# CLINICAL RESEARCH STUDIES

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# A multicenter, randomized, controlled trial of totally percutaneous access versus open femoral exposure for endovascular aortic aneurysm repair (the PEVAR trial)

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***Objective:*** **The first multicenter randomized controlled trial was designed and conducted to assess the safety and effectiveness of totally percutaneous endovascular aortic aneurysm repair (PEVAR) with use of a 21F endovascular stent graft system and either an 8F or 10F suture-mediated closure system (the PEVAR trial, NCT01070069). A noninferiority trial design was chosen to compare percutaneous access with standard open femoral exposure.**
***Methods:*** **Between 2010 and 2012, 20 U.S. institutions participated in a prospective, Food and Drug Administration–approved randomized trial to evaluate percutaneous femoral artery access and closure by a "preclose" technique in conjunction with endovascular abdominal aortic aneurysm repair. A total of 151 patients were allocated by a 2:1 design to percutaneous access/closure (n = 101) or open femoral exposure (n = 50 [FE]). PEVAR procedures were performed with either the 8F Perclose ProGlide (n = 50 [PG]) or the 10F Prostar XL (n = 51 [PS]) closure devices. All endovascular abdominal aortic aneurysm repair procedures were performed with the Endologix 21F profile (outer diameter) sheath-based system. Patients were screened by computed tomography with three-dimensional reconstruction and independent physician review for anatomic suitability and adequate femoral artery anatomy for percutaneous access. The primary trial end point (treatment success) was defined as procedural technical success and absence of major adverse events and vascular complications at 30 days. An independent access closure substudy evaluated major access-related complications. Clinical utility and procedural outcomes, ankle-brachial index, blood laboratory analyses, and quality of life were also evaluated with continuing follow-up to 6 months.**
***Results:*** **Baseline characteristics were similar among groups. Procedural technical success was 94% (PG), 88% (PS), and 98% (FE). One-month primary treatment success was 88% (PG), 78% (PS), and 78% (FE), demonstrating noninferiority vs FE for PG ($P = .004$) but not for PS ($P = .102$). Failure rates in the access closure substudy analyses demonstrated noninferiority of PG (6%; $P = .005$), but not of PS (12%; $P = .100$), vs FE (10%). Compared with FE, PG and PS yielded significantly shorter times to hemostasis and procedure completion and favorable trends in blood loss, groin pain, and overall quality of life. Initial noninferiority test results persist to 6 months, and no aneurysm rupture, conversion to open repair, device migration, or stent graft occlusion occurred.**
***Conclusions:*** **Among trained operators, PEVAR with an adjunctive preclose technique using the ProGlide closure device is safe and effective, with minimal access-related complications, and it is noninferior to standard open femoral exposure. Training, experience, and careful application of the preclose technique are of paramount importance in ensuring successful, sustainable outcomes. (J Vasc Surg 2014;59:1181-94.)**

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**Table I.** Patient selection criteria

- Man or woman at least 18 years old
- Informed consent form understood and signed and patient agrees to all follow-up visits
- Abdominal aortic aneurysm with maximum diameter ≥5 cm or rapidly expanding
- Have a suitable ipsilateral CFA for percutaneous access with a preclose technique
  - At least 2-cm segment for access, 10 mm above the origin of the profunda femoris branch and 10 mm below the lower margin of the inferior epigastric artery as determined on preoperative high-resolution contrast-enhanced computed tomography scan
  - Calcification of CFA target area not covering entire anterior wall, not present circumferentially, and not >50% of the circumference from the posterior wall
- Absence of: prior groin incision; hematoma or significant scarring at the ipsilateral arterial access site; clip-based vascular closure device placement ever; collagen-based vascular closure device placement in either arterial access site within prior 90 days; femoral artery needle puncture in either arterial access site within the prior 30 days
- Absence of: active localized groin infection; traumatic vascular injury; femoral artery aneurysm, arteriovenous fistula, or pseudoaneurysm
- Anatomically eligible for the Endologix System per the indications for use
- Life expectancy >1 year as judged by the investigator
- Absence of: allergy to any device component; coagulopathy or uncontrolled bleeding disorder; active systemic infection; connective tissue disease; prior renal transplant
- Serum creatinine level ≤1.7 mg/dL (unless dialysis dependent)
- Free from cerebrovascular accident or myocardial infarction within 3 months of enrollment
- No planned major intervention or surgery within 30 days after the study procedure
- Not morbidly obese (body mass index <40 kg/m$^2$)

*CFA*, Common femoral artery.

Suture-mediated closure devices were developed to facilitate rapid and secure common femoral artery (CFA) hemostasis after diagnostic or interventional procedures with 5F to 8F sheaths and up to 10F sheaths (Perclose ProGlide [PG] and Prostar XL [PS], respectively; Abbott Vascular, Inc, Redwood City, Calif). Owing to the utility of these closure devices, their use has been adapted to CFA closure in conjunction with large-sheath endovascular aortic aneurysm repair (EVAR). This requires use of a more complex, closure device-specific "preclose" technique. This concept was first described for PS in 1999[1] and for PG in 2007.[2] Technique feasibility has been reported in several single-center experiences, with each using various large-bore sheaths.[2-19] Among these reports, percutaneous EVAR (PEVAR) technical success rates of 71% to 96% (PS) and 88% to 98% (PG) are reported with improvement over time and increasing experience. Limited operator experience[7,10] and "hostile" femoral anatomy[3,4,9,10] have been identified as predictors of technical failure, whereas larger sheath diameter was inconsistently predictive. In observational reports of PEVAR and standard femoral exposure (FE) EVAR, benefits attributed to PEVAR included shorter procedure times,[6,16] lower complication rates[9,12,15,17] and shorter hospital stays.[9,14] One single-center randomized pilot study reported PS technical success in 14 of 15 PEVAR cases, with significantly reduced times to procedure completion and ambulation among PEVAR patients.[5]

Despite this growing experience, no multicenter, randomized trial was previously available delineating the risks and benefits of PEVAR facilitated with an adjunctive pre-close technique. Therefore, we conducted the first prospective, multicenter, randomized controlled trial of PEVAR using an endograft system incorporating a precannulated contralateral limb that is indicated for standard contralateral percutaneous (9F) access (Endologix, Inc, Irvine, Calif).[20] Because of the prevalent use of PG and PS, both were included in the trial. We hypothesized that PEVAR would be noninferior to standard EVAR/FE.

## METHODS

Twenty U.S. centers having prior training and experience in EVAR using both standard FE and suture-mediated closure device preclose percutaneous techniques participated. Each investigator was required (1) to provide evidence of prior Abbott training and experience in the use of the closure devices for small hole closure, (2) to complete the Endologix EVAR training program, and (3) to certify more than 20 PEVAR preclose cases before trial participation. Each site obtained institutional review board approval for human investigation, and written patient informed consent was obtained. Before initiation of the trial randomized phase, all sites were required to complete two PEVAR "roll-in" cases.[20] Preoperatively, high-resolution, contrast-enhanced computed tomography (CT) scan imaging with three-dimensional reconstruction (M2S, Inc, West Lebanon, NH) of the thoracic and abdominal aorta was performed to determine anatomic eligibility. To verify a suitable access artery for the preclose procedure, additional assessments of CFA dimensions and quality were conducted by an independent vascular surgeon with experience in percutaneous endovascular techniques. Physical examinations, ankle-brachial indices (ABI), and blood laboratory evaluations were performed. These baseline assessments were used to determine patient suitability for enrollment (Table I). Health-related quality of life (QOL) was also assessed before and after the procedure by the Medical Outcomes Study short form SF-36 tool (Medical Outcomes Trust, Boston, Mass).[21]

### Randomization/patient allocation

Randomization was conducted by study site, using two block sizes (3 or 6) with random choice of block size order. One set of sealed randomization envelopes was provided to each site after completion of roll-in cases and on sponsor

approval to initiate the randomized trial. On screening eligibility confirmation, the next sequential randomization envelope was opened and the assignment was immediately allocated. An overall 2:1 randomization scheme (PEVAR:FE) was used to allow equal allocation to two PEVAR groups: PG or PS. Trial enrollment was defined as the time of procedure initiation. Two patients who were randomized but never enrolled (one withdrew consent; one did not meet cardiac clearance requirements) were excluded from analysis.

