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Early Results from the ENGAGE Registry: Real-world Performance of the Endurant Stent Graft for Endovascular AAA Repair in 1262 Patients

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WHAT THIS PAPER ADDS

- The technology of endovascular aneurysm repair (EVAR) for abdominal aortic aneurysms (AAAs) is a dynamic, ever-changing endeavour. The challenge is to decrease complications and re-interventions while safely treating more complex anatomy. As improved devices become available and operators become more proficient with endovascular techniques, EVAR outcomes change. In order to make balanced judgement about the management of AAAs, it important to augment the knowledge base about EVAR in contemporary practice with the latest generation devices. The Endurant Stent Graft Natural Selection Global Postmarket Registry (ENGAGE) has been designed to closely monitor the real-world performance of the Endurant Stent Graft System. Unprecedented in size, scope and geographic representation, it represents a combined experience of 79 sites worldwide.

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ABSTRACT

Objective: The ENGAGE registry was undertaken to examine the real-world outcome after endovascular abdominal aortic aneurysm (AAA) repair (EVAR) with the Endurant Stent Graft in a large, contemporary, global series of patients.
Methods: From March 2009 to April 2011, 1262 AAA patients (89.6% men; mean age 73.1 years, range 43–93 years) were enrolled from 79 sites in 30 countries and treated with Endurant. Results are described following the reporting standards for EVAR. Follow-up data were tabulated for all 1262 patients at a 30-day follow-up and for the first 500 patients at a 1-year follow-up.
Results: Intra-operative technical success was achieved in 99.0% of cases. Within 30 days, adverse events were reported in 3.9% of patients, including a 1.3% mortality rate. Type-I or –III endoleaks were identified in 1.5% of cases. Estimated overall survival, aneurysm-related survival and freedom from secondary interventions at 1 year were 91.6%, 98.6% and 95.1%, respectively. At 1 year, aneurysm size increased ≥5 mm in 2.8% and decreased ≥5 mm in 41.3% of cases.
Conclusion: Early results from this real world, global experience are promising and indicate that endovascular AAA repair with the Endurant Stent Graft is safe and effective across different geographies and standards of practice. Longer-term follow-up is necessary to assess durability of these results.

Abdominal aortic aneurysms (AAAs) are a significant health challenge with an estimated incidence of 20–40 cases per 100 000 population per year. Patients present with varying levels of risk due to aneurysm size, age and concurrent co-morbidities.[1] Since Parodi[2] and Volodos[3] published the first transfemoral

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intraluminal graft implantations for AAA in 1991, the practice of endovascular aneurysm repair (EVAR) has continually improved. Today, this approach is a generally accepted alternative to conventional open surgical repair due to reductions in perioperative mortality and morbidity, blood loss, use of the intensive care unit (ICU) and length of hospital stay.[4] Several randomised trials have confirmed these benefits,[5–7] and one trial confirmed these benefits except for perioperative mortality and major adverse events.[8]

The success of EVAR, however, is dependent upon patient-specific factors, including morphology and dimensions of the aneurysm. Severely angulated or short infrarenal aortic necks and small, tortuous or calcified iliac arteries are related to adverse EVAR outcomes,[9] and thus guidelines for commercially available stent grafts indicate use within a specific range of anatomy. A substantial portion of AAA patients fall outside these generally accepted inclusion criteria,[10] and their advanced disease state or major co-morbidities present a high risk for open surgical repair. Therefore, there is a need for improved stent grafts and endovascular techniques to decrease complications and increase eligibility.

Medtronic Endovascular (Santa Rosa, CA, USA) designed its latest generation product, the Endurant Stent Graft System, to address the limitations of previous stent graft designs. A small amplitude M-shaped proximal stent was designed to improve sealing at the proximal neck while potentially allowing for greater sizing flexibility. Radial strength was also improved while allowing a lower-profile delivery system. The Endurant Stent Graft System received CE mark approval in July 2008 and Food and Drug Administration (FDA) approval in December 2010. After a safety assessment trial conducted in Europe,[11] the Endurant Stent Graft Natural Selection Global Postmarket Registry (ENGAGE) was undertaken to quantify the performance of this recently released endograft within the context of contemporary, real-world use. Herein, we report the perioperative and 1-year results of this global, multicentre, prospective 1262-patient study of the Endurant Stent Graft System.

