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Screening for Familial Thoracic Aortic Aneurysms with Aortic Imaging Does Not Detect All Potential Carriers of the Disease

Matias Hannuksela, MD 1*, Eva-Lena Stattin, MD, PhD 2, Bengt Johansson, MD, PhD 3, Bo Carlberg, MD, PhD 3

1 Department of Surgical and Perioperative Science, Heart Centre, Umeå University, Umeå, Sweden
2 Department of Medical Biosciences, Medical and Clinical Genetics, Umeå University, Umeå, Sweden
3 Department of Public Health and Clinical Medicine, Umeå University, Umeå, Sweden

Abstract

Background: About 20% of patients with thoracic aortic aneurysm or dissection (TAAD) have a first-degree relative with a similar disease. The familial form (FTAAD) of the disease is inherited in an autosomal-dominant pattern. Current guidelines for thoracic aortic disease recommend screening of first-degree relatives of TAAD patients. In known familial disease, screening of both first- and second-degree relatives is recommended. However, the outcomes of such a screening program are unknown.

Methods: We screened all first- and second-degree relatives in seven families with known FTAAD with echocardiography. No underlying gene defect had been detected in these families.

Results: Of 119 persons investigated, 13 had known thoracic aortic disease. In the remaining 106 cases, we diagnosed 19 additional individuals with a dilated ascending thoracic aorta; for an autosomal-dominant disease, the expected number of individuals in this group would have been 40 (p<0.0001). Further, only one of the 20 first-degree relatives younger than 40 years had a dilated aorta, although the expected number of individuals with a disease-causing mutation would have been 10.

Conclusions: In most families with TAAD, a diagnosis still relies on measuring the diameter of the thoracic aorta. We show that a substantial number of previously unknown cases of aortic dilatation can be identified by screening family members. It is, however, not possible to consider anyone free of the condition, even if the aortic diameter is normal, especially at a younger age.

Key Words
Aorta • Aortic aneurysm • Aortic dissection

Introduction

Acute dissection of the thoracic aorta is a serious condition associated with a high risk of complications in different organ systems and an in-hospital mortality rate that averages 20-25% [1-3]. Thoracic aortic aneurysms are usually asymptomatic until acute dissection or aortic rupture occurs; therefore, they often remain undetected until an acute and catastrophic complication arises.

Thoracic aortic aneurysms and dissections (TAAD) can be divided into sporadic and inherited forms. An estimated 20% of patients with TAAD have a family history of the disease, indicating a significant genetic component [4]. The inherited forms might be either syndromic or nonsyndromic, with the most common syndromic forms occurring with Marfan syndrome, (MS; FBN1 gene), vascular Ehlers-Danlos syndrome (vEDS; COL3A1 gene), and Loeys–Dietz syndrome.
The inheritance shows an autosomal-dominant pattern in most syndromic and nonsyndromic familial forms.

The clinical heterogeneity of familial TAAD (FTAAD) suggests that multiple genes are involved, and several have been identified, including ACTA2, MYH11, MYLK, and the PRKG1 genes [5, 6]. Even though several genes are associated with FTAAD, only about 20% of TAAD families have mutations in these genes [4]. Mutation carriers in the genes for LDS do not always develop the syndromic form of the disease but may present with a milder phenotype or an isolated TAAD. The penetrance is depressed and the expression varies in gene mutations associated with FTAAD.

The risk of rupture increases with an increasing diameter of the thoracic aorta. An ascending aortic diameter of greater than 55 mm indicates a high risk for dissection, and prophylactic intervention is recommended at this stage. Studies additionally suggest that dissections occur at a younger age and a smaller diameter in the inherited forms compared with the sporadic forms [4]. The risk of aortic dissection is also determined by the specific underlying gene defect, and the gene defect influences the localization of an aneurysm. Aneurysms in MS are mainly localized to the aortic root, whereas aneurysms in LDS and vEDS can arise all over the arterial tree, including the aortic root or the ascending aorta (AoA). Aneurysms in sporadic forms are often found in the AoA.

In the 2010 multi-specialty Guidelines for Diagnosis and Management of Patients with Thoracic Aortic Disease, aortic imaging is recommended for first-degree relatives of patients with an aortic aneurysm or a dissection [7]. In familial forms, defined as more than one family member having an aortic aneurysm or dissection, aortic imaging is recommended for both first- and second-degree relatives if none of the known disease-causing genes are identified. If the genetic cause is known, aortic imaging is performed only in the carriers of the mutant gene.

We investigated how many new cases with a dilated aorta that could be identified by screening families with an inherited form of TAAD. In addition, we address questions that arise when a screening program for a genetic disorder is applied.

**Methods**

**Study Population**

The study population consisted of the first seven families referred to the Centre for Cardiovascular Genetics, Umeå University Hospital, with FTAAD in whom the genetic cause was unknown. Each family had a history of at least two verified TAADs, and 11 individuals from these families had died from aortic dissection. All first- and second-degree family members older than 18 years without TAAD were offered participation in the study. The families consisted of 135 family members of whom 13 living individuals had had an aortic dissection, an elective repair of a dilated thoracic aorta, or a known dilatation, and thus were not included in the screening (Figure 1). Sixteen individuals did not participate in the study. Seven of them, mainly adolescents, declined participation. Eight individuals living in other cities did not have the opportunity to participate. One individual was not offered participation because of concomitant serious disease.

The remaining 106 family members formed the study population and were screened for thoracic aortic aneurysms. No exclusion criterion other than age was applied. A total of 56 individuals were first-degree relatives, and 50 individuals were second-degree relatives.

The individuals were judged to have arterial hypertension or coronary artery disease if they had medical therapy for these diagnoses.

The regional ethical review board at Umeå University approved the study. Signed informed consent was obtained from the participants after both oral and written information was provided.

**Molecular Genetic Analysis**

DNA was extracted from peripheral blood lymphocytes using a standard salting-out method and sent to an accredited laboratory. No disease-causing gene mutations had been identified in the families. In families 1–3, the genes ACTA2, COL3A1, COL5A1, COL5A2, EFEMP2, FBN1, FBN2, GATA5, MYH11, MYLK, NOTCH1, SLCA10, SMAD3, TGFBR2, TGFBR1, and TGFBR2 were analyzed. In families 4–7, the genes FBN1, COL3A1, TGFBR1, TGFBR2, ACTA2, and SMAD3 have so far been analyzed.

**Measurements**

**Clinical Measurements.** Height and weight were measured using a calibrated stadiometer and scale. Body surface area (BSA) was calculated according to the formula by DuBois and DuBois [8].

**Transthoracic Echocardiographic Examination.** All patients underwent transthoracic echocardiographic examination with a Vivid 7 (GE Medical Systems, Horten, Norway) echocardiography machine equipped with a 2D transthoracic transducer. The aortic diameter was measured from the parasternal long-axis view at the sinuses of Valsalva (SoV) and at the widest level of the AoA; thus, AoA measurements were not made at exactly the same level in all patients.

All measurements were made in end-diastole, considering the inner-edge-to-inner-edge distance from the parasternal...
Figure 1. The pedigrees of the families.
long-axis view. Measurements were made in M-mode after verifying correct position and alignment in the 2D image (Figure 2).

All examinations were performed by one of two sonographers. The studies were then reviewed and analyzed offline by one investigator with an international accreditation in echocardiography. The average of three measurements in different cardiac cycles was calculated.

As a reference for the echocardiographic measurements, data published by Mirea et al. were used [9]. That study has defined normal aortic diameters based on 500 individuals with normal echocardiographic findings, and the measurements were performed by inner edge convention in diastole in both SoV and AoA, as in our measurements. The diameters were indexed to age, sex, and body surface area (BSA). The upper normal limit was set to the mean + 2SD.

Magnetic Resonance (MR). All individuals underwent Magnetic Resonance Imaging. The diameter measured by MR was used if the ascending aorta was not visualized clearly enough with echocardiography. Imaging was performed on a 3.0 Tesla MR system (Achieva, Philips, Best, The Netherlands) with the patient in the supine position. All imaging was cardiac gated with a three-lead vector ECG and acquired during expiratory breath hold. Localizer sequences were followed by transaxial T1- and T2-weighted “black blood” sequences over the heart and the great vessels. The internal diameters of the ascending and descending aorta were measured at the level of the pulmonary bifurcation by a single reader without knowledge of the diameters obtained with echocardiography.

As reference values for the MR measurements in the ascending and descending aorta, data published by Davies et al. were used [10].

Statistical Analysis

All data were analyzed using a commercially available software package (SPSS 22, IBM, Armonk, NY, USA). Summary statistics were compared by Chi² tests for categorical variables. P values less than 0.05 were considered statistically significant.

Results

The median age of acute dissection among the family members who had experienced one was 48 years. In those who survived the dissection, the median age was 46 years (n=6, range 38–49 years) and 64 years (n=11, range 15–75 years) in those who died from it. The two youngest persons, 15 and 23 years, were in the group that died because of the dissection. In these two cases, the thoracic aortas were not dilated at autopsy. Although the youngest persons were in this group, overall, those who died from their dissection were older than those who survived the dissection (59 vs. 46 years). The diameter at the time of dissection varied between 44–55 mm in family members in which aortic imaging had been done and the examination could be reviewed.

Eleven individuals had been operated with a graft in the AoA, five of them prophylactically because of an aneurysm and six of them acutely because of an aortic dissection type A (Table 1). Two individuals had a known dilatation of the AoA and are currently included in a periodic follow-up program.

A total of 106 individuals without known disease were investigated. The demographic data for the population are shown in Table 2. Nineteen individ-
Approximately 50% of the family members (57 of 106) were younger than 40 years, but only five of them had a dilated AoA. The diameters in these individuals were quite modest; in one, it was 30 mm. Three individuals were dilated at the SoV to a diameter of 35–37 mm, and one participant was dilated at both levels.

No dilatation was diagnosed in the descending aorta at the level of the pulmonary artery bifurcation. The diameter in the descending aorta varied between 14–24 mm in women and 17–29 mm in men.

Of the 24 individuals with previous aortic involvement, 20 (83%) were men, and 4 (17%) were women. Of the 19 new cases, 11 (58%) were men, and 8 (42%) were women. In three participants, the AoA was poorly visualized with echocardiography; accordingly, they were investigated with MR imaging only.

**Table 2.** Demographic data of the first- and second-degree relatives.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Total</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of individuals, (%)</td>
<td>106</td>
<td>59 (56)</td>
<td>47 (44)</td>
</tr>
<tr>
<td>Age 18y-29y, n</td>
<td>28</td>
<td>13</td>
<td>15</td>
</tr>
<tr>
<td>Age 30y-39y, n</td>
<td>29</td>
<td>17</td>
<td>12</td>
</tr>
<tr>
<td>Age 40y-49y, n</td>
<td>24</td>
<td>11</td>
<td>13</td>
</tr>
<tr>
<td>Age 50y-59y, n</td>
<td>13</td>
<td>10</td>
<td>3</td>
</tr>
<tr>
<td>Age 60y-69y, n</td>
<td>11</td>
<td>8</td>
<td>3</td>
</tr>
<tr>
<td>Age 70y+, n</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Age, y (range)</td>
<td>40 (18–73)</td>
<td>42</td>
<td>38</td>
</tr>
<tr>
<td>Weight, kg (range)</td>
<td>78 (49–121)</td>
<td>87</td>
<td>67 (49–95)</td>
</tr>
<tr>
<td>Height, cm (range)</td>
<td>175 (157–198)</td>
<td>181</td>
<td>168 (157–182)</td>
</tr>
<tr>
<td>Current smoker, n (%)</td>
<td>11 (10.4)</td>
<td>6 (10)</td>
<td>5 (11)</td>
</tr>
<tr>
<td>Arterial hypertension, n (%)</td>
<td>19 (18)</td>
<td>11 (19)</td>
<td>7 (15)</td>
</tr>
<tr>
<td>Coronary artery disease, n (%)</td>
<td>2 (1.7)</td>
<td>2 (3)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Other arterial disease, n (%)</td>
<td>0 (0)</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

The majority of individuals with dilatation of the aorta were found among first-degree relatives. The number of new cases (19) was significantly lower than would be expected for dominant inheritance (40).

Six individuals were dilated only in the aortic root at the level of the Sinuses of Valsalva (SoV), nine individuals were dilated only in the AoA, and four individuals were dilated at both levels. One of the participants dilated at both levels had a previously undiagnosed bicuspid aortic valve with an asymptomatic mild to moderate aortic regurgitation. No other participants in the study population had bicuspid aortic valves.

In these 19 individuals the diameter at the level of SoV varied between 35 to 50 mm (18.4–23.6 mm/m²); at the AoA, the diameter varied from 30 to 46 mm (18.7–22.8 mm/m²) (**Table 4**).

