Editor's Choice - Endurant Stent Graft in Patients with Challenging Neck Anatomy "One Step Outside Instructions for Use"

Endurant Stent Graft in Patients with Challenging Neck Anatomy "One Step Outside Instructions for Use": Early and Midterm Results from the EAGLE Registry

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WHAT THIS PAPER ADDS

This is the first prospective registry study to focus solely on abdominal aortic aneurysm treatment by endovascular aneurysm repair (EVAR) outside the instructions for use (IFU). The results show acceptable outcomes of EVAR treatment "one step" outside the IFU at three year follow up. However, longer follow up should be awaited to draw more definitive conclusions. Reporting on these outcomes is important as it will aid the future choice of treatment strategy for this challenging group of patients.

Objective: The aim of the Endurant for Challenging Anatomy: Global Experience (EAGLE) registry is to evaluate prospectively the technical and clinical success rate of a stentgraft used in patients with challenging neck anatomy outside the instructions for use (IFU) but within objective anatomical limits.

Methods: This was a prospective, international, multicentre, observational study. From 1 February 2012 to 1 September 2017, patients with an abdominal aortic aneurysm with a challenging infrarenal neck that were deemed suitable for endovascular aneurysm repair were included prospectively at 23 European centres. Patients were distributed by anatomy into three groups: short neck (SN; infrarenal neck 5 − 10 mm in combination with suprarenal angulation [α] $\leq$ 45° and infrarenal angulation [β] $\leq$ 60°); medium neck (MN; infrarenal neck 10 − 15 mm with $\alpha \leq 60°$ and β 60° − 75° or α 45°− 60° and $\beta \leq 75°$; and long angulated neck (LN; infrarenal neck $\geq$ 15 mm with $\alpha \leq 75°$ and β 75°− 90° or α 60°− 75° and $\beta \leq 90°$. All computed tomography scans were reviewed by an independent core laboratory. Primary outcomes were technical and clinical success. Secondary endpoints were peri-operative major adverse events, all cause mortality, aneurysm related mortality, endoleaks, migration, and secondary intervention.

Results: One hundred and fifty patients (81.3% male) were included (SN = 55, MN = 16, LN = 79). The median follow up was 36 $\pm$ 12.6 months. In the overall cohort, the technical success rate was 93.3%. Estimated freedom from aneurysm related death was 97.3% at three years. Freedom from secondary interventions was 84.7% at three years. Estimated clinical success was 96.0%, 90.8%, and 83.2% at 30 days, one year, and three years, respectively. Estimated freedom from all cause mortality, late type IA endoleak, and migration at three years was 75.1%, 93.7%, and 99.3%, respectively.

Conclusion: The early and midterm results of the EAGLE registry show that endovascular repair with the Endurant stentgraft in selected patients with challenging infrarenal neck anatomy yields results in line with large "real world" registries. Long term results are awaited for more definitive conclusions.

Keywords: Abdominal aortic aneurysm, Challenging anatomy, Endovascular procedures, Infrarenal neck, Instructions for use
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INTRODUCTION

Endovascular aneurysm repair (EVAR) has changed the treatment of abdominal aortic aneurysms (AAAs) tremendously since its introduction in 1991.[1,2] Currently, EVAR is considered the standard of care. However, challenging aneurysm morphology can impede successful aneurysm

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exclusion.[3,4] Stent manufacturers specify anatomical guidelines within the instructions for use (IFU) of their devices. The IFU is drafted on pre-clinical data and experience with previous devices. Based on the IFU, 19.3% − 37% of patients with an AAA are excluded from EVAR, predominantly due to infrarenal neck morphology.[5–7]

Increased experience and technical advances have resulted in better outcomes and initiated the exploration of the limits of EVAR and how to overcome them.[8–10] Adjunctive procedures during standard EVAR, for example endoanchors or bare metal stents, can be applied to increase proximal stability and seal.[11] Advanced and custom endovascular solutions for challenging anatomy, such as fenestrated EVAR (fEVAR) and chimney EVAR (chEVAR) are gaining popularity but remain technically challenging and are not widely available nor applicable.[12,13]

The Endurant Stent Graft System (Medtronic Vascular, Santa Rosa, CA, USA) is designed to accommodate complex infrarenal neck morphology by means of improved fixation, conformability, and proximal seal.[14] Various studies suggest that this stent graft performs well in patients with challenging infrarenal neck anatomy.[10,15,16] However, challenging neck anatomy and "outside IFU" is a device specific and broad concept, with a large range of complexity.