### Procedural conduct

In centers where the operator was an interventionist, a qualified surgeon was required to be present in all PEVAR cases in the event that surgical cutdown or intervention was needed. At initiation of PEVAR procedures, appropriate ipsilateral CFA puncture was documented angiographically in an oblique projection. For FE-randomized patients, the study protocol reflected a vascular cutdown to be performed by a small oblique incision with direct exposure and control of the femoral artery from inguinal ligament to the femoral bifurcation. Management of the arteriotomy with a purse-string suture vs formal clamping and a transverse arteriotomy was left to the surgeon's preference. The selected endograft was then implanted under fluoroscopy. Anticoagulant was administered on establishing access with a targeted activated clotting time of more than 250 seconds. In all cases, postdeployment graft positioning/aneurysm exclusion was confirmed angiographically. Arteriotomy closure was performed by the preplaced sutures as described later in PEVAR groups or direct artery repair with a standard polypropylene-sutured closure followed by layered wound closure in FE patients. Hemostasis and preserved distal flow were to be confirmed, or any complications identified were to be addressed immediately intraoperatively, in all patients regardless of access type before procedure completion. Anticoagulation reversal was used selectively at the operator's discretion.

All patients received a single intravenous preoperative dose of antibiotics and were admitted for at least overnight observation. Times of ambulation and normal diet were recorded. Clinical examination, laboratory/ABI testing, and femoral ultrasound (US) examinations were performed before discharge. Patients were asked to grade their groin pain bilaterally with a 10-point visual analog scale (0 = none; 10 = worst imaginable). One-month follow-up included clinical examination, laboratory/ABI testing, CT scan, SF-36 QOL, and groin pain assessments. Final 6-month follow-up included these same clinical assessments, with repeated femoral US examination and optional CT scans at the investigator's discretion.

### Device description

The Endologix endograft system consisted of a unibody bifurcated device preloaded into a 21F profile (outer diameter) delivery system containing an integrated 19F introducer sheath. After seating of the bifurcated device at the aortoiliac bifurcation, the inner core was removed, leaving the hemostatic sheath in place. Additional devices, if needed, were advanced through this same sheath to complete the repair. Details of the stent-graft design and anatomic fixation technique are available.[22,23]

The design and application of the PG and PS devices in preclose techniques have been described.[11,22,24] Briefly, each PG includes a single monofilament polypropylene suture having a pretied knot, whereas each PS delivers two braided polyester sutures without a pretied knot. Arterial access was obtained percutaneously at an oblique angle ($\sim 45^\circ$) with or without US guidance at operator discretion. A small skin opening was made to permit PG or PS advancement, limited blunt dissection of subcutaneous tissues was allowed, and the closure device was advanced over a 0.035-inch guidewire and deployed. Two sutures were placed in each arteriotomy by use of either two PG devices sequentially deployed with opposite 30° rotation in a "cross-hair" configuration or a single PS device, and suture tails were secured.

EVAR was performed following standard practice. On final sheath removal, the preplaced sutures were secured over the guidewire. In PG cases, the pretied knots were advanced to the CFA access site to achieve hemostasis; in PS cases, a fisherman's knot was tied manually for each suture set. At operator discretion, an additional device and supplemental manual compression were applied as needed. Skin closure was per operator preference (eg, Steri-Strip, single absorbable suture, adhesive). In cases in which hemostasis was not achieved or limb ischemia was suspected, closure failure was determined and surgical cutdown with arterial repair employed.

### Definitions

Table II provides study protocol definitions. The primary end point of treatment success reflects the comparison in overall EVAR strategies between total percutaneous access and conventional femoral exposure. The substudy end point of access site closure looks more directly at the technical success of femoral vessel closure.

### Statistical analyses

**Primary end point: Treatment success.** Sample size was based on literature-based feasibility data, identifying a minimum sample size of 44 patients per group. To account for deviations from assumptions, a sample size of 50 per group was targeted. Primary end point analysis was performed by a one-sided Blackwelder test for noninferiority within a margin of 0.10 and $\alpha = .025$. No other allowance for multiple comparisons was made. This strategy provided >80% power for end point detection. Analyses were conducted at exact time points: 1 month = 30 days; 6 months = 210 days. An independent Clinical Events Committee adjudicated adverse events, and an independent Data Safety Monitoring Board reviewed safety data. For continuous variables, summary statistics included means and standard deviations; groups were compared by *t*-tests. For ordinal variables, group comparisons were typically performed by the exact Wilcoxon rank-sum test. Comparisons of proportions use Fisher exact test. $P < .05$ defined statistical significance. Analyses

**Table II.** Protocol-specified definitions

| *Term* | *Definition* |
|---|---|
| Procedural technical success | Successful vascular access and closure per randomized assignment, and successful endograft delivery, deployment, and catheter removal, without serious complication or need for vascular exposure in the percutaneous group |
| Closure device technical success | Successful vascular access per randomized assignment and closure without serious complication or need for vascular exposure in the percutaneous group. This includes successful deployment and function of the closure device itself in the percutaneous group. |
| Major adverse events | All-cause mortality; aneurysm rupture; bowel ischemia; cardiac morbidity (acute myocardial infarction/cardioversion; pacemaker placement/new onset; exacerbated congestive heart failure/surgical or percutaneous coronary intervention); conversion to open repair; neurologic complications (paraplegia, spinal ischemia, stroke, transient ischemic attack); renal failure (temporary or permanent dialysis; >0.5 mg/dL increase in serum creatinine level from baseline); respiratory complications (pneumonia or respiratory failure requiring ventilator support >24 hours postoperatively); and secondary procedure for type I/III endoleak |
| Vascular complications | Arteriovenous fistula; femoral neuropathy; hematoma requiring drainage or surgical intervention; hemorrhage (access site bleeding requiring blood transfusion or surgical or percutaneous intervention); infection; lymphocele; vascular (iliac or femoral artery) injury or pseudoaneurysm requiring surgical repair; stenosis, distal emboli or thrombosis/occlusion; and ABI reduction ≥0.15 from baseline not attributable to disease progression |
| Treatment success (primary end point) | Composite end point inclusive of procedural technical success and absence of major adverse event or vascular complication at 1 month |
| Major ipsilateral access site vascular complications (independent access site closure substudy end point) | Access site related: vascular injury requiring surgical repair, angioplasty, US-guided compression, or thrombin injection; new-onset lower extremity ischemia attributed to arterial access or closure requiring intervention; bleeding requiring transfusion; infection requiring intravenous antibiotics or prolonged hospitalization; nerve injury (permanent or requires surgery) |
| Times to hemostasis, ambulation, and normal diet | Time from sheath removal: to first observed complete cessation of CFA bleeding; to when the patient walks independently a minimum of 20 feet; and to tolerance of solid food consumption |

*ABI*, Ankle-brachial index; *CFA*, common femoral artery; *US*, ultrasound.

were performed with SAS software version 9.1 (SAS Institute, Cary, NC).

**Independent access site closure substudy.** The safety and effectiveness of PG and PS were assessed separately in ipsilateral 21F access site closure (1-month major ipsilateral access site vascular complications) in comparison to FE. Analysis was performed by a one-sided Blackwelder test for noninferiority with a margin of 0.10 and $\alpha = .05$.

## RESULTS

**Enrollment/procedural outcomes.** Fig 1 shows randomization and patient allocation. Among 179 consenting/screened patients, 153 were found eligible and randomized between July 2010 and February 2012. Reasons for screen failure included unsuitable anatomy for the endograft, poor CFA quality (eg, circumferential calcification, pseudoaneurysm), morbid obesity (body mass index >40), and inadequate CT scan quality. Excluding the two randomized/nonenrolled patients, 151 were enrolled with 2:1 allocation to PEVAR (n = 101) or FE (n = 50). PEVAR patients were divided by closure device: PG (n = 50) and PS (n = 51). Among the 18 sites participating in the randomized phase, 9 used PG, 7 used PS, and 2 used both. Preoperative group comparisons among the three groups are shown in Table III (demographics), Table IV (comorbidities), and Table V (aneurysm and vascular characteristics). Baseline characteristics were typical of this population, and groups were well matched.