Methods

Patient population

Between March 2009 and April 2011, eligible patients from 79 sites in 30 countries (Appendix) were enrolled in the ENGAGE registry. The study protocol strongly encouraged consecutive enrolment of at least five patients in a row to minimise selection bias. Ruptured AAAs were not considered for enrolment into ENGAGE. Prior to the index procedure, computed tomography angiography (CTA) imaging of the abdomen and pelvis was undertaken to determine the morphological eligibility for elective endovascular treatment with an Endurant Stent Graft. To reflect the real-world clinical practice, eligibility criteria for participation were kept comprehensive. Although the study design included that individual morphological variables (proximal neck diameter and length, infrarenal and suprarenal angulation and distal iliac fixation diameter and length) were consistent with Endurant's Instructions for Use (IFU) (Table 1), enrolment of patients who fell outside the IFU guidance was accepted. Patients considered unlikely to adhere to the follow-up regimen and patients with concurrent trial participation were excluded from study enrolment. A signed consent for authorisation of data release was required. The trial was conducted according to the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines, and approved by local medical ethics committees.

Table 1
Endurant® indications for use.

One of the following criteria:
■ Infrarenal neck length ≥10 mm with non-significant calcification, and/or non-significant thrombus in combination with ≤45° suprarenal angulation and ≤60° infrarenal angulation.
■ Infrarenal neck length ≥15 mm with non-significant calcification and/or non-significant thrombus in combination with ≤60° suprarenal angulation and ≤75° infrarenal angulation.
And all of the following criteria:
■ Adequate iliac/femoral access
■ Proximal AAA neck diameter ≥19 mm and ≤32 mm
■ Distal iliac fixation site diameter ≥8 mm and ≤25 mm
■ Distal non-aneurysmal iliac fixation length ≥15 mm bilaterally

Study procedure

Technical specifications of the Endurant Stent Graft System have been published previously.[11,12] Preoperatively, each patient had a customised plan made with respect to stent diameters and length, dependent on their aortic and iliac dimensions. For optimal sealing, it was advised to oversize the stent diameter by approximately 20% based on inner vessel diameter. All endovascular procedures were performed under fluoroscopic control. Local, regional or general anaesthetics, antibiotics and heparin were administered according to each site's standard regimen. Arterial access was conducted by operator's preference. If necessary, coil embolisation of the hypogastric or inferior mesenteric artery, or other adjunctive procedures were performed and documented before or during the implant procedure. A completion angiogram was performed to document the status after stent graft implantation.

Imaging and follow-up

Follow-up was planned according to standard practice at each clinical site, with the exception of the requirement for 30-day and 1-year imaging studies No specific tests or procedures that fell outside a site's standard regimen for AAA follow-up were required. Diagnostic images were analysed at both time points for technical outcomes and AAA changes. The presence of endoleak was classified by type and recorded as well as changes in aneurysm size.

'End' points and definitions

The ENGAGE registry was designed to assess effectiveness of the Endurant Stent Graft at 12 months post-implantation, with follow-up extended to 5 years. This manuscript describes the initial procedural data and outcomes, the technical observations, adverse events and major adverse events (MAEs) within 30 days and 12 months, along with stent graft migration and aneurysm expansion (>5 mm) between 30 days and 12 months.

The primary effectiveness 'end' point was the initial procedural success, a composite of technical success and clinical success at the time of the index procedure. Technical success was defined as successful delivery and deployment of the Endurant Stent Graft in the planned position without unintentional coverage of one or both internal iliac arteries or visceral aortic branches and with successful removal of the delivery system. In the case of primary conversion, technical success failed. Initial clinical success was defined as technical success without intra-operative death or presence of a type-I/III endoleak at the conclusion of the index procedure.

