Assessment of a new ventricular contractile index obtained with transoesophageal echocardiography before and after cardiopulmonary bypass in cardiac surgical patients

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Summary
We have compared a new contractile index “left ventricular end-systolic wall stress–heart rate-corrected velocity of circumferential fibre shortening (v_{cfc})” with conventional contractile indices in 13 patients undergoing coronary artery bypass grafting. We generated the slopes of the “end-systolic wall stress–v_{cfc}”, “end-systolic wall stress–area” and “peak arterial pressure–area” relationships by altering arterial pressure before and after cardiopulmonary bypass (CPB). In all patients, significant correlations were obtained for end-systolic wall stress–area and peak arterial pressure–area relationships before and after CPB. In all patients, significant inverse linear correlations were obtained for the end-systolic wall stress–v_{cfc} relationship before CPB; however, inverse linear correlation was absent in eight patients after CPB. It may be that the increased afterload had less influence on left ventricular systolic function after CPB as a possible mechanism of loss of the inverse linear correlation in the end-systolic wall stress–v_{cfc} relationship. (Br. J. Anaesth. 1997; 79: 759–765).

Key words

The left ventricular pressure–volume relation developed by Suga and Sagawa has been used widely as a contractile index that is relatively insensitive to loading conditions,\textsuperscript{1,3} and clinical use of this method has been reported for assessment of ventricular function in cardiac surgical patients.\textsuperscript{4–6} The pressure–volume relationship requires invasive techniques to construct left ventricular pressure–volume loops and acute alteration of loading conditions by vena cava occlusion to obtain the end-systolic pressure–volume relationship. A relatively less invasive technique is available by examining the slope of the left ventricular end-systolic wall stress–dimension relationship by echocardiography. This relationship is based on the concept of the pressure–volume relationship, and is constructed by manipulating arterial pressure with vasoactive agents.\textsuperscript{7,8} The end-systolic wall stress–dimension relationship correlates linearly within the physiological range and is sensitive to the inotropic state.\textsuperscript{7,8}

Recently, a new echocardiographic assessment of contractility became available by examining the relationship between left ventricular end-systolic wall stress and heart rate-corrected velocity of circumferential fibre shortening (v_{cfc}).\textsuperscript{9} The slope of the end-systolic wall stress–v_{cfc} relationship was found to be inversely linear over a wide physiological range, relatively independent of preload and sensitive to changes in contractility.\textsuperscript{9,10} In the analysis of this relationship, an upward shift of the slope indicates an increased inotropic state, and a downward shift of the slope indicates a depressed contractile state.\textsuperscript{9,10} Although the left ventricular end-systolic wall stress–v_{cfc} relationship appears to be useful for assessment of ventricular contractility,\textsuperscript{9–11} there is no information on this contractile index in cardiac surgical patients. Accordingly, we compared the left ventricular end-systolic wall stress–v_{cfc} relationship with the conventional end-systolic wall stress–area and peak arterial pressure–area relationships before and after cardiopulmonary bypass (CPB) in patients undergoing coronary artery bypass grafting.

Patients and methods
After obtaining approval from the Department of Medical Ethics Committee and informed consent, we studied 13 patients undergoing elective primary coronary artery bypass grafting. Patients with an ejection fraction of less than 45%, previous history of myocardial infarction, regional wall motion abnormalities (diagnosed as severe hypokinesis, akinesis, dyskinesis or aneurysmal), valvular disease or congenital heart disease diagnosed by previous cardiac angiographic or echocardiographic examination were excluded. Also excluded were patients with atrial fibrillation or any oesophageal or gastric...
pathology diagnosed as a contraindication to transoesophageal echocardiography.

