Roentgen Videodensitometric Determination of Left to Right Shunts in Experimental Ventricular Septal Defect

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Dilution curves of Renovist®-indocyanine green dye solutions and blood oxygen saturation and pressure levels were studied in 6 dogs 21 to 45 days after creation of a ventricular septal defect. Left to right shunt indexes, after right- and left-sided circulatory injections, were determined from the following: (1) the ratio of the area under roentgen videodensitometric dilution curves recorded over the silhouettes of the pulmonary artery and aorta during replays of videotaped angiograms; and (2) the ratio of the area under indocyanine green dye curves in blood from the same circulatory segments. These left to right shunt indexes were also compared with values calculated from oxygen saturation levels of pulmonary arterial and caval blood. After correction for rapid circulation of Renovist by way of distal pulmonary, bronchial and intercostal vasculature superposed in the densitometric pulmonary arterial window, a high correlation was demonstrated between values determined by each method. Phasic variations in shunted Renovist occurred during the cardiac cycle.

Roentgen videodensitometry is an indicator-dilution method that uses a roentgenopaque substance as the indicator.[1,2] This method has been used for the investigation of valvular regurgitation,[3-6] left to right shunts through atrial septal defects[7] and, recently, measurement of coronary blood flow.[8] In our study, videodensitometry was used for the quantitation of left to right shunting through surgically created ventricular septal defects in dogs. The shunt values were compared with values calculated from blood oxygen saturation values and by conventional dye-dilution technique using indocyanine green dye. The dynamic response of the roentgen video system (60 samples/sec) was fast enough to permit analysis of the cyclic changes in opacity at selected sites over the right ventricle; the changes presumably were due to phasic variations in shunt flow during individual heartbeats.

Materials and Methods

In 6 dogs, weighing 13.0 to 19.0 kg, a ventricular septal defect was created with a circular punch in the mid-portion of the ventricular septum through a right ventriculotomy.[9] The diameter of the punch was 7 mm in 2 dogs and 12 mm in 4 dogs.

At cardiac catheterization, 21 to 45 days after operation, all dogs had recovered completely, and were studied without thoracotomy under morphine (2.4 to 3.5 mg/kg body weight) and sodium pentobarbital (16.7 to 20.5 mg/kg body weight) anesthesia. The defects created with the 7 mm punch were healed at this time, and these dogs served as control animals. Two 5F

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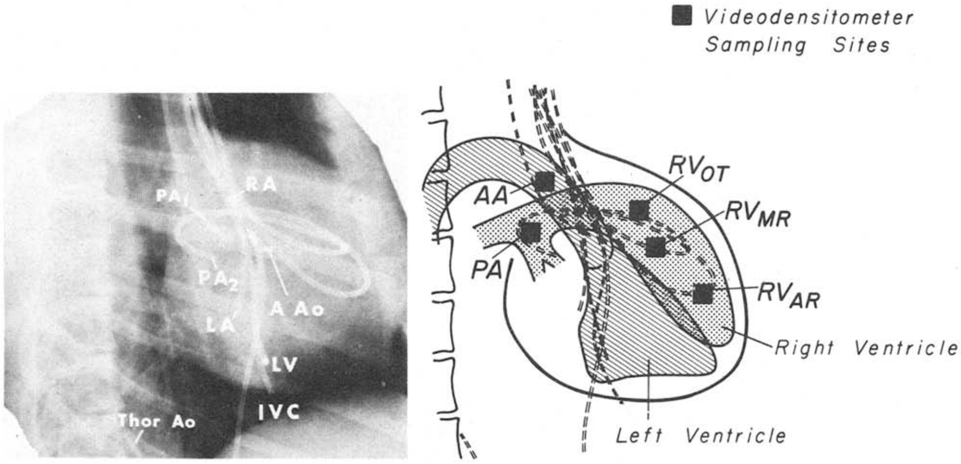

FIGURE 1. Positions of tips of catheters and videodensitometer sampling sites (left anterior oblique projection). **Left panel,** peripheral pulmonary artery (PA_2), main pulmonary artery (PA_1), right atrium (RA), inferior vena cava (IVC), left atrium (LA), left ventricle (LV), ascending aorta (A Ao) and thoracic aorta (Thor Ao). **Right panel,** AA and PA are videodensitometer sampling sites for quantitation of left to right shunts; and RV_{OT}, RV_{MR} and RV_{AR} are sampling sites (outflow tract, mid-region and apical region) used to study regional differences in roentgen density of right ventricle caused by left to right shunting of Renovist-blood mixtures by way of the septal defect.

catheters were positioned to record pressure in the thoracic aorta and dye-dilution curves from the abdominal aorta. One 5F Rodriguez catheter was placed in the ascending aorta, 1 to 2 cm downstream to the aortic valve, for the injection of indocyanine green or roentgen contrast medium (69 percent Renovist-indocyanine green dye mixture). Two 6F catheters were positioned transseptally, 1 in the left atrium and 1 in the left ventricle, for pressure recordings and for injection of indicator. Three 6F catheters were positioned with their tips in the peripheral and proximal pulmonary arteries, and in either the right atrium or inferior vena cava for pressure or dye-dilution curve recordings or the injection of indicator. Intracardiac and intravascular pressures were measured by strain gauges (Statham P23Dd and P23Dg). Two 6F bipolar electrode catheters were positioned in the right atrium and the outflow tract of the right ventricle for pacemaker control of heart rate and atrial-ventricular interval. The position of these catheters is shown in Figure 1.