The secondary 'end' points consisted of technical observations, adverse events and MAE. Technical observations included: stent graft kinking; stent graft wire form fracture; suprarenal bare stent fracture or detachment from fabric; occlusion (defined as 100% obstruction); stenosis (defined as partial obstruction); and

presence of an endoleak. Secondary conversion to open repair, aneurysm rupture and secondary interventions were stated as adverse events. All-cause mortality, bowel ischaemia, myocardial infarction, paraplegia, renal failure (requiring dialysis or elevated serum creatinine two times baseline value), respiratory failure (need for >24 h mechanical ventilation postoperatively or reintubation for any reason), stroke and procedural blood loss ≥1000 cc were noted as MAEs. All deaths within 30 days postoperative were judged to be aneurysm-related. All-cause mortality, aneurysm-related mortality and secondary procedures were separately assessed as 1-year Kaplan–Meier estimates.

Data management, quality control and statistical analysis

Data collected on each patient were recorded on a web-based electronic case report form (Veracity™ Clinical Asset Management, MERGE Healthcare, Chicago, IL, USA) to ensure reliable data collection, data management, secure authentication and traceability. Data were entered by, or under supervision of, sites' principal investigators. Data management and biostatistical analysis were performed by the Medtronic Biostatistics & Data-Management Department (Santa Rosa, CA, USA). It reviewed 100% of data to detect missing or inconsistent data to generate queries to the investigators for resolution. In addition to this, Medtronic Bakken Research Centre BV (Maastricht, the Netherlands) randomly monitored over 40% of patients' source documentation against the data entered. They also performed a verification of all 1262 patient informed consents and essential study documents at each site.

All variables are reported descriptively with no hypothesis testing. For categorical variables, frequency and percentage were calculated. For continuous variables, mean, standard deviation, minimum and maximum were calculated. A per protocol analysis was performed for the technical observations. All other variables were evaluated on an intention-to-treat basis.

Results

From March 2009 until April 2011, 1266 patients from 79 sites in 30 countries were initially recorded in the database. Four patients however, were excluded from the study for the following reasons; one patient refused immediate treatment, but underwent emergency EVAR for a ruptured AAA 3 months later; one patient underwent open surgical treatment instead, because of unsuitable anatomy on preoperative imaging; one patient was operated on at a non-participating site; and with one patient, the informed consent form was missing. Data for the remaining 1262 patients comprise the basis of this report. At time of writing, a sub-cohort of the first 500 operated patients (39.6%) had the opportunity to complete 12-month follow-up. Their data form the basis of the 1-year outcome analysis.

Baseline characteristics

Patients' demographics and risk factors (Table 2) were typical of an AAA population. They were predominantly male, elderly and American Society of Anaesthesiologists (ASA) class II or III, with a high prevalence of cardiovascular risk factors and co-morbidities. The primary indication for EVAR was an AAA diameter >5 cm in 88.1% of cases and 83.9% of patients were asymptomatic. Table 3 describes baseline aneurysm characteristics. The mean maximum AAA diameter was 60.3 ± 11.7 mm. The proximal aortic neck had a mean diameter of 23.7 ± 3.6 mm, with a non-aneurysmal length of 27.0 ± 12.4 mm (27 (2.2%) patients with neck length <10 mm) and a mean infrarenal neck angulation of 30.3 ± 23.8°. Notably, 226 patients (17.9%) were implanted outside the IFU criteria (Table 4).

Table 2
Patient demographics and risk factors (ITT analysis).

Variable		$N = 1262$[a]
Age (years) Mean ± SD (range)	73.1 ± 8.1	(43–93)
Gender		
Male	89.6%	(1131/1262)
Female	10.4%	(131/1262)
ASA[b] Classification		
Class I	6.1%	(77/1261)
Class II	41.8%	(527/1261)
Class III	41.5%	(523/1261)
Class IV	10.6%	(134/1261)
Symptoms		
A-symptomatic AAA[c]	83.9%	(1059/1262)
Symptomatic AAA[c]	16.1%	(203/1262)
Indication by AAA[c] diameter		
>5 cm	88.1%	(1112/1262)
4–5 cm (≥0.5 cm increase in last 6 months)	6.3%	(79/1262)
≥1.5x reference infrarenal aorta	2.9%	(42/1262)
Other	2.3%	(29/1262)
Risk factors		
Tobacco use	49.3%	(607/1231)
Hypertension	75.4%	(939/1245)
Hyperlipidaemia	60.4%	(718/1188)
Diabetes	19.0%	(236/1244)
Cancer	20.5%	(254/1241)
Cardiac disease		
Myocardial infarction (MI)	26.3%	(318/1210)
Arrhythmia	16.0%	(198/1234)
Coronary artery disease (CAD)	34.6%	(422/1218)
Cardiac revascularisation	27.1%	(337/1244)
Pulmonary disease	25.1%	(311/1241)
Renal insufficiency	15.3%	(191/1251)
Cerebrovascular disease		
Transient ischaemic attack (TIA)	4.9%	(61/1249)
Cerebral vascular accident (CVA)	5.3%	(67/1255)
Gastro-intestinal complications	19.5%	(246/1261)

