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Echocardiographic and Hemodynamic Indexes of Left Ventricular Preload in Patients with Normal and Abnormal Ventricular Function

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Background: Transesophageal echocardiography (TEE) is used to diagnose hypovolemia despite the lack of validation studies. The objective was to determine the effects of acute graded hypovolemia on TEE and conventional hemodynamic determinants of left ventricular (LV) preload in anesthetized patients with normal and abnormal LV function.

Methods: Determinants of LV preload derived from TEE and hemodynamic monitoring were measured serially in 35 anesthetized cardiac surgical patients without valvular heart disease. Patients were stratified into two groups: those with normal LV function (group 1, n = 17) and those with LV wall motion abnormalities (group 2, n = 13). Patients in groups 1 and 2 were subjected to graded hypovolemia produced by collecting 6 aliquots of blood, each equal to 2.5% of their estimated blood volume (EBV). A third group of patients (group 3, n = 5), not subjected to graded hypovolemia, were studied to test for time-dependent changes.

Results: Group 2 had a significantly greater baseline (mean ± SD) pulmonary artery occlusion pressure (17 ± 6 *vs.* 11 ± 6 mmHg), LV end-diastolic area (23 ± 5 *vs.* 18 ± 4 cm^2), LV end-diastolic wall stress (23 ± 10 *vs.* 14 ± 6 × 10^3 $dyne \cdot cm^{-2}$), and smaller fractional area change (35 ± 13 *vs.* 59 ± 7%). In groups 1 and 2, the LV end-diastolic area, pulmonary artery occlusion pressure, and LV end-diastolic wall stress decreased linearly in response to blood loss in the range of 0–15% of the EBV. No significant changes in the measured parameters occurred in group 3. A significant decrease in the central venous pressure, pulmonary artery occlusion pressure, and LV end-diastolic area was detected in response to a 2.5% EBV deficit (approximately 1.75 $ml \cdot kg^{-1}$) in groups 1 and 2. The mean change in LV end-diastolic area (0.3 cm^2/1.0% EBV deficit) in response to equivalent EBV deficits was the same in groups 1 and 2. In contrast, the mean change in cardiac output and LV end-diastolic wall stress was less in group 2 despite a greater decrease in pulmonary artery occlusion pressure. Compared to group 1, a greater EBV deficit (7.5% to 12.5% *vs.* 2.5% to 5%) was required in group 2 to cause a significant decrease in the cardiac output, stroke volume, mixed venous oxygen saturation, and LV end-diastolic wall stress.

Conclusions: TEE and hemodynamic determinants of LV preload detected changes in LV function caused by acute blood loss. Acute blood loss caused directional changes in LV end-diastolic area, pulmonary artery occlusion pressure, and LV end-diastolic wall stress even in patients with LV wall motion abnormalities. Changes in LV end-diastolic wall stress, derived from both TEE and hemodynamic measurements corresponded to changes in cardiac output, stroke volume, and mixed venous oxygen saturation that occurred during acute blood loss. (Key words: Anesthesia: cardiac. Heart: ventricular function. Hemorrhage: hemodynamics. Hypotension: hemorrhage; hypovolemia. Monitoring: hemodynamics; hypovolemia; pulmonary artery catheter; transesophageal echocardiography.)

DETECTING and monitoring changes in left ventricular (LV) function caused by acute blood loss are important for the clinical management of anesthetized patients during surgical operations. The ability to diagnose hypovolemia and assess the therapeutic responses to intravascular volume expansion in anesthetized patients is limited because conventional monitors that measure changes in heart rate (HR), intravascular pressures, and cardiac output (CO) provide no information about LV size.[1–4] Transesophageal echocardiography (TEE) can potentially provide information about LV cavity dimensions and wall thickness. The clinical observation that TEE measurements often improved the ability to diagnose hypovolemia prompted the study to determine whether quantitative TEE indexes of LV preload could detect and monitor changes in LV function during graded hypovolemia caused by acute blood loss.

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Clinical and investigational reports suggest that two-dimensional echocardiography is capable of detecting acute changes in LV preload.[5–8] TEE has even been used to diagnose hypovolemia in the clinical setting.[9] Despite these reports, quantitative TEE indexes for measuring changes in LV preload caused by hypovolemia have not been established, nor have TEE determinants been directly compared to hemodynamic determinants to detect acute changes in LV preload. The influence of LV wall motion abnormalities on the accuracy of TEE-derived measurements to quantify changes in LV preload also has not been studied. Problems encountered in developing quantitative approaches for monitoring LV preload include: the lack of a uniform method for defining and producing graded changes in LV preload that is representative of hypovolemia in the clinical setting,[5–8] the difficulties associated with estimating LV volume using cross-sectional imaging,[10,11] the influence of LV asymmetry on TEE-derived measures of LV size, and the uncertainty of which echocardiographic or hemodynamic determinants best detect and quantify acute changes in LV preload.

To compare echocardiographic and hemodynamic methods for quantifying changes in LV preload, acute hypovolemia produced by graded blood withdrawal based on body weight was studied in anesthetized patients during autologous blood collection. The changes produced by acute hypovolemia were compared in patients with normal LV function to those with LV regional wall motion abnormalities to determine whether echocardiographic indexes of LV preload based on single plane short-axis images were interpretable when LV asymmetry was present.

Methods and Materials

After approval by the University of Pennsylvania Committee on Studies Involving Human Beings and written informed consent, 35 patients undergoing elective coronary artery bypass operations were studied prospectively. Patients undergoing emergency operations, patients with a preoperative hemoglobin concentration less than 12.5 $g \cdot dl^{-1}$ or serum creatinine concentration greater than 2.0 $mg \cdot dl^{-1}$, and patients with clinical or laboratory evidence of valvular heart disease, esophageal disease, congestive heart failure, or cardiac rhythm other than sinus rhythm were excluded from the study.

Morphine sulfate 0.05–0.1 $mg \cdot kg^{-1}$, scopolamine hydrobromide 0.3–0.4 mg, and midazolam hydrochloride 0.5–5.0 mg were administered to patients for preoperative sedation. Radial artery and right internal jugular venous oximetric pulmonary artery catheters (Arrow, Reading, PA) were inserted prior to the induction of general anesthesia. General anesthesia was induced and maintained with fentanyl citrate 50–100 $\mu g \cdot kg^{-1}$, a nondepolarizing muscle relaxant (vecuronium bromide 0.1 $mg \cdot kg^{-1}$ or pancuronium bromide 0.1 $mg \cdot kg^{-1}$), and isoflurane (0–0.4 volume%). After intubation of the trachea, a 5 MHz TEE probe (Hewlett Packard, Andover, MA) was inserted into the distal esophagus or stomach to image the short-axis of the left ventricle at the mid-papillary muscle level. Patients were studied while supine with the legs elevated 20 cm above the bed, the standard position for surgical skin preparation. Data for each patient were collected during povidone iodine skin preparation. Intravenous fluid administration was discontinued and no changes in vasoactive drug therapy or isoflurane concentration were made during the study.

