Aortic function quantified: the heart’s essential cushion

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Aortic function quantified: the heart’s essential cushion. J Appl Physiol 113: 1285–1291, 2012. First published August 30, 2012; doi:10.1152/japplphysiol.00432.2012.—Arterial compliance is mainly developed by the elasticity of proximal large-conduit arteries of which the aorta is the largest contributor. Compliance forms an important part of the cardiac load and plays a role in organ (especially coronary) perfusion. To follow local changes in aortic compliance, as in aging, noninvasive determination of compliance distribution would be of great value. Our goal is to determine regional aortic compliance noninvasively in the human. In seven healthy individuals at six locations, aortic blood flow and systolic/diastolic area (ΔA) was measured with MRI. Simultaneously brachial pulse pressure (ΔP) was measured with standard cuff. With a transfer function we derived ΔP at the same aortic locations as the MRI measurements. Regional aortic compliance was calculated with two approaches, the pulse pressure method, and local area compliance (ΔA/ΔP) times segment length, called area compliance method. For comparison, pulse wave velocity (PWV) from local flows at two locations was determined, and compliance was derived from PWV. Both approaches show that compliance is largest in the proximal aorta and decreases toward the distal aorta. Similar results were found with PWV-derived compliance. Of total arterial compliance, ascending to distal arch (segments 1–3) contributes 40% (of which 15% is in head and arms), descending aorta (segments 4 and 5) 25%, and “hip, pelvic and leg arteries” 20%. Pulse pressure method includes compliance of side branches and is therefore larger than the area compliance method. Regional aortic compliance can be obtained noninvasively. Therefore, this technique allows following changes in local compliance with age and cardiovascular diseases.

arteries and is not equally distributed over the aorta (43, 46, 51, 53). It was also shown that, with age, the distribution of the elastic modulus changes over the aorta (25), implying that local changes in aortic compliance with age and arterial disease do occur but are, up until now, not easily measured noninvasively.

Total arterial compliance C is defined as arterial volume changes over transmural pressure changes (C = ΔV/ΔP). Since volume changes are difficult to obtain, several methods have been developed over the years to derive arterial compliance (45, 54). Most of the derivations require measurement of pressure and flow or pressure and stroke volume. Regional (local) aortic compliance or area compliance (Ca = ΔA/ΔP), where ΔA is systolic/diastolic area, requires measurements of pressure and aortic cross-sectional area (or diameter) at different locations.

The goal of this study is to assess the feasibility of noninvasive assessment of local aortic compliance in the human using two independent methods: one using MRI flow and the other MRI area. These two methods will be compared with the compliance as determined by pulse wave velocity (PWV).

MATERIALS AND METHODS

Seven healthy individuals were studied. All subjects gave informed consent, approval was obtained from the university hospital ethics review board, and the investigation conforms to the principles outlined in the Declaration of Helsinki.

Locations of measurement. Regional flow and area were measured at six aortic levels: 1) ascending aorta, 2) proximal aortic arch, 3) distal aortic arch, 4) descending aorta, 5) aorta at diaphragm, and at 6) aortic bifurcation (see Fig. 1).

For this localization, first an MRI image was acquired displaying both the aortic arch and the descending aorta in one image plane. This image was ECG triggered, acquired in mid-diastole of the cardiac cycle and at relaxed end expiration.

Measurements of local flows and areas. MRI was performed with a Siemens 1.5-T “Avanto” whole body scanner (Siemens Healthcare, Erlangen, Germany) equipped with a phased-array body coil. One investigator performed all magnetic resonance acquisitions.

The orientation of the image plane was orthogonal to the aorta, at the locations mentioned above and shown in Fig. 1. Phase-contrast velocity imaging was performed during continuous breathing. We performed a retrospectively ECG-gated, spoiled gradient-echo MRI sequence, with through-plane velocity encoding and a velocity sensitivity of 150 cm/s. This pulse sequence was run with the following parameters: slice thickness 6 mm, field of view 240 × 320 mm², matrix size 140 × 256, echo time 3.4 ms, temporal resolution 13.2 ms, and flip angle 25°. As one phase-encoding line per heartbeat was acquired, the measurement extended over 140 consecutive heartbeats during which the subject was breathing normally.

