Measurement of total pulmonary arterial compliance using invasive pressure monitoring and MR flow quantification during MR-guided cardiac catheterization

Vivek Muthurangu,1 David Atkinson,1 Maxime Sermesant,1 Marc E. Miquel,1 Sanjeet Hegde,1 Robert Johnson,1 Rado Andriantsimiana,1 Andrew M. Taylor,1,3 Edward Baker,2 Robert Tulloh,2 Derek Hill,1 and Reza S. Razavi1,2

1Cardiac MR Research Group, Division of Imaging Sciences, King’s College London; 2Department of Congenital Heart Disease, Guy’s Hospital; and 3Cardiothoracic Unit, Institute of Child Health and Great Ormond Street Hospital, London, United Kingdom

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Measurement of total pulmonary arterial compliance using invasive pressure monitoring and MR flow quantification during MR-guided cardiac catheterization. Am J Physiol Heart Circ Physiol 289: H1301–H1306, 2005. First published May 6, 2005; doi:10.1152/ajpheart.00957.2004.—Pulmonary hypertensive disease is assessed by quantification of pulmonary vascular resistance. Pulmonary total arterial compliance is also an indicator of pulmonary hypertensive disease. However, because of difficulties in measuring compliance, it is rarely used. We describe a method of measuring pulmonary arterial compliance utilizing magnetic resonance (MR) flow data and invasive pressure measurements. Seventeen patients with suspected pulmonary hypertension or congenital heart disease requiring preoperative assessment underwent MR-guided cardiac catheterization. Invasive manometry was used to measure pulmonary arterial pressure, and phase-contrast MR was used to measure arterial flow. The calculated pulmonary arterial pressure and flow. The calculated ratio of stroke volume to pulse pressure. There was good agreement between the two estimates of compliance (r = 0.89, P < 0.001). However, in response to 20 ppm nitric oxide, NO), total arterial compliance was calculated using the pulse pressure method (parameter optimization of the 2-element windkessel model) and the ratio of stroke volume to pulse pressure. There was good agreement between the two estimates of compliance (r = 0.89, P < 0.001). However, there was a systematic bias between the ratio of stroke volume to pulse pressure and the pulse pressure method (bias = 61%, upper level of agreement = 84%, lower level of agreement = 38%).

In response to 20 ppm NO, there was a statistically significant fall in resistance, systolic pressure, and pulse pressure. In seven patients, total arterial compliance increased >10% in response to 20 ppm NO. As a population, the increase did not reach statistical significance. There was an inverse relation between compliance and resistance (r = 0.89, P < 0.001) and between compliance and mean pulmonary arterial pressure (r = 0.72, P < 0.001). We have demonstrated the feasibility of quantifying total arterial compliance using an MR method.

Address for reprint requests and other correspondence: R. Razavi, 5th Floor, Guy’s Hospital, London SE1 9RT, UK (E-mail: reza.razavi@kcl.ac.uk).

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Innovative Methodology

H1302 A METHOD TO ASSESS PULMONARY ARTERIAL COMPLIANCE

this previous work to evaluate the feasibility of calculating total arterial compliance in humans undergoing MR-guided cardiac catheterization. In this study, compliance was calculated using the pulse pressure method and the ratio of stroke volume to pulse pressure. In addition, measurement of other pulmonary hemodynamic parameters allowed a preliminary study of the relation between compliance and resistance and between compliance and pressure, particularly in response to NO.

MATERIALS AND METHODS

Study population. The study population consisted of 17 children and adults [mean 9.58 yr of age (SD12.95)]; inclusion criteria were suspected pulmonary hypertension or congenital heart disease requiring preoperative assessment. Twelve patients had suspected pulmonary arterial hypertension secondary to a congenital systemic-to-pulmonary shunt, three had pulmonary hypertension associated with disorders of the respiratory system, one patient had pulmonary arterial hypertension associated with human immunodeficiency virus infection, and one had pulmonary venous hypertension secondary to repaired mitral stenosis. All patients were in class I or II in the World Health Organization stratiﬁcation of pulmonary hypertension. There is overlap with the patient population from our previous study, in which the feasibility of measuring pulmonary vascular resistance with MR-guided cardiac catheterization was evaluated. However, patients were excluded if previous surgery of the pulmonary artery had been performed. All patients were in sinus rhythm. The study was approved by the Local Research Ethics Committee. Informed consent was given by the patient or a parent/guardian (patients <16 yr of age).

