Endografting in the Aortic Arch — Does the Proximal Landing Zone Influence Outcome?

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Abstract  Objectives: To analyse early and midterm results of thoracic aortic endografting (TEVAR) in the aortic arch.
Methods: Between January 1997 and February 2009 178 patients received TEVAR in the aortic arch at our institution. This population was subdivided into four groups according to the proximal landing zone (LZ) classification in the aortic arch by Ishimaru et al. and a retrospective analysis regarding perioperative mortality, morbidity and endoleak formation was performed.
Results: The overall 30-day mortality rate was 14% with no statistical significant difference between LZ's 0–3 (p=0.274). Renal insufficiency (hazard ratio (HR) 2.5; p=0.0119), age >75 years (HR 3.1; p=0.0019) and emergency procedures (HR 8.9; p < 0.0001) were independent predictors of death. There was no significant difference regarding type I (p=0.07) or type III (p=0.49) endoleaks between the proximal LZs, but a significant difference regarding the development of type II endoleaks (p=0.01).
Conclusions: The present study showed no influence of the proximal LZ on perioperative mortality and morbidity rate. Furthermore it did not influence relevant (type I/III) endoleak formation.

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Vascular pathologies involving the aortic arch are considered to be a special challenge for vascular and cardiovasucular surgeons. Conventional open aortic arch replacement using extracorporal circulation, selective antegrade cerebral perfusion and moderate hypothermia is associated with a relevant morbidity and mortality rate. As a consequence thoracic endovascular aortic repair (TEVAR) as a potentially less invasive treatment alternative seems especially appealing in high-risk patients. While the development of fenestrated endografts is still ongoing, frequently hybrid procedures, combining supra-aortic vessel debranching to achieve sufficient landing zone and TEVAR are necessary. These re-routing procedures have an increasing invasiveness and perioperative morbidity and mortality from subclavian transposition or bypass grafting to hemiarch or complete debranching.
The aim of this study was therefore to analyse short and midterm results of TEVAR in the aortic arch regarding peri-operative mortality and morbidity as well as midterm survival, stratified by the required proximal landing zone.

Methods

Patient population

Between January 1997 and February 2009 a total of 236 consecutive patients received TEVAR in our institution; the aortic arch was involved in 178 patients (126 men, median age 72 years, range: 64−79). This patient population was subdivided into four groups according to the proximal landing zone (LZ) classification in the aortic arch by Ishimaru et al. (Zone 0−3).8

Indications for treatment in all four groups are given in Table 1 and show the complete spectrum of aortic pathologies with the greatest proportion of emergency operations in zones 2 and 3. This is caused by the high amount of acute aortic dissections (n=23) and traumatic transections (n=14), which are typically localised in this aortic section (zone 3) and the referral pattern of our university hospital.

Baseline characteristics and cardiovascular risk factors for patients in group 0−3 are given in Table 2 and reveal a statistical significant difference regarding history of smoking, renal insufficiency and diabetes mellitus between the groups. For risk stratification the logistic EuroScore and ASA classification were used, which showed no statistical difference between the patients of zone 0−3.9,10 The EuroScore is a commonly used pre-operative risk stratification system for cardiac and open thoracic aortic surgery that includes demographic, cardiac-related and surgery-related variables.9,10

Pre-interventional imaging

All patients received pre-operative computed tomography (CTA) or magnetic resonance angiography (MRA). Volumetric imaging (isotropic voxel with thin slice thickness, ideally ≤2 mm), image post-processing in three dimension (3D) using multi-planar reformation (MPR) and centreline measurements were used for procedure- and stent-graft selection as well as pre-operative planning of the implantation strategy whenever possible. Aortic diameters and length, and thus stent-graft selection was calculated using centreline measurements.11 A sufficient LZ was defined as a thrombus-free, non-calcified, >2-cm-long segment of the arch with a maximum diameter ≤15−20% of the largest available stent-graft diameter.