Phase offset errors were corrected by subtracting the velocity images measured at a stationary water-phantom using the same acquisition settings and an artificial ECG mimicking the patient’s ECG.
The next step was to identify the aortic lumen boundary. The lumen area was measured on the magnitude images, for every temporal phase during the cardiac cycle. The signal intensity was measured along 60 radial lines across the aortic wall. Along all these lines, the gradient of signal intensity is calculated, and the boundary of the lumen is detected from the steep gradient of signal intensity. The boundary detection of all 60 radial lines is then combined to form the complete lumen boundary (14). After determining this lumen boundary, the volumetric flow in milliliters per second was calculated in each temporal phase of the cardiac cycle by summing the product of velocity and pixel size over the whole cross section of the aorta.

The lumen boundary was also used to calculate the local systolic and diastolic cross-sectional area in each temporal phase of cardiac cycle at all six locations.

In this boundary detection method, only the initial position estimate of the center of the lumen is carried out by the operator; all following steps are automated. The inter- and intraobserver variability was assessed earlier in a study addressing the stroke volume derived from the aortic flow (28).

**Local pressure.** We used noninvasive pressures derived at the brachial level with standard brachial cuff suitable for MRI during the MRI procedure. From brachial pressure, the proximal aortic Ps (Psa) and Pdb were derived as first described by Kelly and Fitchett (18) as 0.6Pda (4, 6, 49), where Psb is brachial Ps. This gives for central aortic Pm (Pma). We used the following form factors (FFs) (the ratio of (Pm – Psa)/pulse pressure (PP)) to derive mean brachial Pm over PP:

\[ P_{sa} = 0.83P_{sb} + 0.15P_{db} \]  \hspace{1cm} (1)

Note that, for the methods described below to obtain compliance, wave shape are not required: only systolic and diastolic values are used.

Next we derived aortic pressures at the different locations where flows and cross-sectional area were measured. The pressure amplification along the aorta was assumed linear based on previous studies that measured pressures along the aorta invasively (26, 33, 40). These studies report, when averaged, Ps in the distal aorta at the bifurcation (Pdaa) to be \(-8\) mmHg higher than in the ascending aorta (Psa). The Pd at the bifurcation (Pdss) is \(-1\) mmHg lower than in the ascending aorta (Pdss). We then calculated Psa and Pd at the locations where blood flow and cross-sectional areas were measured as:

\[ P_s(L) = P_{ssa} + 8(L/L_{tot}) \]  \hspace{1cm} (2)

\[ P_d(L) = P_{dss} - (L/L_{tot}) \]  \hspace{1cm} (3)

with L is distance from aortic root (location 1) to measurement location, and Ltot is distance from aortic root to bifurcation (location 6). The distances, L, between two locations were assessed longitudinal in the middle of the aorta. These distances were measured on the MRI localizer image displaying both the aortic arch and the descending aorta in one image plane.

**Analysis.** Volume compliance was obtained in two ways, namely with the PP method (PPM) (44, 46) and the CA method (ACM). Finally, compliance by PWV was derived from flow measured at three locations (i.e., 2 sections) and used for comparison.

The PPM uses the two-element Windkessel model with flow waveform and peripheral resistance (Pm over mean flow) as inputs to estimate the compliance value (C_{PPM}) that best predicts Ps and Pd (44). This method gives the total compliance distal of the measurement location. By subtracting compliance at location 2 from compliance at
location 1, the segmental compliance between sites 1 and 2 is found, etc. Hence in general

$$C_{ppm,n} = C_n - C_{n+1}$$

(4)

In total, five segmental compliances are thus obtained.

The second approach, the ACM, derives local volume compliance by first calculating $C_A$, i.e., the ratio of $\Delta A/PP$, where $\Delta A$ is systolic minus diastolic area, i.e., $P_s$ minus $P_d$. By averaging the $C_A$ at two measured locations, the $C_A$ in between the two sites is obtained. Then this $C_A$ times aortic segment length between the two locations, $L_n$, gives volume compliance of the segment ($C_{segment}$).

$$C_{segment,n} = (C_{A,n} + C_{A,n+1})L_n/2$$

(5)

In total, five segmental compliances are thus obtained.

