Pressure Fields by Flow-Sensitive, 4D, Velocity-Encoded CMR in Patients With Aortic Coarctation

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ABSTRACT

This study compared pressure fields by 4-dimensional (4D), velocity-encoded cine (VEC) cardiac magnetic resonance imaging (CMR) with pressures measured by the clinical gold standard catheterization. Thirteen patients (n = 7 male, n = 6 female) with coarctation were studied. The 4D-VEC-CMR pressure fields were computed by solving the Pressure-Poisson equation. The agreement between catheterization and CMR-based methods was determined at 5 different measurement sites along the aorta. For all sites, the correlation coefficients between measures varied between 0.86 and 0.97 (p < 0.001). The Bland-Altman test showed good agreement between peak systolic pressure gradients across the coarctation. The nonsignificant (p > 0.2) bias was +2.3 mm Hg (± 6.4 mm Hg, 2 SDs) for calibration with dynamic pressures and +1.5 mm Hg (± 4.6 mm Hg, 2 SDs) for calibration with static pressure. In a clinical setting of coarctation, pressure fields can be accurately computed from 4D-VEC-CMR–derived flows. In patients with coarctation, this noninvasive technique might evolve to an alternative to invasive catheterization. (J Am Coll Cardiol Img 2014;7:920–6)

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Coarctation of the aorta (CoA) accounts for 5% to 8% of all congenital heart defects (1). Surgical or interventional treatment of CoA is associated with low morbidity. Current treatment strategies are focusing on the elimination of pressure gradients across the site of CoA. According to clinical guidelines, intervention is recommended, among others, at a systolic gradient of >20 mm Hg measured by catheterization in children or by catheterization or noninvasively in adults (1). Hence, for medical decision making, cardiac catheterization is still considered the clinical gold standard despite its known drawbacks concerning invasiveness, ionizing radiation exposure, and costs.

Alternative methods for estimating pressure differences in the aorta have been investigated extensively. Doppler echocardiography tends to overestimate the gradient, and measurements are sometimes difficult to obtain due to the posterior position of the aorta, particularly in the adult patient (1). Cardiac magnetic resonance (CMR) provides high-quality anatomic information of the aorta, whereas 4-dimensional (4D) velocity-encoded cine (VEC) CMR provides time-resolved blood flow velocities in a 3-dimensional (3D) volume that can cover the...
entire aorta. From these velocity fields, dynamic pressure differences along the course of a vessel (4D pressure fields) can be computed by solving the Pressure–Poisson equation (2). Briefly, the Pressure–Poisson equation is derived from the momentum equation of the Navier–Stokes equations for incompressible fluids by applying the divergence operator. The validity of 4D pressure fields has been evaluated in systematic phantom and initial human studies (2).

Our goal was to investigate the method’s accuracy in a clinical setting in patients with CoA. In this context, we investigated the agreement between VEC-CMR-based 4D pressure fields and cardiac catheterization as the clinical gold standard.

Thirteen consecutive patients (n = 7 male, n = 6 female, age range 13 to 52 years, mean age 23 ± 12 years) with clinical indications for cardiac catheterization due to CoA and a preceding CMR study were included between October 2011 and January 2013. Two patients had native CoA and the remaining had recurrent CoA after balloon angioplasty (n = 3) or surgical treatment (n = 8). Exclusion criteria were patients with stents in the aorta, young age that would have required sedation for CMR, and general contraindications to CMR. The study was approved by the institutional research ethics committee following the ethical guidelines of the 1975 Declaration of Helsinki. Written informed consent was obtained from the participants and/or their guardians.

The CMR study was conducted in a whole-body 1.5-T magnetic resonance scanner (Achieva R 3.2.2.0, Philips Medical Systems, Best, the Netherlands) using a 5-element cardiac phased-array coil (Philips Medical Systems).

Three directional blood flow velocities were measured over the cardiac cycle using anisotropic k-space segmented 4D-VEC-CMR with retrospective electrocardiographic gating. The acquired volume covered the thorax from the apex of the heart to the aortic arch in the feet-to-head direction, the external border and spine in the anterior-to-posterior direction, and the ascending and descending aorta in the right-to-left direction. Exemplary scan parameters of this sequence were: field of view feet-to-head 180 mm, anterior-to-posterior 200 to 230 mm (depending on size of the patient), right-to-left 90 to 105 mm (depending on number of slices used), acquired voxel 2.5 × 2.5 × 2.5 mm, reconstruction matrix 128 × 128, reconstructed voxel 1.7 × 1.7 × 2.5 mm, flip angle 5°, shortest repetition and echo time, nominal temporal resolution varying with heart rate for 25 cardiac phases, and velocity encoding 400 cm/s. Scan time varied between 8.5 and 14 min, depending on the size of the patient’s chest.

