From the Society for Vascular Surgery

Fourteen-year outcomes of abdominal aortic endovascular repair with the Zenith stent graft

Fabio Verzini, MD, PhD, FEBVS,[a] Lydia Romano, MD,[a] Gianbattista Parlani, MD,[a] Giacomo Isernia, MD,[a] Gioele Simonte, MD,[a] Diletta Loschi, MD,[a] Massimo Lenti, MD, PhD,[a] *and* Piergiorgio Cao, MD, FRCS,[b]
Perugia and Rome, Italy

ABSTRACT

Objective: Long-term results of abdominal aortic aneurysm (AAA) endovascular repair are affected by graft design renewals that tend to improve the performance of older generation prostheses but usually reset the follow-up times to zero. The present study investigated the long-term outcomes of endovascular AAA repair (EVAR) using the Zenith graft, still in use without major modification, in a single center experience.

Methods: Between 2000 and 2011, 610 patients underwent elective EVAR using the Zenith endograft (Cook Inc, Bloomington, Ind) and represent the study group. Primary outcomes were overall survival, freedom from AAA rupture, and freedom from AAA-related death. Secondary outcomes included freedom from late (>30 days) reintervention, freedom from late (>30 days) conversion to open repair, freedom from aneurysm sac enlargement >5.0 mm and freedom from EVAR failure, defined as a composite of AAA-related death, AAA rupture, AAA growth >5 mm, and any reintervention.

Results: Mean age was 73.2 years. Mean aneurysm diameter was 55.3 mm. There were five perioperative deaths (0.8%) and three intraoperative conversions. At a mean follow-up of 99.2 (range, 0-175) months, seven AAA ruptures occurred, all fatal except one. Overall survival was 92.8% ± 1.1% at 1 year, 70.1% ± 1.9% at 5 years, 37.8% ± 2.9% at 10 years, and 24 ± 4% at 14 years. Freedom from AAA-rupture was 99.8% ± 0.02 at 1 year (one case), 99.4% ± 0.04 at 5 years (three cases), and 98.1% ± 0.07 at 10 and 14 years. Freedom from late reintervention and conversion was 98% ± 0.6 at 1 year, 87.7% ± 1.5 at 5 years, 75.7% ± 3.2 at 10 years, and 69.9% ± 5.2 at 14 years. Freedom from aneurysm sac growth >5.0 mm was 99.8% at 1 year, 96.6% ± 0.7 at 5 years, 81.0% ± 3.4 at 10 years, and 74.1% ± 5.8% at 14 years. EVAR failure occurred in 132 (21.6%) patients at 14 years. At multivariate analysis, independent predictors of EVAR failure resulted type I and III endoleak (hazard ratio [HR], 6.7; 95% confidence interval [CI], 4.6- 9.7; $P < .001$], type II endoleak (HR, 2.3; 95% CI, 1.6-3.4; $P < .001$), and American Society of Anesthesiologists grade 4 (HR, 1.6; 95% CI, 1.0-2.6; $P = .034$).

Conclusions: EVAR with Zenith graft represents a safe and durable repair. Risk of rupture and aneurysm-related death is low, whereas overall long-term survival remains poor. Novel endograft models should be tested and evaluated considering that one-fourth of the operated patients will still be alive after 14 years. (J Vasc Surg 2017;65:318-29.)

Endovascular abdominal aortic aneurysm (AAA) repair (EVAR) entered routine medical practice over 20 years ago. The benefits of this less invasive technique have been confirmed in randomized controlled trials.[1-4] Although EVAR offers the immediate advantage of lower perioperative morbidity and mortality rates, it does require lifelong surveillance for potential graft-related complications.[5-13] Indeed, mid- and long-term data have shown a higher rate of reinterventions, compared with open surgery repair (OSR), to prevent aneurysm rupture and death.[1-4,14]

To improve the long-term results and to extend the indications for treatment of aneurysms with complex anatomy, stent grafts have been modified over the years leading to the introduction of lower profile devices with stable fixation modes, low porosity, and adaptability to anatomic constraints.[15-18] Currently, multiple devices are available in Europe: some represent the evolution of previous models, with small structural changes compared with the previous ones (ie, the low porosity Excluder endograft; W. L. Gore & Associates Inc, Flagstaff, Ariz), whereas others present completely new structural and conceptual models (ie, the Nellix device; Endologix Inc, Irvine, Calif). These new generation endografts promise to afford better results compared with those ascertained in the randomized trials that up to date constitute the best

From the Vascular Surgery Unit, S. Maria della Misericordia Hospital, University of Perugia, Perugia[a]; and Gruppo Villa Maria (GVM) Research and Care, Rome.[b]

Author conflict of interest: F.V. is a paid as a consultant for Cook Inc (Bloomington, Ind), W. L. Gore & Associates Inc (Flagstaff, Ariz), and Medtronic (Santa Rosa, Calif).

Presented at the 2016 Vascular Annual Meeting of the Society for Vascular Surgery, National Harbor, Md, June 8-11, 2016.

Correspondence: Fabio Verzini, MD, PhD, FEBVS, Vascular Surgery Unit, S. Maria della Misericordia Hospital, University of Perugia, Piazzale Menghini, 1, Perugia 06129, Italy (e-mail: fabio.verzini@unipg.it).

The editors and reviewers of this article have no relevant financial relationships to disclose per the JVS policy that requires reviewers to decline review of any manuscript for which they may have a conflict of interest.

0741-5214

http://dx.doi.org/10.1016/j.jvs.2016.07.117

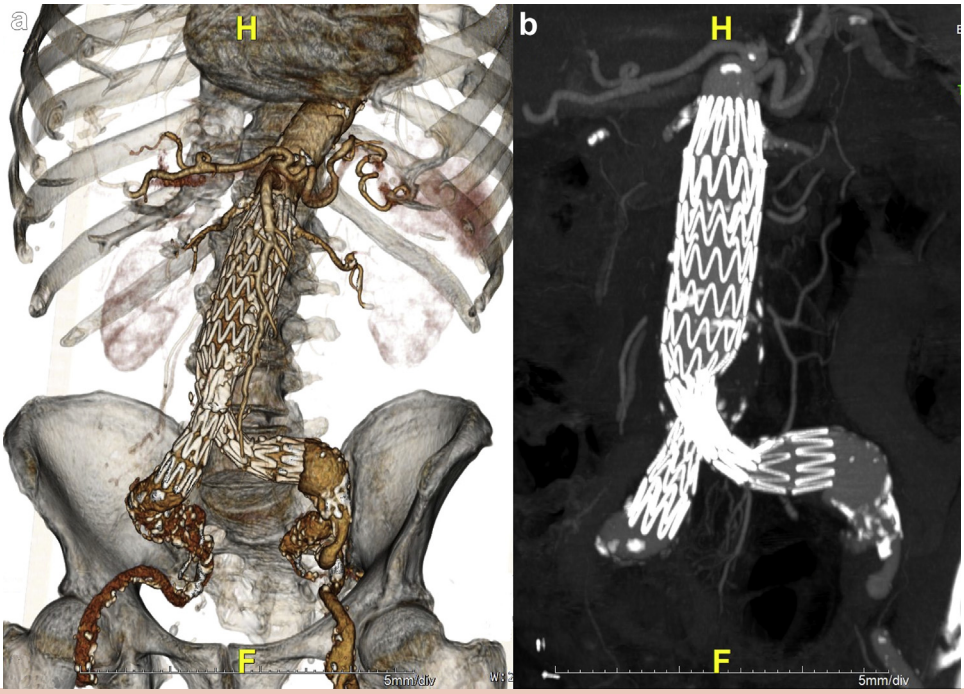


Fig 1. Computed tomography (CT) scan control performed 101 months after endovascular abdominal aortic aneurysm (AAA) repair (EVAR) with Cook Zenith graft. **a,** Three-dimensional reconstruction. **b,** The almost complete shrinkage of the aortic aneurysm is detectable (maximum intensity projection image). Patient presents bilateral recurrent common iliac artery aneurysm, less than 30 mm in axial diameter, currently in follow-up.