[a] Denominator differs when there are missing values.
[b] American Society of Anesthaesiologists.
[c] Abdominal aortic aneurysm.

Intra-operative outcome

The procedure was performed under general, regional and local anaesthesia in, respectively, 62.3%, 26.2% and 11.5% of cases. The mean procedural duration was 99.5 ± 45.0 min (range 20–387 min), with a mean total fluoroscopic time of 20.5 ± 12.4 min (range 0–92 min) and a mean contrast volume used of 130.7 ± 70.6 ml (range 0–400 ml). Mean intra-operative blood loss was 208.4 ± 220.1 ml (range 0–2700 ml). ICU admission rate was 34.2%, and 6.0% were admitted longer than 24 h. The

Table 3
Baseline aneurysm characteristics (ITT analysis).

Variable	Mean ± SD	$N = 1262$ (range)
Maximum AAA[a] diameter (mm)	60.3 ± 11.7	(30–118)
Proximal neck diameter (mm)	23.7 ± 3.6	(15–45[b])
Proximal non-aneurysmal neck length (mm)	27.0 ± 12.4	(0[c] – 80)
Distal iliac fixation site diameter (mm)		
Right	14.1 ± 3.6	(2–29)
Left	13.8 ± 3.5	(6–30)
Infrarenal neck angle (°)	30.3 ± 23.8	(0–130)
≤60°	89.8%	
60–75°	6.0%	
Suprarenal neck angle (°)	18.8 ± 18.5	(0–120)
≤45°	92.5%	
45–60°	4.5%	

[a] Abdominal aortic aneurysm.
[b] Upper range of 45 mm: Tapered aortic neck, with a proximal diameter of 45 mm, a diameter of 22 mm immediately above the aneurysm and a 15 mm non-aneurysmal neck length.
[c] Lower range of 0 mm: Case performed with a "chimney technique".

Table 4
Patients implanted outside IFU[a] (ITT analysis).

Variable		$N = 1262$
Total implanted outside of IFU[a] guidance	17.9%	(226/1262)
Non-primary indications	2.3%	(29/1262)
Proximal neck diameter < 19 mm or >32 mm	5.7%	(72/1255)
Proximal neck length < 10 mm	2.2%	(27/1248)
Proximal neck length ≥ 10 mm and <15 mm[b]	2.1%	(26/1248)
Angulation suprarenal > 60° or infrarenal > 75°	4.7%	(59/1248)
Distal iliac fixation site diameter <8 mm	1.5%	(19/1262)
Distal iliac fixation site diameter >25 mm	0.6%	(8/1262)

[a] Instructions for use.
[b] In combination with suprarenal angle > 45° or infrarenal angle > 60°.

mean hospital stay from the date of the initial procedure was 4.83 ± 5.07 days (median 4.00; range 0.5–68 days).

Technical success was achieved in 1250 patients (99.0%). The Endurant was delivered to the planned location and successfully deployed in 99.4% of patients (Table 5). Attempts at endovascular repair were discontinued in six (0.5%) patients: four cases with access problems due to tortuous or stenotic iliac arteries, two of whom were eventually converted to open repair after 2 and 49 days respectively. One patient required immediate conversion after unintentional coverage of both renal arteries, when the suprarenal stent was released before accurate placement of the covered stent. In another case, one of the proximal struts got stuck in the tip-capture portion of the delivery system, resulting in the inability to remove the device and necessitating immediate conversion to open surgery. There were no intra-operative deaths.

