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Prophylactic Perigraft Arterial Sac Embolization During EVAR: Minimizing Type II Endoleaks and Improving Sac Regression

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Background: Type II endoleaks (ELII) are the most common complication following endovascular aneurysm repair (EVAR). Persistent ELII require continual surveillance and have been shown to increase the risk of Type I and III endoleaks, sac growth, need for intervention, conversion to open or even rupture, directly or indirectly. These are often difficult to treat following EVAR, and there are limited data regarding the effectiveness of prophylactic treatment of ELII. The aim of this study is to report the midterm outcomes of prophylactic perigraft arterial sac embolization (pPASE) performed in patients undergoing EVAR.

Methods: This is a comparison of 2 elective cohorts of those undergoing EVAR using the Ovation stent graft with and without prophylactic branch vessel and sac embolization. Patients who underwent pPASE at our institution had their data collected in a prospective, institutional review board-approved database. These were compared against the core lab-adjudicated data from the Ovation Investigational Device Exemption trial. Prophylactic PASE was performed at the time of EVAR with thrombin, contrast, and Gelfoam if the lumbar or mesenteric arteries were patent. Endpoints included freedom from ELII, reintervention, sac growth, all-cause mortality, and aneurysm-related mortality.

Results: Thirty-six patients (13.1%) underwent pPASE, while 238 patients (86.9%) had standard EVAR. Median follow-up was 56 months (33−60 months). The 4-year freedom from ELII estimates were 84% for the pPASE versus 50.7% for the standard EVAR group ($P = 0.0002$). All aneurysms in the pPASE group remained stable in size or demonstrated regression, whereas aneurysm sac expansion was seen in 10.9% of the standard EVAR group, $P = 0.03$. At 4 years, mean AAA diameter decreased by 11 mm (95% CI 8−15) in the pPASE group versus 5 mm (95% CI 4−6) for the standard EVAR group, $P = 0.0005$. There were no differences in the 4-year freedom from all-cause mortality and aneurysm-related mortality. However, the difference in reintervention for ELII trended toward significance (0.0% vs. 10.7%, $P = 0.1$). On multivariable analysis, pPASE was associated with a 76% reduction in ELII [(95% CI): 0.24 (0.08−0.65), $P = 0.005$].

Conclusions: These results suggest that pPASE in those undergoing EVAR is safe and effective in the prevention of ELII and significantly improves sac regression over standard EVAR while minimizing the need for reintervention.

Conflict of interest: The authors have nothing to disclose.

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INTRODUCTION

EVAR is the dominant modality of abdominal aortic aneurysm (AAA) repair today, accounting for an estimated 74% of all intact AAA repairs in 2014.[1] Numerous studies have demonstrated lower perioperative morbidity and mortality with EVAR compared to open aneurysm repair,[2–4] but these benefits have been shown to decrease over time due to late complications and reinterventions.[5–7]

ELII are the most common complication following EVAR.[8] Ignoring lumbar arteries and a patent inferior mesenteric artery remains one of the major differences between EVAR and open aneurysm repair and is one of the main reasons why EVAR requires more surveillance. Persistent type II endoleaks require continual surveillance and have been shown to increase the risk of type I and III endoleaks, sac growth, need for intervention, conversion, or even rupture.[9,10] Current techniques of secondary intervention for ELII remain costly and have unclear long-term efficacy due to continued sac expansion.[11] Thus, primary prevention of ELII may provide benefits in terms of both patient care and healthcare costs.

Preoperative side branch embolization or intraoperative sac embolization have shown potential to prevent future occurrence of ELII, although current evidence remains limited.[12]

The sac coil embolization for prevention of endoleak randomized trial demonstrated that aneurysm sac coil embolization significantly decreased reintervention rates as well as aneurysm diameter and volume at 2 years.[13] The rate of ELII in the experimental arm was lower at 1, 6, and 12 months but not significant at 2 years.

We previously reported the results of prophylactic perigraft arterial sac embolization (pPASE) in a prospectively maintained institutional database.[14] The aim of this study is to compare results from this database against core lab adjudicated data from the Ovation stent graft Investigational Device Exemption (IDE) trial to evaluate midterm outcomes of pPASE in patients undergoing EVAR with the Ovation device. This analysis serves to provide a control arm for our pPASE patients while additionally removing variability in stent graft choice as a potential effect modifier.

Type of Research

- Retrospective comparison between a single-center prospectively maintained database cohort and an IDE trial cohort.