Table VI shows procedural access technique/closure device use. All patients underwent the assigned treatment. Ipsilateral preclose access was attempted in all PEVAR cases; surgical cutdown was performed in all FE cases. US-guided percutaneous access was used in 36% (PG) and 27% (PS); in the remainder, anatomic landmarks were fluoroscopically visualized. In all cases, angiographic imaging confirmed appropriate access location. Procedural technical success in the roll-in phase was 95% (21 of 22 PG and 18 of 19 PS), with both acute failures to achieve hemostasis resolved with surgical cutdown/vessel repair. Randomized phase procedural technical success among PG, PS, and FE groups was 94% (47 of 50), 88% (45 of 51), and 98% (49 of 50), respectively. In PG, three ipsilateral preclose failures occurred: two surgical cutdowns for excessive bleeding or to resolve stenosis at the femoral bifurcation and return to the operating room for percutaneous stent placement to address significant stenosis. In PS, six technical failures occurred: surgical cutdown for excessive bleeding (5) and rheolytic thrombectomy/iliac stenting for thrombosis. Three PS bleeding events were associated with technique problems (ie, needle nonengagement with artery wall, suture break at knot tying, pull-out from artery). Among PEVAR technical failures, US guidance was used in two of three (PG) and two of six (PS). In FE, one external iliac dissection with excessive bleeding required switching to the lower-profile Endologix AFX system (19F outer diameter) for EVAR and external iliac artery stenting. Standard percutaneous (9F) access and

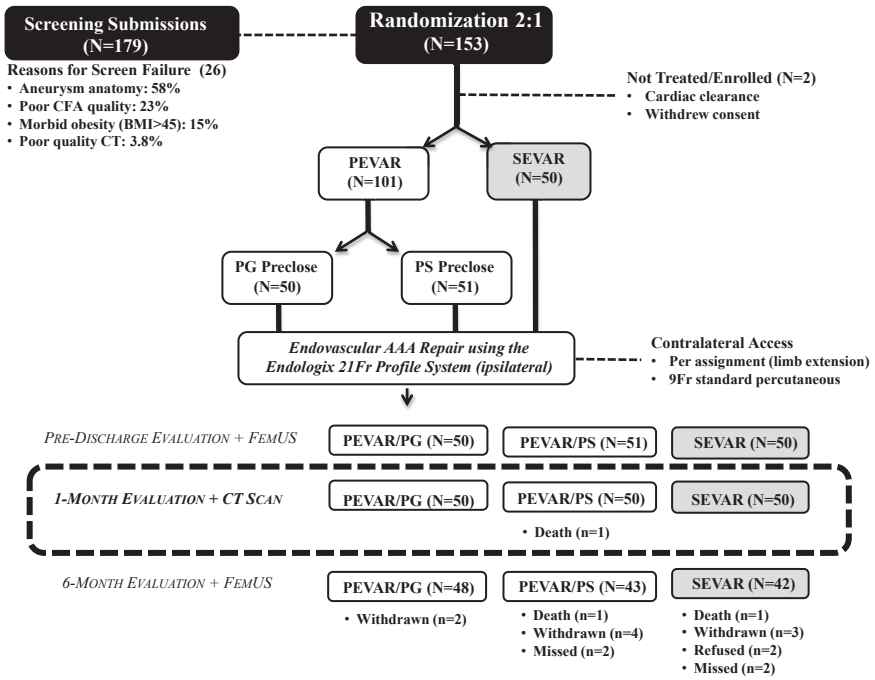



**Fig 1.** Patient flow diagram. *AAA*, Abdominal aortic aneurysm; *BMI*, body mass index; *CFA*, common femoral artery; *CT*, computed tomography; *FEMUS*, femoral ultrasound; *PEVAR*, percutaneous endovascular aortic aneurysm repair; *PG*, ProGlide; *PS*, Prostar XL; *SEVAR*, standard endovascular aortic aneurysm repair.

**Table III.** Baseline demographics

| *Characteristic* | *PEVAR/PG (n = 50)* | *PEVAR/PS (n = 51)* | *FE (n = 50)* | *PG vs FE*[a] | *PS vs FE*[a] |
|---|---|---|---|---|---|
| Age, years | 70 ± 6.6 | 74 ± 11 | 73 ± 8.8 | .033 | .984 |
| Gender | | | | | |
| Male | 47 (94) | 44 (86) | 45 (90) | .715 | .760 |
| Female | 3 (6.0) | 7 (14) | 5 (10) | | |
| Race | | | | | |
| White | 46 (92) | 44 (86) | 47 (94) | 1.000 | .318 |
| Nonwhite | 4 (8.0) | 7 (14) | 3 (6.0) | | |
| ASA | | | | | |
| Class 1 or 2 | 18 (36) | 39 (76) | 30 (60) | .014 | .077 |
| Class 3 or 4 | 32 (64) | 12 (24) | 20 (40) | | |
| Height, cm | 179 ± 6.9 | 173 ± 9.7 | 175 ± 8.5 | .122 | .079 |
| Weight, kg | 93 ± 13 | 83 ± 19 | 86 ± 15 | .017 | .025 |
| Body mass index | 29 ± 3.9 | 28 ± 4.7 | 28 ± 4.7 | .115 | .922 |

*ASA*, American Society of Anesthesiology; *FE*, femoral exposure; *PEVAR*, percutaneous endovascular aortic aneurysm repair; *PG*, ProGlide; *PS*, Prostar XL. Results shown as number (% of group) or as mean ± standard deviation.
[a] *P* values determined by a two-sided Wilcoxon rank-sum test or two-sided Kruskal-Wallis test for singly ordered table (ASA class).

closure were used contralaterally in most patients (92% PG; 90% PS; 84% FE). The remaining patients received 17F outer diameter Endologix limb extensions. In these cases, patients underwent the same preclose technique or FE per randomization assignment. All contralateral access techniques, implants, and closures were successful. Significantly fewer PG patients underwent concomitant ipsilateral vascular procedures (2% PG vs 16% FE and PS; $P < .01$) including iliac artery stenting, embolectomy, hypogastric artery coiling, and CFA endarterectomy or reconstruction.

Table VII shows procedural results. Local anesthesia per physician preference was used in 16% PG, 37% PS, and 24% FE patients. Time to hemostasis was significantly reduced in PEVAR groups vs FE ($P < .002$). Mean total procedure time was significantly shorter by 34 minutes (PG) and 46 minutes (PS) vs FE ($P < .001$). Several nonsignificant trends favoring one or both PEVAR groups were observed: (1) reduced mean blood loss; (2) fewer PG patients requiring transfusion; (3) hospital discharge on average a half-day earlier; and (4) fewer PEVAR patients