Adjunctive procedures were performed before or during implant procedures in 96 (7.6%) and 171 (13.5%) cases, respectively (Table 5). Primarily coil embolisation of the internal iliac artery or inferior mesenteric artery. Unplanned additional stents (other than Endurant) were placed in 44 (3.5%) patients, mainly to resolve intra-operative type-I/III endoleaks. The final completion angiogram revealed type-I and type-III endoleaks in 14 (1.1%) and four (0.3%) cases, respectively, predominantly in patients with regular neck configurations. Among patients with type-I endoleaks, one patient underwent secondary placement of a proximal cuff. Another patient died of a myocardial infarction before 30-day imaging was performed. In all remaining cases, the endoleaks were absent at 30-day CTA and no secondary interventions were performed.

Perioperative outcome

One-month imaging was performed in 91.6% of the 1256 implanted patients (Table 6). One or more graft-related problems, including endoleaks, were reported in 191 (16.6%) of these patients. Occlusion of one of the iliac limbs was reported in 23 patients (2.0%) and graft stenosis was detected in 16 (1.4%). Stent graft kinking occurred in 20 (1.7%) cases. One report of occlusion of a (right) renal artery occurred. This did not result in major clinical event or re-intervention. There were no stent fractures or stent graft migrations reported in any patient through 30 days.

Endoleaks were present in 138 (12.0%) patients at 30 days, of which in seven cases the type could not be specified. type-I and/or -III endoleaks were identified in 17 (1.5%) patients, including one patient with both types present. One of the type-I endoleaks had been observed at the time of operation and persisted to day 32, when it was successfully treated. The remaining endoleaks were newly diagnosed on the 30-day imaging study. Among these, eight type-I endoleaks were treated with an extension or remodelling of the graft, four spontaneously resolved without intervention and two had not yet reached the 12-month follow-up visit. The patient with both a type-I and -III endoleak present had persistent endoleaks at the 12-month images, and was scheduled for re-intervention thereafter. The other type-III endoleak was resolved on follow-up images.

Table 5
Initial procedural data and evaluation (ITT & PP analysis).

Placement procedure (ITT)		$N = 1262$
Pre-implant adjunctive procedure performed	7.6%	(96/1262)
Coil embolization IIA[a]	4.3%	(54/1262)
Coil embolization IMA[b]	1.1%	(14/1262)
Other	2.4%	(30/1262)
Associated procedures performed during procedure		
Coil embolization IIA	5.1%	(64/1262)
Coil embolization IMA	0.6%	(7/1262)
Other	8.7%	(110/1262)
None	86.5%	(1091/1262)
Additional device used during implant procedure		
Balloon catheter	76.5%	(965/1262)
Unplanned	6.0%	(76/1262)
Stent (other than Endurant)	6.2%	(78/1262)
Unplanned	3.5%	(44/1262)
Other	6.8%	(86/126)
Placement of proximal end of device		
With suprarenal stent crossing both renal arterie	75.7%	(955/1262)
With suprarenal stent crossing one renal artery	6.0%	(76/1262)
Below both renal arteries	17.5%	(221/1262)
Placement of distal end of device		
Right limb distal to the IIA	8.8%	(111/1262)
Left Limb distal to the IIA	8.3%	(105/1262)
Endurant stent-graft implanted into a patient	99.5%	(1256/1262)
2 components implanted	43.0%	(540/1256)
3 components implanted	27.5%	(345/1256)
4 components implanted	21.9%	(275/1256)
≥5 components implanted	6.6%	(83/1256)
Primary effectiveness endpoints (ITT)		**$N = 1262$**
Technical success	99.0%	(1250/1262)
Endurant stent-graft successfully delivered	99.4%	(1255/1262)
Endurant stent-graft successfully deployed	99.4%	(1255/1262)
No unintended coverage of IIA or any VABs[c]	99.5%	(1253/1259)
Endurant delivery system successfully removed	99.9%	(1261/1262)
Intra-operative clinical success	97.6%	(1232/1262)
Technical success	99.0%	(1250/1262)
Freedom from intra-operative death	100.0%	(1262/1262)
Freedom from type I/III endoleak	98.6%	(1238/1256)
Initial technical observations (PP)		**$N = 1256$**
Stent graft malfunctions		
Kinking	1.0%	(13/1253)
Twisting	0.5%	(6/1252)
Wire form fracture	0.0%	(0/1253)
Suprarenal bare stent fracture	0.0%	(0/1253)
Other malfunctions	0.3%	(4/1256)
Endoleak (Uncorrected)[d]	16.0%	(201/1256)
Type I	1.1%	(14/1256)
Type II	12.4 %	(156/1256)
Type III	0.3%	(4/1256)
Type IV	1.8%	(22/1256)
Undetermined	0.7 %	(9/1256)