Anaesthesia was induced with fentanyl 10 μg kg⁻¹, diazepam 0.15–0.2 mg kg⁻¹ and vecuronium 0.15 mg kg⁻¹, and maintained with high-dose fentanyl (up to a total dose of 60 μg kg⁻¹) supplemented with benzodiazepines (diazepam or midazolam, or both) and 1–1.5% sevoflurane. Vecuronium was given to facilitate mechanical ventilation with 60% oxygen in air before CPB, or 100% oxygen after CPB. All patients were monitored with leads II and V5 of the electrocardiogram, and with radial and pulmonary artery catheters. After tracheal intubation, a gastroscope tipped with a 5-MHz multi-plane transoesophageal ultrasonic transducer (Hewlett Packard, Andover, MA, USA) was inserted into the oesophagus and positioned behind the left ventricle to obtain a short axis view at the level of the midpapillary muscles. The transducer was connected to an ultrasonograph (Sonos 1500, Hewlett Packard, Andover, MA, USA). While arterial pressure and heart rate were being recorded, two-dimensional echocardiograms were recorded on S-VHS videotapes by the attending anaesthetists (M. K., T. I. and T. O.) with at least 3 yr experience with intraoperative transoesophageal echocardiography.

After pericardiotomy, before aortic and right atrium cannulations, haemodynamic and echocardiographic data were obtained. Cardiac output was measured during apnoea at the end of expiration, in duplicate, by the thermodilution technique with 10 ml of iced saline at 0°C using a pulmonary artery catheter (Opticath with Oximetrix 3 50130, Abbott Lab., North Chicago, IL, USA). Any cardiac output measurement significantly different (greater than ±10%) from its pair was excluded, and a repeat measurement was obtained. Peak systolic arterial pressure was adjusted to 90–110 mm Hg, as the baseline value, by continuous infusion of phenylephrine or prostaglandin E₁ (PGE₁), or both. To generate the slopes of the contractile indices, peak systolic arterial pressure, measured by a radial artery catheter, was increased to 30% of baseline by continuous infusion of phenylephrine 0.5–2.0 mg kg⁻¹ min⁻¹, and then decreased to baseline by continuous infusion of PGE₁ 0.05–0.2 mg kg⁻¹ min⁻¹. Arterial pressure was recorded continuously on a multichannel recorder (78576A, Hewlett Packard, Andover, MA, USA) at a paper speed of 25 mm s⁻¹, and two-dimensional echocardiograms of the left ventricular short axis view with an electrocardiogram lead II were recorded on videotape while haemodynamic data were recorded simultaneously. We synchronized the video and the strip chart recorder to match the pressure values with the echocardiograms. All haemodynamic measurements were made during the expiratory pause phase of the ventilator cycle. Haemodynamic indices were calculated from pressure and cardiac output data with the use of standard formulae.

CPB was conducted using a Cobe CML membrane oxygenator with a non-pulsatile flow of 2.2 litre min⁻¹ m⁻². The system was primed with 1500 ml of balanced salt solution, 150 ml of 15% mannitol and hetastarch 500 ml. In all patients, hypothermia (25–28°C) and aortic cross-clamping with cold hyperkalaemic cardioplegia were used. After the primary surgical operation, patients were warmed to a bladder temperature of 36.5–37°C. The heart was defibrillated after cardiac reperfusion if sinus rhythm did not resume spontaneously. As a pressure gradient between central aortic pressure and radial artery pressure was often observed (sometimes more than 15–20 mm Hg) before weaning from CPB, femoral arterial pressure was monitored routinely to estimate central aortic pressure rather than radial artery pressure. A significant aortic-to-radial artery pressure gradient has been reported during and after CPB in a previous study and femoral arterial pressure reproduces central aortic pressure more reliably than radial arterial pressure after CPB. Patients were weaned from CPB using dopamine 5–8 μg kg⁻¹ min⁻¹ or nitroglycerin 0.5–1.0 μg kg⁻¹ min⁻¹, or both, started before weaning to achieve a systolic arterial pressure >90 mm Hg and pulmonary capillary wedge pressure (PCWP) ≤18 mm Hg. Left ventricular preload was assessed by PCWP and left ventricular cavity area. After completion of CPB and protamine administration, measurements were repeated after aortic and right atrium decannulations but before sternal closure if patients were haemodynamically stable without new regional wall motion abnormalities. During manipulation of arterial pressure, the rates of i.v. volume infusion and continuous infusion of dopamine 5–8 μg kg⁻¹ min⁻¹ were kept constant, and bolus administration of i.v. anaesthetic drug was not performed. Sevoflurane was not used in any patient after weaning from CPB.

