Secondary Interventions after Elective Endovascular Repair of Degenerative Thoracic Aortic Aneurysms: Results of the European Collaborators Registry (EUROSTAR)

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PURPOSE: The need for secondary interventions is an important indicator of intermediate and long-term success of endovascular repair of degenerative thoracic aortic aneurysm. The purpose of this study was to analyze the occurrence and consequences of secondary procedures.

MATERIALS AND METHODS: Data from 213 patients electively subject to operation for degenerative thoracic aortic aneurysm and achieving primary success and who were enrolled in the EUROSTAR registry were analyzed. Secondary procedures were categorized as follows: transfemoral endovascular reintervention, extraanatomic secondary procedures, and transthoracic surgery.

RESULTS: Overall, 25 (12%) of the patients with an elective treatment for a degenerative thoracic aneurysm had secondary intervention, occurring at a mean of 8 months after the initial procedure. Seventeen (68%) of the secondary interventions were via a transfemoral approach, six (24%) involved a transthoracic procedure, and two (8%) involved extraanatomic bypass. The cumulative percentage of freedom from intervention at 1 and 2 years was 86% and 83%, respectively. Endoleak (relative risk, 5.21) was the most frequent cause for secondary transfemoral intervention. For the other secondary interventions, no principal indication for reintervention could be identified. Patients who needed secondary interventions more frequently suffered from preoperative back pain (20% vs 44%, $P = .008$), and their thoracic aneurysms had a longer length (mean, 95.6 mm vs 133.2 mm, $P = .006$). The 2-year cumulative survival rate of patients without secondary intervention was 85% compared with 58% in the patients who received secondary intervention ($P = .0001$).

CONCLUSIONS: Regular surveillance after endovascular degenerative thoracic aneurysm repair is needed as secondary interventions were required throughout the follow-up period.

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Abbreviations: EVAR = endovascular abdominal aortic aneurysm repair, RR = relative risk, TAA = thoracic aortic aneurysms

ELECTIVE endovascular treatment of thoracic aortic pathology has been applied in a variety of conditions of which degenerative aneurysms are the most frequent indication. The mortality associated with open surgery is considerable and ranges from 5% to 20% in thoracic aortic aneurysmal disease (1–4). The advent of endovascular technology offered a minimally invasive alternative treatment for thoracic aortic aneurysms (TAAs). Several institutional series have reported encouraging early results with this technique (1,5–9).

The need for secondary interventions is an important indicator of intermediate and long-term success of endovascular aortic aneurysm repair. These procedures can be categorized according to their extent as follows: transfemoral endovascular reintervention, extraanatomic secondary procedures, and transthoracic surgery. In this report, data were assessed from patients electively subject to endovascular repair of their TAAs who had been included in the multicenter collaborative European registry (EUROSTAR). Many previous publications reported on a mix of aortic pathologies treated by endovascular repair. We choose to report on a well-defined group of patients with regard to type of disease (ie, elective operation for degenerative aneurysm). The objective was to analyze the incidence and the

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consequences of secondary procedures on short-term and long-term outcomes after endovascular TAA and dissection repair. Furthermore, possible risk factors to develop a secondary intervention were analyzed.

MATERIALS AND METHODS

Data from 213 patients electively subject to operation from October 1998 to October 2005 for degenerative TAA and achieving primary success constituted the basis of this analysis. Patients were enrolled into the EUROSTAR database, which was launched in January 2000. Thirty-seven of the patients had been enrolled retrospectively (operation before January 2000); all others prospectively. The study cohort represented patients from 54 European institutions. Patients were treated with commercially available, Communauté Européenne (CE)-approved devices from four different companies such as the Talent (AVE/Medtronic, Santa Rosa, Calif) (n = 134), TAG (W. L. Gore & Associates, Flagstaff, Ariz) (n = 46), Zenith (William Cook Europe, Bjacverskov, Denmark) (n = 24), and other (n = 9). Inclusion criteria, as defined in the registry protocol, comprised elective or emergency treatment for aneurysmal thoracic disease or dissections in patients with a vascular anatomy suitable for the implantation of stent graft. However, the current analysis involved only patients electively treated for degenerative TAA. We restricted our report to a well-defined group of patients with regard to type of pathology (ie, elective operation for degenerative aneurysm), whereas many previous publications reported on a mixed patient group with a range of aortic pathologies. Restriction to patients with the most frequently occurring pathology enhances the clarity of this report, in which the study population was categorized over the three study groups according to the type of secondary intervention needed An additional advantage of including only patients treated by elective endovascular repair for their degenerative aneurysm is the additional possibility to allow some comparisons with the abdominal EUROSTAR registry, which only includes patients electively treated with endovascular repair for abdominal aortic aneurysm.

