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Left ventricular volume determination in dogs: a comparison between conductance technique and angiocardiography

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Left ventricular (LV) volume was determined simultaneously by monoplane cineangiocardiography and conductivity using a multielectrode conductance catheter at rest and during pressure loading in seven mongrel dogs (mean body weight 22 kg). LV volumes were calculated frame-by-frame (75 frames s^{-1}) by angiocardiography and matched with instantaneous volumes obtained by conductivity. There was an excellent correlation between the two techniques at rest (correlation coefficient, $r = 0{\cdot}96$) and during pressure loading ($r = 0{\cdot}92$) when the data of each dog were pooled. The standard error of estimate of the mean angiographic volume was 4%. The slope of the regression analysis showed a small but significant ($P < 0{\cdot}01$) decrease from 0·365 at rest to 0·289 during pressure loading, whereas the intercept remained unchanged (24 versus 26 ml). Since no calibration for parallel conductivity of the surrounding tissue was performed, LV end-systolic volume was significantly over- and LV ejection fraction significantly underestimated whereas LV end-diastolic volume was estimated correctly by the conductance technique.

It is concluded that LV end-diastolic volume can be determined accurately by the conductance technique in dogs. However, LV end-systolic volume is significantly over- and ejection fraction significantly underestimated. Since there is a good correlation between angiocardiography and conductivity, exact determination of LV volumes and ejection fraction is feasible using a correction factor. The change in slope of the regression equation between angiocardiography and conductivity suggests a change in conductivity of the surrounding tissue during pressure loading which limits the application of the conductance catheter to stable haemodynamic situations or calls for repeated calibrations by an independent technique during acute interventions.

Introduction

Left ventricular pressure and volume are two important variables for the assessment of left ventricular function in man. Systolic ejection fraction has been shown to be a simple but reliable parameter with prognostic implications for the postoperative course and the clinical follow-up in patients with coronary, valvular or myocardial heart disease. Cineangiocardiography has been widely used for the assessment of left-ventricular function[1], but haemodynamics are influenced by the use of contrast medium, and continuous measurements over several cardiac cycles are not possible. Radionuclide ventriculography allows continuous determination of left ventricular ejection fraction but left ventricular volumes cannot be determined accurately due to calibration problems[2]. Baan and co-workers[3,4] recently developed a new technique for determination of left ventricular volume using a multielectrode catheter to measure left ventricular conductivity. In experimental studies it was shown that this technique allows an accurate determination of left ventricular volume and ejection fraction in the isolated heart or in the experimental animal using balloon, ferromagnetic or dilution techniques as reference methods[3–6]. The purpose of the present study was to investigate the accuracy of the conductance technique for the assessment of left ventricular volume at rest and during acute pressure

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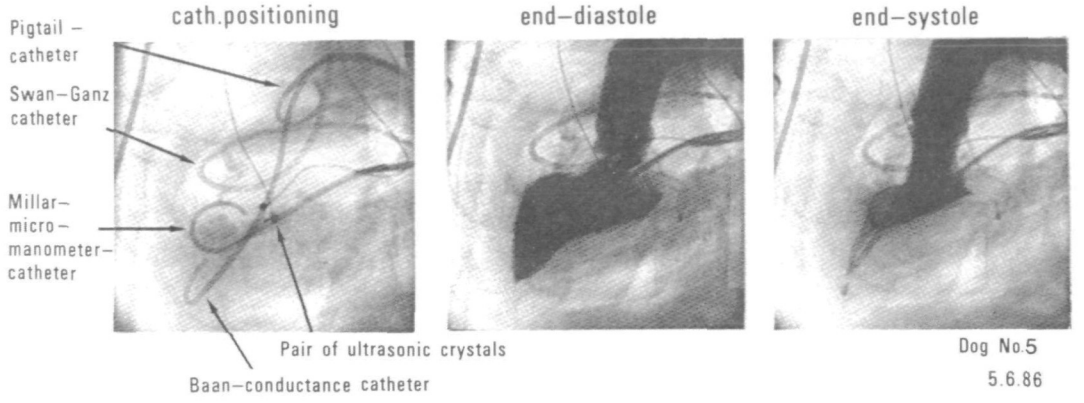

Figure 1 An example of the experimental preparation (see text for further explanation) showing the correct positioning of the different catheters and the ultrasonic crystals before and during angiocardiography (RAO projection) at end-diastole and end-systole It is clearly seen that the conductance catheter is well positioned during the cardiac cycle.

loading using conventional angiocardiography as a reference method.

