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Arterial hypertension and endovascular treatment of adults with coarctation of the aorta: a single-center experience

Short title: Hypertension and coarctation of the aorta

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CONFLICT OF INTEREST: None
INTRODUCTION

Coarctation of the aorta (CoA) is a common cause of secondary arterial hypertension (HTA) in young adults [1,2]. In many cases, however, antihypertensive therapy is initiated without excluding this condition and HTA is very likely to persist. Our study aimed to analyze the diagnostic route and medical therapy of HTA in the population of adult patients undergoing endovascular stenting of CoA.

METHODS

We investigated 24 consecutive adults (78.1% men) with CoA referred for transcatheter intervention at our institution between May 2013 and April 2018. Clinical history was obtained at baseline, with special attention paid to the age at which HTA was first noticed and the age at final diagnosis of CoA. Detailed information on antihypertensive therapy was collected at baseline, discharge and next, by phone contact, after 34±17 months (range 2-63 months).

Blood pressure (BP) was measured at baseline and after stenting using Omron oscillometric device (Omron Healthcare, Kyoto, Japan). HTA was defined in accordance with the European Society of Cardiology guidelines [1].

Endovascular procedures were carried out under general anesthesia in a hybrid operating room. Invasive aortic BP was measured above and below the coarctation directly before and after stenting. Peak systolic pressure gradient defined as difference in peak systolic BP measured across the lesion was calculated. Stents were delivered using femoral approach; bare metal stents were used in 2 (8.3%) patients (LD Max, EV3, Plymouth, USA and
Cheetham Platinum, NuMED, Hopkinton, USA) and covered stents (Covered Cheetham Platinum, NuMED, Hopkinton, USA) in the remaining 22 (83.7%).

Written informed consent was obtained from all patients before the intervention. In accordance with National Ethics Guidance, approval for further analysis was not required as this was a retrospective study with anonymized patient data.

STATISTICAL ANALYSIS

Statistical analysis was performed using SPSS 17.0 (SPSS Inc., Chicago, Illinois). Normally distributed continuous variables were compared with paired-sample t-test and categorical variables with Wilcoxon signed-rank test. A p-value of less than 0.05 was considered significant.

RESULTS AND CONCLUSIONS

The median age at procedure was 36 (range 18 to 77) years. All patients underwent successful stent implantation with significant reduction in peak systolic pressure gradient (see Table). The maximal residual pressure gradient was 6 mmHg. Median hospitalization time was 4 days (lower quartile 3, upper quartile 5 days). No early procedure-related complications, such as neurological deficit, stent migration, balloon rupture or aortic wall injury were observed. One patient died 14 days after procedure from decompensated acute heart failure caused by de novo aortic valve stenosis, it was not considered, however, a complication of stenting. In one of the 2 patients treated with bare metal stents, aortic aneurysm formation was revealed during the follow-up; a successful covered stent implantation (Covered Cheetham Platinum 8Z39)
into the previously implanted Cheetham Platinum 8Z45 was performed 11 months after the original procedure.

At baseline, only 1 patient (4.2%) did not take any antihypertensive medication, while the majority (79.2%) was treated with at least 3 drugs. A significant decrease in both systolic and diastolic BP was observed after procedure (see Table). Medical treatment was reduced or discontinued when possible: 6 patients (26.1%) were discharged without any antihypertensive medication, 10 (52.2%) were prescribed 1 or 2 antihypertensive drugs, and 7 (30.4%) were prescribed at least 3 drugs. The mean number of drugs per patient dropped from 3.1 to 1.9 (see Table).

At follow-up, 15 patients (65.2%) continued their medication, but only 7 (30.4%) required 3 drugs or more. The mean number of drugs per patient was similar to that at discharge (see Table).

CoA was diagnosed in adolescence or adulthood in 20 patients (83.3%)\(^1\). In this subgroup, first clinical manifestation of CoA was predominantly HTA (in 19 patients), cardiac murmur was reported as the first recognized symptom in just 1 patient. The mean age at detection of these abnormalities was 17.1±8.8 years (range 1 to 36), while the mean age at

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\(^1\) Among the 4 patients diagnosed in infancy, 2 were operated before the age of 3 years and currently presented due to re-coarctation; in case of the remaining 2, surgery was deferred on request of their caregivers and, eventually, percutaneous intervention was performed at the age of 35 and 27 years.
diagnosis of CoA was 33.5±14.9 years (range 15 to 60). The mean delay in diagnosis was calculated as 16.4±11.1 (maximally 37) years.

