Aortic dissection and prophylactic surgery in congenital heart disease

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A B S T R A C T

Background: Proximal aortic dilatation in certain congenital heart diseases (CHD) prompts concerns about dissection and consideration of prophylactic surgery. To evaluate contemporary prophylactic practice, we determined incidence of aortic dissection and prophylactic surgery in aortopathy-associated CHD, compared to Marfan syndrome (MFS) and controls.

Methods and results: We followed patients from the CONCOR adult CHD registry (2002–2015), with a native proximal aorta and aortopathy-associated CHD, comprising bicuspid aortic valve/aortic stenosis (‘BAV/AS’; n = 2239) and aortic coarctation/conotruncal defects/univentricular heart/ventricular septal defect (‘At-risk CHD’; n = 5439). As reference, we selected MFS (n = 356) and Control (‘atrial septal defect, pulmonary stenosis; n = 2940’) patients. Cumulative incidences of dissection and prophylactic proximal aortic replacement – considered competing events – were determined, and compared corrected for age and sex. Median follow-up was 6.7 years. Ten-year dissection-incidence was 0.3% (95%CI: 0.0–0.7) in BAV/AS and 0.2% (0.0–0.3) in At-risk CHD, both significantly lower than in MFS (4.1%; 1.8–6.4) and similar to Controls (0.1%; 0.0–0.3). Ten-year prophylactic-surgery incidence was 9.3% (7.6–11.0) in BAV/AS and 0.7% (0.5–1.0) in At-risk CHD, both significantly lower than in MFS (21.3%; 16.3–26.3) and higher than in Controls (0.1%; 0.0–0.3).

Conclusions: In contemporary practice, aortic-dissection incidence is low in adults with aortopathy-associated CHDs, while prophylactic-surgery incidence is high in BAV/AS. To reduce surgical burden, BAV/AS patients could benefit from more individualised prophylactic-surgery algorithms.

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pulmonary atresia, double-outlet right ventricle), univentricular heart (n = 270) and ventricular septal defect (VSD; n = 2293). As reference, we selected patients with MFS (n = 356) and Controls with non-aortopathy-associated CHD (atrial septal defect or pulmonary stenosis; n = 2940). Subjects with BAV and CoA are included as BAV/AS, those with another primary CHD and BAV as a secondary diagnosis were excluded.

Patients were followed for AD and PPAR (not preceded by dissection/rupture; definition: Supplemental Table I). Follow up started 3 months after CONCOR inclusion, to correct for possible inclusion conditional on instantaneous risk (e.g. during (pre)operative hospital admission). Follow-up ended at the outcome, latest medical record review, death or end-of-study (October 10th 2015), whichever occurred first.

Medical imaging records of 91/130 PPARs in BAV/AS and 24/34 in At-risk CHD patients from high-volume centers were retrospectively reviewed for surgical indications (retrieved: 89 BAV/AS, 24 At-risk CHD) and largest pre-operative aortic diameter (retrieved: 78 BAV/AS, 23 At-risk CHD).