Baseline data including comorbidity, estimate of unfitness for open repair, anatomic aspects, and operative details were recorded by the participating institutions on case record forms and submitted for inclusion to the European continental data registry center (10). Findings at follow-up visits, which involved clinical examination, computed tomography (CT) assessment or angiographic magnetic resonance (MR) imaging, or thoracic or transesophageal ultrasound follow-up studies, were recorded on data forms and returned at regular intervals to the data registry centers for processing and analysis. From 2003, all data transfer occurred by Web site (www.eurostar-online.org; KIKA Medical, Nancy, France). There was no outside monitoring of the centers or involvement of a core laboratory for the evaluation of the CT scanning or other imaging studies. Early complications involved endoleaks and device-related, arterial, systemic, and neurologic complications. Primary outcome success was defined as exclusion of the aneurysm survival of the patient and absence of endoleak. Follow-up visits according to the registry protocol were scheduled at 1, 6, and 12 months and annually thereafter. Reminders for overdue follow-up data were regularly sent to the institutions participating in the project. Outcome reporting adhered to the guidelines of the Ad Hoc Committee for Standardized Reporting Practices in Vascular Surgery of the Society for Vascular Surgery/American Association for Vascular Surgery (10). Aneurysm-related mortality was defined as mortality due to aneurysm rupture or occurring 30 days after the initial or secondary intervention.

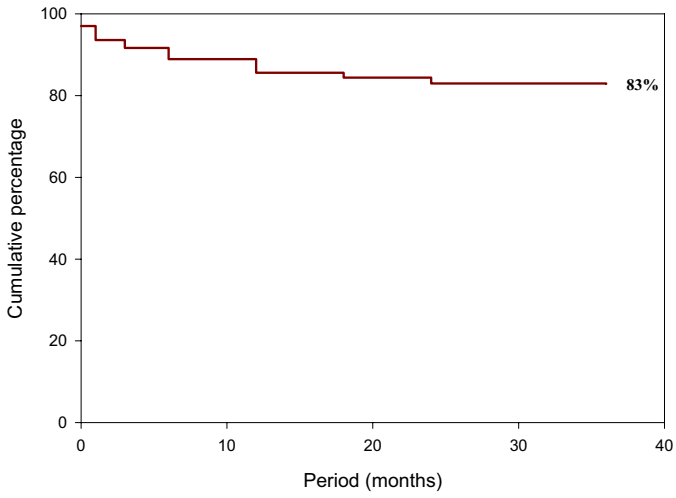
Secondary interventions were defined as any surgical or transfemoral procedure related to the thoracic disorder or its later progression or the imperfect placement of the stent graft (migration, endoleak). Secondary interventions for aneurysmatic disease developing in areas other than the chest or the treatment of nonarterial complications were not included.

Differences in baseline variables were assessed by chi-square or Wilcoxon rank sum test for categorical and continuous data, respectively. Relative risk (RR) values were presented if significant correlations were present. Adverse events that occurred during follow-up were analyzed by Kaplan-Meier analysis. A P value $<.05$ was considered to represent a significant difference. All statistical analyses were performed with SAS statistical software (version 8.02; SAS Institute, Cary, N.C.).