evidence available to sustain the efficacy of EVAR. Unfortunately, these studies included older generation grafts no longer in use, thus, building up evidence that is flawed by the evolving technical improvements. Even our group found a clear advantage in midterm results in patients treated with newer generation endografts compared with the older ones.[11] On the other hand, the new generation endografts have not yet demonstrated efficacy and durability in the long term, thereby leaving uncertainties on the effective perspectives of patients treated today.[18,19]

The only abdominal endograft that is still in use since 1997 without major structural modifications is the Zenith graft (Cook Inc, Bloomington, Ind).[20,21]

The aim of the present study is to analyze the long-term results in our single center experience with the Cook Zenith graft (Fig 1) in a large cohort of patients with a follow-up of up to 14 years.

METHODS

Between February 2000 and December 2011, data of consecutive patients undergoing elective EVAR using the Zenith stent graft (Cook, Inc) at our tertiary care university hospital were retrieved from a prospectively maintained electronic database and analyzed retrospectively. To evaluate follow-up data of at least 3 years, patients treated after December 2011 were excluded from the present analysis.

Patients with ruptured aneurysms or treated for thoracoabdominal or isolated iliac aneurysms were also excluded. Standard indications for EVAR at our center included aneurysms larger than 5 cm in diameter, or patients with smaller aneurysms if associated with iliac aneurysms greater than 3 cm in maximum diameter. Our cohort includes also patients enrolled in the Comparison of surveillance vs Aortic Endografting for Small Aneurysm Repair (CAESAR) Trial, which evaluated EVAR in small AAA (diameter, 4.1-5.4 cm), who underwent immediate intervention or surgery after surveillance.[22] Since 2006, the Cook Zenith iliac side branch device was also used, in addition to the AAA Zenith endograft, in patients with iliac aneurysms and suitable anatomy. All patients signed an informed consent form for inclusion in clinical prospective studies.

Anatomic feasibility was assessed with contrast-enhanced spiral computed tomography (CT) in all patients. A dedicated vascular workstation (Aquarius; Terarecon, Foster City, Calif) was used for CT analysis. Suitable AAA morphology included a proximal neck length $\geq$15 mm, proximal neck diameter in the range of 20-32 mm, and a neck angle $<60^{\circ}$; broader inclusion criteria have been selectively used in case of patients at prohibitive risk for open repair, and a total of 44 patients with proximal neck length $<$15 mm ($n = 43$) and/or proximal neck diameter $>$ 32 ($n = 6$) have been included.

Patient comorbidities were classified according to the Society of Vascular Surgeons/American Association for Vascular Surgery reporting standards.[23] Grading is based on the criteria of the American Society of Anesthesiologists (ASA).[24]

The Zenith endovascular graft is a three-modular system composed by a bifurcated aortic main body and two iliac legs. All devices incorporate self-expanding stainless steel Z-stents that are sutured to a woven polyester graft material. A bare metal stent with staggered barbs is located on top of the main body for suprarenal fixation. Although the Zenith graft has not undergone significant modifications since its introduction, the number of barbs and sutures at the level of proximal stent has been increased over the years.

All procedures were performed in an operating room equipped with a mobile C-arm (OEC 9800; General Electric, Chalfont St. Giles, United Kingdom) until December 2005, and thereafter in a hybrid vascular operating room equipped with a fixed, ceiling mounted X ray imaging system with flat panel detector (Axiom Artis; Siemens, Erlangen, Germany). Surgical access to the femoral artery was used in most of the elderly patients. Procedures were performed preferentially under local anesthesia.

Postoperatively, abdominal and access-site color duplex ultrasound was performed in all patients before discharge to evaluate graft and arterial patency, endoleak, and complications. Clinical and ultrasound evaluations were repeated at 1 month and every 6 months thereafter. The imaging protocol included aortoiliac CT imaging within the first month after implantation, and then yearly, and a plain radiograph at 6 months and annually thereafter. The follow-up protocol was revised after the publication of the European Society for Vascular Surgery guidelines in 2011 and since then, CT after 1 year is reserved only to patients with complications, AAA growth, or endoleaks.[25]

Primary outcomes were (1) overall survival, (2) freedom from AAA rupture, and (3) freedom from AAA-related death, defined as any death occurring within 30 days from the primary or from any secondary aortoiliac intervention or because of AAA rupture or graft infection.

Secondary outcomes included freedom from late reintervention, freedom from late conversion to open repair, freedom from aneurysm sac enlargement >5.0 mm, and freedom from EVAR failure, defined as a composite of AAA-related death, AAA rupture, AAA growth >5 mm, and any aortoiliac reinterventions. Late reintervention was defined as any secondary endovascular or open surgical reintervention after 30 days from primary EVAR, with persistence of endograft in place. Late conversion was defined as any open surgical reintervention with removal of the aortic component of the endograft. In addition, we also analyzed early and late complications, including perioperative major morbidities, reintervention and conversion, endoleaks, graft occlusion, infection, and migration (defined as caudal movement of the proximal portion of the endograft of ≥10.0 mm).

Indications for reintervention were based on occurrence of persisting type II endoleak associated with AAA growth >5 mm, presence or imminence of type I/III endoleak, relevant migration, graft occlusion/rupture/infection, or a combination of these factors associated or not with aneurysm growth/rupture.

Death certificates have been checked in all cases for ascertainment of the cause of death in patients with no clear family and/or general practitioner information.

Statistical analysis. Descriptive statistics are reported as mean ± standard error, median, and interquartile ranges for skewed data. Results for categorical data are expressed as frequencies and percentages. The χ^2 or the Fisher exact test was used for comparison of qualitative variables and the Student *t*-test or the variance analysis for continuous variables. Kaplan-Meier analysis was used to report overall survival, freedom from AAA-rupture, freedom from AAA-related death, and freedom from AAA growth >5 mm, reintervention and conversion to open repair, individually. Estimates up to a standard error <0.10 were considered valid. The independent association between primary and secondary outcomes and risk factors was tested with the χ^2 or Fisher exact test. Cox regression with backward stepwise selection of potential confounders was used to identify variables potentially associated with EVAR failure. Tested variables included AAA diameter, neck length <15 mm, age, smoking status, diabetes mellitus, hypertension, chronic obstructive pulmonary disease, coronary artery disease, renal disease, hyperlipidemia, peripheral arterial disease, anticoagulant therapy, ASA grade = 4, type I or III endoleak, type II endoleak, being a CAESAR patient, and early experience (ie, being among the first 50 patients treated). Results are reported as hazard ratios (HRs) with 95% confidence intervals (CIs). In all analyses a *P* value of ≤.05 indicated statistical significance. Data were analyzed using the SPSS software v 20 (IBM Corporation, Armonk, NY).

