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The Conductance Volume Catheter Technique for Measurement of Left Ventricular Volume in Young Piglets

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ABSTRACT. The conductance catheter has been used extensively in the adult for instantaneous and continuous measurement of left ventricular volumes, but has not been validated for use in the small heart. To determine the accuracy of this technique, we simultaneously measured left ventricular volume by the conductance catheter and biplane cineangiography in nine piglets (2–5 wk of age) over a wide range of volumes experimentally altered by volume infusion, hemorrhage, inferior vena caval occlusion, or administration of phenylephrine, isoproterenol, or propranolol. We performed 110 comparisons and determined parallel conductance of contiguous structures (αV_c) for each comparison using the saline technique. End-systole and end-diastole volumes were estimated by angiography using Simpson's rule. Raw and αV_c-corrected conductance volumes were compared to simultaneously obtained angiographic volumes by multiple regression analyses, using dummy variable coding for the effects of the interanimal variability and the phase of the cardiac cycle. Raw conductance volumes correlated highly with the cineangiographic volumes ($r = 0.97$), and the coefficient of angiographic volumes was near identity (1.11 ± 0.04). The phase of the cardiac cycle did not have a significant effect. However, αV_c-corrected conductance volumes correlated less well ($r = 0.85$), probably related to the fact that estimated αV_c was found to vary with ventricular volume. Thus, the conductance catheter affords a very accurate technique for measuring instantaneous changes in ventricular volume in the small heart, although correction to absolute volumes using the saline technique for estimation of αV_c may induce some inaccuracy. (*Pediatr Res* 31: 85–90, 1992)

Abbreviations

αV_c, parallel conductance

Evaluation of left ventricular systolic and diastolic performance in the pressure-volume plane has been widely investigated, and a variety of indices have been derived that shed light on the intrinsic function of the myocardium during contraction, relaxation and passive filling (1–6). Such studies often require generation of repeated pressure-volume loops during hemodynamic perturbations such as occlusion of the inferior vena cava. The ideal technique would continuously measure volume, preferably instantaneously generating values, so that the loops could be observed during on-line acquisition of data. The technique should not perturb the hemodynamic state of the subject. It is particularly important in the young subject to have a technique that is not subject to observer measurement biases, such as may occur in echocardiographic studies, because small chamber size magnifies the importance of such errors. The conductance catheter meets these requirements better than any previously used technique and has been used in the adult animal and human (7–10). However, validation studies of the conductance technique have not been performed in the small heart. To determine its accuracy in small hearts, we compared volumes measured by the conductance catheter to those simultaneously measured by biplane cineangiography in hearts of young piglets under a variety of volume and contractile conditions.

MATERIALS AND METHODS

Nine piglets between 2 and 5 wk of age (6.1–8.8 kg body wt) were studied on a protocol approved by the Committee on Animal Research at the University of California San Francisco. After sedation with ketamine hydrochloride (8 mg/kg), general anesthesia was induced by α-chloralose (80 mg/kg). A tracheostomy was performed, and ventilation with supplemental oxygen was initiated using a Harvard respirator. Access to the central vasculature was established by the percutaneous placement of 6–7 F Teflon sheaths (Cook, Bloomington, IN) into both right and left femoral veins and femoral arteries. A Teflon sheath was also placed in the left carotid artery by surgical cutdown in some of the piglets.

Catheters were then introduced into the central vasculature via the sheaths. Using fluoroscopic guidance, a 5 F Berman angiographic catheter (Arrow, Reading, PA) was advanced from the femoral vein into the pulmonary artery. A 5 F Fogarty atrial septostomy catheter (Baxter Health Care Corp., McGaw Park, IL) with a 1.8-mL capacity balloon was placed into the contralateral femoral vein and positioned in the inferior vena cava at the level of the diaphragm. A 4–5 F high-flow pigtail catheter (Cook) was passed in a retrograde fashion from the femoral artery into the left ventricle. A 6 F pigtail multielectrode conductance catheter (Webster Laboratories, Baldwin Park, CA), which had a total intraelectrode distance (4 cm) chosen to slightly exceed the left ventricular apex to aortic valve distance (range 3.5–4 cm), was advanced into the left ventricle via the femoral artery or carotid artery sheath. The correct positioning of the distal end of the catheter at the cardiac apex and the proximal electrode just above the aortic valve was confirmed during biplane angiocardiography (Fig. 1).

