Left ventricular endocardial longitudinal and transverse changes during isovolumic contraction and relaxation: a challenge

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Submitted 24 August 2004; accepted in final form 17 January 2005

METHODS

Six adult Targhee sheep (58 ± 18 kg; Sherick Farm, Missoula, MT) were implanted with 13 ultrasonic crystals via a cardiopulmonary bypass. After the animals were weaned from bypass and the pericardial sac was closed, recordings were obtained under stable hemodynamic conditions.

All animals received humane care in accordance with the Principles of Laboratory Animal Care, formulated by the Animal Welfare Act in the National Institutes of Health (NIH) Guide for Care and Use of Laboratory Animals [DHHS Pub. No. (NIH) 85-23, Revised 1996]. The protocol for the use of these animals for this research was also reviewed and approved by the Institutional Animal Care and Use Committee of The University of Montana.

Surgical protocol. The sheep were premedicated with ketamine (1.0 mg/kg) and propofol (4.0 mg/kg). Artificial ventilation was achieved using a volume-regulated respirator (North American Drager, Telford, PA). Electrocardiogram was monitored continuously.

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The venous and arterial cannulas were removed, and the heparin was neutralized with protamine. The pericardium was closed with a 3-0 polypropylene suture. Recordings were obtained after the animal was hemodynamically stable (≥30 min after the animal was weaned from cardiopulmonary bypass) to ensure the presence of normal loading conditions.

**Definition of the phases of the cardiac cycle.** Geometric changes were time related to each phase of the cardiac cycle defined from the aortic and LV pressure curves. The end of diastole was defined as the point of increasing LV pressure trace (dP/dt > 0). The end of IVC was defined as the beginning of ejection at the crossing point of the LV and aortic pressure curves (LV pressure/aortic pressure = 0). The dicrotic notch in the aortic pressure curve defined end ejection. The end of IVR, or the initial phase of diastole, was defined by the mitral valve opening determined by the initial separation of the crystals located in the leaflets’ free edge (AL–PL) (7).

**Definition of anatomic regions.** Longitudinal axes were defined as distances between the apex and the base of the aortic valve RCS, the fibrous trigones (T1 and T2), the lateral mitral annulus (P1 and P2), and the PMA. Movements of the mitral valve were recognized by the changes in distance between the crystals on the AL and PL.

Transverse diameters were defined as the distance between SW and AW and the distance between the crystals on M1 and M2 (Fig. 1).

**Data acquisition.** Distances between crystals were measured with a digital ultrasonic measurement system (TRX series, Sonometrics) using 13 transmitter/receiver crystals. A postprocessing program (Sonometrics) was used for examination of each individual distance between crystals and for three-dimensional reconstruction of the crystal coordinates. The data sampling rate was 200 Hz, with a time frame of ~5 ms and smallest measurable change in distance of 0.024 mm, which allowed us to investigate distance changes during IVC and IVR.

Pressure transducer control units (model TCB 600, Millar Instruments) and Mikro-Tip pressure transducers (Millar Instruments) were used to obtain the LV and aortic pressures. Pulmonary and left atrial pressures were measured directly through a 20-gauge needle and a conventional pressure transducer. Aortic flow was recorded using an ultrasonic flow probe (models T206 and 20A, Transonic Systems) placed around the ascending aorta. Flow readings were used to calculate stroke volume. All distances, flows, and pressures were displayed and recorded simultaneously on the same screen by the Sonometrics system to ensure that all data were synchronized and recorded on the same time line. An effort was made to record the measurements under stable hemodynamic conditions of heart rate and loads with a closed pericardium.