### Table 3. Number of new and expected cases.

<table>
<thead>
<tr>
<th>Age, y</th>
<th>1st-degree relative, n</th>
<th>Dilated aorta, n</th>
<th>2nd-degree relative, n</th>
<th>Dilated aorta, n</th>
<th>Dilated aorta, total n</th>
</tr>
</thead>
<tbody>
<tr>
<td>18–30</td>
<td>10</td>
<td>0</td>
<td>18</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>30–39</td>
<td>10</td>
<td>1</td>
<td>19</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>40–49</td>
<td>13</td>
<td>6</td>
<td>11</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>50–59</td>
<td>11</td>
<td>5</td>
<td>1</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>60–69</td>
<td>10</td>
<td>3</td>
<td>1</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>70+</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>56</td>
<td>15 (28)</td>
<td>50</td>
<td>4 (12.5)</td>
<td>19 (40.5)</td>
</tr>
</tbody>
</table>

The majority of individuals with dilatation of the aorta were found among first-degree relatives. The number of new cases (19) was significantly lower than would be expected for dominant inheritance (40).

### Discussion

The international consensus guidelines recommend screening by aortic imaging for all first-degree relatives of patients with sporadic TAAD and all first- and second-degree relatives in families with TAAD in which the genetic cause is not known. The result of this guideline is that many individuals will be screened. In our study, we have followed the guide-
variant is 50%, and for second-degree relatives, it is 25%. In our families, 56 individuals were first-degree relatives, and 50 were second-degree relatives (Table 3). Thus, 40 individuals (28 first-degree and 12 second-degree relatives) on average would be expected to be carriers of a disease-causing, dominant allele. However, not all mutation carriers will experience an aortic dissection because of reduced penetrance and variable expressivity of the disease. In particular, very few carriers with aortic disease below the age of 40 years could be detected with this method. A single screening with echocardiography is feasible for identifying patients with dilated aortas who should enter a follow-up program or be offered surgery. However, a single screening is definitely not enough for excluding individuals from risk or from being carriers of FTAAD-related alleles, in particular young individuals. Thus, screening in patients with an inherited disease highlights several clinical problems and ethical questions.

One of these questions involves defining when the thoracic aorta is dilated. Several studies have addressed reference values of normal aortic diameters with different imaging modalities [9, 11-14]. The method of measuring aortic diameter varies from study to study (external vs. internal diameter, leading edge-to-leading edge vs. inner edge-to-inner edge convention, systole vs. diastole). Some studies only measured the aortic root or AoA, whereas others have measured the thoracic aorta at different levels. All of the studies point out the importance of taking age, sex, and body size into account when judging whether the aorta is dilated. It is important to consider which imaging modality was used and how the measurements were taken. We measured the internal diameter in diastole with echocardiography so that the values could be compared with those from other imaging modalities (computed tomography, MRI) in which the internal diameter was measured. Transthoracic echocardiography has several advantages (rapid, bedside, accurate, cost-effective) and permits adequate assessment of several aortic segments. However, in some individuals, the proximal thoracic aorta cannot be visualized and another imaging modality must be used.

All aneurysms in the current work were located in the aortic root or AoA. The diameters in the aortic root and performed screening of all first- and second-degree relatives in seven families with FTAAD. In these families, 14 individuals had previously had a dissection and six of them were still alive. Five individuals had undergone surgical repair of an aneurysm, and two were in a surveillance program because of an aneurysm. Therefore, the concern in relatives is substantial, and family members want to know if they are at risk for aortic dissection.

In these families, of 106 individuals, we identified 19 persons (18%) with a dilated SoV and/or AoA. However, we would have expected many more to be carriers of a disease-causing gene mutation. In an autosomal-dominant disease, the risk for first-degree relatives of inheriting the pathogenic sequence lines and performed screening of all first- and second-degree relatives in seven families with FTAAD. In these families, 14 individuals had previously had a dissection and six of them were still alive. Five individuals had undergone surgical repair of an aneurysm, and two were in a surveillance program because of an aneurysm. Therefore, the concern in relatives is substantial, and family members want to know if they are at risk for aortic dissection.

In these families, of 106 individuals, we identified 19 persons (18%) with a dilated SoV and/or AoA. However, we would have expected many more to be carriers of a disease-causing gene mutation. In an autosomal-dominant disease, the risk for first-degree relatives of inheriting the pathogenic sequence

---

**Table 4.** Aortic dimensions for individuals with a dilated aorta on screening.

<table>
<thead>
<tr>
<th>Case</th>
<th>Age (years)</th>
<th>Sex (M/F)</th>
<th>BSA (M²)</th>
<th>SoV/BSA (mm/m²)</th>
<th>AoA/BSA (mm/m²)</th>
<th>SoVdiam (mm)</th>
<th>AoA-diam (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>48</td>
<td>F</td>
<td>1.75</td>
<td>20.8</td>
<td>20.5</td>
<td>36</td>
<td>36</td>
</tr>
<tr>
<td>2</td>
<td>26</td>
<td>F</td>
<td>1.55</td>
<td>18.3</td>
<td>19.5</td>
<td>28</td>
<td>30</td>
</tr>
<tr>
<td>3</td>
<td>59</td>
<td>M</td>
<td>1.98</td>
<td>21.4</td>
<td>18.2</td>
<td>42</td>
<td>36</td>
</tr>
<tr>
<td>4</td>
<td>31</td>
<td>M</td>
<td>2.00</td>
<td>18.5</td>
<td>19.3</td>
<td>37</td>
<td>39</td>
</tr>
<tr>
<td>5</td>
<td>43</td>
<td>M</td>
<td>2.24</td>
<td>17.1</td>
<td>18.7</td>
<td>38</td>
<td>42</td>
</tr>
<tr>
<td>6</td>
<td>47</td>
<td>M</td>
<td>2.13</td>
<td>18.8</td>
<td>20.5</td>
<td>40</td>
<td>44</td>
</tr>
<tr>
<td>7</td>
<td>55</td>
<td>M</td>
<td>2.00</td>
<td>18.8</td>
<td>20.0</td>
<td>38</td>
<td>40</td>
</tr>
<tr>
<td>8</td>
<td>60</td>
<td>F</td>
<td>1.87</td>
<td>21.3</td>
<td>22.8</td>
<td>40</td>
<td>43</td>
</tr>
<tr>
<td>9</td>
<td>65</td>
<td>M</td>
<td>1.93</td>
<td>21.3</td>
<td>18.8</td>
<td>41</td>
<td>36</td>
</tr>
<tr>
<td>10</td>
<td>35</td>
<td>F</td>
<td>1.64</td>
<td>21.7</td>
<td>16.3</td>
<td>36</td>
<td>27</td>
</tr>
<tr>
<td>11</td>
<td>58</td>
<td>M</td>
<td>2.05</td>
<td>19.5</td>
<td>19.8</td>
<td>40</td>
<td>40</td>
</tr>
<tr>
<td>12</td>
<td>56</td>
<td>M</td>
<td>1.99</td>
<td>16.9</td>
<td>19.9</td>
<td>34</td>
<td>40</td>
</tr>
<tr>
<td>13</td>
<td>39</td>
<td>M</td>
<td>2.03</td>
<td>18.4</td>
<td>14.1</td>
<td>37</td>
<td>29</td>
</tr>
<tr>
<td>14</td>
<td>65</td>
<td>F</td>
<td>1.72</td>
<td>20.4</td>
<td>22.7</td>
<td>35</td>
<td>39</td>
</tr>
<tr>
<td>15</td>
<td>37</td>
<td>F</td>
<td>1.75</td>
<td>19.9</td>
<td>17.1</td>
<td>35</td>
<td>30</td>
</tr>
<tr>
<td>16</td>
<td>48</td>
<td>F</td>
<td>1.79</td>
<td>15.9</td>
<td>21.4</td>
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<td>17</td>
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<td>F</td>
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<td>17.8</td>
<td>20.5</td>
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<tr>
<td>18</td>
<td>55</td>
<td>M</td>
<td>2.12</td>
<td>23.6</td>
<td>20.4</td>
<td>50</td>
<td>43</td>
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<tr>
<td>19</td>
<td>49</td>
<td>M</td>
<td>2.09</td>
<td>22.0</td>
<td>16.5</td>
<td>46</td>
<td>34</td>
</tr>
</tbody>
</table>

The diameter and indexed values at two levels, SoV and AoA, are shown. The pathological values are in bold. BSA, body surface area; SoV, sinuses of Valsalva; AoA, ascending aorta; M, male; F, female.
varied from 35 mm to 50 mm and in the AoA from 30 mm to 44 mm. Individuals with a small body size tend to have relatively small aortic diameters, which can be seen in Table 4. The upper normal limits used in clinical practice today are likely higher than those presented in the latest studies. Most often, one common upper normal limit is used for men and women, and the values are not always related to age and body size. The upshot is a substantial risk of not identifying all dilated aortas. At the same time, it is justifiable to ask if some diagnoses are false positives in patients who are not carriers of a disease-related allele. In such cases, these patients may be exposed to unnecessary clinical controls and anxiety.

Another question that requires attention is the kind of information family members should receive. Before a cascade screening of individuals with a genetic disorder is started, they must receive information about the advantages and the limitations. If the disease-causing mutation is not known, the diagnosis relies on measuring the thoracic aortic diameter. In some cases, a clearly pathologically dilated thoracic aorta can be found; however, the majority of individuals will have a normal aortic diameter. As the calculation of individuals at risk for being carriers shows, we do not identify them all by measuring aortic size, at least not at younger ages. Therefore, it is not possible to conclude that individuals with a normal aortic diameter at a young age do not need to be followed. A control program is probably needed even for those with normal diameter. However, such a program would result in a large number of examinations, higher health care costs, and increased anxiety for individuals, some of whom would not be at risk for aortic dissection.

A third question related to the screening guidelines is how to organize families for screening, especially if they are spread over a large geographic area. The controls might be difficult to manage, and there is a risk that family members will have different surveillance in different health care units. Knowledge about inherited thoracic aortic dissections is still limited in the health care system in general, and the disease might be confused with abdominal aneurysms. Special units with a focus on inherited cardiovascular diseases might organize the controls in a systematic way.

Future Perspectives

With a known disease-causing mutation in the family, it is possible to offer genetic counselling and predictive testing to first-degree relatives. Mutation carriers will be offered prevention and surveillance, and noncarriers will benefit from certain knowledge of not being at risk. However, at this time only about 20% of families with FTAAD will gain from genetic testing. Whole-exome sequencing will hopefully increase the rate and efficiency of novel gene identification and allow us to understand the pathophysiology involved in the genetics of aortic aneurysms and dissections.

We will also study mechanical properties of the thoracic aorta, such as compliance, in order to identify other potential markers for progression of the disease than diameter.

Conclusion

In this study, we have shown that screening for aortic aneurysms is encouraged in families with thoracic aortic disease and that family members with a dilated aorta can be identified. Still, screening carries many limitations and a normal aortic diameter is definitely not sufficient for excluding a person from being at risk for aortic disease, in particular in young individuals.

Acknowledgments

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Conflict of Interest

The authors have no conflict of interest relevant to this publication.
References


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Abstract
Recent technological advances have allowed researchers to interrogate the genetic basis of abdominal aortic aneurysms in great detail. The results from these studies are expected to transform our understanding of this complex disease with both multiple genetic and environmental risk factors. Clinicians need to keep abreast of these genetic findings and understand the implications for their practice. Patients will become increasingly informed on genetic risk, and a new era of individualized risk assessment for AAA is just beginning. This brief update aims to provide the clinician with a succinct précis of the recent progress in this area.

Introduction
Abdominal aortic aneurysms (AAAs) are a common condition that affects approximately 4-8% of individuals greater than 65 years of age [1]. AAAs are a multifactorial disease, and we know that there is a significant genetic contribution to their formation [2]. Since the 1970s, clinicians have observed that an important risk factor for AAA formation is a positive family history for the disease with an estimated increased individual risk between two and eleven fold [3-7]. Several studies have described familial aggregation of AAA [7-10], the largest one of these studies with 233 multiplex families [11]. The AAA families displayed multiple forms of inheritance patterns suggesting that AAA is a complex, multifactorial disease.

Based on a recent twin study in Sweden, the estimated genetic contribution to overall susceptibility for AAA formation is approximately 70% [6]. In this study, 265 twins with AAA, including seven monozygotic and five concordant pairs with the disease, were identified in a Swedish population and disease registries. The odds ratio (OR) of the disease in monozygotic twins was 71 [95% confidence interval (CI): 27–183] and for dizygotic twins 7.6 (95% CI: 3.0–19).

Genetic Studies: Have We Made Any Progress?

The evidence supporting a strong genetic component to AAA formation has encouraged a number of research groups to perform hypothesis-driven candidate gene association studies for AAA; some of these studies have yielded highly significant findings, which we summarize in Table 1. With unbiased genome-wide association studies (GWAS), researchers have been able to interrogate the entire genomes of AAA patients, resulting in the dis-
covery of four reproducible chromosomal regions that confer susceptibility to AAA formation:

i. The G-allele of a single nucleotide polymorphism (SNP), rs10757278, located on chromosome 9p21.3 in the noncoding RNA CDKN2B-AS was first discovered in an analysis of patients with coronary artery disease (CAD) [12] and then found to be associated with multiple vascular phenotypes including AAA with an OR of 1.31 (95% CI: 1.22–1.41) and a highly significant p = 1.2 × 10⁻¹² [13,14]. The potential role of this SNP in AAA formation is discussed below.

