

Update on the EUROSTAR Registry

This review looks at the EUROSTAR Registry with special emphasis on the relationship between the AAA diameter and outcome of EVAR.

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Several years after Juan Parodi, MD, had reported the deployment of straight-tube endografts into the aortas of five patients with infrarenal aortic aneurysms¹ and Claude Miahle, MD, had designed and successfully applied a modular bifurcated device in similar patients in 1994,² the EUROSTAR (European Collaborators on Stent/graft Techniques for aortic Aneurysm Repair) Registry program was established. Although the feasibility of endovascular aneurysm repair (EVAR) was well established, the efficacy and durability of EVAR were questionable.^{3,4}

The goal of EUROSTAR was to audit results carefully for

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scientific and ethical reasons. Currently, 135 centers in 18 different European countries are contributing data to the EUROSTAR Registry. The registry provides valuable insight into the risks as well as the advantages of EVAR. For example, the unacceptably high risk of delayed treatment failure associated with the use of early-generation endografts was recognized quickly, and further detailed analysis of the database provided vital information about the modes of failure, which has influenced the evolution of subsequent generations of endografts and clinical applications of EVAR.³ This article reviews some of the important findings that were made during the course of 8 years, with special emphasis on the relationship between the diameter of the AAA and the outcome of EVAR.

METHODS

The data of 5,466 patients treated over 6 years and enrolled prospectively into the EUROSTAR database constituted the basis of this analysis. An account of the organization of the EUROSTAR Registry and reports on various aspects after EVAR have been published previously.⁵⁻⁷ All patients had a minimal follow-up of 1 month. Patients with an aneurysm smaller than 4 cm in diameter, including those

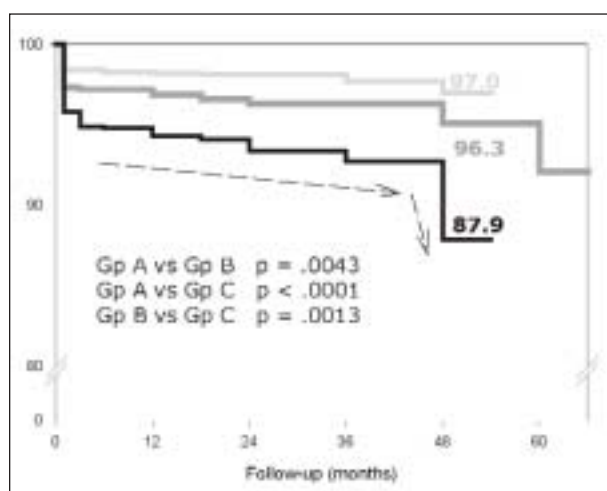


Figure 1. Cumulative freedom from aneurysm-related death. Dashed arrows indicate low attrition of survival in first 3 years and rapid attrition in fourth year of follow-up.

with large iliac aneurysms, had been excluded from this study cohort. This cohort represents patients from 110 European institutions. All patients were treated with commercially available, CE-approved devices from different companies. Device brands that were used in the study cohort were: AneuRx (Medtronic, Inc., Santa Rosa, CA), EVT/Ancure (Guidant Corporation, Indianapolis, IN), Excluder (W.L. Gore & Associates, Flagstaff, AZ), Vanguard (Boston Scientific Corporation, Natick, MA), Stentor (MinTec Inc., Bahamas), Talent (Medtronic), Zenith (Cook Incorporated, Bloomington, IN), and "other."

Inclusion criteria, as defined in the registry's protocol, comprised elective treatment for AAA and vascular anatomy suitable for the implantation of a stent graft. Baseline data including comorbidity, estimate of unfit for open repair,⁸ anatomic aspects, and operative details were recorded by the participating institutions on Case Record Forms and submitted for inclusion to the Data Registry Center. Findings at follow-up visits, which involved clinical examination, CT assessment, or (in 5% of the visits) angiographic, MRI, or ultrasound follow-up studies were recorded on data forms and returned at regular intervals to the Data Registry Center for processing and analysis. Follow-up visits according to the protocol were scheduled at 1, 6, 12, 18, and 24 months, and annually thereafter. Deaths that occurred within 30 days of the initial procedure were categorized as operative deaths; late deaths were defined as those occurring after 30 days. Deaths were also classified as aneurysm-related or unrelated deaths. Aneurysm-related deaths included operative deaths and deaths that occurred as a result of aneurysm rupture, endograft infection, or within 1 month after a secondary surgical procedure for late complications of the aneurysm.

