Retrograde Ascending Aortic Dissection During or After Thoracic Aortic Stent Graft Placement

Insight From the European Registry on Endovascular Aortic Repair Complications

Holger Eggebrecht, MD; Matt Thompson, MD; Hervé Rousseau, MD; Martin Czerny, MD; Lars Lönn, MD; Rajendra H. Mehta, MD, MS; Raimund Erbel, MD; on behalf of the European Registry on Endovascular Aortic Repair Complications

Background—Single-center reports have identified retrograde ascending aortic dissection (rAAD) as a potentially lethal complication of thoracic endovascular aortic repair (TEVAR).

Methods and Results—Between 1995 and 2008, 28 centers participating in the European Registry on Endovascular Aortic Repair Complications reported a total of 63 rAAD cases (incidence, 1.33%; 95% CI, 0.75 to 2.40). Eighty-one percent of patients underwent TEVAR for acute (n=26, 54%) or chronic type B dissection (n=13, 27%). Stent grafts with proximal bare springs were used in majority of patients (83%). Only 7 (15%) patients had intraoperative rAAD, with the remaining occurring during the index hospitalization (n=10, 21%) and during follow-up (n=31, 64%). Presenting symptoms included acute chest pain (n=16, 33%), syncope (n=12, 25%), and sudden death (n=9, 19%) whereas one fourth of patients were asymptomatic (n=12, 25%). Most patients underwent emergency (n=25) or elective (n=5) surgical repair. Outcome was fatal in 20 of 48 patients (42%). Causes of rAAD included the stent graft itself (60%), manipulation of guide wires/sheaths (15%), and progression of underlying aortic disease (15%).

Conclusions—The incidence of rAAD was low (1.33%) in the present analysis with high mortality (42%). Patients undergoing TEVAR for type B dissection appeared to be most prone for the occurrence of rAAD. This complication occurred not only during the index hospitalization but after discharge up to 1050 days after TEVAR. Importantly, the majority of rAAD cases were associated with the use of proximal bare spring stent grafts with direct evidence of stent graft–induced injury at surgery or necropsy in half of the patients.

Key Words: aorta • TEVAR • stent graft • complications • dissection

Thoracic endovascular aortic repair (TEVAR) continues to be increasingly used as a less invasive treatment option for patients with thoracic aortic aneurysms and dissections, particularly in those deemed at high risk for conventional open surgical repair.1,2 Growing technical experience and improving stent graft devices have resulted in better patient outcomes and expanded clinical indications. Available observational nonrandomized data suggest that the risk of acute complications of TEVAR, most notably paraplegia and stroke, appears to compare favorably with open surgery.3 However, as with any new technology, TEVAR bears the risk of unusual, previously unanticipated, severe complications. One of these complications is retrograde ascending aortic dissection (rAAD), which has been highlighted as a potentially lethal complication of TEVAR in previous case series, raising significant concern about the safety of this relatively minimally invasive procedure.4–11 However, the small number of patients in these case series (maximum, n=7 in a single series11) precludes reliable insight into the true incidence and patient- and procedure-related factors associated with this event and its outcomes in large number of patients undergoing TEVAR. This information may provide the opportunity for designing appropriate strategies not only to minimize this complication but also to diagnose and treat this complication early and effectively once it occurs, in the hope of improving future procedural safety and outcomes.

We analyzed data from the European Registry on Endovascular Aortic Repair Complications (EuREC, www.tevarcomplications.eu)
an interdisciplinary registry designed to collect cases of unusual complications after TEVAR at referral centers in Europe and China. The main goal of the current study was to estimate the incidence of rAAD after TEVAR and to describe patient and procedural characteristics, the current clinical management of rAAD, and patient outcomes.

Methods

Patient Selection
The EuREC was founded by an interdisciplinary team of TEVAR experts (H.E., M.T., H.R., M.C., L.L.). The registry was designed to provide an independent open scientific platform dedicated to collecting unusual and severe complications of TEVAR. The rarity of many of unusual complications after TEVAR precludes a large number of cases with these complications even at a very large tertiary care single center. Thus, EuREC was designed to collect information on unusual TEVAR complications across several referral sites to accumulate information on large numbers of cases with otherwise rare complications after TEVAR, with the hope of providing mechanistic insights in to its pathophysiology.

