were smokers and 14% had DM. Nasal culture was SA

Table I. Baseline characteristics of the study population randomized for the main device (*MD*), introduced through percutaneous or open access

	Percutaneous access of MD (n = 73)	Open surgical access of MD (n = 64)
Patients' characteristics		
Age, years	72.6 (8.1)	72.4 (6.2)
Male	67 (92)	56 (88)
BMI, kg/m^2	27.5 (3.6)	27.2 (3.7)
Smoker	20 (27)	20 (31)
DM	8 (11)	11 (17)
SA-positive nose culture	15 (21)	18 (29)
SA-positive groin culture	3 (4)	3 (5)
Procedural characteristics		
Anesthesia		
General	26 (36)	22 (34)
Locoregional	34 (47)	27 (42)
Local	13 (18)	15 (23)
Ultrasound guidance	71 (99)	63 (98)
DOS, minutes	118 (33)	125 (32)
Blood loss, mL	206 (195)	211 (225)
Sheath right	18.4F (2.2)	18.3F (2.8)
Sheath left	16.4F (1.9)	17.1F (2.1)

BMI, Body mass index; *DM*, diabetes mellitus; *DOS*, duration of surgery; *SA*, *Staphylococcus aureus*.
Categorical variables are presented as number (%). Continuous variables are presented as mean (standard deviation).

positive in 25% of patients, and 4.5% had an SA-positive groin. The percutaneous and open groups had comparable baseline characteristics, as shown in Table I.

Most patients (45%) were operated on under locoregional anesthesia. Median DOS was 120 minutes (range, 60-279 minutes), and blood loss was 208 mL (range, 0-1300 mL).

Sheath sizes were smaller in the left groin (mean, 16.7F; range, 12F-23F) compared with the right groin (mean, 18.4F; range, 12F-26F), and this was statistically significant ($P < .01$). Surgeons chose the right side for the MD in 80% of cases because of their right-sided position during the operation and the patient's anatomy. Seven conversions were recorded (5.1%) in 137 patients: six conversions for the MD and one for the CLD. None of the conversions resulted in complications. Patients with a conversion were still included in the analysis according to an intention-to-treat principle.

Primary outcome. Two SSIs were recorded, both in open access, of the total 274 groin approaches, one MD and one CLD. There was no significant difference between open and percutaneous access (Table II). Because of the small numbers, no CI could be calculated for the group as a whole.[21] In the subanalysis of the MDs alone, the SSI difference was not statistically significant (OR, 3.3; 95% CI, 0.31-347; $P = .34$; Table III).

Secondary outcomes. Five hematomas (3.6%) were reported in the percutaneous group compared with four (2.9%) in the open access (OR, 0.79; 95% CI, 0.2-3.3; $P = .74$). Two pseudoaneurysms were recorded, both after percutaneous access procedures (1.5%); one was treated with thrombin injection and the second required an extra operation. Both patients recovered without further complications. Three seromas and one wound dehiscence were reported, all after open access (together 2.9%). ARVI was reported in two percutaneous procedures; one dissection of the external iliac artery during the operation was treated with ballooning, and a CFA occlusion was treated with an open endarterectomy 1 day after EVAR (Table II). There was no statistically significant difference in complications between the percutaneous and the open access group. Adjustment for age, sex, BMI, smoking, DM, DOS, blood loss, and positive nose or groin culture did not alter this outcome (Table II).

Ancillary analysis. On analyzing only the MDs, 12 complications were recorded after 137 incisional access procedures (8.8%). Again, no significant difference was found (Table III). Similar outcomes were found for the CLD group (11/137 [8%]).

VAS scores and SWA scores of 137 groin access procedures were compared, involving the MDs only. The first day after intervention, a statistically significant difference in VAS scores of 0.77 (95% CI, 0.32-1.22; $P = .001$) was found, in favor of the percutaneous access technique (Fig 2). Adjustment for age, sex, BMI, smoking status, DM, DOS, blood loss, and positive SA cultures of nose or groin showed a similar result of 0.69 point difference in VAS (95% CI, 0.27-1.12; $P = .001$), in favor of percutaneous access.

