Does parallel conductance vary during systole in the human right ventricle?

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Abstract

Objectives: Right ventricular (RV) contractile performance remains poorly characterised, particularly in humans. Conductance catheter techniques have the potential to overcome the geometric difficulties in RV volume measurement that have hindered systematic studies of RV pressure volume relations. The present study examines changes in parallel conductance (Vc) that may occur during the cardiac cycle in the human right ventricle. Methods: Using signals obtained from custom-built conductance catheters, six isochronal systolic values of Vc (Vc(t)) were measured during hypertonic saline wash-in. Studies were performed in nine patients undergoing right heart catheterisation. Their ages ranged from 7 to 39 years (median = 16) and their weights ranged from 20.3 to 84.7 kg (median = 50.0 kg). Measurements of mean Vc and isochronal Vc(t) and its variability during systole were assessed. Mean Vc was measured using the Baan technique (Vc(Baan)), Vc(t) was measured from six systolic isochrones obtained during the same period of hypertonic saline wash-in. Results: The temporal changes in Vc(t) were small (mean 5.8%, median = 4.4%, range = 0.6-17.9%) of total corrected end-diastolic volume (mean maximal variation of 7.7 ml). The value of Vc(t) obtained at dp/dtmax (mean = 99.1 ml; median = 104.75 ml; range 20.15-196.7 ml) was not significantly different to that obtained at dp/dtmin (mean = 100.0 ml; median = 110.87 ml; range = 20.0-204.2 ml) (P > 0.05), but both were higher than the single Vc measurement (Vc(Baan)) obtained using the standard approach (P = 0.02). The correlation between Vc(Baan) and Vc(t) for group data; (Vc(Baan) = 89.69 ml, s.d. = 43.73 ml; Vc(T) = 98.16 ml, s.d. = 50.16 ml) produces a regression slope of 0.99 for all studies (P = 0.02). Conclusion: We conclude that parallel conductance does vary during systole in the human right ventricle of adults and older children after repair of congenital abnormalities but there is no significant difference in Vc(t) between dp/dtmax and dp/dtmin. However, there was a significant difference when the isochronal Vc(t) measurement is compared with the standard single value technique (Vc(Baan)) obtained using the hypertonic saline wash-in method. The excellent correlation between Vc(T) and Vc(Baan) suggests that the correction of Vc for the phase of the cardiac cycle is unnecessary for most purposes when studying the human right ventricle.

Keywords: Parallel conductance; Conductance catheter; Human; Pressure-volume area

1. Introduction

Right ventricular (RV) contractile performance remains poorly characterised, particularly in humans. Measurement of ventricular volume is important in the investigation of ventricular function and the description of changes in left ventricular volume related to time and pressure has been fundamental in the development of current concepts of left ventricular performance. Numerous techniques have been used to measure right ventricular volume [1-5], but most require geometric assumptions and labour intensive off-line image contouring. The conductance technique has been developed to enable a real time, beat to beat assessment of left ventricular volume [6-9] and is a potentially useful technique for continuous measurement of right ventricular volume.
We have previously shown that a conductance catheter can reliably measure the volume of right ventricular models made from human post-mortem hearts [10]. A drawback of this technique in vivo is that structures such as the myocardium and left ventricular blood pool also conduct current, a phenomenon known as parallel conductance (Vc). There is no systematic evaluation of Vc in the human left or right ventricle and validation is needed to determine its stability during the cardiac cycle. The hypertonic saline wash-in technique for determining parallel conductance has been widely reported for the left ventricle in animal models [8,11]. This technique yields a single value for parallel conductance volume, Vc(Baan), i.e., it assumes no significant variation during the cardiac cycle. Animal studies have suggested that any such variation is insignificant in the left ventricle [12,13] but there are no data currently available for the right.

In this study we present a method of determining parallel conductance throughout the systolic phase of the cardiac cycle to investigate the potential variation of Vc in the human right ventricle.

