Independence of left ventricular pressure-volume ratio from preload in man early after coronary artery bypass graft surgery


ABSTRACT  The response of the maximum value of the left ventricular pressure-volume ratio to preload augmentation by blood or plasma expanders was studied in 11 patients during the first 24 hr after coronary artery bypass graft surgery. Increasing the mean left atrial pressure from 10 to 15 and 20 mm Hg resulted in no change in the maximum pressure-volume ratio in the group as a whole. In certain individual patients, however, the maximum pressure-volume ratio changed with volume infusion, and these changes were accompanied by simultaneous changes in afterload. The observed changes in pressure-volume ratio were in the same direction as the changes in afterload (systolic pressure), suggesting a dependence of maximum pressure-volume ratio on afterload. These results show that the maximum pressure-volume ratio is independent of preload in the first 24 hr after coronary artery bypass graft surgery with the pericardium open; thus the maximum pressure-volume ratio is a useful index of postoperative left ventricular function when afterload is unchanged. However, because this ratio (a single-point assessment of the pressure-volume relationship) may not be a good estimate of Emax, we recommend a more complete determination of the locus of the “upper left corners” of the pressure-volume loops for measurement of Emax to provide a more accurate indicator of the myocardial contractile state.


The points on pressure-volume diagrams of the left ventricle where the ratio of instantaneous ventricular transmural pressure to instantaneous ventricular volume is at a maximum (i.e., the upper left corners of the loops, which occur at a time near end-systole) lie on a straight line that is independent of loading conditions over a wide range. The slope of this line, which has been called Emax, changes with inotropic interventions and has been shown to be a useful index of left ventricular contractility. Various assessments of Emax, based on measurement of pressure-volume, pressure-dimension, stress-dimension, and similar relationships, can be very useful indexes of ventricular performance.

The ratio of end-systolic pressure to end-systolic volume, a popular estimate of Emax, is reduced in patients with chronic volume overload, and end-systolic volume (even when uncorrected for its pressure dependence) is a useful prognostic indicator in such patients. A single measurement of the end-systolic stress-volume ratio can be a useful predictor of operative risk in patients with chronic mitral regurgitation.

It is compelling to think that a simple ratio, calculated from single measurements of left ventricular pressure and volume near end-systole, might reflect the myocardial contractile state accurately enough to be clinically meaningful. Moreover, such an approach would markedly reduce the technical complexity and number of interventional procedures required for assessment of the contractile state.

We therefore tested the hypothesis that the maximum left ventricular systolic pressure-volume ratio \([P/V]_{\text{max}}\) is independent of preload in intact man, using a technique that allowed repeated measurement of left ventricular pressure-volume relationships as frequently as desired in the first 24 hr after cardiac surgery.
Methods

Patient selection and surgical procedure. Before elective coronary artery bypass graft surgery, written informed consent was obtained for implantation of permanent myocardial markers, instrumentation, and performance of postoperative studies. The study protocol was approved by the Institutional Committees on the use of Human Subjects in Research. Our study group comprised 11 men 37 to 68 years old (mean 54). All patients had multiple-vessel disease, and five had suffered at least one previous myocardial infarction. Wall motion was normal in seven, and wall motion abnormalities were evident in four. Mean preoperative ejection fraction was 0.62 (range 0.39 to 0.79).

Patients were anesthetized with fentanyl and diazepam. Moderate systemic hypothermia (30° C) and single-dose, cold, hyperkalemic cardioplegic solution (supplemented with continuous profound topical hypothermia) were used for myocardial protection.

Seven patients had three grafts placed, and four had four grafts. Mean aortic cross-clamp time was 54 min (SD 12 min).

Seven tantalum markers were placed in the left ventricular myocardial midwall: three along the inferior wall, one at the apex, and three along the anterior wall, providing a silhouette of the left ventricle when fluoroscopically viewed in the 30 degree right anterior oblique projection. Two metallic clips were attached to the aortic adventitia to delineate the position of the aortic valve.\textsuperscript{18} Temporary bipolar pacing leads were sutured to the right atrium. A micromanometer-tipped No. 4F catheter (Millar Instruments PC340) was inserted via the right superior pulmonary vein into the left ventricle (figure 1) and a fluid-filled catheter (16-gauge Teflon) was placed in the left atrium. The pericardium was left widely open; mediastinal drainage tubes and two pericardial pressure catheters (a fluid-filled 16-gauge Teflon catheter for calibration of the accompanying micromanometer, a Millar PC350, No. 5F) were inserted, the chest was closed, and the patient was transferred to the surgical intensive care unit.

There were no perioperative myocardial infarctions or complications associated with the surgical implantation of markers or subsequent postoperative studies.

Preload augmentation and data acquisition. To increase preload, blood volume was augmented by intravenous infusion of blood, albumin, or crystalloid solutions to achieve targeted values of mean left atrial pressure of 10, 15, and 20 mm Hg. Doses of any drugs (inotropic or afterload-reducing agents) were maintained at a constant level throughout the volume loading series.