Cardiac catheterization. Subjects underwent cardiac catheterization in an MR interventional suite (maximum gradient performance = 30 mT/m amplitude, slew rate = 150 T/m·s−1; 1.5-T Intera I/T MRI scanner, Philips Medical Systems) with X-ray backup (BV Pulsera cardiac X-ray unit, Philips Medical Systems) in the same room (XMRI suite). General anesthesia was induced and maintained with propofol. The catheter was advanced under MR guidance or with a combination of X-ray and MR guidance, depending on ease of catheter manipulation. Angiographic catheters (4- to 6-Fr) with CO2-filled balloons were used for all procedures, allowing visualization in both imaging modalities. Hemodynamic variables were collected at 30% O2 (condition 1) and at 20 ppm NO + 30% O2 (condition 2). MR catheter visualization. All imaging was performed using an adult or pediatric two-element receive-only phased-array radio-frequency coil (Flex L or Flex M, Philips Medical Systems); transmission was performed using the body coil. An interactive steady-state free precession sequence (TR = 2.9 ms, TE = 1.45 ms, matrix = 128 × 128, field of view = 250–350 mm, 10–14 frames/s, flip angle = 45°, slice thickness = 6–8 mm, free breathing acquisition) was used to visualize the catheter balloon during manipulation within the heart and great vessels. The imaging plane could be manipulated in real time into any plane to follow the catheter (17).

Flow and pressure quantification. Pulmonary arterial ﬂow data were acquired using a ﬂow-sensitive, fast-ﬁeld echo sequence (TR = 9 ms, TE = 5 ms, matrix = 128 × 192 × 256, ﬁeld of view = 250–350 mm, ﬂip angle = 15°, slice thickness = 5–7 mm, free breathing acquisition). 3 signal averages, retrospective gating, 40 phases in plane and through-plane resolution optimized to patient size). A dedicated nonlinear phase-correction ﬁlter, based on Chebichev polynomials (Philips Medical Systems), was used to correct for phase errors introduced by eddy currents and Maxwell terms. In addition, the image plane was centered in the bore of the magnet to further reduce the phase errors. Image planes were located at the midpoint of the pulmonary artery. Systolic pressure (P systole), diastolic pressure (P diastole), and mean pressure (P mean) were collected during MR ﬂow data acquisition by means of standard ﬂuid-ﬁlled catheters coupled to a computerized data-recording system, with a quoted measurement error of ±2 mmHg (S5 collect system, Datex Ohmeda). Pulse pressure (P pulse) was calculated as P systole − P diastole.

Data analysis. Pulmonary blood ﬂow and stroke volumes were generated from phase-contrast MR data using a semiautomatic vessel edge-detection algorithm (Flow, Medis) with operator correction. Pulmonary artery cardiac output is the product of pulmonary blood stroke volume and heart rate. Resistance (R) was calculated by dividing mean pulmonary arterial pressure by the pulmonary artery cardiac output and indexing to body surface area (23).

Calculation of total arterial compliance and elastance. The equation defining the two-element windkessel model is as follows (16)

\[
Q(t) = \frac{P(t)}{R} + \frac{dP(t)}{dt}
\]

where P is pressure and C is total arterial compliance. A flow curve [Q(t)] with 50 cardiac cycles was constructed by repeating the same cardiac cycle phase-contrast MR ﬂow curve. Q(t) was used as an input to the windkessel model. R was a known variable for each patient at each condition and was entered into the model. For a given C, the equation was integrated using P(0) = 0 as an initial condition, generating a 50-cardiac-cycle pressure curve. The modeled P systole and P diastole are the minimum and maximum pressures between the 40th and 50th cycles, at which point the pressure curve has stabilized and is independent of initial conditions. The modeled P pulse = modeled P systole − modeled P diastole. A series of pressure curves were generated using values of C between 0.001 and 7 ml/mmHg. The modulus of the difference between the modeled P pulse and the invasively measured P pulse was calculated, and an error plot was produced. The compliance that coincides with the global minimum of the error plot is taken as the best estimate of C, which was indexed to body surface area (which we call C mean). All windkessel modeling was performed using Matlab (Mathworks). Elastance (E) is the inverse of C.