2. Method

2.1. Preparation

Studies were performed in nine patients undergoing cardiac catheterisation for a variety of clinical conditions. Their ages ranged from 7 to 39 years (median = 16 years) and their weights ranged from 20.3 to 84.7 kg (median = 50.0 kg). There were seven males and two females. All patients were in sinus rhythm. Patient characteristics are detailed in Table 1. All had undergone surgical or transcatheter treatment of congenital heart defects and were being re-evaluated as part of their routine follow-up. None had any evidence of residual intra- or extracardiac shunting, outflow tract obstruction, atriointerventricular valve regurgitation or myocardial dysfunction. This study was approved by the hospital ethics committee and informed written consent was obtained from all patients. The investigation conforms with the principles outlined in the Declaration of Helsinki [14]. All subjects were sedated, intubated and receiving intermittent positive pressure ventilation at the time of study. A 2.5 French Millar micromanometer (Millar Instruments Inc., Houston, TX, USA) and a 5 or 7 French custom-built “8-electrode” conductance catheter (Cordis-Webster, Roden, The Netherlands) with an appropriate total interelectrode distance to match the length from the apex to the tricuspid valve (range 5–8 cm), was advanced via the femoral vein into the right ventricle and positioned with the distal end in the apex. The catheter size was selected so that the most proximal electrode of the conductance catheter was at the level of the tricuspid valve. Correct placement of the conductance catheter was achieved mainly by fluoroscopy and verified by monitoring segmental volume phase relationships and counterclockwise pressure-volume loop genesis. The conductance catheter was connected to a Sigma 5 DF signal conditioning and processing unit (Cardiodynamics, The Netherlands). Analogue signals representing the five segmental conductances, left ventricular pressure and ECG were digitised (12 bit, 250 Hz), monitored on line and stored on a microcomputer for later analysis using custom software.

2.2. Conductance catheter

The principles of the conductance technique to estimate ventricular volume have been described in detail elsewhere and extensively evaluated in the left ventricle [7–9]. Briefly, the conductance catheter method to determine ventricular volume is based on the measurement of the electrical conductance of blood in a ventricular cavity. The conductance catheter used in all measurements had eight equally spaced platinum ring electrodes.

An electric current of 20 kHz and 30 μA is applied between the two outermost electrodes (electrodes 1 and 8) to generate an intracavitary electric field. The remaining electrodes are used to measure the potential difference and therefore derive the time varying conductance (Gt) of five ventricular segments. Total right ventricular conductance is calculated as the sum of the segmental conductances. The

Table 1

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (years)</th>
<th>Weight (kg)</th>
<th>Sex</th>
<th>Clinical condition (repaired)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>15</td>
<td>40.95</td>
<td>M</td>
<td>PA + VSD</td>
</tr>
<tr>
<td>2</td>
<td>16</td>
<td>20.00</td>
<td>M</td>
<td>PS + PR</td>
</tr>
<tr>
<td>3</td>
<td>7</td>
<td>20.30</td>
<td>M</td>
<td>AVSD + Fallots</td>
</tr>
<tr>
<td>4</td>
<td>18</td>
<td>59.15</td>
<td>M</td>
<td>Fallots</td>
</tr>
<tr>
<td>5</td>
<td>30</td>
<td>84.70</td>
<td>M</td>
<td>Fallots + PS + PR</td>
</tr>
<tr>
<td>6</td>
<td>21</td>
<td>80.10</td>
<td>F</td>
<td>Fallots</td>
</tr>
<tr>
<td>7</td>
<td>39</td>
<td>38.05</td>
<td>F</td>
<td>PS + Fallots + VSD</td>
</tr>
<tr>
<td>8</td>
<td>16</td>
<td>60.00</td>
<td>M</td>
<td>Fallots</td>
</tr>
<tr>
<td>9</td>
<td>14</td>
<td>46.00</td>
<td>M</td>
<td>PS + Pulmonary valvotomy</td>
</tr>
</tbody>
</table>