A total of 71 European and 1 Chinese major referral centers with significant TEVAR experience were contacted by e-mail. Centers were identified as having significant TEVAR experience from publications listed in PubMed (search terms: “aorta” and “stent graft”), from presentations on TEVAR topics at major scientific meetings, or by personal recommendation by one of the principal investigators (H.E., M.T., H.R., M.C., L.L.).

Initially, centers were asked to provide the total number of rAAD cases after TEVAR as well as the total number of TEVAR procedures performed in their local institution as of April 2008. This initial survey was aimed at getting an estimate on the incidence of rAAD after TEVAR. Therefore, centers were also included if they did not encounter this complication during their experience to avoid under-reporting bias. In a second step, an individualized password providing access to an Internet-based database was sent to each center to obtain detailed information on the individual patients in whom rAAD after TEVAR occurred.

Overall, 27 European centers and 1 Chinese center participated in the registry. During the period from 1995 to 2008, a total of 4750 TEVAR procedures were performed in these 28 centers (median, n = 3714; range, 18 to 443).

Data Collection
An electronic case report form with 28 variables including demographics, history, procedural characteristics, clinical presentation and management, and outcomes of patients was developed by EuREC investigators (H.E., M.T., H.R., M.C., L.L.). Data were retrospectively collected by physician review of hospital charts and entered into an Internet-based database. Case report forms were reviewed for clinical face validity and analytic internal validity by the lead author (H.E.). In the case of inconsistencies, the local investigators were contacted. On-site monitoring for data validation was not performed.

Definitions
Aortic dissection was considered an acute event if it occurred within the first 14 days from onset of symptoms, whereas it was considered chronic beyond 14 days.12 Classification of a proximal stent graft landing zone in the aortic arch was performed using the classification proposed by Ishimaru et al.13

Statistical Analysis
Categorical data are presented as frequencies; continuous variables are expressed as median and range. Comparisons were made with the Fisher exact test for categorical variables. A probability value of <0.05 was considered statistically significant. All statistical analyses were performed using the SPSS software package (version 15.0, SPSS Inc, Chicago, Ill).

### Table 1. Patient Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All Patients (n=48)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>56.5 (32–80)</td>
</tr>
<tr>
<td>Men</td>
<td>31 (65)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>40 (83)</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>5 (10)</td>
</tr>
<tr>
<td>Previous aortic surgery</td>
<td>2 (4)</td>
</tr>
<tr>
<td>Underlying aortic disease</td>
<td></td>
</tr>
<tr>
<td>Acute aortic dissection</td>
<td>26 (54)</td>
</tr>
<tr>
<td>Chronic aortic dissection</td>
<td>13 (27)</td>
</tr>
<tr>
<td>Thoracic aortic aneurysm</td>
<td>8 (17)</td>
</tr>
<tr>
<td>Penetrating aortic ulcer</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Presumed etiology of aortic disease</td>
<td></td>
</tr>
<tr>
<td>Atherosclerotic</td>
<td>26 (54)</td>
</tr>
<tr>
<td>Connective tissue disease (Marfan)</td>
<td>4 (8)</td>
</tr>
<tr>
<td>Traumatic</td>
<td>1 (2)</td>
</tr>
</tbody>
</table>

Data are presented as mean (range) or n (%).

Results

The initial survey revealed a total of 63 cases of rAAD after TEVAR, as reported by the centers (overall incidence, 1.33%; 95% CI, 0.75 to 2.40). The median number of rAAD cases per center was 2 (range, 0 to 11). Of these, 48 patient cases from 22 centers (total number of TEVAR procedures: n = 3714; median, n = 149; range, 18 to 443) with complete data sets on patient and procedural characteristics, presentation, management, and outcomes of retrograde ascending aortic complications formed the basis for the present analysis.