Local volume compliance is calculated from PWV ($C_{pwv}$) from the foot of the local flow, according to the formula (56):

$$C_{pwv} = A \cdot L_s/1.06 \cdot PWV^2$$

(6)

The area, $A$, was set equal to average area between the measurement sites. Since the time resolution of flow is limited, we only calculated PWV over longer lengths, namely segments 3-4 and segment 5.

**RESULTS**

Table 1 summarizes the characteristics of the seven healthy subjects, five men and two women, with an average age of $32.7 \pm 7.1$ yr, and an average body mass index of $23.4 \pm 1.6$ kg/m$^2$. All subjects had normal blood pressures. The average brachial artery pressure was $124 \pm 10$ mmHg systolic and $72 \pm 8$ mmHg diastolic. From this brachial pressure, individual ascending aorta pressures were derived (average $113 \pm 8$ and $72 \pm 8$ mmHg, systolic and diastolic, respectively). The local $P_s$ and $P_d$ were then calculated as given above. The average $P_d$ was $121 \pm 8$ and $70 \pm 8$ mmHg, systolic and diastolic, respectively.

In Fig. 1, a schematic representation and MRI image of the aorta are illustrated. In addition, an example of local flows is given.

The aortic diameters at the six locations in Fig. 1 are (systolic and diastolic, given in cm) $2.86 \pm 0.29$ and $2.55 \pm 0.32$, $2.79 \pm 0.26$ and $2.42 \pm 0.28$, $2.28 \pm 0.19$ and $2.01 \pm 0.22$, $2.25 \pm 0.2$ and $1.98 \pm 0.21$, $1.92 \pm 0.21$ and $1.62 \pm 0.21$, $1.57 \pm 0.14$ and $1.40 \pm 0.15$ cm, respectively.

In Fig. 2, top, averaged areas of the aorta are given in systole and diastole. The averaged ascending aorta area is $6.47 \pm 1.35$ cm$^2$ in systole and $5.17 \pm 1.31$ cm$^2$ in diastole. The areas decrease toward the periphery, and areas just above the bifurcation in systole and diastole are $1.94 \pm 0.35$ and $1.55 \pm 0.33$ cm$^2$, respectively.

For area change over the cardiac cycle (Fig. 2, middle), we observed that it is the highest in the proximal aortic arch ($1.49 \pm 0.39$ cm$^2$) followed by the ascending aorta ($1.30 \pm 0.41$ cm$^2$). From the distal arch to diaphragm level, the area change is more or less equal ($0.86 \pm 0.18$ cm$^2$), but is much reduced at the level of the bifurcation (average $0.40 \pm 0.13$ cm$^2$).

$C_A$ (i.e., $\Delta A/PP$) (Fig. 2, bottom) shows the same trend as the area change. $C_A$ is the largest in the proximal aortic arch and the smallest at the bifurcation.

In Fig. 3, left, the volume compliance derived with the PPM at the six locations shows a decrease from ascending aorta (average $1.54 \pm 0.44$ ml/mmHg) toward the bifurcation (average $0.30 \pm 0.10$ ml/mmHg). Note that location 6 (bifurca-

<table>
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<th>Subject No.</th>
<th>Sex</th>
<th>Age, yr</th>
<th>Length, cm</th>
<th>BMI, kg/m$^2$</th>
<th>HR, beats/min</th>
<th>Bif (Systolic/Diastolic), mmHg</th>
<th>Dist Arch (Systolic/Diastolic), mmHg</th>
<th>Desc Arch (Systolic/Diastolic), mmHg</th>
<th>Prox Arch (Systolic/Diastolic), mmHg</th>
<th>Ascend (Systolic/Diastolic), mmHg</th>
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<td>M</td>
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<td>77</td>
<td>56</td>
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<td>117/67</td>
<td>112/67</td>
<td>124/78</td>
</tr>
<tr>
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<td>M</td>
<td>38</td>
<td>197</td>
<td>95</td>
<td>61</td>
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Table 1. Characteristics of the subjects