**Table IV.** Baseline comorbidities

| *Characteristic* | *PEVAR/PG (n = 50)* | *PEVAR/PS (n = 51)* | *FE (n = 50)* | *PG vs FE*[a] | *PS vs FE*[a] |
|---|---|---|---|---|---|
| Arrhythmia | 17/50 (34) | 15/51 (29) | 13/50 (26) | .513 | .821 |
| Cancer | 10/50 (20) | 15/51 (29) | 16/50 (34) | .254 | .831 |
| Cerebrovascular accident | 3/50 (6.0) | 6/51 (12) | 2/50 (4.0) | 1.000 | .269 |
| Chronic obstructive pulmonary disease | 15/50 (30) | 15/51 (29) | 17/50 (34) | .831 | .672 |
| Coagulopathy or uncontrolled bleeding disorder | 0 | 0 | 0 | — | — |
| Congestive heart failure | 8/50 (16) | 7/51 (14) | 11/50 (22) | .611 | .309 |
| Coronary artery disease | 19/50 (38) | 26/51 (51) | 24/50 (48) | .419 | .843 |
| Diabetes | 14/50 (28) | 15/51 (29) | 11/50 (22) | .645 | 1.000 |
| Family history of abdominal aortic aneurysm | 11/50 (22) | 5/50 (10) | 9/50 (18) | .388 | .388 |
| Gastrointestinal abnormality | 26/50 (52) | 20/51 (39) | 29/50 (58) | .688 | .074 |
| Heart valve disease | 4/50 (8.0) | 9/51 (18) | 4/50 (8.0) | 1.000 | .234 |
| Hypertension | 42/50 (84) | 45/51 (88) | 44/50 (88) | .774 | 1.000 |
| Hyperlipidemia | 45/50 (90) | 46/51 (90) | 42/50 (84) | .554 | .389 |
| Liver disease | 5/50 (10) | 2/51 (3.9) | 1/50 (2.0) | .204 | 1.000 |
| Myocardial infarction | 6/50 (12) | 12/51 (24) | 8/50 (16) | .774 | .455 |
| Peripheral arterial occlusive disease | 7/50 (14) | 11/51 (22) | 7/50 (14) | 1.000 | .437 |
| Prior abdominal surgery | 13/50 (26) | 14/51 (27) | 11/50 (22) | .815 | .646 |
| Prior aortic valve repair or replacement | 0 | 1/51 (2.0) | 0 | — | 1.000 |
| Prior coronary artery bypass grafting | 9/50 (18) | 13/51 (25) | 13/50 (26) | .470 | 1.000 |
| Prior pacemaker or implantable cardioverter-defibrillator implant | 2/50 (4.0) | 12/51 (24) | 3/50 (6.0) | 1.000 | .023 |
| Prior percutaneous coronary intervention | 10/50 (20) | 10/51 (20) | 10/50 (20) | 1.000 | 1.000 |
| Renal failure | 1/50 (2.0) | 0 | 2/50 (4.0) | 1.000 | .243 |
| Smoking | 43/50 (86) | 35/51 (69) | 34/50 (68) | .056 | 1.000 |
| Thoracic aortic aneurysm | 0 | 1/51 (2.0) | 2/50 (4.0) | .495 | .617 |

*FE*, Femoral exposure; *PEVAR*, percutaneous endovascular aortic aneurysm repair; *PG*, ProGlide; *PS*, Prostar XL.
Results shown as number (% of group).
[a]*P* values determined per two-sided Fisher exact test.

**Table V.** Baseline aneurysm and vascular characteristics

| *Measurement or characteristic* | *PEVAR/PG (n = 50)* | *PEVAR/PS (n = 51)* | *FE (n = 50)* | *PG vs FE*[a] | *PS vs FE*[a] |
|---|---|---|---|---|---|
| Maximum aneurysm sac diameter, mm | 56 ± 6.1 | 53 ± 6.3 | 56 ± 8.1 | .715 | .096 |
| Proximal nonaneurysmal neck diameter, mm | 22 ± 3.4 | 23 ± 3.2 | 24 ± 2.8 | .031 | .951 |
| Distal nonaneurysmal neck diameter, mm | 26 ± 3.6 | 26 ± 3.3 | 25 ± 3.6 | .115 | .390 |
| Proximal neck length, mm | 30 ± 13 | 27 ± 13 | 29 ± 12 | .700 | .320 |
| Irregular proximal neck[b] | 40 | 41 | 42 | 1.000 | 1.000 |
| Neck angle to sac, degrees | 28 ± 15 | 26 ± 15 | 30 ± 14 | .702 | .235 |
| Distal renal to aortic bifurcation length, mm | 121 ± 26 | 108 ± 15 | 110 ± 23 | .010 | .032 |
| Aortic bifurcation diameter, mm | 25 ± 9.4 | 26 ± 11 | 32 ± 40 | .294 | .656 |
| Narrow aortic bifurcation[c] | 20 | 14 | 16 | .602 | 1.000 |
| Right common iliac artery diameter, mm | 12 ± 2.7 | 13 ± 2.1 | 14 ± 3.9 | .062 | .107 |
| Right external iliac artery diameter, mm | 8.9 ± 1.9 | 9.2 ± 1.5 | 12 ± 13 | .156 | .211 |
| Bifurcation to right hypogastric artery length, mm | 55 ± 18 | 51 ± 21 | 54 ± 35 | .843 | .560 |
| Left common iliac artery diameter, mm | 13 ± 2.8 | 12 ± 2.1 | 13 ± 3.0 | .561 | .675 |
| Left external iliac artery diameter, mm | 8.8 ± 1.5 | 12 ± 15 | 9.2 ± 1.3 | .093 | .376 |
| Bifurcation to left hypogastric artery length, mm | 59 ± 20 | 52 ± 25 | 56 ± 32 | .585 | .387 |

*FE*, Femoral exposure; *PEVAR*, percutaneous endovascular aortic aneurysm repair; *PG*, ProGlide; *PS*, Prostar XL.
Results shown as % of group or as mean ± standard deviation.
[a]*P* values determined per two-sided Wilcoxon rank-sum test, two-sided unequal variance *t*-test, or Fisher exact test.
[b]Defined as >2-mm diameter change over the first 15 mm of length.
[c]Defined as diameter <21 mm.

prescribed analgesics for groin pain (15% vs 30%, FE). No differences were observed in times to ambulation or normal diet. Prolonged hospital stay occurred in five patients because of spinal ischemia (FE [17 days]); stroke, renal failure, and respiratory failure (FE [6 days]); significant bleeding and re-exploration of the groin/extended incision secondary to distal ischemia with postoperative hypotension monitored and resolved (FE [6 days]); heart failure and 33% ABI reduction (PS [6 days]); and contrast nephropathy (PG [5 days]).

**Table VI.** Procedural access technique and closure devices used

| *Technique* | *PEVAR/PG (n = 50)* | *PEVAR/PS (n = 51)* | *FE (n = 50)* |
|---|---|---|---|
| Ipsilateral | | | |
| Preclose[a] (successful) | 48 (96) | 46 (90) | 0 |
| Preclose [a] → cutdown | 2 (4.0) | 5 (9.8) | 0 |
| Cutdown | 0 | 0 | 50 (100) |
| Contralateral | | | |
| Preclose[b] | 4 (8.0) | 5 (9.8) | 0 |
| Cutdown | 0 | 0 | 8 (16) |
| Standard percutaneous (9F sheath) | 46 (92) | 46 (90) | 42 (84) |
| Angio-Seal[c] | 14 | 4 | 12 |
| Manual compression | 0 | 11 | 6 |
| ProGlide | 32 | 11 | 17 |
| Prostar XL | 0 | 18 | 7 |
| StarClose[d] | 0 | 2 | 0 |

*FE,* Femoral exposure; *PEVAR,* percutaneous endovascular aortic aneurysm repair; *PG,* ProGlide; *PS,* Prostar XL.
Results shown as number (% of group).
[a]The group closure device (PG or PS) was used in a preclose technique.
[b]The group closure device (PG or PS) was used in a preclose technique before limb extension placement (17F outer diameter).
[c]St. Jude Medical, Inc (St Paul, Minn).
[d]Abbott Vascular, Inc (Redwood City, Calif).

No early mortality or withdrawals occurred among PG or FE groups. In PS, one patient withdrew (day 7) and one cardiac death occurred (day 28). Two late cancer deaths occurred on days 75 (PS) and 201 (FE). Excluding patients who withdrew consent or refused/missed the visit, 48 PG, 43 PS, and 42 FE patients completed final 6-month follow-up.

**Primary end point analysis.** Treatment success results are shown in Table VIII. Compared with FE (78%), noninferiority was achieved for PG (88%; $P = .004$) but not for PS (78%; $P = .102$). On analysis of results by site, no significant trends were identified between randomized groups. Adjustment for baseline covariates with $P < .10$ did not alter these results. Procedural technical failures were described previously. Although the incidence of major adverse events and vascular complications were similar among groups, the overall rate trended lower in PG (12%) vs PS (22%) or FE (22%).

