Rapid Estimation of Left Ventricular Contractility from End-Systolic Relations by Echocardiographic Automated Border Detection and Femoral Arterial Pressure

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Background: Automated echocardiographic measures of left ventricular (LV) cavity area are closely correlated with changes in volume and can be coupled with LV pressure to construct pressure–area loops in real time. The objective was to rapidly estimate LV contractility from the end-systolic relations of cavity area (as a surrogate for LV volume) and femoral arterial pressure (as a surrogate for LV pressure) in patients undergoing cardiac surgery.

Methods: Studies were attempted on 18 consecutive patients with recordings of LV pressure, LV area, and femoral arterial pressure on a computer workstation interfaced with the ultrasound system. End-systolic pressure–area relations (in terms of pressure–area elastance [Em]) from pressure–area loops during inferior vena cava occlusions were determined before and immediately after cardiopulmonary bypass using both LV and arterial pressure by semiautomated and automated iterative linear regression methods.

Results: Data sets were available for 13 patients before and 8 patients after bypass (21 studies in 14 patients). Em by arterial pressure was closely correlated with Em by LV pressure: r = 0.96, standard error of the estimate = 2 mmHg/cm², y = 1.01 × -0.7 by the semiautomated method and r = 0.94, standard error of the estimate = 3 mmHg/cm², y = 1.02 × -0.5 by the automated method. Analysis of semiautomated and automated estimates of Em from arterial pressure and Em using LV pressure by the Bland-Altman method showed no systematic measurement bias and calculated limits of agreement of 8 and 9 mmHg/cm², respectively. Similar decreases in Em by arterial and LV pressure occurred from before to after bypass in 7 patients with paired data sets: 32 ± 12 to 15 ± 6 mmHg/cm² and 32 ± 15 to 15 ± 7 mmHg/cm², respectively (P < 0.05 for both).

Conclusions: On-line femoral arterial pressure and LV area data by echocardiographic automated border detection may be used to rapidly calculate Em as a means to estimate LV contractility in selected patients. (Key words: Heart; end-systolic elastance; left ventricular performance; pressure–volume relation. Measurement techniques: transesophageal echocardiography.)

The end-systolic pressure–volume relation has been established as an important measure of the left ventricular (LV) contractile state because of its relative insensitivity to loading conditions. The technical and invasive demands of continuous measurement of LV volume, such as sonomicrometry or conductance catheter techniques, and the need for placement of a LV pressure-sensing catheter have limited intraoperative and other clinical applications. Although intraoperative transesophageal echocardiography has been useful as a monitoring tool, in particular for visualizing LV wall motion, quantitative determinations of LV function from these data have required time-consuming off-line analysis. Recently, echocardiographic automated measures of LV cross-section cavity area have provided an opportunity to estimate changes in LV volume online. We have shown that these echocardiographic data can be coupled with LV pressure data to construct real time pressure–area loops as a means to assess LV performance in a manner analogous to pressure–volume relations. Previous investigators have used central aortic and brachial arterial pressure to estimate LV systolic pressure in the absence of aortic stenosis...
or LV outflow tract obstruction. Accordingly, the objective of this study was to determine if femoral arterial pressure data coupled with simultaneous on-line measures of LV cavity area can estimate the end-systolic pressure–area relation as a rapid and less invasive means to assess LV contractility in humans.

**Materials and Methods**

Eighteen consecutive patients, aged 66 ± 12 yr (range 35–77 yr), 16 men and 2 women, who were undergoing coronary artery bypass surgery were studied. The protocol was approved by the Institutional Review Board on Biomedical Research and each patient gave written informed consent. Patients with aortic stenosis or LV outflow tract obstruction by previous cardiac catheterization or Doppler echocardiographic studies were excluded. Validation data from 13 of these patients that showed linearly related changes in pressure–area relations to simultaneous pressure–volume relations were previously reported. The mean preoperative LV ejection fraction by contrast ventriculography was 53 ± 12% (range 35–78%); in 3 cases it was ≤40%.

Patient wall motion abnormalities included posterobasal hypokinesis in 3, anterolateral hypokinesis in 3, and anterior, apical and posterolateral hypokinesis in 2. In all patients the heart was in sinus rhythm.