**TRANSEOSEPHAGEAL ECHOCARDIOGRAPHIC ANALYSIS**

Echocardiographic analysis was performed by offline tracings with the Hewlett Packard Sonos 1500 ultrasonograph system. Images were analysed by the authors (M. K., T. I. and T. O.) with previous published experience in the analysis of ventricular function. We identified at least 10 data points at end-expiration for each regression line to generate the slopes of contractile indices in each patient. We traced the left ventricular short-axis endocardium at end-diastole to obtain end-diastolic area (EDA) and end-diastolic circumference (EDC). We traced endocardium and epicardium at end-systole to obtain end-systolic area (ESA) with papillary muscles included, end-systolic circumference of endocardium (ESC), and total area (At) enclosed by the left ventricular epicardium and right side of the septum. Leading-edge to leading-edge methods were used to trace the endocardium and epicardium. Left ventricular ejection time (LVET) was determined using the number of frames (one every 33 ms) from end-diastole to end-systole. We identified ventricular end-diastole by the peak of the R wave and end-systole by the minimal left ventricular dimension. Fractional area change (FAC) and systolic circumferential fibre shortening (CFS) were determined as follows:
We determined Esfc and end-systolic wall stress (index of afterload) as follows:

\[
\text{Esfc} = \text{CFS} \times (\text{RR})^{1/2}/(\text{LVET} \times 100)
\]

where RR = interval between cardiac cycles, measured as the number of frames from the peak of the R wave to the next peak of the R wave, and EDC and ESC are measured in centimetres.

End-systolic wall stress =

\[
(1.35 \times \text{Psyst} \times \text{ESA})/(\text{At} - \text{ESA})
\]

where end-systolic wall stress is measured in g cm\(^{-2}\), Psyst = peak systolic arterial pressure (mm Hg), At and ESA are measured in cm\(^2\) and 1.35 is a factor to convert mm Hg to g cm\(^{-2}\). Each parameter of area in this equation was obtained with two-dimensional echocardiography. For practical convenience with this equation was obtained with two-dimensional echocardiography, this original equation has been modified to one with endocardial diameter and M-mode echocardiogram, indicating that end-systolic wall stress with peak systolic arterial pressure correlated well with invasively measured wall stress in a variety of clinical conditions.

**STATISTICAL ANALYSIS**

One- and two-way analysis of variance followed by the Bonferroni multiple comparison test were used to compare changes in haemodynamic and echocardiographic data before and after CPB, and changes in those data during manipulation of arterial pressure.

In each patient, we plotted end-systolic wall stress on the X-axis against Esfc on the Y-axis, and plotted end-systolic area on the X-axis against end-systolic wall stress or peak arterial pressure on the Y-axis. At least 10 data points were plotted to generate each regression line in each patient. The linear regression equation was calculated by simple linear regression analysis with the least squares method. Statistical analysis was conducted using statistical software (Statview 4.0, Super ANOVA, Abacus Concept, Inc., Berkeley, CA, USA). P < 0.05 was considered statistically significant, and all data are expressed as mean (SD).

**Results**

The heart was in sinus rhythm in all patients, and no new regional wall motion abnormalities, ST-segment changes or arrhythmias were observed. In these patients, a short axis view was obtained satisfactorily and echocardiographic analysis was performed. Three patients received two bypass grafts (one internal mammary artery and one saphenous vein), and 10 patients received three bypass grafts (one internal mammary artery and two saphenous veins). Patient data are given in table 1. Haemodynamic and echocardiographic variables before and after CPB are summarized in table 2. Heart rate and cardiac index after CPB were significantly higher than those before CPB, and systemic vascular resistance index after CPB was significantly lower than that before CPB. There was no significant difference in any other haemodynamic or echocardiographic variables between before and after CPB.