Mean course of the SWA scores over time is shown in Fig 3. Occurrence of SWA scores ≥II was similar in both groups on the first postoperative day. In the percutaneous group, SWA scores ≥II gradually declined to 0 within 6 weeks. By contrast, the proportion of SWA scores ≥II in the open access group increased during the first 2 weeks and declined to baseline level (3%) after 6 weeks. Both crude and adjusted logistic GEE analyses showed that open access was associated with a significantly increased risk of an SWA score ≥II. After adjustment, the open access group had a significantly higher risk of an SWA score ≥II (OR, 3.57; 95% CI, 1.02-12.44; $P = .046$).

Serious adverse events. Seven serious adverse events were recorded during the study. Two patients required an open repair, unrelated to percutaneous or surgical access. One was treated 3 months after EVAR for a type III endoleak on the left side with an Amplatz occlusion and a femorofemoral crossover bypass. The other patient required urgent repair with open reconstruction of an acute occlusion of the endoprosthesis 3 days after EVAR. An additional intervention was required in a

Table II. Number of primary and secondary outcomes of the intervention based on the access technique per groin

	Percutaneous access (n = 137), No. (%)	Open access (n = 137), No. (%)				
Percutaneous closure device failure						
Conversion	7 (5.1)					
Postoperative complications (<30 days)			**Univariable analyses**		**Multivariable analyses**	
			OR (95% CI)	***P***	**OR (95% CI)**	***P***
SSI	0	2 (1.5)	NA[a]		NA	
Seroma	0	3 (2.2)	NA		NA	
Neuropathy	1 (0.7)	3 (2.2)	3.04 (0.31-30)	.34	3.29 (0.32-33.7)	.32
Hematoma	5 (3.6)	4 (2.9)	0.79 (0.19-3.27)	.74	0.79 (0.19-3.27)	.74
Pseudoaneurysm	2 (1.5)	0	NA		NA	
ARVI	2 (1.5)	0	NA		NA	
Dehiscence	0	1 (0.7)	NA		NA	
Complications	10 (7.3)	13 (9.5)	0.997 (0.99-1.0)	.21	0.998 (0.99-1.0)	.39

ARVI, Access-related vascular injury; *CI*, confidence interval; *NA*, not applicable; *OR*, odds ratio; *SSI*, surgical site infection.
[a]Insufficient data for analysis (Hessian matrix singularity).

Table III. Number of primary and secondary outcomes of the intervention based on the access technique per main device (MD)

	Percutaneous access (n = 73), No. (%)	Open access (n = 64), No. (%)				
Percutaneous closure device failure						
Conversion	6 (8.2)					
Postoperative complications (<30 days)			**Univariable analyses**		**Multivariable analyses**	
			OR (95% CI)	***P***	**OR (95% CI)**	***P***
SSI	0	2 (3.1)	5.98 (0.47-830)	.18	3.25 (0.31-347)	.34
Seroma	0	2 (3.1)	5.98 (0.47-830)	.18	5.24 (0.31-792)	.27
Neuropathy	0	1 (1.6)	3.53 (0.18-519)	.41	2.16 (0.11-210)	.59
Hematoma	2 (2.7)	2 (3.1)	1.16 (0.17-7.73)	.87	1.35 (0.2-9.48)	.74
Pseudoaneurysm	2 (2.7)	0	0.23 (0.002-2.8)	.27	0.21 (0.00-3.07)	.27
ARVI	1 (1.4)	0	0.38 (0.003-7.3)	.53	0.47 (0.004-8.73)	.58
Dehiscence	0	0	1.16 (0.006-215)	.94	1.15 (0.2-112)	.93
Complications	5 (6.8)	7 (9.6)	0.92 (0.39-2.11)	.84	0.77 (0.30-1.91)	.58

ARVI, Access-related vascular injury; *CI*, confidence interval; *OR*, odds ratio; *SSI*, surgical site infection.

patient with CFA occlusion and ischemic complaints 1 day after EVAR. One patient with a pseudoaneurysm after percutaneous access and one patient with persisting pain after open access needed a second surgical procedure. The groin was re-explored under local anesthesia and the nerve entrapment relieved after transection of a subcutaneous suture. Two patients were readmitted because of wound complaints of the open access site.