The Endurant for Challenging Anatomy: Global Experience (EAGLE) registry was initiated to evaluate the technical and clinical success rate of stent grafts being used in patients with short and angulated necks outside IFU but within objective anatomical limits. In particular, short and angulated infrarenal necks are potentially associated with insufficient sealing, and hence with an increased risk of type IA endoleaks and/or migration.[3,4] The hypothesis was that, within certain limits, patients with short or angulated necks can be treated with standard EVAR devices without compromising outcome. Therefore, the anatomical inclusion criteria were whittled down to three groups, each "one step" outside the IFU.

METHODS

Study design

The EAGLE registry is a physician initiated, prospective, multicentre, single device registry of patients treated with an Endurant Stent Graft System (Medtronic Vascular). The study protocol was published previously by Stokmans *et al.*,[17] and was registered at the US National Library of Medicine (ClinicalTrials.gov: NCT01810250). In contrast to the study protocol, no quality of life data were assessed owing to insufficient data. Between 1 February 2012 and 1 September 2017, patients were included from 23 European centres each with extensive experience of the use of the Endurant stentgraft. Sites that performed over 50 EVAR cases each year and had performed at least 25 Endurant cases were eligible to participate.

Inclusion criteria

All patients aged 18 years and older with a non-ruptured AAA and an indication for EVAR were eligible if the infrarenal neck was regarded as "outside the IFU". Indication for EVAR and the use of the Endurant system was at the discretion of the treating physician. Computed tomography (CT) scans were reviewed by an independent core laboratory. Based on the report provided by the core laboratory, anatomical eligibility for the registry and allocation into one of the three pre-specified registry subgroups was determined. The subgroups consisted of short neck (SN), medium neck (MN), and long angulated neck (LN). The specific anatomical definitions are detailed in Figure 1.

Patients with ruptured aneurysms or planned adjunctive procedures to accommodate a challenging infrarenal neck were excluded. Patients who were unlikely to adhere to the follow up protocol were also not eligible for enrolment.

A signed informed consent form for inclusion in the study and authorisation of data release was obtained from all patients. The trial was conducted according to the Declaration of Helsinki and the International Conference on Harmonisation Good Clinical Practice guidelines, and was approved by the local medical ethics committees. The study was also approved by the Dutch Health Inspection.

Procedure and follow up

Graft sizing was assessed by the treating physician. The implant procedure was performed according to the local protocol. There were no restrictions with regard to approach (cutdown or percutaneous), type of anaesthesia, or other procedure specifics.

Ideally, follow up was performed at 30 days, one year, and annually thereafter. If the local follow up protocol did not correspond with this schedule, dates closest to these points were computed as 30 days, one year, and annually thereafter. Both duplex ultrasound and CT angiogram were considered as adequate imaging modalities for follow up.

Outcomes

The outcomes were reported in accordance with the reporting standards for endovascular aortic aneurysm repair.[18] The primary outcomes were technical success and clinical success. Technical success was defined as successful deployment of the stent graft system without type I or III endoleaks, or unintentional coverage of renal and hypogastric arteries on the final intra-operative angiogram and without conversion, death, or graft limb obstruction within 24 hours of the procedure. Clinical success was defined as absence of late type I or III endoleak, stent graft migration $>$ 10 mm, graft limb occlusion, conversion, or aneurysm related death. All deaths within 30 days or in hospital were considered to be related to the aneurysm. Secondary endpoints were peri-operative major adverse events, all cause mortality, aneurysm related mortality, endoleaks, aneurysm sac enlargement ($\geq$ 5 mm, 30 days as baseline), migration, and secondary intervention. Endoleaks were divided into peri-operative, within 30 days, and late endoleaks, defined as those occurring after 30 days. Peri-operative major adverse events included all cause mortality, colonic ischaemia, myocardial infarction, paraplegia, procedural