Procedure

All surgical procedures were performed in an operation theatre equipped with fluoroscopic and angiographic capabilities (Series 9800; OEC Medical Systems, Inc., Salt Lake City, UT, USA until April 2007, after that Axiom U, Siemens, Forchheim, Germany) and a carbon fibre operating table. Our procedure protocol has been published before.12

All cases of LZ 0 were performed under general anaesthesia. In LZ 1−3 epidural or spinal anaesthesia could be applied in 5 cases (3%), local anaesthesia was used in 11 patients (6%) and 91% of all patients received general anaesthesia.

For exact stent-graft positioning in the aortic arch we aimed for an adenosine-induced cardiac arrest (AICA) for all patients with LZ 0−1. This technique could be applied in all elective cases except a few emergency ones.

Routine vascular access was obtained by transfemoral incision in 130 patients (73%). In 35 cases (20%) with small femoral vessel diameters a Dacron conduit prosthesis to the right iliac common artery was used.

Hybrid procedures

Hybrid procedures with supra-aortic debranching were performed in 32 cases. All LZ 0 cases received revascularisation of the supra-aortic branches via bypass grafting from the ascending aorta. In all LZ 1 patients, extra-anatomic revascularisation of the left common carotid artery with carotid−carotid crossover bypass or transposition was performed. An additional 14 patients received primary revascularisation of the left subclavian artery (LSA) in this group.

Revascularisation of the LSA was performed in six patients before TEVAR in LZ 2 (coverage of the LSA). Selection criteria

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Indications for TEVAR in all patients with aortic arch pathologies (n=178).</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Indications</strong></td>
<td>Zone 0 (n=10)</td>
</tr>
<tr>
<td>TAA</td>
<td>6</td>
</tr>
<tr>
<td>TAAA</td>
<td>2</td>
</tr>
<tr>
<td>TAT</td>
<td>–</td>
</tr>
<tr>
<td>AAD</td>
<td>–</td>
</tr>
<tr>
<td>CEAD</td>
<td>–</td>
</tr>
<tr>
<td>PAU/IMH</td>
<td>2</td>
</tr>
<tr>
<td>ABF</td>
<td>–</td>
</tr>
<tr>
<td>Emergency procedures</td>
<td>3 (30)</td>
</tr>
</tbody>
</table>

Values are presented as n (%).

TEVAR in the Aortic Arch

Table 2  Pre-operative characteristics of all patients stratified for different proximal landing zones (classification by Ishimaru et al.)

<table>
<thead>
<tr>
<th>Zone 0 (n = 10)</th>
<th>Zone 1 (n = 25)</th>
<th>Zone 2 (n = 55)</th>
<th>Zone 3 (n = 88)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age 64.8 (61–84)</td>
<td>63.8 (32–84)</td>
<td>63.2 (28–84)</td>
<td>66.7 (2–89)</td>
<td>0.136</td>
</tr>
<tr>
<td>Gender (male) 8 (80)</td>
<td>17 (68)</td>
<td>38 (69)</td>
<td>62 (70)</td>
<td>0.932</td>
</tr>
<tr>
<td>ASA III + IV 10 (100)</td>
<td>22 (88)</td>
<td>41 (75)</td>
<td>75 (85)</td>
<td>0.186</td>
</tr>
<tr>
<td>logEuroscore 20.9 (12–80)</td>
<td>27.3 (3–73)</td>
<td>18.1 (3–65)</td>
<td>21.3 (3–94)</td>
<td>0.489</td>
</tr>
<tr>
<td>Hypertension 10 (100)</td>
<td>23 (92)</td>
<td>42 (78)</td>
<td>77 (88)</td>
<td>0.186</td>
</tr>
<tr>
<td>History of smoking 8 (80)</td>
<td>10 (40)</td>
<td>21 (38)</td>
<td>55 (63)</td>
<td>0.005</td>
</tr>
<tr>
<td>CHD 6 (60)</td>
<td>10 (40)</td>
<td>14 (26)</td>
<td>33 (38)</td>
<td>0.162</td>
</tr>
<tr>
<td>Renal insufficiency 2 (20)</td>
<td>5 (20)</td>
<td>7 (13)</td>
<td>31 (35)</td>
<td>0.019</td>
</tr>
<tr>
<td>COPD 3 (30)</td>
<td>4 (16)</td>
<td>6 (11)</td>
<td>23 (26)</td>
<td>0.117</td>
</tr>
<tr>
<td>Diabetes 4 (40)</td>
<td>4 (16)</td>
<td>2 (4)</td>
<td>10 (11)</td>
<td>0.010</td>
</tr>
<tr>
<td>Previous aortic surgery 2 (20)</td>
<td>5 (20)</td>
<td>9 (16)</td>
<td>24 (27)</td>
<td>0.492</td>
</tr>
</tbody>
</table>