Events by group were as follows:

- PG: Ipsilateral distal thrombosis in two patients manifested as loss of pedal pulses and Doppler signals immediately after the procedure due to posterior plaque-induced stenosis at the CFA bifurcation in which endarterectomy/patch angioplasty restored perfusion; loss of Doppler signal after the procedure in one patient attributed to stenosis was resolved with stenting.
- PS: Iliofemoral thrombosis in one patient was managed with rheolytic thrombectomy of the external iliac/CFA followed by stenting.
- FE: Acute lower extremity ischemia in two patients discovered after initial wound closure was addressed with immediate reoperation and endarterectomy/patch angioplasty after the index procedure; one CFA occlusion on day 7 was treated with thrombectomy/patch angioplasty.

**Independent access site closure substudy analysis.** One-month results are shown in Table IX. Compared with FE (10% failure), noninferiority was achieved for PG (6%; $P = .005$) but not for PS (12%; $P = .100$). A 10% PS rate would have achieved noninferiority per Blackwelder test. Events by group were as follows:

- PG: inability to complete the preclose technique with the closure device because of bleeding and distal thrombosis (2).
- PS: inability to complete the preclose technique with the closure device because of bleeding (3), vascular injury/bleeding repaired surgically (2), iliofemoral thrombosis, and transfusion for bleeding.
- FE: vascular injury (groin re-exploration with bilateral endarterectomy/patching), distal thrombosis (2), transfusion for bleeding, bleeding/vessel dissection requiring surgical repair/stenting/transfusion, and nerve injury (persistent thigh numbness).

**Other 1-month outcomes.** Serious adverse events are shown in Table X. Compared with the incidence rate in FE (26%), a trend toward reduced serious adverse events was seen in PG (10%; $P = .066$) with similar incidence in PS (31%). The incidence of individual events was low. No specific trends were identified. Comparable mean ABI and laboratory results were observed. Fig 2 shows SF-36 QOL results among all eight domains in two dimensions, physical and mental health. Reductions in 1-month mean scores were observed for both role limitation domains; slightly less reduction occurred in PEVAR groups. Overall mean scores were similar at each time point, although 1-month changes were greater in PG (+9) and PS (+6) vs FE (0). Pain scale results are provided in Fig 3 showing relatively low groin pain bilaterally. Compared with FE, prescribed analgesics for groin pain trended lower in PG (18% vs 34%; $P = .241$) and were significantly lower in PS (12% vs 34%; $P = .039$).

**Final 6-month outcomes.** Fig 4 shows the 6-month Kaplan-Meier analysis of treatment success. The 1-month noninferiority analysis results persisted (PG vs FE, $P = .008$; PS vs FE, $P = .118$). Between days 31 and 210, 3 PG, 4 PS, and 4 FE patients (one of whom had an early event) were identified with a major adverse event or vascular complication; there were no major access-related complications. Late major adverse events and vascular complications included the following: PG: renal failure treated medically and two ABI decreases/no intervention; PS: cancer death (day 75), critical left renal artery stenosis requiring stenting, three secondary procedures for endoleak (days 41, 54, and 121), and ABI decrease/no intervention; FE: cancer death (day 201), two secondary procedures for endoleak (days 81, 131), and lymphocele.

**Table VII.** Procedural and in-hospital outcomes

| *Measurement or characteristic* | *PEVAR/PG (n = 50)* | *PEVAR/PS (n = 51)* | *FE (n = 50)* | *PG vs FE*[a] | *PS vs FE*[a] |
|---|---|---|---|---|---|
| Activated clotting time achieved, seconds | 257 ± 51 | 257 ± 39 | 260 ± 55 | .778 | .759 |
| Contrast volume, mL | 120 ± 78 | 123 ± 56 | 144 ± 90 | .113 | .172 |
| Fluoroscopy time, minutes | 26 ± 16 | 22 ± 8.5 | 24 ± 14 | .433 | .359 |
| Estimated blood loss, mL | 213 ± 205 | 193 ± 198 | 280 ± 290 | .115 | .083 |
| Blood transfusion | 4.0 | 16 | 14 | .187 | 1.000 |
| Procedure time, minutes | 107 ± 45 | 95 ± 35 | 141 ± 73 | .006 | <.001 |
| Ipsilateral time to hemostasis, minutes | 9.8 ± 17 | 13 ± 19 | 23 ± 23 | .002 | <.001 |
| Time to ambulation, hours[b] | 17 ± 7.2 | 16 ± 9.1 | 19 ± 16 | .388 | .256 |
| Time to normal diet, hours[c] | 14 ± 9.4 | 10 ± 8.4 | 15 ± 22 | .728 | .135 |
| ICU length of stay, hours | 26 ± 9.0 | 31 ± 15 | 35 ± 38 | .269 | .614 |
| Medication for groin pain | 18 | 12 | 30 | .241 | .029 |
| Time to hospital discharge, days | 1.3 ± 0.7 | 1.4 ± 0.9 | 1.8 ± 2.4 | .135 | .213 |

*FE,* Femoral exposure; *ICU,* intensive care unit; *PEVAR,* percutaneous endovascular aortic aneurysm repair; *PG,* ProGlide; *PS,* Prostar XL.
Results shown as % of group or as mean ± standard deviation.
[a] *P* values determined per an unequal variance two-sample *t*-test or Fisher exact test.
[b] Calculated as time from sheath removal to time patient walks 20 feet.
[c] Calculated as time from sheath removal to time patient consumes solid food.

**Table VIII.** Primary end point results: Treatment success at 1 month

| *Outcome* | *PEVAR/PG (n = 50)* | *PEVAR/PS (n = 51)* | *FE (n = 50)* | *PG vs FE* | *PS vs FE* |
|---|---|---|---|---|---|
| Treatment success | 44 (88) | 40 (78) | 39 (78) | .004[a] | .102[a] |
| Unsuccessful (failure) treatment[c] | 6 (12) | 11 (22) | 11 (22) | .287[b] | 1.000[b] |
| Procedural technical failure | 3 (6.0) | 6 (12) | 1 (2.0) | .242[b] | .027[b] |
| Ipsilateral access failure | 3 (6.0) | 6 (12) | 0 | | |
| Endovascular device failure | 0 | 0 | 1 (2.0) | | |
| Major adverse event | 2 [3] (4.0) | 5 [7] (9.8) | 5 [7] (10) | .436[b] | .741[b] |
| Death | 0 | 1 [1] (2.0) | 0 | | |
| Aneurysm rupture | 0 | 0 | 0 | | |
| Conversion to open repair | 0 | 0 | 0 | | |
| Bowel ischemia | 0 | 0 | 0 | | |
| Cardiac morbidity | 0 | 2 [2] (3.9) | 0 | | |
| Neurologic complication | 0 | 0 | 3 [3] (6.0) | | |
| Renal failure | 2 [2] (4.0) | 1 [1] (2.0) | 1 [1] (2.0) | | |
| Respiratory complication | 1 [1] (2.0) | 2 [2] (3.9) | 1 [1] (2.0) | | |
| Secondary procedure | 0 | 1 [1] (2.0) | 2 [2] (4.0) | | |
| Vascular complication | 4 [5] (8.0) | 8 [9] (16) | 8 [11] (16) | .357[b] | 1.000[b] |
| Arteriovenous fistula | 0 | 0 | 0 | | |
| Femoral neuropathy | 0 | 0 | 1 [1] (2.0) | | |
| Hematoma | 0 | 0 | 0 | | |
| Hemorrhage | 1 [1] (2.0) | 4 [5] (7.8) | 3 [4] (6.0) | | |
| Infection | 0 | 0 | 0 | | |
| Lymphocele | 0 | 0 | 1 [1] (2.0) | | |
| Thrombosis/occlusion | 2 [3] (4.0) | 1 [1] (2.0) | 3 [3] (6.0) | | |
| Vascular injury | 1 [1] (2.0) | 3 [3] (5.9) | 1 [2] (2.0) | | |
| Major adverse event + vascular complication | 6 [8] (12) | 11 [16] (22) | 11 [18] (22) | | |

