Editorial Comment

The Conductance Method of Left Ventricular Volume Estimation
Methodologic Limitations Put Into Perspective

Daniel Burkhoff, MD, PhD

The search for a means of measuring left ventricular volume (LVV) accurately and continuously throughout the cardiac cycle has been long standing. Such efforts have intensified during the past 15 years with the growing appreciation for the wealth of useful information available from analysis of systolic and diastolic ventricular pressure-volume relations. Recently, much effort has gone into developing and testing the conductance method of measuring LVV. The technique is based on a multielectrode catheter, positioned within the LV cavity, that is used to set up an electrical current field and measure time varying voltage potential gradients within the LV chamber. From these voltage gradients, intraventricular conductance and, in principle, LVV are estimated. The electric field theory that underlies the technique is quite complex. However, a few simplifying assumptions make estimation of LVV from the measured voltage gradients relatively easy. To the extent that these assumptions pertain to the heart in situ, this method provides a means of measuring LVV on-line with a percutaneously placed catheter.

Several groups have worked on developing this technique, and a brief history of the various contributions has been provided. Efforts to test the accuracy of the method have focused largely on the conductance catheter system developed by Baan and colleagues, which is available from Leycom (The Netherlands). This has included comparison of 1) conductance catheter-derived stroke volume (SV$_{cath}$) with that measured by electromagnetic flow probe or thermistor in open-chest dogs, 2) SV$_{cath}$ with that measured by ventriculography in humans, and 3) continuous volume estimated by conductance catheter method (V$_{cath}$) with volumes measured with an intraventricular balloon in isolated ejecting dog hearts. Results of all these studies were favorable in that the conductance system provided a signal that was linearly and highly correlated to the LVV measured by the alternate method over a broad range of either absolute volume or stroke volume (SV). However, the relation between real volume (abscissa) and V$_{cath}$ (ordinate) does not fall on the line of identity. Rather, the slope ($\alpha$) is usually less than unity, and there is a large offset volume, referred to as $\alpha$V$_{c}$. Thus, when real volume is zero, V$_{cath}$ still has a positive value. The sources of these deviations from ideal behavior have been reviewed.

From a simplistic standpoint, these calibration factors result from conductive structures surrounding the LV cavity (e.g., myocardium, right ventricular chamber, lung) that contribute to the overall conductance signal and the fact that the equipotential electric field lines are not exactly parallel in the ventricular chamber (which is one of the assumptions referred to above that simplifies estimation of LVV from measured voltage gradients). Baan and colleagues have outlined a method for determining $\alpha$V$_{c}$ in the intact animal using a bolus of hypertonic saline injected into the pulmonary artery; there is no simple way to determine the slope $\alpha$. Importantly, none of the aforementioned validation studies serves to adequately validate application of the conductance method for continuous measurements of absolute LVV under in situ conditions.

Recently, two groups of investigators sought to test the accuracy of the conductance method of absolute LVV measurement in the in situ heart. Both groups used Leycom’s Sigma-5 volume conductance system. Boltwood et al estimated $\alpha$V$_{c}$ by repeated saline injections under a variety of loading conditions. They found that $\alpha$V$_{c}$ was not constant but varied with loading conditions. Results from stepwise regression analysis suggested that the most important factor that affected $\alpha$V$_{c}$ was end-systolic LVV itself. These investigators also compared V$_{cath}$ with volumes determined from biplane cine ventriculography during cardiac cycles and found linear correlations. While there was a trend for the relation to vary depending on the steady-state loading conditions on the ventricle, these trends did not reach statistical significance. Finally, they found a poor correlation...
between stroke volume determined by ventriculography and that determined by the conductance method.

Applegate et al\(^8\) compared \(V_{\text{cath}}\) with volumes estimated from three orthogonal pairs of endocardially placed sonomicrometer crystals (\(V_{\text{sono}}\)) in open-chest dogs. This relation was reasonably linear during the volume excursions of a normal cardiac cycle. However, when determined over a large volume range accomplished by simultaneous superior and inferior vena caval occlusions, the \(V_{\text{cath}}-V_{\text{sono}}\) relation was nonlinear. This was interpreted as indicating that again, rather than being constants, both \(\alpha\) and \(\alpha V_{c}\) varied as volume was changed. This study also investigated the impact of such nonlinearity on several indexes of systolic ventricular function: end-systolic pressure-volume relations (ESPVR), stroke work-end-diastolic volume (SW-EDV) relation, and the \(dP/dt_{\text{max}}\)-end-diastolic volume (\(dP/dt_{\text{max}}\)-EDV) relation. They found that the slope and volume-axis intercept of the ESPVR was significantly underestimated with volume measured by the conductance method as compared with when volume was measured by sonomicrometry. However, relative changes in the slope in response to autonomic blockade and to dobutamine were essentially the same with both methods of volume measurement. The parameters of the SW-EDV and \(dP/dt_{\text{max}}\)-EDV relations were similar with both methods, although the individual data points obtained did not superimpose. In contrast to Boltwood et al,\(^7\) Applegate et al\(^8\) found an excellent correlation between SVs determined from \(V_{\text{cath}}\) and \(V_{\text{sono}}\) with a slope of unity.