The dogs were placed in the right decubitus position in a half-body molded Lucite® cast and positioned so that the plane of the ventricular septum was parallel to the X-ray beam. The dogs were ventilated with room air by way of a cuffed endotracheal tube at an inspiratory pressure of 10 cm H_2O and rate of 12 to 20 breaths/min. Respiration was temporarily suspended during all data recordings by opening the airway to ambient pressure.

Videoangiograms were recorded on video tape. Dilution curves of indocyanine green dye were recorded simultaneously from the pulmonary artery and abdominal aorta before, during and after injection of 0.15 to 0.4 ml/kg body weight of a solution of 0.3 mg indocyanine green/ml of 69 percent Renovist (meglumine and sodium diatrizoate) into the peripheral pulmonary artery or vein, left atrium, left ventricle and ascending aorta. Roentgen contrast medium was injected by a pneumatically powered syringe triggered by the R wave of the electrocardiogram, and the duration of the injections was adjusted to extend over 1 to 4 heart cycles.

The electrocardiogram, left ventricular pressure and the position of the piston of the injection syringe were recorded simultaneously on data channels of the same video tape.

The oxygen saturation levels of blood samples withdrawn simultaneously from the pulmonary artery, aorta and right atrium were determined by successively reinfusing the samples by way of a cuvette oximeter.

Intracardiac and intravascular pressures and the dilution curves of indocyanine green dye and Renovist were recorded repeatedly during control hemodynamic conditions with sinus rhythm, during incremental increases in heart rate up to 180 beats/min produced by atrial pacing or during combined atrial and ventricular pacing with a fixed atrial-ventricular stimulus interval.

The videoangiograms were analyzed by replaying the video tapes and recording the changes in roentgen density from sampling windows positioned over the main pulmonary artery and over the ascending aorta downstream to the aortic valve (Fig. 2). The data obtained from videodensitometer and electrocardiogram and the position of the injection syringe piston were fed into a time-shared digital computer by a 10-bit analog to digital converter. The nonspecific variations in roentgen density associated with each cardiac cycle were measured and averaged at successive 1/60 second intervals, from the R wave of each of 5 heartbeats just before injection of the contrast medium. This mean cardiodensographic value (Fig. 3) was subtracted from the original videodensographic value in exact temporal relation to the R wave of all successive cycles during the entire period of the videodensitometric recording to obtain a compensated videodensographic value, as described previously.[1] The method of calibration, linearity and sensitivity of videodensograms have been previously described.[2,3,10]

Dye-dilution curves were recorded from densitometers (Waters XC 250A) calibrated by withdrawing solutions of indocyanine green of known concentration in the dog's blood through the densitometer. Areas under the dye-dilu-

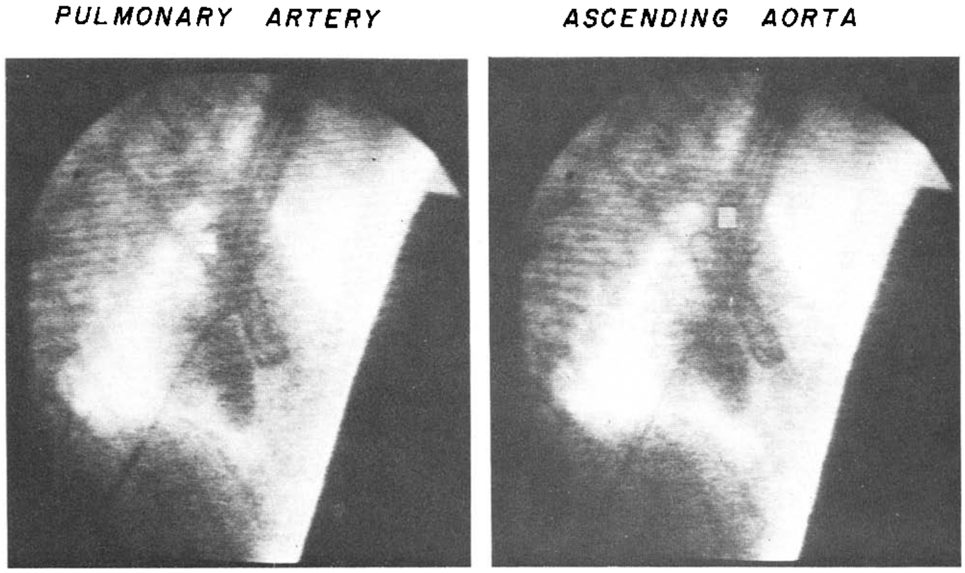

FIGURE 2. Television images of a tape-recorded left ventricular angiogram. Rectangular 7 by 6 mm videodensitometer sampling windows (brightened areas) are located over the pulmonary artery **(left panel)** and the ascending aorta **(right panel)** for quantitation of left to right shunting in ventricular septal defect.