*FE,* Femoral exposure; *PEVAR,* percutaneous endovascular aortic aneurysm repair; *PG,* ProGlide; *PS,* Prostar XL.
Results shown as number of patients (% of group) except for major adverse events and vascular complications, which are shown as number of patients [number of events] (% of group).
Major adverse events and vascular complication events included the following: PG: serum creatinine increases (2), pneumonia, bleeding repaired surgically, distal thrombosis (2), and ankle-brachial index (ABI) decrease; PS: cardiac death, congestive heart failure (2), dialysis, pneumonia, secondary angiography (to rule out endoleak), bleeding repaired surgically (5), iliofemoral thrombosis, femoral pseudoaneurysm, and decreased bilateral ABI; FE: stroke, transient ischemic attack, spinal ischemia, serum creatinine increase, 2-day postoperative intubation, secondary interventions (angiographic endoleak rule out and type Ia endoleak repair), persistent thigh numbness, blood transfusion (2), bleeding/vessel dissection requiring surgical repair/transfusion, lymphocele, distal thrombosis (2), bilateral endarterectomy/patching, and ABI decrease due to stenosis.
[a] *P* values determined per one-sided Blackwelder test (noninferiority).
[b] *P* values determined per two-sided Fisher exact test.
[c] The total number of patients with procedural technical failure, a major adverse event, or a vascular complication.

**Table IX.** Independent ipsilateral access site closure substudy results at 1 month

| *Outcome* | *PEVAR/PG (n = 50)* | *PEVAR/PS (n = 51)* | *FE (n = 50)* | *PG vs FE*[a] | *PS vs FE*[a] |
|---|---|---|---|---|---|
| Major access-related complications | 3 (6.0) | 6 (12) | 5 (10) | .005 | .100 |
| Vascular injury | 1 (2.0) | 5 (10) | 1 (2.0) | | |
| Lower extremity ischemia | 2 (4.0) | 1 (2.0) | 2 (4.0) | | |
| Bleeding/transfusion | 1 (2.0) | 1 (2.0) | 2 (4.0) | | |
| Nerve injury | 0 | 0 | 1 (2.0) | | |

*FE,* Femoral exposure; *PEVAR,* percutaneous endovascular aortic aneurysm repair; *PG,* ProGlide; *PS,* Prostar XL.
Results shown as number (% of group). Some patients experienced >1 event.
[a]*P* values determined per one-sided Blackwelder test (noninferiority).

**Table X.** Serious adverse events at 1 month

| *System organ class* | *PEVAR/PG (n = 50)* | *PEVAR/PS (n = 51)* | *FE (n = 50)* | *PG vs FE*[a] | *PS vs FE*[a] |
|---|---|---|---|---|---|
| Patients with ≥1 serious adverse event | 5 [10] (10) | 16 [28] (31) | 13 [23] (26) | .066 | .661 |
| Blood and lymphatic system disorders[b] | 1 [1] (2.0) | 1 [1] (2.0) | 3 [3] (6.0) | .617 | .362 |
| Cardiac disorders | 0 | 2 [2] (3.9) | 0 | — | .495 |
| Gastrointestinal disorders | 0 | 1 [1] (2.0) | 1 [1] (2.0) | 1.000 | 1.000 |
| General disorders/administration site conditions | 1 [1] (2.0) | 3 [3] (5.9) | 1 [1] (2.0) | 1.000 | .618 |
| Infections and infestations | 1 [1] (2.0) | 3 [3] (5.9) | 0 | 1.000 | .243 |
| Injury, poisoning, and procedural complications | 0 | 1 [1] (2.0) | 1 [1] (2.0) | 1.000 | 1.000 |
| Investigations | 3 [4] (6.0) | 1 [1] (2.0) | 4 [5] (8.0) | 1.000 | .362 |
| Metabolism and nutrition disorders | 1 [1] (2.0) | 1 [1] (2.0) | 0 | 1.000 | 1.000 |
| Nervous system disorders | 0 | 1 [1] (2.0) | 3 [3] (6.0) | .242 | .362 |
| Renal and urinary disorders | 2 [2] (4.0) | 4 [4] (7.8) | 2 [2] (4.0) | 1.000 | .678 |
| Respiratory, thoracic, and mediastinal disorders | 0 | 2 [3] (3.9) | 2 [2] (4.0) | .495 | 1.000 |
| Surgical and medical procedures | 0 | 1 [1] (2.0) | 0 | — | 1.000 |
| Vascular disorders | 0 | 4 [5] (7.8) | 4 [5] (8.0) | .118 | 1.000 |

*FE,* Femoral exposure; *PEVAR,* percutaneous endovascular aortic aneurysm repair; *PG,* ProGlide; *PS,* Prostar XL.
Results shown as number of patients [number of events] (% of group). Some patients experienced >1 event.
[a]*P* values determined per two-sided Fisher exact test.
[b]Blood and lymphatic system disorders detail by study arm: PEVAR/PG: anemia on postoperative day 1, treated by transfusion (two units of packed red blood cells); PEVAR/PS: anemia beginning on postoperative day 2, treated with blood transfusion; standard FE: intraprocedural hemorrhage of 1500 mL treated with nine units of packed red blood cells, anemia on postoperative day 1 treated with two units of packed red blood cells, and exacerbation of anemia beginning on the day of the procedure treated by blood transfusion.

No 6-month differences in other evaluations were observed. No stent fracture, device obstruction/occlusion, migration, or aneurysm sac increase was seen in any patient.

## DISCUSSION

This trial provides strong evidence for the safety and efficacy of totally percutaneous EVAR incorporating a preclose technique using the ProGlide suture-mediated closure device. Both academic and community institutions participated, with vascular surgeons (70%) and interventional specialists (30%) as part of a multidisciplinary team to permit broader assessment of PEVAR. Suitable, defined patient selection criteria were applied, and we have observed excellent outcomes in a representative patient population. Roll-in and trial phase technical success rates were similar for PEVAR/PG but were disparate for PEVAR/PS. This may suggest a difference in preclose technique-specific requirements necessary to ensure success.

With this study design, primary noninferiority of PEVAR/PG vs FE was achieved with respect to treatment success at both 1 and 6 months. A low incidence of PG major access-related complications was observed (6%). Technical failure primarily resulted in inadequate hemostasis control, but distal ischemia and access vessel stenosis were also observed. The PEVAR/PS arm did not achieve noninferiority in part because of a higher rate of technical failures. The rate of failures seen in the standard approach EVAR/FE arm probably reflects the active investigation and oversight mandated by the protocol and the independent adjudication incorporated into this trial. This degree of oversight was applied to all arms equally, however. The raw numbers of failures in both the PEVAR/PS and the FE groups were small, however, so further evaluation is likely to be warranted.

Clinical utility benefits after PEVAR included significantly reduced times to hemostasis and procedure completion. Nonsignificant trends favoring PEVAR were observed with respect to blood loss and time to hospital discharge. Our mean times to ambulation (16-19 hours) were shorter than those reported in the only single-center randomized trial (20-33 hours),[5] probably representing improved overall protocols. Overall 6-month mortality among the cohort is low (1.0%), with few serious adverse events in late follow-up, reflecting excellent standard of care among trial sites.