Patients entered into the study were stratified into two groups before analysis of the data: those with normal LV function (group 1, n = 17) and those with abnormal LV function (group 2, n = 13). A third group of random patients who met the inclusion criteria (group 3, n = 5) were used as a control group to test whether the echocardiographic or hemodynamic parameters changed over time. Patients in group 3 were not stratified based on their LV function and were not subjected to blood withdrawal. Normal LV function was defined as the absence of regional LV wall motion abnormalities by echocardiography at the time of the study. Abnormal LV function was defined as the presence of LV regional systolic wall motion abnormalities (hypokinesis, akinesis, or dyskinesis) diagnosed by echocardiography at the time of the study (table 1). The echocardiographic interpretations of LV regional wall motion abnormalities were verified by a noninvasive cardiologist who was blinded to the patients' clinical condition.

Autologous Blood Collection

Graded hypovolemia was produced by incremental collection of autologous blood from the 8.5-French internal jugular vein introducer sheath into citrate-phosphate-dextrose-adenine blood collection bags via a sterile closed circuit. The autologous blood was stored

Table 1. Description of Left Ventricular Regional Wall Motion Abnormalities in Patients with Abnormal Left Ventricular Function (Group 2)

Patient Number	Echocardiographic Left Ventricular Regional Wall Motion Abnormality
4	Posterior-inferior, anterior-septal, and lateral hypokinesis
9	Anterior-septal and lateral hypokinesis, posterior-inferior akinesis
14	Anterior-septal and lateral hypokinesis, posterior-inferior akinesis
15	Posterior-inferior akinesis
18	Posterior-inferior hypokinesis, anterior-septal akinesis
20	Posterior-inferior hypokinesis
24	Posterior-inferior, anterior-septal, and lateral hypokinesis
25	Posterior-inferior, anterior-septal, and lateral hypokinesis
26	Posterior-inferior, anterior-septal, and lateral hypokinesis
28	Posterior-inferior, anterior-septal, and lateral hypokinesis
29	Posterior-inferior and septal hypokinesis
30	Posterior-inferior, anterior-septal, and lateral hypokinesis
34	Posterior-inferior and septal hypokinesis

at room temperature and readministered after cardiopulmonary bypass. Six aliquots of blood, each equal to 2.5% of the patient's estimated blood volume (EBV), were measured volumetrically and collected serially immediately after each set of measurements were performed to achieve a final EBV deficit equal to 15% of the EBV. The EBV of each patient was calculated with the following formulas: (1) males, EBV (ml) = 70 × body weight (kg) and (2) females, EBV (ml) = 65 × body weight (kg). Autologous blood collection was discontinued if the systolic blood pressure decreased to less than 85 mmHg or acute myocardial ischemia was detected on the electrocardiogram.

Hemodynamic Measurements

The position of the pulmonary artery catheter was confirmed by characteristic pressure waveforms transduced from the pulmonary artery and right atrial ports of the catheter. The pulmonary artery occlusion pressure (PAOP) was defined as the pressure obtained immediately after the a-wave and before the v-wave that corresponded to electrocardiographic and echocardiographic end-diastole during balloon occlusion.[12] Pressure measurements were performed using Sorenson 47616-10 transducers (Abbott Critical Care Systems, Chicago, IL) zeroed at the patient's midaxillary line and interfaced to a Hewlett Packard Merlin Model 66 monitoring system with a six-channel chart recorder (Hewlett Packard) that also recorded the electrocardiogram and carbon dioxide expirogram. Pressures were averaged over 5–7 cardiac cycles. Cardiac output (CO) and stroke volume (SV) were measured by thermodilution using 10 ml of normal saline at ambient temperature (21–23°C, measured by thermistor) as the indicator. The baseline CO was the average of three measurements. Subsequent COs were obtained from single measurements during end-expiration. The mixed venous oxygen saturation (Sv_{O_2}) was measured continuously by oximetry. Heart rate (HR) was determined from the average of 5–7 R-R intervals. All measurements were made during a brief period of apnea at end-expiration. In each patient, a complete set of echocardiographic and hemodynamic data were recorded immediately before blood collection and immediately after the withdrawal of each aliquot of blood (2.5% EBV deficit).

Two-dimensional Transesophageal Echocardiography

Echocardiographic images were recorded on-line together with the electrocardiogram at a frame rate of 30 Hz on 0.5-inch videotape. Recordings were made simultaneously during procurement of the hemodynamic data. Echocardiographic measurements were made off-line from the videotape recording using the Hewlett Packard Sonos 1000 by experienced echocardiographers (ATC, JSS, SJW) who were blinded to the hemodynamic data. End-diastole was defined as the frame corresponding to the largest LV cross-sectional area immediately after the R-wave peak on the electrocardiogram. End-systole was defined as the frame corresponding to the smallest LV cross-sectional area.

Left ventricular short-axis end-diastolic cross-sectional area (EDA), end-systolic cross-sectional area (ESA), end-diastolic endocardial circumference, and end-systolic endocardial circumference were measured by manual planimetry of the area circumscribed by the leading edge of the left ventricular endocardial border. The anterolateral and posteromedial papillary muscles were excluded in the area and circumference determinations. The leading edge to leading edge technique was used to measure end-diastolic and end-systolic LV anterior-posterior cavity diameter and LV posterior-inferior wall thickness. All echocardiographic dimensions used for analysis were the mean of three measurements performed on separate cardiac cycles. The fractional area change and fractional circumferential shortening were calculated using the formulas:

fractional area change (%)

$= 100 \times (EDA - ESA)/EDA$, and

fractional circumferential shortening (%)

$= 100 \times$ [(end-diastolic circumference) − (end-systolic circumference)]/(end-diastolic circumference).

indexes of LV end-diastolic meridional wall stress and LV end-systolic meridional wall stress were calculated using the following formulas[13]:

LV end-diastolic meridional wall stress

$(\times 10^3$ dyne · cm$^{-2})$

$= (0.334)(PAOP)(AEDD)/[(EDWT)(1 + EDWT/AEDD)]$

where

$AEDD = (2)(EDA/\pi)^{1/2}$ and

EDWT = end-diastolic LV posterior wall thickness.

