Effects of Changes in Ventricular Size on Regional and Surface QRS Amplitudes in the Conscious Dog

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SUMMARY Eight conscious dogs instrumented with wall thickness somicmeters and 11 subcutaneous electrodes in a modified McFee vectorcardiographic array were studied during changes in ventricular volume. Simultaneous measurements were made of QRS amplitudes of the endocardial and epicardial ECG, QRS spatial vector magnitudes (SVM), end-diastolic wall thickness (EDT), end-systolic wall thickness (EST) and the amount of systolic thickening (ΔWT). Ventricular size was decreased by atroventricular and infusion of 0.02 μg/kg/min of isoproterenol to increase the mean heart rate from 81 ± 5 beats/min (mean ± SEM) to 174 ± 10 beats/min (p < 0.001), and was reflected by an increased mean EDT (9.06 ± 0.64 mm to 9.94 ± 0.61 mm, p < 0.005). The endocardial QRS amplitude increased in each dog (mean increase 21.55 ± 1.36 mV to 25.13 ± 1.35 mV, p < 0.001), whereas the SVM decreased from 7.69 ± 0.75 mV to 6.18 ± 0.48 mV (p < 0.02). Ventricular size was then increased by rapid saline infusion and was reflected by a decrease of EDT from 9.65 ± 0.66 mm to 9.09 ± 0.66 mm (p < 0.001), while heart rate remained unchanged. Endocardial amplitude decreased in each dog (average decrease 3.59 ± 0.25 mV, p < 0.001), while the SVM increased in each dog (average increase 0.81 ± 0.18 mV, p < 0.005). The mean epicardial amplitudes did not change significantly during either increases or decreases in ventricular volume. In each dog, there was a linear relation between EDT and endocardial amplitudes (r values > 0.88) and an inverse linear relation between EDT and SVM (r values > −0.80). The relations between EST or ΔWT and regional and QRS surface amplitudes were nonlinear. We conclude that in the conscious dog changes in endocardial QRS amplitudes and SVM amplitudes were inversely related to wall thickness, a finding that may relate in part to alterations in the distance of the heart from the chest wall.

THE MECHANISMS underlying regional and surface QRS amplitude changes during acute forms of stress are unclear, and it has not been established whether changes in left ventricular volume are directly or inversely related to QRS amplitudes. In model systems and in animal experiments an increase in ventricular volume produces an augmentation of the initial portions of the QRS potentials in the body surface ECG and vectorcardiogram (VCG), but in human subjects the direction of such changes has been controversial. Lekven et al. recently reported that the endocardial QRS amplitude decreased during volume increases in open-chest dogs, an effect opposite to that described in the surface ECG. It has also been proposed that changes in the ventricular ejection fraction relate to surface QRS-amplitude changes. However, clear relations between left ventricular ejection fractions, left ventricular volumes and alterations in surface QRS amplitudes during exercise in man have not been found. We hypothesized that QRS-amplitude changes at different locations might be related to changes in ventricular wall thickness and to the distance of the heart from the surface recording electrodes. Accordingly, a chronic dog preparation was developed to allow measurements of regional left ventricular wall dynamics simultaneously with the local ECG and body surface VCG leads. This animal model has been applied to study the effects of alterations in ventricular volume and function on both regional and surface QRS-amplitude changes.

Methods

Eight adult mongrel dogs weighing 26-35 kg were anesthetized with sodium pentobarbital (30 mg/kg i.v.) and ventilated with a Harvard respirator. Using sterile technique, the chest was opened through the left fifth intercostal space, and the pericardial sac was incised parallel to the phrenic nerve. A pair of miniature ultrasonic crystals was placed, one crystal in the endocardium and one at the epicardium, in a region near the base of the posterior papillary muscle to measure regional wall thickness, as described previously, as well as regional endocardial and epicardial ECGs. The chest was closed, leaving the pericardium open; all wires and tubing were passed subcutaneously to the back of the dog and brought through the skin between the scapulae. To record surface ECG potentials, 11
stainless-steel electrodes were implanted subcutaneously in a modified McFee VCG array and the wires were tunneled dorsally to the base of the neck.