Table 1. Summary of Genetic Variants Significantly Associated with AAA Risk from Candidate Gene Association Studies.

<table>
<thead>
<tr>
<th>Study with Literature Citation</th>
<th>Type of Study</th>
<th>Gene and Variant(s)</th>
<th>Potential Functional Role</th>
<th>Odds Ratio [95% Confidence Interval]</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Galora et al. 2013 [36]</td>
<td>Association study</td>
<td>LR5: rs3781590 and rs4988300</td>
<td>Lipoprotein metabolism</td>
<td>2.16 [1.41 – 3.29]</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Jones et al., 2013 [37]</td>
<td>Association study</td>
<td>SORT1: rs599839</td>
<td>Lipid metabolism</td>
<td>0.81 [0.76 – 0.85]</td>
<td>7.2 × 10⁻¹⁴</td>
</tr>
<tr>
<td>Helgadottir et al., 2012 [38]</td>
<td>Association study</td>
<td>LPA: rs10455872a and rs3798220a</td>
<td>Increased atherosclerotic burden</td>
<td>1.23 [1.11 – 1.36]</td>
<td>6.0 × 10⁻⁵</td>
</tr>
<tr>
<td>Harrison et al., 2012 [39]</td>
<td>Meta-analysis</td>
<td>IL6R: rs7529229 (Asp358As)</td>
<td>Reduction in downstream targets in response to IL6 signaling</td>
<td>0.85 [0.80 – 0.89]</td>
<td>2.7 × 10⁻¹¹</td>
</tr>
<tr>
<td>Saracini et al., 2012 [40]</td>
<td>Meta-analysis</td>
<td>MMP13: rs2252070 (-77A/G)</td>
<td>Altered remodeling of extracellular matrix</td>
<td>1.37 [1.04 – 1.82]</td>
<td></td>
</tr>
<tr>
<td>Biros et al., 2011 [41]</td>
<td>Meta-analysis</td>
<td>TGFBR2: rs764522</td>
<td>Altered regulation of vascular remodeling</td>
<td>1.69 [1.28 – 2.25]</td>
<td>2.7 × 10⁻⁴</td>
</tr>
<tr>
<td>McColgan et al., 2009 [42]</td>
<td>Meta-analysis</td>
<td>IL10: rs1800896 (nt -1082)</td>
<td>Interleukin signaling</td>
<td>1.51 [1.13 – 2.02]</td>
<td>0.006</td>
</tr>
<tr>
<td>Giusti et al. 2008 [44]</td>
<td>Association study</td>
<td>MTHFD1: rs8003379</td>
<td>Methionine metabolism</td>
<td>0.41 [0.26 – 0.65]</td>
<td>&lt; 0.0001</td>
</tr>
</tbody>
</table>

Studies are listed in chronological order with the most recent one first. Only studies with a minimum of 400 AAA cases and 400 controls and highly significant (p < 0.01) results were included. Gene symbols: ACE, angiotensin converting enzyme; AGTR1, angiotensin II type 1 receptor; IL10, interleukin 10; IL6R, interleukin 6 receptor; LRP5, low density lipoprotein receptor-related protein 5; LPA, apolipoprotein a; MMP3, matrix metalloproteinase 3; MMP13, matrix metalloproteinase 13; MTHFD1, methylenetetrahydrofolatedehydrogenase (NADP+ dependent) 1; MTHFR, 5,10-methyltetrahydrofolate reductase; MTRR, 5-methyltetrahydrofolate-homocysteine methyltransferase reductase; SORT1, sortilin 1; TGFBR1, transforming growth factor beta receptor 1; and TGFBR2, transforming growth factor beta receptor 2.

*Analyses were performed by combining the risk alleles of both variants in the same gene.

ii. The A-allele of SNP rs7025486 located near a gene called DAB2-interacting protein (DAB2IP) on chromosome 9q33.2 was associated with AAA with an OR of 1.21 (95% CI: 1.14–1.28) and a highly significant p = 4.6 × 10⁻¹⁰ [15]. DAB2IP encodes a potent inhibitor of cell growth and survival, which results in increased smooth muscle cell susceptibility to apoptosis via the ras GTPase [16].

iii. The C-allele of SNP rs1466535 located on chromosome 12q13.3 within intron 1 of the gene for low-density-lipoprotein receptor-related protein 1 (LRP1) had a significant association with AAA...
with an OR of 1.15 (95% CI: 1.10–1.21) and a highly significant \( p = 4.52 \times 10^{-10} \) [17]. The LRP1 protein is involved in the regulation of extracellular matrix remodeling as well as vascular smooth muscle cell migration and proliferation, all of which are plausible mechanisms in AAA pathogenesis [18].

iv. The A-allele of SNP rs6511720 located on chromosome 19p13.2 in the gene for low-density-lipoprotein receptor (LDLR) had a significant association with AAA with an OR of 0.76 (95% CI: 0.70–0.83) and a highly significant \( p = 2.08 \times 10^{-10} \) [19]. This same variant has also been associated with lipid levels and CAD [19]. In each of these three traits, it is the A-allele that is associated with a protective effect (OR < 1) [19]. These findings suggest that AAA and CAD have at least some shared biological pathways that contribute to disease initiation or progression.

These studies have begun to unravel the genetic variants contributing to the heritability of AAA. Little, however, is known about the biological mechanisms and how they may contribute to the complex disease process. AAA is a difficult phenotype to study due to a number of aspects. It is a late-age-at-onset disease that is often fatal, which can hinder extended family analysis. Similarly, “unaffected” family members may not have manifested the disease at the time of the study but may develop AAA in due course. Overall, GWAS studies have identified loci that collectively account for a very small fraction of the observed heritability of AAA. This raises the questions: Where are the missing genetic variants contributing to AAA heritability, how to find them, and what do these variants do?

**Emerging Fields in Genetic Research**

With the advent of increasing technological advances in the field of DNA sequencing, the capacity for in-depth sequencing within laboratories has risen exponentially, called Next Generation Sequencing (NGS). A task that used to take months to perform is now possible in a matter of days at a vastly reduced cost, which will drive the search for AAA genes into new and exciting frontiers. Considerable success has been made using these techniques to discover novel DNA variants that underpin the heritability of rare clinical phenotypes, such as Miller syndrome [20]. The next challenge for geneticists is to begin to sequence the whole exomes and genomes of AAA patients for missing variants predisposing to AAA formation.

Using exome sequencing, a novel frame-shift mutation in the SMAD3 gene was identified in a family with autosomal dominant inheritance of thoracic aortic aneurysms with intracranial aneurysms and AAA [21]. This study illustrated the effectiveness of NGS in discovering variants if extended families are available for analysis. Researchers are, however, faced with a number of challenges when applying NGS analysis to AAA to identify causal mutations. Currently, exome coverage is not 100%, some exons are poorly sequenced, and methods for calling small insertion/deletions (so called INDELs) and copy number variants (CNVs) are in further development [22]. Additional challenges related to NGS are low reproducibility of detection of variants and uncertainty about which variants are truly clinically important [23]. Another difficulty for AAA is that, when sequencing families, the segregation of the phenotype in the family may be due to nongenetic, lifestyle factors rather than a genetic sequence variant.

**Beyond the SNPs: Where Do We Go from Here?**

Identifying the risk conferring DNA variants is the first step in a long process to understanding the underlying disease mechanism; the next step is the challenging task of deciphering how the variant is predisposing to disease. For example, GWAS established that the sequence variant rs10757278-G on 9p21.3 confers an increased risk for CAD and AAs [13]. The loss of the INK4a/ARF/INK4b region on chromosome 9p21 was first identified in 2006 as a key process in the cytogenetic events resulting in tumorigenesis, with further characterization since then [24, 25]. Mouse models were used to discover the mechanism by which sequence polymorphisms on chromosome 9p21 confer an increased risk of arterial disease. In culture, aortic smooth muscle cells obtained from mice with a 70-kb deletion encompassing rs10757278 showed excessive proliferation and altered regula-
tion of the neighboring genes [26]. CDKN2B, a tumor suppressor gene, lies within the risk locus on 9p21. An elegant study by Leeper et al. [27] demonstrated an increased aortic diameter in Cdkn2b knockout mice using the elastase AAA model. Furthermore, in vitro studies using cultured human cells showed marked apoptosis of smooth muscle cells related to increased p53 signaling pathways. Pharmacological inhibition of p53 signaling in the Cdkn2b knockout mice reversed the vascular phenotype in the elastase model. The authors concluded that reduced CDKN2B expression and increased smooth muscle cell apoptosis may underlie the 9p21.3 association with AAA. In depth sequencing of the 9p21.3 region within the Framingham cohort identified additional sequence variants [28]. Harismendy et al. [29] interrogated the 9p21 risk alleles (rs10811656 and rs10757278) further and demonstrated their location within enhancer intervals that interact physically with an interval downstream of IFNA21 (interferon, alpha 21). Their work established a connection between the 9p21 risk variants and aberrant vascular cell responses to inflammatory signaling, leading to CAD susceptibility. These promising advances demonstrate that we are only starting to embark on a new era in understanding aneurysm formation directed by genetic discoveries.

Moving Towards an Era of Individualized Risk Assessment: The Future of AAA Diagnoses

Until recently, classical risk factors for AAA have been used to identify patients in the general population for aneurysm screening. These risk factors have formed the basis of the national AAA screening program in the UK: for example, age over 65 years, male sex, and positive family history for the disease (http://aaa.screening.nhs.uk/). Large-scale epidemiological studies have enabled more complex scoring algorithms for AAA risk to be constructed. Greco et al. [30] evaluated 3.1 million individuals screened for AAA and recorded their demographics and environmental risk factors. Using multivariable logistic regression analysis, they developed a novel scoring system for AAA risk that included several clinical variables and achieved a predictive accuracy C statistic of 0.82. The benefits of a healthy lifestyle including exercise, maintaining normal weight, and dietary habits were reinforced in this study, which showed that these factors do contribute to lowering risk and were included in the algorithm [30,31].

As we continue to identify additional genetic variants associated with AAA, individual genetic profiling in addition to environmental risk assessment will become possible. Recent studies on other complex diseases have shown that screening the population for only a single genetic variant for each disease has a poor predictive value; however, a profile of 50 variants, each with odds ratios of 1.02–1.15, may improve the accuracy of disease prediction [32]. Using simulated genetic models, some studies have concluded that substantial predictive power is only achieved when a large number of genetic variants (n = 100–160) with greater effect sizes is employed [33,34].

The future challenge is to use the variants identified in genetic studies to produce integrated genetic and environmental predictive models to more accurately identify at risk individuals in the population that, in turn, will allow alignment of individuals to different types and intensities of screening.

Conclusions

The field of AAA genetics is rapidly progressing with new high-throughput genotyping and DNA sequencing technologies, identifying increasing numbers of genetic variants associated with the disease. With an emerging number of international collaborative projects generating GWAS data, meta-analysis of GWAS data will be required. Once a larger number of variants are identified, the possibility of integrated genetic and environmental predictive models may become a reality for personalized risk assessment and screening.

Acknowledgments

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Conflict of Interest

The authors have no conflict of interest relevant to this publication.

Comment on this Article or Ask a Question

References


1. What do you recommend in terms of genetic testing for AAA patients outside of investigational protocols? What specific tests should we order? Where do we send samples?

We currently do not recommend genetic testing for AAA patients outside of investigational protocols. Unfortunately, current genetic variants related to abdominal aneurysm formation have a poor predictive value when tested in isolation. An increased number of variants with greater effects are required to create integrative predictive models for future testing by clinicians.

If a patient wishes to investigate their genetic risk further, a number of private genetics services are available; these, however, are not in the patients’ best interests due to a lack of supporting evidence for this practice and uncertainty with the interpretation of results.

2. Are there specific genetic variants in AAA that predict a more malignant clinical behavior? If so, which?

Current research is beginning to characterize genetic subtypes of AAA. A preliminary report with a small sample size was recently published [1] that used logistic regression studies to identify genetic variants in LRP1 associated with an aggressive AAA phenotype. In the future, the results of these studies may enable us to categorize patients into indolent and aggressive phenotypes, and tailor monitoring and treatment to the individual.