Key Findings

- In this study, we included patients who underwent endovascular aneurysm repair (EVAR) with the Ovation stent graft, the use of prophylactic perigraft sac embolization was associated with a significant reduction in the incidence of type II endoleak (ELII) and sac expansion.

Take Home Message

- Prophylactic perigraft sac embolization proves to be safe and effective in the prevention of ELII and sac expansion.

METHODS

Study Population

This is a comparison of 2 elective cohorts of those undergoing EVAR using the Ovation stent graft with and without prophylactic branch vessel and sac embolization. Patients who underwent pPASE at our institution were compared against the core lab-adjudicated data from the Ovation IDE trial.

pPASE Cohort

We performed a retrospective review of a prospectively maintained database of all patients who underwent prophylactic PASE at the time of EVAR between 2015 and 2021. Patients with large common iliac aneurysms requiring EVAR and those with ruptured aneurysms were excluded from the study. Prophylactic PASE was performed in patients with patent IMA or LA on sac angiogram at the time of EVAR using a combination of thrombin, contrast, and Gelfoam as previously described.[14]

In our institution, pPASE is accomplished within 5–10 min, and the cost of a Gelfoam sheet and 2,000 units of synthetic thrombin is $41.

The institutional review board approved this study, and individualized patient consent was waived since the study involved only deidentified data.

Ovation IDE Cohort

This group comprised 238 consecutive patients who underwent EVAR with the Ovation stent graft between November 2009 and October 2012 as part of the Ovation IDE pivotal and continued access trials. A detailed description of the trial design has been previously published.[15]

The study protocol and informed consent were approved by an institutional review board or ethics

committee, and all study participants gave written informed consent before participating in the trial.

Endpoints

The primary endpoint was freedom from ELII at 4 years. Secondary endpoints included 4-year freedom from reintervention for ELII, freedom from any aneurysm-related reintervention, aneurysm sac size changes, freedom from all-cause mortality (ACM), aneurysm-related mortality (ARM), and nontarget embolization (NTE) for the pPASE group.

Statistical Analysis

Continuous and categorical covariates were analyzed using the Student's *t*-test, medians, the Fisher exact test, and the χ^2 test as appropriate. Kaplan-Meier curves were used to estimate survival distributions. A comparison between survival curves was performed with the Mantel-Cox log-rank test. Multivariate Cox regression models were used to assess the impact of pPASE on the main outcomes. The variables included in the models were selected based on clinical and anatomic relevance or significance level ($P < 0.1$) in univariate analysis.

Statistical significance was estimated at $P < 0.05$. All statistical analysis was performed using Stata 16 software (StataCorp LLC, College Station, Tex.).

RESULTS

Study Cohort

Thirty-six patients (13.1%) underwent pPASE, while 238 patients (86.9%) had standard EVAR. Median follow-up was 56 months (IQR: 33−60). Patients in the standard EVAR group were older (73.3 ± 8.3 years vs. 70.4 ± 8.9 years, $P = 0.05$) and more likely to be female (18.9% vs. 0%, $P = 0.004$). Regarding lifestyle variables and comorbidities, patients undergoing pPASE were more likely to be smokers (100% vs. 71.4%, $P < 0.001$) and had significantly higher rates of congestive heart failure (19.4% vs. 8.4%, $P = 0.03$) and chronic kidney disease (25% vs. 13.4%, $P = 0.07$) whereas patients in the standard EVAR group were more likely to have hypertension (86.1% vs. 66.7%, $P = 0.003$) and hyperlipidemia (75.2% vs. 58.3%, $P = 0.03$).

Preoperative AAA diameter was significantly larger among patients undergoing pPASE (58 ± 11 mm vs. 54±8 mm, $P = 0.006$). Additionally, EVAR was performed outside the instructions for use (IFU) of the Ovation stent graft in 36.1% ($N = 13$) of the pPASE cases, with 1 (8%) patient having had previous iliac stents, 5 (38%) patients requiring renal stent venting of the proximal cuff, 2 (16%) patients with renal venting stents as well as previous iliac stents, and 5 (38%) patients having unilateral or bilateral hypogastric preservation with eyelet technique using kissing stents.

All patients in the Ovation IDE cohort underwent EVAR within the IFU of the device.

A complete summary of baseline characteristics is provided in Table I.

