Effects of Variations in the Strength of Left Ventricular Contraction on Aortic Valve Closure in the Dog

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ABSTRACT

The efficiency of aortic valve closure was studied in five experiments on three normal dogs by simultaneous roentgen videodensitometry, upstream sampling of dye dilution and recording of flow velocity and direction in the ascending aorta using a chronically implanted electromagnetic flowmeter. The aortic valve closed effectively during regular ventricular contractions. However, aortic reflux was observed whenever a weak ventricular contraction produced an opening of the aortic valve that was barely detectable, as evidenced by a minimal aortic pressure pulse and stroke volume. This type of aortic regurgitation was mild and invariably occurred at the end of ventricular ejection, coincident with the aortic incisura. Such regurgitation may be clinically significant in some instances of bigeminal rhythm or rapid atrial fibrillation, and is especially important for the evaluation of aortic angiograms. It further supports the concept that competent aortic valve closure depends on vortex formation in the sinus of Valsalva of sufficient degree to keep the aortic valve leaflets in partial apposition during ejection of blood from the ventricle across the aortic valve.

KEY WORDS: cardiac arrhythmias and aortic valve closure, stroke volume, regurgitation across normal aortic valve, aortic flow and pressure pulses, mechanism of aortic valve closure, electromagnetic flowmeter, roentgen videodensitometry.

The normal aortic valve works so efficiently that no appreciable amount of blood is regurgitated. Recently, however, reproducible mild aortic reflux was observed after weak ventricular beats in the course of experiments on normal dogs (1). In the present study, aortic reflux after weak ventricular contractions in normal dogs was analyzed systematically, and the implications for the understanding of the mechanism of normal aortic valve closure are discussed.

Material and Methods

Five experiments were made on three normal mongrel dogs weighing 14 to 18.5 kg. A cuff type of electromagnetic flow transducer was implanted around the ascending aorta 3 to 12 weeks before the experiments. Also, to carry out studies at slow heart rates, complete heart block was produced by a percutaneous technique (2).

During the experiments, the dogs were anesthetized with initial injections of morphine, 2.5 mg/kg im, and pentobarbital, 15 mg/kg iv; pentobarbital was given as necessary to maintain light anesthesia. Heart rate and temporal sequence of atrial and ventricular contractions were controlled by bipolar electrode catheters positioned against the wall of the right atrium and the outflow tract of the right ventricle and connected to coupled electronic pacemakers. A 6-F Lehman catheter was placed in the main pulmonary artery and used for injections of indocyanine green for measurement of cardiac output. Additional 5-F or 6-F Lehman catheters with their tips positioned in the aortic arch or thoracic aorta were connected to coupled electronic pacemakers. A 5-F blind-end, spray-tipped catheter for injection of a solution of contrast medium and dye (0.3 mg indocyanine green per ml 69% Renovist [Squibb]) was positioned via a femoral artery into the ascending aorta.

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aorta with its tip 1 to 2 cm downstream to the aortic valve. With the exception of the left atrial and left ventricular catheter, all catheters were introduced percutaneously. All catheters were connected to strain gauges (Statham P23D or P23G). The left ventricular and femoral arterial catheters were connected to the side arm of two-way stopcocks interposed between cuvette densitometers (Waters XC250A) for measurement of concentration of indocyanine green and their respective strain gauges.

Variations in the strength of left ventricular contraction were produced by electric induction of ventricular extrasystoles near or shortly after completion of the aortic injections of contrast medium and dye used to evaluate the competency of the aortic valve. To accomplish this, the upstroke of the plunger of the injecting syringe, recorded on a linear potentiometer, was used to gate the electrocardiographic signal into an electronic circuit connected to the right ventricular pacing catheter and designed to stimulate a single ventricular extrasystole. Thus it was possible to induce single ventricular extrasystoles of any desired degree of prematurity with respect to the preceding heart cycle at or just before completion of the injection. Depending on their timing, these ventricular extrasystoles ranged from frustrate contractions, that is, contractions too weak to open the aortic valve, to effective contractions that ejected stroke volumes of varied magnitude. Isolated weak ventricular contractions during fast driving of the atrium and ventricle were also produced by inducing an atrial asystole by omitting a single atrial pacing stimulus at the selected instant in relation to the injection of the contrast medium into the ascending aorta.