**Table 1** Patient characteristics (mean ± sd or range) or number) (n = 13)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Pre-CBP (n = 13)</th>
<th>Post-CBP (n = 13)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>62 (52–74)</td>
<td></td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>10/3</td>
<td></td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>55.6 (12.0)</td>
<td></td>
</tr>
<tr>
<td>Height (cm)</td>
<td>158.2 (9.7)</td>
<td></td>
</tr>
<tr>
<td>Body surface area (m(^2))</td>
<td>1.6 (0.2)</td>
<td></td>
</tr>
<tr>
<td>Cross-clamp time (min)</td>
<td>75 (15)</td>
<td></td>
</tr>
<tr>
<td>Cardiopulmonary bypass time (min)</td>
<td>140 (26)</td>
<td></td>
</tr>
</tbody>
</table>

Heart rate (beat min\(^{-1}\))

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Pre-CBP (n = 13)</th>
<th>Post-CBP (n = 13)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate (beat min(^{-1}))</td>
<td>65 (12)</td>
<td>97 (7)*</td>
</tr>
<tr>
<td>AP (mm Hg)</td>
<td>107 (14)/52 (5)</td>
<td>98 (8)/47 (5)</td>
</tr>
<tr>
<td>PAP (mm Hg)</td>
<td>24 (5)/12 (3)</td>
<td>29 (6)/15 (5)</td>
</tr>
<tr>
<td>PCWP (mm Hg)</td>
<td>11 (4)</td>
<td>13 (4)</td>
</tr>
<tr>
<td>CVP (mm Hg)</td>
<td>9 (4)</td>
<td>8 (4)</td>
</tr>
<tr>
<td>CI (litre min(^{-1}) m(^{-2}))</td>
<td>2.4 (0.5)</td>
<td>3.2 (0.5)*</td>
</tr>
<tr>
<td>SVI (m l beat(^{-1}) m(^{-2}))</td>
<td>38 (11)</td>
<td>33 (7)</td>
</tr>
<tr>
<td>SVRI (dyn cm(^{-1}) m(^{-2}))</td>
<td>2372 (569)</td>
<td>1481 (323)*</td>
</tr>
<tr>
<td>PVRI (dyn cm(^{-5}) m(^{-2}))</td>
<td>208 (64)</td>
<td>196 (86)</td>
</tr>
<tr>
<td>FAC (%)</td>
<td>52.5 (10.0)</td>
<td>54.9 (14.0)</td>
</tr>
<tr>
<td>Esfc (circ s(^{-1}))</td>
<td>0.712 (0.249)</td>
<td>0.769 (0.323)</td>
</tr>
<tr>
<td>ESWS (g cm(^{-2}))</td>
<td>46.9 (21.6)</td>
<td>36.4 (11.2)</td>
</tr>
<tr>
<td>EDA (cm(^2))</td>
<td>12.8 (3.6)</td>
<td>12.1 (2.3)</td>
</tr>
<tr>
<td>ESA (cm(^{2}))</td>
<td>6.2 (2.5)</td>
<td>5.7 (1.9)</td>
</tr>
</tbody>
</table>
with administration of PGE₁ before CPB, and increased significantly from 98 (8)/47 (5) (65 (4)) to 130 (11)/62 (5) (83 (5)) mm Hg after administration of phenylephrine, and then decreased to 101 (12)/50 (4) (67 (4)) mm Hg after administration of PGE₁ after CPB. During alteration of afterload, there was no significant change in EDA (index of left ventricular preload) before CPB (12.4 (3.3) cm² at baseline, 13.2 (3.8) cm² after administration of phenylephrine and 12.6 (3.7) cm² after PGE₁), or after CPB (11.9 (2.3) cm² at baseline, 13.1 (2.8) cm² after phenylephrine and 12.2 (2.5) cm² after PGE₁), and there was no significant difference in EDA in each state between before and after CPB. Manipulation of arterial pressure was accomplished within 15–20 min in all patients.