When the target value of mean left atrial pressure was achieved, infusion of fluid was adjusted to maintain this pressure for about 5 min. The chest tube suction and respirator were disconnected for a few seconds, allowing the airway pressure to equilibrate with room air pressure. A videofluorogram of marker positions was recorded on an Ampex DR10A video disk recorder at 30 frames/sec for 3 consecutive beats. (The respirator and suction were restored immediately after recording.) The left atrial, pericardial, and left ventricular pressures and the electrocardiogram were also recorded. The left ventricular and pericardial pressures were electronically subtracted to provide left ventricular transmural pressure, which was recorded on the fluorographic image as an analog signal.

Heart rate was controlled by atrial pacing to maintain a constant rate of 100 beats/min when necessary. Unpaced cardiac cycles were recorded only if a patient’s normal sinus rate was between 95 and 105 beats/min.

Data reduction. The video images were replayed in stop-motion (frame-by-frame) mode on a video monitor, and the position of each marker and the analog left ventricular transmural pressure signal were digitized with a light pen coupled to a Hewlett-Packard 2115A digital computer. The x,y coordinates of each marker image were corrected for image magnification and distortion and transmitted to an IBM System/34 computer. Left ventricular volume, transmural pressure, and pressure-volume ratio were obtained by further computer analysis of the corrected digitized coordinates.\textsuperscript{19, 20}

Estimates of left ventricular volume were paired with the simultaneously measured value of left ventricular transmural pressure, and pressure-volume diagrams such as those depicted in figure 2 were plotted.

Each patient’s volumes were expressed as volume index in an effort to compensate for different body sizes, and mean left ventricular end-diastolic volume and volume index were calculated for each 3 beat sequence. \(\frac{P}{V}\)max was calculated for each beat

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(P/V)_{\text{max}} = \text{MAX} \left\{ \frac{(LV \text{ transmural pressure})}{(LV \text{ volume index})} \right\}
\]

and the mean value of \(\frac{P}{V}\)max for each 3 beat sequence was calculated.

Analysis of variance by randomized blocks\textsuperscript{21} was used to determine whether end-diastolic volume index or \(\frac{P}{V}\)max had been affected by changes in mean left atrial pressure. A p value of less than .05 was considered significant.

![Figure 1](http://circ.ahajournals.org/)

**FIGURE 1.** Schematic representation of the monitoring apparatus. Micromanometer-tipped catheters provided pressure measurements in the left ventricle (LV-M) and the pericardium (PC-M). Fluid-filled catheters measured left atrial pressure (LA-FF) and provided calibration (PC-FF) of the micromanometer PC-M at regular intervals as the patient’s temperature changed. Bipolar pacing leads (PACEMAKER) in the right atrium allowed electrical control of heart rate when required. Tantalum markers were inserted in the left ventricular midwall at the time of surgery (three in the anterior wall, one at the apex, and three in the inferior wall) to provide a silhouette of the left ventricle when viewed in a 30 degree right anterior oblique fluorogram. The position of the aortic valve was marked by metallic clips (\(\bigcirc\)) placed on the aortic adventitia.
**Results**

Successful loading series (in which two or more of the target mean left atrial pressures were achieved) were obtained in 11 patients. In five of these patients two series were obtained, the series being no more than 4 hr apart. Recording began an average of 10.4 hr after discontinuation of cardiopulmonary bypass.

Overall mean heart rate was 101 beats/min (SD 2 beats/min).

Figure 3 demonstrates the beat-to-beat reproducibility of the position of the “upper left corners” of the pressure-volume diagrams, the point where the maximum pressure-volume ratio occurred. Reproducibility of the pressures at this point expressed as a coefficient of variation (cv = 100 \cdot SD/mean, where SD is the standard deviation obtained by pooling deviations of each of the measurements from its local 3 beat mean for all 42 sequences) was 1.0%. Reproducibility of the volume was 1.9%, and reproducibility of (P/V)max was 2.4%.

To determine the validity of using mean left atrial pressure to assess preload, we compared left ventricular end-diastolic volume index derived from marker images with the measured mean left atrial filling pressures. In these patients the left ventricular end-diastolic volume index correlated strongly with the mean left atrial pressure during the first 24 hr after cardiac surgery, as shown in figure 4. Analysis of variance showed that the use of mean left atrial pressure to estimate preload was reasonable in these patients, with left ventricular end-diastolic volume index strongly dependent on mean left atrial pressure (F = 37.3; df = 2,30).

Mean values of (P/V)max for each sequence in each patient are plotted against mean left atrial pressure in figure 5. Note that there is no apparent correlation between (P/V)max and mean left atrial pressure. Analysis of variance of these data shows that the observed variation in (P/V)max is not due to preload as measured by mean left atrial pressure (F = 1.1; df = 2,30) but rather to variation between individual patients (F = 31.8; df = 14,30).

Although there was no demonstrable dependence of (P/V)max on preload as defined by mean left atrial pressure, the validity of using mean left atrial pressure to assess preload is confirmed by the strong correlation between the mean left atrial pressure and the mean end-diastolic volume index.