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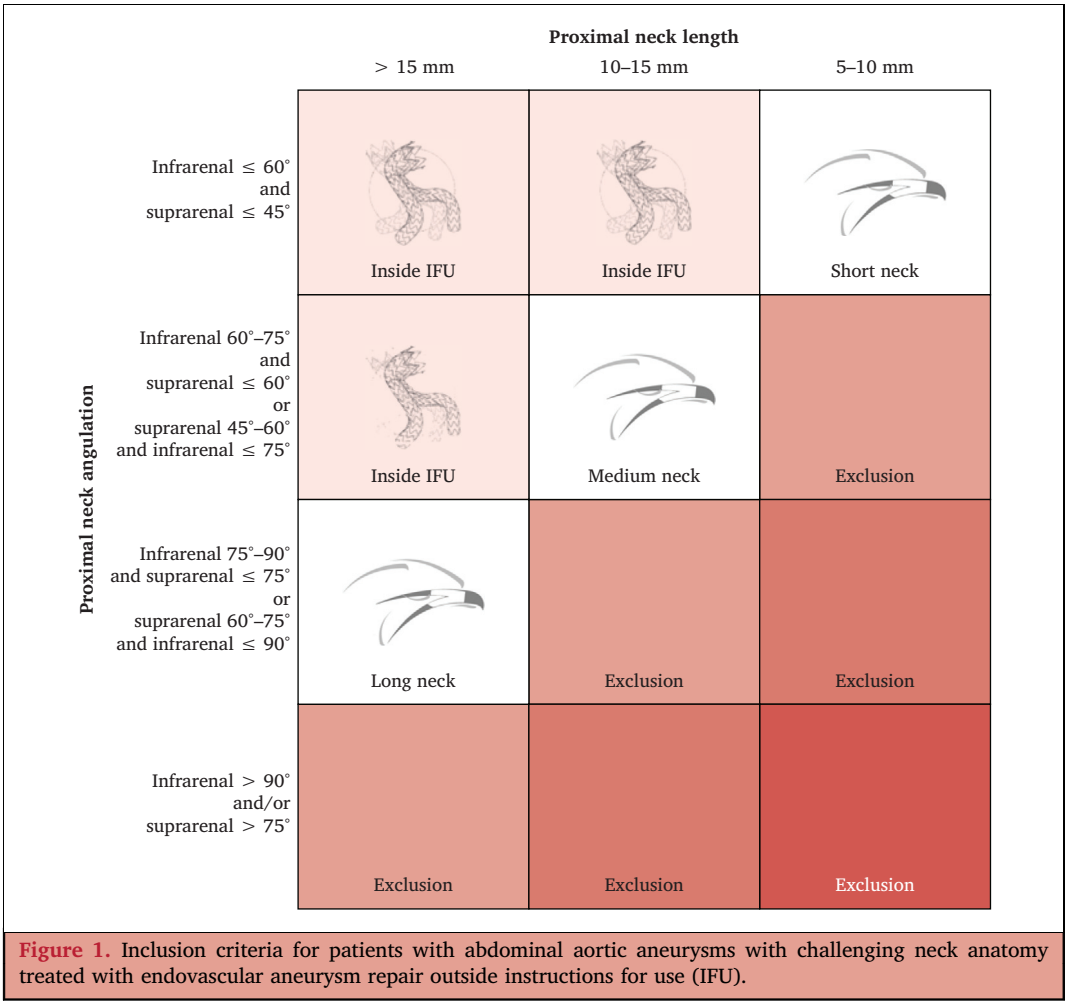

Figure 1. Inclusion criteria for patients with abdominal aortic aneurysms with challenging neck anatomy treated with endovascular aneurysm repair outside instructions for use (IFU).

blood loss > 1 000 mL, renal failure, respiratory failure, and stroke within 30 days. Acute kidney injury was classified as a relative increase of 150% in serum creatinine.[19]

Statistical analysis

Data were collected on standardised case report forms (CRFs) by the local investigators. The CRFs were collected, stored, and analysed by the study coordinators.

Categorical variables are presented as frequencies with percentages. Continuous variables are presented as means ± standard deviation or as median and interquartile range for skewed data. The Shapiro—Wilk and Kolmogorov—Smirnov tests were used to assess distribution normality. Clinical success, aneurysm related mortality, all cause mortality, freedom from re-intervention, and late type IA endoleak were assessed as Kaplan—Meier estimates. All other variables were evaluated on an intention to treat basis. No imputation of missing data was performed.

RESULTS

Two hundred and forty-two patients were screened by the core laboratory. Based on the core laboratory report, 31 patients were excluded because of anatomy within the IFU and 40 were excluded owing to anatomy exceeding the inclusion criteria (extremely complex anatomy). Ten patients did not provide informed consent and 11 received treatment other than EVAR with an Endurant stent graft. Eventually, 150 patients were included (Fig. 2). Baseline characteristics are detailed in Table 1. A total of 81.3% of patients were male and 11.3% had a symptomatic AAA.

Aneurysm morphology

All pre-operative aneurysm details as determined by the core laboratory are presented in Table 2. The majority of aneurysms (n = 79; 52.7%) had a long neck length with severe angulation, while 55 (36.7%) had a short neck length with little angulation and 16 (10.7%) had a medium neck length with moderate angulation.