Left ventricular or arterial pressure was monitored continuously through either the pigtail catheter or the side arm of the femoral artery sheath, using a strain gauge transducer (Statham P23Db, Oxnard, CA) attached to a pressure amplifier and a polygraph (Gould Electronics, Cleveland, OH). The conductance catheter was connected to a model Sigma-5 signal-conditioner-

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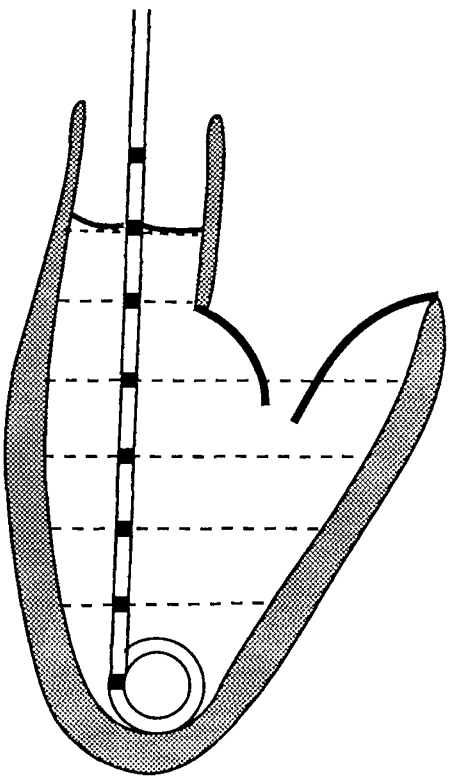

Fig. 1. Diagram of the conductance catheter. A 20-kHz current is applied between the most distal electrode, near the apex of the heart, and the most proximal electrode, above the aortic valve. Conductance of that current is measured between each pair of the other six electrodes.

processor (Leycom, Oestgeest, Netherlands), which supplied a 20-kHz 0.4-mA root mean squared current, measured the segmental conductances, and calculated the total volume from the segmental conductances. The Sigma-5 was also used to measure the conductivity of each piglet's blood and of all injectates. Its output was connected to the polygraph amplifiers for monitoring and to an analog-to-digital data card (National Instruments, Austin, TX) inside a Macintosh II microcomputer (Apple Computer, Cupertino, CA). The data were acquired and simultaneously digitized at 200 Hz and recorded on hard disk for later analysis. The data acquisition and analysis were performed using software developed in our laboratory in the LabVIEW programming environment (National Instruments) on the Macintosh microcomputer.

Between 10 and 17 measurements of ventricular volume were acquired simultaneously by the conductance catheter and cineangiography in each piglet. For each measurement, at least three to seven beats were available from which contrast opacification was sufficient for volume determination by cineangiography. From these beats, maximum diastolic (end-diastolic) and minimum systolic (end-systolic) volumes were measured by the two techniques and mean values were calculated for subsequent data analysis. Data were first acquired under baseline conditions. Subsequently, and in random order, we varied ventricular diastolic and systolic volumes over a wide range by hemorrhage (10 mL/kg, which was immediately returned at the end of data acquisition), volume infusion (10 mL/kg of isoconductive saline), inferior vena caval occlusion, phenylephrine infusion (10–20 μg/kg/dose), isoproterenol infusion (0.1–0.2 μg/kg/dose), and propranolol infusion (1 mg/kg). Heart rate was not controlled, to allow for the greatest changes in volume. We obtained 34 measurements during baseline conditions, eight measurements after volume infusion, four after hemorrhage, 30 during inferior vena caval occlusion, 17 during phenylephrine infusion, 13 during isoproterenol infusion, and four after propranolol infusion. Thus, a total of 110 runs were performed, yielding 220 data sets (110 end-diastolic and 110 end-systolic points) of conductance and angiographic volume estimates. End-diastolic volumes ranged from 4.1 to 29.8 mL, and end-systolic volumes ranged from 1.9 to 20.0 mL, as estimated by angiography.