3D anatomy of the aorta was determined by a clinically-established contrast-enhanced CMR angiography method. The injection dose of contrast agent containing gadolinium (Dotarem, Guerbet, Villepinte, France) was 0.2 ml/kg body weight, corresponding to 0.1 mmol gadoterate meglumine/kg body weight. The typically-used sequence parameters were: echo time 1.1 ms, repetition time 3.2 ms; flip angle 30°, field of view 510 mm; parallel imaging with an acceleration factor of 2 (sensitivity encoding); and half-Fourier acquired voxel size, 1.2 × 1.2 × 2.2 mm³ (reconstructed to 0.9 × 0.9 × 1.1 mm³).

Cardiac catheterization was done with biplane projection angiographies with Philips Allura Xper FD 10/10 (Philips Medical Systems) using injection of contrast agent (Ultravist, Schering, Berlin, Germany).

Catheterization was conducted under conscious sedation by intravenous administration of a bolus of midazolam (0.1 to 0.2 mg/kg, maximum 5 mg), followed by a bolus of propofol (1 to 2 mg/kg, as needed) and continuous infusion of propofol (approximately 4 mg/kg/h).

Pressures were obtained in 6 pre-defined locations (Figure 1A) using 5- to 6-F fluid-filled pigtail catheters (Cordis, Warren, New Jersey) that were connected to pressure transducers (Becton-Dickinson, Franklin Lakes, New Jersey) and amplified, recorded, and analyzed using the Schwarzer Haemodynamic Analyzing System (Schwarzer, Heilbronn, Germany).

Post-processing of 4D-VEC-CMR datasets was done with the MEVISFlow software (Fraunhofer Mevis, Bremen, Germany). In a first step, automatic eddy current correction and a phase-unwrapping algorithm were applied. Thereafter, the aorta was segmented using watershed 3D segmentation of the lumen.

A finite-element-based solution for the Pressure–Poisson equation was applied to the segmented aorta for computing 4D intravascular blood pressure differences at the same 6 locations in the aorta where invasive pressures were obtained (Figure 1A). Because the Pressure–Poisson equation computation is sensitive to errors near the vessel boundaries due to high velocity gradients, we performed a reduction of 5% on the segmented volume of the aorta (to 95% of the initial segmented vessel).

The blood flow velocities, measured by the 4D-VEC-CMR sequence, can be used to calculate only
relative local pressure differences over the cardiac cycle (Figures 1B to 1F). Therefore, the pressure computation algorithm requires a calibration with a known absolute pressure profile over time at a given location in the target vessel. In our study, the reference location was chosen to be in the ascending aorta (location 1, Figure 1A). Calibration was performed in 2 ways:

1. Calibration by dynamic pressures. The pressure at the reference location is considered to change over time during the cardiac cycle, and absolute dynamic pressures from catheterization are applied at the reference location. Physically, this can be the most realistic approach. However, it requires invasive pressure data.

2. Calibration by static pressure. At a reference location, the pressure is considered to be constant at all time points over the cardiac cycle. Therefore, a default 0 value is applied at this reference location and the relative pressure differences to another pre-defined location (in our setting, in the descending aorta at location 6) are computed for each time point. This approach is fully noninvasive. However, it gives only the maximal instantaneous gradient, neglecting the shift in time of peak systolic pressures between the ascending and descending aorta (locations 1 and 6), which is affected, among others, by aortic wall compliance and the distance that the pulse wave has to travel (Figure 2). Therefore, for the assessment of peak systolic pressure gradients (between location 1 and 6), we did not measure the difference of pressures at the same time point, but instead determined the differences between the “peak-to-peak” pressures at their respective time points (Figure 2).

Statistical testing accounted for the fact that, in each patient, multiple measurements were performed at 6 different locations along the aorta. In addition, the measurements at the position used for calibration (location 1, Figure 1A) have been excluded to avoid an underestimation of errors.
The agreement between catheter and CMR measurements was determined with the Bland-Altman analysis for: 1) systolic and diastolic pressures at the 5 locations (locations 2 to 6, Figure 1A); and 2) the peak-systolic pressure gradients between locations 1 and 6 (Figure 1A). In addition, the Pearson correlation coefficients between catheter- and CMR-based measures have been determined separately for the different positions.