During the experiments, the dogs were placed in half-body molded Lucite casts in the right decubitus position so that the plane of the aortic valve was approximately parallel to the x-ray beam (Fig. 1). The dogs were ventilated with air at 25 to 35 cycles/min via auffed, plastic endotracheal tube with intermittent positive pressure of 8 to 10 cm of water. During recordings of angiograms, dye curves, and pressures, the respiration was temporarily suspended by opening the airway to ambient atmospheric pressure.

The degree of competency of the aortic valve was studied by roentgen videodensitometry, the upstream sampling of dye, and an aortic electromagnetic flowmeter. Simultaneous videoangiograms and curves of dye sampling from the left ventricle and femoral artery were recorded along with circulatory pressures and ascending aortic flow before, during, and after injection of 4 to 6 ml of the solution of contrast medium and dye into the aortic root via the spray-tipped catheter. The pneumatically driven syringe was triggered by the R wave of the electrocardiogram, and the injections lasted about 1 second, extending over 1 to 3 heart cycles. During an injection, whenever a ventricular extrasystole had been induced or an atrial systole omitted, the identical cardiac arrhythmia was induced a second time after the clearance of contrast medium from the ascending aorta, at which time...
AORTIC VALVE CLOSURE
707

The roentgen densities of the aorta and ventricle had returned to or near the control level and were relatively stable. By this means, nonspecific changes in left ventricular roentgen density due to variations in left ventricular volume and geometry produced by the abnormal beat could be differentiated from changes produced by aortic regurgitation.

In each experiment, multiple recordings of angiograms, dye curves, aortic flow tracings, and circulatory pressures were obtained at various heart rates, during regular heart action and during induced variations in the strength of left ventricular contractions.

The videoangiograms were analyzed during replay from the video tape by recording the roentgen density within a selected area over the ascending aorta about 0.5 cm downstream from the aortic valve, and from an identical area over the outflow tract of the left ventricle a similar distance upstream from the aortic valve (Fig. 1). The resulting left ventricular and aortic dilution curves of the roentgen contrast medium (video-densograms) were recorded on photokymographic paper. Maximal left ventricular and aortic roentgen densities were measured in roentgen density units with the optical density ruler described by Bassingthwaighte et al. (3). The ratio of maximal left ventricular to maximal aortic roentgen density after injection of contrast medium and dye into the aortic root (regurgitant index) was calculated and used to estimate the presence of, the relative degree of, and the temporal relationship to, the cardiac cycle of the retrograde passage of this solution into the left ventricle.

The videodensitometer was calibrated by passing a calibration wedge constructed of equal density increments of aluminum and a terminal segment of lead through which x-ray transmission is negligible between the dog and the fluoroscopic screen. When the lead segment was interposed in the roentgen beam, that is, black level was being recorded during replay of the video tape, the...
output of the videodensitometer was adjusted to zero volts. By adjusting the videodensitometer to zero output when the fluoroscopic screen was quiescent, that is, at zero x-ray transmission, the relationship between changes in roentgen density and corresponding outputs of the videodensitometer could be measured in roentgen density units by the optical density ruler (3). This relationship was linear independent of the level of background contrast accumulated over the course of the experiment (4).