DISCUSSION

This is the first randomized clinical trial comparing percutaneous CFA access in one groin with open CFA access in the other groin of patients undergoing EVAR. Although patients reported significantly less pain from the percutaneous wound on the postoperative day, no significant differences in wound complications were found. After percutaneous access, a lower SWA score 2 weeks after surgery indicated reduced inflammation. Neither nasal nor groin SA carriage had a significant effect on SSIs, SWA scores, or VAS scores.

When percutaneous devices (ProGlide or Prostar) were first introduced, several limitations were described. Obese patients, calcified or narrow-access vessels, ruptured aneurysms, and scarred groins were considered exclusion criteria for percutaneous access.[4,15,16,23] Postclosure techniques seem to have an advantage in smaller device profiles (<16F).[24] Our clinical success rate of 95% is comparable to the 4% to 15% conversion rate reported in the literature.[3,23,25] The conversions did not lead to additional complications, such as neuropathy or SSIs.

Our complication rate of 8.4% is at the high end for a relatively simple incision in the groin. However, in the

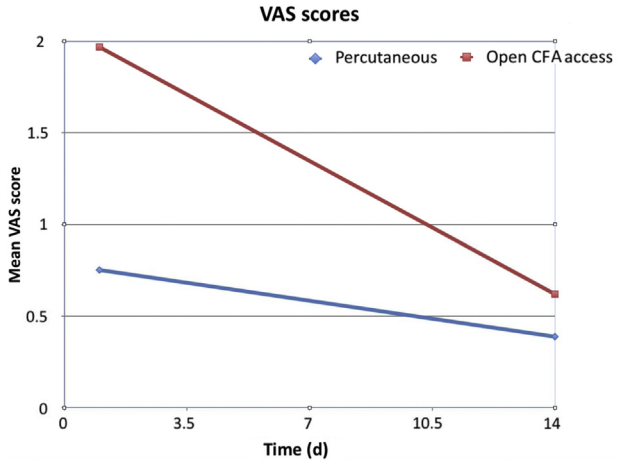

Fig 2. Mean visual analog scale (*VAS*) scores of percutaneous vs open access groins measured at day 1 and 2 weeks postoperatively. *CFA*, Common femoral artery.

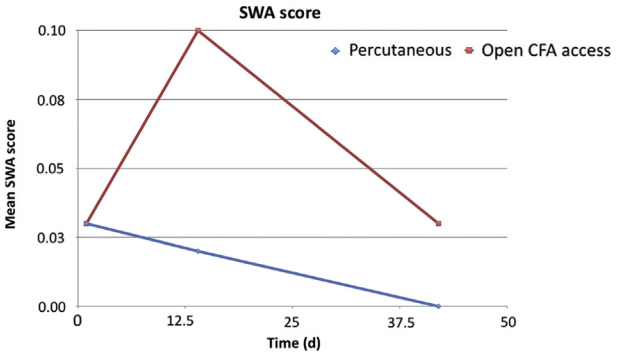

Fig 3. Mean Southampton Wound Assessment (*SWA*) scores of percutaneous vs open access groins measured at day 1, 2 weeks, and 6 weeks postoperatively. *CFA*, Common femoral artery.

course of this prospective study, minor complications were also recorded (eg, seroma and dehiscence). These are not mentioned in the Valve Academic Research Consortium-2 definitions of vascular access site-related complications[26] but were comparable to the outcome of the Percutaneous Endovascular Aneurysm Repair (PEVAR) trial.[7] The number of complications in the percutaneous group was not inferior to that in the open access group. BMI had no impact in the multivariable analysis.

The number of SSIs was unexpectedly low, notwithstanding the craniocaudal incision required in the open access procedure protocol and the normal distribution of SA carriage of 23% to 31% (Table I). The OR for SSI of 3.25 in favor of percutaneous access was far from significant ($P = .34$), but if the difference were to hold in a larger series, it could be clinically relevant.