LV end-systolic meridional wall stress

$(\times 10^3$ dyne · cm$^{-2})$

$= (0.334)(SBP)(AEDS)/[(ESWT)(1 + ESWT/AESD)]$

where

$AESD = (2)(ESA/\pi)^{1/2}$,

ESWT = end systolic LV posterior wall thickness, and

SBP = systolic arterial pressure (mmHg).

Statistical Analysis

All hemodynamic and echocardiographic parameters were analyzed as continuous variables. To determine the relative importance of the variability of repeated intra-observer TEE measurements, the intraclass correlation coefficients were calculated for the EDA and ESA at baseline (EBV deficit = 0%) and at EBV deficits of 12.5%. The intraclass correlation coefficient is defined as (between subject variance)/(between subject variance + within subject variance) and was estimated using one-way analysis of variance (ANOVA) with subject as the single factor.[14] Comparisons between groups were performed using the independent-sample *t*-test. Correlation between measured variables was tested using the Pearson rank correlation coefficient. One-way ANOVA for repeated measures was used to test whether the measured parameters changed in relation to the EBV deficit. Missing values were assigned the mean for that group at the specific time point. Missing values were imputed for the final time point (EBV deficit = 15%) in only 3 patients (2 from group 1 and 1 from group 2) who achieved a final EBV deficit of 12.5%. The minimum detectable blood loss for each measured parameter was defined as the minimum EBV deficit at which a statistically significant ($P < 0.05$) change in the parameter from baseline (EBV deficit = 0%) was detected using ANOVA contrasts for repeated measures with adjustment for multiple comparisons. This definition for the minimum detectable blood loss was used because it was determined based on the magnitude of the measured change in the parameter together with variability inherent in the measurement. Tests for linear contrasts were used to determine if the relationship between the EBV deficit and the measured variables were linear. The mean of the individual-level slopes was compared between groups 1 and 2 using an independent-sample *t*-test to determine whether the rate of change in the measured parameters with respect to the EBV deficit was different in the two groups.

Results

There was no difference in the mean age, body surface area, HR, arterial pressure, and CO between groups, but the mean body weight of group 2 was slightly greater than groups 1 and 3 (table 2). Group 2 had a significantly greater mean PAOP, EDA, ESA, LV end-diastolic wall stress, LV end-systolic wall stress, and lower mean fractional area change and Sv_{O_2} at baseline (table 2). The echocardiographic LV regional wall motion abnormalities present in each patient in group 2 are listed in table 1.

The intraclass correlation coefficients for the EDA and ESA at baseline were 0.982 and 0.976, respectively. The intraclass correlation coefficients for the EDA and ESA at an EBV deficit of 12.5% were 0.971 and 0.984, respectively. The interpretation of the intraclass correlation coefficient is similar to the interpretation of an ordinary correlation coefficient; values of the intraclass correlation coefficient greater than 0.75 are generally considered to represent excellent agreement between repeated measurements.[14]

Table 2. Patient Profiles at Baseline

Parameter	Group 1, Normal LV (n = 17)	Group 2, Abnormal LV (n = 13)	Group 3, Control (n = 5)
Age (yr)	62 ± 9	60 ± 7	61 ± 7
Weight (kg)	80 ± 10	90 ± 13*	84 ± 16
BSA (m^2)	1.95 ± 0.15	2.02 ± 0.15	1.91 ± 0.13
Hb (g/dl)	14.0 ± 1.1	13.6 ± 1.6	14.1 ± 1.3
HR (beats/min)	68 ± 12	69 ± 14	54 ± 8
MAP (mmHg)	83 ± 10	84 ± 10	82 ± 9
CVP (mmHg)	9 ± 3	12 ± 3	12 ± 2
PAOP (mmHg)	11 ± 4	17 ± 6‡	15 ± 3
CO (L/min)	5.0 ± 1.4	4.7 ± 1.2	4.2 ± 0.8
SV (ml)	74 ± 16	69 ± 14	79 ± 21
SvO_2 (%)	88 ± 4	82 ± 5‡	88 ± 1
EDA (cm^2)	17.8 ± 3.8	22.7 ± 5.4†	17.6 ± 2.2
ESA (cm^2)	7.2 ± 1.7	15.2 ± 6.4‡	8.4 ± 2.6
FAC (%)	59 ± 7	35 ± 13‡	53 ± 12
EDWT (cm)	1.08 ± 0.17	1.15 ± 0.28	1.20 ± 0.19
ESWT (cm)	1.51 ± 0.37	1.34 ± 0.40	1.56 ± 0.52
EDWS ($\times 10^3$ dyne/cm^2)	14 ± 7	23 ± 10†	16 ± 5
ESWS ($\times 10^3$ dyne/cm^2)	62 ± 32	114 ± 52†	38 ± 16

Data are the mean ± SD.

No statistical comparisons were performed between groups 1 and 3 and between groups 2 and 3.

LV = left ventricle; BSA = body surface area; Hb = hemoglobin concentration; HR = heart rate; MAP = mean arterial pressure; CVP = central venous pressure; PAOP = pulmonary artery occlusion pressure; CO = cardiac output; SV = stroke volume; SvO_2 = mixed venous oxygen saturation; EDA = end-diastoilc area; ESA = end-systolic area; FAC = fractional area change; EDWT = end-diastolic posterior wall thickness; ESWT = end-systolic posterior wall thickness; EDWS = end-diastolic wall stress; ESWS = end-systolic wall stress.

* $P < 0.05$ (group 2 *vs.* group 1).

† $P < 0.005$ (group 2 *vs.* group 1).

‡ $P < 0.001$ (group 2 *vs.* group 1).

The baseline PAOP correlated significantly with the pulmonary artery systolic and diastolic pressure in groups 1 and 2. The correlation between the PAOP and the EDA was marginally significant ($r = 0.512$, $P = 0.04$) in group 1, but not significant ($r = 0.327$, $P = 0.28$) in group 2. The baseline PAOP correlated with the central venous pressure (CVP) in group 1, but not in group 2. The baseline EDA and PAOP correlated inversely with the fractional area change in group 2. The correlation between the echocardiographic measurements of LV short-axis cavity area, diameter, and circumference were highly significant in groups 1 and 2. Similarly, there was a highly significant correlation between the fractional area change and fractional circumferential shortening (table 3).

