

Physician-modified endovascular grafts for the treatment of elective, symptomatic, or ruptured juxtarenal aortic aneurysms

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Objective: To determine if a physician-modified endovascular graft (PMEG) is a safe and effective method of treating juxtarenal aortic aneurysms in patients considered to be unsuitable for open surgical repair.

Methods: A retrospective, nonrandomized, single institution evaluation of the safety and efficacy of physician modification of a currently Food and Drug Administration-approved device (Zenith Flex; Cook Inc, Bloomington, Ind) to preserve branch vessels when used in the treatment of patients with elective, symptomatic, or ruptured juxtarenal aortic aneurysms.

Results: Forty-seven consecutive patients underwent fenestrated endovascular repair using PMEG over a 3-year period. Thirty-eight patients (80%) were symptomatic or had rapid aneurysm expansion. Eighty-five percent of patients were American Society of Anesthesiologist category III or IV. Eight-two fenestrations were created for 58 renal arteries, 16 superior mesenteric arteries, three celiac arteries, and the rest accessory vessels. Mean follow-up was 607 days, with a range of 425 to 1460 days. Mean contrast usage and fluoro time were 98 mL and 48 minutes. Technical success rate was 98%, and freedom from aneurysm-related death was 98%. There were six complications (13%). Three (6%) were access related, and three (6%) were procedure related and included one stroke, one case of renal failure, and one branch artery dissection. On follow-up, six patients (13%) had endoleak. There was one type 1 endoleak and five type 2 endoleaks. In-hospital and 30-day mortality was 2%, with one patient expiring due to aspiration on the ward after successful endovascular repair. Two patients died during follow-up; one at 58 days due to cessation of dialysis and one at 485 days due to stent graft migration and occlusion of the superior mesenteric artery. There were two deaths in the first year, one in the second year, and zero in the most recent year of experience. One patient with endoleak (2%) had aneurysm sac expansion at 1 year requiring secondary intervention.

Conclusions: PMEG is a safe and effective alternative for treating patients with juxtarenal aneurysms who have no other alternatives for repair. Longer-term follow-up is needed to assess the durability of repair and potential for device-related complications. (*J Vasc Surg* 2012;56:601-7.)

Endovascular treatment of aortic pathology has become mainstream and standard practice in most institutions for the treatment of patients with infrarenal aortic aneurysms who are anatomically suitable for repair. The majority of patients who are not eligible for endovascular repair typically harbor proximal aortic neck deficiencies. Reasons for ineligibility include short proximal necks and juxtarenal aneurysms. In clinical trials in the United States and in other countries, fenestrated technology has been used to extend the applicability of endovascular techniques to more patients who would be deemed ineligible for standard infrarenal bifurcated repair.¹⁻⁷ These grafts are customized to the patient and typically require between 6 and 12 weeks to manufacture. Patients presenting with symptomatic and ruptured juxtarenal aortic aneurysms would therefore be ineligible for these techniques without an “off-the-shelf”

option. The objective of this study was to determine if an immediate physician-modified endovascular graft (PMEG) is a safe and effective method for treating juxtarenal aortic aneurysms in patients deemed unsuitable for traditional open surgical repair or who, while presenting in an urgent fashion, cannot wait for entry into a clinical trial.

METHODS

This study was approved by the Institutional Review Board at the University of Washington and was a retrospective review of a consecutively logged, nonrandomized evaluation of the safety and efficacy of PMEG. This entire study was conducted at Harborview Medical Center in Seattle, Washington, and involved customized device modification of a commercially available and Food and Drug Administration (FDA)-approved aortic stent graft (Zenith Flex Device; Cook Inc, Bloomington, Ind). Patients were chosen based upon presentation with a juxtarenal aortic aneurysm and with no alternative for open repair.