PA = pulmonary atresia; VSD = ventricular septal defect; PS = pulmonary stenosis; PK = pulmonary regurgitation; AVSD = atriointerventricular septal defect; Fallots = tetralogy of fallot.
relationship between time varying volume ($V_t$) with $G_t$ is given by the simple formula [7]:

$$V_t = \frac{1}{\alpha} \cdot L^2 \cdot \rho(G_t - G_p)$$

(1)

Where $\alpha$ is the dimensionless slope factor, $\rho$ is the specific conductivity of blood measured from a blood sample, $L$ is the interelectrode distance and $G_p$ is the parallel conductance. Left and right ventricular tissue, fluid and the associated pericardial tissues also contribute to the total measured conductance. The offset volume, $V_c$, caused by the parallel conductance, $G_p$, is equal to

$$V_c = \frac{1}{\alpha}(L^2 \cdot \rho)G_p$$

(2)

2.3. Vc estimation

Determination of a value for the volume offset due to parallel conductance ($V_c(Baan)$) was performed by a dilution technique previously described by Baan et al. [6], whereby the conductivity of the blood was transiently increased by a bolus injection of hypertonic saline (1–3 ml of 10%) into the femoral vein. After a short period of time the blood-saline mixture entered the right ventricle causing an increase in the right ventricular conductance and perceived increase in amplitude of the volume signal (Fig. 1A). The principal assumption inherent in this method is that infusion of a small bolus of hypertonic saline increases the blood conductivity but not the volume of blood in the right ventricular cavity, while the conductivity of surrounding structures remains constant. From the conductance signal, the two most easily identified points from each successive cycle are the points of maximum ($V_{es}$ or end-diastolic) and minimum ($V_{ed}$ or end-systolic) volume according to

$$V_{es} = mV_{ed} + b$$

(3)

Where $V_{es} = \text{end systole}$ and $V_{ed} = \text{end diastole}$, $m =$ slope, $b =$ y-intercept.

As actual stroke volume is constant, changes in these conductance values are due to altered blood conductivity and not volume. $V_{max}$ is plotted against the subsequent $V_{min}$ of each beat during the ascending phase of the saline wash-in. The theoretical relationship between EDV and ESV represents a straight line thus we perform linear regression analysis on ESV and EDV. This line is used to extrapolate to the line of identity (A'). The volume at this point represents $V_c(Baan)$ (B') (Fig. 1B). This volume is the result of current conducted through structures surrounding the right ventricle equals ($V_c(Baan)$) by:

$$V_c(Baan) = b/(1 - m)$$

(4)

Fig. 2. Pressure volume loops obtained during a saline wash-in technique. The perceived volume increase is due to the increasing conductivity created by hypertonic saline.

where $V_c(Baan) =$ parallel conductance, $b =$ y-intercept, $m =$ slope

2.4. Vc(t)

The method described by Baan et al. [6] yields a single value based on measurements taken at end systole and diastole. This does not take into account potential changes during the cardiac cycle. To assess variability of parallel conductance in the right ventricle multiple estimates were obtained during systole using a method previously described in dogs and mini-pigs in the left ventricle [12,13]. Briefly, the systolic portion of four consecutive cardiac cycles from a hypertonic saline wash-in was divided into six equal time intervals (isochrones) from $dp/dt_{max}$ to $dp/dt_{min}$ and the apparent ventricular volume of each point was obtained by interpolation from the raw data.

The data were then plotted as ventricular volume versus stroke volume for each cardiac cycle. Thus ventricular volume at each isochronal point can be linearly regressed against stroke volume. The volume where the regression line intercepts the y-axis corresponding to zero stroke volume or conductivity corresponds to the parallel conductance volume at each time interval ($V_c(t)$). If there were no change in $V_c(t)$ then the intercept would be identical for each isochrone.