No patients developed acute myocardial ischemia during the study. An EBV deficit of 12.5% was achieved in all (100%) patients. An EBV deficit of 15% was achieved (SBP > 85 mmHg) in 15 out of the 17 (88%) patients in group 1 and in 12 out of the 13 (92%) patients in group 2. The average time required to perform the study in an individual patient was 13 min (range 9–19 min).

Effects of Graded Hypovolemia

Acute EBV deficits in the range of 0–15% of the EBV produced significant decreases in the MAP, CVP, PAOP, CO, SV, Sv_{O_2}, EDA, ESA, LV end-diastolic wall stress, and LV end-systolic wall stress in groups 1 and 2 (figs. 1 and 2). Patients who were not subjected to graded blood loss, group 3, exhibited nonsignificant changes in the measured hemodynamic or echocardiographic parameters over the course of the study (figs. 1 and 2). The HR, fractional area change, and fractional circumferential shortening did not change significantly over time or in response to graded hypovolemia in groups 1, 2, and 3. In both groups 1 and 2, the MAP, CVP, PAOP, CO, SV, Sv_{O_2}, EDA, ESA, LV end-diastolic wall stress, and LV end-systolic wall stress changed linearly based on highly significant linear contrasts in the ANOVA models over the range of EBV deficits produced in the study (table 4).

The ability to detect acute volume deficits using each of the measured parameters of LV preload was determined by finding the minimum EBV deficit that produced a statistically significant ($P < 0.05$) change in the parameter from baseline (EBV deficit = 0%). The minimum detectable EBV deficit for each of the determinants of LV preload in groups 1 and 2 are shown in table 5. An EBV deficit of 2.5% was associated with a significant decrease in the CVP, PAOP, and EDA in groups 1 and 2. Compared to group 1, group 2 required greater EBV deficits to produce significant changes in the MAP, CO, SV, Sv_{O_2}, and LV end-diastolic wall stress.

Group 2 exhibited a greater mean change in the PAOP in response to graded blood volume deficits compared to group 1 (table 4). In contrast, the CO and LV end-diastolic wall stress changed less in response to graded blood volume deficits in group 2 compared to group 1. The mean rate of change in the EDA, MAP, CVP, SV, Sv_{O_2}, ESA, and LV end-systolic wall stress in response to graded blood volume deficits was not significantly different between groups 1 and 2 (table 4).

Table 3. Relation between Parameters of Left Ventricular Preload at Baseline

Parameters	Group 1, Normal LV (n = 17)		Group 2, Abnormal LV (n = 13)	
	r[1]	P	r[1]	P
PAOP *vs.* PAS	0.852	<0.0001	0.781	0.002
PAOP *vs.* PAD	0.898	<0.0001	0.944	<0.0001
PAOP *vs.* CVP	0.896	<0.0001	0.520	0.083
MAP *vs.* SBP	0.822	<0.0001	0.971	<0.0001
MAP *vs.* DBP	0.955	<0.0001	0.957	<0.0001
EDA *vs.* EDD	0.887	<0.0001	0.840	0.0003
EDA *vs.* EDC	0.985	<0.0001	0.990	<0.0001
ESA *vs.* ESD	0.822	<0.0001	0.900	<0.0001
ESA *vs.* ESC	0.965	<0.0001	0.995	<0.0001
FAC *vs.* FCS	0.965	<0.0001	0.990	<0.0001
EDA *vs.* ESA	0.746	0.0006	0.961	<0.0001
EDA *vs.* FAC	0.230	0.374	−0.792	0.001
PAOP *vs.* EDA	0.512	0.036	0.327	0.276
PAOP *vs.* FAC	0.378	0.134	−0.720	0.006
SV *vs.* EDA	0.748	0.0006	0.014	0.965
SV *vs.* ESA	0.645	0.005	−0.051	0.868

[1] Pearson rank correlation coefficient.

LV = left ventricle; PAOP = pulmonary artery occlusion pressure; PAS = pulmonary artery systolic pressure; PAD = pulmonary artery diastolic pressure; CVP = central venous pressure; MAP = mean arterial pressure; SBP = systolic arterial pressure; DBP = diastolic arterial pressure; EDA = end-diastolic area; EDD = end-diastolic diameter; EDC = end-diastolic circumference; ESA = end-systolic area; ESD = end-systolic diameter; ESC = end-systolic circumference; FAC = fractional area change; FCS = fractional circumferential shortening; SV = stroke volume.

Discussion

Intraoperative TEE was found to be effective for detecting and monitoring changes in LV function during graded hypovolemia caused by acute blood loss in anesthetized cardiac surgical patients. The threshold for detecting acute blood loss using serial LV short-axis dimensions measured by TEE was comparable to conventional hemodynamic measurements obtained from pulmonary artery catheterization. Directional changes in LV end-diastolic short-axis area in response to acute blood volume deficits in the range of 0–15% were linear, suggesting that TEE-derived parameters can be used quantitatively to monitor for hypovolemia. The presence of LV wall motion abnormalities did not change the threshold for detecting acute blood loss using TEE or the rate of change in EDA in response to graded blood loss. These findings suggested that TEE-derived parameters of LV preload were applicable for detecting and monitoring hypovolemia even in patients with LV wall motion abnormalities. In contrast, the rate of change in the PAOP in response to graded blood loss differed between patients with normal and abnormal LV function. An index of LV end-diastolic meridional wall stress, obtained by combining measurements from TEE and pulmonary artery catheterization, also correlated linearly with the EBV deficit and corresponded to changes in cardiac output, cardiac stroke volume, and mixed venous oxygen saturation during acute blood loss.

Differences in LV diastolic compliance between individual patients limit the ability to use pressure measurements alone to derive information about LV preload. The weak correlations between the PAOP and EDA suggested that LV diastolic compliance differed among the patients that were studied. Previous studies also have demonstrated that LV pressure measurements alone could not be used to estimate LV volumes.[1–4] In a heterogenous patient population, TEE measurements of LV cavity size provided a source of information about LV preload that was independent of pressure measurements.