Other outcome events observed during follow-up included endoleaks, migration, severe device kinking, occlusion, and aneurysmal growth. Endoleaks were classified into types I to IV. Aneurysmal enlargement was defined as a diameter increase of at least 8 mm relative to the preoperative measurements on CT. The aggregated data are analyzed and published at regular intervals and are now available online at www.eurostar-online.org.

To assess the influence of size on the early and midterm outcome after EVAR, the study cohort was subdivided according to the preoperative aneurysm diameter: group A, 4 cm to 5.4 cm; group B, 5.5 cm to 6.4 cm; and group C, >6.5 cm.⁹

RESULTS

Database

At the end of July 2003, a total of 5,466 patients had been registered. Of these, 1,224 patients were treated prior to July 1, 2003, with early generations of endografts that have now

TABLE 1. DEVICE DISTRIBUTION IN EUROSTAR DATA (JULY 2003)

	Number of Patients (%)
AneuRx	958 (22.6)
EVT	66 (1.6)
Excluder	528 (12.4)
Talent	1108 (26.1)
Zenith	1372 (32.3)
Other	181 (4.3)
<i>29 missing data</i>	

been withdrawn (Ancure, Stentor, and Vanguard). Standard reports currently published by EUROSTAR and exhibited on the Web site do not include data relating to these devices. The devices that are included are Ancure after July 1, 1998, AneuRx, Quantum (Fortron, Cordis Corporation, a Johnson & Johnson company, Miami, FL), Excluder, Lifepath (Edwards Lifesciences, Irvine, CA), Talent, and Zenith (Table 1).

Diameter of the AAA and Its Relationship to EVAR Outcome

The average diameter of the aneurysm sac was 5.72 cm (range, 4-14.5 cm) in minor dimension. Group A consisted of patients with aneurysm diameters of 4 cm to 5.4 cm (1,962 patients), group B consisted of aneurysm diameters of 5.5 cm to 6.4 cm (1,528 patients), and group C consisted of aneurysm diameters of >6.4 cm (902 patients). Patients in group C were on average 1.2 to 3.6 years older, more frequently had an ASA class 3 or 4, and more frequently had cardiac, renal, and pulmonary comorbidity than the other groups. Patients in group C had a higher incidence of significant angulation in the neck, the aneurysm, and the iliac arteries, and on average had a 0.6 mm to 1.2 mm wider infrarenal neck. Operative time was 157 minutes in group C, compared to 140 and 132 minutes in groups A and B, respectively ($P<.0001$). Talent and Zenith endografts were used significantly more frequently in group C (Table 2). Other operative aspects more frequently observed in group C included the use of additional procedures (37% vs 31% in group B and 30% in group A; $P=.0007$), and a higher incidence of type I endoleak at completion angiography (9.9% vs 6.8% in group B and 3.7% group A; group A vs group B, $P=.001$; group A vs group C, $P<.0001$; group B vs group C, $P=.01$).

The overall 1-month mortality was 2.5% (108 patients). This mortality was 4.1% in group C compared to 2.1% in the other groups combined ($P<.0001$, 2.6% in group B and 1.6% in group A). The 1-month mortality in the Stentor/Vanguard category was 3.0% versus 2.2% in other endografts (NS).

One-month systemic complications combined (mainly cardiac and pulmonary) were observed in 17.4%, 12.6%, and 12.0% of patients in groups C, B, and A, respectively (group A vs group C, $P<.0001$; group B vs group C, $P=.001$; group A vs group B, NS). Hospital stay was longer in groups C and B (7.0, 6.1, and 5.5 days in groups C, B, and A, respectively (group A vs group B, $P=.004$; group A vs group C, $P<.0001$; and group B vs group C, $P=.001$).

Mean duration of follow-up was 18.4 months (range, 1 to 72), with 20.9 (range, 1 to 96), 17.4 (range, 1 to 84), and 14.5 (range, 1 to 84) months of follow-up in groups A, B, and C, respectively. Patient survival was 76% at 5 years. Group C had a significantly lower survival compared to groups B and A (62%, 69.6%, and 84.2% at 5 years, respectively) (group A vs group B, $P<.0001$; group B vs group C, $P<.0001$; group A vs group C, $P<.0001$).