What needs to be noted here is that the majority of patients did not receive proper physical evaluation either before starting, or throughout medical treatment (continued for nearly 11 years on average, maximally 25). CoA can often be diagnosed just on physical examination. A discrepancy between upper and lower extremity pulses, and, most importantly, upper-to-lower limb BP difference of >20/10 mmHg are highly suggestive findings [1,2]. Unfortunately, pulses assessment and four-limb BP measurement, although quick and easy to perform, seem to be neglected by many physicians. In fact, all patients from our group claimed to have been prescribed medication without prior evaluation of femoral pulses. Four-limb pressure measurement was not done before referring to a tertiary care hospital in all but 2 cases.

Published data confirm that correction of CoA leads to BP reduction [3-5]. De-escalation or discontinuation of antihypertensive therapy may be achieved in 63-84% of patients after stenting [5-8]. These data are in accordance with our results, where reduction in the number of drugs was observed in 60.1% of patients at discharge and 69.6% at follow-up. Residual hypertension may be due to arterial remodeling resulting from diffuse vasculopathy involving, inter alia, the transforming growth factor beta signaling pathway [3,10].

Endovascular stenting has become an accepted therapeutic procedure in adults with CoA [6,8,9]. We believe that apart from reporting satisfactory results in terms of safety, efficacy and resolution of HTA, our study highlights the need of careful physical examination.

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2 These calculations do not include one patient that died (see further in text), as complete information could not be obtained.
Palpation of brachial and femoral pulses as well as BP measurement in upper and lower extremities should form the integral part of routine office checkup in patients presenting with HTA to avoid unnecessary medication and late complications of long-lasting unrecognized CoA.

The limitations include selection bias, since this single-center study analyzed a relatively small number of patients treated in a tertiary adult heart center. Furthermore, follow-up was short as related to the patients’ expected life span and the follow-up data was based on telephone contact. Last, a standardized method of BP measurement, preferably 24-hour ambulatory BP measurement, should be used to objectively ascertain the efficacy of medication.
REFERENCES


Table 1. BP measured invasively and non-invasively pre- and post-stent implantation; antihypertensive medication at the baseline, discharge and follow-up; data are presented as mean ± standard deviation. Statistically significant differences were marked in bold; SBP – systolic BP, DBP – diastolic BP, n/a – not applicable.

<table>
<thead>
<tr>
<th></th>
<th>Baseline (Pre-procedure)</th>
<th>Discharge (Post-procedure)</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>INVASIVE BLOOD PRESSURE MEASUREMENT</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n=24</td>
<td>n=24</td>
<td>n/a</td>
<td></td>
</tr>
<tr>
<td>ascending aorta SBP, mmHg</td>
<td>115.5 ± 31.7</td>
<td>111.7 ± 24.5</td>
<td>p=0.55 (95% CI -9.2, 16.8)</td>
</tr>
<tr>
<td>descending aorta SBP, mmHg</td>
<td>81.0 ± 23.3</td>
<td>110.4 ± 23.6</td>
<td>p&lt;0.001 (95% CI -42.4, -16.4,)</td>
</tr>
<tr>
<td>peak systolic pressure gradient, mmHg</td>
<td>40.1 ± 15.9</td>
<td>1.3 ± 2.2</td>
<td>p&lt;0.001 (95% CI 32.1, 45.4)</td>
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<tr>
<td><strong>NON-INVASIVE BLOOD PRESSURE MEASUREMENT (UPPER EXTREMITY)</strong></td>
<td></td>
<td></td>
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<tr>
<td>n=24</td>
<td>n=23</td>
<td>n/a</td>
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<tr>
<td>SBP, mmHg</td>
<td>155.8 ± 20.0</td>
<td>131.1 ± 17.2</td>
<td>p&lt;0.001 (95% CI 16.7, 32.6)</td>
</tr>
<tr>
<td>DBP, mmHg</td>
<td>84.2 ± 11.2</td>
<td>78.6 ± 10.1</td>
<td>p=0.04 (95% CI 0.2, 11.1)</td>
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<tr>
<td><strong>ANTIHYPERTENSIVE DRUGS</strong></td>
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<td></td>
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<tr>
<td>n=24</td>
<td>n=23</td>
<td>n=23</td>
<td></td>
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<tr>
<td>at least 1</td>
<td>23 (95.8%)</td>
<td>17 (73.9%)</td>
<td>15 (65.2%)</td>
</tr>
<tr>
<td>p=0.025 (Z=-2.24)</td>
<td>p=0.008 (Z=-2.65)</td>
<td></td>
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<tr>
<td>at least 3</td>
<td>19 (79.2%)</td>
<td>7 (30.4%)</td>
<td>7 (30.4%)</td>
</tr>
<tr>
<td>p=0.001 (Z=-3.46)</td>
<td></td>
<td></td>
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<tr>
<td>average number per patient</td>
<td>3.1 ± 1.3</td>
<td>1.9 ± 1.8</td>
<td>1.9 ± 1.7</td>
</tr>
<tr>
<td>p=0.01 (95% CI -2.1, -0.3)</td>
<td>p=0.009 (95% CI -2.1, -0.3)</td>
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</table>