RESULTS

Between February 2000 and December 2011, 1282 consecutive patients with aortoiliac aneurysms underwent primary elective EVAR at our hospital using different device models. The Zenith stent graft was used in 610 cases (47.5%). In 70 (11.5%) patients, the Zenith iliac side branch device was also used.

Baseline characteristics are listed in Table I. In our cohort, 567 (93%) patients were male, and mean age was 73.2 years (range, 40-95 years). Forty-three (7%) patients had aneurysm neck length <15 mm, and 38 (6.2%) had an aneurysm neck diameter >28 mm. General anesthesia

Table I. Baseline characteristics

Patients	No. (%) (N = 610)
Males, No, %	567 (93)
Age, mean, (range), years	73.7 (48-95)
ASA grade	
2	177 (31.2)
3	309 (54.5)
4	81 (14.3)
Comorbidities	
Hypertension	472 (77.4)
Smoking habit	343 (56.2)
Pulmonary disease	297 (48.7)
Cardiac disease	262 (43.0)
Hyperlipidemia	218 (35.7)
Renal disease	88 (14.4)
Diabetes	84 (13.8)
Cerebrovascular disease	80 (13.1)
Peripheral arterial disease	58 (9.5)
Aneurysm, mean (range), mm	
AAA diameter	55.3 (35-105)
Proximal neck length	24.7 (10-60)
Proximal neck diameter	23.9 (16-34)

AAA, Abdominal aortic aneurysm; *ASA*, American Society of Anesthesiologists.
Categorical data are shown as number (%) and continuous variables as mean (range).

Table II. Perioperative complications

Patients	No. (%)
Early reinterventions	40 (6.5)
Conversion to open repair	3 (0.5)
Iliac branch occlusion	11
Lower limb ischemia	7
Renal stenosis/occlusion	5
Access complications	5
Type I endoleak	4
Type III endoleak	2
Iliac artery rupture	2
Intestinal ischemia	1
Major morbidity	25 (4.0)
Renal	7
Cardiac	4
Pulmonary	4
Cerebrovascular	3
Access complications	3
Lower limb ischemia	3
Intestinal ischemia	1
Total, n (%)	65 (10.5)

Values are shown as number (%).

was used in 107 patients (17.5%). Median postoperative hospital stay was 2 days (range, 1-30 days).

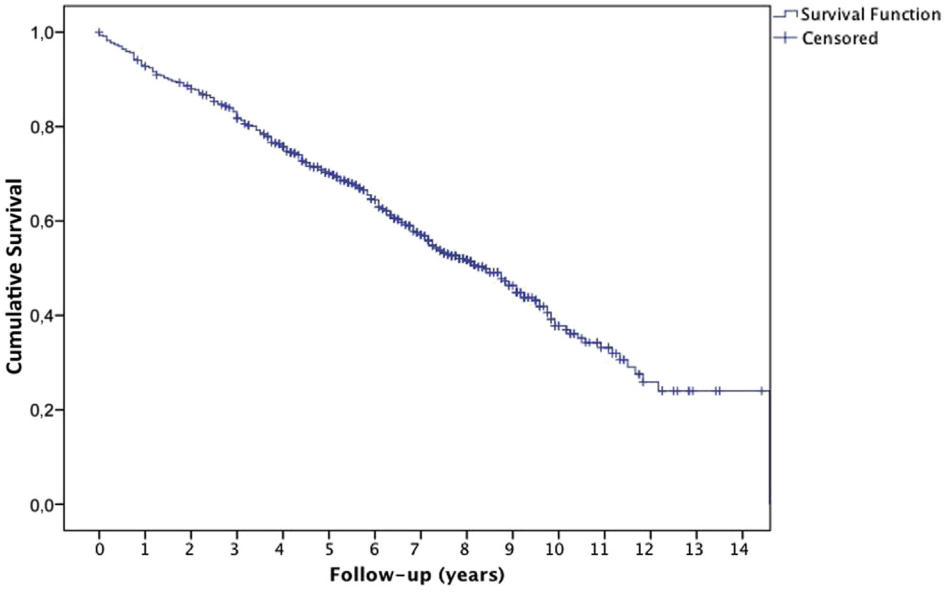
There were five (0.8%) perioperative deaths. Mortality was due to aneurysm rupture at 21 days in one case and the remaining four were attributable to intestinal ischemia, pancreatitis, cardiac complications, or renal failure secondary to occlusion of renal artery. Overall, 65 (10.6%) perioperative complications occurred, 40 (6.5%) requiring reinterventions, as described in Table II. Conversion to open repair during primary EVAR occurred in three cases (0.5%), two of which were due to deployment failure (impossibility to retract the releasing wire), and one for proximal neck rupture after ballooning. Intraoperative endoleaks were 87 (14.2%); 25 (4%) persisted to 30 days (two type I and 23 type II).

Mean follow-up was 99.2 ± 2.9 months (range, 0-175). Ten patients were lost to follow-up. Compliance with imaging follow-up declined over time, and among the 50 patients with a 10-year follow-up, not imaging was performed on four patients in the last 2 years. Overall, survival estimated by Kaplan-Meier analysis was 92.8% ± 1.1% at 1 year, 70.1% ± 1.9% at 5 years, 37.8% ± 2.9% at 10 years, and 24 ± 4% at 14 years (Fig 2).

Seven (1.14%) AAA ruptures occurred, all fatal except one. One fatal rupture happened during the early perioperative period. Among the late ruptures, two were attributable to device infection (one died after conversion to open repair, the other left untreated); two to type I endoleaks (one with distal type I endoleak died after reintervention and the other with proximal type I endoleak refused reintervention); and two to type II endoleak. The patient who survived, had type 1B endoleak and was successfully treated with iliac extension. The Kaplan-Meier estimate of freedom from aneurysm rupture was 99.8% ± 0.02 at 1 year, 99.4% ± 0.04 at 5 years, and 98.1% ± 0.07 at 10 and 14 years (Fig 3).

AAA-related deaths were 12 (2%); five patients died in the perioperative period. During follow-up, five patients died because of late AAA-rupture, and the remaining two to AAA-related reintervention. The Kaplan-Meier estimate of freedom from AAA-related death was 99.2% ± 0.4 at 1 year, 98.4% ± 0.6 at 5 years, and 97.3% ± 0.8 at 10 and 14 years (Fig 4).