For a common analysis of the differences measured at different positions, a mixed linear model has been used. The depending variable was the difference of catheter- and CMR-based measures at the corresponding positions. A common overall mean and a fixed effect for the position have been included, as well as a random person factor. To respect possible dependencies of the measurements at adjacent positions, the position effect has been modeled as a repeated factor with an autoregressive correlation structure of grade 1.

The analyses have been carried out with SPSS version 21 (IBM Corporation, Armonk, New York). Data are expressed as mean ± SD. Effects have been considered significant at p < 0.05.

The sample size necessary to compare catheter and CMR measurements was estimated using power analysis using G*Power 3.1.7 (Franz Faul, Kiel University, Kiel, Germany). The power test was performed for the T-test (differences between 2 dependent means – matched pairs). As input parameters we used: 2-tails, α = 0.05, power = 1 – β (β assumed as 0.8), and effect size ρ = 1.1. Effect size was calculated based on SD of pressure drops measured with a catheter (4.8 mm Hg) and a 5-mm Hg difference between 2 measurement techniques relevant in the clinical setting. On the basis of these parameters, we found that a sample size of 9 patients is necessary for this study.

The patient characteristics are given in Table 1. After diagnostic catheterization, 10 patients received the implantation of a stent, 1 patient received a balloon angioplasty, and in 2 patients, no treatment was judged to be necessary (Table 1).

The dynamic pressure profiles obtained by catheterization and CMR were similar between the methods at all measurement positions (Figure 2). The timing difference between peak systolic pressures in the ascending versus descending aorta is illustrated in Figure 2. The correlation coefficients between both measures (catheter and CMR) varied between 0.938 and 0.973 at the different positions for the systolic pressures and between 0.956 and 0.744 for the diastolic pressures (all p < 0.001 in a test for independence).

There was good agreement between peak systolic and end-diastolic pressures. For the systolic pressures, the bias (mean of differences) was −0.6 mm Hg and the limit of agreement (2 SD) was ±9.6 mm Hg (Figure 3A). The bias suggests only slight underestimation by the CMR method, with differences between the methods being nonsignificant (p = 0.239). For diastolic pressures, the bias was −0.3 mm Hg and the limit of agreement (2 SD) was ±9.7 mm Hg (p = 0.722) (Figure 3B). The mixed model analyses showed that the difference between both measuring methods varied only slightly between the positions (p > 0.2). Also, the differences between the individual patients (person effect) had only a small effect on the variance component (p > 0.05).

The Bland-Altman test showed good agreement among peak systolic pressure gradients between the ascending and descending aorta measured by catheterization and CMR with either calibration method (Figures 3C and 3D). For calibration with dynamic catheter-based pressures, the bias was 2.3 mm Hg and the limit of agreement was ±6.5 mm Hg. The bias suggests only slight underestimation by the CMR method, with differences between the methods being nonsignificant (p = 0.22). For calibration by static pressure, the bias was 1.5 mm Hg, and the limit of agreement was ±4.6 mm Hg. Again, the bias
sponds to not be critical because it was not the scope of our study to investigate pressure conditions near the vessel, such as wall shear stress.

At the level of CMR data processing, we applied a finite-element-based method for solving the Pressure-Poisson equation. This method was reported to considerably limit computation time and, importantly, to be less susceptible to pressure underestimation than the iterative approach reported by Bock et al. (2). In addition, a vessel size reduction by 5% was applied to avoid numerical inconsistencies close to the vessel wall typical of the Pressure-Poisson equation. We consider such minor vessel size reduction to not be critical because it was not the scope of our study to investigate pressure conditions near the vessel, such as wall shear stress.

CMR-derived pressure fields was previously studied with focus on the determination of relative pressure differences between anatomic locations by setting pressures at the reference location to default values. This approach is attractive because it is easy to conduct and is fully noninvasive.

