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Philipp Geisbüsch, Drosos Kotelis, Hendrik von Tengg-Kobligk, Alexander Hyhlik-Dürr, Jens-Rainer Allenberg, Dittmar Böckler

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Thoracic Aortic Endografting in Patients With Connective Tissue Diseases

Philipp Geisbüsch, MD[1]; Drosos Kotelis, MD[1]; Hendrik von Tengg-Kobligk, MD[2]; Alexander Hyhlik-Dürr, MD[1]; Jens-Rainer Allenberg, MD, PhD[1]; and Dittmar Böckler, MD, PhD[1]

[1]Department of Vascular and Endovascular Surgery, Ruprecht-Karls University, Heidelberg, Germany. [2]Department of Radiology, German Cancer Research Center (DKFZ), Heidelberg, Germany.

Purpose: To present midterm results after thoracic endovascular aortic repair (TEVAR) in patients with connective tissue diseases focusing on secondary endoleak and reintervention due to disease progression.
Methods: Between January 1997 and January 2007, 167 patients received 241 thoracic aortic stent-grafts. Eight patients (6 men; median age 48 years, range 32–67) with connective tissue diseases (6 Marfan and 2 Ehlers-Danlos syndrome) treated with stent-graft repair were retrospectively analyzed at a median follow-up of 31 months (range 3–79). Surveillance included postoperative computed tomographic angiography and/or magnetic resonance imaging exams prior to discharge, at 3, 6, and 12 months, and yearly thereafter.
Results: Technical success of endovascular placement was 88% due to 1 primary type I endoleak. There were no perioperative deaths, and there have been no conversions to open surgery so far. Perioperative complications occurred in 2 (25%) of the 8 patients. Endoleaks were observed in 3 patients (primary type I, secondary type I, and type II). The reintervention rate was 38%. Progression of disease resulting in de novo aneurysms or aortic expansion occurred in 4 (50%) patients. Seven (88%) patients are alive. There was no disease- or procedure-related death.
Conclusion: TEVAR in patients with connective tissue diseases is feasible but still questionable regarding their young age and the rates of endoleaks and reintervention due to disease progression. Close surveillance is mandatory. Low morbidity and mortality rates may justify TEVAR in emergencies as a ''bridging'' method.

Key words: Marfan syndrome, thoracic aorta, endovascular repair, stent-graft, connective tissue disease, thoracic aortic endovascular repair

Following pioneering work in endovascular aortic aneurysm repair,[1] the Stanford group subsequently applied this alternative treatment option to thoracic aortic aneurysm (TAA) in the mid '90s.[1,2] Recently, Demers et al.[3] reported the 5-year results of thoracic endovascular aortic repair (TEVAR) from the Stanford group. Over the past 10 years, TEVAR has been used with increasing frequency for a variety of indications, including TAAs, dissections, traumatic transections, and penetrating aortic ulcers.[3–5]

As aortic aneurysm formation and dissection are most commonly associated with atherosclerotic disease, there is a broad experience and a multitude of data regarding

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Address for correspondence and reprints: Philipp Geisbüsch, MD, Department of Vascular and Endovascular Surgery, Ruprecht-Karls University Heidelberg, Im Neuenheimer Feld 110, 69120 Heidelberg, Germany. Fax: 49-6221-565423; E-mail: *Philipp.Geisbuesch@med.uni-heidelberg.de*

TEVAR in these patients.[6–8] In contrast to atherosclerotic TAAs, little data is available on the concept of stent-graft implantation in patients with TAA or dissection associated with connective tissue disorders (CTD), such as Marfan or Ehlers-Danlos syndrome. So far, only case reports and 2 small series have been published.[9–13]

Successful TEVAR requires ''healthy'' proximal and distal landing zones for efficient sealing. Therefore, stent-graft deployment in a potentially completely diseased aorta might seem a hazardous procedure, and the topics of endoleak and disease progression are of special interest. Considering the relatively high peri- and postoperative mortality of open surgery, a less invasive treatment alternative such as TEVAR seems an especially promising alternative, even as a ''bridging method,'' in this young patient cohort, who typically require multiple sequential operations.

The aim of this study was to present and discuss our midterm results of TEVAR in patients with Marfan or Ehlers-Danlos syndrome focusing on secondary endoleak and reintervention due to disease progression.

METHODS

Between January 1997 and January 2007, 167 patients received 241 thoracic stent-grafts for various indications (Table 1), 85 (51%) under emergency conditions. The data of these patients were collected prospectively in a database. The records of 8 patients (6 men; median age 48 years, range 32–67) with Marfan (n=6) or Ehlers-Danlos (n=2) syndrome were reviewed.