During the 3-year period of study and as a point of reference, there were 533 aortic procedures done at Harborview Medical Center. Abdominal aortic procedures accounted for 352 of these procedures. Overall, there were 242 nonruptured abdominal aortic aneurysms, of which 41 were treated using an open approach and 201 using an endovascular approach. One hundred ten patients presented with a ruptured abdominal aortic aneurysm during the study period, of which 32 were treated using an open

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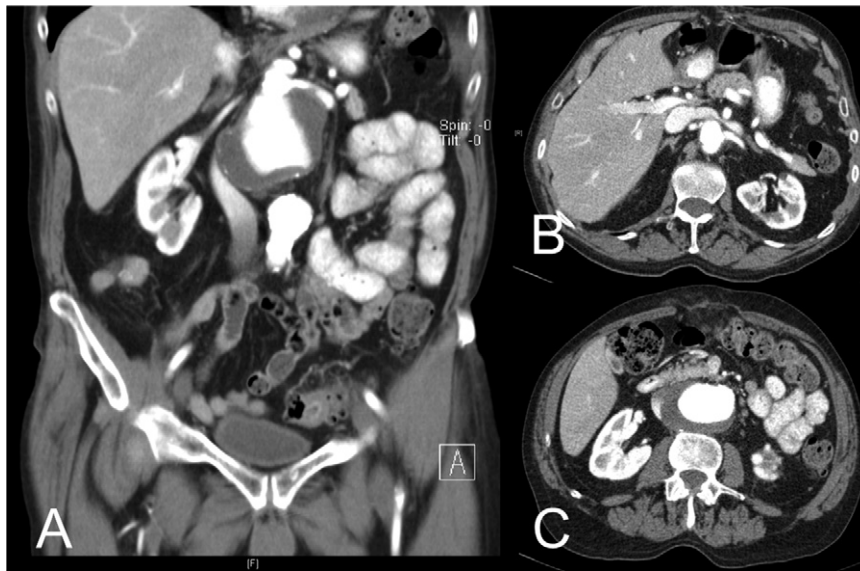


Fig 1. A computed tomographic angiogram from a representative patient demonstrating a short infrarenal aortic neck and a large juxtarenal aneurysm. **A**, Coronal computed tomographic angiogram image. **B**, Left renal artery originating from a short aortic neck immediately cephalad to a large juxtarenal aneurysm (**C**).

approach and 78 using an endovascular approach. Including both nonruptured and ruptured juxtarenal aneurysms, there were a total of 74 patients undergoing open repair versus the 47 patients who serve as the basis for this report on PMEG.

A computed tomographic angiogram from a representative patient is shown in Fig 1 demonstrating a short infrarenal aortic neck and a large juxtarenal aneurysm. Three-dimensional reconstruction imaging software (Aquarius; Tera-Recon, Foster City, Calif) was routinely used for preoperative planning to ensure precise placement of aortic fenestrations in “clock face” positions for branch vessel preservation.

Device preparation. All operative procedures were performed concurrently with back table device modification while the patient was being prepared for surgery. The device was chosen according to standard instructions for use sizing guidelines, and a routine aortic oversizing of 10% to 15% for the main body graft was utilized. The bifurcated graft was unshathed on a separate table, and a sterile marking pen was used to mark the location of the fenestrations based on both length and clock face measurements that had been previously determined with reconstruction imaging software. Minor adjustments were made in localization of the fenestrations to allow for maximum usage of strut-free fenestrations when possible. When this was not possible and multiple fenestrations were required, struts within fenestrations were preferentially avoided for the renal arteries. An ophthalmic Bovie cautery device (Medtronic, Minneapolis, Minn) was used to carefully burn the Dacron fabric to create all fenestrations and thus avoid fabric fraying. Gold, 15-mm Amplatz Gooseneck Snares (ev3 Endovascular Inc, Plymouth, Minn) were then used to