Patients were instrumented with 18-G fluid-filled femoral arterial catheters, connected to strain-gauge pressure transducers (Baxter Summit, Irvine, CA). This femoral arterial pressure system has a resonant frequency of approximately 40 Hz and a damping ratio of approximately 0.6, which is typical for a fluid-filled catheter system in clinical use. A median sternotomy was performed and a high-fidelity fiberoptic pressure catheter (Camino Laboratories, San Diego, CA) was advanced into the LV through the right superior pulmonary vein. The frequency response characteristics of this LV catheter were superior to those of fluid-filled catheter systems with a resonant frequency of 120 Hz. An inferior vena caval (IVC) vascular ligature was placed to rapidly alter preload by occlusion and release.

A 64-element single-plane 5-MHz transesophageal echocardiographic transducer of an automated border detection ultrasound system (77035A, Hewlett-Packard, Andover, MA) was used. Echocardiographic images were recorded from the transgastric midventricular short-axis plane by using the midpapillary muscle as an anatomic landmark and orienting the transducer to obtain the image that had the most circular overall geometry. Echocardiographic images were considered technically adequate for automated border detection if at least 75% of the endocardial circumference could be visualized. This criterion was adopted from previous reports of quantitative echo analysis. Manual adjustments of the automated border detection ultrasound gain settings were made by visual inspection as previously described.

In brief, the overall transmit, time gain compensation, and lateral gain control features were adjusted as a compromise between lateral dropout and cavity clutter. A region of interest was manually drawn immediately beyond the LV endocardial border to exclude the right ventricular cavity. The automated border detection ultrasound system acquired area data at the frame rate of the echoscanner (approximately 33 Hz), and the data were internally converted to an analog signal. The echo system was configured to allow direct recording of this analog area signal through a customized hardware and software interface. This area signal was digitized at a sampling rate of 150 Hz for display and storage on a computer graphics workstation (DN3550, Apollo Computer, Chelmsford, MA) with an acquisition system (RTS-132, Signifcat, Hudson, MA). LV pressure, femoral arterial pressure, LV cavity area, and electrocardiographic (lead II) signals were simultaneously digitized and recorded on the workstation in a similar manner.

All IVC occlusions were made with respirations suspended at end-expiration to minimize translational motion and to control for the effects of cardiopulmonary interactions. Caval occlusions were held for approximately 10 s until a minimum LV area occurred, then released. After a brief interval of positive-pressure ventilation, attempts at IVC occlusions were repeated but limited to a maximum of three challenges per patient and were not repeated if persistent hypotension or ventricular arrhythmias occurred. The entire protocol was attempted before and after cardiopulmonary bypass if the patient was judged to be hemodynamically stable.

**Data Analysis**

Data were analyzed by two methods with investigators blinded to the results of the alternative approach. In the first method, referred to as the “semiautomated method,” pressure, area, and electrocardiographic data were transferred from the workstation into a customized personal computer program written in ASYST (ASYST Software Technologies, Rochester, NY). Signals
Fig. 1. (Left) An example of waveform data during inferior vena caval occlusion. Minimum femoral arterial pressure has been realigned with end-diastolic left ventricular pressure and end-diastolic cross-section area. (Right) Corresponding simultaneous ventricular pressure–area loops in dashed lines and superimposed arterial pressure–area loops in solid lines.

were filtered with a low-pass filter that was applied to reduce electromagnetic interference commonly encountered in the operating room. This filtering process uses the inverse Fourier transform of the Blackman window with a cutoff frequency set at 50 Hz to eliminate 60 Hz electrical noise. This filtering procedure does not alter the physiologic signal spectrum while suppressing high-frequency noise.28

The program then separated data into cardiac cycles by determining the R wave of the electrocardiogram with a peak detection algorithm allowing the user to eliminate ectopic beats. One IVC occlusion per patient per condition was selected as the first run in chronological order with enough beats (approximately 7–10) to perform the analysis of end-systolic pressure–area relations described below. We have previously shown the variability of end-systolic pressure–area relation calculations by this technique to be low and within the range of variability of end-systolic pressure–volume relations reported by others.3,15 No increase in heart rate occurred during these first 7–10 beats of IVC occlusion.

To construct LV pressure–area loops, the LV pressure waveform was delayed slightly for the whole caval occlusion run and adjusted individually for each run to account for the time required for the automated ultrasound system to calculate cavity area from each frame (approximately 30 ms). Specifically, LV end-diastolic pressure, defined as the point immediately before isovolumic contraction, was aligned with end-diastolic area, defined as the first occurrence of the maximal area. The amount of delay in the area signal, attributed to the time required by the ultrasound system to make the area calculation, was slightly variable and adjusted for each patient with an average delay of 27 ± 33 ms.

To construct arterial pressure–area loops, arterial pressure waveforms were advanced to manually align the minimum arterial pressure with end-diastolic area previously defined as first occurrence of maximal area for each run (fig. 1). Slight adjustments in timing were made by visual inspection of the pressure–area loops.