Conductance measurements. The volume data from the conductance catheter were calibrated using digitized electrical zero and full-scale values. To convert measurements of segmental conductance, G(i), to absolute segmental volumes V(i), the following formula was used:

$$V(i) = (1/\alpha)\,(L^2/\sigma_b)\,G(i) - V_c$$

where V(i) is the segmental volume, α is a dimensionless slope constant, L is the interelectrode distance of the catheter, σ_b is the specific conductivity of blood, and V_c is a correction term caused by the parallel conductance of structures surrounding the ventricular cavity (10). The conductivity of the blood was determined frequently throughout the study. αV_c was determined at the end of each acquisition by the saline method (10) to correct the conductance signal to "absolute" ventricular volume. This was done by transiently changing the conductivity of the blood in the left ventricle and extrapolating to where the blood conductivity was zero. After the radioopaque dye had completely cleared the left ventricle, a small volume (0.2–0.5 mL) of 3% NaCl solution was injected into the pulmonary artery catheter during continuous data acquisition. End-systolic volume was then plotted against end-diastolic volume during the period when the conductivity of the blood was changing, and linear regression was performed. This regression line was then extrapolated to where end-systolic volume equals end-diastolic volume (to where the conductivity of the blood was zero). At this point, αV_c, all conductance must be through surrounding structures. Conductance volumes throughout the cardiac cycle were determined both without (raw) and with (αV_c-corrected) subtraction of αV_c. End-diastolic and end-systolic volumes for several beats were temporally matched to the angiographic beats during each run.

Cineangeographic measurements. Biplane left ventricular cineangiograms were recorded on videotape in posterior-anterior and lateral projections at a frame rate of 30/s. Before injection, the radioopaque contrast material (Hypaque 76; Sterling-Winthrop, New York, NY) was warmed in a water bath to body temperature, and its conductivity was adjusted to equal that of the blood by dilution with either deionized water (infinitely low

Table 1. *Raw conductance volume: results of multiple linear regression analysis**

				Between pigs							
Variable	b_0	V_{Cine}	C	A1	A2	A3	A4	A5	A6	A7	A8
b	17.8	1.1	0.1	−2.3	12.5	0.9	2.0	−0.3	0.1	−1.1	−2.9
SEM		0.05	0.09	0.55	0.63	0.55	0.55	0.54	0.56	0.45	0.55
p value		<0.001†	>0.5	Coefficients combined: <0.001†							

* The coefficients b are in mL except b_{Vcine}, which is in $mL \cdot mL^{-1}$. b_0, the intercept (overall mean raw conductance volume). Variables: V_{cine} is a continuous variable (mL) representing cineangiographic volume, C is a dummy variable representing cardiac cycle, and A1 through A8 are dummy variables representing the variability among the nine pigs. The regression equation was statistically significant ($p < 0.0001$). The SD of these between-pig coefficients was 4.87 mL. The *p* value is that of the corresponding *F* test for that coefficient or group of coefficients.

† The coefficient or group of coefficients has a significant effect on raw conductance volume.