The pathologies included thoracic and thoracoabdominal aortic lesions. One patient was treated for a TAA, while the other 7 patients were treated for chronic expanding aortic dissection (3 type A, 4 type B). Three patients had previous reconstructive surgery on the ascending aorta; 2 patients underwent prior open thoracoabdominal aortic surgery.

Sizing of the stent-graft was planned by measurements (centerline diameter) from preoperative contrast-enhanced computed tomographic angiography (CTA) and magnetic resonance angiography (MRA) with 3-dimensional

TABLE 1
Indications for Stent-Graft Repair of Thoracic Aortic Pathologies in 167 Patients Treated Between January 1997 and January 2007

	Total*	Elective	Emergency
Thoracic aortic aneurysm	49	34	15
Penetrating aortic ulcer	31	18	13
Thoracoabdominal aneurysm	26	17	9
Chronic expanding aortic dissection	26	21	5
Acute type B dissection	14	—	14
Acute type A dissection	6	—	6
Traumatic rupture	9	—	9
Aortobronchial fistula	9	—	9
Patch rupture	3	—	3
Intramural hematoma	2	—	2

* Multiple indications.

(3D) reconstructions. Two types of stent-grafts were implanted: Talent/Valiant (Medtronic Vascular, Santa Rosa, CA, USA) or TAG (W.L. Gore & Associates, Flagstaff, AZ, USA). For stent-graft diameter selection, 15% oversizing in TAA and 10% in dissections was applied.

All surgical procedures were performed under general anesthesia in an operating theater equipped with fluoroscopic and angiographic capabilities (Series 9800; OEC Medical Systems, Inc., Salt Lake City, UT, USA) and a carbon fiber operating table. For exact visualization of the landing zones, the patient's left shoulder was elevated 40° with both arms fixed beside the body. Each patient received single-shot antibiotic therapy and 3000 units of heparin for anticoagulation. Vascular access was obtained by transfemoral incision; in patients with small femoral arteries, a 10-mm Dacron conduit was created to the left common iliac artery (CIA). A sheath (up to 26 F) was inserted over a 0.035-inch, 260-cm Amplatz Super Stiff guidewire (Boston Scientific, Ratlingen, Germany) and passed to the aortic arch. A 0.035-inch guidewire (Terumo, Frankfurt, Germany) was advanced and exchanged for a 7-F calibrated angiography catheter. Digital subtraction angiography was performed with breath-hold technique followed by manual injection of 20 mL of nonionic contrast medium [iopamidol (Solutrast 300); Byk Gulden, Konstanz, Germany] with the aortic arch turned to about 40° in the left anterior oblique projection. Completion angiography was performed to assess accurate placement and exclusion of the lesion.

Additional procedures were performed in 3 patients. In 2, open surgery was necessary prior to TEVAR: as part of a hybrid arch supra-aortic debranching in one and revascularization of the renal arteries, the superior mesenteric artery, and the celiac trunk via transperitoneal bypass grafting in the other. The third patient had type B dissection, and a renal artery dissection was impairing blood flow to the kidney; a renal stent (Corinthian 7×20 mm) was implanted during the TEVAR procedure.

Surveillance included postoperative CTA scanning prior to discharge; clinical examination, plain chest radiography, and CTA or MRA were performed at 3, 6, and 12 months, and yearly thereafter.

RESULTS

The 8 patients received 12 stent-grafts (8 TAG, 2 Talent, and 2 Valiant), 4 patients receiving multiple devices (Table 2). Technical success was achieved in 7 (88%) patients; there was a primary distal type I endoleak seen on the postoperative CTA in Case 2.

There were no perioperative deaths. Two (25%) postoperative complications occurred: a postoperative bleed and persistent subclavian steal syndrome after intentional overstenting of the left subclavian artery (LSA) in Case 1. There were no neurological complications (strokes, paraparesis, or paraplegia) in this subgroup of patients.

At a median follow-up of 31 months (range 3–79), 7 (88%) patients were alive. One Ehlers-Danlos patient (Table 2, Case 8) died 34 months after endovascular TAA treatment from sequelae of a bilateral embolic stroke.

Endoleaks were observed in 3 (38%) patients. A type II endoleak was seen in a Marfan patient (Case 5) 3 months after endovascular treatment of a chronic type A dissection; he is under close observation with CTA control. A primary distal type I endoleak was observed in a Marfan patient (Case 2) who had undergone emergent TEVAR for acute type B dissection; a distal stent-graft extension was implanted (Figure), but false lumen expansion occurred owing to re-entry from the left CIA, and the patient needed further reinterventions (described below). A secondary distal type I endoleak due to disease progression in the distal landing zone was observed in an Ehlers-Danlos patient (Case 7) 58 months after stent-grafting for expansion of a residual type A dissection of the descending aorta. Stent migration was not observed.