Fig. 2. An example of the effect of timing on arterial pressure–area loops from a patient with a left ventricular pressure–area elastance (Ep) value of 13 mmHg/cm². The amount of time (t) the arterial pressure waveform was advanced with respect to left ventricular (LV) area is shown. (C) These loops (t = 99 ms) were selected for estimation of Ep by the semiautomated method because their configuration most resembled the ejection portion of a typical LV pressure–area loop (systolic pressure–area trajectory bounded by the range of area values). (E) demonstrates how Ep varies as a result of time shift in arterial pressure waveform alignment.
to most approximate LV ejection pressure as shown in figure 2, with the systolic pressure–area trajectory bounded by the range of area values. These adjustments were made by adding or subtracting 33-ms increments to the pressure signals. End-diastole was chosen as the point for alignment because most of the arterial pressure tracings did not have a clearly defined dicrotic notch to indicate end-diastole. LV contractility was then estimated by Suga and Sagawa’s method for calculating the end-systolic pressure–volume relation, or end-systolic elastance, by applying these calculations to the pressure–area loops.1,2,5,15,17 Accordingly, end-systole was defined as the occurrence of the maximal pressure/area point for each pressure–area loop, and the slope of these points from differently loaded beats determined $E_a$ by an iterative linear regression method described previously.15,17 Pressure–area elastance values were designated “$E_a$” to differentiate them from the “$E_{es}$” values of end-systolic elastance from pressure–volume data.

The same IVC occlusion runs were then analyzed by a second automated method, a customized software program written for the same computer workstation used for data acquisition (DN3550, Apollo Computer). This method decreased analysis time by automating the pressure and area waveform alignment by identifying and separating each cardiac cycle by the R wave of the electrocardiogram. Minimum arterial pressure values were automatically aligned with the first occurrence of maximal area values to approximate simultaneous end-diastolic events for each cardiac cycle. Pressure–area loops were then plotted and end-systolic points determined as the maximal pressure/area points (fig. 3). Ectopic ventricular beats were then manually eliminated and $E_a$ values solved with the identical linear regression and iterative technique as above. This automated method allowed for rapid determination of $E_a$ in the operating room by automating waveform alignment and $E_a$ calculation within 3 s, once ectopic beats were eliminated. The variability of the automated echo area signal during IVC occlusions for $E_a$ has been demonstrated in previous studies.12,13,15 Reproducibility of arterial pressure $E_a$ calculations was evaluated by correlating independent automated arterial pressure $E_a$ values with semiautomated results from the same runs by investigators blind to the alternate results.

Statistical Analysis

To assess the degree to which femoral arterial pressure could be used to estimate $E_a$ with LV pressure, linear regression analysis by the method of least squares was performed because $E_a$ derived from high-fidelity LV pressure was the gold standard to which $E_a$ by the arterial pressure signal was compared. Automated arterial pressure $E_a$ values were also correlated with semiautomated arterial pressure $E_a$ values. However, because systematic errors may exist, bias was evaluated for both the semiautomated and the automated arterial pressure $E_a$ calculations by pairing with LV pressure $E_a$ values using the Bland-Altman method for assessing agreement between two methods of clinical measurement.29 Agreement between semiautomated and automated arterial pressure $E_a$ also was evaluated by a similar technique. Estimates of $E_a$ after cardiopulmonary bypass were compared with $E_a$ before bypass by using a Student’s paired $t$ test. Significance is reported as $P < 0.05$. Data are presented as mean ± SD.

Results

Technically adequate simultaneous arterial pressure, LV pressure, and LV area data with IVC occlusions were available on 13 patients before and 8 patients after cardiopulmonary bypass for a total of 21 studies on 14 patients. Two patients had an inadequate echo image before cardiopulmonary bypass, as defined as <75% of the endocardium visualized,21–24 and were eliminated from further analysis. Two patients had frequent ventricular arrhythmias with attempted IVC occlusion that precluded further analysis. After cardiopulmonary bypass; 1 more patient had an inadequate echo image; 2 patients had ventricular arrhythmias with caval occlusion; 2 patients had excessive ventricular catheter artifact; and 1 patient was hemodynamically unstable and IVC occlusion was not attempted. All 3 patients with inadequate echo images were studied before the avail-
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ability of the lateral gain control feature of the ultrasound system. Preload was successfully acutely lowered by IVC occlusion, resulting in a transient decrease in arterial systolic pressure from 110 ± 22 to 70 ± 17 mmHg or a mean decrease of 40 ± 19 mmHg for this group.