In hospital outcomes

Procedural characteristics for all patients and for subgroups are provided in Table 3. The technical success rate was 93.3% (SN 96.4%, MN 87.5%, LN 92.4%). Successful deployment of the stent graft was achieved all patients. In 14 patients, unplanned additional interventions were required to resolve an intra-operative type IA endoleak or to improve apposition: extension cuff (n = 7); bare metal

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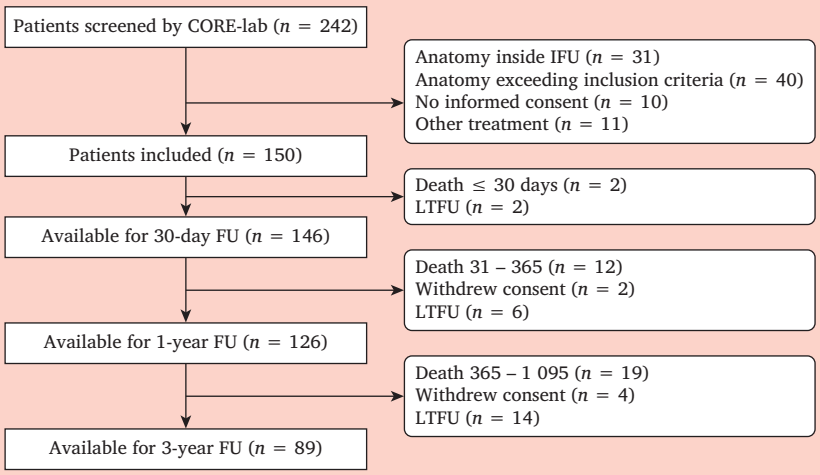

Figure 2. Flow chart of exclusion and compliance with follow up (FU) of patients with abdominal aortic aneurysms with challenging neck anatomy treated with endovascular aneurysm repair outside the instructions for use (IFU). LTFU = lost to follow up.

Table 1. Baseline characteristics of 150 patients with abdominal aortic aneurysms (AAA) with challenging neck anatomy defined as short neck (SN), medium neck (MN), or long angulated neck (LN), and treated with endovascular aneurysm repair outside instructions for use

	Total (n = 150)	SN (n = 55)	MN (n = 16)	LN (n = 79)
Age − y	76.0 ± 7.6	74.4 ± 8.1	74.8 ± 8.8	77.3 ± 6.8
Sex				
Male	122 (81.3)	48 (87.3)	14 (87.5)	60 (75.9)
Female	28 (18.7)	7 (12.7)	2 (12.5)	19 (24.1)
ASA class				
I	12 (8.0)	4 (7.3)	2 (12.5)	6 (7.6)
II	63 (42.0)	22 (40.0)	4 (25.0)	37 (46.8)
III	66 (44.0)	26 (47.3)	9 (56.3)	31 (39.2)
IV	9 (6.0)	3 (5.5)	1 (6.3)	5 (6.3)
Symptomatic AAA	17 (11.3)	6 (10.9)	0 (0)	11 (13.9)
Risk factors				
Tobacco use	67 (44.7)	24 (43.6)	10 (62.5)	33 (41.8)
Hypertension	121 (80.7)	42 (76.4)	16 (100.0)	63 (79.7)
Hyperlipidaemia	113 (75.3)	46 (83.6)	11 (68.8)	56 (70.9)
Diabetes	22 (14.7)	9 (16.4)	2 (12.5)	11 (13.9)
Renal insufficiency	40 (26.7)	11 (20.0)	7 (43.8)	22 (27.8)
Cardiac disease	73 (48.7)	29 (52.7)	11 (68.8)	33 (41.8)
Pulmonary disease	47 (31.3)	15 (27.3)	11 (68.8)	21 (26.6)
Cerebrovascular disease	28 (18.7)	10 (18.2)	2 (12.5)	16 (20.3)

Data are mean ± standard deviation or n (%).

stent (n = 6); and endo-anchor (n = 1). In 10 patients (6.7%), a small type IA endoleak persisted after the additional intervention. In two cases, a right renal artery was partially covered at the index procedure. In both cases, a renal stent was placed during the initial intervention to secure kidney perfusion.

The majority of procedures were performed under general anaesthesia through a surgical cutdown. One tube configuration and four aorto-uni-iliac devices were used in this registry.

During hospitalisation, four (2.7%) secondary interventions were performed. A malpositioned stent graft was extended the following day. One patient had a CT angiography confirmed type IA endoleak that was not recorded during the initial procedure; this was resolved with a non-covered stent 8 days post-operatively. In another patient, a limb occlusion was resolved with kissing stents, and in the fourth patient, there was a type B dissection. A thoracic stent graft was used to treat the dissection. However, after this intervention the patient refused pre-operatively started haemodialysis and died as a result of renal failure. Two additional patients died during hospitalisation: one suffered a fatal cerebral haemorrhage and the other died due to cardiac failure 104 days after treatment.