**Table 1: Patient Characteristics and Pressure Gradients**

<table>
<thead>
<tr>
<th>Patient #</th>
<th>Sex</th>
<th>Age</th>
<th>Diagnosis</th>
<th>Intervention</th>
<th>RR Right Arm, mm Hg</th>
<th>Peak-Systolic Gradient, mm Hg</th>
<th>Catheter</th>
<th>CMR</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>20</td>
<td>Re-CoA</td>
<td>Implantation of a stent</td>
<td>140/60 (84)</td>
<td>27</td>
<td>27</td>
<td>MR</td>
</tr>
<tr>
<td>2</td>
<td>F</td>
<td>14</td>
<td>Re-CoA</td>
<td>Implantation of a stent</td>
<td>136/58 (90)</td>
<td>22</td>
<td>19</td>
<td>MR</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>19</td>
<td>Re-CoA</td>
<td>Implantation of a stent</td>
<td>146/66 (101)</td>
<td>15</td>
<td>18</td>
<td>MR</td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>23</td>
<td>Native CoA</td>
<td>Implantation of a stent</td>
<td>128/62 (88)</td>
<td>15</td>
<td>10</td>
<td>MR</td>
</tr>
<tr>
<td>5</td>
<td>F</td>
<td>13</td>
<td>Re-CoA</td>
<td>None</td>
<td>128/62 (97)</td>
<td>16</td>
<td>11</td>
<td>MR</td>
</tr>
<tr>
<td>6</td>
<td>F</td>
<td>29</td>
<td>Re-CoA</td>
<td>Implantation of a stent</td>
<td>140/75 (102)</td>
<td>16</td>
<td>15</td>
<td>MR</td>
</tr>
<tr>
<td>7</td>
<td>M</td>
<td>52</td>
<td>Re-CoA</td>
<td>Implantation of a stent</td>
<td>158/83 (115)</td>
<td>10</td>
<td>10</td>
<td>MR</td>
</tr>
<tr>
<td>8</td>
<td>M</td>
<td>15</td>
<td>Re-CoA</td>
<td>None</td>
<td>140/55 (87)</td>
<td>16</td>
<td>15</td>
<td>MR</td>
</tr>
<tr>
<td>9</td>
<td>M</td>
<td>15</td>
<td>Re-CoA</td>
<td>Implantation of a stent</td>
<td>128/62 (88)</td>
<td>11</td>
<td>10</td>
<td>MR</td>
</tr>
<tr>
<td>10</td>
<td>M</td>
<td>17</td>
<td>Re-CoA</td>
<td>Balloon dilation</td>
<td>153/72 (100)</td>
<td>15</td>
<td>13</td>
<td>MR</td>
</tr>
<tr>
<td>11</td>
<td>M</td>
<td>15</td>
<td>Native CoA</td>
<td>Implantation of a stent</td>
<td>118/63 (74)</td>
<td>16</td>
<td>13</td>
<td>MR</td>
</tr>
<tr>
<td>12</td>
<td>F</td>
<td>46</td>
<td>Re-CoA</td>
<td>Implantation of a stent</td>
<td>196/88 (122)</td>
<td>19</td>
<td>21</td>
<td>MR</td>
</tr>
<tr>
<td>13</td>
<td>F</td>
<td>21</td>
<td>Re-CoA</td>
<td>Implantation of a stent</td>
<td>151/69 (94)</td>
<td>22</td>
<td>19</td>
<td>MR</td>
</tr>
</tbody>
</table>

*Blood pressure was measured on the right upper arm with the Riva-Rocci (RR) method: systolic/diastolic (mean).
†Gradients were measured between peak systolic pressure values at locations 2 and 6 (Figure 1A).
CoA = coarctation; CMR = cardiac magnetic resonance; Re- = recurrent.
However, the previous studies did not take the timing difference of peak systolic pressures along the aorta into account (2). This patient-specific time shift, depending on the patient’s size and vessel compliance, is related to the pulse wave velocities that exist in the investigated vessel segment. In CoA, the compliance of the aorta can be decreased and further affected by scars after surgery and/or stent implantation. In addition, in the clinical routine, systolic pressure gradients by catheterization are typically measured as peak-to-peak gradients. For these reasons, we accounted in our study for the timing differences of peak systolic pressures at the different locations.

The study was performed in a cohort of 13 patients with CoA that had moderate pressure gradients. Such patients have borderline indications for intervention and are thus the target group for applying the proposed pressure field method as an alternative to diagnostic catheterization. In borderline conditions, pressure gradients are often determined during exercise or pharmacological stress. We did not test if these conditions can be accurately quantified by the method presented here. The 6 defined anatomic positions could be slightly different between catheter- and CMR-based measurements. The segmentation was not time resolved. However, motion was accentuated at the level of the aortic annulus but less so in the distal parts of the ascending aorta, the aortic arch, and the descending aorta. Absolute pressures were measured during catheterization in sedation, whereas CMR was performed in awake patients. This can impact measurement accuracy because pressures and pressure gradients are affected by cardiac output. In the present study, we did not investigate interobserver or interstudy variability. However, previous work showed that 4D-VEC-CMR has relatively low variability.

In conclusion, in a clinical setting of coarctation, pressure fields can be accurately computed from 4D-VEC-CMR-derived flow velocities. This noninvasive technique might evolve into an alternative to diagnostic catheterization.
invasive diagnostic catheterization, with cost savings for the healthcare system, especially in patients with borderline indication for treatment.

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