Thus, the results of these carefully conducted studies carried out in different manners present data that suggest that the relation between actual LVV and conductance-estimated LVV is nonlinear when volume is varied over a broad range. A large part of the evidence to support this conclusion rests on the assumption that LVVs determined by endocardial sonomicrometry or by biplane cine ventriculography are accurate or, at the very least, linearly related to real LVV. It is, therefore, mandatory to reconsider carefully the results of the previous studies in which these other methods of volume measurement have been validated.

The bulk of the data supporting the accuracy of endocardial sonomicrometrically derived LVVs is from comparisons of SVs determined simultaneously by electromagnetic flow probes and the sonomicrometer crystals under a variety of conditions.\(^9\)-\(^13\) The results of all these studies show a linear correlation between SV determined by these two methods. This is the same comparison that was performed with the conductance catheter showing equally high correlations between SV estimates.\(^1\),\(^5\) The regression lines for the sonomicrometric data did not fall on the line of identity, and there was significant variability from one study to the next. Only one study (of four dogs) compared absolute volumes measured by endocardial sonomicrometry with those determined by combining information from flowmeter-derived SV and gated blood pool scan–derived ejection fractions; furthermore, this study was limited only to an examination of end-systolic volumes. The results showed a linear correlation between end-systolic volumes determined by the two methods. However, the range of end-systolic volume variations was not specified. Furthermore, the average regression between LVVs determined by the two methods was far from the line of identity, varied significantly between animals, and even varied significantly within one animal studied on separate days. It was concluded in most of these validation studies that the crystal measurement of LVV yields an index of LVV, not absolute volume.

Biplane cine ventriculography has been validated only by comparison of its volume estimates to known volumes of LV casts or models.\(^7\),\(^14\) Validation of the technique in ejecting hearts with power-injected contrast media has not been done due to lack of a suitable independent measure for comparison.

Thus, in both the Boltwood et al and Applegate et al studies,\(^7\),\(^8\) the conductance method of volume measurement is judged on the basis of measurements made by other techniques that have not been fully validated. In fact, the results of the two studies disagree with each other on at least two important points: SV by conductance method correlated very well with that obtained by sonomicrometry but not that obtained by ventriculography, and the magnitude of changes in \(\alpha V_{c}\) observed during vena caval occlusion was much greater when volumes were measured by sonomicrometry (27-ml decrease) than by ventriculography (7-ml decrease). Part of this latter difference may relate to the fact that Applegate et al\(^8\) may have caused bigger changes in LVV by occluding inferior and superior vena cavae, whereas Boltwood et al\(^7\) occluded only the inferior vena cava.

The finding that \(\alpha V_{c}\), determined by the saline injection technique, varies significantly with end-systolic volume (more specifically, end-systolic conductance) after interventions such as inferior vena caval or aortic occlusion\(^7\) do not depend on a second method of volume measurement. The conclusion that \(\alpha V_{c}\) is a function of end-systolic volume, however, was obtained by statistical analysis of data obtained from hemodynamic maneuvers that simultaneously influenced LVV and right ventricular volumes (RVV). However, right heart volumes were not measured. Rather, right ventricular pressures were used to assess changes in the right ventricular contribution to the \(\alpha V_{c}\). The statistical results may have been different if RVVs had been included in the analysis instead of RV pressures. It would, therefore, be interesting to confirm the conclusion more directly by performing a study in which LVV and RVV were varied independently.