Baseline characteristics of the 48 patients are given in Table 1. The median age of the patients was 56.5 years (range, 32 to 80), and 65% were men. Hypertension was present in the majority of patients (83%). Thirty-nine of the total of 48 patients (81%) underwent TEVAR for aortic dissection, which was an acute event in 26 (54%) and was considered to be chronic in 13 (27%) patients. Etiology of aortic disease was presumed to be atherosclerotic in the majority of patients (n = 26, 54%). Marfan syndrome was present in 4 (8%) patients.

Procedural data are presented in Table 2. TEVAR was performed as an emergency procedure in 16 (33%) patients and as an elective procedure in the remaining 32 (67%). A median of 1 stent graft was used for treatment (range, 1 to 5). The configuration of the proximal stent graft landing zone was free-flow bare spring in 40 (83%) of patients. Stent grafts were positioned within the aortic arch across the left subclavian artery (zone 2) in 26 (54%) patients. Additional balloon dilatation of the stent graft after deployment was performed in 11 (23%) patients. In 9 of these 11, the proximal stent spring was dilated.

Retrograde ascending aortic dissection occurred during the TEVAR procedure (n = 7, 15%), before the procedure during the index hospitalization (n = 10, 21%), and after discharge during follow-up (n = 31, 65%) (Table 3 and Figure 1). In 22 of 48 (46%) patients, rAAD occurred within the first 30 days after the procedure, whereas in 15 of 48 (31%) it occurred beyond 3 months (median time to rAAD, 35 days; range, 0 to
1050 days after the index procedure). Nine patients (19%) had sudden death, and rAAD was diagnosed during necropsy. The majority of patients (44%) presented with symptoms (chest pain, syncope, stroke), but one fourth were asymptomatic (Table 3). There was no difference between patients who had early versus late rAAD with respect to asymptomatic onset (24% versus 26%, \(P=0.1005\)).

For detection of rAAD, computed tomography (CT) was the preferred diagnostic modality and was used in 73% of patients. Management consisted of emergency surgical repair in 25 (64%) patients and elective surgery in 5 (13%) patients. Nine (23%) patients were treated conservatively with tight blood pressure control and repeat imaging.

Overall, 20 of the 48 (42%) patients died, including the 9 sudden deaths. Mortality rates were comparable for conservative management (33%), elective surgery (20%), and emergency surgery (28%, \(P=0.868\)). Death occurred early at median on the day of diagnosis of rAAD (range, 0 to 1160 days). Analysis of subgroups showed that patients in whom rAAD occurred during the TEVAR procedure had the worst outcome compared with patients in whom ascending dissec-

### Table 2. Procedural Data

<table>
<thead>
<tr>
<th>All Patients (n=48)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emergency procedure</td>
</tr>
<tr>
<td>No. of stent grafts placed</td>
</tr>
<tr>
<td>Stent graft device used</td>
</tr>
<tr>
<td>Talent (Medtronic)</td>
</tr>
<tr>
<td>Valiant (Medtronic)</td>
</tr>
<tr>
<td>GoreTAG (Gore)</td>
</tr>
<tr>
<td>Zenith TX2 (Cook)</td>
</tr>
<tr>
<td>Endofit (Le Maitre)</td>
</tr>
<tr>
<td>Relay (Bolton)</td>
</tr>
<tr>
<td>Design of most proximal stent spring</td>
</tr>
<tr>
<td>Free-flow bare spring</td>
</tr>
<tr>
<td>Membrane-covered</td>
</tr>
<tr>
<td>Diameter of most proximal stent graft, mm</td>
</tr>
<tr>
<td>Diameter of ascending aorta, mm</td>
</tr>
<tr>
<td>Oversizing, mm</td>
</tr>
<tr>
<td>Oversizing, %</td>
</tr>
<tr>
<td>Landing zone within aortic arch</td>
</tr>
<tr>
<td>Zone 0</td>
</tr>
<tr>
<td>Zone 1</td>
</tr>
<tr>
<td>Zone 2</td>
</tr>
<tr>
<td>Zone 3</td>
</tr>
<tr>
<td>Method for blood pressure-lowering during stent graft deployment</td>
</tr>
<tr>
<td>Drug-induced hypotension (eg, nitroprusside)</td>
</tr>
<tr>
<td>Adenosine-induced cardiac arrest</td>
</tr>
<tr>
<td>Rapid right ventricular pacing</td>
</tr>
<tr>
<td>Overstenting of arch vessels</td>
</tr>
<tr>
<td>Retraction of stent graft during deployment</td>
</tr>
<tr>
<td>Additional balloon dilatation of the stent graft after deployment</td>
</tr>
</tbody>
</table>