Left ventricular and femoral arterial dye curves were recorded on magnetic tape and directly on photokymographic paper. Cardiac output was calculated on line by a digital computer (CDC 3200), and the femoral arterial dye concentrations after pulmonary arterial injections were summed for the time interval from the middle of injection until decay to 60% of maximal concentration. Because the small degrees of aortic regurgitation encountered in these experiments caused only small deflections in the left ventricular dye curves recorded during aortic injections, no attempt was made to quantify aortic reflux using upstream sampling of dye dilution. Circulatory pressures and aortic flow tracings were analyzed from photokymographic paper after replay from magnetic tape. The area under the flow pulses was determined by planimetry. Zero flow was assumed to be present at end-diastole of normal beats not associated with aortic regurgitation, as judged by videodensitometry. The flowmeter was calibrated in vivo by relating cardiac output as measured by dye curves to the area of simultaneous flow pulses. In vitro calibration of the flow transducers for forward and retrograde flows across the flow transducer, perfusing solution was linear through zero for the range of flows occurring in vivo. Thus the same calibration factor was used to calculate forward and retrograde flows across the flow transducer. The maximal rate of change of flow or maximal acceleration was obtained by differentiating the flow signal with a linear differentiator (Philbrick).

**Results**

No aortic regurgitation was detected during regular ventricular contractions at heart rates ranging from 65 to 300 beats/min in normal dogs. An example of competent aortic valve closure during regular heart rhythm, as
Aortic Valve Closure

Demonstrated by videodensitometry and upstream sampling of dye dilution, is shown in Figure 2.

In contrast to competency of the aortic valve with regular pacing, significant aortic regurgitation was demonstrated in each dog when a ventricular contraction was weak enough to produce an opening of the aortic valve that was barely detectable. Under these conditions, aortic regurgitation occurred independent of the causative nature of the weak ventricular beat.

Figures 3 and 4 demonstrate aortic regurgitation after an electrically induced weak premature ventricular contraction in a normal dog. The systolic pressure of the premature ventricular contraction shown in Figure 4 was just sufficient to open the aortic valve and eject a minimal amount of blood at low velocity, as indicated by the small positive portion of the corresponding aortic flow pulse. The negative portion of this flow pulse, reflecting retrograde flow across the flow probe, coincides with the barely visible aortic incisure of this beat and with the onset of the deflection of the left ventricular videodensogram. It is slightly larger than the small negative deflections seen after normal beats. Figure 5 demonstrates mild aortic regurgitation during a weak ventricular beat after induced omission of the preceding atrial contraction.

Aortic regurgitation after weak ventricular beats always was confined to the time of valve closure, coincident with the incisure on the aortic pressure curve and the negative deflection at the end of ejection on the ascending aortic flow pulse.

No aortic regurgitation was found after ventricular contractions that were too weak to open the aortic valve. Aortic regurgitation was observed within a limited range of prematurity of extrasystolic beats when the aortic pulse pressure was close to 0 mm Hg and stroke volume ranged from 0.6 to 1.4 ml. Aortic regurgitation was not demonstrable when the...
ventricular contraction was either too weak to open the aortic valve or strong enough to eject a stroke volume of 4 ml or more (Fig. 6).

The range of prematurity of extrasystolic beats associated with aortic regurgitation lies early in the cardiac cycle at slow heart rates and progressively later at increasing heart rates, depending on where in the cycle the extrasystolic beats were just strong enough to produce a minimal but just detectable opening of the aortic valve (Fig. 7). The magnitude of the aortic reflux showed no consistent correlation with the heart rate.

Incompetency of the normal aortic valve was confined to a narrow range of aortic pulse pressure, stroke volume, maximal rate, and maximal acceleration of forward flow associated with weak ventricular beats (Fig. 8). Aortic reflux of variable degree was mostly found when, with the aortic valve opened, the aortic pulse pressure was nearly 0 mm Hg, when the stroke volume ranged between 0 and 1 ml, and when the maximal rate and acceleration of forward flow were, respectively, less than 20 ml/sec and 1,000 ml/sec/sec. Conversely, no regurgitation was observed when the aortic valve did not open at all or when the aortic pulse pressure and stroke volume exceeded 5 mm Hg and 4 ml, respectively.