References

Abstract

Endovascular correction of aortic arch pathology remains a challenge, with a variety of techniques proposed over the years to minimize complications and enhance the probability of a successful result. A variety of approaches have been developed in order to deal with the aortic arch pathology and its idiosyncrasies. We review potential interventional techniques for the repair of aortic arch pathologies, beginning with conventional aortic arch surgery, followed by hybrid treatments and those along the endovascular spectrum (parallel and fenestrated endografts, scalloped endografts, and ascending and new branched endografts). We finish with an overview of all the Bolton Medical (Barcelona, Spain and Sunrise, FL, USA) thoracic platforms. Endovascular techniques show acceptable results in selected cases. Both proximal Bolton Relay configurations (with and without a bare stent) offer conformability and accuracy on deployment with very low rates of stroke. Fenestrated and scalloped designs are also useful for selected cases. Ascending and branched Bolton devices are very promising platforms for a serious, full endovascular approach to the aorta.

Key Words

Arch • Endovascular treatment • Endograft

Introduction: Aortic Arch-Related Pathologies

There are an increasing number of patients with thoracic aortic pathology. Enlargement of the thoracic aorta is an increasingly recognized condition that is usually diagnosed incidentally on imaging studies performed to evaluate unrelated conditions. Main pathologies of the thoracic aorta, including the arch section, include aneurysms (and sometimes pseudoaneurysms), dissections, penetrating ulcers, and intramural hematomas (IMHs).

Aneurysms along the arch often develop over many years without symptoms; however, they are a serious pathology, with an incidence around 5 to 10 cases per 100,000 patients/year [1]. Arch aneurysms are dangerous health issues, which often require urgent surgical interventions. The prevalence of arch aneurysms may be at least 3–4% of patients older than 65 years. Aortic aneurysms are the 18th leading cause of death in the USA and the 15th among individuals older than 65 years. Aortic aneurysms cause about 13,000 deaths per year in the USA [2]. Thoracic aneurysms are mainly caused by atherosclerosis and other degenerative diseases of the aorta, and have been historically treated with highly invasive surgery. Due to the significant risks associated with thoracotomy, alternative approaches to treat aortic disease have been developed.

Aortic dissections are relatively uncommon, with a documented incidence of 10–20 cases per million population per year [3]. However, aortic dissection is a serious health condition, with extremely high mortality rates, affecting both young and elderly people. Reported incidence rates are probably underestimates of the true incidence, because of difficulties in diagnosis (symptoms of aortic dissection may mimic those of other diseases, often leading to
errors in diagnosis). The incidence of aortic dissection appears to have increased over time [3]. Hypertension has been considered the most important risk factor for this condition, which most frequently occurs in men between 60 and 70 years of age [4]. Patients with untreated dissections have a high mortality rate, particularly if the dissection involves the ascending aorta. The mortality rate of patients with untreated dissections can be as high as 90% within 1 week to 3 months of diagnosis [4].

Penetrating ulcers and IMHs are radiologically distinct from classic aortic dissection. These variants of the acute aortic pathology are prone to rupture. A rupture incidence between 21–47% has been documented. Untreated patients with IMHs can show mortality rates at 30 days of 46%. The clinical impact of Type A IMH (proximal) tends to have a high frequency of complications (dissection or rupture) and even death. Therefore, urgent treatment is required. Surgery has also been the standard treatment of penetrating ulcers; however, it has been associated with high morbidity and mortality (9–38% of cases) [4-6]. In the case of IMHs, monitoring may be the best approach in cases of nonsevere symptoms, given the risk associated with surgery.

Traditionally, reports using open surgical techniques to treat the aortic arch and ascending aorta show rates of mortality, which range from 0% to 16.5% and stroke rates from 2% to 18% [7].

The correction of aortic arch pathology remains a challenge, with a variety of techniques proposed over the years to minimize complications and enhance the probability of a successful result [8]. In this light, a variety of approaches have been developed in order to deal with aortic arch pathology and its idiosyncrasies.

Treatment: Conventional to State-of-the-Art Endovascular Solutions

Conventional Treatments: Aortic Arch Surgery

This technique, implying replacement of aortic arch portions by synthetic grafts to restore blood flow through the aorta and all branch vessels, has improved during recent years. Different surgical techniques of extracorporeal circulation with selective supraaortic trunk perfusion appear to decrease cerebral ischemia. However, significant rates of mortality and morbidity persist [8,9].

The future of aortic surgery will be influenced by endovascular advances. Despite an interest in developing a unique endovascular approach for the aortic arch, its limitations will probably slow an endovascular replacement of open aortic arch surgery. In addition, some advances of open surgery, including new strategies for cerebral protection (i.e., the use of antegrade cerebral perfusion and the use of more moderate temperatures for hypothermic systemic circulatory arrest) have been made in recent years [4,9].

Hybrid Treatments: A Bridge from Surgery to an Endovascular Approach

Hybrid repair, usually constituting a combination of open supraaortic branch revascularization before the arch and endovascular aortic stent-graft repair, is an alternative option to open surgery for selected patients.

Total arch debranching procedures have been described as safe and relatively less invasive in high-risk patients [10-12].

The few studies showing hybrid repair of aortic arch aneurysms in samples of fewer than 10 cases showed still-relevant adverse consequences (i.e., perioperative mortality or stroke from 0% to 25%) [13].

A recent hybrid series for aortic disease focusing on techniques to avoid endoleaks [14] showed 0% incidences of neurologic events and endoleaks. Previous experiences reported endoleaks in 5% to 30% of cases [15-17].

Different hybrid alternatives have been proposed to treat various aortic pathologies [18], with some optimizing the fixation of the endovascular stent graft [8].

Endovascular: A Rainbow of Solutions for the Arch

The aortic arch is the last frontier for endovascular treatment. This segment presents specific challenges to endovascular repair. In recent years, the number of thoracic endovascular procedures has risen [18,19].

An endovascular procedure has a lower mortality rate compared to open surgical repair and is now being used in individuals with conditions that make them high-risk patients for open surgery.
Endovascular repair results in excellent midterm protection from aortic-related mortality, regardless of presenting pathology and comorbidities. There is a small, but significant, persistent risk of aorta or aneurysm rupture that is higher than that of an open-surgery aneurysm approach [20].

**Parallel Stent-Grafts: The Chimney or Snorkel Technique.** This technique, consisting of endovascular stent placement parallel to the main aortic stent graft in order to preserve or rescue flow to aortic branch vessels and allow proximal extension of endograft fixation zones, has been used in a variety of aortic arch pathologies and is feasible and safe in midterm follow up [21].

This technique is less challenging compared to fenestrated and branched endografting [22] and can be used with a variety of stents, making it applicable in urgent situations.

The incidence of endoleaks and strokes during the perioperative period is 21.6% and 7.8%, respectively [23]. A limitation is that the stents may become obstructed, resulting in stenosis. Future studies should evaluate long-term graft durability and techniques for fixation to the aortic arch.

**Fenestrations.** The thoracic aorta has a three-dimensional angulation and an anatomical peculiarity of three vessels branching at narrow intervals along the arch. Fenestrated endovascular aortic repair enables the continuation of blood flow to the arteries through holes in the graft.

Deployment of the endograft in the arch is necessary to adjust the fenestrations to correspond to each ostium of the vessels. Some second-generation devices have obtained high-quality adaptability to the arch curvature by the use of new materials, short-length stent elements, and the possibility of an expansion stent system.

The need to maintain perfusion of the branch arteries has limited application of endovascular techniques for treatment of more complex aneurysms. The next generation of precurved fenestrated endografts appears to be a good option for aortic arch aneurysms with a less than 15-mm proximal sealing zone. These devices have a significant advantage in cases where the landing zones have a short neck [24].

**Scallops.** A scalloped device may be a treatment option for urgent aortic arch and aneurysms in the distal aortic proximal-descending aorta. This technique does not require surgical revascularization, providing an adequate landing zone while preserving flow (via the scallop) to the left upper limb and posterior cerebral circulation. Limitations of these devices include a possible lack of accuracy of deployment in the diseased arch and the elapsed time for the device customization (product availability of the custom made device takes 3 weeks on average). Variability of the origin of the left subclavian artery may limit the feasibility of use of ready-made scalloped thoracic stent-graft devices.

**New Branched Endografts.** New endografts with modular, small branches for aortic arch branches that are flexibly adapted and connected to the stent implanted into the aortic arch appear to be a promising future approach to aortic arch diseases. Different custom-made and off-the-shelf models have been developed [25-28] with good initial outcomes.

The characteristics of the modular branched grafts are markedly different from previous techniques, allowing precise, optimal positioning of the stent graft and branches.

New-generation stent grafts have good early clinical and radiologic outcomes and avoid the need for open surgery. The off-the-shelf branched solution eliminates adjunctive procedures (hybrid repair, extra-anatomic bypasses, and chimneys). However, demonstration of durability for off-the-shelf branched stent grafts is essential for securing long-term outcomes.

**Bolton Medical Approaches: Focus on the Aortic Arch**

This part of the report concerns the Relay family of stent graft products for Thoracic Endovascular Aneurysm Repair (TEVAR), commercially available since receiving CE approval in 2005, as well as the Treovance stent grafts for Endovascular Aneurysm Repair (EVAR), receiving the CE mark in 2013 (Bolton Medical, Barcelona, Spain and Sunrise, Florida, USA).
Relay Device for the Aortic Arch

The Relay stent grafts are particularly designed to favor tracking, navigation through and upon landing of the device in the aortic arch, even in challenging anatomies that present acute curvatures and angles, or unfavorable proximal landing zones. The following are the main features underlying performance of the Relay grafts in the aortic arch and ascending aorta segments:

Stent Graft

• Presence of an outer curved Nitinol bar (S-bar) that allows for the gentle conformability of the device along the three-dimensional anatomy of the aortic arch.
• Design of the proximal stent graft with 2 configurations to align to the center of the aortic arch: bare stent (Relay) and without bare stent (Relay NBS) (Figure 1 A and B).

Essentially, the device adapts to the aortic anatomy without modifying the vessel morphology.

Figure 1. Two proximal edges are available: With proximal bare stent configuration (Relay) (A) and without bare stent (Relay NBS) (B).

Figure 2. Overall view of the delivery system (A). The polyester sheath offers more flexibility (B). Both proximal end configurations, with (C) and without (D) bare stent, have a capture system for a sequential deployment of the endograft.
Two major international post-market data registries, RELAY Endovascular Registry for Thoracic Disease (RESTORE) and RESTORE II, have been carried out to obtain clinical feedback when using the products in a “real-life” situation, including a variety of different aortic pathologies and patient conditions (e.g., post-trauma patients) [29,30]. Table 1 summarizes the operative results obtained with Relay/Relay NBS in aortic arch lesions in a cohort of 304 patients (RESTORE, European Registry).

Table 2 includes results similar to Table 1 but for the cases included in RESTORE II (worldwide post market surveillance registry). Only elective cases presenting aneurysm or dissection have been included in the study.

Table 1. Summary of RESTORE early Results for arch pathology.

<table>
<thead>
<tr>
<th>Landing Zone</th>
<th>Z0 (%)</th>
<th>Z1 (%)</th>
<th>Z2 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n = 22</td>
<td>n = 36</td>
<td>n = 74</td>
</tr>
<tr>
<td>Etiology</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Aneurysm</td>
<td>15 (68.2)</td>
<td>17 (47.2)</td>
<td>32 (43.2)</td>
</tr>
<tr>
<td>Dissection</td>
<td>7 (31.8)</td>
<td>17 (47.2)</td>
<td>22 (29.7)</td>
</tr>
<tr>
<td>Traumatic</td>
<td>0</td>
<td>1 (2.8)</td>
<td>15 (20.3)</td>
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<tr>
<td>False anastomotic</td>
<td>0</td>
<td>1 (2.8)</td>
<td>4 (5.4)</td>
</tr>
<tr>
<td>Myotic</td>
<td>0</td>
<td>0</td>
<td>1 (1.4)</td>
</tr>
<tr>
<td>Technical success</td>
<td>20 (90.9)</td>
<td>36 (100)</td>
<td>72 (97.3)</td>
</tr>
<tr>
<td>Endoleak rate</td>
<td>1 (4.5)</td>
<td>1 (2.8)</td>
<td>5 (6.7)</td>
</tr>
<tr>
<td>Device related complic.</td>
<td>2 (9.1)</td>
<td>2 (5.6)</td>
<td>6 (1.1)</td>
</tr>
<tr>
<td>Stroke</td>
<td>1 (4.5)</td>
<td>0</td>
<td>1 (1.3)</td>
</tr>
<tr>
<td>Death (in hospital)</td>
<td>1 (4.5)</td>
<td>4 (11.1)</td>
<td>6 (8.1)</td>
</tr>
<tr>
<td>Conversion to open surgery</td>
<td>1 (4.5)</td>
<td>1 (2.8)</td>
<td>0</td>
</tr>
</tbody>
</table>

Table 2. Summary of RESTORE II early Results for arch pathology.