Statistical analysis. Values are means (SD) unless otherwise stated. A two-tailed t-test was used to compare the hemodynamic responses to NO. A two-tailed t-test, correlation coefﬁcients, linear regression analysis, and Bland-Altman analysis (7) were used to compare C ppm with C sv. Bias was the mean of the difference between the two methods, and agreement was the mean (2SD). P < 0.05 was taken as statistically signiﬁcant. Correlation coefﬁcients and linear regression analysis were also used to study the relation between steady-state hemodynamic variables and compliance. Statistical analysis was performed using Matlab.

RESULTS

Feasibility. In nine patients, catheterization of the pulmonary artery was achieved under MR guidance alone. In the other eight patients, the catheter was advanced using a combination of X-ray and MR guidance. Simultaneous invasive pressure and phase-contrast MR data (Fig. 1) were obtained in all 17 patients in conditions 1 and 2. Total arterial compliance in all patients in both conditions was calculated using the pulse pressure method and the ratio of stroke volume to pulse pressure.

Pulmonary hemodynamics: response to 20 ppm NO. Pulmonary hemodynamic parameters (P mean, P systole, P diastole, P pulse, Q, and R) in conditions 1 and 2 are shown in Table 1. At baseline, pulmonary arterial pressures and resistance were raised compared with the normal quoted range. There were statistically signiﬁcant declines in R, P systole, and P pulse in response to 20 ppm NO.

Arterial compliance: C ppm vs. C sv. The mean C ppm and C sv in conditions 1 and 2 are shown in Table 1. Correlation between C ppm and C sv (Fig. 2) was excellent in condition 1 (r = 0.99,
and lower level of agreement between condition 2; and bias $/H11005$ ($r$).

Mean pulmonary hemodynamic parameters (Table 1).

![Fig. 1. Simultaneously flow acquired (measured using phase-contrast MR) and pulmonary arterial pressure (measured using a catheter in the main pulmonary artery).](image)

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Significance is $P$. There was a significant difference between mean $C_{ppm}$ and $C_{sv}$ ($P < 0.05$).

Compliance: response to 20 ppm NO. An increase of $\geq 10\%$ was considered a response to NO (30). A response in $C_{ppm}$ was demonstrated in 7 of 17 patients and in $C_{sv}$ in 9 of 17 patients.

Relation between steady-state hemodynamic variables and compliance. As pulmonary hypertensive disease worsens, compliance is thought to decrease. Thus $R$ and $P_{mean}$ were correlated with $1/C_{ppm} = E$, rather than $C_{ppm}$ (Figs. 4 and 5). There was good correlation between $R$ and $E$ in condition 1 ($r = 0.86$, $P < 0.001$, $m = 0.54, c = -0.22$), condition 2 ($r = 0.92, P < 0.001, m = 0.56, c = -0.19$), and overall ($r = 0.89, P < 0.001, m = 0.55, c = -0.20$). There was moderate correlation between $P_{mean}$ and $E$ in condition 1 ($r = 0.72, P < 0.001, m = 12.6, c = 15.5$), condition 2 ($r = 0.73, P < 0.001, m = 14.0,$ $c = 15.5$).

Table 1. Mean pulmonary hemodynamic parameters in conditions 1 and 2

<table>
<thead>
<tr>
<th>Condition</th>
<th>Condition 2</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$P_{cystolic}$, mmHg</td>
<td>52.3 (24.1)</td>
<td>49.2 (23.7)</td>
</tr>
<tr>
<td>$P_{diastolic}$, mmHg</td>
<td>20.4 (12.2)</td>
<td>20.3 (12.2)</td>
</tr>
<tr>
<td>$P_{pulsec}$, mmHg</td>
<td>31.9 (15.0)</td>
<td>28.9 (14.5)</td>
</tr>
<tr>
<td>$P_{mean}$, mmHg</td>
<td>33.7 (16.1)</td>
<td>32.8 (16.9)</td>
</tr>
<tr>
<td>$Q$, ml/s$^{-1}$·m$^{-2}$</td>
<td>84.0 (45.6)</td>
<td>87.0 (42.2)</td>
</tr>
<tr>
<td>SV, ml/m$^{-2}$</td>
<td>50.9 (27.4)</td>
<td>51.7 (25.6)</td>
</tr>
<tr>
<td>$R$, mmHg·ml$^{-1}$·s·m$^{-2}$</td>
<td>0.56 (0.58)</td>
<td>0.50 (0.51)</td>
</tr>
<tr>
<td>$C_{ppm}$, ml·m$^{-2}$·mmHg$^{-1}$</td>
<td>0.99 (0.68)</td>
<td>1.06 (0.58)</td>
</tr>
<tr>
<td>$C_{sv}$, ml·m$^{-2}$·mmHg$^{-1}$</td>
<td>1.87 (1.28)</td>
<td>2.01 (0.99)</td>
</tr>
</tbody>
</table>