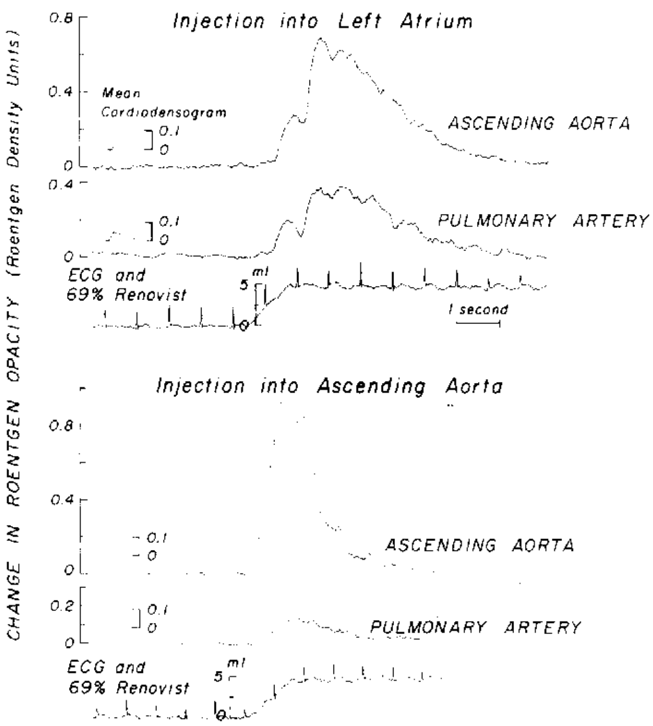

FIGURE 3. Dog 5. Computer replottings of roentgen videodensitometric dilution curves recorded over the pulmonary artery and ascending aorta after injections of roentgen contrast medium into the left atrium **(upper panel)** and ascending aorta **(lower panel)**. Simultaneously recorded electrocardiogram and amount and duration of Renovist injection are shown in the lowest tracing in each panel. Nonspecific variations in roentgen density have been removed from these curves by subtracting the respective mean cardiodensographic value for individual heartbeats (insets above beginning of each curve). The major portion of the large increase in roentgen density of the pulmonary artery after Renovist injection into the left atrium **(upper panel)** is due to the blood-Renovist mixture that was shunted by way of ventricular septal defect. The smaller increase in roentgen density recorded over the pulmonary artery after Renovist injection into the ascending aorta **(lower panel)** is caused by traversal of Renovist through superposed segments of systemic vasculature included in the pulmonary arterial sampling window (see text). The computer-calculated left to right shunt index from these curves was 38 percent.

tion curves obtained in the pulmonary artery or aorta after distal pulmonary arterial, pulmonary venous, left atrial and left ventricular injections of dye were determined by the forward triangle method.[11] The magnitude of the shunt was expressed as the shunt fraction of total pulmonary blood flow:[12]

$$F_{L\text{-}R} = A_{pa}/A_{sa}$$

where $F_{L\text{-}R}$ represents the left to right shunt index; A_{pa}, the area under the dilution curve recorded from the pulmonary artery; and A_{sa}, the area under the dilution recorded from the aorta.

Similarly, the shunt index by videodensitometry was determined from the ratio of the areas of the pulmonary arterial and aortic videodensograms. A small increase in roentgen density was observed uniformly over the pulmonary artery immediately after Renovist was injected into the ascending aorta. This rapidly appearing indicator (demonstrating apparent left to right shunt) over the pulmonary artery is due to the traversal by Renovist of those segments of the systemic circulation that are superposed in the area of the pulmonary arterial sampling window. The following formula was used to exclude this false left to right shunt due to superposition of other vessels:

$$F_{L\text{-}R} = A_{pa} - (A_{sa} \times [A'_{pa}/A'_{sa}])/A_{sa}$$

where A'_{pa} and A'_{sa} represent, respectively, the areas under the pulmonary and aortic videodensograms after injection of Renovist into the ascending aorta.

The phasic changes of videodensograms were analyzed before, during and after injection of the contrast medium, when the sampling window was placed over the right ventricle, close to the site of entry of the left to right shunt.

The locations and sizes of the ventricular septal defects were examined at the end of the experiments in all dogs. The septal defects were located in the muscular mid-portion of the ventricular septum and ranged from 2 to 7 mm in diameter in 4 dogs. The defects had healed in 2 dogs (Table I). There was no damage to the atrioventricular valves in any dog.