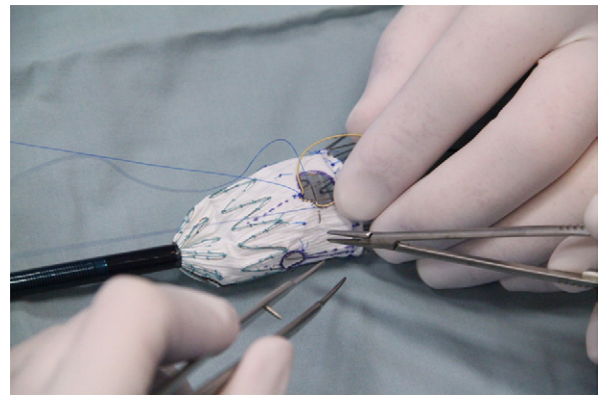


Fig 2. Gold, 15-mm Amplatz Gooseneck Snares (ev3, Plymouth, Minn) were then used to reinforce all fenestrations. These were hand sewn into place using 4-0 Prolene suture in a 720 degree running fashion.

reinforce all fenestrations. These were hand-sewn into place using 4-0 Prolene suture in a 720 degree running fashion (Fig 2). A typical final PMEG device is depicted in Fig 3. Diameter-reducing ties were then used to constrain the device along its posterior border (opposite the superior mesenteric artery [SMA] and or celiac fenestration at 6 o'clock) by rerouting the existing proximal trigger wire through and through the graft material at the midportion of each of the top two Z stents. The constraining ties were then tied down into place over the trigger wire. The bare stent was then reconstrained in the top cap, and the entire graft wetted with heparinized saline and then reloaded into the existing sheath.

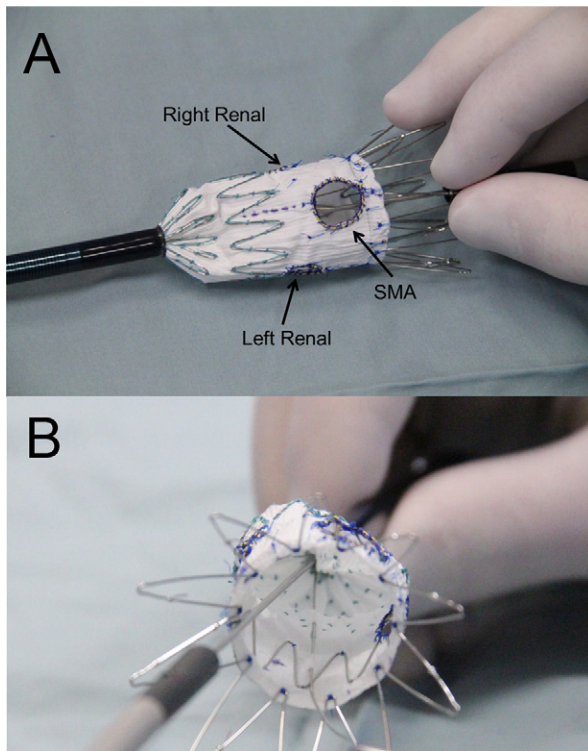


Fig 3. A typical physician-modified endovascular graft (PMEG) prior to device repackaging (A). Fenestrations for the superior mesenteric artery (SMA) (*struts present*) and left and right renal arteries (*strut-free*) were created for this particular patient. B, Rerouting of the trigger wire to allow for placement of graft constraining ties.

PMEG procedural details. The majority of these procedures were performed in a modern angiography suite utilizing a Philips Allura Xper FD 20/10 system (Philips Healthcare, Amsterdam, The Netherlands). Three cases were for rupture and were performed in a standard operating room with a portable imaging unit (OEC 9900 Elite; General Electric, Chalfont St Giles, United Kingdom). Common femoral access was almost always achieved in a standard percutaneous fashion and the stent graft delivered up into position near the visceral vessels. A contrast aortogram with 10 mL of dilute contrast injected at 25 mL/s was performed with the PMEG in place to mark the visceral vessels (Fig 4). Proper orientation of the graft (SMA anterior) was confirmed by rotating the graft clockwise under fluoroscopy and confirming that the SMA fenestration moved from left to right instead of right to left, which would denote a posterior orientation of the SMA fenestration. The graft was then carefully deployed down to the opening of the contralateral limb. The contralateral limb was then selected, and, typically, an 18 to 20 Fr sheath inserted into the contralateral limb over a stiff wire under direct fluoroscopic visualization. Double 6 or 7 Fr Ansel sheaths (Cook Inc) were used through separate punctures in this blank sheath to individually select the renal arteries