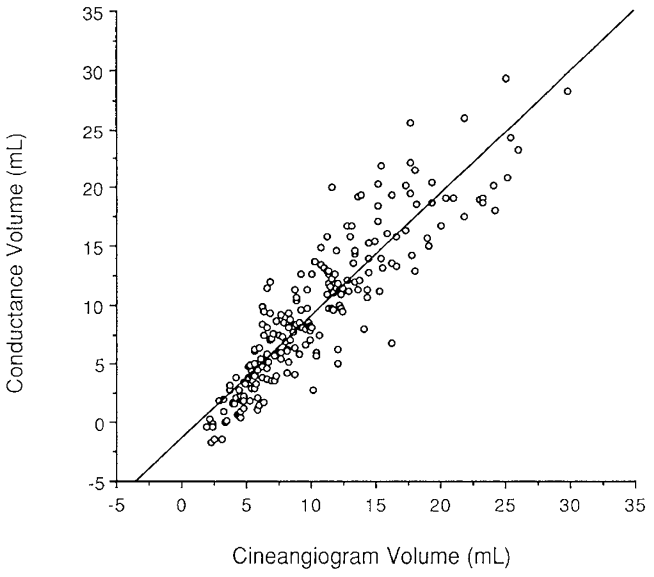

Fig. 2. Scattergram of all of the conductance and cineangiogram data. The conductance volumes have been corrected using the mean αV_c for each piglet to remove the different offset volumes between animals. The *line* shown represents the simple regression between conductance and angiogram volumes. The slope of the line is 1.04, and $r = 0.91$.

conductivity) or saturated sodium chloride solution (very high conductivity). Between 1 and 1.5 mL/kg of radioopaque contrast were injected using a pressure injector for each cineangiogram. The volume catheter with known intraelectrode distances was recorded on videotape in a straight cranial-caudal position with the radiographic equipment positioned as it was for the cineangiograms to determine magnification.

Angiographic ventricular volumes were measured from biplane images using Simpson's rule (11, 12) on a microcomputer equipped with a video card and software designed for image quantification (Microsonics, Indianapolis, IA). End-diastolic and end-systolic volumes were determined for each beat using frame-by-frame comparison of the images. The observer measuring the volumes was blinded to the volume measurements made using the conductance catheter and to the condition under which they were measured. Volumes derived from conductance and angiography were synchronized using the cineangiographic contrast injection (which caused an obvious increase in the volume on the catheter tracing) or by timing of ventricular ectopic beats, which occasionally occurred during contrast injections.

Data analysis. Comparisons between conductance and cineangiographic volumes were made by multiple regression analysis using dummy variables by effects coding (13–15):

$$V_{cond} = b_0 + b_{V_{cine}} V_{cine} + b_c C + \sum_{j=1}^{8} b_{A_j} A_j$$

where the dependent variable V_{cond} is the raw or αV_c-corrected conductance volume, the intercept b_0 is the offset of the conductance volume relative to the cineangiographic volume, V_{cine} is the angiographic volume, C is the dummy variable representing the phase in the cardiac cycle (end-systole was assigned a value of 1, end-diastole, −1), and A_j represents the dummy variables representing interanimal variability. The coefficients (b_0, b_{cine}, etc.) for each variable are the change in V_{cond} relative to a change in that variable.

αV_c has been found to vary relative to end-systolic and end-diastolic volume in the adult dog (16). To determine whether this relationship existed in the newborn piglet, we performed separate multiple regression analyses of parallel conductance against end-systolic and end-diastolic volume and the set of dummy animal variables, A_j.

RESULTS

Multiple regression analysis of raw conductance volumes showed a high correlation ($r = 0.97$), an offset volume b_0 (equivalent to the y-intercept in simple regression) of 17.9 mL, and no significant effect of cardiac cycle (Table 1). The coefficient of the angiographic volume was 1.11 ± 0.04, indicating that a change in conductance volume relative to a change in angiographic volume was near identity. This coefficient corresponds to α, the slope of the simple linear regression of conductance *versus* angiographic volume. The strength of the association can be appreciated in Figure 2, which shows a scattergram of all data sets of conductance volume corrected using mean αV_c. This was done to remove the different offset volumes between animals. From simple linear regression analysis of conductance *versus* cineangiogram volume, the slope of the regression equation was very similar (1.04) to that found by multiple regression analysis. Attempts to fit a polynomial equation to these data did not yield a significantly greater correlation.

When conductance volumes were corrected for individual αV_c for each run, the correlation of the resultant regression equation was not quite as good ($r = 0.85$), and the coefficient for the angiographic volume was lower (Table 2). Thus, it is likely that the correction of conductance volume using αV_c introduced some error in the estimation of conductance volume.

