The volume-dependency of parallel conductance throughout the cardiac cycle and its consequence for volume estimation of the left ventricle in patients

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Abstract

Objective: To study the hypothesis that the electrical conductance of tissues and fluids (parallel conductance ($G_p$)) around the ventricle depends on left ventricular volume throughout the cardiac cycle. Methods: We extended a recently developed method to determine $G_p$ throughout the cardiac cycle. First, we compared the estimates of parallel conductances obtained with the new method ($G_p^*$) with those of the conventional one ($G_p^1$), both averaged over the cardiac cycles. Secondly, $G_p^*$ was determined throughout the cardiac cycle and its volume dependency was assessed. Thirdly, the factor $\alpha$ was calculated as the ratio between stroke volume, obtained by the conductance method using $G_p^*$, and that obtained by a thermodilution method. Because the non-homogeneous field was indicated to be the reason for the dependency of $G_p$ on left ventricular volume as well as for the need for $\alpha$, we tested whether the hypothesis implies that a correction with $\alpha$ is not needed if $G_p$ is determined throughout the cardiac cycle. Results: We found a negative linear relation between $G_p$ and left ventricular volume. This relation appeared to be reproducible within each patient. Furthermore, we found that $\alpha$ deviates from 1 primarily due to the dependency of $G_p$ on left ventricular volume. Conclusion: To obtain stroke volume or to determine absolute left ventricular volume continuously within a cardiac cycle, $G_p$ should be determined throughout each cardiac cycle and if a constant $G_p$ throughout the cardiac cycle is used a correction with the factor $\alpha$ should be made to correct for a possible influence of electrical field heterogeneity.

Keywords: Cardiomyopathy; Cardiovascular surgery; Contractile function; Heart failure; Ventricular function

1. Introduction

We expect that in the near future the assessment of pressure–volume relationships in both ventricles will become more and more important in the determination of cardiac function in a clinical setting. Therefore, besides pressure, absolute ventricular volume should be determined continuously. The electrical conductance catheter has been used to measure the volume of a cardiac chamber continuously by positioning a catheter in the right or left ventricle and relating the electrical conductance of blood in the ventricle to its volume [1–20]. Besides blood, the tissues surrounding the ventricle contribute to the measured conductance and cause an offset in the conductance signal, i.e. parallel conductance ($G_p$). Conventionally parallel conductance is determined by plotting values at end-systole ($G_{sys}$) versus those at the preceding end-diastole ($G_{dias}$) during a beat-to-beat increase in conductivity of blood after the injection of hypertonic saline. The linear regression line through $G_{sys}-G_{dias}$ values is extrapolated to the identity line to estimate parallel conductance ($G_p^1$) [2]. For this estimation it is assumed that $G_p^1$ is constant

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within a cardiac cycle. Theoretical studies, however, predict a dependence of parallel conductance on volume [21–23]. If the ventricle becomes larger, the density of electric current at the myocardial boundary and therefore parallel conductance will be smaller due to the nonhomogeneous electrical field. If a constant $G_p$ during a cardiac cycle is assumed as with the conventional conductance method, stroke volume, estimated with the conductance catheter, was different from stroke volume obtained by an independent method [1,2,7]. A correction factor $\alpha$, being the ratio between conductance-derived stroke volume and a reference stroke volume, was used to relate both stroke volumes. The reason for this factor $\alpha$ was attributed to a non-homogeneous electrical field within the ventricle [2,8].

In various studies, parallel conductance was indeed found to depend on left ventricular volume [7,8,10] whereas in other studies no such dependency was found [15,18,24,25]. Recently, we described a new method to estimate parallel conductance ($G^*_p$), based on the determination of the area under a conductance dilution curve and the determination of flow and conductivity of blood, which appeared to be (four times) more precise than the conventional method [26]. In the present study, we extended the new conductance-dilution method to test the hypothesis that parallel conductance depends on left ventricular volume throughout the cardiac cycle. The non-homogeneous field has been shown to be the causal factor for the dependency of parallel conductance on left ventricular volume [23], as well as for the need for $\alpha$ [2]. Therefore, we also tested whether the hypothesis implies that a correction with $\alpha$ is not needed if parallel conductance is determined throughout the cardiac cycle.

First, we compared the estimates of real parallel conductances $G_p^*$ and $G_p'$, averaged over the cardiac cycles within the dilution curves. Secondly, $G_p^*$ was determined throughout the cardiac cycle and its volume dependency was assessed. Thirdly, the factor $\alpha$ was calculated as the ratio between stroke volume, obtained by the conductance method using the conventional method to estimate parallel conductance, and that obtained by a thermodilution method.