Results of individual E's calculations from single IVC occlusion runs by the semiautomated and automated methods appear in Table 1. The r values shown are the results of the iterative linear regression analysis of end-systolic pressure-area points. Excessive signal noise on the echo area on one patient after bypass prevented use of the automated program, but semiautomated analyses were possible. To test the sensitivity of the results of the semiautomated process of signal alignment to operator technique, E's values were recalculated for each patient by adding and subtracting a 33 ms shift of the arterial pressure signal. Recalculated group mean E's values obtained by subtracting 33 ms from the arterial pressure signal were 23 ± 15 mmHg/cm² and were 18 ± 11 mmHg/cm² for adding 33 ms to the arterial pressure signal. Neither of these group mean values was significantly different from the group mean value of 20 ± 13 mmHg/cm² obtained by the operator selected signal alignment described above. These analyses suggest relative insensitivity of the results of the semiautomated E's calculations to operator technique, and this is illustrated by the typical flat part of the curve of E's versus time shift in arterial pressure (fig. 2E).

Estimates of E's from arterial pressure were closely correlated with E's from LV pressure: r = 0.96, standard error of the estimate = 2 mmHg/cm², y = 1.01 X - 0.7 by the semiautomated method, (fig. 4), and r = 0.94, standard error of the estimate = 3 mmHg/cm², y = 1.0 X - 0.5 by the automated method (fig. 5). Both semiautomated and automated arterial pressure E's covaried over a wide range of values that did not deviate from the line of identity (fig. 6).

Analysis by the Bland-Altman method of the semiautomated and automated estimates of E's from arterial pressure and E's from LV pressure are shown in figure 7. No systematic measurement errors are seen. The calculated limits of agreement of E's by arterial pressure

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<th>Table 1. Estimation of Left Ventricular End-Systolic Elastance from Pressure-Area Relations</th>
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* Pre and immediately post cardiopulmonary bypass studies.
E's = end-systolic elastance, mmHg/cm².

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and the semiautomated and automated methods of signal alignment with $E'_{es}$ by LV pressure were 8 and 9 mmHg/cm², respectively. All but three measures for the group demonstrate $<5$ mmHg/cm² or $<25\%$ difference relative to group mean $E'_{es}$ values. Because the clinical change in $E'_{es}$ after cardiopulmonary bypass was usually greater than $50\%$, this measurement error was less than the degree to which clinical changes in $E'_{es}$ could be measured. In addition, automated arterial pressure $E'_{es}$ were in agreement with semiautomated arterial pressure $E'_{es}$ with $<5$ mmHg/cm² difference relative to mean $E'_{es}$ values in all but one comparison.

In patients with paired data sets before and after cardiopulmonary bypass, similar decreases in $E'_{es}$ values occurred by both arterial and LV pressure methods (figs. 8 and 9). Mean $E'_{es}$ was $32 \pm 15$ mmHg/cm² by the automated arterial pressure method and $32 \pm 12$ mmHg/cm² by LV pressure before cardiopulmonary bypass. Similar significant decreases occurred in $E'_{es}$ immediately after cardiopulmonary bypass with values of $15 \pm 7$ and $15 \pm 6$ mmHg/cm² by arterial pressure and LV pressure methods, respectively ($P<0.05$ for both). These findings are consistent with the previously reported immediate decrease in LV function after cardiopulmonary bypass. Although these findings have not been accepted universally, they are thought to result primarily from hypothermia or ischemia–reperfusion.

**Discussion**

This study demonstrates that measures of LV cavity area by echocardiographic automated border detection
and arterial pressure may be combined to construct online pressure–area loops. This study shows the feasibility of using femoral arterial pressure acquired with fluid-filled catheters and remote pressure sensors to simulate LV ejection pressure in the construction of $E'_m$, as a means to serially assess LV contractility in selected patients. In addition, pressure–area data may be automatically analyzed during acute alterations of load, such as IVC occlusion to determine $E'_m$. Bland-Altman bias analysis demonstrates that no systematic measuring errors were seen between measures of $E'_m$ by high-fidelity LV pressure catheters or fluid-filled arterial pressure catheters. Although the number of patients with paired data sets was relatively small, the degree of agreement between $E'_m$ by both pressure sources was great enough to identify significant decreases in $E'_m$ after cardiopulmonary bypass making the substitution of femoral arterial pressure for LV pressure in the construction of $E'_m$ a potentially practical clinical endpoint.