Results

In dogs with a ventricular septal defect, roentgen density increased rapidly over the pulmonary artery when Renovist was injected into a peripheral pulmo-

TABLE I

Data on Dogs with a Surgically Created Ventricular Septal Defect

Dog no.	Body Weight (kg)	Time of Study (postoperative day)	Size of Defect (mm)	Pressure (mm Hg) Ao	LV	PA	RV	Left to Right Shunt (% pulmonary blood flow) Oximetry	Dye Method	Heart Rate (beats/min)
1	15.5	31	Closed	149/113	141/8	21/8	21/3	0	0	81
2	18.0	30	5 × 4	116/97	116/18	29/10	33/8	58	58	66
3	13.0	31	7 × 5	88/71	89/9	23/10	23/3	82	79	135
4	19.0	45	Closed	126/113	128/10	18/9	19/4	0	0	126
5	18.5	34	2 × 2	134/103	134/6	16/9	16/2	27	14	90
6	19.0	21	7 × 6	132/102	128/26	37/14	35/4	70	51	132

Ao = aortic; LV = left ventricular; PA = pulmonary arterial; RV = right ventricular.

nary artery or vein, left atrium and left ventricle (Fig. 3). A small but significant increase in roentgen density over the pulmonary artery was also observed (Fig. 4) in the 2 dogs with healed ventricular septa. In every dog, some increase in roentgen opacity was detected over the pulmonary artery after Renovist was injected into the ascending aorta. This increase was due to the superposition of segments of systemic vessels in the sampling window (Fig. 3 and 4). The ratio of the areas of the curves recorded simultaneously over the pulmonary artery and ascending aorta after injections into the ascending aorta ranged between 10 and 25 percent (average 17 percent).

Comparison of simultaneous determinations of the left to right shunt indexes by dye densitometry and videodensitometry is depicted in Figure 5. There was a high correlation between the shunt index values of the 2 methods.

Reproducibility for the shunt index by videodensitometry was evaluated by comparing the values obtained from independent computer analyses of successive replays of the recorded angiograms. Excellent agreement between the paired values was obtained (Fig. 6).

In 3 dogs, the videodensograms were recorded while the heart rate and the atrial-ventricular interval were controlled by pacing (Fig. 7). When the heart rate was increased to 180 beats/min, the magnitude of the left to right shunt increased in 2 dogs and was unchanged in 1 dog.

A typical videodensogram recorded with the sampling window over the right ventricle near the septal defect is depicted in Figure 8. After the injection of Renovist into the peripheral pulmonary artery or vein, left atrium and left ventricle, the videodensogram showed an increase in roentgen density during both systole and diastole on its build-up slope in the 4 dogs with ventricular septal defect, although this phenomenon was not observed in the 2 control dogs under the same conditions. The phasic rate of opacification of the cardiodensograms, presumably as a result of phasic changes in shunt flow, was greater in all dogs during diastole than during systole at heart rates of less than 110 beats/min. When the heart rate was increased by atrial pacing to a rate of 180 beats/min, the increase in density occurred mainly during the systolic phase of the cardiac cycle (Fig. 8).

When the sampling window was placed over the outflow tract of the right ventricle, the phasic rate of opacification of videodensograms showed nearly the same pattern as that obtained from the mid-region;