2. Methods

2.1. The conductance method

The general principles of the conductance method [2,6] and the configuration used for this study (7F conductance catheter (Sentron, The Netherlands), Leycom CFL512 (CD Leycom, Zoetermeer, The Netherlands)) have been described extensively elsewhere [26]. Also, the conventional method and the new approach to determine parallel conductance averaged over a cardiac cycle have been described elsewhere [2,6,26]. For this new approach, the indicator dilution method for hypertonic saline is described by a mass balance, in which the amount of ions injected is equal to the change in amount of ions detected. The amount of injected ions (indicator) influencing conductance is the product of the injected volume and the NaCl ion-concentration difference between the hypertonic saline and the blood before injection. The amount of detected ions is the product of flow and the integrated area under the NaCl ion-concentration, i.e. conductivity of blood mixed with NaCl, dilution curve. If the injection is given as a bolus and if blood flow ($Q_b$) is constant with the assumption of complete mixing of indicator and blood, the following can be formulated:

$$Q_s \cdot (\sigma_i - \sigma_b) = \dot{Q}_b \cdot \int_{t_1}^{t_2} \Delta \sigma_b(t)dt$$  \hspace{1cm} (1)

where $Q_s$ is the volume of the injectate, $\sigma_i$ the electrical conductivity of the injectate at blood temperature, $\sigma_b$ the conductivity of the blood before injection, $\dot{Q}_b$ blood flow, $t$ is time, $t_1$ the time of injection, $t_2$ the time when all indicator has passed the detector site and $\Delta \sigma_b$ the change in conductivity of the blood due to the injection of the hypertonic saline. For left ventricular measurements, the volume of the left ventricle ($Q_s$) between two measuring electrodes at any time $t$ can be calculated as:

$$Q_s(t) = \frac{1}{\alpha} \cdot \frac{L^2}{\sigma_b} \cdot [G(t) - G_p(t)]$$  \hspace{1cm} (2)

where $L$ is the distance between the electrodes, $G(t)$ the time-varying conductance and $G_p(t)$ the time-varying parallel conductance. If $\alpha$ is assumed to be 1, Eqs. (1) and (2) can be combined and written as:

$$G^*_p(t) = G(t) - \frac{\sigma_b \cdot \dot{Q}_b \cdot \int_{t_1}^{t_2} \Delta G(t)dt}{Q_s \cdot (\sigma_i - \sigma_b)}$$  \hspace{1cm} (3)

where $G^*_p(t)$ is the time-varying parallel conductance as determined with the conductivity dilution method. The total sum of the conductance signals of the segments were used to calculate total parallel conductance. To study $G^*_p(t)$ during a cardiac cycle, the conductance signal was subdivided into 10 equal time intervals for each cardiac cycle during the dilution curve. The first interval started at the beginning of diastole, i.e. minimum blood volume in the left ventricle, and the last interval ended at the end of systole, i.e. also minimum blood volume in the left ventricle. For every $x$th interval, the conductance signal was averaged and plotted versus time (asterisk in Fig. 1A). In Fig. 1B,C, conductance is averaged for the first (*) and the sixth interval (**) for each of the cardiac cycles in the dilution curve, respectively. Again a dilution curve was plotted through the average conductance versus time values and the area under the dilution curve was obtained by subtracting baseline conductance: $\tilde{G}(t)$. It should be noted that the baseline of a dilution curve is different for
been approved by the medical ethics committees of the various hospitals where the patients were accommodated [19]. The investigation conformed to the principles outlined in the Declaration of Helsinki [31]. Informed patient consent was obtained for insertion of catheters and subsequent measurements. The patients were heparinized before catheterization. A Swan Ganz thermodilution catheter was positioned in the pulmonary artery and a lumen of this catheter, positioned near the entrance of the right atrium, was used for the injection of hypertonic saline. The conductance catheter was inserted via a femoral artery into the left ventricle.

2.3. Data analysis

First, both estimates of parallel conductances $G^1_p$ and $G^a_p$, averaged over the cardiac cycles within the dilution curve, were compared using a paired $t$-test. Secondly, $G^a_p$ was determined for each of the 10 intervals within a cardiac cycle and plotted versus the corresponding left ventricular volume ($Q_v$) and analysed using linear regression. To obtain stroke volume, end-diastolic minus peak systolic ventricular volume was calculated with the conductance method, assuming a constant parallel conductance $G_{pa}$ and also with the time-varying parallel conductance $G^a_p$. Because left ventricular volume $Q_v^c$ is an average value of a certain interval within the cardiac cycle, the maximum and minimum $Q_v^c$ within the cardiac cycle will be slightly under- and over-estimated, respectively. Therefore, we used the maximum and minimum conductance found in each cardiac cycle during the dilution curve to calculate stroke volume $Q_v$. This stroke volume was compared to stroke volume obtained by thermodilution ($Q_{TD}^v$) using a paired $t$-test.