Although the end-systolic pressure–volume relation is useful to describe LV performance because of its ability to predict the contractile state, clinical applications have been limited by technical difficulties in rapidly acquiring and analyzing volume data throughout the cardiac cycle. Standard imaging techniques have required frame-by-frame manual analysis, and the invasive conductance catheter and sonomicroscopy techniques are not well suited to many clinical settings. Transesophageal echocardiography is increasingly used for monitoring of LV function intraoperatively, and high-quality automated border detection data have been demonstrated with this approach in humans. These data can be combined with arterial pressure data, which also are often routinely acquired in the operating room for hemodynamic monitoring. The use of arterial pressure data obviates the need for additional instrumentation and the potential added risk associated with LV catheter placement. An additional advantage of not requiring LV catheter placement is the likely reduction in LV ectopic arrhythmias, which frequently occur from catheter contact with the ventricular wall during IVC occlusion.

The use of femoral arterial pressure, however, to represent LV systolic pressure is a limitation of this method. The femoral arterial pressure waveform may vary with respect to LV pressure because of the viscoelastic properties of the vessels and the acceleration and deceleration of aortic flow or the impedance characteristics of the arteries. However, the time shift in the arterial pressure signal we performed demonstrated that femoral arterial pressure may be a reasonable substitute for LV ejection pressure in $E'_m$ calculations. Previous investigators have shown that LV systolic pressure can be described by ascending aortic pressure, with the only differences being the short isovolumic contraction and relaxation intervals and the slight relative decrease in lateral wall pressure as blood gains kinetic energy. Although a small progressive rise in systolic pressure has typically been demonstrated from the ascending aorta to the peripheral arteries, this pressure wave amplification is most pronounced in smaller, more distal arteries, such as brachial or radial arteries. Femoral arterial pressure, therefore, appears...
to be an adequate substitute for LV pressure for practical purposes. More importantly, changes in femoral arterial systolic pressure with IVC occlusions are similar to changes in LV pressure, although differences in their absolute values may exist. Another limitation of this study is the exclusion of patients with aortic stenosis or LV outflow tract obstruction because of existing differences in arterial and LV pressure. These patients, however, may be easily identified and prospectively excluded as part of a transesophageal echocardiographic and Doppler examination. Arterial pressure data in this study were acquired with fluid-filled catheters in routine clinical use. The frequency-response characteristics of these pressure recording catheters may be improved by use of high-fidelity catheters. The similar results in $E_s$ values from arterial pressure compared with $E_s$ values from high-fidelity LV pressure, suggests that these pressure data are adequate.

An obvious limitation of this technique is the use of two-dimensional data to represent three-dimensional volume. Although no known reliable method exists to calculate absolute LV volume values from cross-section area measurements, previous investigations have shown a predictable linear relation between changes in area and changes in volume within physiologic ranges. We have demonstrated this relation by using echocardiographic automated border detection in an isolated canine heart preparation, in a canine preparation with an intact circulation, and in humans. The midventricular short axis plane selected in this study can easily be acquired by using the papillary muscles as internal anatomic landmarks. We and others have more recently shown that LV pressure–area relations determined by echocardiographic automated border detection are closely correlated with pressure–volume relations during alterations in load and behave in a physiologically predictable fashion with positive and negative inotropic modulation.

These validation studies have been performed on ventricles with predominantly normal geometry and function. Limited data are available on patients with significant segmental wall motion abnormalities outside of the imaging plane or serial studies on patients with new or changing segmental dysfunction. One would predict that these scenarios may alter the area-volume relation and thus represents potential limitations to the applications of this technique. This limitation may be somewhat overcome by excluding patients who have severe alterations in ventricular geometry outside of the imaging plane, such as aneurysms.

Although LV area and arterial pressure data can only serve as estimates of the LV end-systolic pressure–volume relation, changes in this value occurred in a similar magnitude and direction as the end-systolic pressure–area relation from before to after cardiopulmonary bypass in patients with paired data sets. These data suggest that the LV end-systolic pressure–area relation determined by femoral arterial pressure may be a physiologically significant and less invasive method for serial assessment of ventricular contractility in individual pa-

![Fig. 9. Data from seven patients with paired data sets showing similar decreases in end-systolic elastance ($E_s$) by arterial pressure and left ventricular (LV) pressure from before to immediately after bypass surgery.](image-url)
tients. Although this technique requires further eval-
uation, it has promise to rapidly assess LV performance
in selected patients in the operating room and perhaps
other clinical settings such as the intensive care unit.
These potential applications, although exciting, remain
to be studied.

The authors thank Christie Bennett for preparation of this
manuscript.

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