[a] Internal iliac arteries.
[b] Inferior mesenteric arteries.
[c] Visceral aortic branches.
[d] Uncorrected: Detected, but chosen not to treat within initial procedure.

The overall 30-day mortality rate was 1.3. One or more major adverse events within 30 days, including all-cause mortality, were reported in 3.9% of patients (Table 7); bowel ischaemia was recorded in three patients (0.2%), myocardial infarction in 14 patients (1.1%), renal failure in four patients (0.3%), stroke in two patients (0.2%) and blood loss ≥1000 cc was recorded in 18 (1.4%) patients. No patient developed paraplegia or respiratory failure.

Within the first month, three (0.2%) cases were converted to open surgery, two as emergencies and one electively, as mentioned earlier. Secondary interventions were required in 19 (1.5%) cases,

Table 6
Technical performance at 30-days (PP analysis).

Variable		$N = 1151$[a]
One or more technical observations	16.6%	(191/1151)
Stent graft kinking	1.7%	(20/1151)
Stent graft twisting	0.1%	(1/1151)
Stent graft wire form fracture	0.0%	(0/1151)
Suprarenal bare stent fracture	0.0%	(0/1151)
Suprarenal bare stent detachment from fabric	0.1%	(1/1151)
Stent graft occlusion	2.0%	(23/1151)
Stent graft stenosis	1.4%	(16/1151)
Stent graft migration	0.0%	(0/1151)
Endoleak	12.0%	(138/1151)
Type I	1.4%	(16/1151)
Type II	9.9%	(114/1151)
Type III	0.2%	(2/1151)
Type IV	0.1%	(1/1151)
Undetermined	0.6%	(7/1151)
Type I and/or III	1.5%	(17/1151)
Other technical observation	0.6%	(7/1151)

[a] Only implanted patients with 1-month imaging study included in the analyses.

within the first 30 days of follow-up; eight (0.6%) cases required endovascular intervention for graft occlusion, stenosis or kinking; one case was for contralateral leg implant; six (0.5%) cases required a bypass procedure; and four (0.3%) cases required endovascular intervention to correct a type-I endoleak.

One-year outcome

A sub-cohort of 500 patients was followed for at least 12 months, with compliance to follow-up of 98.6%. Baseline characteristics and perioperative outcome measures of this sub-cohort were comparable to those of the total study population. Therefore, further analysis on this sub-cohort was considered to be valuable.

The 1-year Kaplan–Meier estimate for overall survival was 91.6 ± 1.4%. The 1-year estimate for aneurysm-related survival was 98.8 ± 0.5%, with no device-related deaths (Fig. 1). One or more MAEs, including all-cause mortality, were reported in 11.2% of patients within 1-year follow-up; including five (1.0%) cases of renal failure, nine (1.8%) myocardial infarctions, two (0.4%) cases of stroke, two (0.4%) case of bowel ischaemia and one (0.2%) case of respiratory failure.

The Kaplan–Meier estimate for 1-year secondary intervention-free survival was 95.1 ± 1.1% (Fig. 2). Within the first year after implantation, secondary interventions were required in 23 (4.6%) patients. Endovascular procedures were performed in 10 patients to resolve graft occlusion, stenosis or kinking; in six patients to correct a type-I/III endoleak; and in three patients to resolve a persistent type-II endoleak. Five patients underwent a by-pass procedure for an occluded iliac limb. Notably, stent graft migration or loss of device integrity was never observed within the first year after implantation. In addition, there were no reports of aneurysm rupture. At 1-year, aneurysm size increased by ≥5 mm in 2.8% of cases, was stable in 55.9% of cases and decreased by ≥5 mm in 41.3% of cases.