**Study Protocol**

The experiments were performed at least 7 days postoperatively, when the dogs had completely recovered from the operation. During the study, the conscious dog was resting quietly on its right side, on the floor. An intravenous catheter was inserted into a calf vein and 30 minutes later a control recording of wall thickness, endocardial and epicardial ECGs, and the X, Y and Z leads of the VCG were made for at least 5 minutes. Atropine (2 mg i.v.) was then injected, and 2 minutes later 0.02 µg/kg/min of isoproterenol was infused for 1.5 minutes. When heart rate, regional function and ECGs had returned to control (usually more than 1 hour later), a second dose of atropine (2 mg) was injected, and 2 minutes later 250 ml of saline was infused under pressure over 1.5–2.5 minutes (mean 2 minutes).

Within 7–14 days of the studies described above, the position of the endocardial and epicardial wall thickness crystals was studied at postmortem examination and determined to be in proper alignment; the endocardial crystals lay within the inner one-third of the left ventricular wall in all dogs.

**Data Analysis**

All variables were recorded simultaneously on a Brush eight-channel, forced-ink recorder. Systolic regional thickening (ΔWT) was calculated as the difference between end-diastolic wall thickness (EDT) (measured at the time of peak deflection of the QRS complex of the endocardial ECG) and end-systolic wall thickness (EST). EST was measured at the maximum wall thickening during ventricular systole. In other experiments (100 observations in five dogs), it was found that end-ejection, identified on the ventricular pressure tracing just before peak −dP/dt, followed the termination of the T wave of the endocardial ECG by 50 ± 20 msec (sd). Therefore, in the present experiments, maximum systolic shortening was identified as the excursion on the wall thickness tracing that followed the termination of the endocardial ECG T wave by approximately the same time interval (small, vertical arrow, bottom tracing, fig. 1). The Q-wave amplitude of the endocardial ECG and the R-wave amplitude of the epicardial ECG were measured from the PR segment, which was taken as the isoelectric line. The spatial magnitude of the VCG QRS amplitudes (spatial vector magnitude [SVM]) was measured at the time of the greatest potential in one of the three vector planes and calculated as previously described:  

\[ SVM(mV) = \sqrt{X^2 + Y^2 + Z^2} \]

All data points were averaged over 10 consecutive beats at a paper speed of 50 mm/sec.

The differences between control vs atropine, control vs isoproterenol, and atropine vs isoproterenol were analyzed using an analysis of variance with repeated measures. The difference between atropine vs volume infusion was analyzed using a paired t test. A least-squares fit regression analysis was used for analyzing the relation between EDT and regional and surface QRS amplitudes. The level of statistical significance was p < 0.05. All results are presented as mean ± SEM.

**Results**

**Decreased Ventricular Size**

Two minutes after the injection of atropine, there was a significant increase in mean heart rate, from 81 ± 5 beats/min to 150 ± 9 beats/min, and a significant increase in mean EDT, from 9.06 ± 0.65 mm to 9.63 ± 0.64 mm, changes that reflected a reduction in left ventricular volume (fig. 2). Mean endocardial Q-wave amplitude increased significantly from control, by 2.1 ± 0.4 mV to 23.64 ± 0.74 mV; the mean SVM decreased from 7.69 ± 0.75 mV to 6.86 ± 0.55 mV (fig. 3). The mean EST (fig. 2) and epicardial
amplitude (fig. 3) did not change significantly from control with atropine.

After 1.5 minutes of isoproterenol infusion, the mean heart rate increased further by 24 ± 3 beats/min, the mean EDT decreased from 9.63 ± 0.64 mm to 9.94 ± 0.61 mm and the mean EST increased significantly, by 0.84 ± 0.14 mm, changes that are consistent with further decrease in ventricular volume (fig. 2). Endocardial Q-wave amplitude increased further, by 1.49 ± 0.07 mV, while the mean surface SVM decreased significantly (p < 0.01), from 6.86 ± 0.55 mV to 6.18 ± 0.48 mV (fig. 3). The epicardial ECG amplitude decreased in five dogs, increased in two and did not change in one; however, the mean change in epicardial ECG amplitude was not significant (figs. 3 and 4).

Representative tracings in figure 5 show that reducing ventricular size increased the endocardial QRS amplitude and decreased the surface QRS amplitude.

Increased Ventricular Size

After the administration of atropine and rapid infusion of saline, the mean heart rate was unchanged (fig. 2). EDT decreased significantly, from 9.65 ± 0.66 to 9.09 ± 0.66, indicating increased ventricular volume, and the mean EST decreased by 0.27 ± 0.05 mm (fig.