2. Results

2.1. Baseline characteristics

Baseline characteristics and outcome data per group. Table 1

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>BAV/AS</th>
<th>At-risk CHD</th>
<th>MFS</th>
<th>Control</th>
<th>p-Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>2239</td>
<td>5439</td>
<td>356</td>
<td>2940</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age, years</td>
<td>35.0(23.4–48.6)</td>
<td>29.7(21.6–42.3)</td>
<td>33.8(24.4–45.6)</td>
<td>39.7(26.6–54.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Male</td>
<td>1449(64.7)</td>
<td>2762(50.8)</td>
<td>157(44.1)</td>
<td>1041(35.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>AVR</td>
<td>373(16.7)</td>
<td>93(1.7)</td>
<td>1(0.3)</td>
<td>14(0.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Tertiary center</td>
<td>1427(63.7)</td>
<td>3894(71.6)</td>
<td>320(89.9)</td>
<td>1641(55.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Follow up time, years</td>
<td>6.0(2.8–9.4)</td>
<td>7.1(3.6–10.3)</td>
<td>9.3(5.8–11.3)</td>
<td>6.1(3.0–9.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total</td>
<td>13,959</td>
<td>37,752</td>
<td>2970</td>
<td>17,872</td>
<td></td>
</tr>
<tr>
<td>ADs in follow up</td>
<td>4(0.2)</td>
<td>6(0.1)</td>
<td>12(3.4)</td>
<td>2(0.1)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>2(0.0)</td>
<td>4(66.7)</td>
<td>3(25.0)</td>
<td>2(100)</td>
<td></td>
</tr>
<tr>
<td>Age at AD, years</td>
<td>44.3(34.4–75.1)</td>
<td>48.8(32.4–69.6)</td>
<td>44.1(31.2–54.5)</td>
<td>67.7(64.2–….)</td>
<td>0.506*</td>
</tr>
<tr>
<td>Fatal AD</td>
<td>3(75.0)</td>
<td>4(66.7)</td>
<td>2(16.7)</td>
<td>2(100)</td>
<td>0.024*</td>
</tr>
<tr>
<td>PPARs in follow up</td>
<td>130(5.8)</td>
<td>34(0.6)</td>
<td>63(17.7)</td>
<td>1(0.0)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>90(69.2)</td>
<td>25(73.5)</td>
<td>38(60.3)</td>
<td>1(100)</td>
<td></td>
</tr>
<tr>
<td>Concomitant AVR</td>
<td>98(75.4)</td>
<td>25(73.5)</td>
<td>19(30.2)</td>
<td>0(0.0)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Age at PPAR, years</td>
<td>40.7(29.5–50.4)</td>
<td>37.4(29.6–47.4)</td>
<td>36.1(26.6–46.0)</td>
<td>36.2</td>
<td>0.123*</td>
</tr>
<tr>
<td>Died &lt;3 months after PPAR</td>
<td>2(1.5)</td>
<td>2(5.9)</td>
<td>0(0.0)</td>
<td>0(0.0)</td>
<td>0.141*</td>
</tr>
</tbody>
</table>

Categorical variables are summarized as number (%), and compared using the χ² or Fisher’s exact test. Continuous variables are summarized as median (interquartile range), and compared using the Kruskal Wallis or Mann-Whitney U test.

Abbreviations: AS, aortic stenosis; AVR, aortic valve replacement; BAV, bicuspid aortic valve; CHD, congenital heart disease; MFS, Marfan syndrome.

* Overall across-group comparison.
† BAV/AS vs MFS: p = NS. All other pairwise: p < 0.008.
‡ At-risk CHD vs MFS: p = NS. All other pairwise: p < 0.008.
¶ At-risk CHD and Control vs MFS: p = NS. All other pairwise: p < 0.008.
∥ All pairwise comparisons: p < 0.008.
§ BAV/AS vs Control: p = NS. All other pairwise: p < 0.008.
¶ Overall pairwise: p = NS.
** BAV/AS and At-risk CHD vs MFS: p < 0.008. All other pairwise: p = NS.

3. Aortic dissection and prophylactic surgery

3.1. Baseline characteristics

Baseline characteristics are presented in Table 1. BAV/AS patients were older, and had proportionately more males and baseline AVR than the others. MFS and At-risk CHD were relatively more often followed in tertiary centers.

Table 1

Baseline characteristics and outcome data per group.
and if the indication for surgery included valve dysfunction (43.0 [6.3] mm, no valve dysfunction: 52.0 [3.5] mm, p = 0.001). In At-risk CHD, it differed by indication (included valve dysfunction: 44.9 [3.2] mm, no valve dysfunction: 54.1 [5.6] mm, p < 0.001), not by concomitant AVR. In BAV/AS, mean diameter was similar between periods of different guideline-recommended diameter-thresholds for PPAR, and there was no correlation between calendar-time and pre-operative diameters (overall, and stratified by AVR and indication).

Aortic-dissection incidence was not different between patients with BAV with and without CoA, PPAR incidence was significantly higher in the latter (Supplemental Fig. 1).