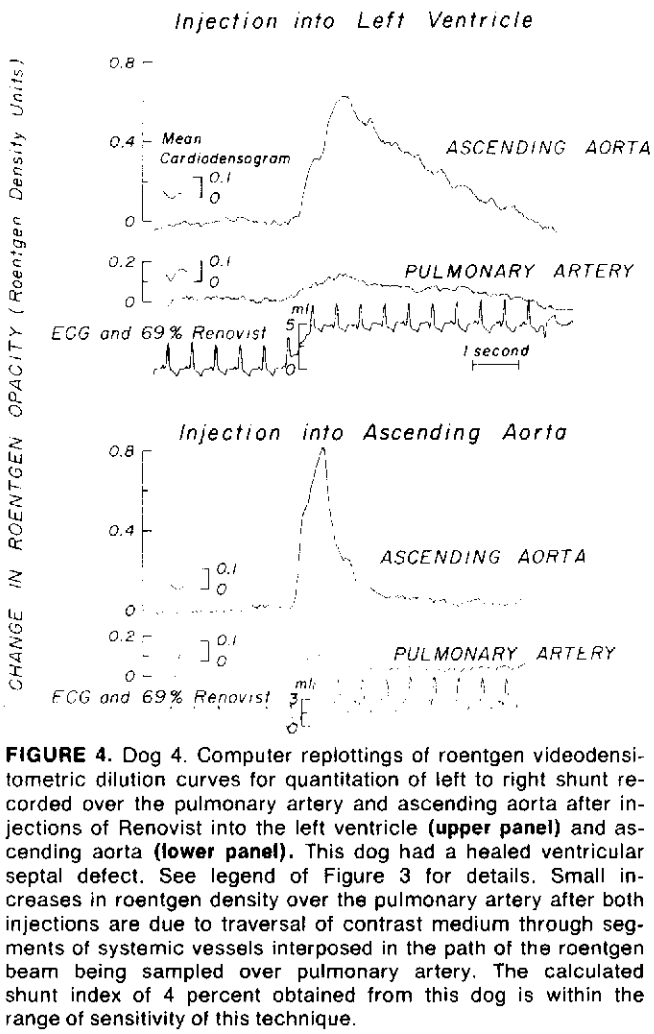

FIGURE 4. Dog 4. Computer replottings of roentgen videodensitometric dilution curves for quantitation of left to right shunt recorded over the pulmonary artery and ascending aorta after injections of Renovist into the left ventricle **(upper panel)** and ascending aorta **(lower panel).** This dog had a healed ventricular septal defect. See legend of Figure 3 for details. Small increases in roentgen density over the pulmonary artery after both injections are due to traversal of contrast medium through segments of systemic vessels interposed in the path of the roentgen beam being sampled over pulmonary artery. The calculated shunt index of 4 percent obtained from this dog is within the range of sensitivity of this technique.

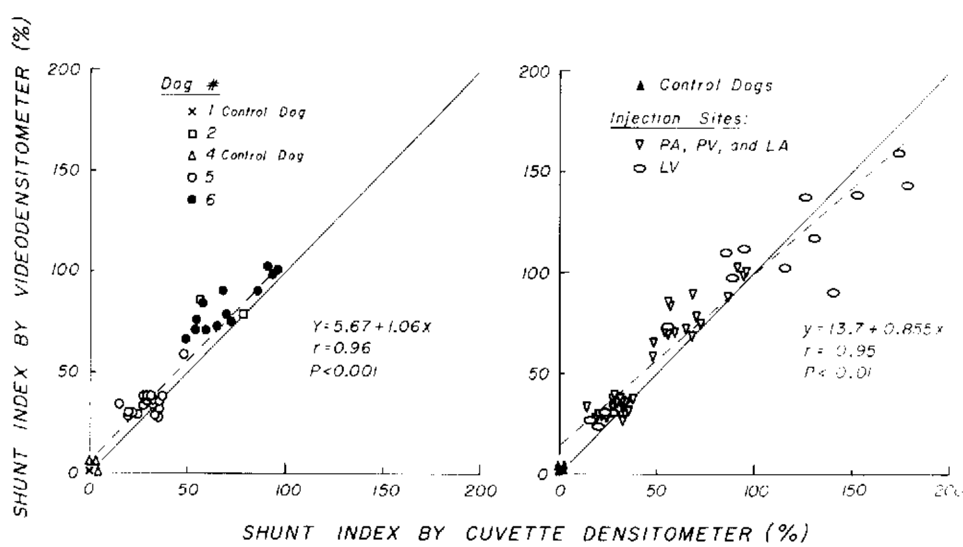

FIGURE 5. Comparison of left to right shunt indexes measured simultaneously by conventional double-sampling indocyanine green-dilution technique and videodensitometric method. **Solid line** is the line of identity, and the **dashed line** is the regression line for paired sets of values. *Left panel,* values obtained by curves after Renovist injections into the peripheral pulmonary artery or vein, or the left atrium. Values from individual dogs are shown by different symbols. *Right panel,* values obtained by curves recorded after Renovist injections into the left ventricle (ellipses). The erroneously high (>100 percent) shunt values obtained when indicator was injected into left ventricle are presumably due to incomplete blood-indicator mixing and preferential flow of indicator across the defect.

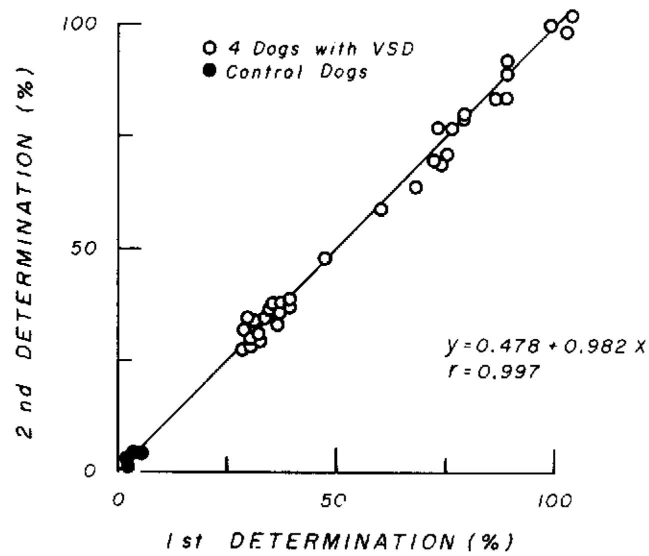

FIGURE 6. Variability of replicate measurements of left to right shunt index by videodensitometry. Each shunt index was plotted against measurements obtained from curves recorded during successive replays of angiograms from video tapes. **Solid line** is the line of identity between paired values.