**Figure 2.** Changes in left ventricular wall thickness during changes in left ventricular volume. End-systolic thickness (EST), end-diastolic thickness (EDT) and amount of thickening during systole (ΔWT [mm]) are shown with the heart rate. Each point represents the mean value (± SEM) for the eight dogs.

**Figure 3.** Changes in endocardial amplitude (ENDO ECG AMP), epicardial amplitude (EPI ECG AMP) and the spatial magnitude of vectorcardiographic (VCG) amplitudes (SPATIAL VCG) during alterations in left ventricular volume. Each point represents the mean value (± SEM) for eight dogs.

2). The mean endocardial Q-wave amplitude decreased significantly, from 24.41 ± 1.41 mV to 20.83 ± 1.31 mV, while the mean SVM increased from 7.03 ± 0.67 mV to 7.84 ± 0.81 mV (fig. 3). The

**Figure 4.** Epicardial QRS amplitude changes from control to saline (NaCl) infusion and from control to isoproterenol infusion in each dog. Open circles represent the mean ± SD.
epicardial ECG QRS amplitudes increased in three dogs and decreased in five during the saline infusion, but the mean change was not significant (figs. 3 and 4).

Representative tracings in figure 1 show that increasing ventricular size decreased the endocardial QRS amplitude and increased the surface QRS amplitude.

Correlations

To determine the relations between geometric changes and QRS-amplitude alterations, changes in EDT, EST and ΔWT were related to endocardial and surface QRS-amplitude changes during the interventions mentioned above. Both the endocardial QRS amplitudes (fig. 6A) and the surface QRS amplitudes (fig. 6B) were linearly related to EDT in each dog. However, the relations between amplitudes and EST or ΔWT were nonlinear (figs. 6A and 6B). In all dogs the correlation coefficients between EDT and endocardial QRS amplitude were high (≥0.88) and positive; between EDT and SVM the correlation coefficients were high (≥0.80) and negative, indicating an inverse relation (table 1).

Discussion

The present study in the intact, conscious dog shows that changes in endocardial QRS amplitudes are opposite to those of the simultaneously measured body

Table 1. The Correlation Coefficients (r) for Endocardial Q-wave Amplitudes and the Spatial Magnitude of Vectorcardiographic Amplitudes vs End-diastolic Thickness in Each Dog

<table>
<thead>
<tr>
<th>Dog</th>
<th>r (EDT vs endo amp)</th>
<th>r (EDT vs SVM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.97</td>
<td>-0.80</td>
</tr>
<tr>
<td>2</td>
<td>0.90</td>
<td>-0.86</td>
</tr>
<tr>
<td>3</td>
<td>0.91</td>
<td>-0.87</td>
</tr>
<tr>
<td>4</td>
<td>0.89</td>
<td>-0.90</td>
</tr>
<tr>
<td>5</td>
<td>0.88</td>
<td>-0.99</td>
</tr>
<tr>
<td>6</td>
<td>0.98</td>
<td>-0.95</td>
</tr>
<tr>
<td>7</td>
<td>0.96</td>
<td>-0.91</td>
</tr>
<tr>
<td>8</td>
<td>0.98</td>
<td>-0.97</td>
</tr>
</tbody>
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Abbreviations: endo amp = endocardial Q-wave amplitude; SVM = spatial vector magnitude; EDT = end-diastolic thickness.
surface leads during acute changes in left ventricular volume. The change of the endocardial potential was directionally similar and linearly related to that of left ventricular EDT, while the QRS amplitude on the body surface behaved in an opposite manner.

In this chronic dog preparation, surface ECG recordings were obtained using an implanted, modified McFee VCG system.\textsuperscript{15, 16} This array has been reported to be more stable in the dog than other surface ECG recording systems and less sensitive to positional changes.\textsuperscript{21}

Our approach for determining SVM is slightly less accurate in our experience than computer approaches,\textsuperscript{22} but in practice provides reasonable accuracy. The use of single, rather than multiple electrograms is a potential limitation, but the number of wires that can be placed in the conscious dog is limited (14 were used in this study), and responses in the sub-endocardial leads were uniform despite some differences in location in each dog.

