Interatrial Septum Motion but Not Doppler Assessment Predicts Elevated Pulmonary Capillary Wedge Pressure in Patients Undergoing Cardiac Surgery

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ABSTRACT

Background: Left atrial pressure and its surrogate, pulmonary capillary wedge pressure (PCWP), are important for determining diastolic function. The role of transthoracic echocardiography (TTE) in assessing diastolic function is well established in awake subjects. The objective was to assess the accuracy of predicting PCWP by TTE and transesophageal echocardiography (TEE) during coronary artery surgery.

Methods: In 27 adult patients undergoing on-pump coronary artery surgery, simultaneous echocardiographic and hemodynamic measurements were obtained immediately before anesthesia (TTE), after anesthesia and mechanical ventilation (TTE and TEE), during conduit harvest (TEE), and after separation from cardiopulmonary bypass (TEE).

Results: Twenty patients had an ejection fraction (EF) of 0.5 or greater. With the exception of E/e′ and S/D ratios, echocardiographic values changed over the echocardiographic studies. In patients with low EF, E velocity, deceleration time, pulmonary vein D, S/D, and E/e′ ratios correlated well with PCWP before anesthesia. After induction of anesthesia using TTE or TEE, correlations were poor. In normal EF patients, correlations were poor for both TEE and TTE at all five stages. The sensitivity and specificity of echocardiographic values were not high enough to predict raised PCWP except for a fixed curve pattern of interatrial septum (area under the curve 0.89 for PCWP ≥17, and 0.98 for ≥18 mmHg) and S/D less than 1 (area under the curve 0.74 for PCWP ≥17, and 0.78 for ≥18 mmHg).

Conclusion: Doppler assessment of PCWP was neither sensitive nor specific enough to be clinically useful in anesthetized patients with mechanical ventilation. The fixed curve pattern of the interatrial septum was the best predictor of raised PCWP.

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LEFT ventricular diastolic function assessment is a strong independent risk factor for poor outcome in the general population.[1] Similarly, elevated left ventricular end-diastolic pressure is an independent predictor of mortality in patients undergoing cardiac surgery.[2–4]

Current guidelines recommend assessment of left ventricular diastolic function with transthoracic echocardiography (TTE) in awake, spontaneously breathing patients utilizing two-dimensional, spectral and tissue Doppler and color M-mode techniques.[5,6] There are few data, however, investigating the reliability of these measurements for diastolic assessment under general anesthesia or with the use of transesophageal echocardiography (TEE).

Recent reviews[7,8] addressing intraoperative and perioperative diastolic assessments identify limited evidence for the assessment of left ventricular diastolic function using TEE. In a retrospective study in patients undergoing coronary artery bypass surgery, Swaminathan *et al.*[9] found in a large cohort of cardiac surgery patients that few could be classified using the American Society of Echocardiography (ASE) TTE grading guidelines by using intraoperative TEE, but most were able to be classified using preoperative TTE by measurement of

What We Already Know about This Topic

- Left ventricular diastolic dysfunction is a strong independent risk factor for poor outcome in the general population. Left atrial pressure and its surrogate, pulmonary capillary wedge pressure (PCWP), are important for determining diastolic function.
- This study compared transthoracic echocardiography and transesophageal echocardiography and identified the effect of anesthesia on the accuracy of estimation of PCWP.

What This Article Tells Us That Is New

- Doppler assessment of PCWP was neither sensitive nor specific enough to be clinically useful in anesthetized and mechanically ventilated patients requiring cardiac surgery. The fixed curve pattern of the interatrial septum was the best predictor of raised PCWP only when the PCWP was 17 mmHg or greater.

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peak early transmitral inflow (E) to peak early lateral mitral annulus tissue velocity (e′) ratio. Mahmood *et al.*[10] suggested a simplified approach to the assessment of diastolic function in cardiac surgery patients with intraoperative TEE, based on guidelines recommended by the ASE[6] using tissue Doppler measurement of the peak lateral mitral annulus velocity.

The current standard method of left ventricular diastolic function assessment in mechanical ventilated patients is measurement of pulmonary capillary wedge pressure (PCWP). This requires pulmonary arterial catheterization, which has significant limitations in accuracy and rare but potentially lethal complications. If echocardiography accurately predicts left atrial pressure (LAP) in these patients, then risks of pulmonary artery catheterization can be avoided.