The choice between which echocardiographic dimension was best for monitoring acute changes in LV function appeared to be inconsequential. Nearly perfect correlations between independent echocardiographic measurements of LV cross-sectional area, di-

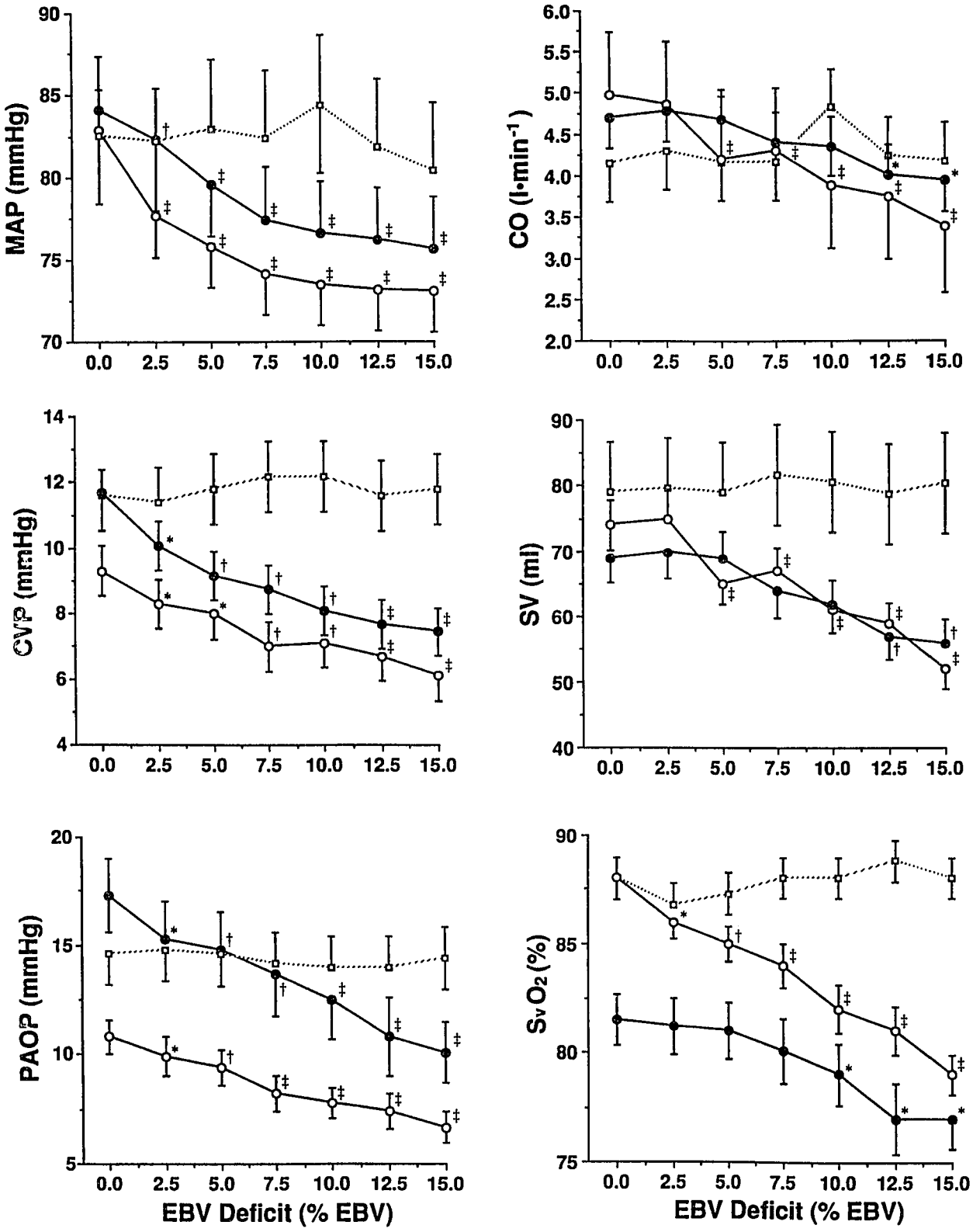

Fig. 1. Hemodynamic indexes of left ventricular (LV) preload at baseline (EBV deficit = 0%) and in response to graded hypovolemia (EBV deficits = 0–15%) in patients with normal LV function (group 1, -○-, n = 17) and patients with LV wall motion abnormalities (group 2, -●-, n = 13). Control patients (group 3, —□—, n = 5) were not subjected to graded blood volume deficits. All values are mean ± SEM. CO = cardiac output; CVP = central venous pressure; EBV = estimated blood volume; MAP = mean arterial pressure; PAOP = pulmonary artery occlusion pressure; SV = stroke volume; Sv_{O_2} = mixed venous oxygen saturation. *$P < 0.05$ *versus* baseline. †$P < 0.005$ *versus* baseline. ‡$P < 0.001$ *versus* baseline. Analysis of variance for repeated measures adjusted for multiple comparisons.

ameter, and endocardial circumference were observed. For this reason only the EDA was used for statistical comparisons. However, the correlation coefficients suggested that statistical comparisons performed using any of the three TEE-derived LV short-axis dimensions would yield similar results.

The absolute determination of LV volumes and meridional wall stress was limited by discrepancies between PAOP measurements and actual LV end-diastolic pressures and by problems inherent in estimating LV cavity volumes using single short-axis images. Despite these limitations, directional changes in LV short-axis dimensions and an index of LV wall stress decreased linearly in response to graded blood volume deficits in the range of 0–15% of the EBV. This finding was consistent with clinical and experimental studies that have demonstrated a linear relation between LV cavity dimensions and volumes over small physiologic ranges.[15,16] Because changes in the TEE- and hemodynamically derived determinants of LV preload were based on actual measurements obtained after removal of known volumes of blood, applying these indexes for detecting acute blood loss did not require any assumptions to be made relating the echocardiographic and hemodynamic determinants to absolute values of LV volume, pressure, or wall stress.

Patients with LV wall motion abnormalities were analyzed as a separate group because LV wall motion abnormalities are known to impair the ability to measure LV volumes using single LV short-axis dimensions.[10,17] Left ventricular wall motion abnormalities diagnosed by TEE at the time of the study were used to stratify patients because LV wall motion abnormalities detected by cardiac catheterization in the preoperative period may have been caused by acute reversible myocardial ischemia and were not always present at the time of operation. Visual interpretation of the echocardiograms were used for the stratification of patients because it is regarded as the present standard.[18] The patients with abnormal LV function constituted a heterogenous group of patients with varying degrees of LV dysfunction (table 1), but as a group, had a different baseline hemodynamic profile compared to group 1 (table 2). The weak correlation between LV dimensions and SV in the group of patients with LV wall motion abnormalities was consistent with the unpredictable relationship between single short-axis LV dimensions and absolute LV volumes when LV asymmetry was present.