The possibility raised by these studies that \(V_{\text{cath}}\) is nonlinearly related to actual ventricular volume prompts several questions. First, are the results of studies published previously using the conductance method valid? The answer to this question can be
provided only through a case-by-case analysis of how such nonlinearities would impact on the results. One example may be illustrative. It was argued by Boltwood et al \(^7\) that because of a nonlinearity in conductance method of volume estimation, it was not an ideal modality for assessing nonlinearity of the ESPVR as was done by Kass et al.\(^{15}\) Recognizing the possible existence of this problem, Kass et al performed an analysis to determine how a varying \(\alpha V\) would have influenced their finding of a nonlinear ESPVR. The result of that analysis indicated, in fact, that such a situation would tend to underestimate curvilinearity when volumes were determined by conductance method. Results presented in Figure 9 of the article by Applegate et al\(^8\) illustrate this point nicely. The ESPVR shown in that figure, which was obtained using sonomicrometric dimensions, is curvilinear, with concavity toward the volume axis, whereas that obtained simultaneously by the conductance method was more shallow and linear. Thus, the assertion by Kass et al\(^{15}\) that potential variations in \(\alpha V\) would not change the qualitative conclusion regarding the type of nonlinearities they observed seems reasonable.

A second important question is whether the conductance method of LVV estimation, even at its current level of technology, can still provide useful physiologic or clinical information. The answer appears to be a conditional "yes." There does seem to be general agreement that the conductance method can provide a reasonably accurate measure of SV. Even Boltwood et al\(^8\) concede that their comparison to ventriculographically determined SVs may not be as accurate as those provided by electromagnetic flow probes. There also seems to be a consensus that over the range of volume excursions occurring during the cardiac cycle, \(V_{\text{cath}}\) provides a signal that is linearly related to volumes as determined by other methods. Finally, it was shown by Applegate et al\(^8\) that relative changes in the parameters of the ESPVR, SW-EDV, and \(dP/dm_{\text{max}}\)-EDV relations in response to pharmacologic agents are nearly the same as those obtained when sonomicrometry is used to measure LVV. Therefore, the major restriction imposed by the current findings would be for the use of the conductance method in instances requiring absolute volume measurements during transient loading changes over a broad range of volumes.

The primary advantage offered by the conductance method is the continuous volume signal output in the closed-chest (clinically relevant) setting and the absence of any tedious poststudy image processing, which permits the evaluation of several important physiologic parameters. This advantage cannot be overstated. In this regard, it can be pointed out that the usefulness of this, or any other commonly used method of LVV estimation, is not necessarily linked to the absolute accuracy of its volume estimation. The main requirement is that the method provides information that is clinically or physiologically meaningful, or both. The ability to assess relative changes in various systolic pressure-volume relations, as demonstrated for the conductance method by the results of Applegate et al\(^8\) would represent a significant advancement for studies of patients and unperturbed closed-chest animals.

Nonlinearities between \(V_{\text{cath}}\) and real LVV have been predicted on theoretic grounds.\(^{23}\) However, the degree to which they might impact on the accuracy of the method have not been exposed previous to these two studies. It should be recognized that the results of these two studies pertain to the Leycom Sigma-5 system, which takes a simple approach to estimating LVV from measured voltage potential gradients. Several technologic improvements in the technique have been explored, but they have been only partially tested (e.g., dual frequency excitation\(^{16}\) and guard currents\(^{17}\)). The system being developed by Cardiac Pacemakers, Inc. (CPI, Minneapolis, Minnesota) uses an algorithm of LVV estimation that is complex; it is only recently that details of this algorithm have become available.\(^{3,18,19}\) The CPI system, while technically more sophisticated, remains less rigorously tested than the Leycom Sigma-5. Such testing would seem important because there is no guarantee that its performance would be better than that of the Leycom system. It is reasonable to expect that improvements in technology will appear that will further enhance the ability of this method to estimate LVV from conductance measurements.

Conclusions

Results of two recent studies\(^7,8\) raise the possibility of important limitations in the conductance method of measuring absolute ventricular volume as implemented by the Leycom Sigma-5 system under in situ conditions. These studies have limitations of their own, especially with regard to lack of adequate validations of sonomicrometry and ventriculography to measure absolute LVV over broad ranges. It is vital that these potential limitations of the conductance method be considered when designing an experiment or clinical application in which the method is to be used, and accounted for in the interpretation of results. This maxim applies not only to the conductance catheter but also to all methods of measuring ventricular volumes. The results of both studies also suggest that there are many conditions under which the limitations of the conductance method appear to be insignificant. Some investigators may abandon this method because of the results of these two studies. It would be unfortunate if results obtained by others using the method were ignored or rejected, provided that its limitations are dealt with in a meaningful way. No other method on the immediate horizon offers the possibility of measuring ventricular volumes continuously without ever having to invade the chest wall. Hopefully, the results of these studies will provide an impetus for physiologists, physicists, and engineers to advance the technology of volume measurement by a conductance
technique to the next level of sophistication to overcome such limitations.

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D Burkhoff

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