**Measurement and statistical analysis methods.** Distances were explored in a coordinate-independent analysis, using only distance measurements (5). After close examination of the data, three consecutive heartbeats that contained the least amount of noise were chosen for analysis. The summary statistics are reported as means ± SE. Normal distribution of measured data was rejected by Kolmogorov-Smirnov (Lilliefors) test. Therefore, data were tested by Wilcoxon’s
Fig. 2. A: phases of the cardiac cycle with changes in longitudinal and transverse diameters in 1 sheep. B: phases of the cardiac cycle with changes in mean longitudinal and transverse diameters in 1 sheep. 1, Beginning of isovolumic contraction; 2, beginning of ejection; 3, end of ejection; 4, end of isovolumic relaxation. AA pressure, aortic pressure.
plateau at the beginning of IVR and decreased further by 4.55% of its total expansion (9.33 ± 1.23 mm), with a fast decrease from 95.55 ± 1.80% to 69.39 ± 3.99% followed by a small notch at the beginning of ejection and a subsequent continuous shortening during systole (Fig. 2A). Simultaneously, during IVC, the mean longitudinal diameter increased by 30.80 ± 9.54% of its total expansion (5.74 ± 1.01 mm), with a fast lengthening from 64.21 ± 3.76% to 95.01 ± 1.28%, reaching its peak precisely at the beginning of ejection and then shortening throughout the remainder of systole (Table 3).

IVR. LV mean transverse diameter reached maximum shortening of 2.65 ± 0.79% of its total expansion (9.33 ± 1.23 mm) exactly at the end of ejection and started to expand by 11.01 ± 3.18% of total expansion during IVR (Fig. 2A). The shortening in the LV longitudinal diameter during ejection reached a small notch at the beginning of IVR and decreased further by 21.37 ± 6.91% of its total expansion (9.33 ± 1.23 mm) from 24.43 ± 7.16% at end ejection to maximum shortening of 3.06 ± 0.86% precisely when the mitral valve started to open (Table 4).

DISCUSSION

Mitral valve closure. Contrary to the general opinion that the mitral valve closes at the very beginning of IVC, we found that it was still open at that moment. Our data show that the mitral valve is open during the first three-quarters of IVC. It closed at the beginning of the last quarter, confirming data presented previously by our group (14, 15) (Fig. 2B). Given that motion must be preceded by an acceleration phase and that acceleration in fluids is driven by pressure gradients, it makes sense that a pressure gradient must significantly precede the flow that closes the mitral valve. An instantaneous closure would only be possible with a weightless, incompressible fluid.

Yellin et al. (33) implanted a flow probe in the LV inflow tract and showed a negative flow at the mitral orifice during IVC. They interpreted this finding as an artifact, because they assumed that the mitral valve must already be closed at the onset of IVC. Also, finding that the first heart sound occurred during the rapid ventricular pressure development (or IVC), and not at end diastole as expected, they concluded that this sound was generated by the vibration of the already closed and tense mitral valve. Our data clearly show that the mitral valve remains open during most of IVC, while there is a rapid rise in LV pressure. As found by Yellin et al., some degree of regurgitation through the open mitral valve is likely. If this is so, the concept of an isovolumic phase is open to criticism. We can also probably assume that closure of the mitral valve at the last quarter of IVC contributes to the generation of the first heart sound, which occurs ~7 ms before ejection (8, 12, 33). Therefore, it might be incorrect to define IVC as the interval between the start of LV rising pressure and the opening of the aortic valve. Furthermore, previous work in our laboratory showed that the aortic valve leaflets start to separate while a negative gradient still exists between the LV and the ascending aorta (13). Again, the concept of an isovolumic phase becomes doubtful.

IVC phase. On the basis of the early experiments of Rushmer et al. (23–25), it has been accepted that the LV becomes more spherical during IVC. This phenomenon is easily visible intraoperatively in the beating heart. Intracardially, we found the opposite pattern. During the initial phase of LV contraction, the endocardial shape of the LV became more elliptical (i.e., its...
longitudinal diameter increased while its transverse diameter decreased; Fig. 2B). This discrepancy is explained by the thickening of the LV wall during contraction (20, 31). This thickening results in an epicardial outward and an endocardial inward displacement and, consequently, a reduction in the LV endoluminal transverse diameter. According to Laplace’s law (7), it can be hypothesized that this reduction in LV radius should reduce wall tension before ejection. The LV longitudinal diameter lengthened during IVC. As described by Robinson and associates (21), this longitudinal fiber stretch stores elastic kinetic energy that will be supplied during the beginning of longitudinal shortening.