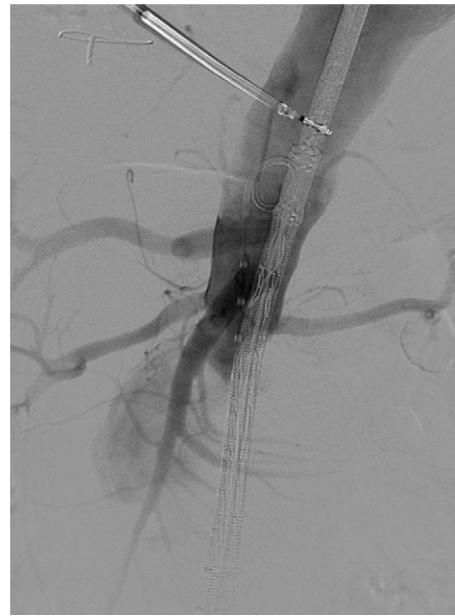


Fig 4. Contrast aortography demonstrating the origins of all four visceral vessels with the physician-modified endovascular graft (PMEG) device in situ prior to deployment.

while maintaining stability of the PMEG device. Once the renal arteries were completely selected with each 6 or 7 Fr sheath, diameter-reducing ties were freed by pulling the proximal trigger wire out, then the top cap was released and the main body deployed. At this time, the remainder of the main body device was deployed, the top cap retrieved, and a CODA balloon (Cook Inc) was used to seat the proximal portion of the graft in the zone of the visceral aortic stent graft segment (Fig 5). The renal arteries were then individually stented with appropriately sized iCAST stents (Atrium USA, Hudson, NH), and the stents were flared proximally into the aortic stent graft using either 8 or 9 mm standard angioplasty balloons. The remainder of the procedure involved standard placement of docking limbs to the level of each iliac bifurcation and seating of the stent graft overlap and seal zones with a molding balloon (CODA, Cook Inc). A completion aortogram was performed at the completion of each procedure (Fig 6).

RESULTS

A total of 47 patients with asymptomatic, symptomatic, or ruptured juxtarenal aortic aneurysms were treated between April 2007 and April 2010. Thirty-eight patients (80%) were either symptomatic (abdominal pain or aneurysms that were tender to palpation) or had documented rapid aneurysm expansion as evidenced by an increase in aneurysm diameter of 0.5 cm in the previous 6 months or 1.0 cm in the previous year. Forty patients (85%) were American Society of Anesthesiology (ASA) category 3 or 4. Mean follow-up was 607 days, with a range of 425 to 1460 days. Follow-up imaging of the procedure described above is depicted in Fig 7.

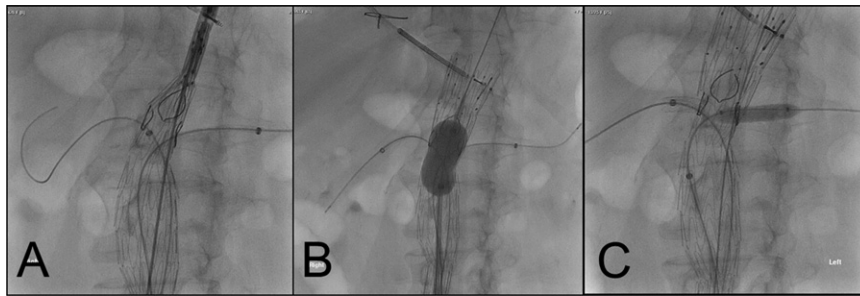


Fig 5. Physician-modified endovascular graft (PMEG) procedure. **A**, Both renal arteries have been selected through the renal fenestrations and a sheath advanced into the left renal artery. **B**, Seating of the proximal graft with the renal sheaths securely in place. **C**, Stent grafting and subsequent flaring of the renal artery stents.



Fig 6. Completion aortogram demonstrating absence of endoleak and good alignment of all three visceral vessel fenestrations.