Values are presented as n (%) or median (range). Abbreviations: CHD: coronary heart disease, COPD: chronic obstructive pulmonary disease, ASA: American Society of Anaesthesiologists classification.

for revascularisation included patients with an increased risk for paraplegia (previous aortic surgery, long covered aortic segment, etc.), previous aorto-coronary bypass grafting using the internal mammary artery or an insufficient contralateral vertebral artery. A total of 17 patients required additional thoraco-abdominal hybrid procedures (LZ 0: two patients, LZ 1: two patients, LZ 2: three patients and LZ 3: 10 patients). Our early experience with hybrid procedures in TAAA has been published recently.13 Stent-grafts

A total of 293 endografts were implanted, with 108 patients receiving a single stent-graft. Four types of stent-grafts were implanted: Talent and Valiant (Medtronic Vascular, Santa Rosa, CA, USA), TAG (W.L. Gore & Associates, Flagstaff, AZ, USA) and Zenith (Cook Inc., Bloomington, Indiana, USA).

For stent-graft diameter selection 15–20% oversizing in aneurysms and 10% in aortic dissections or transections were applied.

Follow-up

The follow-up protocol included post-operative CTA before discharge, clinical examination, plain chest radiography and CTA/MRA 6 and 12 months post-operatively and annually thereafter. Additionally, all patients with hybrid procedures received duplex scanning to exclude bypass stenosis or occlusion. A total of 11 patients were lost in follow-up (seven patients refused serial aortic imaging and four patients could not be located). Mean follow-up was 33.2 months (range 0.1–141.5 months).

Definitions and statistical analysis

The definitions of technical and clinical success are according to the reporting standards for endovascular aortic aneurysm repair.13 Endoleaks were categorised as previously described by White et al.14 and specified as primary endoleaks if apparent on intra-operative control angiography or primary post-operative CTA control. Secondary endoleaks were defined as occurring during follow-up.

A retrospective analysis of the prospectively collected data was performed. Continuous data are described by mean ± SD or median (range). Survival rates were estimated by Kaplan—Meier. The log-rank test was used for comparison of survival distributions between subgroups defined by LZ. For categorial data comparison of subgroups was carried out by Fisher’s exact test and in case of continuous or ordinal data Mann—Whitney U-test was used. Cox proportional hazard model (Cox regression analysis) and logistic regression analysis were used to identify independent risk factors affecting survival and endoleak formation. All statistical analysis was performed using SAS for Windows, (Version 9.2, SAS Institute Inc., Cary, NC, USA) and MedCalc (Version 9.5.2, MedCalc software, Mariakerke, Belgium). A p value <0.05 was defined as statistically significant.

Results

Mortality and morbidity

Operative results are presented in Table 3. Overall 30-day mortality was 14%, with the highest perioperative mortality in LZ 2 and 3 (p = 0.274). Cox proportional hazard regression showed renal insufficiency (HR 2.5; 95% confidence interval (CI) 1.2–4.9), age >75 years (HR 3.1; 95% CI 1.5–6.2) and the necessity for an emergency procedure (HR 8.9; 95% CI 3.1–25.2) as independent predictors of death. (Table 4).