Outcomes

During follow-up, 116 patients were diagnosed with an ELII, of which 112 (96.6%) were in the standard EVAR group. No NTE was observed in the pPASE group. The 4-year freedom from ELII estimates were 84% for the pPASE versus 50.7% for the standard EVAR group ($P = 0.0002$) (Fig. 1). After adjusting for potential confounders, pPASE was associated with a 76% reduction in ELII [aHR (95% CI): 0.24 (0.08−0.65), $P = 0.005$] (Table II). Similarly, patients in the pPASE group achieved significantly higher rates of freedom from all reintervention (85.4% vs. 80.3%, $P = 0.03$). However, on multivariable analysis, the difference could not be observed [aHR (95% CI): 0.9 (0.32−2.55), $P = 0.8$].

None of the patients who underwent pPASE required a reintervention for ELII compared to 21 patients in the standard EVAR group, yielding a freedom from reintervention for ELII rate of 100% for the pPASE group versus 89.3% for the standard EVAR group at 4 years, $P = 0.1$.

All aneurysms in the pPASE group remained stable in size or demonstrated regression, whereas aneurysm sac expansion was seen in 10.9% of the standard EVAR group, $P = 0.03$.

At 4 years, mean AAA diameter decreased by 11 mm (95% CI 8−15) in the pPASE group versus 5 mm (95% CI 4−6) for the standard EVAR group, $P = 0.0005$ (Fig. 2). After adjustment, pPASE was associated with a 6.7 mm decrease in sac size (CI %: 3−10, $P < 0.001$).

There were no differences in the 4-year freedom from ACM and ARM (Table II).

DISCUSSION

The Ovation stent graft system (Endologix, Irvine, CA) is a commercially available stent graft system with a unique network of inflatable channels and sealing rings. 5-year results from the FDA-IDE clinical trial of the Ovation system demonstrated excellent durability with 95% freedom from type I and

Table I. Baseline characteristics by pPASE groups

Variable	pPase ($N = 36$, 13.1%)	No pPase ($N = 238$, 86.9%)	*P*-value
Age	70.4 ± 8.9	73.3 ± 8.3	0.05
Male sex	36 (100)	193 (81.1)	0.004
Smoking	36 (100)	170 (71.4)	<0.001
Diabetes	10 (27.8)	54 (22.7)	0.5
HTN	24 (66.7)	205 (86.1)	0.003
HLD	21 (58.3)	179 (75.2)	0.03
COPD	8 (22.2)	66 (27.7)	0.48
CHF	7 (19.4)	20 (8.4)	0.03
CKD	9 (25)	32 (13.4)	0.07
Off IFU	13 (36.1)	0 (0)	<0.001
AAA Diameter, mm	58 ± 11	54 ± 8	0.006

HTN, hypertension; HLD, hyperlipidemia; COPD, chronic obstructive pulmonary disease; CHF, congestive heart failure; CKD, chronic kidney disease; IFU, instructions for use; AAA, abdominal aortic aneurysm.

type III endoleak and 99% freedom from aneurysm-related mortality despite 41% of patients having anatomy unfit for other stent grafts.[16] Although overall freedom from secondary interventions was 80.2% in the standard EVAR group, type II endoleak was the most common indication, accounting for 63.1% of reinterventions.

In our previous report on outcomes of pPASE with thrombin, contrast, and gelfoam in our prospectively maintained institutional database, pPASE was successful in all measured endpoints including freedom from ELII, reintervention, nontarget embolization, aneurysm sac size changes, ACM, and ARM.[14] In this study, we sought to compare outcomes of patients receiving the Ovation stent graft in this database against core lab adjudicated data from the Ovation stent graft IDE trial.[16]

Previous reports have shown that nonadherence to anatomic guidelines specified in the manufacturer's IFU is associated with an increased risk of aneurysm-related complications.[17] However, at 4 years, our pPASE cohort achieved a higher freedom from reintervention rate when compared to the Ovation IDE cohort, despite EVAR being implanted outside the IFU of the graft in 36% of cases. This may suggest that even relative to patients with more complex anatomy, EVAR with pPASE can outperform standard EVAR in several key outcomes. Also, this study may suggest that, institutional experience and improved device technology has allowed us to safely perform EVAR in high-risk anatomic patients and obtain a proximal seal with unfavorable neck anatomy using commercially available devices.