Progression of disease resulting in de novo aneurysms or aortic expansion occurred in 4 (50%) patients. The Marfan patient (Case 2) who underwent the emergent TEVAR procedure described above showed a chronic expanding type B dissection after initially successful endovascular closure of the entry site. She underwent a thoracoabdominal hybrid procedure (visceral revascularization and stent-grafting). Two patients (Cases 7,8) with de novo aneurysms involving the aortic arch and ascending aorta, respectively, underwent open replacement.

Reinterventions were necessary in 3 (38%) patients, including the Marfan patient (Case 2) who has had 4 endovascular reinterventions so far. Patient 1 needed staged transposition of the LSA due to persistent symptomatic impairment of cerebral perfusion after LSA occlusion during TEVAR. Patient 7 needed distal stent-graft extension to close the secondary distal type I endoleak. No patient needed early or late conversion to open procedures.

DISCUSSION

Poor early and long-term results, with a mortality rate up to 30%,[14] have been reported in Marfan patients needing secondary open aortic surgery for descending aortic pathologies after primary aortic root surgery. In our small series, the low mortality (0%) and morbidity (25%) rates are comparable to those reported in the literature,[9,10,14–18] which indicates that TEVAR is an alternative to open surgery in patients with connective tissue disease (CTD).

One major advantage of TEVAR is a low neurological complication rate. None of our patients had stroke, paraparesis, or paraplegia, which matches the experiences reported by Baril et al.[10] and Ince et al.[9] By comparison, this complication occurs in ~8% of patients after open descending aortic surgery.[19]

Table 2
Characteristics of 8 Patients With Arteriopathies and Thoracic Aortic Pathologies Treated With Stent-Grafts

Sex/Age, y	Pathology/ Previous Aortic Surgery	CTD	Endograft Model/ Size, mm	Endo-leak	Additional Disease-Related Procedures	Procedure-Related Re-interventions	Outcome
1. M/36	Type A CEAD; TLC; ascending aortic surgery; CIA-renal artery bypass	Marfan	TAG/31×120	None		Transposed LSA for subclavian steal syndrome	Alive at 79 mo
2. F/32	Type B CEAD; emergent TEVAR for acute type B dissection	Marfan	TAG/28×100 TAG/31×150	Distal type I		TA hybrid procedure; secondary distal stent-graft extension; CIA stent-graft; distal re-entry closure with CIA stent-graft	Alive at 57 mo
3. M/67	Type B CEAD	Marfan	Talent/36×130 Talent/36×130 Renal stent	None		None	Alive at 28 mo
4. F/55	Type B CEAD	Marfan	TAG/31×150	None		None	Alive at 17 mo
5. M/66	Type A CEAD; Bentall procedure; aortic arch replacement; membrane resection, fenestration, and aortobi-iliac-bypass	Marfan	Valiant 36/150 Valiant 40/150	Type II		None	Alive at 3 mo
6. M/41	Type B CEAD; aortic arch hybrid	Marfan	TAG/28×150 TAG/28×100	None		None	Alive at 13 mo
7. M/41	Type A CEAD; ascending aortic surgery; TA aortic replacement; membrane resection and fenestration	ED	TAG/37×200	Distal type I	Bentall procedure; aortic arch replacement	Distal stent-graft extension	Alive at 58 mo
8. M/65	TAA	ED	TAG/40×150	None	Preplanned aortic root replacement	None	Died at 34 mo

CTD: connective tissue disease, CEAD: chronic expanding aortic dissection, TA: thoracoabdominal, ED: Ehlers-Danlos syndrome. TLC: true lumen collapse, LSA: left subclavian artery, TAA: thoracic aortic aneurysm, CIA: common iliac artery, TAA: thoracic aortic aneurysm.

Primary technical success of endovascular stent-graft placement varies from 88% in our experience to 100% in the literature.[9,10] Especially in chronic dissections, wire cannulation of the true lumen or an existing elephant trunk prosthesis can be difficult; an additional wire via a brachial or radial access can be helpful in special cases.

Type I endoleak and stent-graft migration in the setting of a potentially completely diseased aorta or rapidly progressing aortic disease such as CTD is of special interest; in some centers, this scenario would be considered a contraindication to TEVAR. In our subgroup of patients, the 38% endoleak rate was somewhat high, but no stent-graft migration has occurred so far. Baril et al.[10] reported 1 (17%) type III endoleak in their 6 patients.