The overall post-operative morbidity rate was 53% with no significant difference between LZ 0–3 (p = 0.370), although the greatest proportion of cardiac, respiratory and renal complications were seen in patients with LZ 0. Neurological complications (stroke and paraplegia) occurred in 6.1% (11/178) patients. The perioperative stroke rate was 3.3%, with a maximum in LZ 1 (8%) and a minimum in LZ 0 (0%). Paraplegia was seen in five patients (2.8%). This includes three patients with simultaneous thoraco-abdominal aortic hybrid procedures, one patient
who required simultaneous infrarenal open aortic replacement and TEVAR for a contained ruptured TAAA thoracoabdominal aortic aneurysm and one patient with an acute aortic dissection Type B.

**Technical success**

The technical success rate was 89% with 19 patients showing a primary type I or III endoleak and one patient requiring early conversion (n = 20/178; 11%). The technical success rate was 80% in LZ 0 (two patients endoleak type I), 76% in LZ 1 (six patients endoleak type I), 95% in LZ 2 (three patients endoleak type I) and 90% in LZ 3 (seven patients endoleak, type I + 1 patient endoleak type III + 1 early conversion). All patients are described in detail in the following.

**Endoleaks and re-intervention**

Primary endoleaks were detected in 36 patients (20%), with an increasing incidence towards the proximal aortic arch (from LZ 3 (14%) to LZ 0 (40%)), although this just did not reach statistical significance (p = 0.05). Endoleaks type II from the left subclavian artery were seen in 10 patients. This included one patient in LZ 0, 2 patients in LZ 1 and seven in LZ 2. These endoleaks sealed spontaneously in seven patients during follow-up, while three patients required surgical intervention. Early conversion (0.6%) was necessary in a 65-year-old patient with a TAA in the beginning of the TEVAR era (1998) due to a stent-graft collapse that could not be resolved intra-operatively by endovascular means.

Secondary endoleaks occurred in seven patients (4%) that included two patients with a type III endoleak. One patient underwent successful endorepair, the second one required late conversion due to an aorto-oesophageal fistula caused by the fractured stent wire.14

The total rate of endoleak formation (primary + secondary) was independently predicted by a more proximal LZ (OR 0.612, 95% CI 0.421–0.8884) and an increasing number of endoprosthesis used in one procedure (OR 1.438, 95% CI 1.011–2.045) (Table 5).

The overall re-intervention rate was 23% with an increasing proportion of re-interventions towards the more proximal LZs (Table 3).

**Midterm survival analysis**

A total of 21 patients died during follow-up, 14 due to aortic or procedure unrelated causes. The causes of death in these patients were myocardial infarction in six patients, pneumonia in three patients, lung cancer in two patients and stroke/intracerebral bleeding in two patients. One patient died of a sepsis caused by an osteomyelitis after repeated spine surgery.

Aortic-related death during follow-up occurred in seven patients (4%). This included two patients with an aortic rupture caused by a primary type I endoleak. Both patients refused further re-intervention and/or were incompliant regarding post-operative follow-up. Two patients died of

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**Table 3** Operative results, specified for different proximal landing zones.