2.5. Protocol

Arterial, right atrial and pulmonary artery pressures and ECG were continuously monitored. Having obtained an optimum conductance catheter position in the right ventricle, blood resistivity, $\rho$, was measured and entered into the signal conditioning and processing unit along with the
interelectrode distance. Parallel conductance was measured during the injection of 3 ml of 10% saline into the femoral vein during continuous data acquisition. If ectopy occurred during data collection, we performed another injection in order to obtain at least two acceptable recordings. If changes in heart rate or ventricular pressure were apparent during the saline injection, the injection was repeated with a smaller volume. Each dataset was acquired for approx. 20 s during suspended ventilation.

2.6. Data analysis / statistics

The significance of variation from the mean of six isochronal values of \( V_c(t) \) during systole was assessed using analysis of variance. The \( V_c(t) \) values obtained at \( d_p/dt_{\text{max}} \) were also compared directly to those at \( d_p/dt_{\text{min}} \) using a paired sample \( t \)-test. The possibility of a relationship between the absolute measurement of \( V_c(\text{Baan}) \) and its deviation during the cardiac cycle was assessed by linear regression. The null hypothesis was rejected when \( P < 0.05 \).

3. Results

Fig. 2 shows an example of the pressure volume loops recorded after injecting 3 ml of hypertonic saline into the femoral vein. The single value technique yielded values of \( V_c(\text{Baan}) \) which ranged from 19 to 166.4 ml (median = 99 ml, s.d. = 43.75 ml). The correlation coefficients (\( r \)) of the relationship when \( V_{\text{max}} \) is plotted against the subsequent \( V_{\text{min}} \) to obtain \( V_c(\text{Baan}) \) ranged from 0.80 to 0.99 (mean = 0.93, s.d. = 0.07).

The time varying \( V_c(t) \) determination was obtained from each of six isochrones during the systolic portion of the cardiac cycle (Fig. 3). Each of the lines displayed on the graph represents one of the isochrones ranging from minimum to maximum \( d_p/dt \) and the numerical value is reflected by the \( y \)-intercept for each regression line. Isochrone 1 represents maximum positive \( d_p/dt \) and isochrone 6, minimum \( d_p/dt \). Each isochrone in between can be identified from its \( y \)-intercept. The six \( V_c(t) \) values, \( V_c(t) \) at \( d_p/dt_{\text{min}} \) and \( d_p/dt_{\text{max}} \) and from the normal saline technique (\( V_c(\text{Baan}) \)) are summarised in Table 2. The close correlation between \( V_c(\text{Baan}) \) and \( V_c(t) \) for group data (\( V_c(\text{Baan}) = 89.69 \text{ ml, s.d.} = 43.74 \text{ ml;} \ 0.60 \text{ to } 1.90 \text{ ml} \text{ above the mean; } V_c(t) \) mean decreased to a minimum of \(-2.60 \text{ ml} \text{ at midystole changing to } 1.90 \text{ ml} \text{ at max} \) in this study of left ventricular pressure-volume relationships in animals [8,15,16] and adults with a variety of heart diseases [7,11]. Extensive validation has been published and it has been recently demonstrated that left ventricular parallel conductance remains fairly constant during the cardiac cycle [12,13]. There is no theoretical reason why this technique should not be applied to study human right ventricular function. A prerequisite of this technique is the determination of the parallel conductance or volume offset \( V_c \) due to the conductivity of tissues surrounding the ventricular blood pool. Early studies assumed this offset to be constant [6,17], but there are several potential sources of \( V_c \) variability including respiration, atrial filling, right ventricular ejection, and myocardial blood volume changes. Of these, in clinical practice, changes with respiration are the largest and were even more marked in this study of right ventricular volumes than we have seen in the left ventricle. For this reason all measurements made using this technique should be recorded during suspended ventilation.