<table>
<thead>
<tr>
<th>Landing Zone</th>
<th>Z0 (%)</th>
<th>Z1 (%)</th>
<th>Z2 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n = 10</td>
<td>n = 15</td>
<td>n = 57</td>
</tr>
<tr>
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<td></td>
<td></td>
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<tr>
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<td>13 (86.7)</td>
<td>18 (31.6)</td>
</tr>
<tr>
<td>Dissection</td>
<td>3 (30.0)</td>
<td>2 (13.3)</td>
<td>39 (68.4)</td>
</tr>
<tr>
<td>Traumatic</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>False anastomotic</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Myotic</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Technical success</td>
<td>10 (100.0)</td>
<td>15 (100.0)</td>
<td>54 (94.7)</td>
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<tr>
<td>Endoleak rate</td>
<td>0</td>
<td>0</td>
<td>7 (12.3)</td>
</tr>
<tr>
<td>Device related complic.</td>
<td>0</td>
<td>0</td>
<td>4 (7.0)</td>
</tr>
<tr>
<td>Stroke</td>
<td>1 (10.0)</td>
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</tr>
<tr>
<td>Death (in hospital)</td>
<td>0</td>
<td>0</td>
<td>3 (5.3)</td>
</tr>
<tr>
<td>Conversion to open surgery</td>
<td>0</td>
<td>0</td>
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</tr>
</tbody>
</table>

**Delivery Device**

A dual (inner and outer) sheath system provides sufficient pushability in the lowest aortic segment (from the vascular access site to the diaphragm), whereas the flexible Nitinol-made inner tube provides trackability to the operator, even in acute (e.g., Gothic arch) and complicated curves (Figure 2 A–D).

There are four differently designed solutions among Bolton Medical grafts to be considered when treating the aorta from the aortic valve to the aortic isthmus: Relay and Relay NBS standard (CE mark) stent grafts and three custom-made tailored devices—Proximal Scalloped Relay, Ascending Relay, and Branched Relay—when commercially available products are not sufficient to address a specific anatomical limitation.

**Relay and Relay NBS.** More than 15,000 Relay and Relay NBS stent grafts have been implanted worldwide so far. The treatment indication described in the instructions for use for the use of these devices in the aorta includes the treatment of aneurysm, pseudoaneurysm, dissection, intramural hematoma, and atherosclerotic ulcers. The design features described above favor the use of Relay and Relay NBS in aortic arch lesions.

Two major international post-market data registries, RELAY Endovascular Registry for Thoracic Disease (RESTORE) and RESTORE II, have been carried out to obtain clinical feedback when using the products in a “real-life” situation, including a variety of different aortic pathologies and patient conditions (e.g., post-trauma patients) [29,30]. Table 1 summarizes the operative results obtained with Relay/Relay NBS in aortic arch lesions in a cohort of 304 patients (RESTORE, European Registry).

Table 2 includes results similar to Table 1 but for the cases included in RESTORE II (worldwide post market surveillance registry). Only elective cases presenting aneurysm or dissection were included in the study.

These results from aortic arch surgery are considered satisfactory. The low rate of complications, especially for stroke (1.5% and 1.2%, for RESTORE and RESTORE II, respectively), suggests that both the
stent graft and the delivery device are effective for this aortic segment.

**Proximal Scalloped Relay.** Proximal scalloped as well as ascending and branched Relay devices are custom-made, designed, and exclusively manufactured under medical prescription. This process requires about 2 to 3 weeks.

Proximal scallops are sized depending on the measurement of the upper trunk (or trunks) to be included in the scallop. A lateral positioning of the scallop is also a good solution when the upper branch does not arise from the center plane of the aorta.

Strategically placed tubular radiopaque markers are positioned surrounding the scallop. This feature is helpful when manipulating the delivery device for effective matching of the opening with the ostium of the upper branch. The X-ray tube is angulated and changed from left-anterior-oblique to right-anterior-oblique projections to assure both the longitudinal and lateral positioning of the scallop.

Control of systolic arterial pressure is another strongly recommended maneuver during the deployment of the stent graft. Rapid pacing is probably the most effective technique to obtain a near-zero blood pressure level.

Some technical restrictions apply when designing the customization, specifically related to the width of the scallop but not the length, which can be as long as needed to include one, two, or even three upper trunks in the "window." Scallops as long as 55 mm in length have been manufactured in cases where the inclusion of all the upper trunks was required (Figure 3).

![Figure 3. Planning sketch of proximal scallop endograft. D2 is proximal diameter; D4 is distal diameter and L2 is the total length.](image)

![Figure 4. Example of a pseudoaneurysm of the ascending aorta after cardiac surgery (A) treated with a Bolton Medical device (B).](image)

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Relay for Ascending Aorta. As short as 4–7-cm long, customized Relay devices to treat the ascending aorta have been designed and implanted using its nonbare stent configuration to avoid any interference with the aortic valve (Figure 4).

The anatomical limits to take into account in the ascending aorta are the coronary ostia at the proximal end and the brachiocephalic trunk at the distal end. Thus, a careful analysis of the aortic anatomy when making pre-case assessments and measurements is essential.

As for the proximal scalloped devices, rapid pacing is recommended for the treatment of the ascending aorta; one single systolic peak could incite a partial migration of the device and the unintentional covering of the brachiocephalic trunk.

Branched Relay. A new device with branches for the upper trunks has recently been utilized in patients [32].

The device is based on the Relay NBS platform but incorporates a “roof-positioned” aperture connected to two internal tunnels for easy cannulation of the two branches (Figure 5).

Technically, stent-graft positioning is facilitated by the flexibility of the delivery device’s inner Nitinol hy-

Table 3. Summary of Relay double Branched endograft early results.

<table>
<thead>
<tr>
<th>#</th>
<th>Age/Sex</th>
<th>Pathology</th>
<th>Endoleak</th>
<th>Intraoperative Complication</th>
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<td>69/M</td>
<td>TAA</td>
<td>N</td>
<td>R SCA coverage¹</td>
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<td>2</td>
<td>73/F</td>
<td>TAA</td>
<td>N</td>
<td>L CCA dissection¹</td>
</tr>
<tr>
<td>3</td>
<td>78/F</td>
<td>TAA</td>
<td>N</td>
<td>LV perforation¹</td>
</tr>
<tr>
<td>4</td>
<td>79/F</td>
<td>TAA</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>5</td>
<td>66/M</td>
<td>Dissection</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>6</td>
<td>77/M</td>
<td>TAA</td>
<td>N</td>
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</tr>
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<td>71/M</td>
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<td>N</td>
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<tr>
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<td>70/M</td>
<td>TAA</td>
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<td>TAA</td>
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<tr>
<td>21</td>
<td>59/M</td>
<td>Dissection</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>22</td>
<td>68/M</td>
<td>PAU</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>23</td>
<td>82/M</td>
<td>TAA</td>
<td>N</td>
<td>Y²</td>
</tr>
<tr>
<td>24</td>
<td>65/F</td>
<td>TAA</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>25</td>
<td>74/F</td>
<td>TAA</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>26</td>
<td>72/M</td>
<td>TAA</td>
<td>N</td>
<td>N</td>
</tr>
</tbody>
</table>

F: Female; M: Male; TAA: Thoracic Aortic Aneurysm; N: None; RSCA: Right Subclavian Artery; LCCA: Left Common Carotid Artery; LV: Left Ventricle.

Patients status by August 2014: ¹ Alive. ² Dead caused by multiple stroke.

International clinical studies (retrospective and prospective) are ongoing in order to collect clinical data to confirm the good results published by several authors experienced with this device [31].

Figure 5. Overview of a double branched Bolton Medical endograft for the aortic arch.
potube (as it is for the ascending Relay). The presence of pared “driving-wires” (support wires) allows for a precise proximal landing in Zone 0 and for progressive apposition of the proximal stent-graft segment against the aortic wall.

One of the main concerns in this type of device is potential dislocation of the branches during deployment due to the asynchronous motion of the aorta. In this case, there is a locking mechanism (inner dull barbs in the internal tunnels) that prevents separation of the bridging stent.

The operative results with the dual branched device in clinical application are presented in Table 3.

Conclusions

Aortic arch repair is a challenging surgical procedure. Endovascular techniques show acceptable results in selected cases. A total endovascular approach with branched endografts will be a useful alternative for high-risk patients. Both proximal Bolton Relay configurations (with and without a bare stent) offer conformability and accuracy on deployment with low rates of stroke. Fenestrated and scalloped designs are useful for selected cases. Ascending and branched Bolton devices are promising platforms for a full endovascular approach to the aorta.

Acknowledgments

We would like to thank Roger Ferrer MSc (Bolton Medical, Barcelona) for providing all clinical data and Emili González-Pérez PhD, MSc (TFS, Barcelona) and Roger for their help during the writing process.

Conflict of Interest

The author is consultant and proctor for Bolton Medical, Medtronic Inc and WL Gore & Associates. Also he is proctor for Cook Medical.

References

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Abstract
There is a growing body of literature expanding the indication of endovascular aneurysm repair, from prophylactic treatment of aneurysms to other indications such as ruptured and complicated ruptured abdominal aneurysms. Concomitant aortocaval fistula is rare, and reports of open and endovascular repair exist. We report a unique hybrid approach to a case of a ruptured abdominal aortic aneurysm with aortocaval fistula, repaired primarily via endovascular approach in a hybrid, two-staged fashion. Representative images are presented in addition to a short review of this pathology.

Key Words
Ruptured abdominal aortic aneurysm • Aortocaval fistula • EVAR

Introduction
Spontaneous aortocaval fistula (ACF) is a rare complication of abdominal aortic aneurysm (AAA), present in fewer than 1% of all AAAs and up to 6% of ruptured AAAs [1]. In addition to the classic triad of hypotension, flank/back pain, and a pulsatile abdominal mass seen in ruptured AAAs, the clinical presentation of a ruptured AAA with ACF may include a continuous machinery murmur, lower extremity swelling, and high-output cardiac failure [1]. Conventional open repair of a ruptured AAA has a high mortality rate and is decreasing in frequency [2]. In select patients, the preferred treatment for ruptured AAAs and ruptured AAA complicated by ACF is endovascular aneurysm repair (EVAR), which avoids the morbidity of open repair [3]. However, data are conflicting on whether there is a significant survival benefit of EVAR over an open approach in the repair of ruptured AAA [2-4]. A review of the literature reveals there is scant data on the management of ruptured AAA presenting with ACF. We report a case of ruptured AAA with ACF successfully repaired via a two-stage hybrid approach.

Case Report
An 85-year old man with a 72 pack-year smoking history, but otherwise no significant past medical history, was transferred to our hospital for emergent repair of a ruptured AAA after presenting to another hospital with a 5-day history of lower back pain and one day of hematemesis. Prior to presentation, he had been in good health and denied symptoms of peripheral venous hypertension. Computed tomography angiography (CTA) showed a 9.2-cm AAA with
extensive rupture into the retroperitoneum, a right hypogastric artery aneurysm with iliocaval fistula, a duplicated caval system, and an occluded left iliac artery (Figure 1). On exam, the patient was hypotensive and had a soft, minimally distended abdomen. Given the patient's clinical status and features of the AAA, the decision was made to proceed to the operating room for endovascular repair. Intraoperative ultrasound also showed a right common femoral artery aneurysm and occlusion of the left common femoral artery (Figure 1). On exam, the patient was hypotensive and had a soft, minimally distended abdomen. Given the patient's clinical status and features of the AAA, the decision was made to proceed to the operating room for endovascular repair. Intraoperative ultrasound also showed a right common femoral artery aneurysm and occlusion of the left common femoral artery. Subsequently, a femoral cutdown was performed on the right groin. Planned coverage of the right hypogastric artery was executed due to the fact that the iliocaval fistula was emanating from the right hypogastric vessel. Dual C3 Gore Excluder main body bifurcated devices (Flagstaff, Arizona, USA) were deployed with exclusion of the right hypogastric artery in an aorto-uniliac fashion. Hemodynamic changes consistent with coverage of an arteriovenous fistula were observed, including a rise in blood pressure and a decrease in cardiac output as measured on transeosophageal echocardiogram. Completion intraoperative angiogram showed complete exclusion without evidence of obvious endoleak and obliteration of the iliocaval fistula. The right common femoral aneurysm was then repaired and a right-to-left femoral-femoral bypass was performed.

One week following the initial operation, the patient developed symptoms suggestive of high-output cardiac failure. Follow-up CTA showed a type II endoleak (T2E) with continued communication between the aneurysmal right hypogastric artery and the inferior vena cava (Figure 2). The patient was taken back to the operating room for open ligation of the right hypogastric artery aneurysm and inferior mesenteric artery. Once the aneurysm was excluded, it was interrogated with intraoperative ultrasound. There was continued pulsatility within the aneurysm with no flow detected in the sac on ultrasound. Flow patterns in the vena cava also demonstrated normal venous phasic flow. Repeat CTA one week later demonstrated patency of the graft and completed exclusion of the endoleak (Figure 3). Postoperative course was uneventful and the patient was discharged from the hospital in improved condition. At the 9-month follow-up, he was in good health with repeat CTA re-demonstrating patency of the graft without evidence of rupture or leak, as well as decrease in the size of the AAA.