When conductance volumes were corrected using the mean of αV_c for each piglet rather than the individual αV_c for each run, the resultant correlation improved substantially ($r = 0.91$) and the coefficient for the angiographic volume, V_{cine}, increased to 1.1, similar to the coefficient for the raw conductance volume analysis (Table 3). This improvement indicates that there is error in measurement of αV_c that is partially eliminated by averaging. For actual volume measurements, this small error was not physiologically important. Figure 3 shows data from a representative piglet where the mean αV_c for this piglet was subtracted from the raw conductance volume, showing excellent correlation between volumes measured by the two techniques. Again, polynomial regression did not yield a significantly greater correlation.

Regression analyses of αV_c showed that it varied significantly with both end-systolic and end-diastolic ventricular volumes (Tables 4 and 5). A moderate and similar effect of both volumes on αV_c was seen, with a predicted change in αV_c of 0.46 and 0.76 mL in conjunction with a 1 mL change in end-systolic volume and end-diastolic volume, respectively.

Table 2. *Individual αV_c corrected conductance volume: results of multiple linear regression analysis**

Variable	b_0	V_{Cine}	Between pigs							
			A1	A2	A3	A4	A5	A6	A7	A8
b	1.16	0.77	2.0	0.2	−0.1	−0.4	−0.4	0.6	0.4	−1.2
SEM		0.05	0.64	0.78	0.66	0.66	0.64	0.62	0.53	0.63
p value		<0.001†	Coefficients combined: >0.5							

* The SD of the between-pig coefficients was 0.94 mL. See Table 1 for abbreviations and statistical significance. The *p* value is that of the corresponding *F* test for that coefficient or group of coefficients.

† The coefficient or group of coefficients has a significant effect on corrected conductance volume.

Table 3. *Mean αV_c corrected conductance volume: results of multiple linear regression analysis**

Variable	b_0	V_{Cine}	Between pigs A1	A2	A3	A4	A5	A6	A7	A8
b	−2.1	1.1	−0.1	2.1	0.8	0.3	0.0	1.7	0.9	−0.9
SEM		0.04	0.53	0.59	0.54	0.55	0.54	0.55	0.45	0.55
p value		<0.001†	Coefficients combined: >0.5							

* The SD of the between-pig coefficients was 1.17 mL. See Table 1 for abbreviations. The *p* value is that of the corresponding *F* test for that coefficient or group of coefficients.

† The coefficient or group of coefficients has a significant effect on corrected conductance volume.

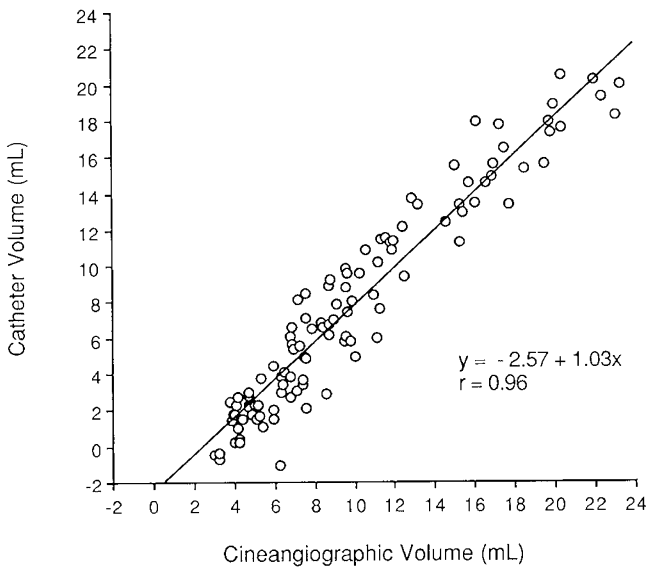

Fig. 3. Scattergram of conductance and cineangiogram data for a representative piglet. The conductance volumes have been corrected using the mean αV_c for the piglet. The *line* shown represents the simple regression between conductance and angiogram volumes.

DISCUSSION

This study demonstrates that the conductance catheter technique is accurate for determining instantaneous ventricular volumes in small hearts. The technique was more accurate when comparing raw rather than αV_c-corrected conductance volumes to cineangiographic volumes. This suggests that correction using the saline method to measure αV_c introduced a small error in calculation of absolute volume. We also found that αV_c varies with ventricular volume, similar to the findings of Boltwood *et al.* (16) in the adult dog. This is in contrast to the lack of such a relationship in the newborn lamb (17), in which αV_c remained remarkably constant over a very wide range of ventricular volumes.