The other types of complications were variable and therefore difficult to compare; three additional operations were performed in the percutaneous group because of the access technique. In open CFA, only one additional operation was performed (not significant), but open CFA access complications caused prolonged complaints (SSI, seroma, neuropathy). These complaints were not seen in the "crude" VAS scores after 2 weeks.

In EVAR treatment, complications contribute to a large part of additional costs. A second surgical procedure is more expensive than local wound care. From the preceding, we may conclude that more surgical complications than percutaneous access complications seem to resolve with local wound care. The percutaneous access complications required up to three additional surgical interventions. This increased cost of VCDs may become an issue. Typically, for a percutaneous EVAR, four ProGlides are deployed (two per groin), adding an additional $1200 to the medical costs. Because DOS and hospital length of stay do not seem to decrease,[5] the single gain seems to be increased comfort of the patient.

Strengths and limitations. A major strength of the PiERO trial is the comparison of two techniques in one patient. This approach has not been performed before, and it enables the patient to judge both techniques but entails a statistical challenge too. One patient may present as his or her own control, yet outcome cannot be seen as unrelated. This is why analyses were first performed for all groins as well as for MDs separately, both using the GEE technique. This amounts to a clear advantage of the percutaneous technique compared with the surgical technique in terms of the patient's comfort. Other studies do not report this.

This study has some other limitations that need to be addressed. Despite randomization, the two groups deferred 11 patients. After thorough analysis of the imbalance, only one explanation seemed plausible; randomization was performed with envelopes at each center, and the remainder of the envelopes was large enough to cause the imbalance. Centralization of randomization would have prevented this imbalance.

This was a multicenter trial, and the large number of surgeons and interventional radiologists may have caused a sizable variation in surgical techniques and experience. Despite the detailed protocol for longitudinal incisions in the open CFA access group and the required advanced training, preference for the right-sided position during the operation may have caused an inherent bias. However, this variability does add to the applicability in daily practice.

In this study, two devices were used, the Prostar device delivering two sutures and the ProGlide device delivering one suture. Although both devices require a similar small incision, the difference in knot tying and the monofilament vs braided sutures in the devices may have caused different outcome. Other series have combined these techniques and found no different outcomes.[27] The PEVAR trial showed more technical failures in Prostar,[7] but in our series, conversions were equally divided (Prostar/ProGlide, 3/4). No infections were reported in the percutaneous arm, and the required experience with the technique should have prevented bias.

The sample size analysis of this study resulted in an underestimation of the required number of patients because of a high number of SSIs reported (6.8%).[6,15-18] Only 1.5% of our open access surgical wounds became infected. The point estimate of the OR (3.3) could be clinically relevant, but the large CI demonstrates no difference statistically. A new sample size analysis would result in a study requiring 632 patients in each group, which seems an unrealistic number given the limited profit.

Despite previous sample size analysis, this randomized study seems to be underpowered. An interim analysis could have prevented this lack of power. Prolongation of this study could have produced a significant difference in SSIs, but the clinical relevance remains disputable. The robust increase in comfort of the patients is the only gain that stands firm in this comparison.

CONCLUSIONS

Percutaneous access of the CFA in endovascular procedures is a safe technique but does not seem to alter the number of wound complications significantly. Patients do experience less pain and less inflammation after the first day and 2 weeks after surgery, respectively. The patient's comfort does improve.

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AUTHOR CONTRIBUTIONS

Conception and design: BV, RP, MO, JB, CZ
Analysis and interpretation: BV, MM
Data collection: BV, RP, MO, MP, TK, RH, OW, MM, CZ
Writing the article: BV, RP, MO, MM, CZ
Critical revision of the article: MP, TK, RH, OW, JB
Final approval of the article: BV, RP, MO, MP, TK, RH, OW, JB, MM, CZ
Statistical analysis: BV, MM
Obtained funding: BV
Overall responsibility: BV

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