**Discussion**

Ruptured AAA is a potentially lethal condition for which emergent surgical intervention is required. The addition of the rare complication of ACF presents a particularly unique treatment challenge. In those patients with ruptured AAA whose anatomy is suitable for endovascular repair, EVAR may confer a lower operative mortality and perioperative morbidity than conventional open repair [3]. However, data is conflicting on whether this early benefit persists beyond the operative and perioperative period [2-4]. Data are even more limited in cases of ruptured AAA with the rare complication of ACF.
Additionally, in the emergent management of this life-threatening condition, treatment decisions must be tailored to the unique aspects of the case. In this case, once the orifice to the internal iliac artery was covered in the first stage, we no longer had access to the vessel using endovascular techniques. However, it is our standard of practice at our institution to plug or coil-embolize internal iliac arteries or perform iliac-preserving techniques when extension is needed into the external iliac artery. Secondly, due to immediate availability, Dual GORE Excluder devices were used rather than an off-the-shelf aorto-uni-iliac device from another company. In the second stage, an open transabdominal rather than retroperitoneal approach was taken given the relative complexities of the patient’s anatomy: The large internal iliac artery aneurysm and the desires for the ability to have proximal control and to analyze the aneurysm sac using direct duplex ultrasound.

In the presence of ACF, endovascular repair is accompanied by the theoretical concern of high flow T2Es, which could lead to persistent aortocaval communication. T2Es occur after EVAR and are caused by retrograde flow of collateral arteries into the excluded aneurysm sac, leading to repressurization and consequent aneurysm growth and, ultimately, possible rupture [5]. Without surgical intervention, a T2E in the setting of persistent aortocaval communication may lead to high-output cardiac failure and sac growth. In many cases, the flow of a T2E may be small enough as to not lead to sac enlargement of a continuous ACF. However, in the setting of a rupture, the integrity of the wall of the aorta is already compromised, and there is an increased risk of progression in the presence of both a T2E and venous fistula. Although the role of intervention in patients with T2Es remains controversial in the literature, there is consensus that this pathology is accompanied with high risks of morbidity and mortality.

Figure 2. A. Computed tomography angiogram showing persistent aortocaval fistula (arrow). B. Type II endoleak from backfilling aneurysmal hypogastric artery (arrow). C. Three-dimensional reconstruction with contrast filling around the graft (arrows).
stability was achieved with endovascular exclusion of the AAA and exclusion of an aortocaval fistula with an aortic-uni-iliac stent graft. In the second stage, an open repair of a T2E allowing persistent arteriovenous communication was performed without the high risks associated with open repair of ruptured AAA and associated ACF.

The literature on AAA with ACF is sparse, limited to case studies, and those patients presenting in the emergent setting of a freely ruptured AAA with ACF are rarer still. The paucity of data hinders the comparison of outcomes of open versus endovascular repair of this rare and complicated condition. The emergent management of these cases, therefore, presents a unique and difficult challenge. As described above, endovascular placement of a stent graft can potentially act as an initial damage control therapy in the setting of a life-threatening ruptured AAA and may create a role for the staged repair of concomitant, but not immediately life-threatening lesions, such as ac-

Figure 3.  A. Computed tomography angiogram showing resolution of aortocaval fistula (arrow). B. Resolution of type II endoleak (arrow). C. Three-dimensional reconstruction with resolution of endoleak (arrow) and patent bilateral runoff.
cessory aneurysms or ACF. This hybrid, staged strategy may prove to be the preferred approach for select patients presenting with this rare complication. Further study is necessary to better evaluate the efficacy and safety of this method.

Ruptured AAA complicated by ACF is rare and life threatening. We present the successful treatment of a freely ruptured AAA with ACF via a staged, hybrid approach. EVAR may serve as the preferred initial management approach followed by open repair of concomitant but not immediately life-threatening lesions, such as ACF.

References


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Ruptured Pneumococcal Aortic Aneurysm Presenting as ST-Elevation Myocardial Infarction
Case Report and Literature Review

Xiaoyue Mona Guo, BA1, Pramod Bonde, MD2*

1 Bonde Artificial Heart Laboratory, Yale University School of Medicine, New Haven, Connecticut, USA
2 Section of Cardiac Surgery, Department of Surgery, Yale University School of Medicine, New Haven, Connecticut, USA

Abstract
Ruptured mycotic aneurysms occur infrequently in current clinical practice, and a pneumococcal etiology is even more rare. This case report describes a patient who initially presented with catheter lab activation for an acute ST-elevation myocardial infarction, receiving a full Plavix load. She was subsequently found to have a ruptured aortic aneurysm and underwent emergency surgical repair, with intraoperative findings of an aorta seeded with Streptococcus pneumoniae. A retrospective evaluation of her history revealed clues of a previous upper respiratory infection and long-standing back pain. The subsequent literature review summarizes presentations and outcomes in previously reported, ruptured pneumococcal aneurysms and describes the relatively common occurrence of aortic conditions masquerading as acute myocardial infarctions. We provide recommendations to help approach similar situations in the future.

Key Words
Mycotic • Aneurysm • STEMI • Streptococcal • Rupture

Introduction
Rapid diagnosis of myocardial infarction is vital for optimal treatment and patient outcome [1]. As such, in order to minimize door-to-balloon times, emergency medical services (EMS) are encouraged to perform and evaluate electrocardiograms to assist in pre-hospital activation of the “cath lab” if suspicion is strong enough for an ST-segment elevation myocardial infarction (STEMI) [2]. However, in a small but significant number of patients, suspected STEMIs mask other disorders. In those cases, routine myocardial infarction management can be dangerous and cause catastrophic outcomes. We describe a unique case of a ruptured mycotic aortic aneurysm due to Streptococcus pneumoniae presenting with STEMI, which led to the patient receiving antiplatelets and anticoagulants before being sent to the operating room for emergency aneurysm repair.

Case Report
The patient was a 56-year-old African American woman brought in by EMS from home for mid-sternal chest pain, with cath lab activation from the field for ST elevation in V4-V6 and Q waves in the inferior wall. She reported a several month history of intermittent chest pain with multiple evaluations, but her current episode began the night before with associated dyspnea, nausea, and back pain worse on inspiration. She otherwise denied fever, syncope, cough, abdominal pain, or vomiting. Her medical history was pertinent for HIV with unknown CD4 count and viral load, hypertension, ½ pack per day smoking for the past 4
years, active crack cocaine use approximately once a week and no alcohol consumption.

On presentation to the resuscitation bay, her vitals were within normal limits except for a blood pressure of 96/61 and a respiratory rate of 22. She was in mild distress but cooperative and her exam was notable only for distended jugular veins. Her labs showed an elevated white blood cell count of 13,800/mm³ with left shift, mild anemia with hemoglobin of 11.3g/dl and a hematocrit of 33.9%, and negative troponins. Her electrocardiogram (ECG) confirmed ST-elevation in leads II, III, and aVF and the patient received a Plavix load of 600 mg and aspirin and was started on a heparin infusion with PTT aimed for between 60 to 80 seconds in preparation for coronary angiogram. As she was waiting to go to the cath lab, chest radiograph revealed a widened mediastinum (Figure 1).

The patient was emergently sent for computed tomography with angiogram (CTA) as per dissection protocol, which revealed a pseudoaneurysm of the aorta and a large mediastinal hematoma (Figure 2). There were also prominent lymph nodes in the chest and nonspecific hypodensities in the spleen raising the possibility of mycotic disease. She was emergently transferred to the operating room (OR) for resection and repair of the ruptured aneurysm.

The patient was put on bypass via groin vessel cannulation with systemic cooling prior to sternal opening. After opening the sternum, the ruptured aneurysm was immediately evident even without dissection of the mediastinal fat. Operative findings included a large intrapericardial ruptured ascending aortic and arch aneurysm involving the bovine arch. The patient’s dynamic ECG changes could be attributed to physiologic compromise of coronary ostial blood flow by the aneurysm itself. Transesophageal echocardiogram did not show evidence of vegetation or endocarditis on any of the heart valves. The rest of the aorta was normal in caliber.

The entire arch and the ascending aorta up to the sinotubular junction were resected and replaced with a Hemashield Platinum graft under deep hypothermic arrest, and the arch vessels were implanted as an island. Due to the saccular nature of the aneurysm with anterior projection, OR cultures and pathology of the resected tissue were sent to the lab. The wound culture was eventually positive for S. pneumonia, and the patient was treated with intravenous ceftriaxone. She was discharged 2 weeks later on four more weeks of intravenous antibiotics coverage (for a total of 6 weeks of ceftriaxone, 2 grams daily). At last follow up 4 months after the inciting event, the patient remained asymptomatic.

Figure 1. Chest plain film revealed new widening of the mediastinum (B, double-headed arrow) compared to three weeks prior (A).

Guo, X.M. et al. Ruptured Mycotic Aneurysm of the Arch
Case Report

Between 1.4 to 15% of patients presenting with acute chest pain with STE do not have an acute MI (AMI) [3] and approximately 1 to 3% of aortic aneurysms are of mycotic etiology [4-6]. We report a unique case of a combination of these two relatively rare occurrences in a ruptured S. pneumoniae mycotic aortic aneurysm presenting as a STEMI.

Commonly described conditions misdiagnosed as AMI generally fall into four categories: (1) transient STE from acute coronary syndrome, (2) cardiac conditions not affecting the coronary arteries such as peri- or myocarditis, (3) vascular events including pulmonary emboli and aortic dissections, and (4) other etiologies like acute cholecystitis or pancreatitis [3]. The pathophysiological processes of these conditions may manifest with cardiac symptoms, such as when coronary ostia are compressed during a dissection or when inflammation mimics AMI via viral infections, immunological change, or induced platelet abnormalities [7, 8]. In the pre-antibiotic era, this mimicry may have been more common as infected aneurysms were overwhelmingly due to endocarditis, with a smaller subset being due to lung and bone infections. The most commonly perpetrated organism was non-hemolytic Streptococcus although Staphylococcus, Pneumococcus, and Gonococcus also were implicated. Another common pre-antibiotic era mycotic aneurysms included syphilitic mycotic aneurysms. Aneurysm formation was described at the time to be either due to the lodging of infected emboli into the vessel walls or a contiguous infection from affected valves [9].

With the onset of antibiotic use and decreased rates of endocarditis, the incidence of mycotic aneurysms is decreasing and the microbiological profile is changing. Staphylococcus aureus, Salmonella peripheral and other Gram-negative organisms are now more frequently seen [10-13]. However, the clas-

![Figure 2. Emergency CTA showed a 5.2cm by 4.2cm pseudoaneurysm (*) arising at the origin of the common trunk of the right brachiocephalic and left common carotid arteries.](image-url)
sification of mycotic aneurysms remains basically the same: primary bacteremic seeding (such as from endocarditis, pneumonia, and cellulitis) to a weakened vessel wall, secondary traumatic inoculation (such as from intravenous drug use), and contiguous infection from a nearby source [5, 14]. *S. pneumoniae* in particular presently accounts for approximately 9-36% of all mycotic aneurysms [4, 12, 15, 16]; Cartery et al. [14] found 52 cases reported in the literature from 1924 to 2007, and we found an additional 16 cases since 2007 [6, 16-23]. Perhaps not surprisingly, the majority of these patients have an antecedent history compatible with a lower respiratory infection in the near past [12, 14, 24].

Compared to typical aortic aneurysms, the tendency for a mycotic aneurysm to rupture is substantially higher, with sources citing a risk between 34% and 83% [6, 12, 16, 22, 25]. In our review, 12 patients since 1923, including our current case, had a ruptured *S. pneumoniae* aneurysm [10, 13, 14, 17, 19, 20, 25-28]. These aneurysms were located in the infrarenal abdominal aorta in five patients (41.7%), the descending aorta in three (25%), an unspecified abdominal aortic location in two (16.7%), and multiple locations including descending thoracic, suprarenal abdominal, and common iliac in one (8.3%). The case we described is the only reported such aneurysm of the aortic arch (Table 1). All patients had a recent history of infection that provided a primary source for the aneurysm and a nidus for an inflammatory response which may lead to mimicry of AMI. Thus, patients with ruptured mycotic aortic aneurysms in the right location can be misdiagnosed as AMI due to both coronary ostia compression and mimicry.

The elevated rupture rate may partially account for the high mortality of 14% to 75% associated with mycotic aneurysms [4, 15, 16, 21], although this patient population tends to have a frailer baseline; up to 60% of the patients have an immunocompromising condition such as a history of prolonged steroid or immunosuppressive agent use, alcoholism, irradiation, chronic renal disease, diabetes, or malignant illness [4, 16]. In the 12 patients we described, all those with listed medical histories were immunocompromised, further suggesting atypical presentations of illnesses.