The conductance catheter has major advantages over other techniques for estimating left ventricular volume. Although left ventricular angiocardiography is an accepted method of measurement of time-varying left ventricular volume, it requires human judgment (18) and is very time-consuming (18–20), even with the use of an image quantification computer. Variability is noted in the studies validating angiocardiography as a technique for volume measurement (18, 21, 22), and it frequently overestimates true volume (18, 21–24). More importantly, angiocardiography alters the loading conditions and contractile function of the ventricle (25). Volumes measured using cross-sectional echocardiography have considerable variability (26–28), often underestimate volume when compared to cineangiography (26, 27), and require substantial time for calculation of volume. In addition, echocardiographic definition of the entire endocardial surface is often difficult. Other methods of volume measurement, including computed tomography (29, 30), magnetic resonance imaging (31–34), and gated radionuclide imaging (35–39) measure volume from images obtained over many beats. These techniques cannot reflect the beat-to-beat changes in volume required for comparison to simultaneously measured pressures. First-pass radionuclide imaging (36, 40) provides images of only one cardiac cycle and similarly cannot reflect beat-to-beat changes in volume. Radionuclide imaging is further limited by its poor resolution and inability to perform multiple studies because of radiation exposure. The technique of volume estimation with similar advantages to the conductance catheter is multidimensional sonomicrometry. However, it can only be performed in animal models and has other disadvantages in the small heart. The placement of six crystals on the heart is technically very difficult, and because of the small size of the heart, may cause significant dysfunction of a relatively large portion of myocardium. The accuracy of the technique has not been established in the small heart. In the adult heart, limited validation studies have shown marked variability in the slope of the relationship between sonomicrometry volumes and "true" volumes (41).

In studies that use estimates of volume based on one or two dimensions of the left ventricle for calculation of indices of cardiac function, assumptions are made regarding both the geometry of the ventricle and uniformity of ventricular motion. These assumptions may not be valid for a great many normal and diseased hearts. Volumes measured using the conductance volume catheter do not strictly require similar geometric assumptions. However, several assumptions of the behavior of the electrical field in the ventricle are required for calculation of volume. These assumptions may not be entirely valid, and work is ongoing to try to better define the electrical field in the ventricle (42).

The determination of αV_c affects estimation of true volume in two ways: first, αV_c is dependent on ventricular volume and, second, αV_c may vary because of technical problems associated with its estimation. The latter appears more important in this

Table 4. *αV_c vs end-systolic volume: results of multiple linear regression analysis**

Variable	b_0	V_{Cine}	Between pigs A1	A2	A3	A4	A5	A6	A7	A8
b	14.4	0.46	−4.5	11.4	1.3	1.8	1.3	0	−1.7	−2.6
SEM		0.08	0.99	1.2	0.95	0.98	0.86	0.84	0.79	0.84
p value		<0.001†	Coefficients combined: >0.1							

* The SD of the between-pig coefficients was 4.79 mL. See Table 1 for abbreviations. The *p* value is that of the corresponding *F* test for that coefficient or group of coefficients.

† The coefficient or group of coefficients has a significant effect on a V_c.

Table 5. *αV_c vs end-diastolic volume: results of multiple linear regression analysis**

Variable	b_0	V_{Cine}	Between pigs A1	A2	A3	A4	A5	A6	A7	A8
b	14.5	0.76	−6.0	10.9	1.3	2.0	0.9	0.8	−1.5	−2.0
SEM		0.12	1.1	1.2	0.95	0.97	0.84	0.87	0.79	0.84
p value		<0.001†	Coefficients combined: >0.1							

* The SD of the between-pig coefficients was 4.83 mL. See Table 1 for abbreviations. The *p* value is that of the corresponding *F* test for that coefficient or group of coefficients.