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Table 2. Baseline characteristics of 150 abdominal aortic aneurysms (AAA) with challenging neck anatomy defined as short neck (SN), medium neck (MN), or long angulated neck (LN), and treated with endovascular aneurysm repair outside the instructions for use

	Total (n = 150)	SN (n = 55)	MN (n = 16)	LN (n = 79)
Fusiform/saccular aneurysm	148/2	54/1	16/0	78/1
Maximum AAA diameter − mm	59 (54–70)	58 (54–69)	62 (57–70)	60 (55–70)
Proximal neck diameter − mm	23 (21–25)	23 (21–25)	24 (22–25)	23 (20–24)
Neck length − mm	16 (9–29)	8 (7–9)	12 (11–13)	28 (21–38)
Infrarenal angle − degrees	68 (44–77)	31 (17–50)	67 (61–74)	77 (74–82)
Suprarenal angle − degrees	33 (16–52)	17 (10–28)	32 (11–48)	49 (32–66)
Access vessel diameter right − mm	9 (8–10)	9 (8–10)	9 (8–10)	9 (8–11)
Access vessel diameter left − mm	9 (8–10)	9 (8–10)	9 (8–10)	9 (8–11)
Mural thrombus or calcification circumference − %	15 (0–28)	15 (0–25)	15 (0–25)	15 (0–25)
Right CIA tortuosity				
Mild	94 (62.7)	37 (67.3)	11 (68.8)	46 (58.2)
Moderate	53 (35.3)	17 (30.9)	4 (25.0)	32 (40.5)
Severe	3 (2.0)	1 (1.8)	1 (6.3)	1 (1.3)
Left CIA tortuosity				
Mild	80 (53.7)	30 (55.6)	9 (56.3)	41 (51.9)
Moderate	58 (38.9)	22 (40.7)	7 (43.8)	29 (36.7)
Severe	11 (7.4)	2 (3.7)	0 (0)	9 (11.4)
Right CIA aneurysm	58 (38.7)	17 (30.9)	5 (31.3)	36 (45.6)
Left CIA aneurysm	61 (40.7)	18 (32.7)	10 (62.5)	33 (41.8)

Data are presented as n (%) or median (interquartile range). CIA = common iliac artery.

Overall, the in hospital mortality rate was 2.0% (n = 3). Peri-operative major adverse events were recorded in five cases (3.3%): all cause mortality in three cases, post-operative myocardial infarction in one, and procedural blood loss > 1000 mL in one.

Thirty day outcomes

Follow up was available for 96.7% of patients. The outcomes are shown in Table 4. Post-operative imaging was performed in 96.6% of patients. In 14 patients, CT was performed prior to discharge instead of at the 30 day follow up.

Table 3. Procedural data of 150 patients with abdominal aortic aneurysms (AAA) with challenging neck anatomy defined as short neck (SN), medium neck (MN), or long angulated neck (LN), and treated with endovascular aneurysm repair outside the instructions for use

	Total (n = 150)	SN (n = 55)	MN (n = 16)	LN (n = 79)
Anaesthesia type				
General	111 (74.0)	42 (76.4)	14 (87.5)	55 (69.6)
Spinal	28 (18.7)	10 (18.2)	0 (0)	18 (22.8)
Local	11 (7.3)	3 (5.5)	2 (12.5)	6 (7.6)
Procedure duration −min	88 (70–110)	82 (60–105)	105 (79–131)	90 (75–110)
Contrast volume − mL	85 (65–125)	80 (60–124)	98 (74–170)	85 (68–123)
Fluoroscopic time − min	18 (14–24)	15 (12–19)	23 (15–35)	20 (15–25)
Blood loss − mL	200 (100–300)	200 (100–300)	250 (100–425)	200 (100–350)
Main section type				
Bifurcated	145 (96.7)	52 (94.5)	16 (100)	77 (97.5)
AUI	4 (2.7)	2 (3.6)	0 (0)	2 (2.5)
Tube	1 (0.7)	1 (1.8)	0 (0)	0 (0)
Access type				
Surgical cutdown	131 (87.3)	50 (90.9)	14 (87.5)	67 (84.8)
Percutaneous	19 (12.7)	5 (9.1)	2 (12.5)	12 (15.2)
Intra-operative endoleak	29 (19.3)	11 (20.0)	3 (18.8)	15 (19.0)
Type IA	10 (6.7)	2 (3.6)	2 (12.5)	6 (7.6)
Type II	16 (10.7)	8 (14.5)	0 (0)	8 (10.1)
Type III	0 (0)	0 (0)	0 (0)	0 (0)
Undetermined	3 (2.0)	1 (1.8)	1 (6.3)	1 (1.3)
Technical success	140 (93.3)	53 (96.4)	14 (87.5)	73 (92.4)
Post-operative hospital stay − days	3 (2–5)	2 (1–4)	4 (2–8)	3 (2–5)
Acute kidney injury	1 (0.7)	0 (0)	1 (6.2)	0 (0)

Data are presented as n (%) or median (interquartile range). AUI = aorto-uni-iliac device.