The literature lists frequent presenting symptoms as fever, abdominal pain, back pain, and palpable pulsatile masses in the case of abdominal aortic aneurysms [15, 24, 25]. Of the patients we described, 72.7% (8/11) complained of back or flank pain, 54.5% (6/11) had a fever, and 36.3% (4/11) had abdominal pain. These symptoms had often been worsening for several weeks before presentation. Of note, our case was the only patient presenting with chest pain or shortness of breath. Diagnostically, the results obtained in these 12 patients agreed with those found in the literature, where increased markers of inflammation such as C-reactive protein (CRP) were seen in 50% and leukocytosis in 61.5% of cases [16]. For imaging, 80% (8/10) of patients had CT scans, all of which were diagnostic; of the two patients without CT, one had a positive MRI. Two of three patients had concerning findings on chest radiography, and TTE did not elucidate any abnormality in either of the two patients in whom it was performed. Other than our case presentation, electrocardiographic results were not noted for any patient.

Treatment of mycotic aortic aneurysms requires prompt surgical involvement, as sole medical management with antibiotics is almost inevitably fatal [14, 19, 23]. After surgical debridement and resection, generally accepted guidelines are for appropriate antibiotic treatment intravenously for at least 6 to 12 weeks until blood cultures clear [14]. There is little consensus for long-term oral antibiotic treatment but it has been suggested that erythrocyte sedimentation rate or CRP could be used to both guide response to and duration of antibiotic treatment [12, 25]. In our described patients, all but one underwent open surgery with resection and/or graft, as well as intravenous antibiotic treatment for 1 to 8 weeks. Of the survivors, 62.5% (5/8) continued oral antibiotics from 6 weeks to lifelong treatment after that. With an aggressive approach, survival is purported to reach 100%, compared to 62.5% prior to 1998 [14]. In these 11 cases post-2000, survival was 73% to discharge; however, in two of the three patients who died, surgical intervention had been delayed.

**Conclusions and Recommendations**

In this reported case, it was fortuitous that there was delay in communication with the catheter lab...
### Table 1. Characteristics of patients in literature with ruptured S. pneumoniae mycotic aortic aneurysms.

<table>
<thead>
<tr>
<th>Year</th>
<th>Age/ Sex</th>
<th>Significant Medical History</th>
<th>Preceding Symptoms</th>
<th>Presenting Symptoms</th>
<th>Infection Source</th>
<th>Aneurysm Location</th>
<th>Diagnostics</th>
<th>Treatment (in order performed)</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>1988</td>
<td>51/M</td>
<td>N/A</td>
<td>&quot;Flu-like illness&quot; x 2 wk PTA, new onset DM</td>
<td>Lower back pain, abdominal pain, myalgias</td>
<td>Possible PNA</td>
<td>Abdominal</td>
<td>N/A</td>
<td>N/A</td>
<td>Died</td>
</tr>
<tr>
<td>2000</td>
<td>61/M</td>
<td>N/A</td>
<td>New onset AF, thyrotoxicosis</td>
<td>Lower back pain, fever, difficulty urinating x 4 wk</td>
<td>Mesenteric abscess</td>
<td>Infrarenal abdominal</td>
<td>+ CT 1WBC</td>
<td>Resection  Bypass IV abx (2 wk) Oral abx (24 wk)</td>
<td>Alive</td>
</tr>
<tr>
<td>2001</td>
<td>61/F</td>
<td>Smoking, alcohol abuse, HTN</td>
<td>PNA x 6 wk PTA</td>
<td>Low back pain x 1 wk</td>
<td>Possible PNA</td>
<td>Descending thoracic</td>
<td>+ CT 1WBC</td>
<td>Dacron graft IV abx (8 wk) Oral abx (8 wk)</td>
<td>Alive</td>
</tr>
<tr>
<td>2001</td>
<td>67/F</td>
<td>MI, AF, MM, IPF</td>
<td>Rectovaginal fistula and pneumococcal meningitis x 8 wk PTA</td>
<td>Sudden onset abdominal and back pain</td>
<td>Possible meningitis</td>
<td>Descending thoracic</td>
<td>+ CT 1WBC</td>
<td>Dacron graft IV abx (3 wk) Oral abx (6 wk)</td>
<td>Alive</td>
</tr>
<tr>
<td>2002</td>
<td>65/M</td>
<td>N/A</td>
<td>Meningitis x 2 years PTA</td>
<td>Fever, loss of consciousness</td>
<td>Meningitis</td>
<td>Descending thoracic</td>
<td>+ CXR, + CT 1WBC, TCRP</td>
<td>IV abx</td>
<td>Dacron graft Wedge lung resection IV abx (6 wk) PO abx (life)</td>
</tr>
<tr>
<td>2003</td>
<td>52/M</td>
<td>COPD, alcohol abuse</td>
<td>PNA x 4 wk PTA</td>
<td>Flank pain, fever, dysuria, anorexia</td>
<td>Possible PNA</td>
<td>Descending thoracic, suprarenal abdominal, common iliac</td>
<td>- CXR, -TTE, + MRI 1WBC</td>
<td>Dacron graft IV abx (6 wk) PO abx (life)</td>
<td>Alive</td>
</tr>
<tr>
<td>2007</td>
<td>65/M</td>
<td>N/A</td>
<td>PNA x 32 wk PTA</td>
<td>Hematemesis, abdominal pain, back pain x 8 wk</td>
<td>Possible PNA</td>
<td>Infrarenal abdominal</td>
<td>- US abdomen, - Bone scan</td>
<td>Graft</td>
<td>IV abx (1 wk)</td>
</tr>
<tr>
<td>2010</td>
<td>77/F</td>
<td>DM, HTN, rectal cancer</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>Infrarenal abdominal</td>
<td>N/A</td>
<td>PTFE graft IV abx (5 days) PO abx (12 wk)</td>
<td>Alive</td>
</tr>
<tr>
<td>2010</td>
<td>59/M</td>
<td>N/A</td>
<td>N/A</td>
<td>Lower abdominal pain, fever</td>
<td>N/A</td>
<td>Infrarenal abdominal</td>
<td>+ CT 1WBC, TCRP</td>
<td>Declined surgery IV abx (5 wk)</td>
<td>Re-reruption</td>
</tr>
<tr>
<td>2011</td>
<td>75/M</td>
<td>Alcohol abuse, DM, HTN, alcohol-induced CM</td>
<td>Hypogastric pain x 3 wk PTA, newly diagnosed bladder cancer</td>
<td>Fever, pelvic pain, weight loss</td>
<td>PNA</td>
<td>Infrarenal abdominal</td>
<td>+ CT 1ESR, TCRP</td>
<td>IV ab (1 wk)</td>
<td>Surgical resection</td>
</tr>
<tr>
<td>2011</td>
<td>63/M</td>
<td>DM, smoking</td>
<td>Fever without complications 8 wk PTA</td>
<td>Back pain, fever</td>
<td>N/A</td>
<td>Abdominal</td>
<td>- CT, + PET-CT, -TTE, -TEE, + CTA 1WBC, TESR, TCRP</td>
<td>Oral abx (5 days)</td>
<td>IV abx (10 days)</td>
</tr>
<tr>
<td>2014</td>
<td>56/F</td>
<td>HTN, HIV, drug abuse</td>
<td>Intermittent chest pain x several months</td>
<td>Chest pain, back pain, shortness of breath x 4 wk</td>
<td>Possible PNA</td>
<td>Aortic arch</td>
<td>+ ECG, + CXR, + CT 1WBC</td>
<td>Graft</td>
<td>IV abx (5 wk)</td>
</tr>
</tbody>
</table>

N/A, not applicable; DM, diabetes mellitus; AF, atrial fibrillation; MM, multiple myeloma; IPF, idiopathic pulmonary fibrosis; COPD, chronic obstructive pulmonary disease; CM, cardiomyopathy; HIV, human immunodeficiency virus; PNA, pneumonia; PTA, prior to admission; wk, week(s); CT, computed tomography; CXR, chest x-ray; TTE, transthoracic echocardiography; MRI, magnetic resonance imaging; US, ultrasound; PET, positron emission tomography; TEE, transesophageal echocardiography; CTA, CT angiography; WBC, white blood cell count; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; +, diagnostic results; -, normal; IV, intravenous; abx, antibiotics; PTFE, polytetrafluoroethylene (Gore Medical, Flagstaff, Arizona, USA).
upon patient arrival to the emergency department allowing for a chest radiograph to be obtained, albeit after full loading with antiplatelet agents. Had the patient received additional antiplatelets or anticoagulants, or had she undergone catheterization, her outcome likely would have been fatal. It has previously been reported that demographically similar patients with aortic dissections who were misdiagnosed as having AMI had a mortality rate double those with typical Type A dissections (36% vs 17%, respectively) [29].

On reflection, the patient’s presentation was somewhat odd despite the classic STE seen on ECG; particularly, her relatively short past medical history and description of back pain worse on inspiration should prompt further workup. In one study of patients referred for primary percutaneous coronary intervention (PCI) for suspected STEMI who had a final non-MI diagnosis, those misdiagnosed individuals less often had traditional cardiac risk factors like smoking, symptoms of angina, or family history of cardiac disease [3]. Moreover, her history of chest pain for several months would have been important to indicate that this was not a conventional STEMI.

It is evident that there needs to be a balance between speed and safety in diagnosis, especially for immunocompromised patients who tend to have atypical presentations for every disease process. Controversy exists over the evaluation and diagnostic algorithm for these patients. The majority of research is on misdiagnosed aortic dissections, likely because of the devastating effect of mainstream MI treatment in those patients, but the results may still be applicable.

Some investigators suggest using TTE and D-dimer as screening tests if there is a concern for possible dissection [29], although neither of the two performed TTEs showed any pathology in the patients we described. Other authorities are more specific, suggesting aortic imaging in either those with STEMI and symptoms suggestive of an aortic dissection, or all non-STEMI cases because dissection is statistically more likely to occur with nonspecific ECG changes [8]. However, as classic symptoms often do not occur, more individualized recommendations are for a multimodal imaging approach with CT and ECG to evaluate patients with dynamic ST abnormalities that are suspicious for intermittent coronary artery occlusions [30].

Our review further shows that patients with mycotic aortic aneurysms tend to have heightened leukocyte counts and markers of inflammation, both of which are easily and quickly obtained via point-of-care testing and can help triage patients towards an infectious etiology. Finally, it is important to note that patients uniformly report a recent infectious event and that taking a good history overrides all diagnostic testing.

**Conflict of Interest**

The authors have no conflict of interest relevant to this publication.

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EDITOR’S COMMENTS

Ion S. Jovin, MD, Department of Medicine, Virginia Commonwealth University and McGuire VAMC, Richmond, VA, USA.

Reminding ourselves that uncommon things are uncommon

The report by Guo and Bonde presents a case of a patient with ruptured mycotic aneurysm of the ascending aorta caused by Streptococcus pneumoniae presenting as an acute ST segment elevation myocardial infarction (STEMI). The authors then review the literature and present 12 other patients from other papers who presented with ruptured aortic aneurysms caused by the organism.

Cite this article as: Guo XM, Bonde P. Ruptured Pneumococcal Aortic Aneurysm Presenting as ST-Elevation Myocardial Infarction. AORTA 2015;3(Issue 1):36-37. DOI: http://dx.doi.org/10.12945/j.amc.403701.

Case Report

Cardiol. 1993;16:67-71. DOI: 10.1002/ccl.4960160115


Case Report

AORTA, February 2015

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Volume 3, Issue 1: 30-37
The report is interesting but raises several controversial issues: The main issue is that, while the authors recognize the difficulty of distinguishing entities that present with ST segment elevations on ECG yet are not true acute coronary syndromes from STEMI, they do not put matters adequately into perspective in terms of the relative (in)frequency of ruptured aortic aneurysms presenting as STEMI. Thus, their discussion does not account for the “needle in a haystack” nature of this case. Perhaps going into more detail on this aspect would help the reader interested in the topic. Moreover, while the authors state that between 1.4 and 15% of patients presenting with ST elevations on ECG do not have an acute myocardial infarction, they reference a paper from the Netherlands that reported only a 2.3% rate of patients presenting with ST elevations and taken for primary percutaneous intervention who did not have a myocardial infarction, among 820 consecutive patients. Of note, less than 1% of patients had aortic dissections [1]. Also, the authors do not discuss the feasibility of investigating such patients for alternative causes before they are taken emergently to the cardiac catheterization laboratory, a proven contemporary strategy that is associated with the best outcomes [2].

Moreover, the authors claim in the abstract that they “provide recommendations for ensuring a similar situation is not misdiagnosed in the future”. It would be more useful to provide a discussion of how the large number of STEMI and the improved outcomes of patients treated with a primary PCI constitute a very powerful argument for striving for a short door-to-balloon time. The cost to pay for a strategy aimed at accomplishing the likely unattainable goal of eliminating all misdiagnoses of rare masquerading conditions may be the late diagnosis of the very frequent patients with true coronary syndromes presenting with appropriate features of STEMI. It would be unrealistic to expect all patients presenting with a typical coronary picture to have full laboratory studies including white cell count and CRP as well as chest X rays and/or computed tomographic angiography before deciding to activate the cardiac catheterization laboratory; such a requirement would significantly prolong door-to-balloon time, which is one of the important determinants of the outcomes of patients with STEMI.