Improved intraoperative monitoring of LV preload would be potentially most useful in patients with underlying LV dysfunction. However, previous studies have demonstrated poor correlations between echocardiographic LV short-axis dimensions and angiographic LV end-diastolic volumes.[10,17] Those studies were performed by comparing measurements between different patients and not designed to compare serial measurements in individual patients. The correlation between graded EBV deficits and serial EDA measurements even in patients with abnormal LV function suggested that fixed LV wall motion abnormalities did not impair the ability of TEE to detect and monitor acute blood loss in individual patients.

The effect of acute blood loss on LV performance differed in patients with normal and abnormal LV function. In the group of patients with normal LV function, acute blood loss caused early decreases in PAOP, EDA, and LV end-diastolic wall stress that were associated with early decreases in LV performance as measured by CO, SV, and Sv_{O_2}. In the group of patients with abnormal LV function, acute blood loss caused early decreases in their PAOP and EDA, but a greater EBV deficit was required to produce significant decreases in LV end-diastolic wall stress, CO, SV, and Sv_{O_2}. Furthermore, the mean decrease in CO and LV end-diastolic wall stress in response to equivalent acute blood volume deficits was less in patients with abnormal LV function despite the greater decrease in their PAOP. Whereas the lack of statistical significance for parameters of LV performance at smaller EBV deficits could, in part, be attributed to the small number of patients with abnormal LV function, the statistical results seemed to reflect

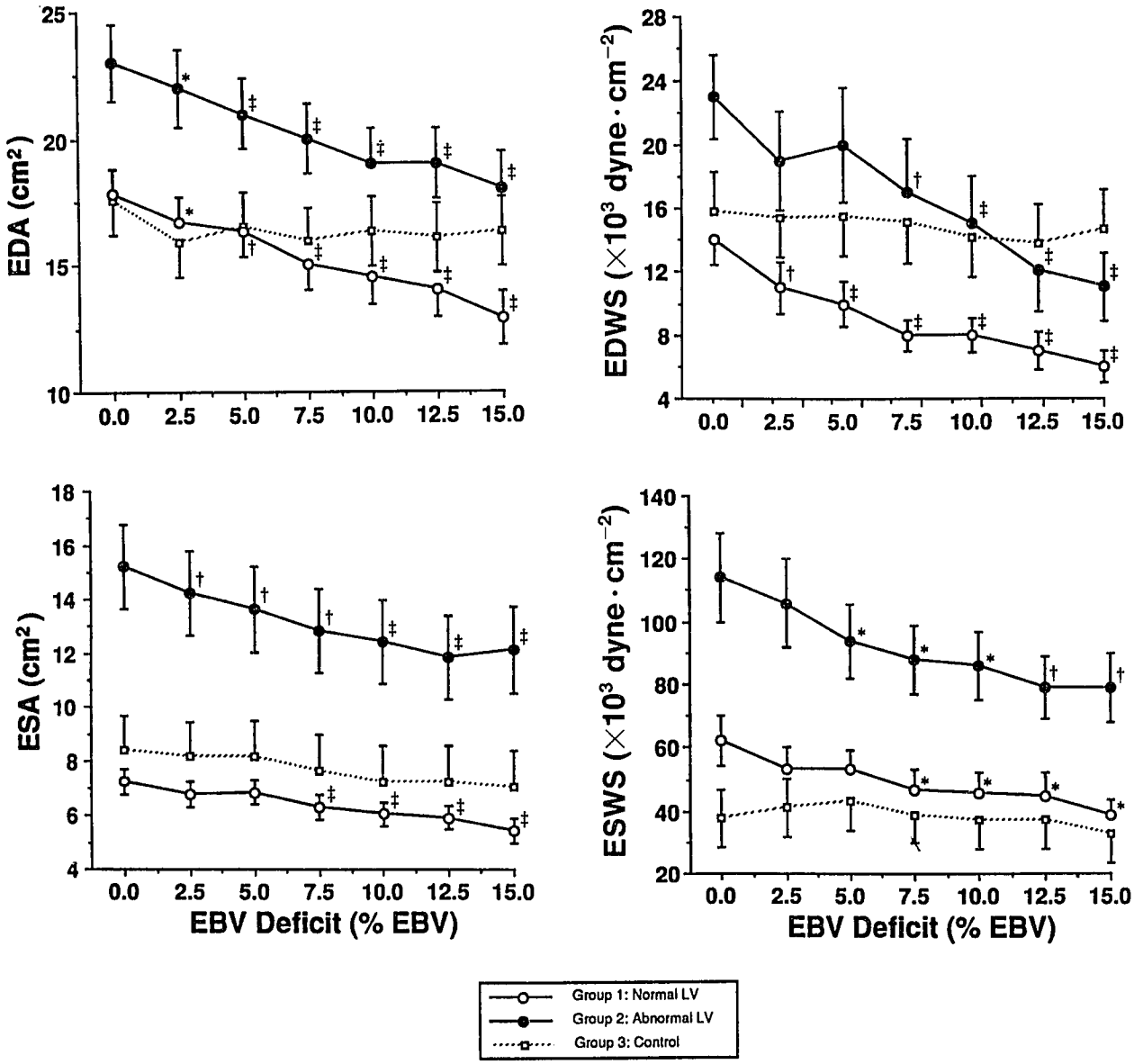

Fig. 2. Echocardiographic indexes of left ventricular (LV) preload at baseline (EBV deficit = 0%) and in response to graded hypovolemia (EBV deficits = 0–15%) in patients with normal LV function (group 1, -○-, n = 17) and patients with LV wall motion abnormalities (group 2, -●-, n = 13). Control patients (group 3, —□—, n = 5) were not subjected to graded blood volume deficits. All values are mean ± SEM. EBV = estimated blood volume; EDA = end-diastolic area; EDWS = end-diastolic meridional wall stress; ESA = end-systolic area; ESWS = end-systolic meridional wall stress. *$P < 0.05$ *versus* baseline. †$P < 0.005$ *versus* baseline. ‡$P < 0.001$ *versus* baseline. Analysis of variance for repeated measures adjusted for multiple comparisons.

real physiologic differences. The group of patients with LV wall motion abnormalities had a greater mean baseline PAOP, EDA, and LV end-diastolic wall stress compared to patients with normal LV function, suggesting that their volume status at baseline may have exceeded their optimal LV preload. In other words, the group of patients with abnormal LV function were operating in the "flat" region of their diastolic ventricular function curve and their LV performance was less responsive to acute changes in blood volume. The concept of an