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**FIGURE 2.** Left ventricular pressure-volume diagrams showing three sequences (each of 3 beats) at three different conditions of preload. Left ventricular volume is plotted along the abscissa, and left ventricular transmural pressure is plotted on the ordinate. (Notice that peak systolic pressure has increased with preload augmentation in this patient.) Solid line, Mean left atrial pressure 10 mm Hg; dashed line, mean left atrial pressure 15 mm Hg; dashed-dotted line, mean left atrial pressure 20 mm Hg.

**FIGURE 3.** Upper left corners of the pressure-volume diagrams shown in figure 2. Mean and SD of volume and pressure at the point of (P/V)max (circles) are shown for each 3 beat sequence.

**FIGURE 4.** End-diastolic volume index (EDVI) plotted against mean left atrial pressure (LAP), showing the strong dependence of EDVI on mean LAP (p < .0005).
pressure for the group as a whole, in some patients (P/V)max did change with volume loading. In these cases, systolic pressure had changed markedly as well, in the same direction as the change in (P/V)max. This suggests a possible afterload dependence of (P/V)max. A plot of (P/V)max against afterload (defined as the left ventricular transmural pressure at the time of maximum systolic pressure-volume ratio) is shown in figure 6. Values of (P/V)max are found to be strongly correlated with this measure of afterload (mean slope $= 0.01; p < .01$).

Discussion

Because mean left atrial pressure is easily measured in postoperative surgical patients and because it is commonly used to guide the course of blood volume replacement, we used mean left atrial pressure to assess preload in this study while validating that increases in mean left atrial pressure brought about the desired increases in end-diastolic volume (figure 4). Two patients showed only slight volume increases with increased left atrial pressure, and one showed a decrease in volume. These variations might be caused by stiff ventricles associated with postmyocardial infarction scarring, right ventricular influences on the left ventricular filling characteristics, or a combination of both of these effects. Despite these atypical responses, our data show that augmentation of blood volume sufficient to increase mean left atrial pressure can be expected to increase end-diastolic volume ($p < .0005$). Although mean left atrial pressure was a reasonable assessment of left ventricular preload, our patients all had widely open pericardia. It is clear that the pericardium influences the filling characteristics of the left ventricle, so caution is recommended in the extrapolation of our results to other patient groups or to the normal ventricle.

It was interesting that in each of the 126 beats we examined in the present study, a good estimate of (P/V)max could be obtained with the highest (peak systolic) transmural pressure as the numerator and the smallest (end-systolic) volume index as the denominator of the ratio. That is to say, the upper left corner of the pressure-volume loop was well defined by the uppermost and leftmost limits of the loop. Previous investigators have shown, however, that if the shape of the pressure-volume loops is different for any reason, this observation may not be applicable.$^{22, 23}$

Although (P/V)max was shown to be independent of preload, individual variations occurred after augmentation of blood volume. These changes can be explained by the accompanying changes that occurred in left ventricular systolic pressure (figure 6; $p < .01$). This finding corroborates those of other investigators.$^{24, 26}$ (The variability of afterload response to preload augmentation is probably caused by the interpatient differences in afterload-reducing therapeutic agents such as nitroprusside.) Although systolic wall stress or the systolic wall stress-time integral may be more suitable measurements of afterload than systolic pressure,$^{27}$ it is clear that (P/V)max and the maximum stress-volume ratio are both explicitly dependent on afterload.

We did not systematically control afterload in this study, but the finding that (P/V)max was increased at higher afterloads [assessed by the left ventricular transmural pressure at the time of (P/V)max] is in perfect agreement with the recent findings of Kono et al.$^{26}$ in
their work with the isolated canine heart. Current studies in our laboratory, using appropriate afterload alterations,11, 28 are being carried out to determine the dependence of (P/V)max on afterload in intact man.

On theoretical grounds, one would expect that the peak left ventricular pressure-volume ratio derived from a single pressure volume loop is not as reliable as an index of myocardial contractile state as Emax. As can be seen in figure 7, the dashed line (which has a slope equal to the maximum pressure-volume ratio) might be a poor estimate of the solid line, whose slope is Emax. Only when the volume intercept, Vo, which has been called the “dead volume” or more properly “unstressed volume,” is zero are the lines collinear. Generally, when afterload conditions are varied, the upper left corner of the pressure-volume diagram moves up or down on the solid line (at constant Emax). This results in a changing value of (P/V)max with changing afterload. This fact has been pointed out previously by other investigators.26, 29, 30

We conclude that in intact man early after coronary artery bypass graft surgery with the pericardium left open, the maximum value of the left ventricular pressure-volume ratio is independent of preload. This ratio is probably not independent of afterload, nor is it realistically expected to be. Because (P/V)max or a similar single assessment of the pressure-volume relationship may not be a good estimate of Emax, we recommend a more complete determination of the locus of the “upper left corners” of the pressure-volume loops for measurement of Emax (and Vo) to provide a more accurate indicator of the myocardial contractile state.

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