Whether the patient described in this report got her chest X ray because of a delay in activating the cardiac catheterization laboratory or because the emergency room clinician had a clinical suspicion based on subtle atypical features of the patient is not clear. Ultimately, though, the authors’ suggested strategy to investigate every patient fully with the goal to avoid very rare misdiagnoses of unusual conditions is difficult to justify in terms of its risk: benefit ratio and thus not feasible in real life.

References

Latrogenic Aortic Transection in a Child

Ram Chandra Sherawat, MS*, Anil Sharma, Mch, Sunil Dixit, Mch, Mohit Sharma, MS, Sidarth Lukaram, MS
Department of Cardio-Thoracic and Vascular Surgery, Sawai Man Singh Medical College, Jaipur, Rajasthan, India

Abstract
The accepted treatment for aortic injury has been repair of the injury as soon as possible. Delayed repair is not generally fruitful, but in our case report, delay in the repair of a ligated and transected abdominal aorta is safe and has a potential positive impact on survival and vascular stability/integrity. This case seems worth reporting.

Key Words
Transected • Abdominal aorta • Superior mesenteric artery • Inferior mesenteric artery

Introduction
No documentation of a case of ligation and transection of the abdominal aorta with delayed repair is available. Sir Astley Cooper in 1817 originally reported ligation of the abdominal aorta if an aneurysm was present. In this case report, the patient was referred to our center because of intensive pain in the legs with numbness following radical nephrectomy. Color Doppler showed minimal flow in both common femoral arteries. A completely occluding thrombus was visualized by Doppler in both femoral arteries. Computed tomography showed an abrupt termination of the aorta below the right renal artery. The superior mesenteric artery (SMA) was seen intact. The IMA was not seen.

Under general anesthesia and via a previous incision (Chevron), the abdomen was explored and the aorta was exposed. We found a ligated and totally transected aorta from below the origin of the right renal artery to just proximal to the bifurcation of the aorta. We performed an interposition replacement of the aorta using a 10mm GoreTex graft (Gore Medical, Flagstaff, Arizona, USA) and re-implanted the inferior mesenteric artery (IMA) into the new graft.

Case Report
The patient was a 7-year-old girl. She presented with a history of left radical nephrectomy 3 days earlier for Wilms’s tumor. The patient was referred to our center because of intensive pain in the legs with numbness.

On physical examination, the pulse was 86 bpm, and the blood pressure was 100/60 mm Hg. The legs were cool and mottled, but not cold (Figure 1). The patient was unable to move her legs. There was no sensation. No pulses were palpable in any lower limb arteries. There was no motor power (0/5) in the lower limbs (paraplegia). Color Doppler showed minimal flow in both common femoral arteries. A completely occluding thrombus was visualized by Doppler in both femoral arteries. Computed tomography showed an abrupt termination of the aorta below the right renal artery. The superior mesenteric artery (SMA) was seen intact. The IMA was not seen (Figure 2).

Under general anesthesia and via a previous incision (Chevron), the abdomen was explored and the aorta was exposed. We found a ligated and totally transected aorta from below the origin of the right renal artery to just proximal to the bifurcation of the aorta. The IMA was found ligated. The transected segment gap was approximately 10 cm. The gut was normal with no signs of ischemia. We performed the interposition aortic replacement and re-implanted the IMA into the new graft.

Postoperatively, the patient was maintained on thromboprophylaxis with low-molecular weight heparin. Bilateral femoral pulses were present immediately.
The lower limbs were warm by postoperative day (POD) 1. Sensation returned to both lower limbs on POD 2. Motor power (2/5) returned to both lower limbs on POD 3. Bowel and bladder functions were intact.

The patient was discharged before ambulating to rehabilitation. As of the most recent follow up, the patient has regained motor strength (4/5) bilaterally.

**Discussion**

Because the patient was very young, we decided to operate to perform an aortic repair even with a late presentation (> 72 hours). We were concerned about operating on a patient with a single kidney. We expected enhanced resistance due to her young age. No post-operative complications occurred.

The severity of tissue ischemia depends not only on its duration but on both the level of arterial injury and the efficiency of collateral circulation [1-3]. Additionally, the amount of time since the injury may not necessarily reflect the actual period of ischemia, especially in a closed vessel injury [4,5].

This is not to suggest that delays in revascularization should not be minimized. Conventional logic dictates that the longer the period of ischemia, the higher the chance of limb loss. However, this case illustrates that to condemn limbs as unsalvageable purely on the basis of ischemia time alone is not prudent.

Finally, it must be stressed that both limb salvage and long-term functionality must be considered. Nevertheless, in Asian societies like ours where the physical integrity of limbs often takes precedence over functionality, maintaining even a nonfunctional limb may be desired.

This case illustrates the delayed repair of a ligated and transected abdominal aorta with good outcome.

**Conflict of Interest**

The authors have no conflict of interest relevant to this publication.

Figure 1. Preoperative findings show cool and mottled legs.
Case Report

Figure 2. Pre and post operative computed tomography (2a) preoperative CT Shows an abrupt termination of the aorta below the right renal artery (2b) post operative CT shows normal blood flow.

References


Abstract
An 18-year-old male patient was admitted to our hospital because of a high impact trauma. A computed tomography scan showed massive mediastinal bleeding due to a posteriorly located rupture of the aortic arch with formation of a pseudoaneurysm. Although urgent repair was indicated, open cardiac surgery was not feasible, as this would involve full heparinization in a patient with subarachnoid bleeding. The chosen solution was to perform a percutaneous thoracic endovascular aneurysm repair (TEVAR) and a kissing chimney procedure using a U-shape configuration.

Key Words
Aortic Arch Rupture • Percutaneous TEVAR • Chimney

Introduction
An 18-year-old male patient was admitted to our hospital because of a high impact trauma in which he fell off his motorcycle at high speed. Clinically, an open femur shaft fracture was visualized. Due to a Glasgow coma scale of 3/15 with severe signs of pain and hemodynamic instability, the patient was intubated on site.
to a posteriorly located rupture of the aortic arch with formation of a pseudoaneurysm (Figure 1).

Due to hemodynamic instability, urgent repair was indicated. Open cardiac surgery, however, was contraindicated, as this would involve circulatory arrest and full heparinization. Anticoagulation therapy was especially hazardous because of the subarachnoid bleeding, unknown cerebral damage, and substantial orthopedic trauma. Therefore, an endovascular approach was favored.

A more detailed examination of the CT scan showed a bovine arch with common origin of the brachiocephalic trunk and the left common carotid artery (LCCA), complicating the procedure (Figure 2). Debranching of the LCCA was not possible because the rupture was too close to the origin of the brachiocephalic trunk, thus inducing an unacceptable proximal landing zone (Figure 2).

The chosen solution was to perform a kissing chimney procedure and percutaneous TEVAR.

At first, an endoprosthesis (Medtronic Valiant Captiva) was delivered percutaneously via the right common femoral artery after preclosure with two Pro-Glides (Abbott Perclose ProGlide Suture-Mediated Closure System). Next, we performed chimney stenting of the LCCA (Advanta V12 – 6x59) through access in the left internal carotid artery. After this procedure, substantial leakage was still visible, and, when switching the sheath to provide access to the LCCA, the V12 stent luxated, possibly due to undersizing.

Therefore a more complex option was chosen: This began with an elongation of the endoprosthesis with a second Valiant Captiva placed more distally and overriding the brachiocephalic trunk, which meant placing kissing chimney stents. At the most proximal part of this “kissing chimney” configuration were two Advanta V12 10x38mm and 10x59mm stents (Maquet Cardiovascular, Wayne, New Jersey, USA) introduced via the right brachial and subclavian arteries. This allowed for blood from the ascending aorta to enter the trunk and proceed through the right subclavian artery and the right common carotid artery. The second portion of the chimney allowed blood to enter the LCCA from the brachiocephalic trunk. Dotted area: U-shaped Viabahn stent allowing blood to enter the LCCA from the brachiocephalic trunk. Arrows: blood
between the endoprosthesis and the aortic wall, into the right common carotid artery in a U-shape pattern (see Figure 3 for a schematic version of the entire construction) [1]. The left subclavian artery received blood via a steal phenomenon through the left carotid artery system. The entire procedure was possible under low heparin dosage (Activated Clotting Time < 250 seconds) with immediate antagonistic Protamine administration afterwards.

Although the procedure went well, immediate control comparison revealed a type IA endoleak (Figure 4) which was treated additionally by direct suprasternal puncture of the pseudoaneurysm. Once the correct position of the sheath was verified, filling of the space with Gianturco coils (Cook Medical, Bloomington, Indiana, USA) and Glubran glue (GEM S.R.L., Lu, Italy) resulted in immediate success (Figure 5).

In the second stage, the femoral fracture was treated with external fixation. The patient was weaned from ventilation quite rapidly and further recovered without neurological sequelae. Finally, he was transferred for further rehabilitation to a specialized center.

Today, the patient is in perfect clinical condition without any problems regarding the extensive endovascular repair of his aortic arch and supraaortic vessels. A control CT scan and intraarterial angiogram 1 year later showed a good construction with patent chimneys and no type I or II leakage (Figure 6).

Follow up for this patient is life-long, as we expect future elective open reconstruction of the aortic arch due to his young age.

**Conflict of Interest**

The authors have no conflict of interest relevant to this publication.
Figure 6. Stable control at 1 year. A) frontal view, early contrast phase. B) frontal view, late contrast phase. C) enhanced image. Note the subclavian steal to the left upper extremity (large arrow) and the luxated V12 stent still in situ (small white arrows).

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Cite this article as: Hendriks JMH, Brits T, Van der Zijden T, Monsieurs K, de Bock D, De Paep R. U-Shape Kissing Chimney TEVAR for a Traumatic Arch Rupture in a Polytraumatized Patient. AORTA. 2015;3(Issue 1): 41-45. DOI: http://dx.doi.org/10.12945/j.aorta.2015.14-044
EDITOR’S QUESTIONS

1. You literally saved a life with your creativity. Do you have concerns about long-term durability of this endograft construct in an 18-year-old patient? Do you think the patient is susceptible to sudden brain events?

This indeed was an emergency solution for a young male polytraumatized patient who could not be helped by open cardiovascular surgery. As we stated at the end of the manuscript, intensive follow-up is well organized, and elective surgery with reconstruction of the aortic arch has already been discussed with the patient. Because of his young age, we believe it is too hazardous to allow him to continue with a supraaortic blood supply that relies on a kissing stent solution.

For the moment, however, ultrasound and angiographic controls show good results with adequate flow and no signs of graft failure. For this reason, we don’t expect short-term brain events and will thus allow the patient to focus on the last stages of his recovery. In the future, we will propose aortic arch replacement as a definitive long-term solution after informing the patient of the potential risks of follow-up therapy versus aortic arch surgery.
List of Upcoming Meetings

February

1. 61st Annual Conference of the Indian Association of Cardiovascular and Thoracic Surgeons
   February 19-22, 2015
   Hyderabad, India
   Meeting information available at: www.iactscon2015.org

2. Transcatheter Aortic Valve Implantation
   European Association for Cardio-Thoracic Surgery February 25-26, 2015
   Windsor, UK
   Meeting information available at: www.eacts.org/academy/2015-programme/

March

1. The Houston Aortic Symposium: Frontiers in Cardiovascular Disease, the Eighth in the Series
   March 5-7, 2015
   Houston, TX
   Meeting information available at: www.promedicacme.com

2. Advanced Module: Open and Endovascular Aortic Therapy
   European Association for Cardio-Thoracic Surgery
   March 18-20, 2015
   Windsor, UK
   Meeting information available at: www.eacts.org/academy/2015-programme/

3. Association of Cardiothoracic Anaesthetists / Society for Cardiothoracic Surgery in Great Britain and Ireland: Joint Annual Meeting & Cardiothoracic Forum
   March 25-27
   Manchester, UK
   Meeting information available at: www.scts.org

4. Aortic Valve Repair: A Step by Step Approach
   Institut Mutualiste Montsouris
   March 26-27, 2015
   Paris, France
   Meeting information available at: www.caviaar.com

5. 64th International Congress of the European Society for Cardiovascular and Endovascular Surgery
   March 26-29, 2015
   Istanbul, Turkey
   Meeting information available at: www.escvs2015.org

April

1. 62nd Annual Conference of the Israel Heart Society in Association with the Israel Society of Cardiothoracic Surgery
   April 13-14, 2015
   Tel-Aviv, Israel
   Meeting information available at: http://2015.en.israelheart.com/

2. Australasian Thoracic Aortic Symposium 2015
   April 15-18, 2015
   Melbourne, Australia

3. American Association for Thoracic Surgery 2015 Annual Meeting
   April 25-29, 2015
   Seattle, WA
   Meeting information available at: www.aats.org/annualmeeting/index.cgi