For the echocardiographic data, 292 points were obtained for regression analysis; 146 data points before CPB and 146 data points after CPB. Regression equations, correlation coefficients, and lines between end-systolic wall stress and \( v_{cfc} \), between end-systolic wall stress and area, and between peak pressure and area are illustrated in figure 1. In all patients, the relationships between end-systolic wall stress and area, and between peak pressure and area are significant and linear before CPB, but the correlation was lost in eight patients after CPB (Post-CPB). Between measurements taken before and after CPB, there was no significant difference in ventricular contractility measured by the slopes of the end-systolic wall stress–area and peak pressure–area relationships.

During alteration in arterial pressure, left ventricular end-systolic wall stress increased significantly after administration of phenylephrine and then returned to baseline after PGE₁ administration before and after CPB (fig. 2a). Between before and after

**Figure 1** For the left ventricular (LV) end-systolic wall stress–heart rate-corrected velocity of circumferential fibre shortening (\( v_{cfc} \)) relationship (A), significant inversely linear correlations were obtained in all patients before cardiopulmonary bypass (Pre-CPB), but the correlations were no longer inversely linear in eight patients (broken lines) after CPB (Post-CPB). For the LV end-systolic wall stress–area (B) and peak arterial pressure–area (C) relationships, significant linear correlations were obtained in all patients before and after CPB. ns = not significant.
Discussion

The results of this study indicate that, in patients undergoing coronary artery bypass grafting, assessment of ventricular contractility is possible by examining the slope of the end-systolic wall stress–ecfc relationship and the end-systolic wall stress–area and peak arterial pressure–area relationships before CPB. After CPB, assessment of the contractile state is possible by measurements of the slope of the end-systolic wall stress–area and peak arterial pressure–area relationships, but not the slope of the end-systolic wall stress–ecfc relationship because of loss of the inverse linear correlation. It is possible that increased afterload had less influence on left ventricular systolic function after CPB as a possible mechanism for the loss of the inverse linear correlation between end-systolic wall stress and ecfc.

The end-systolic wall stress–ecfc relationship reported by Colan, Borow and Neumann9 is based on the force–velocity relationship found in isolated human papillary muscle.21 Although several studies have examined a contractile state by using the end-systolic wall stress–ecfc relationship,9–11 there is no report on this contractile index in cardiac surgical patients. In this study, the significant influence of afterload on ecfc and FAC observed before CPB was not detected after CPB, and the significant inverse linear correlations between end-systolic wall stress and ecfc observed in all patients before CPB were lost after CPB. Although both ecfc and FAC are known to be dependent on left ventricular afterload,8 the afterload dependence of ecfc and FAC observed in individual subjects before CPB was not necessarily reproducible after CPB in this study. A possible explanation could be that there was inotropic support with catecholamines during the period after CPB. Beta-receptor stimulation induced by administration of dopamine after CPB might have preserved left ventricular systolic function when afterload increased, although pure alpha adrenergic stimulation by phenylephrine to patients with coronary artery disease has been shown to cause transient impairment of left ventricular function before CPB. Bolus administration of phenylephrine to patients with coronary artery disease has been shown to cause transient increase in ventricular function that has not been observed in response to bolus administration of noradrenaline (alpha- and beta-receptor agonist).22 The other possible explanation could be that there was afterload dependence on the force–velocity relationship found in isolated human papillary muscle. 21 Although several studies on the force–velocity relationship found in isolated human papillary muscle.21 Although several studies on the force–velocity relationship found in isolated human papillary muscle.21 Although several studies on the force–velocity relationship found in isolated human papillary muscle.21 Although several studies

Figure 2. Changes in left ventricular (LV) end-systolic wall stress (A), heart rate-corrected velocity of circumferential fibre shortening (ecfc) (B) and fractional area change (FAC) (C) at baseline, after administration of phenylephrine (Phenyl.) and after administration of prostaglandin E1 (PGE1) before and after cardiopulmonary bypass (CPB). P<0.05 compared with: *baseline; †after CPB.