Material and methods

Seven mongrel dogs weighing 20–30 kg (mean 22 kg) underwent left thoracotomy in the fifth intercostal space under general anaesthesia[7] with 0·25 mg kg^{-1} Polamivet (morphine derivative) and 0·04 mg kg^{-1} Combelen (phenothiazine derivative) in combination with 10 mg kg^{-1} pentothal (barbiturate). The pericardium was opened widely and an 8F Millar pigtail-micromanometer catheter was inserted via the left atrial appendage into the left ventricle (Fig. 1) to measure left ventricular pressure and to inject contrast medium for simultaneous angiocardiography. The conductance catheter was inserted by the retrograde route into the left ventricle from the right femoral artery (Fig. 1). The tip of the catheter was placed in the apex of the left ventricle and its position was checked several times throughout the study. A 7F Swan–Ganz catheter was introduced in the pulmonary artery for taking blood samples and for the injection of hypertonic saline or cold glucose. Finally, an 8F pigtail catheter was positioned in the ascending aorta to measure aortic pressure. Arterial blood gases and serum potassium were closely monitored and corrected when necessary.

CONDUCTANCE MEASUREMENTS

Left ventricular conductivity was measured using a conductance catheter with eight electrodes (Cordis Europa NV, Roden, The Netherlands). This technique has been described previously by Baan and co-workers[3,4]. The electrodes are placed adjacent to each other on the distal 10 cm of the catheter. After positioning of the catheter into the left ventricle, an alternating current of 22·2 kHz and 30 μA was applied between the two driving electrodes Nos 1 and 8. The sensing electrodes 2–3, 3–4 and 4–5 were used for the conductivity measurements. It has been shown experimentally that the sum of the conductances measured by each pair of electrodes is linearly related to the volume[3]. The volume (V) can be calculated according to the following equation:

$$V = (1/a)\,(L^2/qb)\,G_t - V_c$$

where a is a dimensionless constant, L is the distance between two adjacent electrodes (cm), qb is the specific conductivity of the blood in the ventricle (S m^{-1}), G_t is the instantaneous sum of conductances measured between every pair of adjacent electrodes (S = Siemens = 1/ohm), and V_c is the volume intercept for the conductance of the surrounding tissues at zero cavity volume (ml). The specific conductivity of the blood was measured every 30 min with a rho cuvette which was connected to the amplifier (Leycom Sigma 5).

Calibration of the conductance signal was carried out with a built-in calibration system in the amplifier. These volumes have to be corrected for the volume intercept V_c, which varies from dog to dog, to obtain the absolute volumes. Baan *et al.*[4] suggested two calibration methods: the first method

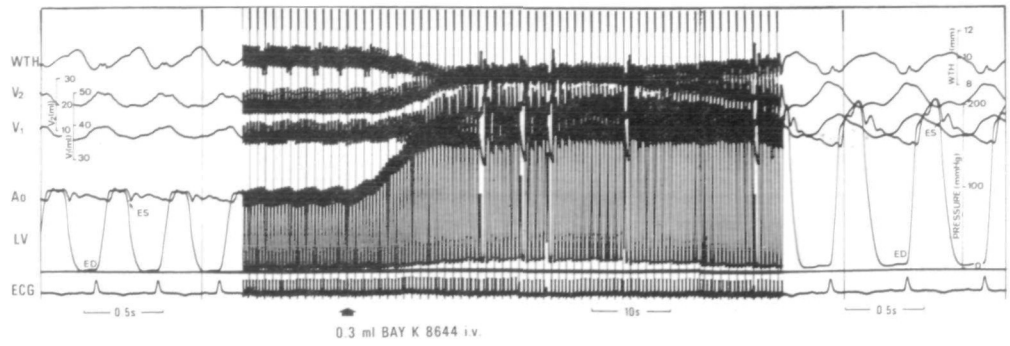

Figure 2 An original tracing showing the haemodynamic variables measured before and during acute pressure loading. WTH, left-ventricular wall thickness (cm) not used in this study; V_1 and V_2, two left-ventricular volume signals (ml); Ao, aortic pressure (mmHg); LV, left-ventricular pressure (mmHg); ED and ES, end-diastole and end-systole, respectively