RESULTS

The mean follow-up for the entire study group of 213 patients was 18.0 months ± 16.1 (range, 1–60 months). Twenty-five (12%) of the patients with an elective treatment for a degenerative thoracic aneurysm required a secondary intervention, occurring at a mean of 8 months (range, 1–60 months) after the initial procedure. There was no significance difference in the rates of reintervention between the different stent-graft brands. The mean total follow-up in patients with a secondary procedure, including the time period after the intervention, was 15.9 months ± 14.3 (range, 1–48 months). Seventeen (68%) of the secondary interventions were via a transfemoral approach, 6 (24%) involved a transthoracic procedure, and 2 (8%) involved an extraanatomic bypass. Secondary interventions were required at a continuous rate throughout the follow-up period. The rates of freedom from intervention at 1 and 2 years were 86% and 83%, respectively (**Fig 1**) Comparison of baseline patient and anatomic characteristics demonstrated that patients subject to secondary interventions more frequently suffered from preoperative back pain (20% vs 44%, P = .008) and had longer thoracic aneurysms (mean, 95.6 mm vs 133.2 mm, P = .006) (**Table 1**). All other risk scores and anatomic measurements were similar in patients with and without subsequent secondary interventions.

All patients had primary outcome success. Patients subject to a secondary intervention had significantly more device-related (migration, occlusion, or stenosis of the device) and access-site complications (bleeding, hematoma, or false aneurysm) (**Table 2**). Neurologic complication (paraplegia, paresis, or stroke) occurred in similar proportions in both study arms. During the follow-up period, patients who needed a secondary intervention more frequently had type 1 and 3 endoleaks.



Period (months)	1	3	6	12	18	24
Patients at risk	228	163	142	130	103	70

Figure 1. Secondary intervention–free survival.

Transfemoral Secondary Intervention

Endoleak was the reason for transfemoral interventions in 14 (82%) of 17 patients. These were nine type 1 endoleaks, one type 2 endoleak, and four type 3 endoleaks. In the other three patients, the reason for intervention was not indicated. Of the 196 patients who did not require a secondary intervention, 31 (17%) were reported to have an endoleak. Of these 31 endoleaks, 14 were type 1, 6 were type 2, and 11 were type 3. The RR of an endoleak being the reason for a transfemoral reintervention was 5.21 (95% CI, 3.52–7.70). In other words, when an endoleak was detected during follow-up (n = 45), the RR to undergo a transfemoral secondary intervention (n = 14) was 17.42 (95% CI, 5.23–58.00). The cumulative percentage from freedom of transfemoral secondary intervention was 90.4% and 85.8% after 1 and 2 years of follow-up, respectively.

Transthoracic Secondary Intervention

Three of the six transthoracic interventions were late (>30 days) conversions to open repair. The reasons for these interventions were a type 3 endoleak, severe stent-graft kinking, and the presence of an infectious fistula. For two patients, the indication was unknown. Freedom from transthoracic secondary interventions reached 96.4% after 1-year of follow-up.

Extraanatomic Secondary Intervention

Two extraanatomic interventions were required: one femoral-femoral bypass for iliac occlusion and one replacement of the femoral artery by a venous graft. No variable recorded during surveillance imaging correlated with this event. The cumulative rate of freedom from extraanatomic intervention was 98.6% after 1 year.

Mortality in the Study Groups

The 2-year cumulative survival rate of patients without a secondary intervention was 73.4% (34 deaths). In the patients who received a secondary intervention, the survival rate after 2 years was 49.0% (9 deaths) (**Fig 2**). This difference was borderline statistical significantly (P = .070). Of the 43 patients who died, four received a transfemoral, four a transthoracic, and one an extraanatomic secondary intervention during the study period. The cause of death in patients with secondary intervention (n = 9) was related to the aneurysm in three patients. The other causes of death were either cardiac failure (n = 2), cerebral emboli (n = 2), sepsis (n = 1), or a fistula (n = 1). Of the patients who did not have secondary interventions, the cause of death (n = 34) was related to the aneurysm in two patients. The other 31 patients died because of either cardiac (n = 9), cerebral (n = 2), pulmonary (n = 1), or multiorgan (n = 4) failure or other/unknown reasons (n = 16).

DISCUSSION

Endovascular repair of the thoracic aorta is an appealing alternative to open surgery because of the avoidance of thoracotomy, aortic clamping, and left-sided heart bypass. Significant progress has been achieved since the first stent graft for thoracic aneurysm exclusion was deployed in 1992 (9). Several reports documented feasibility of different stent-graft systems in a broad spectrum of thoracic pathologies (9,11–13). The need for secondary interventions is an important indicator of the durability of endovascular aortic aneurysm repair.

