Application of an end-systolic pressure-segment length relationship for measuring regional contractility

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Summary

A method for estimating regional contractility is described using the end-systolic relationships between left ventricular pressure and myocardial segment-lengths in rapidly volume-loaded beats. The approach was based on the success of previously developed end-systolic relationships between left ventricular pressure and volume and between variable ejection force and fiber length used to describe global contractility in beating hearts. The regional end-systolic relationship was more complicated than its global counterpart, which was load independent, and appeared curvilinear to rapid volume loading. As an approximation of this relationship, a linear slope was constructed between maximum and minimum (pre-ejection) loaded beats of equal cycle length. Because of its load dependency and in order to compare slope relationships between interventions, slope functions were derived only from similarly loaded beats either within or between interventions. Slopes generated by this technique had a reasonable constancy at control conditions and coronary flows with an average SEM of 9.1% of the slope means. End-systolic slopes also appeared sensitive to changes in contractile state, increasing appropriately following treatments with dobutamine and decreasing after propranolol. Following shifts in the end-systolic slopes were unreliable, however, in describing the regional changes in contractility with ischemia. At milder levels of flow restriction, the slopes declined as expected. At moderate levels of flow restriction, the pressure-segment loops shifted markedly rightward and the slope increased. At advanced levels of ischemia, the loops were so distorted, that end-systole could not be identified accurately and the loops essentially described the diastolic compliance characteristics of the left ventricle.

Thus the slope estimates of regional contractility as described in this report provided a reliable assessment of inotropic background during modifications with positive and negative inotropic drugs but became invalid as systolic shortening was replaced by aneurysmal bulging during high-grade ischemia.

Key words: positive and negative inotropy, dobutamine, propranolol, regional ischemia, working swine hearts

Introduction

A variety of force-velocity-length relationships have been developed in several isolated muscle preparations which accurately reflect the inotropic state of the muscle and are insensitive to changes in initial fiber length (9). Enormous effort has been expended in trying to apply these relationships
to the beating heart. However, to date their transference to more intact preparations has had to rely on several model systems based on either questionable or untested assumptions (6). Early emphasis was placed on evaluating empirically-derived indices of isovolumetric contraction. All (max dp/dt, V_{\text{max}}, V_{10}, V_{\text{CE}}, \text{at max dp/dt}, \text{or peak } V_{\text{CE}}) have since been challenged with respect to their dependency on changes in preload and afterload (15). More recently, attention has shifted to studying certain relationships at end-systole. Time-dependent slopes of pressure-volume (13) and force-length (16) relationships at end-systole have been shown to reliably reflect inotropic background at varying levels of preload and afterload in the isolated and globally supported heart. Early success with these slope relationships has also been reported in pilot clinical trials (1, 5, 7, 12).

However, certain mechanical events are expressed to a greater extent regionally rather than globally, particularly those changes observed with regional ischemia. In intact working canine hearts, it has been shown that the mechanical changes with ischemia are only incompletely represented by global abnormalities in hemodynamic performance (8). It was thus of interest to determine whether the global constructs of contractility previously described at end-systole could be applied in modified form to the regionally supported myocardium. The following is a methods' report of studies designed to test the validity and sensitivity of these measurements in an intact, working, and regionally perfused swine heart preparation.

**Methods**

*Preparation and instrumentation.*

Six adolescent open-chest swine, weighing between 40-62 kg, were studied following general anesthesia with pentobarbital (35 mg/kg i.v.), intubation with positive pressure ventilation and 100 % oxygen flow, and treatment with i.v. heparin (3 mg/kg). Specifics of the intact working swine heart preparation have been previously described (3). Studies were conducted both at native coronary flow states and at regulated coronary perfusion to the anterior descending coronary circulation. For this latter arrangement, arterial blood was obtained from a cannula in a femoral artery and diverted through extracorporeal tubing to a small coronary cannula placed in the anterior descending artery high in its proximal distribution. Flow was supported by a low-flow Sarns perfusion pump. Normal flow was initially determined by matching mean coronary perfusion pressure with peak systemic arterial pressure, after correcting for the internal line resistances of the tubing and cannula. Final adjustments were made based on the coronary venous oxygen saturation (average 45 %) sampled from a catheter inserted into the anterior great cardiac vein running adjacent to the anterior descending artery.

A manometer-tipped, pressure-measuring catheter (Milar) was retrogradely inserted from a carotid artery into the left ventricle. A pair of ultrasonic crystals was placed in the anterior free wall of the left ventricle in the region perfused by the anterior descending artery. The crystals were oriented in an equatorial plane in the mid-myocardium corresponding to the alignment and direction of circumferential fibers. These crystals and dimension system (Schuessler Biomed Instruments) were used to measure regional myocardial shortening. Left ventricular pressures and shortening data were used further to construct instantaneous left ventricular pressure-myocardial segment length relationships throughout a computer (Digital Equipment Corporation PDP 10/10) reconstructed cardiac cycle. A large-bore, 1.8