Demographics and patient characteristics are listed in Table I. Nearly half of the patients had a history of coronary artery disease, nearly one-third had a history of congestive heart failure, and one-third had chronic obstructive pulmonary disease. Mean age was 75 years (range, 54-87 years), mean aneurysm diameter was 5.8 cm, and mean ASA class was 3. Three patients presented with a ruptured juxtarenal aortic aneurysm and were ASA category 4E.

Overall, 82 fenestrations were created for 58 renal arteries, 16 SMAs, three celiac arteries, and five accessory renal arteries. Procedural details are listed in Table II. Mean operative time was 185 minutes (range, 66-349 minutes), mean fluoroscopy time was 48 minutes (range, 4.1-119.2 minutes), and mean contrast usage was 98 mL (range, 30-204 mL). Estimated blood loss was, on average, 119 mL (range, 50-750 mL), and general anesthesia was utilized in 94% ($n = 44$) of cases. Technical success rate was 98%, and freedom from aneurysm-related death was 98%. Mean length of stay was 4 days (range,

2-30 days). Graft modification times averaged 48 minutes but were not recorded on all patients.

Overall, there were six complications in this series (13%). Three were access site-related (6%), and three (6%) were procedure-related, including one stroke, one permanent renal failure, and one renal artery dissection. Six patients had endoleaks (13%). There was one type 1 endoleak that required intervention and subsequent repair. Of the five type 2 endoleaks, one required secondary intervention due to aneurysm sac growth at 1 year.

In-hospital and thirty-day mortality was 2% ($n = 1$). This particular patient had an underlying diagnosis of multiple myeloma and had a “Do Not Resuscitate” order in her medical record. She unfortunately aspirated on the hospital ward on postoperative day 2, and her wishes for no resuscitation were abided by. Two patients died during follow-up. One patient died at 58 days due to voluntary cessation of dialysis, and one patient died at 485 days due to endograft migration and SMA occlusion. The latter patient was an 87 year old who presented with a symptomatic juxtarenal aneurysm, and the fenestrations were not stented. This was early on in our experience and led to a mandatory policy of at least one visceral artery stent per PMEG procedure to mitigate the risk of stent graft migration. Kaplan-Meier survival curves for the entire cohort are depicted in Fig 8.

DISCUSSION

Endovascular repair of aortic aneurysmal disease has become a mainstay of treatment in most modernized countries. The paravisceral segment of the aorta has become a focus of improved device design in order to apply advanced endovascular technologies to more and more patients who would be deemed “unsuitable” candidates based on anatomic criteria. These improved device designs have included both branched and “fenestrated” (fenestra: Latin “window”) constructs. There exists a certain degree of variability in the origins of the visceral vessels in humans, and hence a customized design has been promoted with each device custom-made for any specific patient. As one might imagine, any device customization involves a time delay between patient sizing, the manufacture of the de-

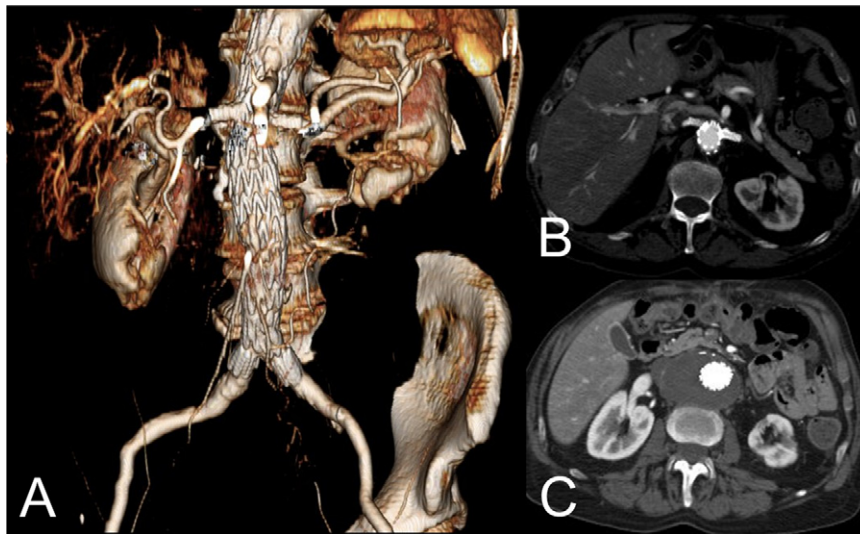


Fig 7. Six-month follow-up imaging in patient depicted in Figs 1-6.