Data are presented as n (%) or mean (range).
servatively (83%). Interestingly, patients with progression of aortic disease underwent elective surgical repair in the majority (57%). Mortality was high and not different with stent graft–induced dissections and wire-related dissections (45% versus 43%). However, patients with rAAD caused by progression of aortic disease had a better outcome (mortality, 14%; \( P = 0.216 \); Figure 3).

**Discussion**

To our knowledge, this is the first multicenter study to provide insight into an unusual but catastrophic complication of TEVAR in a larger series of patients. Our data indicate that rAAD is rare, occurring in only 1.33% of 4750 TEVAR procedures performed across 27 European centers and 1 Chinese center. This event not only occurred during the procedure but occurred even beyond the procedure during index hospitalization as well as after hospital discharge up to 1050 days of follow-up. Additionally, our data suggest that rAAD is not a benign event and is associated with very high mortality despite surgical repair in many.

Iatrogenic aortic dissection (class 5 dissection according to Svensson classification\(^1\)) accounts for approximately 5% of all acute aortic dissections and is a well-known complication of coronary angiography, percutaneous coronary interventions, and open heart surgery.\(^{15} \) Our data add TEVAR to this list of the procedures resulting in iatrogenic dissection. The risk of iatrogenic dissection of the ascending aorta after TEVAR is

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\begin{align*}
\text{Figure 1.} & \quad \text{A, Preoperative contrast-enhanced CT scan showing type B aortic dissection with true lumen (TL) and false lumen (FL) in the descending thoracic aorta. B, Angiography after successful TEVAR shows complete exclusion of the false lumen. C, Contrast-enhanced CT 4 hours after TEVAR performed for sudden hemiplegia and aphasia shows rAAD with perfused TL and FL. Note the stent graft and the completely thrombosed FL in the descending thoracic aorta. D, Multiplanar CT reconstruction reveals stent graft–induced rAAD with ascending aortic injury related to the proximal bare spring of the endoprosthesis.}
\end{align*}
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\begin{align*}
\text{Figure 2.} & \quad \text{Mortality in relation to the onset of rAAD.}
\end{align*}
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\begin{align*}
\text{Figure 3.} & \quad \text{Choice of treatment regimen and mortality in relation to the presumed etiology of rAAD.}
\end{align*}
\]
widely unknown and has only been recently acknowledged with expanding indications and clinical application of this novel emerging technique.\textsuperscript{10,11} Previous reports have estimated the risk of rAAD after TEVAR to range between 1.9\% and 2.4\%\textsuperscript{1,10,11} to as high as 6.8\%\textsuperscript{9} in a single-center experience involving a relatively small number of procedures. The incidence of TEVAR-related dissection was low in the current study and perhaps represents a much more stable estimate of this event due to the large number of patients evaluated.

Our data suggest several potential mechanisms of rAAD in patients undergoing TEVAR. Although some of them appeared to be related to the TEVAR procedure itself (ie, manipulation of wires and sheaths), the majority (60\%) were related to the trauma caused by the semi-rigid stent graft either during implantation or subsequently after implantation caused by repeated subtle back-and-forth motion of the stent graft with the cardiac cycle. Others were related to the underlying aortic disease process that eventually led to aortic dilation or initial tearing requiring the initial TEVAR procedure.