<table>
<thead>
<tr>
<th>Zone 0 (n = 10)</th>
<th>Zone 1 (n = 25)</th>
<th>Zone 2 (n = 55)</th>
<th>Zone 3 (N = 88)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>30-day mortality</td>
<td>1 (10)</td>
<td>1 (4)</td>
<td>11 (20)</td>
<td>12 (13.6)</td>
</tr>
<tr>
<td>Perioperative morbidity</td>
<td>8 (80)</td>
<td>13 (52)</td>
<td>29 (53)</td>
<td>44 (50)</td>
</tr>
<tr>
<td>Stroke</td>
<td>0 (0)</td>
<td>2 (8)</td>
<td>1 (1.8)</td>
<td>3 (3)</td>
</tr>
<tr>
<td>Paraplegia</td>
<td>0 (0)</td>
<td>1 (4)</td>
<td>1 (1.8)</td>
<td>3 (3)</td>
</tr>
<tr>
<td>Cardiac complications</td>
<td>5 (50)</td>
<td>2 (8)</td>
<td>7 (13)</td>
<td>12 (14)</td>
</tr>
<tr>
<td>Respiratory failure</td>
<td>4 (40)</td>
<td>4 (16)</td>
<td>15 (27)</td>
<td>18 (20)</td>
</tr>
<tr>
<td>Renal failure</td>
<td>4 (40)</td>
<td>1 (4)</td>
<td>6 (11)</td>
<td>13 (15)</td>
</tr>
<tr>
<td>Wound infection</td>
<td>1 (10)</td>
<td>3 (12)</td>
<td>2 (4)</td>
<td>8 (9)</td>
</tr>
</tbody>
</table>

Open conversion
- Early | 0 (0) | 0 (0) | 0 (0) | 1 (1) |
- Late | 0 (0) | 0 (0) | 3 (5) | 3 (3) |

ICU stay in d
- Revascularisation | 3 (1–60) | 2 (1–12) | 3 (0–5) | n.a. |
- TEVAR | 3 (1–60) | 2 (0–12) | 2 (1–40) | 2 (0–47) |

Endoleak: primary + secondary
- Type I | 3 (33) | 6 (24) | 6 (11) | 8 (9) | 0.073 |
- Type II | 3 (33) | 2 (8) | 9 (16) | 4 (5) | 0.015 |
- Type III | 0 (0) | 0 (0) | 0 (0) | 3 (3) | 0.499 |
- Re-intervention | 5 (50) | 9 (36) | 10 (18) | 17 (19) |

Values are presented as n (%) or median (range).
Discussion

The present study shows that endografting in the aortic arch is associated with a relevant mortality (14%) and morbidity rate (53%). No statistically significant difference regarding the proximal LZe could be shown, but these results are prone to serious limitations (see section titled 'Limitations'). This result is in line with other series that demonstrated no influence of the proximal LZe or the debranching procedure on perioperative mortality.

Nevertheless, it is obvious that complete debranching procedures represent a different procedure category (compared to partial re-routing) with an increased mortality and morbidity rate that could possibly not be shown in this series due to the relatively small number of patients in this cohort. Mortality rates after TEVAR in the aortic arch vary from 0% to 8% and are thus below our reported mortality of 14%.15–17 This might be explained as a result of the large proportion (54%) of emergency procedures performed in our patient cohort, which are associated with an increased perioperative mortality (HR: 8.8; \(p < 0.0001\)) as shown in our study. Besides the necessity for emergency procedures, age >75 years (HR 3.1; \(p = 0.0019\)) and renal insufficiency (HR 2.5; \(p = 0.0119\)) could be identified as independent risk factors influencing perioperative survival. The strong influence of renal insufficiency could be explained by the inclusion of patients with acute, complicated aortic dissections in LZ 2/3 and thus reflect the poor outcome in this subgroup. This is supported by the fact, that patients with LZ 2/3 showed the highest 30-day mortality in this cohort. Additionally, Gottardi et al. could demonstrate in their series of 73 patients with aortic arch hybrid procedure that survival was predicted by higher logistic EuroSCORE levels (OR 1.8; \(p = 0.020\)), also reflecting increased patient co-morbidities and emergency situations.15 Furthermore, we are not aware of any other series focussing on risk factor analysis in the aortic arch.