Aneurysm-Related Deaths According to the Size of the AAA

Freedom from aneurysm-related death in the entire study cohort was 93.9% at 5 years. Aneurysm-related deaths occurred in 53 patients in group C, 52 patients in group B, and 39 patients in group A, resulting in a freedom-from-aneurysm-related-death rate at 5 years of 87.9%, 95%, and 97%, respectively (Figure 1).

The majority of the aneurysm-related deaths in groups B and C during follow-up occurred in the fourth year. In group C, the aneurysm-related death rate was 1% annually in the first 3 years (operative deaths omitted) and 8% in the fourth year. In group B, the aneurysm-related annual death

rate was 0.3% in the first 3 years and 2.1% in the fourth and fifth year. This pattern can be described as a gradual increase in the first 3 years, followed by an accelerated increase of aneurysm-related deaths in the fourth year in groups B and C (Figure 1). This trend was not apparent in group A.

A multivariate model of variables observed at follow-up with aneurysm-related deaths omitting the first-month deaths (ie, late aneurysm-related death) as outcome event indicated an independent significant correlation with large aneurysms (size group C), proximal endoleak (type I), kinking of the device, and aneurysm expansion during follow-up.

Aneurysm-Related Complications According to the Size of the AAA

Rupture after EVAR occurred in 32 patients of the entire study cohort, with 16 ruptures in group C, nine in group B, and seven in group A. Freedom-from-rupture after 4 years was observed in 97.2% in the entire group, 90.5% in group C, 98.3% in group B, and 98.3% in group A (group A vs group B, $P=.13$; group A vs group C, $P<.0001$; group B vs group C, $P<.0001$) (Figure 2). Ruptures occurred in patients who received an AneuRx (three of 877), Excluder (one of 341), Stentor (six of 282), Talent (five of 821), Vanguard (15 of 905), and Zenith (one of 891), and other (one of 108) device. No single device brand was significantly associated with a higher risk of rupture after EVAR.

Late conversion to open repair (after the first postoperative month) had a higher incidence in group C (86.2% freedom from conversion at 4 years) compared to group A

TABLE 2. DEVICE DISTRIBUTION BY SIZE GROUPING (N=4,392 PATIENTS)

	Number of Devices Used	Group A 4 cm-5.4 cm (1,962 patients)		Group B 5.5 cm-6.4 cm (1,528 patients)		Group C >6.5 cm (902 patients)	
AneuRx	877	438	(50%)*	296	(34%)	143	(16%)
EVT/Ancure	150	62	(41%)	56	(37%)	32	(21%)
Excluder	341	158	(46%)	129	(38%)	54	(16%)
Stentor	282	142	(50%)	93	(33%)	47	(17%)
Talent	821	307	(37%)	322	(39%)	192	(23%)†
Vanguard	905	438	(48%)††	295	(33%)	172	(19%)
Zenith	891	344	(37%)	300	(34%)	247	(28%)§
Other	108	62	(57%)**	31	(29%)	15	(14%)
Unknown	17	11	(65%)	6	(35%)	0	0

* $P=.0002$ more frequent use in groups A; † $P<.0001$ more frequent use in group C; § $P<.0001$ more frequent use in group C;

** $P=.004$ more frequent use in group A; †† $P=.04$ more frequent use in group A.

(93.4%, $P=.003$) and group B (93.2%, $P=.01$). Variables observed during follow-up with an independent correlation with the decision to open conversion included large aneurysm size (group C), proximal endoleak (type I), midgraft endoleak (type III), type II endoleak, device migration, limb occlusion, and aneurysm expansion.

Other Important Findings of the EUROSTAR Registry *Comparison of outcomes after EVAR with current and withdrawn devices.*

Thirty-day clinical outcomes were similar in the two groups. However, despite a higher-risk patient population, comparison of the medium term results showed a statistical advantage in favor of current devices with respect to all outcome measures, with the exception of the rupture rate, which was too low to reach statistical significance. Aneurysm-related death at 3 years associated with current devices was approximately half of that for withdrawn devices.

Significance of type II endoleak.