Table 7
Patient outcome within 30-days (ITT analysis).

Variable		$N = 1262$
One or more major adverse events (MAE)	3.9%	(49/1262)
All-cause mortality	1.3%	(16/1262)
Bowel ischemia	0.2%	(3/1262)
Myocardial infarction	1.1%	(14/1262)
Paraplegia	0.0%	(0/1262)
Renal failure	0.3%	(4/1262)
Respiratory failure	0.0%	(0/1262)
Stroke	0.2%	(2/1262)
Procedural blood loss ≥1000 cc	1.4%	(18/1262)
Conversion to open surgery	0.2%	(3/1262)
Secondary surgical procedure	1.5%	(19/1262)
Endovascular for occlusion, stenosis or kinking	0.6%	(8/1262)
Endovascular to correct Type I/III endoleak	0.3%	(4/1262)
Open bypass procedure	0.5%	(6/1262)
Other	0.1%	(1/1262)
Aneurysm rupture	0.0%	(0/1262)

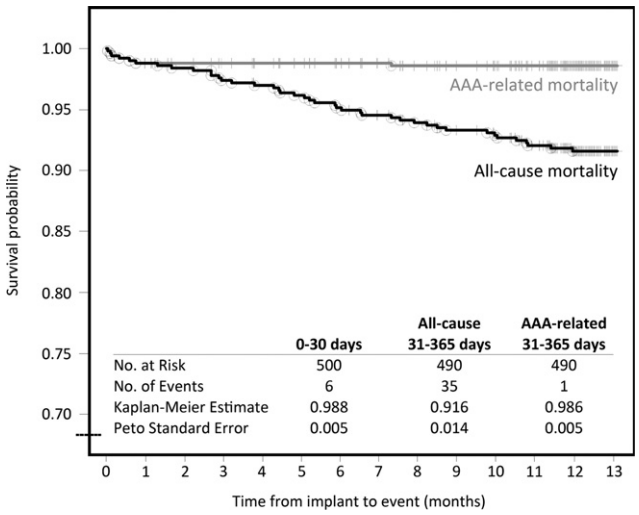

Figure 1. Kaplan–Meier estimates for all-cause mortality & AAA-related mortality.

Discussion

The technology of EVAR for AAAs is a dynamic, ever-changing endeavour. The challenge is to decrease complications and re-interventions while safely treating more complex anatomy, especially for those cases unfit for open repair. As improved devices with wider inclusion criteria become available and operators become more proficient with endovascular techniques, the proportion of patients suitable for EVAR increases.[13] However, overall outcomes may not improve if broadening the application rate results in poorer outcomes despite improvements in operator skill and device design. This ever-evolving trade-off implies that results from older series using previous generations of devices may

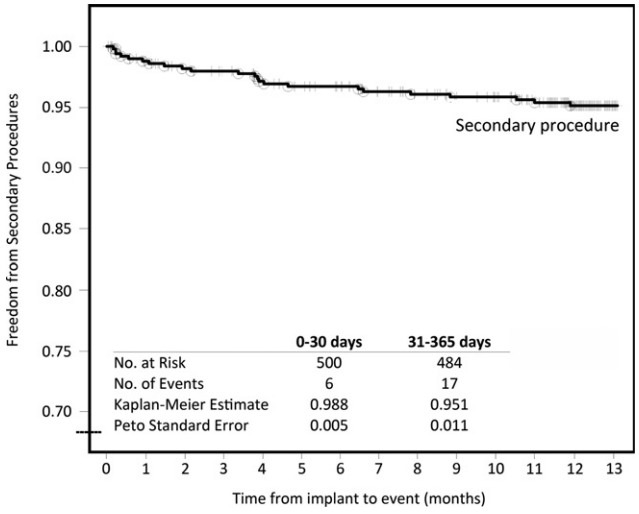

Figure 2. Kaplan–Meier estimates for secondary procedures.

not reflect the current status of EVAR. As a consequence, results of the performance of latest generation devices in contemporary, real-world settings are important. High-quality, well-designed observational studies are increasingly believed to provide complementary evidence to randomised controlled trials (RCTs).[14] Therefore, they are essential in making a balanced judgement about the management of AAAs.