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Table 4. Thirty day, one year, and three year outcomes of 150 patients with abdominal aortic aneurysms (AAA) with challenging neck anatomy defined as short neck (SN), medium neck (MN), or long angulated neck (LN), and treated with endovascular aneurysm repair outside the instructions for use

Outcome	Total (n = 150)	SN (n = 55)	MN (n = 16)	LN (n = 79)
30 day outcomes				
30 day follow up	146 (97.3)	55 (100)	14 (87.5)	77 (97.5)
Imaging performed	140 (93.3)	53 (96.4)	14 (87.5)	72 (91.1)
CT	124 (82.7)	52 (94.5)	13 (81.2)	59 (74.7)
Duplex	16 (10.7)	1 (1.8)	1 (6.3)	13 (16.5)
Clinical success	144 (96.0)	54 (98.2)	13 (81.3)	77 (97.5)
All cause mortality	2 (1.3)	0 (0)	1 (6.3)	1 (1.3)
30 day endoleak				
Type IA	3 (2.0)	2 (3.6)	0 (0.0)	1 (1.3)
Type IB	1 (0.7)	0 (0.0)	0 (0.0)	1 (1.3)
Type II	13 (8.7)	4 (7.2)	1 (6.3)	8 (10.1)
Type III	0 (0)	0 (0)	0 (0)	0 (0)
Secondary intervention	5 (3.3)	1 (1.8)	3 (18.8)	1 (1.3)
1 year outcomes				
1 year follow up	127 (84.7)	47 (85.5)	11 (68.7)	69 (87.3)
Imaging performed	116 (77.3)	45 (81.8)	9 (56.3)	62 (78.5)
CT	59 (39.3)	26 (47.2)	2 (12.5)	31 (39.2)
Duplex	57 (38.0)	19 (34.5)	7 (43.8)	31 (39.2)
1 year clinical success	136 (90.7)	50 (90.9)	13 (81.3)	73 (92.4)
All cause mortality	14 (9.3)	4 (7.3)	1 (6.3)	9 (11.4)
Aneurysm related mortality	4 (2.7)	2 (3.6)	1 (6.3)	1 (1.3)
Secondary intervention	13 (8.7)	5 (9.1)	3 (18.8)	5 (6.3)
Conversion	1 (0.7)	1 (1.8)	0 (0.0)	0 (0.0)
Late endoleak > 30 days	14 (9.3)	4 (7.3)	0 (0)	10 (12.7)
Type IA	3 (2.0)	1 (1.8)	0 (0)	2 (2.5)
Type IB	0 (0)	0 (0)	0 (0)	0 (0)
Type II	9 (6.0)	3 (5.4)	0 (0)	6 (7.6)
Type III	1 (0.7)	0 (0)	0 (0)	1 (1.3)
3 year outcomes				
3 year follow up	89 (59.3)	38 (69.1)	9 (56.3)	42 (53.2)
Imaging performed	83 (55.3)	35 (63.6)	8 (50.0)	40 (50.6)
CT	35 (23.3)	11 (20.0)	3 (18.8)	21 (26.6)
Duplex	48 (32.0)	24 (43.6)	5 (31.3)	19 (24.1)
3 year clinical success	129 (86.0)	48 (87.3)	13 (81.3)	68 (86.1)
All cause mortality	32 (21.3)	10 (18.2)	2 (12.5)	20 (25.3)
Aneurysm related mortality	4 (2.7)	2 (3.6)	1 (6.3)	1 (1.3)
Re-intervention < 3 years	23 (15.3)	7 (12.7)	3 (18.8)	13 (16.5)
Late endoleak > 30 days				
Type IA	7 (4.7)	4 (7.3)	0 (0.0)	3 (3.8)
Type IB	1 (0.7)	0 (0.0)	0 (0.0)	1 (1.3)
Type II	20 (13.3)	6 (10.1)	1 (6.2)	1 (1.3)
Type III	2 (1.3)	0 (0.0)	0 (0.0)	1 (1.3)
Conversion	2 (1.3)	1 (1.8)	0 (0.0)	1 (1.3)

Kaplan—Meier estimated clinical success at 30 days was 96% (SN 98.1%, MN 81.3%, LN 97.5%). Thirty day and in hospital mortality was 2% (n = 3). At the 30 day follow up, 80.0% (n = 8/10) of intra-operative type IA endoleaks had resolved spontaneously. In addition to the two persisting endoleaks, one new type IA endoleak and one type IB endoleak were reported; these were all planned for secondary intervention. A type II endoleak was seen in 13 cases; none required treatment. No type III or IV endoleaks were identified. Migration was reported in one case and caused the abovementioned new type IA endoleak. Secondary interventions within 30 days were performed in five cases. In addition to the abovementioned four secondary interventions during admission, a fifth case underwent an axillofemoral bypass due to a right limb occlusion 22 days after the index procedure.