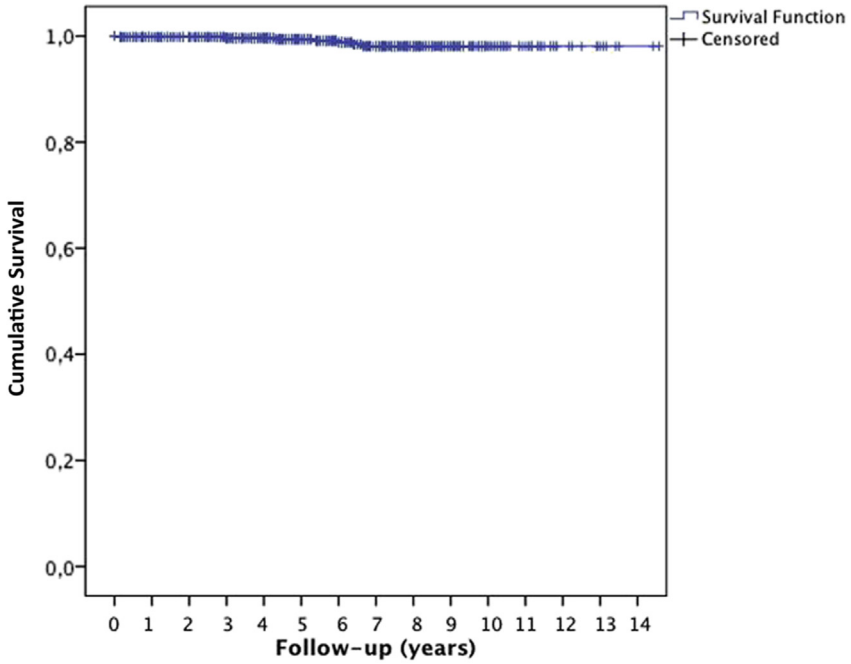
Conversion to OSR occurred in 11 (1.8%) patients. The Kaplan-Meier estimate of freedom from late conversion to OSR was 99.5% at 1 year, 98.4% at 5 years, and 95.3% at 10 years, and 91.2% ± 4.3% at 14 years (Fig 5). Conversion was due to an infected aneurysm in one case (the patient died after conversion); to type II endoleak in three; to type I endoleak in five; to type III endoleak in 1, and to endotension in 1. During follow-up, 91 (14.9%) patients required at least one secondary intervention (Table III). The Kaplan-Meier estimate of freedom from late reintervention and conversion was 98% ± 0.6 at 1 year, 87.7% ± 1.5 at 5 years, 75.7% ± 3.2 at 10 years, and 69.9% ± 5.2 at 14 years (Fig 6).



Years	*0*	*1*	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*	*10*	*11*	*12*	*13*	*14*
N at risk	610	599	535	493	436	371	307	241	161	96	50	30	14	4	2
Survival, %[a]	100	92.8	88	81.8	75.7	70.1	64.4	57.0	51.9	46.4	37.8	33.2	25.8	24	24

[a]Estimated from Kaplan-Meier survival life-table

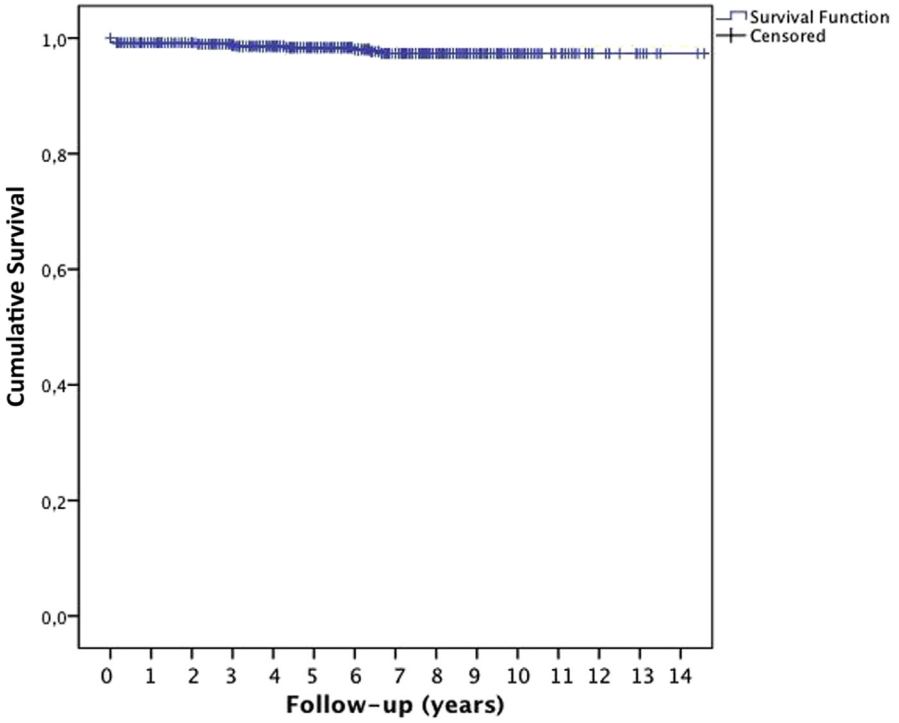
Fig 2. Kaplan-Meier estimate of the cumulative probability of overall survival.



Years	*0*	*1*	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*	*10*	*11*	*12*	*13*	*14*
N at risk	610	565	536	494	439	371	311	244	160	95	86	29	12	7	2
Survival, %[a]	100	99.8	99.8	99.6	99.6	99.4	98.8	98.4	98.1	98.1	98.1	98.1	98.1	98.1	98.1

[a]Estimated from Kaplan-Meier survival life-table

Fig 3. Kaplan-Meier estimate of the cumulative probability of aneurysm rupture.



Years	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
No at risk	610	566	535	495	439	374	313	249	168	101	55	30	13	7	2
Survival, %[a]	100	99.2	99.2	98.8	98.8	98.4	98.0	97.3	97.3	97.3	97.3	97.3	97.3	97.3	97.3

[a]Estimated from Kaplan-Meier survival life-table

Fig 4. Kaplan-Meier estimate of the cumulative probability of aneurysm-related death.

Late aneurysm sac growth >5 mm occurred in 41 (6.7%) patients leading to reintervention in 22 cases and to conversion to open repair in six (Table IV). The Kaplan-Meier estimate of freedom from aneurysm sac growth >5.0 mm was 99.8% at 1 year, 96.6% ± 0.7 at 5 years, 81.0% ± 3.4 at 10 years, and 74.1% ± 5.8% at 14 years (Fig 7).

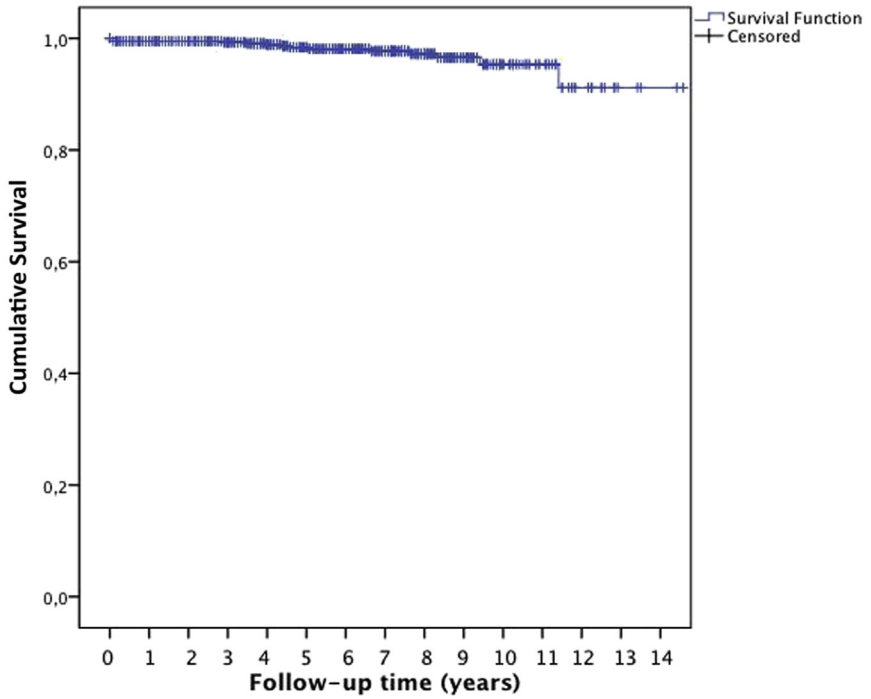
A total of 140 (22.9%) patients developed endoleaks at any time; 41 were classified as type I, 104 type II, and 11 type III. Endograft migration occurred in seven (1.1%) cases (Fig 8), however, only two exceeded 10 mm and required reintervention (ie, proximal endograft extension). Twenty-one (3.4%) iliac limb occlusion were observed, 11 of which occurred in the first 30 days and required reintervention (in one patient limb occlusion recurred and required reintervention during follow-up), whereas 10 developed during follow-up and required surgical revision in six cases.