The ENGAGE registry was undertaken to quantify the performance of a recently released endograft within the context of contemporary, real-world use. This prospective observational study represents the collective experience of 79 centres in 30 countries across five different continents with the Endurant Stent Graft. As eligibility was for the most part, left to the discretion of the investigator, the outcomes in the 1262 AAA patient series are expected to have high external validity. Follow-up protocols were kept as close as possible to standard site regimens, to keep treatment to real world practice. In order to be able to produce meaningful analysis, a large quantity of data was recorded. To guarantee high quality and completeness of data, efforts were made to achieve onsite quality control and continual monitoring of reported data, which is evident in the high level of compliance to follow-up in this registry.

The necessity for secondary interventions is considered the Achilles' heel of EVAR.[18,19] Secondary interventions were the main reason that EVAR was not considered cost-effective at long-term follow-up in the DREAM (Dutch Randomised Endovascular Aneurysm Management) trial.[20] A re-intervention rate of 4.6% is comparable to re-intervention rates of earlier reports and the recent OVER (Open Versus Endovascular Repair) trial, and compares favourably to the landmark studies EVAR −1 (Endovascular Repair versus Open Repair) and DREAM.[5–7,15–17] The type II endoleak rate of 9.9%, which is remarkably lower than in these older studies, might have contributed to the lower rate of secondary procedures. Comparison of re-intervention rates at 1-year with other studies is hampered by several factors; in particular, the treatment of type-II endoleaks has changed over time. On the other hand, in the ENGAGE Registry, 17.9% of patients were treated outside IFU, primarily due to complex anatomy; therefore, it should also be taken into consideration that the eligibility criteria for ENGAGE were less strict than for DREAM and OVER.[6,7]

The majority of re-interventions in our study were performed for iliac limb occlusion or stenosis. Van Keulen et al.[17] also found a higher iliac limb occlusion rate together with a 1-year re-intervention rate of 5% after implantation of an Endurant Stent Graft. At this moment, we are unable to conclude if there is any causality between occurrence of iliac occlusions and the wider inclusion criteria associated with the Endurant Stent Graft, or the stent graft itself.

Despite numerous cases of short- or angulated necks, rates of early type-I endoleaks were low, with no ruptures and 42% of reported aneurysm-sac shrinkage. So far, few re-interventions were required to resolve endoleaks. A comparison with the literature on type-I/III re-interventions or shrinkage of the aneurysm awaits availability of longer-term follow-up.

Compared with the landmark studies EVAR-1 and DREAM, in this study both perioperative mortality and the aneurysm-related mortality rates after 1 year were comparable. The all-cause mortality rate in this study compares favourably to EVAR-1 and DREAM.[5,6] This is remarkable given the proportion of ASA class IV patients (10.6%) in the ENGAGE study population; in all previously assessed RCTs, ASA class IV patients were excluded.

Conclusion

ENGAGE is an unprecedented registry in scope and magnitude to characterise the performance of the Endurant Stent Graft in a contemporary series of 1262 AAA patients treated with the stent graft in 30 countries. The early results of the Endurant Stent Graft in a real-world, global experience are promising despite the fact that 10.6% of patients were classified ASA class IV and 17.9% of the patients were treated outside IFU. Longer follow-up is needed to assess durability of safety and effectiveness in a broader spectrum of AAA patients treated via endovascular methods.

Registration

ClinicalTrials.gov Identifier NCT00870051, registered since 25 March 2009.

Contributions

Study design: RS, JT, DB, VR, PH and MvS
Data collection: JT, TF, DB, PP, VR, PH and MvS
Data analysis: RS, JT, TF, VR and MvS
Writing: RS, JT, TF, DB, PP, VR, PH and MvS

Conflicts of Interest

JT, TF, DB, PP, VR, PH and MvS have in the past received contributions from Medtronic AVE for giving oral presentations. JT, TF, DB, PP, VR and PH have been proctors for Medtronic AVE in the past.

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Appendix A

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