The importance of device-related (types I and III) endoleaks was recognized at an early stage. But, the significance of aortic side-branch (type II) endoleaks was less certain. In 2002, EUROSTAR published a definitive article on the importance of endoleaks.⁵ A total of 2,463 patients were included in the analysis. Type II endoleaks occurred in 191 patients (7.8%); types I and III endoleaks occurred in 297 patients (12%). Analysis confirmed that device-related endoleaks were associated with a high risk of adverse, clinically significant events, including rupture. However, type II endoleaks were not statistically associated with any adverse events, except secondary intervention—an event that depends on the discretion of the physician. The relevance of this finding to clinical practice is that type II endoleaks do not require treatment by secondary intervention unless there is evidence of progressive expansion of the aneurysm sac.

Analysis of the causes of late failure after EVAR (first-generation devices).

Data relating to withdrawn and current devices were included in this analysis. However, only follow-up data extending to 5 years for first-generation endografts were available; therefore, information derived about the rates and modes of delayed failure of endovascular repair related principally to these devices.⁴ There was a total of 2,464 patients, 221 of whom had been followed for more than 6 years. During this period, 27 patients had unequivocal rupture of their aneurysm. Patients who collapsed and died suddenly without CT, operative, or autopsy evidence of rupture were not included. Therefore, the rate of late rupture could have

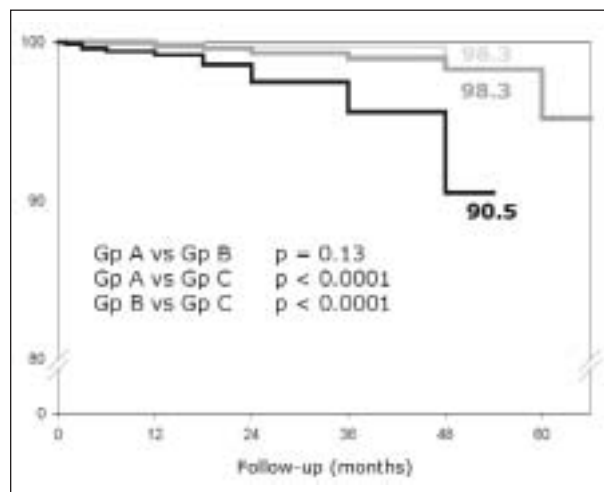


Figure 2. Cumulative freedom from rupture post-EVAR.

been considerably higher than that recorded. The cumulative rate of rupture displayed an alarming exponential curve, increasing to 12.44% at 6 years.

Univariate analysis of potential risk factors identified a number that were statistically associated with rupture. However, when the same factors were subjected to multivariate analysis, only three were found to be independently linked with a risk of rupture: (1) the last measured Dmax; (2) migration of fixation stents; and (3) type III endoleak. A large aneurysm diameter increased the risk of rupture only slightly (RR, 1.057), however, migration (RR, 5.335) and type III endoleak (RR, 7.474) both had major adverse impact upon the risk of rupture. Therefore, these were the principal modes of failure of early generations of endograft. The results indicate that delayed type I endoleaks occur secondarily to migration. The results also pointed to the need for stent graft design modifications directed toward minimization of migration and a structure to resist the erosion of materials, fatigue, and separation of components that were responsible for type III endoleaks.

SUMMARY

Several conclusions can be drawn as a result of this analysis:

1. An open audit is an essential tool for the clinical evaluation of new technologies.
2. To date, the EUROSTAR Registry has formed the basis of 22 papers in peer-reviewed journals, 10 chapters in textbooks and other publications, and 51 presentations at scientific meetings. The total volume of data available today is immense, and it continues to provide valuable insight into the risks as well as the advantages of EVAR.
3. EVAR works extremely well in treating small AAAs. These data support the argument in favor of earlier treat-

ment of AAAs by EVAR. The risk of rupture in small aneurysms (diameter <5.5) after EVAR was 0.002 ruptures per patient-year, which compares favorably with 0.008 in the similar size category in the trial arm with the initially conservative management from the UK Small Aneurysm Trial.

4. There is a need for change in follow-up protocol. Adverse events as measured by aneurysm-related death increase in frequency at 4 years after operation—these data argue in favor of increasing rather than decreasing the intensity of follow-up with time after operation.

5. New devices perform better than the first-generation devices.

6. As long as the aneurysm does not enlarge, type II endoleak can be safely monitored. ■

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Participating centers can be viewed online at www.evto-day.com.

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