In our series, 3 (38%) patients needed procedure-related reintervention during a

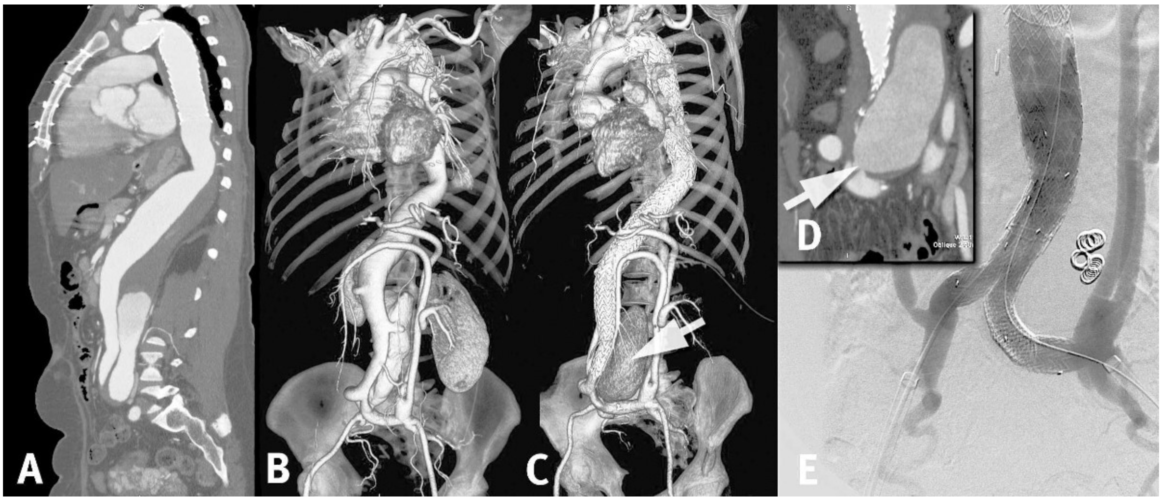

Figure ◆ (**A**) This CTA scan shows aortic expansion after initial TEVAR for acute type B aortic dissection in a Marfan patient. (**B**) The 3D volume rendering CTA reconstruction after visceral revascularization. (**C**) Thoracoabdominal stent-grafting with distal type I endoleak; the arrow indicates false lumen perfusion. (**D**) Re-entry (arrow) from the left CIA. (**E**) Completion angiography after distal stent-graft extension.

median follow-up of 31 months, including a young female Marfan patient who underwent multiple reinterventions. Baril et al.[10] reported a reintervention rate of 50%. Although Ince et al.[9] reported no reinterventions, they did have 2 (33%) conversions due to persistent false lumen perfusion and expansion in patients with aortic dissection; a third patient was being considered for open surgical conversion. The authors concluded that stent-grafting should be considered more a bridging maneuver than a curative treatment modality.[9]

In CTD patients, disease progression is expected, and a higher rate of ancillary interventions could be anticipated compared to non-CTD-related pathologies. Baril et al.[10] reported 2 of their 6 Marfan patients needed consecutive disease-related interventional procedures; another patient underwent repeated peripheral bypass grafting. Half of our patients had pathology related to their CTD; 2 required additional open aortic repairs. Although disease progression might seem like the Achilles' heel of TEVAR in CTD patients, one must keep in mind that open aortic replacement in these patients, with direct resection and anastomosis to a diseased vessel, also bears a high rate of anastomosis failure and de novo aneurysms.[20]

An interesting observation is that physicians often face a well-informed patient who is well aware of possible complications of open surgery and who requests aortic stent-graft repair, attracted by the ''minimal invasiveness'' of this procedure. Discussing both therapeutic options is an important factor in decision making in this rather young patient cohort.

The high rates of endoleaks, reinterventions, and disease progression necessitating open conversion or additional open aortic surgery described in this series and others[9,10,14,15,17,18,21] underline the importance of lifelong follow-up with close serial aortic imaging. In our previously published series of non-CTD patients with chronic expanding type B dissection, TEVAR also carried a low mortality (0%) rate, an estimated 2-year survival rate of 90%, and a 74% freedom from reintervention after 2 years.[5]

CONCLUSION

This small series demonstrates that endovascular treatment of patients with thoracic aortic pathologies and underlying connective tissue diseases is feasible but questionable regarding the young age of the patients and the relevant endoleak and reintervention rates due to disease progression. Lifelong close surveillance is mandatory. Low morbidity and mortality rates may justify using endovascular stent-grafts in emergency situations as a ''bridging'' method.

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