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Volume compliance obtained with the ACM (i.e., $C_A$ times aortic segment length) is shown in Fig. 3, right, and shows a more gradual linear distribution. Overall, the values of each segment obtained with ACM are smaller than segment compliance obtained with the PPM, because compliances of the side branches are included in the PPM. This is especially clear for the compliance of segment 2 (Fig. 3, middle and right). Compliance of segment 2 obtained using the PPM includes head and arm vessels, whereas, using the $C_A$ and its length, only the compliance of the aortic part is obtained (see DISCUSSION). Thus the compliance of the head and arm arteries is 0.21 ml/mmHg, namely the difference between PPM segment 2 and $C_A$ segment 2. The compliance of “pelvic, hip, and leg arteries”, beyond location 6 (see Fig. 1), is 0.3 ± 0.09 ml/mmHg.

In Fig. 4, the relative distribution of total compliance is depicted. The fraction of total compliance of each segment is depicted for the ACM. According to the ACM, 35% is in the ascending aorta and arch, and 72% is in the ascending aorta until diaphragm level. According to the PPM, 65% of total compliance is in the entire aorta, 15% is in the arch arteries, and 20% in the “pelvic, hip, and leg arteries” (beyond aortic bifurcation).

The PWV (Fig. 5, left) assessed at the level of the abdominal aorta (segment 5) is higher compared with the descending thoracic aorta (segments 3+4). The volume compliance derived from PWV of segments 3+4 and 5 (Fig. 5, middle) is not different from the values obtained by ACM (Fig. 5, right).

DISCUSSION

The present study demonstrates that, using two new methods, it is feasible to assess local aortic compliance noninva-
sively in the human and therefore allows for studying changes in local compliance over time as in aging. We found in healthy humans that 65% of total arterial compliance is located in the aorta and thoracic and abdominal branches, of which almost 40% is in the proximal aorta (proximal ascending aorta minus distal arch). The aortic arch arteries contain 15% and the “pelvic, hip, and leg” arteries 20% of total compliance.

The decreasing arterial compliance toward the periphery is in accordance with previous studies (23, 43, 46, 53). In contrast to these studies, the present study measured aortic compliance in humans directly and noninvasively. In one study, it was shown that, in a single human isolated aorta setup (ex vivo), ~45% of total arterial systemic compliance is within the ascending and proximal descending aorta (43). A value of ~50% of total arterial compliance between aortic valve and proximal descending aorta was found by Latham et al. (23). Westerhof et al. (53) reported a value of an ~40% in the ascending aorta in an electrical model of the human arterial tree. The study by Stergiopulos et al. (46) using the PPM showed that the entire aorta contains 60–70% of the total arterial compliance, which is close to our data. Their study used invasively derived pressure and flow from dogs to determine regional compliance.

Segmental compliances derived using the PPM are higher than the values obtained using the ACM, because, with PPM, compliance of side branches is included. The arch compliance (segment 2), using the PPM (Fig. 2, middle), appears much larger than the value derived using the ACM (Fig. 2, left). This difference results from the considerable contribution of the arch branches (anonyma, common carotid artery, and left subclavian artery). Thus, from the difference in compliance of segment 2 between PPM and ACM, the compliance of the arch arteries can be estimated by subtraction, and we found that they contribute ~15% to total compliance. This is close to the value reported in the study of Westerhof et al. (53).

Aortic compliance, its effect on (systolic) blood pressure, and its association with aging (25) and various cardiovascular diseases (e.g., connective tissue disease, aortic aneurysm, chronic kidney disease, atherosclerosis, etc.) are increasingly being investigated (5, 31, 37, 41). The methods proposed in this study could thus be of value.