Table I. Demographics and patient characteristics

Demographics	N (%)
Male	27 (57.4)
Coronary artery disease	23 (48.9)
Congestive heart failure	13 (27.7)
Hypertension	45 (95.7)
Chronic obstructive pulmonary disease	16 (34.0)
Diabetes mellitus	10 (21.3)
Hyperlipidemia	34 (72.3)

Table II. Physician-modified endovascular graft procedure details

Procedural details	Mean or % (range)
Operative time	185 minutes (66-349 minutes)
Fluoroscopy time	48 minutes (4.1-119.2 minutes)
Contrast usage	98 mL (30-204 mL)
Estimated blood loss	119 mL (50-750 mL)
General anesthesia	94%

vice, and the actual implantation event. Currently, this process takes, in the best of circumstances, 8 to 12 weeks. These emerging devices are widely available in countries outside the United States and unfortunately only in select centers within the United States under an umbrella of an investigational trial.

The concept of fenestrated stent grafting was first described by Park et al in a canine model,⁸ and early experience in humans was described by Chuter et al in 1999.⁹ There have been several single center^{2,4,5,7} and few multi-center trials^{1,3,6} evaluating the use of fenestrated endografts in patients with juxtarenal aneurysms. These studies all share remarkable results of low mortality, averaging 1% to 2% at 30 days, and low rates of branch

vessel occlusion. In all but one of these studies, there were zero aneurysm-related deaths. The only aneurysm-related death was in a patient who experienced massive bleeding during redo surgery for infection.⁴ In an attempt to offer this technique to some patients who have no other options for aneurysm repair, some authors have attempted to modify existing stent grafts.^{10,11} The durability of this approach has yet to be vetted and is the basis for this report on our initial experience. Until an “off-the-shelf” device is available, patients with rapidly expanding, symptomatic, or ruptured juxtarenal aneurysms who are poor candidates for open surgical repair have limited options other than immediate physician modification or PMEG.

Our results with PMEG compare favorably with the existing literature. PMEG was associated with a 2% 30-day mortality in a single patient who died of an aspiration event on the first postoperative day. Immediately apparent when analyzing our data is that our average number of fenestrations per patient is 1.75 compared with two to three in other studies.^{1-3,6} We began this program in April 2007, treating patients with discrepant renal arteries and a single fenestration for one low-lying renal artery. After a dozen or so patients, we began to reach higher into more normal aorta, realizing that the ability to seal was better when the seal zone was in the healthiest portion of aorta. This required more precise planning and incorporation of between two and four fenestrations per procedure.

There exists an obvious legal risk to modifying an existing FDA-approved medical device that involves product liability. Once a physician decides to modify a device that has been intended for other indications, the manufacturer can deny any responsibility for a malfunctioning device, and the physician who chose to modify the device becomes the responsible party. Due to ethical and legal