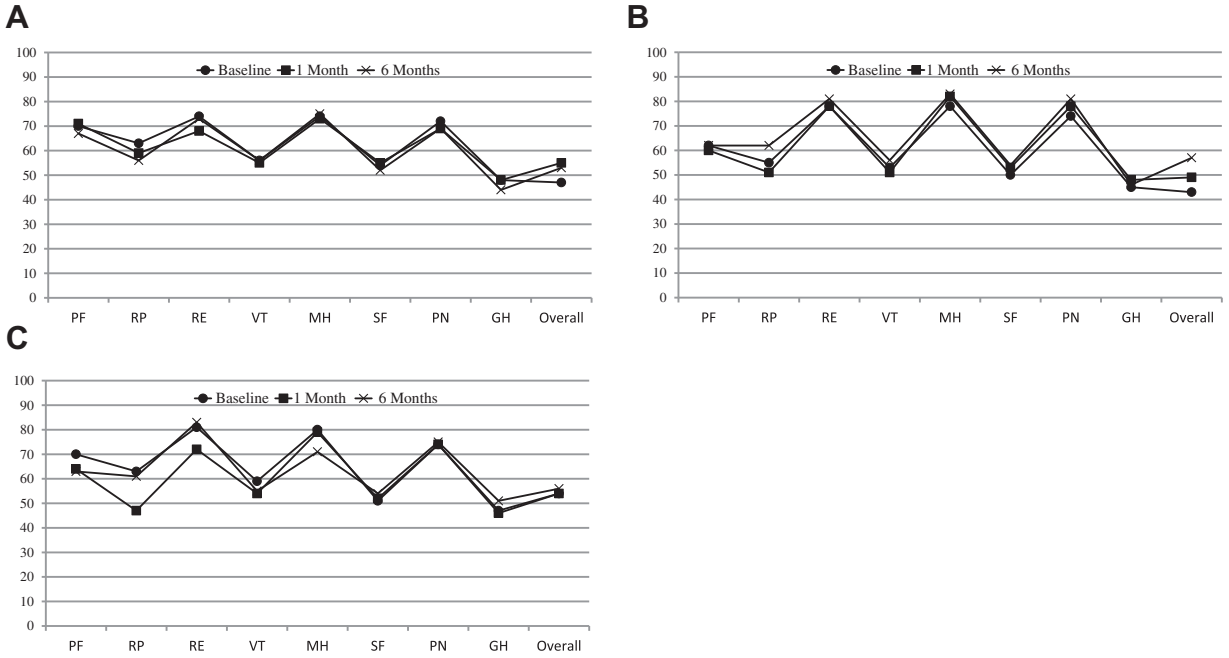



**Fig 2.** SF-36 quality-of-life questionnaire results over time. **A,** Percutaneous endovascular aortic aneurysm repair (PEVAR) ProGlide (PG) group results. **B,** PEVAR Prostar XL (PS) group results. **C,** Standard femoral exposure (FE) group results. The horizontal axis shows the SF-36 domain: *PF,* Physical function; *RP,* role limitation, physical; *RE,* role limitation, emotional; *VT,* vitality; *MH,* mental health; *SF,* social functioning; *PN,* bodily pain; *GH,* general health; overall.

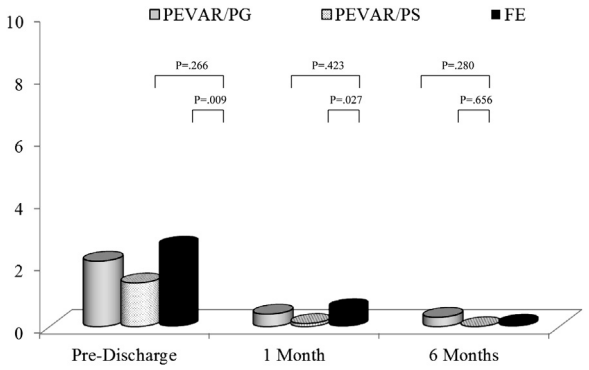
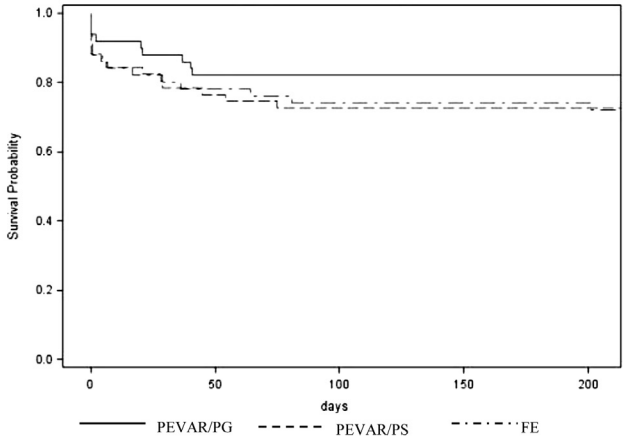



**Fig 3.** Ipsilateral groin pain. *P* values calculated by a two-sample *t*-test. *FE,* Femoral exposure; *PEVAR,* percutaneous endovascular aortic aneurysm repair; *PG,* ProGlide; *PS,* Prostar XL.

These results in a prospectively randomized population support the generalizability of totally percutaneous EVAR with this sheath-based endograft system and the ProGlide closure device using the study patient selection criteria. Patient selection criteria were applied to permit a realistic group comparison while avoiding inappropriate patient anatomies (eg, circumferential CFA calcification). Consequently, two groups in particular are not adequately addressed by these results. First, morbidly obese patients were excluded (body mass index cutoff of 40 kg/m$^2$); however, many think that this population may realize the greatest benefit of PEVAR because of morbidity reduction associated with groin incisions. Single-center evidence suggests PEVAR safety in the morbidly obese,[14] but we cannot conclude such. Second, our cohort included only 9.9% women, making broad generalization difficult. Consistent with recent reports that female patients are anatomically less likely to meet device eligibility criteria for EVAR in general[25] or for PEVAR,[16] only a small number of women met our inclusion criteria. Treatment success in women among groups in this study was similar (7 of 10 PEVAR; 4 of 5 FE), consistent with single-center studies suggesting PEVAR to be safe in carefully selected women.[16] Appropriate caution should be taken in expanding the applicability of this technique.[8,14]

Additional study limitations are noted. US guidance for CFA location/puncture was strongly recommended but not protocol mandated. The relatively infrequent use among study sites probably represents physician experience and comfort with PEVAR without US guidance. Although there are reports that US guidance aids in precise CFA preclose punctures and is a predictor of technical success,[26-28] its limited use in this trial did not influence PG success; nonetheless, it is not clear to what extent this influenced PS success. Also, the choice of anesthetic strategy was left up to the implanting physicians. Although local anesthesia or monitored anesthesia care has been suggested for PEVAR,[17] utilization in this trial was limited, so no specific conclusions can be drawn. This probably represents the comfort of each study site with local anesthesia protocols




| Days Post-Procedure | PEVAR/PG | | PEVAR/PS | | FE | |
|---|---|---|---|---|---|---|
| | No. at Risk | Survival (95% CL) | No. at Risk | Survival (95% CL) | No. at Risk | Survival (95% CL) |
| 0 | 50 | 1.00 | 51 | 1.00 | 50 | 1.00 |
| 30 | 44 | 0.88 (0.79, 0.97) | 40 | 0.78 (0.67, 0.90) | 39 | 0.78 (0.67, 0.89) |
| 90 | 41 | 0.82 (0.71, 0.93) | 37 | 0.73 (0.60, 0.85) | 37 | 0.74 (0.62, 0.86) |
| 210 | 41 | 0.82 (0.71, 0.93) | 37 | 0.73 (0.60, 0.85) | 36 | 0.72 (0.60, 0.84) |

Log-rank P=.437

**Fig 4.** Treatment success composite end point Kaplan-Meier analysis. *CL,* Confidence limit; *FE,* femoral exposure; *PEVAR,* percutaneous endovascular aortic aneurysm repair; *PG,* ProGlide; *PS,* Prostar XL.

(eg, if general anesthesia was used for EVAR previously, it was generally used during the trial). Mandated use of local anesthesia in the PEVAR arm would have biased results. It stands to reason that local anesthesia becomes more attractive with PEVAR adoption, but several other factors influence this decision (anesthesiologist experience/comfort, patient cooperation). Further, a recent report suggests that ambulatory, outpatient PEVAR is safe in up to 40% of patients.[29] This is likely where this procedure is headed.