PWV presently is considered the gold standard as measure of aortic stiffness, mainly because of its noninvasive character (27). The advantage of using PWV is that it does not require calibrated pressures or flows to determine local proximal stiffness. With PWV based on applanation tonometry, it is possible to quantify arterial stiffness of whole thoracic and abdominal aorta, but not including the ascending aorta and proximal arch. With MRI flow and diameters/area, it is also possible to measure PWV over the entire aorta (12), but local PWVs over short segments are not accurate, because the time differences are small with respect to the temporal resolution of the MRI (38). Moreover, to calculate compliance from PWV using the Newton-Young equation (see Eq. 6), the average area over the (assumed uniform) segment is required, while aortic tapering is not negligible (1, 13, 15). The methods we propose are much less strongly dependent on temporal resolution. Our PWV-derived compliance on the basis of MRI flow agrees over longer segments fairly well with the other methods (Fig. 5) and are in line with the data of Hickson et al. (15).

The pressure wave shape changes from brachial to central aorta and from central aorta to peripheral arteries and, therefore, alters the FF. To derive $P_{sa}$ and $P_{da}$, we used averaged FFs of brachial artery and aorta according to the Kelly and Fitchett method (18). The Kelly and Fitchett method is an accepted one, and pressure amplification in the aorta is small. Nevertheless, the calculations are performed on averages, while it may depend on conditions that affect aortic elasticity (e.g., hypertension, age) (8, 9, 19). Several methods are available to measure radial (17, 20, 34) and carotid pressure waveforms (10, 20, 48) accurately by applanation tonometry. Then via a transfer function for radial pressure (16, 18), and after calibration of either waveform, the FF is required to obtain central $P_{sa}$ and $P_{d}$ (18, 34, 36). An alternative for the transfer function is through the assumption that integrated $P_{sa}$ and $P_{d}$ are the same at peripheral and central sites, to calculate central $P_{sa}$ and PP (34, 36). Another method is the finger pressure, which is a calibrated peripheral pressure and only requires a (generalized) transfer function to obtain central aortic pressure magnitude and wave shape (47).

$P_{sa}$ and $P_{d}$ in the aorta are based on assumed aortic amplifications estimated from an assumed linear relation based on experimental data. It should be emphasized that, for both of our proposed methods (which assume constant FF of 33% at the brachial artery and 40% at the ascending aorta), only $P_{sa}$ and $P_{d}$ are required, not pressure wave shape.

The PPM is, compared with the ACM, more difficult to obtain local compliance, because it is sensitive to flow wave shape, whereas the ACM requires only vessel size (e.g., diameter or area change) and PP. In addition, as stated above, the PPM considers the aorta and the vascular bed beyond the measurement site (i.e., side branches), and the ACM is limited...
to the aortic segments only. Thus these differences of the two methods give complementary information, since the differences between them give information on the distal beds.

**Limitations.** A constant FF to derive central $P_a$ and $P_d$ from brachial pressures was used. However, the FF is influenced by age, sex, hypertension, etc. (8, 9, 19, 25). The $P_e$ and $P_{da}$ are assumed to relate linearly with distance over the aorta with a general amplification (distal $P_e$ and $P_{da}$ 8 mmHg higher and 1 mmHg lower than proximal aortic pressure, respectively). The amplification over the aorta in principle could be individualized by measuring iliac pressures with MRI-compatible upper leg cuff, as an estimate of distal aortic pressure. Furthermore, compliance derived from PWV assumes a uniform (constant diameter, branchless) tube, while the human aorta is known to be tapering.

In conclusion, this study demonstrates the feasibility to assess regional arterial compliance noninvasively in the human. The methods presented here allow following local aortic compliance changes over time noninvasively and may give information of treatment and give insight how (old age) hypertension and cardiovascular diseases relate to changes in local and total arterial compliance.

**DISCLOSURES**

No conflicts of interest, financial or otherwise, are declared by the author(s).

**AUTHOR CONTRIBUTIONS**

Author contributions: N.S., A.V.N., and N.W. conception and design of research; N.S. and J.T.M. performed experiments; N.S. and N.W. analyzed data; N.S., A.V.N., and N.W. interpreted results of experiments; N.S. and N.W. prepared figures; N.S., A.V.N., and N.W. drafted manuscript; N.S., J.T.M., A.V.N., and N.W. edited and revised manuscript; N.S., J.T.M., and N.W. approved final version of manuscript.

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