There was a significant relationship \((r = 0.59, P < 0.05)\) with the difference between maximum and minimum \( V_c(t) \) \([\Delta V_c(t)]\) and the \( V_c(t) \) averaged from all of the six isochrones. This suggests that the magnitude of variability is proportional to the amount of parallel conductance itself. However, overall the \( V_c(t) \) averaged for the group represented 5.73% (s.d. = 5.75%) of total corrected end-diastolic volume (mean maximal variation of 7.66 ml), and 2.47% (s.d. = 2.23%) as a percentage of \( V_c(t) \).

4. Discussion

The conductance technique has been widely applied to the study of left ventricular pressure-volume relationships in animals [8,15,16] and adults with a variety of heart diseases [7,11]. Extensive validation has been published and it has been recently demonstrated that left ventricular parallel conductance remains fairly constant during the cardiac cycle [12,13]. There is no theoretical reason why this technique should not be applied to study human right ventricular function. A prerequisite of this technique is the determination of the parallel conductance or volume offset \( V_c \) due to the conductivity of tissues surrounding the ventricular blood pool. Early studies assumed this offset to be constant [6,17], but there are several potential sources of \( V_c \) variability including respiration, atrial filling, right ventricular ejection, and myocardial blood volume changes. Of these, in clinical practice, changes with respiration are the largest and were even more marked in this study of right ventricular volumes than we have seen in the left ventricle. For this reason all measurements made using this technique should be recorded during suspended ventilation.
We have previously shown that a conductance catheter can reliably measure the volume of human right ventricular casts [10], and Dickstein et al. [18] in a recent study in open chest pigs suggested the technique may be particularly useful for the study of RV function in vivo. In their study a consistent change in RV end-systolic P-V relationships with loading and inotropic intervention was shown.

Parallel conductance determination in the study of Dickstein et al. [18] was measured using the single value, linear technique first described by Baan et al. (Vc(Baan)) [7]. Validation studies in animals [18,19] with structurally normal right ventricles suggest that Vc measured using Baan’s technique is relatively stable over a wide volume range. This commonly used method of estimating Vc has the theoretical disadvantage of utilising only two points in the cardiac cycle and does not, therefore, allow for change in Vc that may occur between these times. Parallel conductance determination tends to be higher in the right ventricle [18], presumably reflecting a greater current leakage through the thin wall and proximity to mediastinal structures. This may introduce the potential for a greater error in absolute volume determination. Furthermore, the thin ventricular wall makes Vc measurements more sensitive to changes that occur within the cardiac cycle, e.g., atrial filling and LV ejection. To date, however, there are no animal or human data concerning right ventricular parallel conductance during the cardiac cycle.

Lankford et al. [12] devised a method for estimating changes in Vc during the cardiac cycle which, they argue, is more robust and less susceptible to noise within the system. By using 20 isochrones throughout systole they were able to demonstrate, in the isolated heart, minimal changes in left ventricular Vc(t), although there were more marked changes which approximated 4% of the end-diastolic volume, in the in situ preparations. Despite this temporal variation there remained an extremely good correlation between Vc(Baan) and Vc(t). It was also shown that the conductance volume signal was only minimally sensitive to changes in the blood content of the surrounding myocardium.

We used a similar method to examine changes in Vc(t) that occur during the cardiac cycle in the right ventricle. Our data show that small changes in parallel conductance occur during systole, representing 6% of the end-diastolic volume, but no significant difference between Vc(t) at \(dp/dr_{max}\) and \(dp/dr_{min}\). Interestingly, in common with the study of left ventricular parallel conductance by Lankford et al. [12], the parallel conductance at both of these points and the Vc(t) from the six systolic isochrones exceeded that obtained using the single value Baan technique (Vc(Baan)). Importantly, however, there was a close linear relationship between Vc(t) and Vc(Baan) (r = 0.99). Thus for most clinical and experimental preparations, where relative volume is important, either method will allow durable, repeatable and comparable results.