One and three year outcomes

Follow up was available for 127 (84.6%) patients at one year and for 89 (59.3%) at three years. Median follow up was 36 ± 12.6 months. A flow chart of follow up compliance is presented in Figure 2. Imaging was performed in 116 of 127 patients (91.3%) at one year and in 83 of 89 (93.3%) at three years. Duplex ultrasound was used in 49.1% of patients at one year and in 57.8% at the three year visit. The

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Kaplan–Meier estimate of clinical success was 90.8% at one year (SN 90.2%, MN 81.3%, LN 93.2%) and 83.2% at three years (SN 84.7%, MN 81.3%, LN 82.8%). Estimated freedom from aneurysm related death and all cause mortality was 97.2% and 90.8% at one year, respectively, and 97.2% and 75.1% at three years, respectively (Fig. 3). In addition to the 30 day deaths, two patients died after secondary intervention for a type IA endoleak detected at 30 days. One of these occurred after an open surgical conversion that resulted in multi-organ failure. The second occurred after rupture of a renal artery during endovascular treatment of a type IA endoleak.

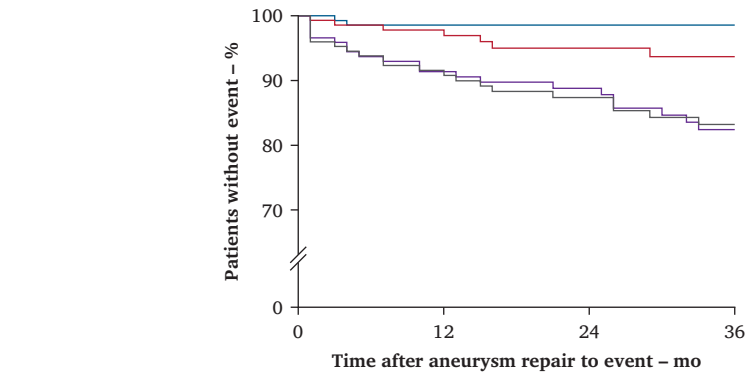
At the three year follow up, a late type IA endoleak (> 30 days) was found in seven patients (4.7%). Kaplan–Meier estimated freedom from type IA endoleaks at three years was 93.7% (SN 91.3%, MN 100.0%, LN 94.7%). Type II endoleaks were seen in 20 cases (13.3%). Two (1.3%) late type III endoleaks were reported. At one year, aneurysm sac expansion (≥ 5 mm, 30 day baseline) was present in five cases (5.2%), a stable diameter in 38 cases (39.2%), and sac shrinkage was present in 54 cases (55.7%). At the three year follow up, the Kaplan–Meier estimate of freedom from aneurysm sac enlargement was 91.5% No new cases of migration were reported. In total, secondary interventions within one year were performed in 13 cases (8.7%), and within three years in 23 cases (15.3%). All one and three year outcomes are presented in Table 4.

DISCUSSION

Since the introduction of EVAR, knowledge of aneurysm pathophysiology and endovascular technical skills have increased tremendously. This has led to an exploration of the boundaries of EVAR. However, after the long term results of landmark randomised controlled trials, sentiment has changed towards a more cautious use of EVAR, especially outside the IFU.[20] Nevertheless, according to recent literature, 17.9% – 44% of AAAs are still treated outside the IFU.[14,21,22] This prospective, multicentre, single device registry reports outcomes of treatment outside the IFU, within certain anatomical limits for the infrarenal neck.

Considering the challenging anatomy included in this registry, the 97.2% freedom from aneurysm related death at three years, 93.7% freedom from late type IA endoleak, 91.5% freedom from aneurysm sac expansion, and 84.7% freedom from secondary intervention at the three year follow up are acceptable outcomes. These results are similar to the results of "real world" registries like the ENGAGE registry at the five year follow up, which reported 97.8% freedom from aneurysm related death, 95.2% freedom from type IA endoleak, and a 15.7% secondary intervention rate.[23] Moreover, the GREAT registry reported 90.6% freedom from all cause mortality and 91.5% freedom from late re-interventions at the two year follow up. Furthermore, the secondary intervention rate is similar to that of the DREAM trial at three years, which included a highly selected group of patients without challenging anatomy.[24] This suggests that endovascular treatment of challenging anatomy with the Endurant stent graft system in a select group of patients within certain boundaries can be a promising alternative to open surgery or customised endografts in experienced centres. This study does not indicate that treating patients outside the IFU is safe. Only within the strict anatomical boundaries shown in Figure 1 can it be concluded that the results of the study are acceptable. It should be noted that the follow up is currently too short to draw any definitive conclusions.