Estimation of LAP is a core component of differentiating mild *versus* clinically important diastolic dysfunction, with ASE grade II and III requiring evidence of raised LAP. There are two factors that are likely to influence the estimation of LAP with echocardiography: the hemodynamic effects of anesthesia and positive pressure ventilation, and the modality and different Doppler alignment of TTE compared with TEE. For a measurement technique to be clinically useful in the perioperative setting, it must be sufficiently sensitive and specific, be reproducible over a range of hemodynamic conditions, be suitable for good and poor left ventricular function, and show equivalence between TTE and TEE.

Our aim was to compare the modality of TTE and TEE and to identify the effect of anesthesia on the accuracy of estimation of PCWP. The null hypothesis is that there is no difference in the correlation between PCWP measurements and estimates by TTE or TEE and no difference between echocardiographic estimates in awake and anesthetized states.

Material and Methods

Ethics Approval and Consent

The study was approved by the Melbourne Health Human Research and Ethics Committee, The Royal Melbourne Hospital, Melbourne, Victoria, Australia, and all patients provided written informed consent.

Patient Selection

Adult male and female patients aged 18 yr or older and undergoing on-bypass elective coronary artery surgery were recruited at The Royal Melbourne Hospital sequentially by convenience sampling between July and December 2011. Exclusion criteria included off-bypass cardiac surgery, greater than mild cardiac valvular insufficiency or stenosis (any valve), acute coronary syndrome requiring emergent surgery, atrial fibrillation, and contraindication to TEE.

Patient Preparation

Before induction of anesthesia, an intraarterial cannula (radial or femoral artery) and right internal jugular vein intermittent thermodilution pulmonary artery catheter (834HF75; Baxter Healthcare Corporation, Irvine, CA) were inserted under local anesthesia as per our routine institutional practice. After anesthesia induction and institution of mechanical ventilation, a Philips X7 multiplane TEE transducer (Philips Healthcare, Bothell, WA) was inserted. The zero reference point for PCWP was the anterior aspect of the left atrium, measured from the parasternal short-axis view using TTE in the supine position and marked on the lateral chest wall skin. Other routine intraoperative monitoring included 5-lead electrocardiography, pulse oximetry, capnography, bispectral index encephalography, nasopharyngeal temperature, and TEE, consistent with standard care at our institution.

Anesthesia was conducted according to anesthesiologist preference which included either inhalational volatile anesthesia (sevoflurane or desflurane) or total intravenous anesthesia (propofol or fentanyl/midazolam) or both. Analgesia included either intravenous fentanyl (5 to 10 μ/kg) or, in a few patients, high thoracic epidural ropivacaine (0.2%). Neuromuscular blockade was maintained with either intravenous pancuronium or rocuronium. The cardiopulmonary bypass circuit was primed with 2 l of crystalloid solution and maintained at a temperature of 33° to 35°C. Cardiopulmonary bypass was performed with median sternotomy and standard aorto-caval cannulation. The ascending aorta was cross-clamped and cardiac arrest induced by administration of tepid blood cardioplegia (20° to 25°C) with both antegrade and retrograde delivery. Further doses of maintenance cardioplegia were given following completion of each graft anastomosis. Rewarming commenced at the start of the last distal anastomosis, with the heat exchanger not exceeding 37°C. The hemoglobin was maintained at greater than 70 g/l.

Echocardiography Assessment

Due to the interference generated when using simultaneous TTE and TEE, measurements were performed in sequence using one machine only (Philips IE 33 with C5-1 Sector Array TTE probe and X7-2t Live 3D TEE probe; Philips Healthcare). Each patient underwent five echocardiographic studies by an experienced echocardiographer in the following order:

1. TTE study conducted before induction of anesthesia (pre-An TTE)
2. TTE study conducted after induction of anesthesia and institution of mechanical ventilation (post-An TTE)
3. TEE study conducted immediately after completion of the postinduction TTE (post-An TEE)
4. TEE study conducted during harvest of the left internal mammary artery (graft harvest TEE)
5. TEE study conducted after separation from cardiopulmonary bypass (postcardiopulmonary bypass TEE)