The present series demonstrates that endoleak formation was associated with a more proximal LZe (OR 0.612; \(p = 0.0098\)). However, the sub-analysis showed that this result is not caused by relevant (type I/III) endoleaks but influenced by a significantly increased amount of type II endoleaks. This is in line with Melissano et al. who showed no significant difference regarding primary or secondary endoleak formation for the different aortic arch segments.16 Additionally, Gottardi et al. recently proved that the type of arch re-routing (and thus the LZe) was not associated with an increased risk of early or late endoleak formation.15

In their series, early and late endoleak formation was predicted by an increasing number of endoprostheses used per procedure, which was proved in our series (OR 1.438; \(p = 0.0427\)) as well. A possible explanation for this could be an increase of type III endoleaks, which we have not seen in our series. The amount of endoprostheses used might therefore reflect more complex TEVAR procedures including thoraco-abdominal stent-graft placement with an increasing risk of type II endoleaks.

Patients with a proximal LZe 3 showed the lowest rate of endoleaks in our series, which has clearly influenced the overall results. The inclusion of these patients is certainly debatable as many authors would consider LZe 3 as 'pure' descending aorta. In our concern, the proximal LZe 3 is located just distal of the left subclavian artery in the transition of the distal arch to the descending aorta. Depending of the location of the left subclavian artery (e.g., in patients with a bovine arch) the LZe 3 might therefore even end up in the mid-arch section in some cases. Additionally, we think that this section of the aorta is still exposed to the heavy pulsatile movements of the aortic arch, reflected by the high amount of pathologies (e.g., dissections) in this aortic segment. Stent-graft procedures in the aortic arch with or without concomitant debranching represent technical challenging procedures. Frequently, the stent-graft does not adapt to the inner curve of the aortic arch but tends towards the outer curve, leaving a triangular space between the endograft and the inner curve (bird peak sign) at risk for endoleak formation, endograft compression or collapse. This is especially prevalent in the mid-aortic section (LZe 1 and 2) and should be considered while planning these procedures. Future device development should therefore include longer, flexible devices, especially designed for the aortic arch, as this might substantially reduce endoleak formation. Published technical success rates from other groups vary between 66% and 100% and are thus in line with our results.16,18–20

Our results showed a sustained treatment success regarding midterm survival with 75% and 67% survival rates after 1 and 3 years, which is also in line with the literature.4 Nevertheless, we experienced aortic-related death and secondary endoleak formation in a relevant (4%) proportion of patients, which underscores the outstanding relevance and necessity for continued follow-up, including dedicated serial aortic imaging and image post-processing.21

Current surgical treatment alternatives for aortic arch pathologies include open conventional arch replacement with/without (frozen) elephant trunk technique.22–26 A comparison of these techniques with endovascular procedures, especially aortic arch hybrid procedures seems difficult due to selection bias, as the patient populations frequently show decisive differences regarding age or co-morbidities. Recently, techniques that allow a total

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds Ratio</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of stent-graft used</td>
<td>1.438</td>
<td>1.011–2.045</td>
<td>0.0427</td>
</tr>
<tr>
<td>Proximal landing zone</td>
<td>0.612</td>
<td>0.421–0.888</td>
<td>0.0098</td>
</tr>
</tbody>
</table>

Table 5 Risk factor analysis regarding primary and secondary endoleak formation.
endovascular repair of arch pathologies using branched endografts are developing and show encouraging initial results. 27–29 Although these techniques might represent the future of aortic arch repair, a broader application, particularly in emergency situations (~50% of all arch pathologies) is still limited by the availability of these custom-made endoprostheses today.

Limitations

The major limitation of these results concern the heterogeneity of the study population in regard to (a) the aortic pathologies (b) the different proportion of emergency procedures in the subgroups and (c) the revascularisation procedures used. Additionally our study covers a large time period (12 years) with significant improvements in stent-graft technology, operative and perioperative management. These influences could mean that a true comparison between mortality and morbidity for different LZs can not be made.

Conclusions

The present study could show no influence of the proximal LZ on perioperative mortality and morbidity rate, but serious study limitations have to be taken into account while drawing this conclusion. Age, renal insufficiency and emergency procedures were independent predictors of death. The proximal LZ did not influence relevant (type I/II) endoleak formation.

Conflict of Interest/Funding

None.

References