4. Discussion

This study reassuringly shows low aortic-dissection risk in patients with aortopathy-associated CHD types and a native proximal aorta in contemporary practice: similar to controls and much lower than in MFS. Incidence of prophylactic aortic replacement was high in BAV/AS, but not in other aortopathy-associated CHD.

Low aortic-dissection risk in BAV/AS agrees with observations in population-based [1,9] and post-AVR [10] BAV cohorts. The latter also found ~12× lower risk compared to MFS [10]. Present aortic-surgery incidence was comparably high. This is likely due to proportionately more valve dysfunction requiring AVR, a predictor for aortic surgery [9], in our clinical cohort with predominantly native valves. For other aortopathy-associated CHD, low dissection risk in is in line with sporadically reported dissections in these patients, while data on aortic-surgery incidence is lacking [1].

During the study-period (2002–2015), guideline-recommended aortic-diameter thresholds for prophylactic surgery in BAV ranged from conservative (55 mm) in 2002, via aggressive (40 mm) in 2010, back to currently conservative (55 mm, or 50 mm with risk-factors). It ranged between 40 and 50 mm (currently 45 mm) at the time of AVR for dysfunctional BAV [2,3,5]. No specific guidelines for aortic dilatation in other aortopathy-associated CHDs exist [1,2]. While the observational nature of this study precludes conclusions concerning its efficacy, present results reflect clinical practice over the study period.

Regarding BAV/AS, low dissection- and high prophylactic-surgery incidence may either indicate effective contemporary prophylactic practice with justifiably high surgical burden, or substantiate the notion that aggressive guidelines induce unnecessary prophylactic operations, possibly worsening overall outcome [5]. Importantly, many prophylactic aortic replacements were performed with AVR for valve dysfunction, often at moderate dilatation in reviewed cases. However, observational data in BAV patients with moderately dilated aortas showed no long-term difference in dissections or repeat operations compared with isolated AVR [11], while concurrent aortic replacement may increase operative risk [12]. Maximum pre-operative aortic diameters in the present study suggest rather aggressive prophylactic practice, constant over the study-period despite changing guidelines. This may reflect influence of operator and/or patient preference on timing of surgery [4]. Importantly, guidelines are based on nonrandomized data and expert consensus. Moreover, aortic diameter is an imperfect marker for dissection-risk [13], while hemodynamic and genetic factors probably contribute in the heterogeneous BAV-associated aortopathy [4]. Of note, European guidelines consider CoA a risk factor for dissection in BAV patients, eliciting surgery at the reduced (50 mm) threshold [2]. However, we found CoA associated with similar dissection risk, despite lower prophylactic-surgery incidence, in BAV patients. Systematic data and reliable markers for dissection-risk are necessary to provide targeted prophylactic algorithms with a strong evidence-base, and thus improve uniform clinical practice and ultimately reduce surgical burden [4].

Regarding aortopathy-associated CHD other than BAV/AS, dissection-risk was low without frequent surgery. While a restrictive policy following general aortic-disease guidelines (55 mm) seems appropriate in these patients, aortic surgery was sometimes performed at lower aortic diameters, particularly if surgery was indicated for aortic valve dysfunction [1–3].

This study is limited by its observational nature. Known risk-factors for, and determinants of dissection and treatment decisions were unavailable. Locations (proximal/distal) of dissections, important regarding the rationale of prophylactic proximal aortic surgery, were not recorded. Surgical indications and pre-operative diameters were retrospectively collected for a proportion of cases. Our clinical cohort from secondary/tertiary centers likely represents a selection with more severe/overt disease from the CHD-population, particularly for BAV, which may remain asymptomatic well into adulthood. Longer follow-up in MFS and At-risk CHD reflects CONCOR inclusion starting in tertiary centers, thus including patients with more severe CHD earlier [14].

In conclusion, the present study confirms contemporary aortic risk in aortopathy-associated CHD is much lower than in MFS. As incidence of prophylactic surgery is high in BAV/AS, research should focus on identifying patients at highest risk, to target surgery and reduce surgical burden in BAV/AS patients. A restrictive approach seems appropriate in other aortopathy-associated CHD-types.

Declarations of interest

None.
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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcard.2018.09.038.

References