The cumulative rate of freedom from intervention at 2 years was 83%, which equates with an intervention rate of almost 10% per year. This is remarkably similar to the annual risk rate reported previously after endovascular abdominal aortic aneurysm repair (EVAR) using first- and second-generation stent grafts (14). However, the rate of secondary interventions after stent-graft repair of abdominal aortic aneurysm demonstrated a significantly lower (5%) annual rate of reinterventions when current endografts were used (15). This may indicate that the thoracic aorta poses more extreme mechanical conditions for the endovascular technique with regard to flow and pulsatility, causing greater wear and tear to stent-graft materials.

The absolute 12% secondary intervention rate observed after elective endovascular degenerative thoracic aneurysm repair was slightly lower than the 18% reported in the first EUROSTAR report after elective abdominal aortic aneurysm repair and was slightly higher than the 9% reported recently with current-generation endografts (14,15).

The distribution of types of secondary interventions after elective thoracic aneurysm repair was as follows:

Table 1
Patient, Morphologic, and Operative Characteristics of Patients With and Without Secondary Interventions After the Endovascular Treatment of Degenerative TAA

	No Reintervention (n = 188)	Secondary Intervention (n = 25)	P Value
Patient characteristics			
Age at operation (years)	69.6 ± 8.7	70.2 ± 8.9	NS
Male gender	140 (74.5%)	20 (80.0%)	NS
ASA ≥3	106 (56.4%)	11 (44.0%)	NS
Unfit for open thoracic surgery	65 (34.6%)	8 (32.0%)	NS
Preoperative symptoms			
No symptoms	145 (77.1%)	13 (52.0%)	.0070
Back pain	38 (20.2%)	11 (44.0%)	.0079
Symptoms of side branch occlusion	1 (0.5%)	0 (0%)	NS
Aneurysm measurements, mm			
Maximal diameter aneurysm	65.0 ± 13.3	66.6 ± 9.9	NS
Length of aneurysm	95.6 ± 55.9	133.2 ± 90.3	.0060
Fusiform morphology	119 (64.3%)	22 (88.0%)	.0180
Localization aneurysm: category			
A (proximal one-third descending thoracic aorta)	50 (26.6%)	3 (12.0%)	NS
B (proximal + middle)	25 (13.3%)	4 (16.0%)	NS
C (middle)	37 (19.7%)	5 (20.0%)	NS
D (middle + distal)	28 (14.9%)	2 (8.0%)	NS
E (distal)	18 (9.6%)	2 (8.0%)	NS
F (proximal + middle + distal)	18 (9.6%)	7 (28.0%)	.0072
Details of operation			
Regional/local anesthesia	16 (8.5%)	1 (4.0%)	NS
Duration (minutes)	146.8 ± 105.2	153.2 ± 95.0	NS
Days until discharge	10.3 ± 13.2	9.7 ± 12.13.1	NS

NS, not significant; ASA, American Society of Anesthesiologists.

Table 2
Complication Rates in Patients With and Without Secondary Interventions After the Endovascular Treatment of Degenerative TAA

	No Reintervention (n = 188)	Secondary Intervention (n = 25)	P Value
Early (≤30 day) complications			
Device-related complications	15 (8.0%)	2 (8.0%)	NS
Failure to complete procedure	1 (0.5%)	0 (0%)	NS
Arterial complications	18 (9.6%)	4 (16.0%)	NS
Neurologic sequelae	17 (9.1%)	2 (8.0%)	NS
Systemic complications	38 (20.3%)	7 (28.0%)	NS
Procedure- and device-related complications	1 (0.5%)	6 (24.0%)	<.0001
Access site complications	10 (5.4%)	4 (20.0%)	.0073
Late (>30 day) complications			
Endoleak	31 (16.5%)	14 (56.0%)	<.0001
Type 1	14 (7.4%)	8 (32.0%)	.0001
Type 2	6 (3.2%)	1 (4.0%)	NS
Type 3	11 (5.9%)	5 (20.0%)	.0118
Kinking	9 (4.8%)	1 (4.0%)	NS
Stenosis/thrombosis	3 (1.6%)	0 (0%)	NS
Migration	2 (1.1%)	0 (0%)	NS