EVAR failure occurred in 132 (21.6%) patients at 14 years. At multivariate analysis, independent predictors of EVAR failure resulted: type I-III endoleak (HR, 6.7; 95% CI, 4.6-9.7; $P < .001$), type II endoleak (HR, 2.3; 95% CI, 1.6-3.4; $P < .001$), and ASA grade 4 (HR, 1.6; 95% CI, 1.0- 2.6; $P = .034$). In addition, although a trend toward an increased risk of EVAR failure with early experience (ie, first 50 cases) was observed, experience was not a significant predictor of EVAR failure (HR, 1.7; 95% CI, 0.99-2.92; $P = .052$) at multivariate analysis.

DISCUSSION

The present study provides long-term information on a wide, unselected population of patients with AAA treated with the oldest EVAR graft still in use without major modification.

The first observation refers to prognosis of patients with AAA treated with a minimally invasive procedure. After 14 years, three-fourths of them died, mainly from cardiovascular disease. These data are in line with recent observations focusing on the persistence of poor long-term prognosis of this population, even with advances in medical treatment and reduced invasiveness of the intervention. In a recent article from Bahia et al,[26] the systematic review of the literature on late survival after AAA repair surprisingly resulted in only 36 studies published between 1969 and 2011 with a follow-up of at least 4 to 6 years. Authors underlined that 5-year survival remains poor, with a mean 69% rate, and that there has been no measurable improvement over time because of increasing treatment of elderly patients. A message toward the need for a focused research to



Years	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
No at risk	610	564	533	490	434	372	309	243	173	105	53	32	15	4	2
Survival, %[a]	100	99.5	99.5	99.3	98.9	98.4	98.1	97.7	97.2	96.6	95.3	95.3	91.2	91.2	91.2

[a]Estimated from Kaplan-Meier survival life-table

Fig 5. Kaplan-Meier estimate of the cumulative risk of conversion to open repair.

Table III. Secondary interventions during follow up

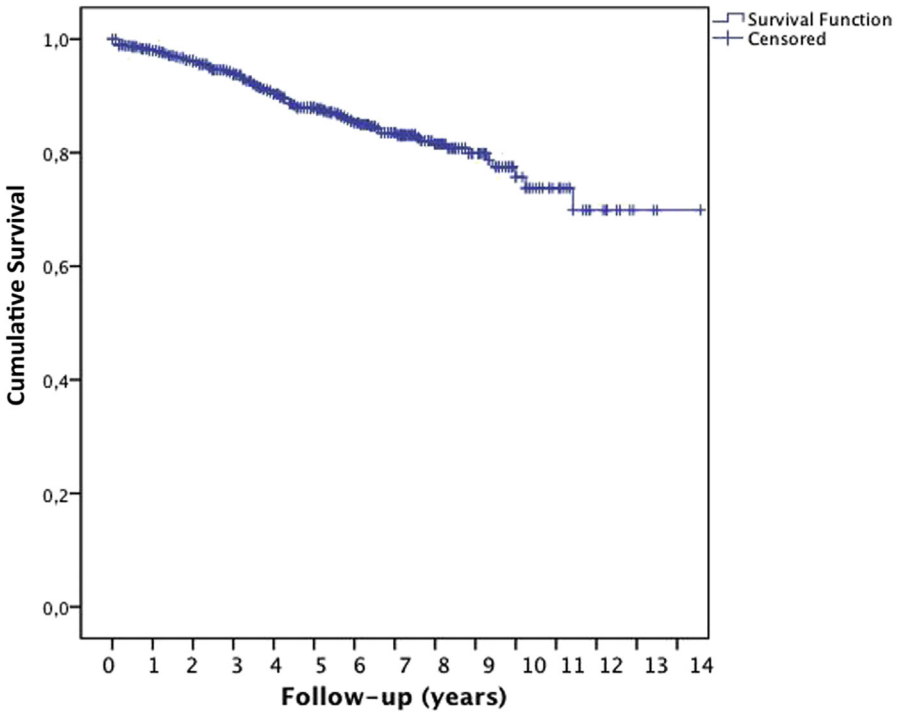
Patients	No. (%) (N = 610)
Reinterventions	80 (13.1)
Endoleak type 1-III	34
Endoleak type II	22
AAA rupture	2
Graft occlusion	7
Graft migration	2
Renal stenosis/occlusion	3
Conversions	11 (1.8)
Endoleak type 1-III	6
Endoleak type II	3
Endotension	1
AAA rupture and graft infection	1
Total	91 (14.9)

AAA, Abdominal aortic aneurysm.
Values are shown as number (%).

further improve the survival of AAA patients is clearly evident from these observations.

On the other hand, if we consider that after 14 years from treatment, one-fourth of the operated patients are still alive with their endograft in place, we have to forecast durable repairs with endografts able to withstand mechanical stresses for a long time. Up until now, legal constraints dictate in vitro fatigue testing for aortic endografts of at least 400 million cycles to reproduce 10 years of activity. In addition, these tests cannot mimic the in vivo stresses of an implanted endograft that is exposed to an ever-changing environment because of anatomic plasticity, sac remodeling, and appearance and disappearance of endoleaks, among others. To date, few other studies have reported long-term results of EVAR with single models of endograft, most were able to demonstrate increasing rates of mechanical failure with oldest endografts that determined the abandonment of graft production, like in the case of the oldest Vanguard endograft (Boston Scientific/Scimed, Natick, Mass).[27] More recently, 10-year follow-up data have been published for the Talent abdominal stent graft (Medtronic, Santa Rosa, Calif, no longer available). In an article by Pitton et al,[28] in a cohort of 127 patients, the risk of reinterventions was approximately around 45% at 5 years, and approximately 65% at 10 years.

Our results compare very favorably to those numbers. In the present cohort, the risk of reintervention is 12.1% at 5 years, 25% at 10 years, and 30% at 14 years, in accordance with other long-term Zenith cohorts.[5,29,30] In the Japanese experience reported by Ivakoshi et al,[29] using the Zenith device in 127 patients followed-up for 10 years,



Years	*0*	*1*	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*	*10*	*11*	*12*	*13*	*14*
No at risk	610	555	514	466	399	333	269	212	140	84	43	26	12	3	1
Survival, %[a]	100	98	96.1	93.8	90.3	87.9	85.3	83.5	81.5	79.9	75.7	73.7	69.9	69.9	69.9

[a]Estimated from Kaplan-Meier survival life-table

Fig 6. Kaplan-Meier estimate of the cumulative risk of overall late reinterventions (reintervention and conversion).