Previous investigators have speculated that the proximal bare spring designed to improve stent graft fixation within the aortic arch may potentially increase the risk of rAAD.\textsuperscript{10,11} Indeed, in 40 of the 48 (83\%) patients of our series stent grafts with proximal bare springs were used. Moreover, in patients in whom rAAD was classified as being stent graft-induced, proximal bare spring stent grafts were used in 27 of 29 patients (93\%). Conversely, in rAAD presumed to be related to progression of aortic disease, proximal bare spring stent grafts were used less frequently (4 of 7 [57\%] patients), with the remaining being covered stent grafts. Nevertheless, our finding that rAAD was not limited to a specific endograft device but occurred with various commercially available endografts and with proximally covered stent grafts may also suggest that it is the semi-rigid stent graft design rather than the proximal bare spring that may be responsible for the tear in the aorta. Unfortunately, the retrospective design of the present registry made it impossible to draw definitive conclusions regarding the device-specific nature of rAAD. Excessive radial force due to oversizing of the stent graft prosthesis to >20\% in relation to the diameter of the aorta has also been proposed as a potential factor to be associated with rAAD after TEVAR.\textsuperscript{11} There was only a median of 6\% oversizing of the stent graft in relation to the aorta in our series, rendering oversizing less likely as a contributing factor to the occurrence of rAAD.

As in cases of other percutaneous diagnostic or interventional cardiovascular procedures, rAAD may also result from manipulation of guide wires and sheaths as well as the large-bore stent graft delivery system within the aortic arch and was suspected to be the case in 15\% of the present series. Even discrete localized intimal tears that occur during such manipulation may ultimately extend into the ascending aorta during days, weeks, or months after the procedure.\textsuperscript{11} Previous investigators have proposed postdilation of the stent graft with a balloon for better alignment of the stent graft to the curved geometry of the aortic arch to be related to rAAD after TEVAR.\textsuperscript{11} Balloon inflations of the stent graft and even of the proximal stent spring were less often associated with occurrence of rAAD in our series than in the series of Kpodonu et al.\textsuperscript{11} Nevertheless, dilatation of the stent graft after deployment may be harmful in other ways such as rupturing the dissecting membrane, particularly in those patients undergoing TEVAR for acute type B dissection.

Our results confirm previous reports suggesting that patients undergoing TEVAR for aortic dissection are particularly prone to have rAAD after TEVAR.\textsuperscript{8,10} In fact, of the total of 48 patients with rAAD, 40 (83\%) had TEVAR performed either for acute or chronic aortic dissection. This is not surprising, given that the aortic wall is particularly friable in patients presenting with spontaneous aortic dissection and even minor injury during guide wire manipulation, or, stent graft deployment or subtle movement during the cardiac cycle of the semi-rigid stent graft may ultimately result in retrograde ascending aortic dissection. The hypothesis that friability of the aortic wall is an important factor in rAAD in patients undergoing TEVAR is further substantiated by the relatively high number of Marfan patients in the present series who had this complication, supporting the restrictive use of TEVAR in patients with connective tissue diseases such Marfan syndrome, Ehler-Danlos syndrome, and polycystic kidney disease.

Not surprisingly, management of retrograde dissection was different, based on the timing of dissection in relation to the procedure and on the presumed mechanism of the tear. Intraprocedural stent graft–induced dissection more often prompted emergency surgery, whereas dissection presumably due to manipulation of wires or sheaths was treated conservatively, much akin to that done for similar scenarios during other percutaneous cardiovascular procedures. In contrast, patients presenting with retrograde dissection presumed to be due to the progression of underlying aortic disease underwent elective surgical repair with fairly good outcomes.