consists of a transient reduction of the left ventricular volume to zero through suction which is, however, not possible in the living animal. The second method is based on a change in the specific conductivity of blood (qb) by injection of hypertonic saline or cold glucose into the pulmonary artery. Assuming no change in left ventricular volume and ejection fraction during saline or glucose injection, the volume measured by the conductance catheter at zero cavity volume (V_c) can be calculated from the regression line between the end-systolic and end-diastolic conductivity during saline or glucose injection[4,6]. The second technique was applied in the present study by injecting hypertonic saline (10 and 20%) or cold glucose solution (5%) into the pulmonary artery. However, no significant change in the specific conductivity of the blood was observed by the conductance catheter within the left ventricle. Therefore, this calibration technique was abandoned. Baan *et al*[4] reported also in some patients no response of the conductance catheter to saline injections. Since no direct calibration procedure was possible for the determination of V_c, the regression equation between angiocardiography and conductivity was used to correct left ventricular volumes obtained by the conductance technique.

ANGIOCARDIOGRAPHY

Monoplane left ventricular cineangiocardiography was performed in the right anterior oblique projection. The contrast medium (Urografin 76%) was injected (40 ml with a flow rate of 10 ml s^{-1}) via the 8F Millar pigtail-micromanometer catheter into the left ventricle. The filming rate was 75 frames s^{-1} and the volumes were calculated frame-by-frame using the 'area–length' method[1]. Extrasystolic and post-extrasystolic beats were excluded from the analysis. The volume signals of the conductance catheter and left ventricular pressures were

Table 1 Standard haemodynamic data

Dog No.	HR (bpm)	LVEDP (mmHg)	LVSP (mmHg)	SVR (dyn s cm^{-5})
Control run				
1	145	8·4	111	2154
2	142	5·5	110	2653
3	124	7·7	130	3507
4	161	5·5	119	1730
5	154	6·5	121	3329
6	137	5·2	111	2394
7	173	9 3	101	2715
Mean	148	6·9	115	2640
±1 SD	±16	±1·6	±9	±627
Pressure loading				
1	137	9·0	143	2668
2	129	3·2	191	4670
3	107	11·8	199	4713
4	129	5·5	172	3620
5	145	6·7	171	5995
6	116	6·0	150	4630
7	163	8·4	161	4490
Mean	132	7·2	169	4398
±1 SD	±18	±2·8	±20	±1032
P	<0·005	NS	<0·001	<0·001

HR, heart rate; LVEDP, left ventricular end-diastolic pressure; LVSP, left ventricular systolic pressure; SVR, systemic vascular resistance.

recorded simultaneously during cineangiocardiography on an oscillograph 'Electronics for Medicine VR 12' at a paper speed of 250 mm s^{-1}[8]. Angiographic volumes were compared on a frame-by-frame (every 13·4 ms) basis with left ventricular volumes obtained from the conductance catheter. Since there was a good correlation between these two techniques, the angiographic data were used to correct left ventricular volumes obtained from the conductance catheter (see below).

EXPERIMENTAL PROTOCOL

After completion of the instrumentation, an interval of 10 to 15 min was allowed for haemodynamics to return to baseline conditions. Then the control run was begun and pressure and volume measurements were carried out simultaneously during left ventricular cineangiocardiography (Fig. 1). After an interval of 20 min which was allowed for dissipation of the haemodynamic effects of the contrast medium, pressure and volume measurements were repeated. Acute pressure loading was then performed using a new calcium agonist Bay K 8644[9,10]. The drug was injected intravenously and the mean dosage amounted to 0·55 mg ranging between 0·3 and 1·2 mg (mean 0·02 mg kg^{-1}). Steady state was usually achieved 1 to 2 min after injection of the drug. Immediately after a steady state was reached, pressure and volume measurements were recorded simultaneously with a second cineangiocardiogram.