The aortic regurgitation in these experiments was mild, but we were unable to determine its absolute magnitude. Whereas the mixing of regurgitant blood in the left ventricle is surprisingly good in anatomic aortic insufficiency (5), this is not true for the transient small degrees of aortic regurgitation via the normal valve associated with weak ventricular beats. Consequently, the regurgitant index does not allow quantification of the

![Aortic Regurgitation Diagram]

Demonstration of mild aortic regurgitation during weak ventricular beats caused by omission of atrial contraction in normal dog (15.5 kg) with aortic and ventricular paced at 100 beats/min. Asterisks identify both the ECG complexes of ventricular systoles with absent P waves, that is, those lacking preceding atrial contractions, and the incisurae on the just perceptible aortic pressure pulses associated with these same weak ventricular beats.

There is no further increase in left ventricular roentgen density associated with identically weak beats caused by control omission of atrial contraction induced after contrast medium was cleared from ascending aorta. This suggests that the slight increase in left ventricular roentgen density coincident with the injection is due to transient regurgitation of contrast material from aorta and not to variations in volume and geometry of left ventricle associated with atrial systoles. (See legend for Fig. 3.)
Relationship of degree of prematurity of ventricular extrasystoles to stroke volume, aortic pulse pressure, and competency of aortic valve in normal dog (15.5 kg) at heart rate of 90 beats/min. Cycle length was 667 msec. Aortic pulse pressure was determined as the difference of maximal aortic pressure during and the aortic pressure just before left ventricular ejection. Regurgitant indices within shaded area in this figure and in Figure 7 represent video signals within range seen in absence of aortic regurgitation, while values above shaded area indicate visible aortic regurgitation. The three extrasystoles with the shortest delay in respect to preceding normal beat (open symbols) were frustrate contractions, that is, the maximal pressure generated by these beats was insufficient to open aortic valve.

Variation of competency of aortic valve with prematurity of extrasystolic beats in normal dog (15.5 kg). Number on top of each curve indicates the preceding ventricular stimulus interval of the extrasystole associated with the highest degree of reflux at each heart rate studied. (See legend for Fig. 6.)

Regurgitant volume in this type of aortic regurgitation. Analysis of the negative component of the aortic flow pulse at the time of valve closure also does not permit quantitative...
assessment of these small degrees of aortic reflux, because it represents retrograde flow across the flow transducer rather than necessarily true regurgitant flow across the valve.

The relation between the negative component of the aortic flow pulse, aortic regurgitation as estimated by videodensitometry, and the presence or absence of regurgitation detectable by the human eye when viewing the angiograms from three dogs is shown in Figure 9. In dog 1, the negative portion of the flow pulse tended to be larger when there was demonstrable aortic reflux. In dogs 2 and 3, however, there was no apparent correlation, indicating that the negative portion of the flow pulse is not uniformly directly related to these small degrees of regurgitation.

When the negative component of flow pulses was plotted against the positive component (that is, stroke volume) of the same pulses, an inverse correlation was demonstrable between the magnitude of flow pulses producing stroke volumes of more than 1 ml and the negative flow component of these pulses (Fig. 10). However, for very small stroke volumes (less than 1 ml), a statistically significant positive correlation was demonstrated in dogs 2 and 3 between the...
AORTIC VALVE CLOSURE

FIGURE 9
Relationship of regurgitant index of aortic valve determined by roentgen videodensitometry and retrograde flow recorded by aortic flowmeter in normal dogs. Circled values indicate instances when regurgitation of contrast medium into left ventricle was of sufficient magnitude to be visible by eye during replay of videocinogram.

FIGURE 10
Relationship of positive and negative components of individual flow pulses in ascending aorta of normal dogs. Numbers associated with vertical arrows indicate number of pulses analyzed for beats with stroke volumes greater than 6 ml.