3. Results

Baseline haemodynamic conditions such as heart rate and cardiac output as determined with thermodilution are shown in Table 1. In total, 24 measurements, i.e., 12 pairs, obtained in the left ventricle of 12 patients were used to calculate parallel conductance values with the conventional $G^1_p$-method and the new $G^a_p$-method. The values obtained by both methods to estimate parallel conductance averaged over various cardiac cycles were not significantly different, whereas the mean difference $= 4.04 \pm 6.3$ S.E. (S).

Fig. 2 shows a typical example of the values of parallel conductance ($G^a_p$) and left ventricular volume ($Q_v^c$) both plotted as a function of the 10 intervals occurring within the cardiac cycle. The first interval started at the end of diastole and the last interval ended at the end of systole. At the interval where left ventricular volume was maximal (usually interval 3, 4 or 5), parallel conductance was minimal for each measurement. The $G^a_p$ averaged over a certain interval minus the $G^1_p$ averaged over the whole interval.
Table 1. Haemodynamic conditions such as heart rate and cardiac output as determined with thermodilution and slopes of the linear regression lines through the $G_p^a$ versus $Q_{sv}$ values.

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>Heart rate (bpm)</th>
<th>Cardiac output (l/min)</th>
<th>Slope±95% (S/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>87</td>
<td>4.45</td>
<td>−0.56±0.05</td>
</tr>
<tr>
<td>2</td>
<td>62</td>
<td>4.38</td>
<td>−0.36±0.06</td>
</tr>
<tr>
<td>3</td>
<td>72</td>
<td>5.49</td>
<td>−0.54±0.07</td>
</tr>
<tr>
<td>4</td>
<td>56</td>
<td>5.34</td>
<td>−0.40±0.04</td>
</tr>
<tr>
<td>5</td>
<td>45</td>
<td>6.15</td>
<td>−0.24±0.15</td>
</tr>
<tr>
<td>6</td>
<td>61</td>
<td>6.41</td>
<td>−0.56±0.02</td>
</tr>
<tr>
<td>7</td>
<td>115</td>
<td>5.30</td>
<td>−0.54±0.22</td>
</tr>
<tr>
<td>8</td>
<td>62</td>
<td>3.85</td>
<td>−0.34±0.05</td>
</tr>
<tr>
<td>9</td>
<td>67</td>
<td>4.43</td>
<td>−0.50±0.07</td>
</tr>
<tr>
<td>10</td>
<td>51</td>
<td>7.27</td>
<td>−0.78±0.14</td>
</tr>
<tr>
<td>11</td>
<td>53</td>
<td>4.82</td>
<td>−0.70±0.23</td>
</tr>
<tr>
<td>12</td>
<td>51</td>
<td>3.80</td>
<td>−0.50±0.14</td>
</tr>
</tbody>
</table>

The slopes of the 12 linear regression lines and their corresponding 95% confidence intervals of their estimates are given in Table 1.

3.1. Stroke volume and $1/\alpha$

Fig. 5 clearly shows that stroke volume obtained from the new conductance-dilution method, assuming conductance to be volume-dependent, resembles stroke volume obtained with the thermodilution method better than stroke volume obtained with the conventional conductance method. Stroke volume obtained from the new conductance-dilution method ($Q_{sv}^a$), did not differ significantly from stroke volume obtained from the thermodilution ($Q_{sv}^{TD}$) (paired $t$-test, $Q_{sv}^{TD} - Q_{sv}^a = 1.90$, 95% CI = −3.99, 7.80, S.E. = 2.88 (ml)) (Fig. 5). Thus, left ventricular volume did not need a correction with $1/\alpha$ (Eq. (2)), i.e. $\alpha$ is not significantly different from 1, if the new method to estimate parallel conductance is used. Stroke volume obtained by the conventional conductance method ($Q_{sv}^1$) was significantly smaller than $Q_{sv}^{TD}$ (paired $t$-test, $Q_{sv}^{TD} - Q_{sv}^1 = 46.07$, 95% CI = 35.89, 56.25 [ml]) (Fig. 5). Therefore, $1/\alpha$ ($Q_{sv}^{TD}/Q_{sv}^1$) differed significantly from 1 (paired $t$-test, $1/\alpha = 3.09$, 95% CI = 2.40, 3.78).

4. Discussion

Using an extension of a recently developed method to derive parallel conductance [26], we have shown in heart failure patients that parallel conductance decreased linearly within a cardiac cycle if left ventricular volume increased. In each patient, for a duplicate measurement, this relation between parallel conductance and left ventricular volume was similar, but between patients, variation in this relation

Fig. 2. For one typical measurement blood volume of the left ventricle ($Q_{sv}$) (■) and parallel conductance ($G_p^a$) (○) are plotted versus the corresponding 10 equally sub-divided time-intervals within the cardiac cycle.
was found (Table 1). This variation is probably due to variance in hydration level and therefore the conductivity of the tissues and the fluids surrounding the left ventricular cavity and other patient-related factors such as anatomy.