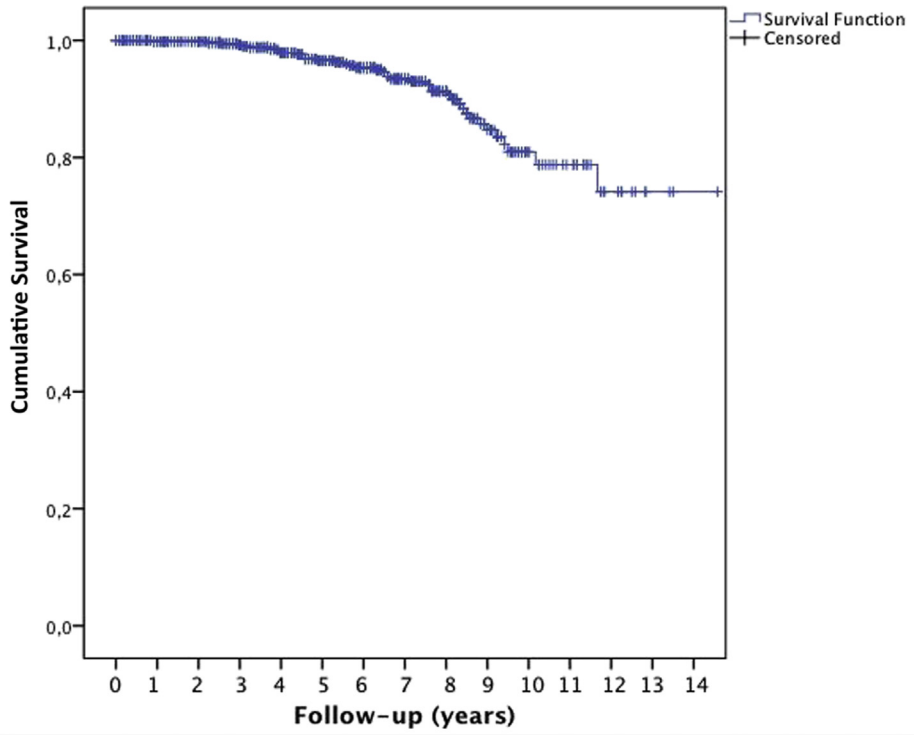
Table IV. Abdominal aortic aneurysm (AAA) growth > 5 mm

Patients	No. (%) (N = 41)
Reinterventions	22 (53.6)
Endoleak type I-III	10
Endoleak type II	12
Conversions	6 (14.6)
Endoleak type I-III	3
Endoleak type II	2
Endotension	1
No treatment	13 (31.7)
Endoleak type I-III	3
Endoleak type II	7
Endotension	3
Total	41 (6.7)

the risk of reintervention was 30%, with a 7% risk of aneurysm-related death. A larger cohort was investigated in the Zenith multicenter trial that enrolled 739 patients both in the pivotal arm and in the continued access trial.[29] The reported 5-year results sustained long-term durability of Zenith repairs with a low risk of aneurysm-related death (2% and 4% in standard- and high-risk patients, respectively). Our similar risk of 1.6%, at the same follow-up interval suggests that the graft performs equally well in a selected population with rather strict inclusion criteria, such as the American one, and in a cohort with broader indications, like ours.

Very recently, the preliminary 5-year results of a latest generation endograft have been presented. The performance of EVAR with Endurant Medtronic is being investigated in the multicenter U.S. investigational device exemption trial that enrolled 150 patients.[31] Authors reported a 0.8% risk of AAA-related death, with a risk of re-intervention of 11% at 5 years.[32] If these trends will be confirmed in the long term, we probably could expect similar results with our Zenith cohort, with a small proportion of patients still at risk of failure in the long run, even with the newest endografts. This may imply that clinical and imaging follow-up cannot be stopped any time after EVAR, to detect and treat potential causes of late AAA ruptures, at least in selected subgroups of patients.

Variable outcomes of different graft models suggest that mixing up results of older generation endografts with those of newer ones may carry the risk of underestimating the true updated results of EVAR. In



Years	*0*	*1*	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*	*10*	*11*	*12*	*13*	*14*
No at risk	610	565	536	494	439	371	311	244	160	95	86	29	12	7	2
Survival, %[a]	100	99.8	99.8	99.2	97.9	96.6	95.4	93.4	91.3	84.7	81.0	78.8	74.1	74.1	74.1

[a]Estimated from Kaplan-Meier survival life-table

Fig 7. Kaplan-Meier estimate of the cumulative risk of aneurysm sac growth >5.0 mm.

the randomized trials comparing EVAR and open repair, at least one-third to one-half of the patients have been enrolled with grafts no longer in use. Both EVAR 1 and 2 trials and Open vs Endovascular Repair (OVER) trial suggested different results between different graft generations, already at midterm. In the United Kingdom trials, secondary interventions occurred more frequently with Talent than with Zenith graft, with nonstatistically significant difference: 8.6 vs 6.4 events per 100 patient-years in the EVAR 1 trail (HR, 0.79 [0.51-1.21]); in the EVAR 2 trial, the difference was more pronounced, with 15.1 vs 9.6 events per 100 patient-years. In the OVER trial, the risk of death demonstrated a less favorable outcome after endovascular repair with AneuRx device (Medtronic) compared with other endovascular systems. Hopefully, long-term follow-up will clarify the role of technology on the late outcomes of EVAR.

Unfortunately, with the introduction of newer generation endografts, follow-up lengths have to be reset to zero, and, therefore, experiences such as the present one may be of value to predict the fate of currently operated patients in the long term. The real advantage of newest, thinnest endograft models, with completely different designs from the older ones (like ultra-thin fabrics, squared metallic wires instead of rounded, bags with polymers as sealing methods, among others) cannot be derived by assimilation of their early results with those at long term presented here.

Even if the Zenith endograft is being replaced, at least in Europe, by newer generation endografts, its long-term results remain valuable because its basic structure is preserved in the currently available fenestrated models. The low risk of migration (1.1%) observed in our series is, therefore, reassuring. In fact, eventual migration of fenestrated endografts may carry high risk of complications because of the potential occlusion of visceral stent grafts and vessels, when angulations may become prohibitive to preserve the flow. Our data are in line with the largest experience on fenestrated Cook devices.[33] In over 9 years of follow-up, Mastracci et al[33] reported only seven migrations in 650 patients (1.1%), four cases required a branch-related reintervention to preserve visceral patency.

Previous reports suggested that iliac limb occlusion risk might represent a weakness of the Zenith endograft, mainly because of the segmented long stents design of its skeleton.[21,30,34-37] However, our cumulative occlusion rate was 3.4%, most of the cases occurring in the early postoperative period. With growing experience, we learned to avoid the use of this graft in very tortuous anatomies and to detect graft kinks at the intraoperative