Discussion
In these experiments on normal dogs, the aortic valve was always found to close...
effectively after normal ventricular contractions. In contrast, ineffective closure of the aortic valve was demonstrable in all dogs after a transient weak ventricular contraction that opened the aortic valve to a degree that was barely detectable and one that was associated with a low-velocity ejection of a minimal amount of blood. This aortic reflux always occurred at the time of closure of the aortic valve, coincident with the incisura of the aortic pressure curve produced by the weak beat.

During a normal left ventricular ejection (Fig. 11, left), vortices are believed to form in the aortic sinus (6-9). These vortices make the pressure on the sinus side of the cusps exceed that on the aortic side (10), thereby causing the valve cusps to project during ejection into the aortic lumen and to close almost instantaneously and competently at the end of ejection. There is a small amount of retrograde flow in the ascending aorta at the end of left ventricular ejection, as indicated by the normally seen, small negative deflections on the aortic flow pulse coincident with the aortic incisura. This retrograde flow probably corresponds to the volume of blood that is displaced by closure of the valve cusps rather than by true regurgitation across the valve. The closure of the aortic valve during diastole is maintained by the aorta-to-left-ventricle pressure gradient.

With smaller-than-normal stroke volumes ejected with low velocity (Fig. 11, middle), there is probably less or no vortex formation in the aortic sinus during ejection. Consequently, the aortic valve cusps may float into a wider opened position. Hence the volume of retrograde flow in the ascending aorta coincident with the return of the valve cusps to the fully closed position is increased. This would
AORTIC VALVE CLOSURE

explain why the volume of retrograde flow in the aorta at end of ejection tended to increase with decreasing stroke volume and that the presence and volume of this flow were not necessarily associated with or proportional to the magnitude of valvular reflux (Figs. 9 and 10). Without normal vortex formation in the aortic sinus during ejection, closure of the aortic valve is left partly to deceleration of the aortic flow during the terminal phases of ejection and is therefore less prompt and efficient than under normal conditions. This would explain why (Fig. 12) the maximal acceleration of retrograde flow at the end of ejection tends to be lower in beats with smaller stroke volume than in beats with larger stroke volume.

With weak ventricular contractions which just barely open the aortic valve (Fig. 11, right), only a minimal amount of blood is ejected into the aorta. The aortic valve is closed by deceleration of aortic flow, followed by reversal of the pressure gradient across the valve from the aorta to the ventricle. The closure is sluggish and usually associated with a small amount of retrograde flow into the left ventricle (Fig. 8). However, retrograde flow in the ascending aorta is frequently not detectable by a flowmeter because of minimal displacement of the valve cusps when opened and the small degree of actual regurgitation across the valve which may occur.

There is disagreement in the literature in regard to the frequency of regurgitation across the normal aortic valve. Nelson et al. (11) emphasized competency of the normal aortic valve in dogs when a closed-tip catheter was used for injection in aortic angiography. However, Fabian and Abrams (12) found aortic reflux in 35% of 190 contrast injections into the aorta in normal dogs. The incidence of regurgitation increased with increasing injection rates and intrabronchial pressure. Armelin et al. (5), using upstream sampling of dye dilution, observed a minimal degree of aortic regurgitation in 7 of 22 dogs with normal aortic valves after unsynchronized injections of dye. When short, synchronized injections of dye were given, the incidence of minimal aortic regurgitation increased when the injection was timed to occur during closure of the aortic valve.

Incompetent closure of the normal aortic valve after weak ventricular beats, as demonstrated in our experiments, is likely to occur in humans and may have been responsible for the observation of Lehman et al. (13), who noted "on rare occasions, with a transient bradycardia or asystole, a slight 'puff' of opaque medium issuing through a competent aortic valve and entering the left ventricle." Because the incompetence of the normal aortic valve after weak ventricular beats is of mild degree, it is probably of no hemodynamic significance when it occurs after isolated extrasystolic beats. It may, however, assume clinical significance in a rare case of bigeminal rhythm or rapid atrial fibrillation. It should also be kept in mind during interpretation of aortic angiograms in the presence of cardiac arrhythmias.

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