Values are means (SD). $P_{mean}$, mean pulmonary arterial pressure; $P_{cystolic}$, systolic pulmonary arterial pressure; $P_{diastolic}$, diastolic pulmonary arterial pressure; $P_{pulsec}$, pulse pressure; $Q$, pulmonary artery flow; SV, stroke volume; $R$, resistance; $C_{ppm}$, pulse pressure compliance; $C_{sv}$, ratio of SV to $C_{ppm}$. Significance is $P < 0.05$.

![Fig. 2. Scatter plot of compliance estimated using the ratio of stroke volume to pulse pressure ($C_{sv}$) and the pulse pressure method ($C_{ppm}$). Plotted line represents line of regression.](image)

Fig. 2. Scatter plot of compliance estimated using the ratio of stroke volume to pulse pressure ($C_{sv}$) and the pulse pressure method ($C_{ppm}$). Plotted line represents line of regression.

![Fig. 3. Bland-Altman plot of percent difference between $C_{ppm}$ and $C_{sv}$ vs. average of $C_{sv}$ and $C_{ppm}$. Bias is the mean percent difference; limits of agreement are bias (2SD) of percent difference.](image)

Fig. 3. Bland-Altman plot of percent difference between $C_{ppm}$ and $C_{sv}$ vs. average of $C_{sv}$ and $C_{ppm}$. Bias is the mean percent difference; limits of agreement are bias (2SD) of percent difference.
arterial compliance (23). The pulse pressure method is based on parameter estimation of a two-element windkessel model and has been found to be an accurate method of calculating the total arterial compliance in the pulmonary (23) and systemic vasculatures (27–29). It does not require measurement of a detailed pressure curve or zero flow conditions in diastole and is well suited to patients with pulmonary hypertension (29). This method requires measurement of volume flow as a function of time (flow curves), pulse pressure, and vascular resistance \((R)\). In the pulmonary artery, pressure can be measured at catheterization with invasive manometry. In animal studies, perivascular flow probes can be used to accurately measure flow curves (23); unfortunately, use of such methods is difficult in humans. In humans, blood flow velocity curves can be measured invasively (15) or noninvasively (14, 30). Combining this data with a measurement of cardiac output (using an indicator-dilution method) allows generation of flow curves (14, 15, 30). However, inaccuracies in measurement of cardiac output by indicator-dilution methods (10, 11) and measurement of blood flow velocities can lead to errors in measurement of volume flow.

**MR-guided cardiac catheterization.** Velocity-encoded phase-contrast MR is a validated technique that enables measurement of flow curves in major vessels (3, 4, 18). It is therefore well suited to generate flow curves for estimation of pulmonary arterial compliance by the pulse pressure method. MR-guided cardiac catheterization is a new technique that allows greater access to physiological and anatomic information (20). We previously demonstrated the feasibility of simultaneously acquiring phase-contrast MR and invasive pressure data in patients undergoing MR-guided cardiac catheterization to calculate pulmonary vascular resistance (18). In this study, we have used these data to calculate total arterial compliance by the pulse pressure method and as the ratio of stroke volume to pulse pressure.