These findings are very similar to those recently published by Szwarc et al. [13] in the much smaller left ventricle of anaesthetised closed chest mini-pigs. In this study a small but significant variation in Vc(t) was found using the isochronal method in the left ventricle of closed chest pigs, although there was no significant difference between Vc(t) at \(dp/dr_{max}\) and \(dp/dr_{min}\). However, a comparison with the single value method was not made in their study.

Implicit in our analysis is an unchanged gain constant (\(\alpha\)) throughout the cardiac cycle. There are remarkably few data in this regard. Most investigators, in left ventricular studies, like us in the right ventricle either ignore \(\alpha\) (assuming it to be constant even over a wide range of conditions [8,17]) or calibrate the conductance signal using angiographic [7] or thermodilution measurements [7,11] (both of which have inherent limitations). In a novel study, examining \(\alpha\) and its potential variation throughout the cardiac cycle and over a broad volume range, Stamato et al. [20] examined seven open and closed chest pigs. The gain constant, \(\alpha\), did not change significantly during the cardiac cycle. However, when stroke volume was compared with that obtained by either thermodilution or pulmonary flow probe (in the open chest animal), over a wide range of volumes, an inverse relation was observed between right ventricular volume and \(\alpha\). Although the exact relationship between a variable \(\alpha\) and a variable Vc has not been definitively described, no matter what this relationship, the overall effect is small when assessed in this clinical preparation.

The effects of hypertonic saline in the myocardial blood vessels were overcome by taking systolic isochrones during the ascending limb of the saline wash-in. This is important, as Baan et al. [7] showed that a transient decrease in left ventricular pressure and in maximal left ventricular \(dp/dr\) occurred when 1.5 ml of 0.6 M of saline was injected directly into the main stem left coronary artery of dogs. Furthermore, there was a transient increase in left ventricular diameter and conductance, amounting to 2% of end diastolic dimension. Lankford et al. [12] and Applegate et al. [21] also observed that the descending phase of the saline wash-in is often accompanied by a slight fall in left ventricular pressure, presumably because of the myocardial depressant effect of the concentrated saline. To avoid these changes, apparently caused by an effect on the myocardium, Vc was measured during the rising limb of the hypertonic saline wash-in in all right ventricular parallel conductance measurements as penetration of salt into the wall during this period is limited.

Our results are important in a number of respects. The temporal variation in Vc(t) in the right ventricle is small and appears to be of the same order of magnitude as that seen in the left ventricle [12,13], although it is theoretically possible that we did not detect larger changes by examining only six isochrones. Nonetheless, despite the potential effects of right atrial filling, varying right ventricular chamber geometry during systole and left sided events,
Vc(t) remains reasonably constant, and so estimations of Vc in the right ventricle should be as accurate as those in the left ventricle. Although these results are encouraging it must be realised that they do not imply that Vc remains constant under all conditions. Indeed Boltwood et al. [22] have demonstrated a significant fall in Vc during extreme off-loading in the canine left ventricle, while Applegate et al. [21] observed a greater decrease in conductance volume as compared to ultrasonic volume during caval occlusion, implying that Vc decreased with extreme preload reduction. However, we have found no significant change in Vc under the more physiological changes seen during fluid loading in humans [23]. Until these findings have been investigated further it remains important, therefore, to make repeated measurements of Vc during acute interventions.

In conclusion we have shown that while Vc(t) varies throughout the cardiac cycle in the human right ventricle of adults and older children after repair of congenital abnormalities, there is no significant difference in Vc(t) at dP/dtmin and dP/dtmax. The fact that the small changes observed in Vc(t) during systole are similar in both the RV and LV suggests that the anatomy of the RV does not preclude the use of conductance catheter technology in the assessment of RV function. Finally, the excellent correlation between Vc(Baan) and Vc(t) suggests that the correction of Vc for the phase of the cardiac cycle is unnecessary for the purposes of most data analysis.

These results provide further evidence that the application of conductance technology to the study of human right ventricular function is both possible and useful.

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