DATA ANALYSIS

Left ventricular pressure tracings were digitized manually for an entire cardiac cycle using an electronic digitizer (Numonics Corp.) interfaced to a

Table 2 Left ventricular volume and ejection fraction

	Angiocardiography			Conductivity					
				Uncorrected			Corrected		
Dog No	EDV (ml)	ESV (ml)	EF (%)	EDV (ml)	ESV (ml)	EF (%)	EDV (ml)	ESV (ml)	EF (%)
Control run									
1	40	12	71	41	31	25	46	9	80
2	46	23	50	44	35	21	49	23	53
3	49	24	52	52	39	25	50	22	56
4	47	13	73	40	30	25	46	13	73
5	30	11	63	32	24	26	31	12	61
6	46	21	54	37	29	21	48	22	54
7	24	7	71	32	24	23	26	7	73
Mean	40	16	62	40	30*	24*	42	16	64
±1 SD	±10	±7	±10	±7	±5	±2	±10	±7	±11
Pressure loading									
1	45	14	69	40	30	24	53	13	76
2	46	21	55	46	38	18	50	21	59
3	58	24	58	46	33	28	55	20	63
4	46	16	65	40	30	25	54	11	80
5	28	11	59	32	27	17	31	13	59
6	39	17	57	35	30	16	41	18	55
7	24	6	75	32	25	22	25	6	76
Mean	41	16	63	39	30*	21*	44	15	67
±1 SD	±12	±6	±7	±6	±6	±5	±12	±5	±10
P (control *vs.* pressure loading)	NS	NS	NS	NS	NS	NS	NS	NS	NS

EDV, end-diastolic volume; ESV, end-systolic volume; EF, ejection fraction; uncorrected, observed volumes obtained by conductivity; corrected, corrected volumes using the individual regression equation between angiocardiography and conductivity.

*$P < 0.001$ (angiocardiography *vs.* conductivity).

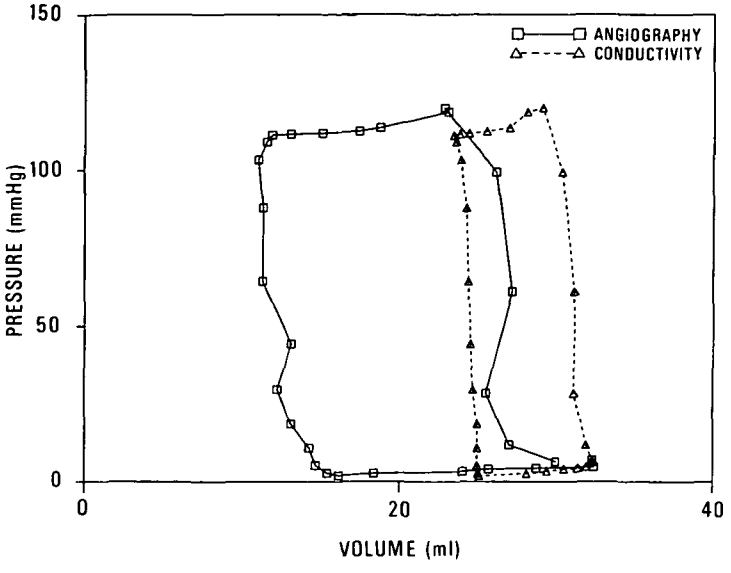

Figure 3 Representative left ventricular pressure-volume loop using angiography and the uncorrected left ventricular volumes measured with the conductance catheter for one cardiac cycle. The end-diastolic volume is estimated exactly by the conductance catheter, but the end-systolic volume and, hence, the ejection fraction are clearly over- and underestimated, respectively.

computer PDP 11/34. Data were printed out every 4·45 ms on a Versatec printer–plotter. Left ventricular end-diastolic pressure (LVEDP) was defined as the pressure at the time 40 ms before peak R wave in the ECG. Left ventricular end-systolic pressure was defined as the pressure at the aortic incisura[8]. Left ventricular volume curves obtained by the conductance technique (Fig. 2) were digitized manually using an electronic digitizer. Data were plotted every 4·45 ms. Three data points (= 13·4 ms) of the volume curves were averaged to match the corresponding angiographic cine-frames (intervals 13·4 ms).

STATISTICS

Statistical comparisons between rest and pressure loading or angiocardiography and conductivity were carried out using the paired Student's *t*-test. The correlation between left ventricular volumes obtained by cineangiocardiography and conductivity was performed using the least-squares regression analysis.

Results

Original tracings illustrating the variables measured are shown in Fig. 2.

STANDARD HAEMODYNAMICS (TABLE 1)

Heart rate decreased slightly although significantly during pressure loading, whereas left ventricular end-diastolic pressure remained unchanged. Systemic vascular resistance increased significantly from 2640 to 4398 dyn s cm^{-5} after administration of the calcium agonist.