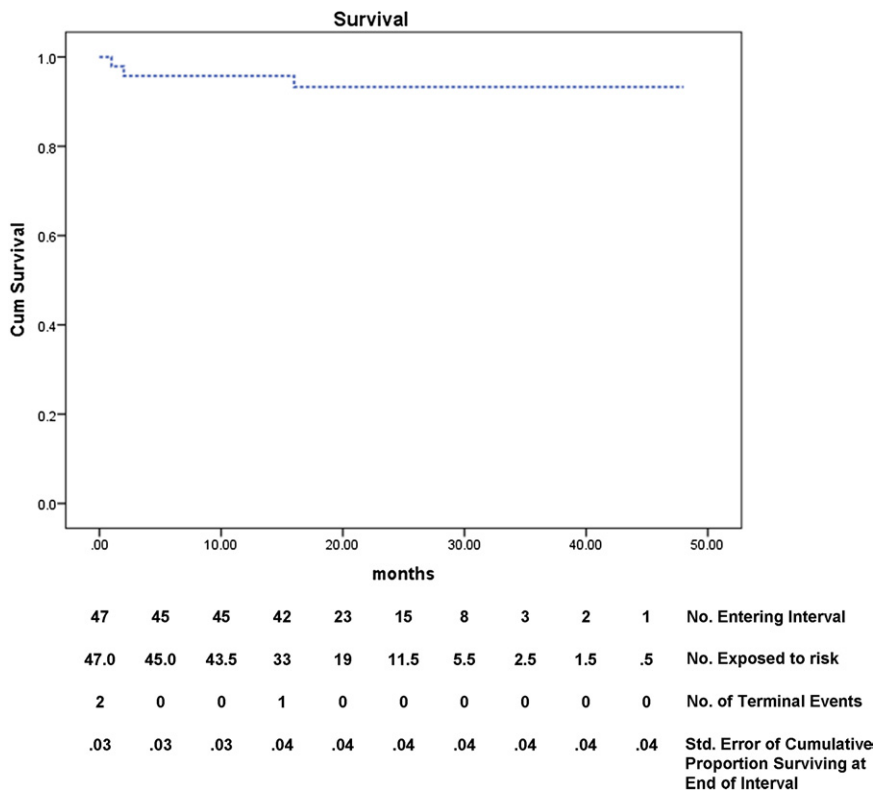


Fig 8. Kaplan-Meier survival curves depicting cumulative survival for the entire cohort of patients undergoing physician-modified endovascular graft (PMEG).

implications of performing device modification without an Investigational Device Exemption (IDE), in April of 2010, we elected to perform an external review of our experience (the basis of this report) under an Institutional Review Board (IRB)-approved protocol at the University of Washington. We then used these data to approach the FDA with a formal IDE application to prospectively study PMEG for patients with juxtarenal aneurysm pathology. In January 2011, we were given full approval from the FDA to conduct this IDE at the University of Washington. We began enrolling patients into this IDE in March 2011 and currently have performed 19 successful PMEG procedures. The practice of PMEG is now being attempted at more and more centers in the United States outside of a formal IDE. It is the author’s opinion that PMEG will definitely play a future role in the management of these complex patients. In fact, in some centers, it may play the only role due to comparative effectiveness and low cost if it can be shown to be just as safe and effective as commercial custom devices, which require extensive manufacture times and may be more costly.

It should be noted that fenestrated endografting in and of itself has not been validated in a prospective, randomized fashion. Mortality rates for open repair of juxtarenal aneurysms are often quoted to be quite low in high-volume centers, which does not accurately reflect the true operative mortality rate in most centers. What is required are accurate

multi-center studies assessing the current true outcomes of open juxtarenal aneurysm repair to benchmark against current fenestrated approaches.

CONCLUSIONS

In conclusion, PMEG seems to be a safe and effective alternative for treating patients with asymptomatic, symptomatic, and ruptured juxtarenal aortic aneurysms who have limited alternatives for repair. Longer-term follow-up is needed to determine the durability of this approach and the potential for device-related complications. In the future, there must be the availability of “off-the-shelf” endografts or the capability of immediate modification of currently available stent grafts to treat patients with symptomatic or ruptured aortic aneurysms. It is the author’s opinion that immediate device modification should be performed only at centers completely familiar with all advanced endovascular aortic and visceral artery techniques and a high volume (at least 30-50 patients per year or two to four per month) of these fenestrated procedures.

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AUTHOR CONTRIBUTIONS

Conception and design: BS

Analysis and interpretation: BS

Data collection: BS

Writing the article: BS

Critical revision of the article: BS

Final approval of the article: BS

Statistical analysis: Not applicable

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Overall responsibility: BS

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