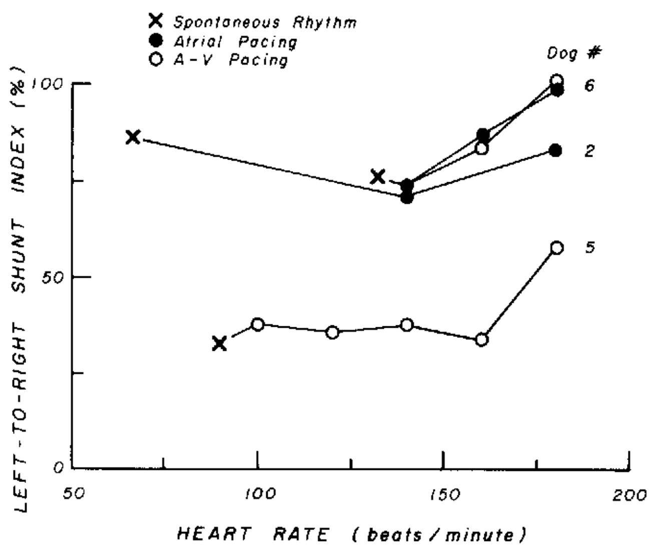

FIGURE 7. Relation between heart rate and left to right shunt index in 3 dogs with a ventricular septal defect. Heart rate and atrial-ventricular interval were controlled by electric pacing. Note the tendency for relative shunt values to increase when the heart rate was increased to 180 beats/min.

the simultaneous recordings over the apical region of the right ventricle showed a different pattern (Fig. 9).

Discussion

The magnitude of the left to right shunt was determined in this study by measuring the amount of rapidly appearing indicator in the dilution curves recorded over the pulmonary artery and aorta after injections of indocyanine green dye or Renovist-dye solution into the peripheral pulmonary artery or vein, left atrium and left ventricle.

However, in the videodensitometric recording of the traversal of the contrast medium through a particular vessel, some superposition of segments of other vessels cannot be avoided. Small increases in roentgen density over the pulmonary artery were observed in the 2 control dogs after Renovist was injected into the peripheral pulmonary artery or vein, left atrium and left ventricle, and in all dogs after

Renovist was injected into the ascending aorta. These increases in roentgen density are due to the traversal of contrast medium through the bronchial, intercostal and other intrathoracic vessels interposed in the path of the roentgen beam being sampled over the pulmonary artery and to rapid recirculation by way of the coronary system.[13,14]

The ratios of the areas of pulmonary arterial-aortic curves (shunt index) obtained by videodensitometry were larger than the indexes obtained from simulta-