Table 4. Relation between Parameters of Left Ventricular Preload and Graded Estimated Blood Volume Deficits

Parameter	Group 1, Normal LV (n = 17)		Group 2, Abnormal LV (n = 13)	
	Slope[1]	P^2	Slope[1]	P^2
HR (beats/min)	−0.12 ± 0.33	0.090	0.06 ± 0.36	0.376
MAP (mmHg)	−0.66 ± 0.39	<0.0001	−0.68 ± 0.58	0.001
CVP (mmHg)	−0.19 ± 0.17	0.0004	−0.26 ± 0.13	<0.0001
PAOP (mmHg)	−0.27 ± 0.12*	<0.0001	−0.48 ± 0.27*	<0.0001
CO (l/min)	−0.11 ± 0.06†	<0.0001	−0.06 ± 0.05†	0.001
SV (ml)	−1.41 ± 0.52	<0.0001	−1.06 ± 0.83	0.001
SvO_2 (%)	−0.56 ± 0.23	<0.0001	−0.40 ± 0.38	0.004
EDA (cm^2)	−0.31 ± 0.11	<0.0001	−0.29 ± 0.14	<0.0001
ESA (cm^2)	−0.11 ± 0.05	<0.0001	−0.21 ± 0.19	0.0004
EDWS ($\times 10^3$ dyne/cm^2)	−2.71 ± 1.61*	<0.0001	−1.50 ± 0.71*	<0.0001
ESWS ($\times 10^3$ dyne/cm^2)	−0.91 ± 0.83	0.001	−0.51 ± 0.96	0.003

[1] Mean ± SD of the individual level slopes for parameter *versus* estimated blood volume deficit (%).

[2] *P* value for linearity from analysis of variance for repeated measures.

LV = left ventricle; HR = heart rate; MAP = mean arterial pressure; CVP = central venous pressure; PAOP = pulmonary artery occlusion pressure; CO = cardiac output; SV = stroke volume; SvO_2 = mixed venous oxygen saturation; EDA = end-diastolic area; ESA = end-systolic area; EDWS = end-diastolic wall stress; ESWS = end-systolic wall stress.

* $P < 0.05$ (group 1 *vs.* group 2).

† $P < 0.02$ (group 1 *vs.* group 2).

"optimal" preload in cardiac surgical patients has also been described by Mangano *et al.*, who demonstrated that acute volume loading was less effective for augmenting ventricular output when the PAOP exceeded 7 mmHg or the end-diastolic volume index exceeded 70 $ml \cdot m^{-2}$.[19]

The finding that end-systolic parameters of LV function correlated with the EBV deficit was expected. Al-

Table 5. Minimum Detectable Blood Loss*

Parameter	Group 1, Normal LV (n = 17)			Group 2, Abnormal LV (n = 13)		
	EBV Deficit†	Mean Difference‡	*P*§	EBV Deficit†	Mean Difference‡	*P*§
MAP (mmHg)	2.5	5.2	0.00006	5.0	4.5	0.005
CVP (mmHg)	2.5	1.0	0.014	2.5	1.6	0.01
PAOP (mmHg)	2.5	0.9	0.007	2.5	2.0	0.006
CO (L/min)	5.0	0.8	0.0004	12.5	0.7	0.007
SV (ml)	5.0	8.7	0.0004	12.5	11.6	0.004
SvO_2 (%)	2.5	1.5	0.03	10.0	2.5	0.045
EDA (cm^2)	2.5	1.1	0.007	2.5	1.0	0.024
ESA (cm^2)	7.5	0.9	0.001	2.5	1.0	0.005
EDWS ($\times 10^3$ dyne/cm^2)	2.5	2.8	0.002	7.5	6.1	0.002
ESWS ($\times 10^3$ dyne/cm^2)	7.5	15.0	0.031	5.0	19.8	0.042

* Minimum EBV deficit (%) that caused a significant change in the parameter compared to its baseline value.

† Estimated blood volume deficit that caused a significant change in the parameter compared to its baseline value.

‡ Mean decrease in the parameter from its baseline value.

§ *P* value for the change in parameter (analysis of variance for repeated measured with adjustments for multiple comparisons).

LV = left ventricle; EBV = estimated blood volume; MAP = mean arterial pressure; CVP = central venous pressure; PAOP = pulmonary artery occlusion pressure; CO = cardiac output; SV = stroke volume; SvO_2 = mixed venous oxygen saturation; EDA = end-diastolic area; ESA = end-systolic area; EDWS = end-diastolic wall stress; ESWS = end-systolic wall stress.

though physiologic models have predicted that LV end-systolic volume and wall stress are insensitive to changes in preload,[20] decreases in arterial pressure associated with hypovolemia could decrease LV afterload and thus influence systolic function. Other investigators also have observed that LV end-systolic dimensions decrease in response to maneuvers known to decrease LV preload.[7,8] The decrease in ESA observed in response to hypovolemia may be explained by decreased LV afterload (LV end-systolic wall stress) as a consequence of reduced LV size and arterial pressure that favored LV ejection. Hypovolemia also may have indirectly increased LV contractility by activating the sympathetic nervous system.

Prior studies that have examined echocardiographic techniques to measure changes in LV preload have relied on either the use of hemodynamic measurements to diagnose hypovolemia,[5,6] the administration of nitroglycerin,[7] changes in body posture,[7] or the application of lower body negative pressure[8] to produce acute alterations in LV preload. The threshold at which TEE can detect acute changes in LV preload could not be determined accurately from the techniques employed in those studies, nor could comparisons be made between TEE and conventional hemodynamic monitoring techniques for detecting acute changes in LV preload. The limitations of using phlebotomy to produce graded changes in intravascular volume status included problems inherent in calculating the EBV based on body weight, changes in intravascular volume caused by the translocation of interstitial fluid into the intravascular space, the circulatory influences of autonomic nervous system reflexes that occur in response to acute blood loss, and the assumption that patients were normovolemic at the start of the study.