**Total arterial compliance.** We have demonstrated the feasibility of calculating total pulmonary arterial compliance in patients undergoing MR-guided cardiac catheterization. As reported in other studies, \(C_{sv}\) was consistently higher than \(C_{ppm}\) (23). It is believed that \(C_{sv}\) overestimates total arterial compliance, inasmuch as it assumes that the total stroke volume is buffered in the arteries (23). In fact, the volume buffered in the arteries is the stroke volume minus the arterial outflow volume.
during ejection. Our results demonstrated excellent correlation between $C_{sv}$ and $C_{ppm}$ in conditions 1 and 2 and overall, as well as good correlation between the percent change in $C_{sv}$ and $C_{ppm}$, in agreement with previous studies (23). These results suggest that $C_{ppm}$ is a precise estimate of true arterial compliance, although we are unable to verify its accuracy, inasmuch as there is no in vivo “gold standard” method of measuring arterial compliance. However, previous work using models of the arterial system has shown $C_{ppm}$ to be an accurate estimate of total arterial compliance (27).

**Relation to hemodynamic variables and response to NO.** Our results show that, within our study population, $R$ and $P_{mean}$ are inversely related to $C_{ppm}$, with good to moderate correlation. There are two possible explanations for these findings: 1) Vascular remodeling, which leads to an increase in $R$ and, thus, in $P_{mean}$, causes vessel distension and reduced compliance. Studies have shown that reduced compliance in systemic arteries is secondary to distension. 2) Vascular remodeling occurs in the large conduit arteries as well as the resistance arteries as part of the pulmonary hypertensive disease process. Vessel wall thickening in large pulmonary arteries has been demonstrated using intravascular ultrasound and is associated with decreased vessel compliance (6, 22). It is probable that both factors contribute to the relation between $R$, $P_{mean}$, and $C_{ppm}$. However, the strong correlation between $P_{mean}$ and $C_{ppm}$ do suggest that distension of the conduit arteries is an important factor. To fully understand the relation between $R$, $P_{mean}$, and $C_{ppm}$, this technique will need to be performed on a larger group of patients with pulmonary hypertensive disease.

Inhaled NO acts on pulmonary vascular smooth muscle, causing smooth muscle relaxation (12). NO causes a fall in resistance due to vasodilation of resistance arteries. In this study, we have demonstrated a hemodynamically significant increase in $C_{ppm}$ in response to NO in seven patients. However, the population change was small and not statistically significant. There was mild correlation between the percent change in $R$ and $1/C_{ppm}$. A possible explanation for these findings is that a decrease in $R$ leads to a decrease in $P_{mean}$, causing less distension and an increase in $C_{ppm}$. In this study group, there was little correlation between the percent change in $P_{mean}$ and $1/C_{ppm}$. Therefore, increase in compliance in response to NO cannot be explained purely in terms of reduced distension. Another explanation is that NO decreases resistance and increases compliance through its actions on smooth muscle distributed throughout the pulmonary vasculature. However, it should be noted that inhaled NO may not have significant bioavailability in the large conduit arteries.

**Limitations.** Phase-contrast MR flow is less accurate in patients with arrhythmias during acquisition and/or turbulent blood flow; the presence of these conditions is a general limitation of this technique, however, we did not encounter these events in our study. We did not repeat previous work internally validating phase-contrast MR in our patient population, inasmuch as we did not wish to prolong the procedure times. The study population was small and inhomogeneous. In addition, the change in hemodynamic parameters in response to NO was limited, possibly because of general anesthesia. This population was sufficient to prove the feasibility of this technique. However, study of the relation between the various hemodynamic parameters was hampered.

**Conclusion.** Using simultaneously acquired invasive pressure measurements and MR flow data, we have demonstrated the feasibility of quantifying total arterial compliance. This additional information can be combined with information regarding resistance to tailor patient management, particularly with the advent of new medical therapies. With proof of the feasibility of this technique, it will be possible to investigate the relation between compliance and other hemodynamic parameters in a larger more homogeneous population. In our facility, cardiac catheterization was accomplished by MR guidance with X-ray backup. Pulmonary artery catheterization can be accomplished without imaging before MR scanning, thus potentially allowing this technique to be used in a conventional cardiac MR scanner. Further investigation using this technique is required to fully elucidate the relation between compliance, pulmonary hypertensive disease, and medical intervention. In conclusion, we believe that measurement of pulmonary arterial compliance will give new insights into the pathophysiology of pulmonary hypertension and may be important in assessing suitability for long-term medical therapy.

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**DISCLOSURES**

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**REFERENCES**