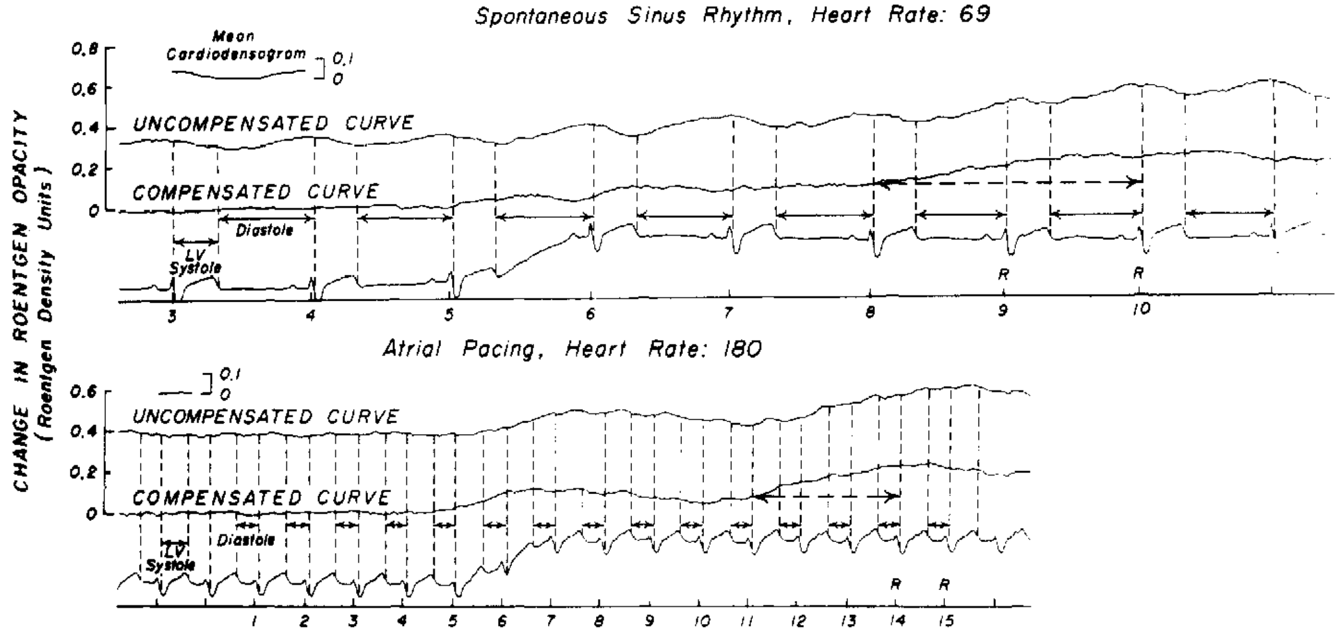

FIGURE 8. Extended time-base Renovist dilution curves, showing phasic relation between changes in right ventricular roentgen density and cardiac cycle during slow **(upper panel)** and fast **(lower panel)** heart rates. Before Renovist injections, cyclic changes in roentgen density are evident in uncompensated (upper) curves, increasing during ventricular diastole and decreasing during systole. Immediately after Renovist injection into the peripheral pulmonary artery, a small increase in roentgen density is observed in all curves (beats 5 to 7 and 5 to 10 in upper and lower panels, respectively) due to traversal of Renovist through segments of peripheral pulmonary circulation included in the pulmonary arterial sampling window. The subsequent increase in roentgen density due to the left to right shunt through the defect occurs during both systolic and diastolic phases of cardiac cycle (see beats 8 and 9 in compensated curve of upper panel—**double-ended dashed arrow**), with the major increase occurring during long-duration diastole at the slow spontaneous heart rate. At higher heart rate of 180 beats min **(lower panel)**, the major portion of increases in density due to left to right shunt (beats 11, 12 and 13 in compensated curve of lower panel—**double-ended dashed arrow**) occurred during systole. **Vertical blips** indicated by numbers and the letter R in the bottom tracing of each panel indicate instances when the computer recognized the R waves of the electrocardiogram.

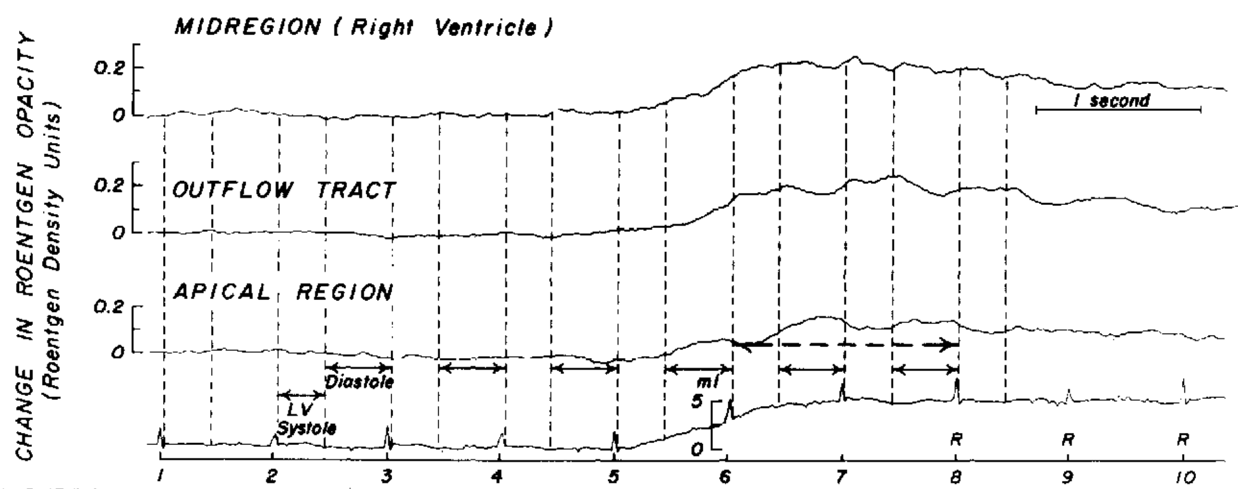

FIGURE 9. Extended time-base simultaneous compensated dilution curves of Renovist, showing regional differences in phasic changes in roentgen density of the right ventricle during video roentgenography, after injection of Renovist into the left atrium. Increases in roentgen density due to left to right shunting occurred during both systolic and diastolic phases of cardiac cycle in the mid- and outflow regions (beats 5 and 6); no increase occurred during the systolic phases of these beats in the apical region (lowest curve). During beats 6 and 7 **(double-ended dashed arrows)**, cyclic changes in roentgen density in the apical region were out of phase with changes in the mid- and outflow regions because of the nonuniform mixing of the shunted blood-indicator mixture in the right ventricle.

neously recorded dilution curves of indocyanine green dye. This systematic difference was eliminated when the ratios of the pulmonary arterial-aortic curves obtained after aortic injections of Renovist were subtracted from the ratios obtained after injections into the peripheral pulmonary artery or vein, left atrium and left ventricle.