† The coefficient or group of coefficients has a significant effect on αV_c.

study, because correction for αV_c introduced inaccuracy in the relationship between conductance and angiographic volumes. Several possible reasons for technical problems in determination of αV_c were present in our study. First, the saline technique assumes that no change in true ventricular volume occurs during injection of hypertonic saline, so that change in apparent volume can be ascribed only to change in conductivity of ventricular blood. To avoid an increase in true left ventricular volume in the small heart, which had absolute end-systolic volumes of 2–4 mL, very small volumes of very hypertonic saline solution are injected. This hypertonic solution itself might change ventricular function as it reaches the coronary circulation and, therefore, will change true ventricular volume. In this study, saline injection probably caused a small but consistent increase in ventricular volume during each estimate of αV_c. This would have a relatively greater impact at the smaller volumes, which might explain the volume dependency of αV_c. Secondly, although every effort was made to insure that the injectate containing radioopaque dye had the same conductivity as the piglet's blood, some error in volume measurement caused by alteration of the blood conductivity was probably introduced by this injection. This may also have contributed to error in measurement of αV_c, which always occurred after angiography. Such an error would only occur in this type of validation study. This would also likely induce volume dependency, because injection of a fixed volume of contrast agent would have different effects in ventricles of different starting volumes. Lastly, we determined αV_c by performing a linear regression of end-diastolic *versus* end-systolic volumes for estimates of total volume, rather than determining the individual αV_c for each catheter segment. Because the best linear fit for each segment (43) appears critical to the accurate determination of αV_c, our technique probably induced some inaccuracy in its determination, although this would not be expected to be volume-dependent. Because averaging of many αV_c measurements for each piglet improved the correlation of corrected conductance volume and cineangiographic volume, it is apparent that there is more inaccuracy to αV_c measurement than systematic variation of αV_c with volume.

Although averaging the αV_c for each animal eliminated some of its variability, this is not a true solution to the problem of error in estimation of αV_c because variation of αV_c with volume still exists. A better solution must be found that makes determination of αV_c more reliable in the piglet heart. This perhaps includes use of even smaller volumes of saline injected very slowly, which would not alter true left ventricular volume. If αV_c appears to be inaccurate or at least volume-dependent in a particular study situation, a decision must be made on how to deal with this problem. One possibility would be to ignore αV_c entirely and allow the differences in αV_c to be represented within interanimal variability in a multiple regression analysis or analysis of variance. Thus, changes in volume rather than absolute volumes would be used in the generation of pressure-volume loops or other techniques for analysis of systolic and diastolic ventricular performance. This is reasonable because many indices of ventricular function do not require knowledge of absolute values of volume but depend upon changes in volume. This is true of many current techniques for estimating ventricular contractility, including the end-systolic pressure-volume relationship, the preload recruitable stroke-work index, and the maximum change in pressure per unit time-end-diastolic volume relationships, where the slope of the relationships is most important and curvilinearity beyond the range of measurement makes extrapolation to "unstressed" volume unreliable. Estimates of diastolic performance are primarily directed to isovolumic relaxation, in which rate of pressure fall alone is analyzed, or to passive filling, in which some estimates of compliance are made. Because compliance is determined by a change in pressure relative to a change in volume, true knowledge of absolute volumes is unnecessary. Alternatively, if an estimate of absolute volume is desired for calculation of absolute stress, for example, it may be possible to define the relationship of an accurate estimate of αV_c *versus* absolute volume and to correct for this during the estimate of that absolute volume. Other techniques for improving the estimation of αV_c that may not show the same volume dependency are being developed (42, 44). Further studies must be performed before they are accepted for general use.

In summary, estimation of ventricular volume using the conductance catheter is accurate in the young piglet. The conductance catheter method does not disturb loading conditions or contractility and is therefore suitable for repeated studies of left ventricular function. Accuracy decreases when correction to absolute volume is attempted by the use of the saline technique for calculation of αV_c. Despite this problem, the conductance catheter will be a very useful tool in conjunction with accurate measurement of instantaneous ventricular pressure for evaluation of ventricular systolic and diastolic performance in the pressure-volume plane in small hearts.

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