LEFT VENTRICULAR VOLUME AND EJECTION FRACTION (TABLE 2)

The angiographic left ventricular end-diastolic and end-systolic volume as well as left ventricular ejection fraction remained unchanged at rest and during pressure loading. Parallel to the angiographic data no change in volume or ejection fraction was observed with the conductance technique but the end-systolic volume was significantly overestimated not only at rest but also during acute pressure loading (uncorrected). As a result left ventricular ejection fraction as obtained by conductivity was significantly underestimated at rest and during pressure loading. Figure 3 shows a representative pressure–volume loop using angiocardiography and the conductance technique (uncorrected data). After correction left ventricular end-diastolic and end-systolic volume as well as

left ventricular ejection fraction were determined adequately by the conductance technique (Table 2) using the linear regression between angiocardiography and conductivity as a correction factor for volume determination (Table 3).

CORRELATIONS BETWEEN ANGIOCARDIOGRAPHY AND CONDUCTIVITY (TABLE 3, FIG. 4)

Correlations between angiocardiographic volumes and those obtained by the conductance technique showed good agreement at rest and during pressure loading. The correlation coefficients were, however, slightly, although not significantly, lower during acute pressure loading (Table 3). The standard error of estimate in percentage of the mean angiographic volume was low ($\leqslant 6\%$) and showed no significant difference between rest and pressure loading. A representative plot of the correlation between angiographic volumes and those obtained by conductivity is shown in Fig. 4, and a representative pressure–volume loop using corrected volumes obtained by conductivity in Fig. 5.

Discussion

Left ventricular volume determination can be performed by several non-invasive and invasive techniques such as echocardiography, radionuclide ventriculography and angiocardiography[1,2,11–13]. The non-invasive techniques are associated with several limitations such as underestimation of the true left ventricular volumes by echocardiography [11–13] or the inability of measuring absolute volumes by radionuclide ventriculography[13]. Invasive techniques such as angiocardiography[1] are accompanied by several limitations including side effects due to the use of contrast medium, injection-related premature ventricular beats and no continuous volume determination over several cardiac cycles. Thus, the advantage of the recently developed conductance technique[3–6] is related to the continuous determination of left ventricular volume over several cardiac cycles. The purpose of the present study was to evaluate the accuracy of the conductance technique for left ventricular volume determination in the anaesthetized dog. Conventional angiocardiography was used as the reference method in the present analysis.

Table 3 Correlation between left ventricular volumes determined by angiocardiography and conductivity

Dog No.	*r*	Slope	Intercept (ml)	SEE (ml)	SEE (%)
Control run					
1	0·959	0·282	27·9	0·88	3·7
2	0 914	0·355	26·8	1·31	3·8
3	0·982	0·486	27·7	1·37	3·8
4	0·977	0·304	26·1	0·75	2·9
5	0·978	0·448	18·6	0·69	3·6
6	0·924	0·296	22·5	1·21	3·8
7	0·963	0·383	21 4	0·73	5·0
Mean	0·956	0·365	24·4	0·99	3·8
±1 SD	±0·027	±0·079	±3·6	±0·30	±0·6
Pressure loading					
1	0·789	0·232	26 7	1·94	6·4
2	0·981	0·283	31·7	0·53	1·6
3	0·935	0·368	25·8	1·43	4·2
4	0·839	0·230	27·3	1·66	5·7
5	0·934	0·299	22·8	0·68	3·5
6	0·961	0·253	24·9	0·55	2·0
7	0·966	0·364	22·4	0·62	4·7
Mean	0·915	0·289	25·9	1·06	4·0
±1 SD	±0·072	±0·058	±3·1	±0·60	±1·8
P	NS	<0·01	NS	NS	NS

r, Correlation coefficient; SEE, standard error of estimate in millilitres and in percent of the mean angiographic volume.