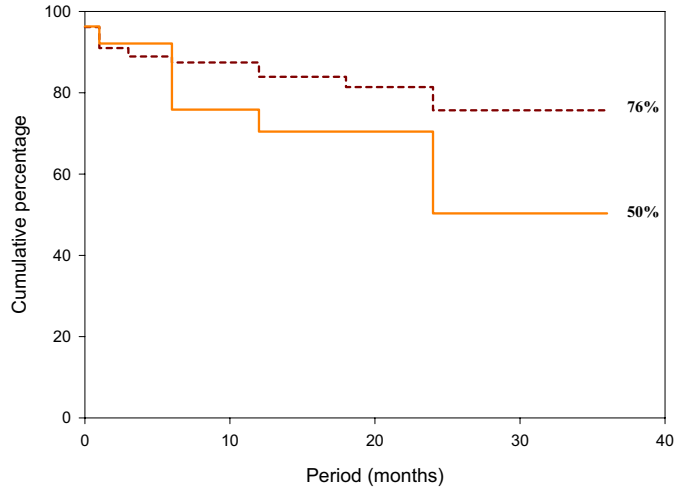
NS, not significant.

68% via a transfemoral approach, 24% involved a transthoracic procedure, and 8% by extraanatomic bypass. After elective abdominal aortic aneurysm (AAA) repair with the early generation of stent grafts, this distribution was 76%, 12%, and 11%, respectively (14). With the current generation of stent graft, the distribution was 60% transfemoral, 23% transabdominal, and 16% extraanatomic (15). This emphasizes that most adverse events can be resolved by appropriate endovascular technique, similarly noticed in EVAR (16,17). The same authors pointed out that transfemoral reinterventions were associated with low morbidity and mortality rates.

Preoperative factors correlating with reintervention were back pain at presentation and a longer extent of a patient's aneurysm. Endoleak was found to be a predictor for transfemoral reintervention. Patients who received a secondary intervention had an elevated mortality risk compared with patients who did not undergo a reintervention. This borderline significant difference was similar after EVAR (14).

After endovascular stent grafting of the thoracic aorta, transfemoral reinterventions of approximately 3.8% have previously been reported in institutional series, which is lower than our observed rate of 8.0% (18,19). From another institution, Grabenwoger et al reported a need for surgical reinterventions of 5% after endovascular thoracic aortic aneurysm and dissection repair, which was comparable with our combined 3.8% rate of transthoracic and extraanatomic interventions (19). Moreover, Hansen et al reported a need for secondary intervention of 23% (14 of 60 patients) after endovascular repair of high-risk and emergent thoracic aneurysm and dissection (20). In this latter report, the majority of reinterventions were secondary to an endoleak. Thus, the rate of required secondary interventions after thoracic aortic stent-graft repair ranges from 4% to 23%. None of the previous studies distinguished the reinterventions according to the indication of the primary stent-graft repair (ie, degenerative aneurysm, dissection, false aneurysm, or trauma). Our initial study on all thoracic stent-graft repairs in the EUROSTAR and UK thoracic registries combined indicated that the secondary intervention rate after 1 year in degenerative aneurysms (5.2%) was higher than the rate in aortic dissections (1.5%) (13).

Possible limitations of this study relate to the potential selective patient



- - Patients without secondary intervention

— Patients with secondary intervention

Period (months)	1	3	6	12	18	24
Patients at risk	200	141	127	120	95	65
Patients at risk	26	22	20	14	13	8

Figure 2. Kaplan-Meier curves of survival in patient with and without secondary intervention.

inclusion in the voluntary registry. To prevent such selective inclusion, enrollment forms were submitted 24 hours before operation to the EUROSTAR data registry center. Furthermore, data collected in a multicenter registry may suffer from relatively large interobserver variation, limited data monitoring, and incomplete follow-up data. Nevertheless, a registry's patient population normally is a good reflection of common-day clinical practice.

More clinical research is necessary to identify patients at risk for reintervention after an endovascular treatment of different thoracic aortic pathologies.

In conclusion, regular surveillance after endovascular degenerative thoracic aneurysm repair is needed because secondary interventions can occur throughout the follow-up period.

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