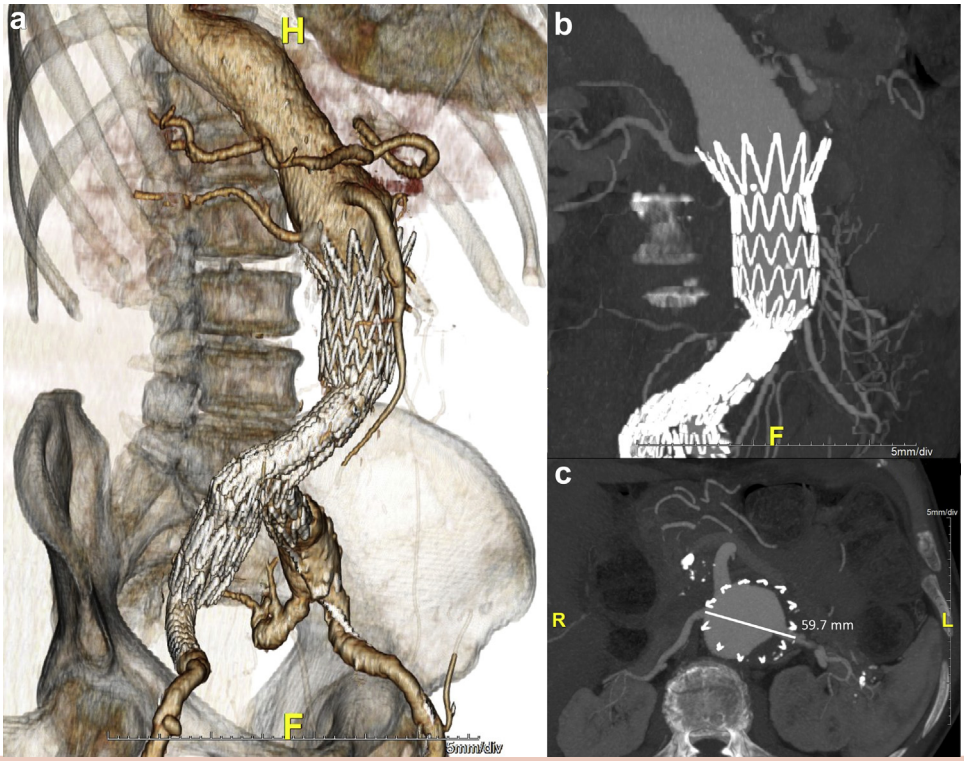


Fig 8. Computed tomography (CT) scan control in a patient that developed recurrent proximal aortic aneurysm in the visceral segment with subsequent distal migration; **a,** Three-dimensional reconstruction; **b,** Maximum intensity projection in coronal; and **c,** Axial view.

control, when the adjunct of a supporting self-expanding stent may limit the risk of subsequent graft thrombosis. Our data are similar to those of the Zenith investigational device exemption trial in which cumulative occlusion rate was 2.6% over 5 years, with all cases occurring in the first 2 years of follow-up.[30] A wide variety of limb graft occlusion risks have been reported in the current literature using different graft models, underlying that operator experience and patient's anatomy may play a major role. In a multiple grafts single center experience, Mantas et al[38] reported highly variable occlusion risk among different endografts (2.2% for Gore Excluder, 5.8% for Cook Zenith; 2.7% for Vascutek Anaconda; and 8.8% for Medtronic Endurant). Authors pointed out that presence of excessive iliac angulation (>60°), calcification (>50% of the circumference), and oversizing (>15%) were independently associated with graft occlusions, whereas endograft model was not statistically significant. Our data are also in line with those of last generation devices, such as Medtronic Endurant. In the Endurant Stent Graft Natural Selection Global Postmarket Registry (ENGAGE) registry, collecting worldwide data on EVAR with the Endurant graft, the occlusion rate, over maximum follow-up of 2 years, was 3.4%; the strongest independent predictors being iliac landing into the external iliac artery; a diameter of the external iliac artery < 10 mm; and iliac kinking.[39]

All these studies reinforce the message that outstretching the indications for endovascular repair carries higher risk of failure. In our experience, among the preoperative risk factors, the only independent predictor of EVAR failure was the ASA 4 status of the patient. This may suggest that in those patients at high risk for conventional open repair, the EVAR procedure was carried out even in the presence of an adverse anatomy, leading, therefore, to worse long-term results.

The current study presents some limitations. The long observation period carries the risk of loss to imaging follow-up in aging patients, with potential underestimation of complications not linked to evident clinical effects. In addition, data from a single center may not be generalized due to the potential of site-specific selection criteria adopted locally. Furthermore, the nonconsecutive patient inclusion because of the concomitant use of different endografts may not reflect the results of other series in which a single graft was used by default.

CONCLUSIONS

Our data show that EVAR with Zenith endograft represents a durable repair. The risk of AAA-related death remains low up to 14 years after intervention, with acceptable rates of reinterventions. However, the prognosis of patients with EVAR remains poor, with only one-fourth of them surviving after 14 years, thereby

advocating a clear call for strategies to reduce cardiovascular mortality in such population. The presence of late AAA growth, even if in a minority of cases, suggests that a lifelong follow-up is still needed in all patients with EVAR.

The authors would like to thank Francesca Zannetti for language editing and technical support and Grazia Pula for clinical assistance.

AUTHOR CONTRIBUTIONS

Conception and design: FV, GP, GI, GS, PC
Analysis and interpretation: FV, GI, GS
Data collection: LR, GI, GS, DL
Writing the article: FV, LR, GP
Critical revision of the article: FV, LR, GP, GI, GS, DL, ML, PC
Final approval of the article: FV, LR, GP, GI, GS, DL, ML, PC
Statistical analysis: FV, LR, GI, GS
Obtained funding: Not applicable
Overall responsibility: FV