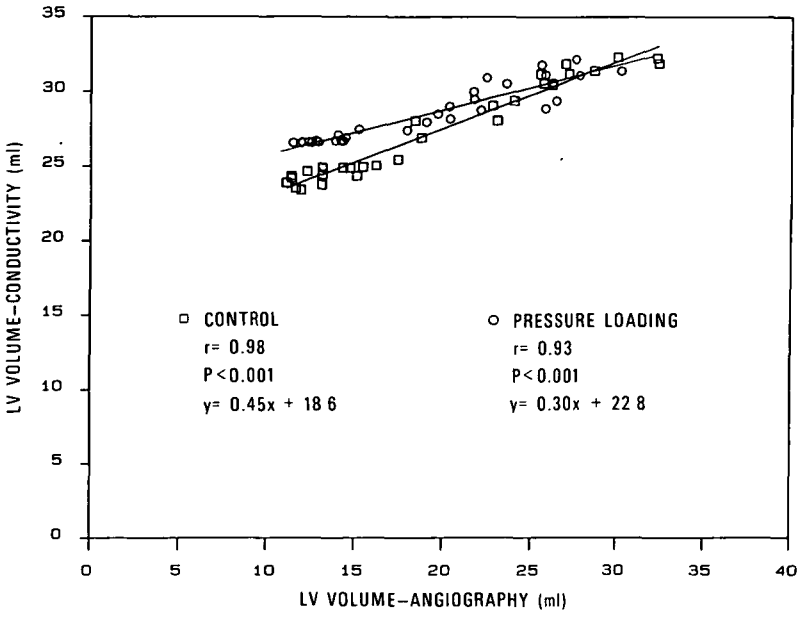

Figure 4 Correlations for left ventricular (LV) volume between angiocardiography and conductivity before and after pressure loading in a representative case (No. 5, Table 3). There is an excellent correlation between the two techniques with a decrease in slope and an increase in intercept during pressure loading.

CARDIOVASCULAR EFFECTS OF THE CALCIUM AGONIST BAY K 8644

The calcium agonist used in the present study is a structural analog of nifidipine with positive inotropic activity. This new compound belongs to the group of dihydropyridines and acts as a competitive antagonist of nifidipine and increases the calcium influx into the muscle cell[9,10] Bay K 8644 is a positive inotropic and vasoconstricting compound which is accompanied with an increase in left ventricular systolic pressure and peripheral vascular resistance (Table 1). This drug was used in the present study as a pressure-raising agent with positive inotropic action. This explains the fact that left ventricular ejection fraction was maintained normal (Table 2) despite a significant increase in afterload. Since the purpose of the present study was a comparison of two different techniques to measure left ventricular volume, the pharmacological effects of this new compound are not further discussed.

CONDUCTANCE TECHNIQUE VERSUS ANGIOCARDIOGRAPHY

An excellent correlation was observed between the two techniques (Table 3) with a mean correlation coefficient of 0·956 for resting conditions and 0·92 for acute pressure loading. The standard error of estimate as a percentage of the mean angiographic volume ranged between 3 and 5% at rest and between 2 and 6% during acute pressure loading. It is generally accepted that an accurate technique has a standard error of estimate of the mean which is less than 10%. Thus, this requirement is fullfilled for the conductance technique using angiocardiography as a reference method. However, the conductance catheter overestimated significantly the end-systolic volume, whereas the end-diastolic volume was determined exactly in most animals (Fig. 3, Table 2). This might have been accidentally due to the fact that a possible underestimation of the true end-diastolic volume by the conductance technique has been balanced by the failing to determine the accurate volume intercept as suggested by Baan *et al.*[4]. Since no calibration was performed for parallel conductivity of the surrounding tissue by injection of hypertonic saline or cold glucose[4], the absolute left ventricular volume could not be determined by the conductance technique itself. Therefore, each individual

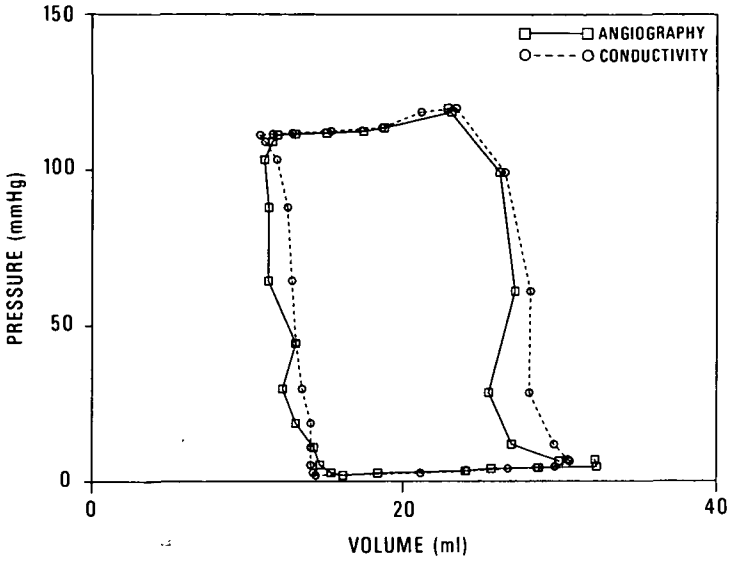

Figure 5 After correction of left ventricular volumes measured with the conductance catheter, left ventricular pressure-volume loops for angiocardiography and conductivity show an excellent correlation.