Additionally, pPASE was associated with a 76% reduction in the incidence of ELII and no reinterventions for ELII or NTE. Although it did not eliminate all ELII's, it has eliminated the need for reintervention in this follow-up period by stabilizing or shrinking the aneurysm size. Thrombin administration directly into the aneurysm sac at the time of EVAR has also been shown to decrease ELII rates, regardless of whether patent branch vessels were coiled. Ronsivalle et al. reported that with the use of thrombin alone, the observed ELII decreased from 15.2 to 2.2% without an increase in NTE.[18] The authors of this study used thrombin alone, and did not mix it with Gelfoam to increase viscosity or with contrast to aid in the successful delivery of the mixture.

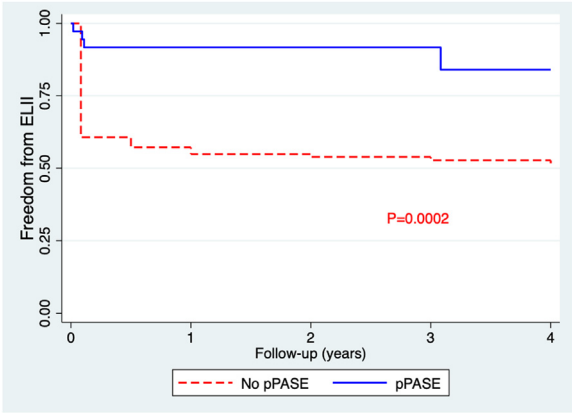

Fig. 1. Freedom from type II Endoleak by pPASE groups.

Prophylactic PASE was also associated with greater freedom from aneurysm sac expansion and decrease in aneurysm diameter. Consistently with our results, from the EUROSTAR database, Marrewijk and colleagues found ELII to be significantly associated with aneurysm sac growth over time.[19]

Limitations of the present study include those inherent to a retrospective study design with a small

Table II. Main Endpoints by pPASE group

4-year outcomes	pPASE ($N = 36$, 13.1%)	No pPASE ($N = 238$, 86.9%)	*P*-value	aHR (95%CI)	*P*-value
Freedom from ELII	84%	50.7%	0.0002	0.24 (0.08−0.65)	0.0005
Freedom from Reintervention	85.4%	80.3%	0.03	0.91 (0.32−2.55)	0.8
Mean sac size decrease, mm	11 (8−15)	5 (4−6)	0.0005	6.7 (3−10)	<0.001
Reintervention for ELII	0%	10.7%	0.1		
Freedom from ACM	64.6%	81.7%	0.07	1.9 (0.8−4.3)	0.12
Freedom from ARM	100%	99.60%	0.7		

ELII, type II endoleak; ACM, all-cause mortality; ARM, aneurysm-related mortality.

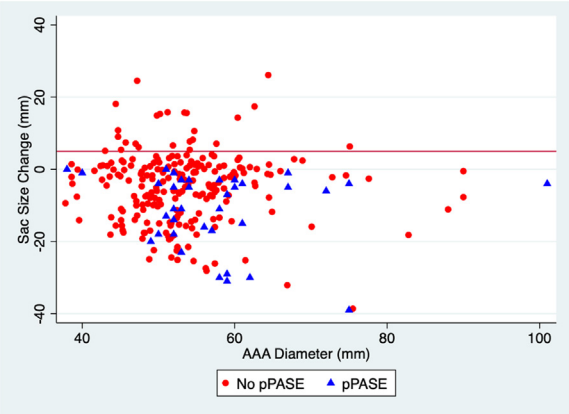

Fig. 2. Mean Change in AAA Diameter by pPASE groups.

sample size. Although the addition of patients from the Ovation IDE trial allows us to include a control group compared to our previous study, the use of patients from 2 separate datasets creates the potential for unmeasured confounders. Despite rigorous adjustment of baseline demographic and procedural characteristics, residual confounding from unmeasured institutional factors such as hospital volume and operator experience are inevitable. Nonetheless, the potential benefit of pPASE that has been demonstrated is promising and warrants continued investigation.

CONCLUSION

In our analysis of patients undergoing EVAR with the Ovation stent graft, pPASE was associated with reduced adjusted hazards of ELII as well as unadjusted freedom from aneurysm sac expansion and a decrease in aneurysm diameter at 4-years. There were no reinterventions for ELII in the pPASE group during the study period, compared to nearly 10% in the standard EVAR group. Additional studies are warranted to continue to characterize the long-term efficacy, safety, and cost of this promising adjunctive technology in EVAR.

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