The use of the conscious dog avoided the adverse hemodynamic and physiologic effects noted during anesthesia and opening of the chest.\textsuperscript{23, 24} The wall thickness crystals were well aligned in the fixed heart, but it was not possible to exclude lateral displacement of one crystal or shear during changes in cardiac size. However, this potential limitation has been shown to have only a minor effect on measurement of wall thickness.\textsuperscript{25} Moreover, simultaneous measurements of left ventricular diameter and wall thickness (by the present method) during acute interventions in conscious dogs have shown an excellent linear inverse correlation ($r = 1.00$) between relative changes in internal chamber diameter and wall thickness.\textsuperscript{14} Thus, although changes in left ventricular volume were not directly measured, increased EDT provides clear evidence of decreased left ventricular chamber diameter, while the decrease in EDT during saline infusion is consistent with an increase in ventricular chamber diameter.

Ventricular electrical activation occurs at end-diastole. Therefore, changes in the size or number of end-diastolic regional dipole moments should influence the regional endocardial potentials at that time. As ventricular end-diastolic diameter increases, EDT decreases proportionally to maintain total ventricular mass constant, but the myocardial mass in proximity to the recording endocardial electrode decreases and may thereby explain the fall in the endocardial QRS potential. When ventricular end-diastolic diameter decreases, EDT increases and could

**Figure 6.** Relations of endocardial ECG amplitude (A) and spatial vectorcardiographic (VCG) amplitudes (B) to end-systolic thickness (EST), end-diastolic thickness (EDT) and amount of systolic wall thickening ($\Delta WT$ [mm]) in a representative dog. Note the linear direct relationship between EDT and both endocardial and spatial VCG amplitudes, and the nonlinear relation between amplitudes and EST or $\Delta WT$. 

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produce higher regional endocardial potentials. Reduction of endocardial potentials has been noted during ischemia and infarction,26, 27 conditions that also may be associated with reduction of wall thickness,13, 14 but whether other mechanisms are involved remains to be established. Further evidence for the possible relationship of endocardial potentials to EDT is the excellent linear relation between these two variables in each dog during various interventions. Lekven et al.6 described similar directional changes of epicardial and endocardial potentials in a few open-chest dogs during volume changes. However, we found no significant mean change in the epicardial potentials, and in three dogs inverse relations between endocardial and epicardial QRS amplitudes during volume infusion occurred (figs. 1 and 4). The reason for these different findings is not clear, although the variable behavior of the epicardial amplitudes might have related in part to the surface attachment of that crystal, whereas the endocardial crystal was imbedded within the wall.

Changes in surface QRS amplitudes have been hypothesized to be influenced by greater size or number of dipoles, as in ventricular hypertrophy,28 or by decreased cancellation within the current generator, as in myocardial infarction.29 Previous observations have also shown the influence of changes in the highly conductive intracardiac blood mass on the surface QRS potentials (Brody effect). Thus, with an increase in the intracardiac blood pool, augmented, radially directed dipoles produce increases in the early portions of the QRS, whereas a decrease in intracardiac blood has the opposite effect.30 In the present study, an excellent linear relation existed between the changes in EDT and surface QRS potentials, but the correlation coefficient was negative, the surface potentials decreasing with increased EDT and vice versa. These observations are not contradictory to those previously made in hypertrophy, which showed increased surface potentials with increased wall thickness, because the changes in wall thickness in the present study were acute and secondary to changes in ventricular size without alteration of total myocardial mass. Thus, during acute ventricular volume changes, it seems clear that mechanisms other than changes in wall thickness or conductivity of the intracardiac blood mass can also influence surface QRS amplitudes. During changes in ventricular volume, the distance of the heart from the recording surface electrodes must also change. Thus, with increased ventricular size, the heart is closer to the chest wall and the surface QRS potentials should increase, whereas with decreased ventricular size the opposite should occur. This mechanism might also help to explain the variable changes in QRS amplitude in normal subjects and patients with coronary disease during exercise.15, 31 An increased QRS amplitude might tend to occur in some patients with poor ventricular function as ventricular volume increases during exercise,32 but changes in the surface potential also depend on other factors. Changes in transfer impedance due to changes in the position of the heart in the thorax and the amount of air in the lungs during exercise, in addition to the changes in ventricular function and volume, could explain exercise-induced changes in surface QRS amplitude. In this connection, we have recently shown that changes in R-wave amplitude during exercise are more closely related to shifts in the angle of the vector loop than to alterations in the computer-processed SVM.33

We conclude that volume-induced changes in EDT are directly related to endocardial QRS amplitude. We postulate that the opposite direction of changes in the simultaneous surface QRS amplitudes may be due in part to changes in the distance of the heart from the recording electrodes.

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