regression equation between angiocardiographic volumes and those obtained by conductivity (Table 3) was used as a correction factor for determination of absolute (corrected) left ventricular volumes by conductivity (Table 2). This approach has been used also by other[14] to circumvent the problems inherent to the calibration procedure using hypertonic saline or glucose solution. It has to be realized that the volume intercept V_c obtained by the calibration procedure with hypertonic saline or cold glucose is not the same as the volume intercept obtained from the correlation between angiocardiography and conductivity (Fig. 4). From a theoretical point of view it would have been preferable to use the original technique of Baan *et al.*[4]. The use of a different technique for calibration purposes is somewhat inconsequent, but certainly a feasible and accurate method especially under clinical conditions with angiography as a routine procedure in the diagnostic evaluation of patients with heart disease.

The correlation between angiographic volumes and the volumes obtained by conductivity was good not only at rest but also during pressure loading. The slope of this relationship was, however, significantly different during pressure loading than at rest. This has to be explained by a change in parallel conductivity of the surrounding tissue or a change in left ventricular geometry. Since left ventricular angiographic volume and ejection fraction remained absolutely unchanged during pressure loading, it seems unlikely that a change in geometry could explain the observed change in slope. It has to be assumed that the parallel conductivity of the surrounding tissue has changed during acute pressure loading probably due to an increase in left atrial or right ventricular volume although left ventricular end-diastolic pressure did not change significantly (Table 1). The administration of a calcium agonist could be associated with pulmonary vasoconstriction of varying degree which could be responsible for an increase in right ventricular pressure and volume. A change in parallel conductivity has also been observed by Kass *et al.*[6] during occlusion of the inferior vena cava; they reported, however, a horizontal shift of the volume curve to the left with a decrease in end-systolic volume of 5–7 ml with no change in stroke volume. Kass *et al.*[6] suggested as possible explanations a change in geometry through septal unloading, or an artifact of the catheter signal recording the acute right ventricular volume decrease during caval occlusion. Small, but measurable, influences of variations in the filling volume of the right ventricle on the left ventricular volume signal have been reported to be in the range of

10%[6]. Under ideal conditions, if the tissues were a perfect insulator, all the measuring current would pass only through the left ventricular cavity, and extremely accurate volume measurements could be obtained[14]. The electrical impedance of the myocardium is approximately 100-fold greater than that of blood[15] and, therefore, tends to contain the current within the left ventricle and to render changes in conductivity of the right ventricle small in comparison with changes in left ventricular conductivity. However, changes in left atrial volume can affect conductance measurements in an important way, because no insulating wall exists between the left atrium and left ventricle. Thus, repeated calibrations by an independent technique have to correct for the changes in parallel conductivity during acute interventions in order to guarantee accurate determination of absolute volumes by the conductance technique.

CLINICAL IMPLICATIONS

The conductance catheter can be used successfully for ventricular-volume determination in humans[4,14]. There are several advantages, but also some disadvantages, of the conductance technique for left ventricular volume determination. One of the most important *advantages* is that ventricular volume can be measured continuously without any negative influences of contrast medium or isotopes. Arrhythmias are usually not a major problem after proper positioning of the catheter in the left ventricular apex (Fig. 1). The major advantage of left ventricular angiocardiography is the high resolution for left ventricular volume determination with the possibility of regional wall-motion analysis and determination of left ventricular wall thickness and muscle mass. The major *disadvantage* of the conductance technique is the need for volume calibration with an independent technique such as angiocardiography or thermodilution techniques[14,15]. An important observation from our study was that the parallel conductivity of the surrounding tissue changes during acute pressure loading with a significant change in the relationship between left ventricular angiographic volume and those obtained by conductance measurements (Table 3, Fig. 4). This observation limits the application of this new technique to haemodynamic situations with no change in parallel conductivity or calls for repeated calibrations during acute interventions.

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