Last, this trial was conducted in centers of excellence with experienced physicians, and thus the results need to be considered in that context. Selected investigators were well past their learning curve with both EVAR and the preclose technique. A recent article[30] reporting 82% PEVAR technical success suggested that the learning curve may be 30 cases. This conclusion, however, was drawn on the basis of an unacceptable 45% single-operator early technical success rate with Prostar XL. On the basis of the performance in our trial and the availability of procedure-specific training with the ProGlide device, we would expect the learning curve to be significantly shorter.

With judicious patient selection and adequate operator training and experience, excellent and sustainable outcomes with PEVAR comparable to those achieved in this trial will be realized. Approval of the Food and Drug Administration for PEVAR with the Endologix endovascular system and the ProGlide vessel closure device studied in this trial and the availability of an approved physician training/certification program have been accomplished. Implementation of the training program with specific attention to hands-on bench training and live case demonstration followed by proctored case completion through the learning curve to demonstrated proficiency is underway. As a result, this less-invasive alternative should be offered to and will benefit similarly selected patients.

## CONCLUSIONS

Among trained operators and in suitably selected patients, a totally percutaneous approach to EVAR using the Endologix sheath-based 21F endograft system with preclose vessel closure facilitated by the ProGlide closure device is safe with a low incidence of access-related complications. PEVAR is less invasive, takes less time to complete and to achieve hemostasis, and may positively influence other aspects of the patient's safety and overall experience. Keys to success are intensive operator training and experience, careful patient selection, and diligent attention to procedural conduct.

The following physicians and institutions were involved in this multicenter randomized controlled trial: J. Michael Bacharach, MD (North Central Heart Institute, Sioux Falls, SDak); Christian Bianchi, MD (VA Loma Linda, Loma Linda, Calif); Lee Goldstein, MD (VA Miami, Miami, Fla); Homayoun Hashemi, MD (Inova Fairfax Hospital, Falls Church, Va); Paul Jones, MD (Mercy Hospital, Chicago, Ill); Nikhil Kansal, MD (VA San Diego, San Diego, Calif); Barry Katzen, MD (Baptist Cardiac and Vascular Institute, Miami, Fla); Zvonimir Krajcer, MD

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## AUTHOR CONTRIBUTIONS

Conception and design: PN, ZK
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Writing the article: PN
Critical revision of the article: PN, ZK, NK, VR, CB, HH, PJ, JB
Final approval of the article: PN, ZK, NK, VR, CB, HH, PJ, JB
Statistical analysis: PN, ZK
Obtained funding: Not applicable
Overall responsibility: PN

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## DISCUSSION

**Dr Zachary K. Baldwin** (*Jackson, Miss*). Despite the lack of high-quality evidence for efficacy, percutaneous access for endovascular aneurysm repair has become commonplace among vascular interventionalists. In the right hands, it has the potential to mitigate the morbidity associated with open groin incision, speed recovery, and accelerate discharge. However, in the wrong hands and without proper training and judgment, there is the potential for grave complication.

With this in mind and with CMS looking over everyone's shoulder in terms of outcomes data and reimbursement, the authors should be commended on putting together a thoughtful multicenter trial of percutaneous EVAR and traditional EVAR. The study provides level 1 evidence of noninferiority when comparing percutaneous to open access. From a clinical standpoint, PEVAR was found to either trend toward or significantly impact procedure time, time to hemostasis, blood loss, and mean time to hospital discharge. The study outcomes suggest that PEVAR has favorable impact on the perioperative course of EVAR patents. Given the stent graft utilized, French size, and closure device, these results appear to be applicable to other EVAR devices on the market.

That being said, the core question of comparative effectiveness research is which treatment works best, for whom, and under what circumstances? Answering these questions using this study is somewhat difficult given that the patient cohort is notable for being predominantly white males with large iliac vessels and average BMIs $<30$. The morbidly obese are thought to be a group likely to benefit from a percutaneous approach. However, it is difficult to confirm or deny these suspicions based on this particular study. Iliac morphology may also play a role in deciding between percutaneous and open vessel access. It has been my experience that advancing and withdrawing sheaths in borderline diameter arteries with significant calcification and/or tortuosity can increase shear at the level of arteriotomy. Are such cases better approached percutaneously, or does open exposure mitigate potential injury?

Finally, one potential benefit of percutaneous access is allowing for an "awake" EVAR. Avoidance of a general anesthetic should have an impact in terms of perioperative morbidity/mortality when performing EVAR. Unfortunately, there is little information as to whether utilization of PEVAR impacted anesthetic choice among participating physicians.

Dr Nelson and colleagues should be congratulated on a very important and timely study that provides much needed evidence for percutaneous access in performance of EVAR. I do not believe that the study can be interpreted by interventionalists as a license to access all patients percutaneously. Instead, the study provides clear evidence of the percutaneous technique's safety and will, hopefully, set the stage for studies in the future defining which patients benefit most from a percutaneous approach.

**Dr Peter R. Nelson.** Thank you, Dr Baldwin, for your comments and for your review of our manuscript. I assure you that you are a candidate for PEVAR. I want to respond to one of the comments that you made. I think we have to be a little careful extrapolating these data to all endovascular devices or all large-bore access procedures since this study was conducted using a single endovascular stent graft system. I fully realize that people are using this technique for other systems, but this trial obviously was specifically focused on one device.

With respect to your first question on obesity, I think we all feel that the obese patient is really where the PEVAR technique could offer the most benefit because the obese suffer the most morbidity from groin wound complications. But, in designing a rigorous clinical trial, we have to be cautious upfront because, in the literature, the obese also have the highest complication rate of percutaneous access. So in terms of this being the first phase of the trial, it was reasonable to exclusion. The 7-cm distance required from the skin to the femoral artery was defined by the length of the micropuncture needle. We felt that if the needle could not reach the femoral artery easily, then maybe that should be an anatomic exclusion. We all know that you can indent the skin and get access in those situations, but at least for the purposes of the trial, 7 cm was the maximum length allowable.

Regarding your second question on anesthetic options used in the trial, investigators came into the trial with a certain established practice or preference in terms of what anesthetic strategy they used, and we did not see a significant change from this baseline practice. I think that if you were a local anesthetic user before, you used it in the trial. If you used general anesthetic, you used it in the trial. We did not see people switching to local anesthesia, and we did not require or suggest that in PEVAR cases. I think your point is very important, however, because this technique definitely opens the door to very feasible use of local anesthetic, which could result in even shorter hospital stays and even move us toward outpatient EVAR, and I think that is where we need to be thinking.

Your third question on iliac morphology is an important question. The trial focused most of the exclusion criteria on the common femoral artery anatomy and calcification, but we did collect data on the degree of calcification in the iliac access vessels. The amount of calcification as I showed was similar between groups and it did not impact the success of the percutaneous access overall. Greater calcification did, however, result in an increased number of iliac interventions, such angioplasties and adjunctive stenting for the access vessel. What I do in my practice is if I have someone who has a heavily calcified iliac access vessel, I still am comfortable doing percutaneous, but in that case, I might more conservatively use a series of hydrophilic dilators to sequentially dilate the access to allow the device to pass. I personally have not had problems with that affecting the success of percutaneous approach itself.

One additional comment regarding the influence of iliac anatomy is that tortuosity, which we did not critically scientifically evaluate in this trial, is a significant variable. If you have a very tortuous iliac system, and anyone who has done this will know, the Proglide device is just a little bit short, such that, in a very tortuous iliac system, you may have difficulty maintaining wire access. If the Proglide device slides back into the iliac system, you have to traverse that tortuosity twice at least to get the access and secure all of your preclosure devices. Therefore, iliac tortuosity is something I think worthy of looking at as you plan cases, since it poses some challenges that may require some thought to ensure success.

## INVITED COMMENTARY

**William A. Marston, MD,** *Chapel Hill, NC*

As devices for endovascular aneurysm repair (EVAR) have been packaged into smaller and more flexible sheath systems, the potential for percutaneous aneurysm repair has been realized with the use of closure devices and specific pre-closure procedures.

In this carefully designed and executed prospective randomized trial, the authors have compared standard surgical femoral access EVAR (SEVAR) with percutaneous EVAR (PEVAR) using two different devices designed for femoral artery closure. Sites