**IVR phase.** We found no relaxation of the entire ventricle during IVR. After ejection, from closure of the aortic valve until opening of the mitral valve, both valves are firmly closed, and LV volume does not change. However, during this time, while the LV transverse diameter starts to increase, the longitudinal diameter continues to shorten (Fig. 2B). Our results are different from those of Nikolic et al. (18), who described a change in LV to an elliptical shape. Again, these dimensional measurements were done with epicardial sonomicrometric markers after mitral valve replacement and, presumably, with the deleterious effects that follow transection of all mitral valve chords (34). Our findings confirm the observations of Rankin et al. (20), who described a change in LV geometry to a spherical shape during the initial isovolumic phase of diastole in the direction opposite that observed during IVC. LV transverse diameter reaches its shortest distance (end of transverse contraction) exactly at the time of closure of the aortic valve and lengthens during IVR. LV longitudinal diameter shortens during systole. After a small plateau corresponding to aortic valve closure, LV endocardial longitudinal diameter continues to shorten during the entire IVR until the exact time of mitral valve opening. Consequently, to term this period relaxation is incorrect, because LV contraction and blood volume redistribution are still occurring. As demonstrated by Ashikaga et al. (1), endocardial sheet shortening occurs during IVR and appears to drive global torsional recoil to aid early diastolic filling.

The predominant paradigm that is used to understand the LV pump function with staccato mechanical parameters should probably be shifted toward a smoother, flow-directed behavior. Recent cardiac flow dynamic studies with three-dimensional MRI velocity mapping (11) and studies on LV mechanics (2–4, 28, 30), anisotropic material properties of myocardium (17), and transmural myocardial deformations (31) might provide a more physiological and real understanding of the fluid continuum of the cardiac phases.

**Limitations of the study.** We are aware that our approach is simple, but the present technology of high-resolution sonomicrometry requires that the number of sonomicrometry crystals be limited to a minimum. Sonomicrometry gives the distance between identical locations with high resolution (200 Hz) and a time frame of 5 ms, making it possible to investigate distance changes during IVC and IVR.

Pictorial methods, such as echocardiography and computed tomography scan, cannot precisely pursue a moving location over several slides; therefore, it is impossible for these methods to give precise distances between two moving points. Additionally, the time frame resolution of these methods is considerably longer (>30 ms). Cinéfluoroscopy (29) with a high-speed camera or ultrafast MRI (6, 22) with true myocardial motion tracking makes it possible to observe the same location during IVC and IVR within 30–60 ms, but these techniques are still experimental. Sonomicrometry is a well-known and established technology.

In this experimental setting, it was impossible to address the rotational motion of the LV, which is essential for understanding LV function. Sonomicrometry allows precise, high-resolution recording of distances, but it cannot distinguish between active contraction and passive reshaping of the myocardium.

The sonomicrometric crystals and their electrodes might have interfered with the normal movements of the different structures. Also, the location of the crystals might vary between animals. To diminish this possibility, all surgeries were performed by the same surgeon.

All data were acquired in an acute, anesthetized, open-chest animal after cardiopulmonary bypass and cardioplegia and with the pericardial cavity surgically closed in all animals. Hemodynamic stability was carefully monitored, and the loading conditions were controlled. Despite this nonphysiological condition, the changes were very consistent among all animals. Additionally, findings in sheep are not necessarily applicable to humans.

**Conclusions.** Our findings from this study are as follows: 1) The mitral valve remains open during three-quarters of the IVC phase. 2) During IVC, the LV endoluminal transverse diameter decreases while its longitudinal diameter increases, resulting in an elliptical shape. 3) During IVR, the LV endoluminal longitudinal diameter continues to shorten as it does during ejection. Simultaneously, the LV transverse diameter increases from its shortest at end ejection. The LV acquires a more spherical
shape. 4) The concept of IVC and IVR phases might need to be revised.

ACKNOWLEDGMENTS

We appreciate the technical assistance of Leslie Trail, Lorinda Smith, and Holly Meskimen in the animal laboratory and the editorial assistance of Jill Roberts.

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