The erroneously high shunt indexes (>100 percent) obtained by both indocyanine green and videodensitometric methods after injection of these indicators into the left ventricle are believed to be due to the nonuniform mixing of blood and indicator in this chamber, coupled with the preferential flow of the indicator through the defect (Fig. 5). Consequently, when an indicator-dilution technique is used for quantitation of left to right shunt through a ventricular septal defect, the injection of indicator should be made upstream to the mitral valve, preferably into a peripheral pulmonary artery in the lower lung fields so as to maximize the likelihood of uniform mixing of blood and indicator before its entrance into the left ventricle.

Advantages of roentgen videodensitometry over conventional techniques: The use of roentgen videodensitometry has several advantages over conventional dye-dilution techniques for the evaluation of shunt flow: (1) Withdrawal of blood for recording of the dilution curves is not necessary. The time delay and distortion in dye-dilution curves caused by withdrawing the dyed blood through the catheter-cuvette-densitometer system are avoided, and the videodensitometer has an excellent dynamic response (60 samples/sec), which is fast enough to permit analysis of the phasic variations occurring within individual heartbeats. (2) By adjusting the site and size of the sampling window over any desired circulatory structure and replaying the video tape, the investigator can, at leisure, record as many dilution curves from as many sites in the roentgen image as desired. (3) The small volume of contrast medium injected, usually 4 to 6 ml, has little effect on circulatory variables. (4) The high level of sensitivity of the instrument (0.5 percent change in roentgen transmission) makes it possible to detect and measure minimal shunts that are not apparent on usual angiograms, particularly when the change in transmission occurs slowly.

Factors influencing phasic variation in shunt flow: The volume of blood passing through a septal defect depends primarily on the size of the defect and the duration and amplitude of the pressure difference across it. If the size of a ventricular septal defect does not change during the cardiac cycle, the expected magnitude of the shunt would be larger during systole than during diastole, in proportion to the increased pressure difference across the defect during systole.

The phasic variations in roentgen density of the right ventricle during individual heartbeats after injections of contrast medium into the pulmonary circulation or left atrium may be caused by phasic variations in the magnitude of the left to right shunt during the cardiac cycle. However, this interpretation cannot be made with certainty because other factors affect the roentgen density of the right ventricle. These include the inflow of blood containing no contrast medium from the right atrium; this inflow varies during the heartbeat, as do the shape and thickness of the transradiated segment of right ventricle included under the sampling window of the videodensitometer. This latter effect should be eliminated or greatly minimzed by the compensation for the cyclic changes in roentgen density determined and averaged for the 5 heartbeats immediately before injection of contrast medium.

The increases in roentgen density of the right ventricle caused by the left to right shunting of the Renovist-blood mixture were greater during diastole than during systole in all dogs when the heart rate was less than 110 beats/min. When the heart rate was increased by atrial pacing, the rate of increase in roentgen density increased during systole and decreased during diastole.

Gamble et al.[15] and Frommer et al.[16] observed in their clinical studies using fiberoptic catheters with response times of 0.07 and 0.1 second, respectively, that the oxygen saturation level of right ventricular blood near the defect increased during systole and decreased during diastole. Because of the nonuniform mixing of blood in the ventricle and the phasic inflow of relatively desaturated blood from the right atrium, which in effect dilutes the oxyhemoglobin in the shunted blood, these changes cannot be attributed with certainty to increases and decreases in the magnitude of the left to right shunt. Gamble et al.[15] observed an increase in oxygen saturation of blood near the defect during diastole in some patients with the Eisenmenger syndrome. An increase in oxygen saturation of right ventricular blood during this phase of the cardiac cycle is indicative of the occurrence of left to right shunting during the diastolic phase.

Applications to study of muscular ventricular septal defects: The demonstration of increases in roentgen density during diastole in our experimental ventricular septal defect, which were not associated with severe pulmonary hypertension, is of physiologic interest in relation to possible determinants of the magnitude of left to right shunting in muscular ventricular septal defects. The size of the experimental ventricular septal defect in the muscular mid-portion of the septum may have decreased by contraction of the surrounding muscle during systole to the degree that the shunt is smaller during systole than during diastole, in spite of the much larger left to right ventricular pressure gradient during the systolic phase of the cycle.

When the heart rate was increased by atrial pacing to 180 beats/min, the pressure gradients between both ventricles did not change significantly; however, the phasic increases in roentgen density of the right ventricle due to the left to right shunt of Renovist-blood mixture were increased during the systolic phases and decreased during the diastolic phases of the cardiac cycle, respectively. The increase in right ventricular opacity was also larger during weak ventricular contractions associated with premature beats and during long diastolic periods due to atrioventricular block. These findings suggest that variations in the effective size of the defect may be an important determinant of the amount of left to right shunting by way of defects in the muscular portions of the ventricular septum such as those present in our dogs.

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