The technical success rate in this study was 93.3% as a type IA endoleak persisted on final intra-operative angiogram in 6.7% of patients. However, the majority (80%) of



No. at risk				
Aneurysm related mortality	150	123	101	82
Type IA endoleak	150	115	81	61
Reintervention	150	114	91	69
Clinical success	150	116	91	71

Figure 3. Cumulative Kaplan–Meier estimate of freedom from aneurysm related mortality, type IA endoleak and re-intervention, as well as clinical success in 150 patients with abdominal aortic aneurysms with challenging neck anatomy treated with endovascular aneurysm repair outside instructions for use. analysis. Note the adapted scale for the *y* axis.

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these had resolved spontaneously at the 30 day follow up. This is consistent with previously reported findings,[25–27] suggesting that, in highly selected cases, the risk of adjunctive procedures or conversion can outweigh the risk of a small, persisting type IA endoleak.

The use of standard EVAR has a low physical impact on the patient, as indicated by the finding of a median procedural time of 88 minutes, a median contrast use of 85 mL, and a limited post-operative hospital stay of three days. This compares favourably with reported procedural times for fEVAR or chEVAR of 180 — 233 minutes, using over 150 mL of contrast.[12,13,28] Moreover, this study reports a post-operative acute kidney injury rate of 0.7%, which is markedly lower than the 17.5% observed in the PERICLES registry for chEVAR.[12]

This study focused specifically on neck length and neck angulation, as these criteria are considered crucial in the IFU. There was no focus on neck diameter, calcification, thrombus, or infrarenal neck conicality, additional parameters for the anatomical severity grading (ASG) score for the infrarenal neck.[29] The experienced interventionist in the EAGLE registry assessed the included patients as suitable for EVAR and may have potentially excluded patients who might have fitted the EAGLE inclusion criteria, taking the "additional" ASG criteria into consideration. This could have created a potential bias.

In the screening process, 71 of 242 patients were excluded by the core laboratory based on anatomy outside of the study parameters. This was probably due to inter-observer variability between treating physicians and the core laboratory. Previous studies have shown significant interobserver variability in aortic neck measurements based on CT imaging.[30] This highlights the importance of an independent core laboratory, especially in studies reporting on complex anatomy.

The strictly defined inclusion criteria combined with the growing popularity of alternative treatment options (i.e., chEVAR, fEVAR, and endo-anchors) made inclusion challenging. The choice of therapy was at the discretion of the treating physician. This may have resulted in a selection bias as patients within inclusion criteria for this registry could still be deemed unsuitable for EVAR by the treating physician based on other criteria. Only patients considered for standard EVAR were presented to the study group for inclusion. Therefore, no data on considerations regarding the type of intervention are available. Moreover, only centres with extensive experience with the Endurant stent graft were participating in this registry. This might hamper the external validity of the results, especially for smaller or less experienced centres.

Owing to duplex ultrasound being the advised modality for follow up imaging in the European and US guidelines, migration or stent fractures might be under reported unless they lead to endoleaks or aneurysm sac growth.[31,32] Furthermore, in the absence of a control group of patients treated inside the IFU, results can only be compared with those in the literature. Because of the strict anatomical neck parameters employed, the included population is a highly selected group, with possible consequent selection bias that confounds comparison with other treatment modalities.

Unfortunately, the follow up rate dropped to 59.3% at three years. Owing to the financial crisis in Greece in 2015, all nine patients from one of the participating centres were lost to follow up. Moreover, due to the COVID-19 pandemic, several patients cancelled or postponed their three year visits, resulting in loss to follow up at the time of the writing.

Conclusion

To the authors' knowledge, the EAGLE registry is the only core laboratory controlled prospective international registry that has focused solely on performance of the Endurant stent graft outside the IFU. Results at midterm follow up show that treatment of patients with challenging anatomy of the infrarenal neck (within certain boundaries) with the Endurant stent graft system can yield results in line with large "real world" registry data. However, long term follow up is awaited for more definitive results.

CONFLICTS OF INTEREST

M.vB.B., Y.'tM., A.S., and G.G., have no competing interests. M.vS., J.T., and P.C. have received unrestricted research grants from Medtronic. J.T. and P.C. have been proctors for Medtronic.

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