**Clinical Implications**

Our findings may have some clinical implications for the management of patients undergoing TEVAR, particularly for the diagnosis and prevention of retrograde aortic dissection. First, it is important to recognize that many cases are diagnosed beyond the procedure and even after discharge up to 1050 days after the procedure. It is possible that some of these events may have already occurred as a small tear during the index procedure, and perhaps careful review of the angiogram may help detect this before the end of procedure, so that remedial measures can be implemented immediately. The role of intravascular (or intracardiac) ultrasound in facilitating early detection of such tears remains unknown.\textsuperscript{16} Second, many cases are not only diagnosed late, but up to 25\% of these cases are asymptomatic, underlining the importance of regular life-long surveillance of all TEVAR patients in general and specifically for the early detection of this complication. Third, the friability of the aortic wall in patients with aortic dissection and particularly in those with Marfan syndrome should be appropriately recognized, and all efforts should be made to minimize manipulation of guide wires and stent graft systems in these at-risk patients. Development of dissection-specific, less-rigid endoprostheses, with improved flexibility and geometry, is currently under way and may help to reduce the risk of rAAD in the future.\textsuperscript{10}
Strengthen and Limitations
Our analysis is the first to provide multicenter data on the incidence and patient characteristics of a rare but potentially lethal complication of TEVAR in a relatively large number of patients undergoing these procedures. Nevertheless, our analysis should be viewed in the light of its limitations. First, our study used a unique approach of collecting detailed data only from patients who developed complications, thereby lacking a control group of TEVAR patients who did not develop rAAD after the procedure. Therefore, identification of risk factors predisposing toward this complication is limited. Our findings should thus be considered as hypothesis-generating. Full descriptive information was available for only 48 of the 63 (76%) cases of rAAD. Furthermore, our study is limited by its retrospective nature, which makes it impossible to provide an accurate estimation of the incidence of rAAD in the classic form of events per patient-year of follow-up.

Conclusions
Our data indicate that retrograde dissection of the ascending aorta is an unusual rare complication of an emerging new treatment strategy, that is, TEVAR occurring in approximately 1.33% of patients undergoing this procedure. Nonetheless, this complication is associated with high mortality rates despite surgical repair in many. Our data provide important insights into underlying pathophysiological mechanisms, timing of occurrence, and mode of presentation of the patients with this complication that may have some clinical implications for minimizing the risk and for the early detection of this catastrophic complication.

Appendix: EuREC Centers
West-German Heart Center Essen, University of Duisburg-Essen, Essen, Germany (Holger Eggebrecht, Raimund Erbel); St George’s Vascular Institute, St George’s Hospital NHS Trust, London, London Kingdom (Matt Thompson); Centre Hospitalier Universitaire, Hopital de Rangueil, Toulouse, France (Herve Rousseau); University of Vienna Medical School, Vienna, Austria (Martin Czermak); Rigshospitalet University Hospital, University of Copenhagen, Copenhagen, Denmark (Lars Lønn); University of Heidelberg, Heidelberg, Germany (Dittmar Böckler); University Hospital S. Orsola, Bologna, Italy (Rosella Fattori); Zhongshan Hospital, Fudan University, Shanghai, China (Weigu Fu, Zhiu Dong); Northern General Hospital, Sheffield, United Kingdom (Peter Gaines); St Antonius Hospital, Nieuwegein, The Netherlands (Robin Heijmen); Gentofte Hospital, Hellerup, Denmark (Sven Just); Odense University Hospital, Odense, Denmark (Per Justesen); European Vascular Center Aachen-Maastricht, University Hospital Aachen, Aachen, Germany (Stephan Langer); Vascular Center Malmö-Lund, Malmö University Hospital, Malmö, Sweden (Martin Malina); Centre Hospitalier Universitaire, Hôpital Sainte Marguerite, Marseille, France (Alessandro Piquet); Department of Cardiovascular Surgery, Thoracic Institute, Hospital Clinic, University of Barcelona, Barcelona, Spain (Vicente Piquet); Miquet P, Lovato L, Dabbech C, Kische S, Gaxotte V, Schepens M, Ehrlich M, Bartoli JM. Results of endovascular repair of the thoracic aorta with the Talent Thoracic stent graft: the Talent Thoracic Retrospective Registry. Eur J Cardiothorac Surg. 2006;132:332–339.


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Disclosures
Dr Thompson reports having received honoraria from Medtronic and Cook; Dr Rousseau serves as a consultant for Gore, Medtronic, and Bolton; and Dr Lönn has received honoraria from Cordis, Cook, Gore, Medtronic, and Boston Scientific, serves as a consultant for Mentice and Orzane Company, and has received payment for speaker’s bureau appointments from Syncron Medical.

References
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