The minimum detectable blood loss for each of the indexes of LV preload reported in this study (table 5) represents changes detected under conditions designed to isolate the acute effects of blood loss. The minimum detectable blood loss for each of the measured parameters depended on both the magnitude of the measured changes in response to acute blood loss and the variability inherent in each of the measurements. In clinical practice, echocardiographic and hemodynamic parameters of LV preload may be influenced by factors other than blood loss. Changes in anesthetic or vasoactive drug therapy, the rate of intravenous fluid administration, the level of surgical stimulation, patient position, or TEE probe position may potentially modify echocardiographic and hemodynamic indexes of LV preload independent of changes in the patient's intravascular volume status. Differences in patient population, instrumentation, echocardiographic image resolution, and the temporal relation of measurements to the respiratory cycle may affect the thresholds for detecting acute blood loss in any individual situation. The minimum detectable changes in LV EDA and ESA found in this study (approximately 1.0 cm^2) were slightly greater than the changes reported by Reich *et al.* (approximately 0.62 cm^2) in a study of anesthetized pediatric patients subjected to a 5–8% reduction in blood volume.[6] Despite those smaller changes in EDA and ESA, Reich found that TEE had a sensitivity of 80–90% and a specificity of 80% for identifying mild reductions in blood volume.[6] The agreement between repeated echocardiographic measurements in this study and reported mean inter-observer differences of 4.03% and 5.08%, in the measurement of EDA and ESA, respectively,[21] suggests that echocardiographic indexes of LV preload are potentially applicable for monitoring acute blood loss in the clinical setting.

This study demonstrated that TEE could be used to detect and monitor the effects of acute blood loss in anesthetized patients undergoing coronary artery bypass grafting. The LV EDA decreased linearly (0.3 cm^2/1.0% EBV deficit) in response to acute blood volume deficits in the range of 2.5–15% of the EBV even in patients with LV wall motion abnormalities. Both TEE and hemodynamic indexes of LV preload had a threshold for detecting an EBV deficit of 2.5% or approximately 1.75 $ml \cdot kg^{-1}$. An index of LV end-diastolic meridional wall stress, obtained by combining TEE and hemodynamic measurements corresponded to changes in cardiac output, cardiac stroke volume, and mixed venous oxygen saturation caused by hypovolemia.

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References

1. Douglas PS, Edmunds LH, St. John Sutton M, Geer R, Harken AH, Reichek N: Unreliability of hemodynamic indexes of left ventricular size during cardiac surgery. Ann Thorac Surg 44:31–34, 1987

2. Thys DM, Hillel Z, Goldman ME, Mindich BP, Kaplan JA: A comparison of hemodynamic indexes derived by invasive monitoring and two-dimensional echocardiography. ANESTHESIOLOGY 67:630–634, 1987

3. Hansen RM, Viquerat CE, Matthay MA, Wiener-Kronish JP, DeMarco T, Bahtia S, Marks JD, Botvinick EH, Chatterjee K: Poor

correlation between pulmonary arterial wedge pressure and left ventricular end-diastolic volume after coronary artery bypass graft surgery. ANESTHESIOLOGY 64:764–770, 1986

4. Ellis RJ, Mangano DT, VanDyke DC: Relationship of wedge pressure to end-diastolic volume in patients undergoing myocardial revascularization. J Thorac Cardiovasc Surg 78:605–613, 1979

5. Leung JM, Levine E, Mangano DT: Intraoperative preload estimation using transesophageal echocardiography (abstract). ANESTHESIOLOGY 3A:A125, 1992

6. Reich DL, Konstadt SN, Nejat M, Abrams HP, Bucek J: Intraoperative transesophageal echocardiography for the detection of cardiac preload changes induced by transfusion and phlebotomy in pediatric patients. ANESTHESIOLOGY 79:10–15, 1993

7. Redwood DR, Henry WL, Epstein SE: Evaluation of the ability of echocardiography to measure acute alterations in left ventricular volume. Circulation 50:901–904, 1974

8. Nixon JV, Murray RG, Leonard PD, Mithcell JH, Blomqvist CG: Effect of large variations in preload on left ventricular performance characteristics in normal subjects. Circulation 65:698–703, 1982

9. Reichert LA, Visser CA, Koolen JJ, vd Brink RBA, van Wezel HB, Meyne NG, Dunning AJ: Transesophageal echocardiography in hypotensive patients after cardiac operations. J Thorac Cardiovas Surg 194:321–326, 1992

10. Teichholz LE, Kreulen T, Herman MV, Gorlin R: Problems in echocardiographic volume determinations: Echocardiographic-angiographic correlations in the presence or absence of asynergy. Am J Cardiology 37:7–11, 1976

11. Clements FM, Harpole DH, Quill T, Jones RH, McCann RL: Estimation of left ventricular volume and ejection fraction by two-dimensional transesophageal echocardiography: Comparison of short-axis imaging and simultaneous radionuclide angiography. Br J Anaesth 64:331–336, 1990

12. Braunwald E, Brockenbrough EC, Frahm CJ, Ross J: Left atrial and left ventricular pressures in subjects without cardiovascular disease. Circulation 24:267–269, 1961

13. Reichek N, Wilson J, St. John Sutton M, Plappert TA, Goldberg S, Hirshfeld JW: Noninvasive determination of left ventricular end-systolic stress: Validation of the method and initial application. Circulation 65:99–108, 1982

14. Fleiss JL: Statistical Methods for Rates and Proportions. 2nd edition. New York, John Wiley & Sons, 1981, pp 225–227

15. Feigenbaum H, Popp RL, Wolfe SB, Troy BL, Pombo JF, Haine CL, Dodge HT: Ultrasound measurements of the left ventricle. Arch Intern Med 129:461–467, 1972

16. Suga H, Sagwa K: Assessment of absolute volume from diameter of the intact canine left ventricular cavity. J Appl Physiol 36:496–499, 1974

17. Schiller NB, Acquatella H, Ports TA, Drew D, Goerke J, Ringetz H, Silverman NH, Brundage B, Botvinick EH, Boswell R, Carlsson E, Parmley WW: Left ventricular volume from paired biplane two-dimensional echocardiography. Circulation 60:547–555, 1979

18. American College of Cardiology/American Heart Association Task Force Report: ACC/AHA guidelines for the clinical application of echocardiography. J Am Coll Cardiol 16:1505–1528, 1990

19. Mangano DT, VanDyke DC, Ellis RJ: The effect of increasing preload on ventricular output and ejection in man: Limitations of the Frank-Starling mechanism. Circulation 62:535–541, 1980

20. Sagawa K: The ventricular pressure-volume diagram revisited. Circ Res 43:677–687, 1978

21. Cahalan MK, Ionescu P, Melton HE, Adler S, Kee LL, Schiller NB: Automated real-time analysis of intraoperative transesophageal echocardiograms. ANESTHESIOLOGY 78:477–485, 1993