Parallel conductance was shown to be inversely related to ventricular volume (Fig. 3A), following the same pattern as that observed by others [15, 24, 25]. We found $G_p$ to deviate significantly on average 13% of the mean at mid-systole, i.e. maximal volume. Szwarc and colleagues also found a significant decrease in $G_p$ at mid-systole in the left ventricles of minipigs but this decrease was rather small [15]. No significant variation in parallel conductance within the cardiac cycle could be detected in the left ventricle of dogs [24] and in the left ventricle of children with a congenital cardiac disease [25].

In contrast to our results where only spontaneous cardiac variations were considered, it was found that if volume was varied artificially over a broad range then parallel conductance decreased with left ventricular volume [7, 8]. Boltwood et al. reported that parallel conductance remained constant, if measured under steady-state conditions or measured during aortic or pulmonary arterial occlusion, but decreased with decreasing left ventricular volume during vena caval occlusion probably due to a decrease in

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**Fig. 3.** $G_p$ averaged over the corresponding time interval minus $G_p$ averaged over the whole cardiac cycle as a percentage of the $G_p$ averaged over the whole cardiac cycle is plotted versus the corresponding 10 equally sub-divided time-intervals within the cardiac cycle. The error bars show the 95% confidence intervals.

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**Fig. 4.** For a typical duplicate measurement $G_p$ is plotted versus $Q_v$. A linear regression line is drawn through these values. The two different symbols indicate the two paired measurements.
the filling of the right ventricle [7]. Applegate et al. compared conductance of left ventricular volumes to those estimated from three orthogonal pairs of endocardially placed sonomicrometer crystals in open chest dogs [8]. This relation was reasonably linear during the volume excursions of a normal cardiac cycle, but non-linear if left ventricular volume was reduced below steady state end-systolic volume, implying that parallel conductance decreased with volume. Cassidy and Teitel [10] found a better correlation between total conductance volume, i.e. volume not corrected for parallel conductance, and volume obtained by cineangiography, than between ventricular blood volume, i.e. volume corrected for cineangiography. They concluded that an error is introduced in the calculation of blood volume, if parallel conductance is assumed to be volume-independent.

The method to estimate parallel conductance within a cardiac cycle, which was used by the other groups [15,24,25] was derived from the $G_p$-method as described by Baan et al. [1]. Furthermore, to estimate average parallel conductance, the $G_p^{\text{ave}}$-method [7,8,10] or a method derived from the $G_p^{\text{ave}}$-method [14] was also used. We found previously that our method, based on the estimation of an area under a dilution curve and knowledge of flow, estimates parallel conductance averaged over various cardiac cycles with a factor four times better repeatability than the $G_p$-method [26]. We therefore assume that our method to determine parallel conductance within a cardiac cycle also estimates parallel conductance more precisely than the method derived from the $G_p$-method and that if a volume-dependency is present, this would be more easily detected with our method. Theoretical and experimental analysis of the area under the dilution curve revealed errors less than 1% made by neglecting the pulsatile character of blood flow [32]. Although this error contributes to the error made in the determination of parallel conductance within the cardiac cycle, we consider this error of minor importance. It should be noted that we determined left ventricular volumes of adult humans after cardiomyoplasty, whereas other studies were performed in the smaller left ventricles of children, dogs, or piglets [7,8,10,14,15,24,25], which might influence the slope of the relation between parallel conductance and volume. However, no relation was found between cardiac output (Table 1) and the slope of the relation between parallel conductance and left ventricular volume (Table 1). To correct for a possible influence of saline accumulation in the ventricular wall, passage of saline in the adjacent ventricle and recirculation on our calculated value of parallel conductance, we subtracted a baseline from the dilution curve. To correct for the influence of breathing, the dilution curve was recorded during a prolonged expiratory pause [26].

The correction factor $\alpha$ is assumed to be a correction for the inhomogeneity of the electrical field [1,8]. A non-homogeneous electrical field was suggested to cause parallel conductance to be volume-dependent [23]. Indeed, we found that if volume dependency of parallel conductance was taken into consideration then the correction with $\alpha$ was not needed because it was not significantly different from one.

To consider volume dependency, only slight changes in the conventional protocol for the determination of parallel conductance are necessary. Those include that the concentration and volume of the injectate should be known and that the injection and recording of the dilution curve should take place during an expiratory pause to eliminate the influence of breathing on the obtained conductivity dilution curve.

In conclusion, parallel conductance should be determined at each average volume level and throughout each cardiac cycle or the conductance of the left ventricle should be corrected with the factor $\alpha$ at the corresponding volume to eliminate a possible influence of electrical field heterogeneity.

References

[5] Baan J, van der Velde ET. Sensitivity of left ventricular end-systolic