REFERENCES

1. The United Kingdom EVAR Trial Investigators. Endovascular versus open repair of abdominal aortic aneurysm. N Engl J Med 2010;362:1863-71.
2. The United Kingdom EVAR Trial Investigators. Endovascular repair of aortic aneurysm in patients physically ineligible for open repair. N Engl J Med 2010;362:18672-80.
3. Blakensteijn JD, De Jong S, Prinssen M, van der Ham AC, Buth J, van Sterkenburg SM, et al. Two-year outcomes after conventional or endovascular repair of abdominal aortic aneurysms. N Engl J Med 2005;352:2398-405.
4. Lal BK, Zhou W, Li Z, Kyriakides T, Matsumura J, Lederle FA, et al; OVER Veterans Affairs Cooperative Study Group. Predictors and outcomes of endoleaks in the Veterans Affairs Open Versus Endovascular Repair (OVER) Trial of Abdominal Aortic Aneurysms. J Vasc Surg 2015;62:1394-404.
5. Prinssen M, Verhoeven EL, Buth J, Cuypers PW, van Sambeek MR, Balm R, et al. A randomized trial comparing conventional and endovascular repair of abdominal aortic aneurysms. N Engl J Med 2004;351:1607-18.
6. EVAR Trial Participants. Endovascular aneurysm repair versus open repair in patients with abdominal aortic aneurysm (EVAR trial 1). Lancet 2005;365:2179-86.
7. Lederle FA, Freischlag JA, Kyriakides TC, Padberg FT, Matsumura JS, Kohler TR, et al. Outcomes following endovascular vs open repair of abdominal aortic aneurysm: a randomized trial. JAMA 2009;302:1535-42.
8. Mertens J, Houthoofd S, Daenens K, Fourneau I, Maleux G, Lerut P, et al. Long-term results after endovascular abdominal aortic aneurysm repair using the Cook Zenith endograft. J Vasc Surg 2011;54:48-57.
9. Schanzer A, Greenberg RK, Hevelone N, Robinson WP, Eslami MH, Goldberg RJ, et al. Predictors of abdominal aortic aneurysm sac enlargement after endovascular repair. Circulation 2011;123:2848-55.
10. Schanzer A, Messina L. Two decades of endovascular abdominal aortic aneurysm repair: enormous progress with serious lessons learned. J Am Heart Assoc 2012;1:e000075.
11. Verzini F, Isernia G, De Rango P, Simonte G, Parlani G, Loschi D, et al. Abdominal aortic endografting beyond the trials: a 15-year single-center experience comparing newer to older generation stent grafts. J Endovasc Ther 2014;21:439-47.
12. Leurs LJ, Buth J, Laheiji RJ; for the EUROSTAR Collaborators. Long-term results of endovascular abdominal aortic aneurysm treatment with the first generation of commercially available stent grafts. Arch Surg 2007;142:33-41.
13. Cieri E, De Rango P, Isernia G, Simonte G, Verzini F, Parlani G, et al. Effect of stent graft model on aneurysm shrinkage in 1450 endovascular aortic repairs. Eur J Vasc Endovasc Surg 2013;46:192-200.
14. Becquemin JP, Pillet JC, Lescalie F, Sapoval M, Goueffic Y, Lermusiaux P, et al; ACE trialists. A randomized controlled trial of endovascular aneurysm repair versus open surgery for abdominal aortic aneurysms in low- to moderate-risk patients. J Vasc Surg 2011;53:1167-73.
15. Sobocinski J, Briffa F, Holt PJ, Martin Gonzalez T, Spear R, Azzaoui R, et al. Evaluation of the Zenith low-profile abdominal aortic aneurysm stent graft. J Vasc Surg 2015;62:841-7.
16. Torsello G, Scheinert D, Brunkwall JS, Chiesa R, Coppi G, Pratesi C. Safety and effectiveness of the INCRAFT AAA stent graft for endovascular repair of abdominal aortic aneurysms. J Vasc Surg 2015;61:1-8.
17. Mehta M, Valdés FE, Nolte T, Mishkel GJ, Jordan WD, Gray B, et al. One-year outcomes from an international study of the Ovation Abdominal Stent Graft System for endovascular aneurysm repair. A Pivotal Clinical Study to Evaluate the Safety and Effectiveness of the Ovation Abdominal Stent Graft System Investigators. J Vasc Surg 2014;59:65-73.e1-3.
18. Hogg ME, Morasch MD, Park T, Flannery WD, Makaroun MS, Cho JS. Long-term sac behavior after endovascular abdominal aortic aneurysm repair with the Excluder low-permeability endoprosthesis. J Vasc Surg 2011;53:1178-83.
19. Böckler D, Holden A, Thompson M, Hayes P, Krievins D, de Vries JP, et al. Multicenter Nellix EndoVascular Aneurysm Sealing system experience in aneurysm sac sealing. J Vasc Surg 2015;62:290-8.
20. Greenberg RK, Lawrence-Brown M, Bhandari G, Hartley D, Stelter W, Umscheid T, et al. An update of the Zenith endovascular graft for abdominal aortic aneurysms: initial implantation and mid-term follow-up data. J Vasc Surg 2001;33(2 Suppl):S157-64.
21. Greenberg RK, Chuter TA, Sternbergh WC 3rd, Fearnot NE. Zenith AAA endovascular graft: intermediate-term results of the US multicenter trial. J Vasc Surg 2004;39:1209-18.
22. Cao P, De Rango P, Verzini F, Parlani G, Romano L, Cieri E; for the CAESAR Trial Group. Comparison of Surveillance Versus Aortic Endografting for Small Aneurysm Repair (CAESAR): Results from a Randomised Trial. Eur J Vasc Endovasc Surg 2011;41:13-25.
23. Chaikof EL, Blankensteijn JD, Harris PL, White GH, Zarins CK, Bernhard VM, et al; Ad Hoc Committee for Standardized Reporting Practices in Vascular Surgery of The Society for Vascular Surgery/American Association for vascular Surgery. Reporting standards for endovascular aortic aneurysm repair. J Vasc Surg 2001;35:1048-60.
24. American Society of Anesthesiologists. New classification of physical status. Anesthesiology 1963;24:111.
25. Moll FL, Powell JT, Fraedrich G, Verzini F, Haulon S, Waltham M, et al. Management of abdominal aortic aneurysms clinical practice guidelines of the European society for vascular surgery. Eur J Vasc Endovasc Surg 2011;41(Suppl 1):S1-58.
26. Bahia SS, Holt PJ, Jackson D, Patterson BO, Hinchliffe RJ, Thompson MM, et al. Systematic review and meta-analysis of long-term survival after elective infrarenal abdominal aortic aneurysm repair 1969-2011: 5-year survival remains poor

despite advances in medical care and treatment strategies. Eur J Vasc Endovasc Surg 2015;50:320-30.
27. Mestres G, Zarka ZA, García-Madrid C, Riambau V. Early abdominal aortic endografts: a decade follow-up results. Eur J Vasc Endovasc Surg 2010;40:722-8.
28. Pitton MB, Scheschkowski T, Ring M, Herber S, Oberholzer K, Leicher-Düber A, et al. Ten-year follow-up of endovascular aneurysm treatment with Talent stent-grafts. Cardiovasc Interventional Radiol 2009;32:906-17.
29. Iwakoshi S, Ichihashi S, Higashiura W, Itoh H, Sakaguchi S, Tabayashi N, et al. A Decade of Outcomes and predictors of sac enlargement after endovascular abdominal aortic aneurysm repair using Zenith endografts in a Japanese population. J Vasc Interv Radiol 2014;25:694-701.
30. Greenberg RK, Chuter TAM, Cambria RP, Sternbergh WC III, Fearnot NE. Zenith abdominal aortic aneurysm endovascular Graft. J Vasc Surg 2008;48:1-9.
31. Kiguchi MM, Forbes TL, Teijink JA, Pliagas GA, Ellozy SH, Böckler D, et al. Clinical application and early outcomes of the aortouni-iliac configuration for endovascular aneurysm repair. J Vasc Surg 2014;60:1452-9.
32. McCallum JC, Buck DB, Darling JD, Soden PA, Zettervall SL, Schermerhorn ML. Five-year results from the Endurant Post-Approval Study of the Endovascular Treatment of Abdominal Aortic Aneurysms in the United States. Eposter P25. 43rd annual symposium SCVS, March 29-April 2, 2015, Miami, FL, USA abstract book SVS 2015.
33. Mastracci TM, Eagleton MJ, Kuramochi Y, Bathurst S, Wolski K. Twelve-year results of fenestrated endografts for juxtarenal and group IV thoracoabdominal aneurysms. J Vasc Surg 2015;61:355-64.
34. Alric P, Hinchliffe RJ, MacSweeney ST, Wenham PW, Whitaker SC, Hopkinson BR. The Zenith aortic stent graft: a 5-year single center experience. J Endovasc Ther 2002;9:719-28.
35. Bos WT, Verhoeven EL, Tielliu IF, Zeebregts CJ, Prins TR, van den Dungen JJ. Results of endovascular abdominal aortic aneurysm repair with the Zenith stent-graft. Eur J Vasc Endovasc Surg 2008;36:653-60.
36. Baum RA, Shetty SK, Carpenter JP, Soulen MC, Velazquez OC, Shlansky-Goldberg RD, et al. Limb kinking in supported and unsupported abdominal aortic stent-grafts. J Vasc Interv Radiol 2000;11:1165-71.
37. Maleux G, Koolen M, Heye S, Nevelsteen A. Limb occlusion after endovascular repair of abdominal aortic aneurysms with supported endografts. J Vasc Interv Radiol 2008;19:1409-12.
38. Mantas GK, Antonopoulos CN, Sfyroeras GS, Moulakakis KG, Kakisis JD, Mylonas SN, et al. Factors predisposing to endograft limb occlusion after endovascular aortic repair. Eur J Vasc Endovasc Surg 2015;49:39-44.
39. Faure EM, Becquemin JP, Cochennec F; ENGAGE collaborators. Predictive factors for limb occlusions after endovascular aneurysm repair. J Vasc Surg 2015;61:1138-45.e2.

Submitted Apr 18, 2016; accepted Jul 19, 2016.