CPB, there was no significant difference in arterial pressure or end-systolic wall stress at baseline, after administration of phenylephrine or after administration of PGE1, ecfc and FAC decreased significantly when end-systolic wall stress increased significantly before CPB, but there were no significant changes in ecfc or FAC after CPB (fig. 2a, 2c). Between patients with an inverse linear correlation (n=5) and those without an inverse linear correlation (n=8) in the end-systolic wall stress–ecfc relationship, there was no significant difference in aortic cross-clamp time (76 (15) vs 75 (15) min), CPB time (135 (35) vs 143 (21) min), dopamine requirements (7.2 (1.0) vs 7.5 (1.0) μg kg⁻¹ min⁻¹), left ventricular EDA (11.9 (2.0) vs 12.3 (1.9) cm²) or ecfc (0.748 (0.236) vs 0.726 (0.230) circ s⁻¹), respectively.
ventricular cavity area and femoral arterial pressure monitoring. Their studies indicated that on-line pressure–area relationships may be clinically useful for estimating ventricular contractility in cardiac surgical patients. The slope of the left ventricular end-systolic wall stress–dimension relationship is also sensitive to the inotropic state. The end-systolic wall stress–dimension relationship can be determined by manipulating arterial pressure with vasoactive agents, and is correlated linearly within the physiological range. O’Kelly and colleagues reported that the slope of the end-systolic wall stress–dimension relationship obtained before surgical incision was useful for measuring ventricular contractility in patients undergoing coronary artery bypass grafting. To our knowledge, our study is the first to examine if the end-systolic wall stress–dimension relationship is useful for assessment of a contractile state after weaning from CPB. In contrast with the end-systolic wall stress–eccentric relationship, our study indicated that the end-systolic wall stress–area and peak arterial pressure–area relationships were useful for assessment of contractile state both before and after CPB. The curvilinearity in a pressure–volume relation has been reported to produce negative values for the extrapolated area–axis intercepts derived from linear regression analysis. The negative area–axis intercept in the peak arterial pressure–area and end-systolic wall stress–area relationships observed in this study might be attributable to such curvilinearity. Wall stress may be a better index of afterload than left ventricular pressure when left ventricular wall thickness is chronically altered, as in ventricular hypertrophy.

We used PGE1 to decrease arterial pressure. In a previous animal study, we showed that PGE1 decreased preload and afterload during 10%, 20% and 30% decreases in mean arterial pressure, but had no inotropic action on myocardial contractility assessed by a load-independent contractile index. PGE1 did not induce significant change in right ventricular contractile state assessed by preload recruitable stroke work as a load-insensitive index in patients after pulmonary resection. Changes in EDA by two-dimensional echocardiography are considered to reflect changes in end-diastolic volume, reflecting a change in LV preload. The absence of significant change in EDA during alteration in afterload indicated that left ventricular preload was affected minimally by afterload manipulations caused by phenylephrine or PGE1. The absence of significant difference in EDA before and after CPB indicated that left ventricular preload conditions were comparable between those states.

An automated border detection system using integrated backscatter imaging (Acoustic quantification, Hewlett Packard, Andover, MA, USA) is useful for real-time measurements of left ventricular cavity area and circumference by identifying ventricular endocardial–blood boundaries. As determination of wall stress required a tracing of epicardium that was not currently available by automated border detection, time-consuming off-line analysis was necessary in this study.

In summary, determining the slope of the end-systolic wall stress–area and the peak pressure–area relationships permits assessment of ventricular contractility, whereas determining the slope of the end-systolic wall stress–eccentric relationship permits assessment of the contractile state before, but not after, CPB, because of the loss of inverse linear correlation.

**References**


Assessment of ventricular contractile indices