The initial TTE and TEE studies included two-dimensional and color flow Doppler imaging to assess left ventricular size and systolic function, valve morphology and function, and wall motion so as to categorize left ventricular function and exclude more than mild valve pathology. Spectral Doppler and tissue Doppler echocardiographic parameters were measured according to ASE guidelines.[6] These parameters included early (E) and late (A) transmitral peak velocities, early mitral inflow deceleration time (DT), septal and lateral wall tissue Doppler velocities of mitral annulus for TTE (e′ and a′), and lateral wall tissue Doppler velocity for TEE and systolic and diastolic pulmonary vein peak velocities (S and D). In addition, the shape and movement of the interatrial septum were recorded for all studies from the apical four-chamber or subcostal views (TTE) and from the mid esophageal aortic valve short-axis view (TEE). A pattern of "fixed curve" of the interatrial septum, where the shape of the septum is bowed from left to right throughout the cardiac cycle and was categorized as a high LAP state, was differentiated from "mid-systolic reversal," where the septum reverses direction to bow toward the left atrium during systole which was categorized as a normal LAP state.[11] Examples are shown (online echocardiographic videos, Supplemental Digital Content 1, http://links.lww.com/ALN/B67, and Supplemental Digital Content 2, http://links.lww.com/ALN/B68). The following Doppler ratios were calculated: E/e′ (lateral wall), E/e′ (septal wall—TTE only), E/A, and S/D. Digital echocardiographic measurements were measured off-line by two independent echocardiographers using Synapse Cardiovascular software (Fujifilm, Akasaka, Minato, Tokyo, Japan), who were blinded to hemodynamic data. Reported values are the average of three consecutive beats per observer.

Hemodynamic Measurements

Immediately before each echocardiographic study, a set of hemodynamic measurements were recorded using a pulmonary artery catheter. PCWP (mmHg) was measured during end expiration or apnea. Cardiac output was measured using the thermodilution technique, averaging three measurements that were concordant within 10%, and indexed to body surface area. Heart rate, central venous pressure (mmHg), mean systemic arterial pressure (mmHg), and diastolic, systolic, and mean pulmonary artery pressures (mmHg) were recorded. The systemic vascular resistance index was calculated according to the formula systemic vascular resistance index = 80× ((mean systemic arterial pressure – central venous pressure)/cardiac index) dynes s^{-1} cm^{-5} m^{-2}.

Statistical Analysis

The sample size calculation was performed using the concept of Lin in estimating sample size for agreement analyses including the Bland–Altman technique. Using nQuery Advisor 7.0 (Statistical Solutions Ltd., Farmer's Cross, Cork, Ireland), and using previous data from our research group, α of 0.05, and user-defined acceptable concordance of 0.9 between methods, a sample size of 27 was required. We considered that an acceptable "limits of agreement" using the Bland–Altman method was ±2.5 mmHg. This is different to the methods used in this article. The original intention was to assess agreement in a subsequent cohort of patients using derived formulae from this study. As there are multiple types of analysis (correlation, sensitivity and specificity, and agreement analysis), the ethics committee favored the sample size estimation based on the Bland–Altman method, as it is primarily an estimate based on precision. However, after conducting this component of the study, we found that the correlation, sensitivity, and specificity analyses were not sufficient to proceed to agreement analysis in a subsequent cohort of patients.

All statistical analysis was performed in SPSS version 20 (IBM, Greenwood, SC). All graphical displays were produced in GraphPad Prism (GraphPad Software, La Jolla, CA). Statistical significance was defined as a *P* value of less than 0.05; all tests are two tailed. Continuous data are presented as mean ± SD and (range). Pearson correlations were used to explore the relationship between echocardiography measurements and PCWP.

As there were repeated measures for each patient, to analyze the relationship between echocardiography measurements and PCWP over time, a linear mixed model using the restricted maximum likelihood method with a random effect for patient was implemented for each parameter. This enables identification of changes in the relationship between each parameter and PCWP for the five echocardiographic studies.[12] The fixed effects were time of echocardiography study and PCWP. The interaction between time of echocardiography study and PCWP was also considered to determine if this relationship between the measured parameters and PCWP changed across the five studies. As well as overall tests of the effect of PCWP, time of study, and their interaction, pairwise comparisons of measured echocardiographic parameters were conducted to identify differences in means between pre-An TTE and post-An TTE studies to assess the effect of anesthesia and between post-An TTE and post-An TEE studies to assess the effect of echocardiography modality.

Pairwise comparisons were corrected for multiple testing with the Ryan–Holm–Bonferroni procedure within families of endpoints (P'). The families for Doppler measurements were mitral inflow Doppler, tissue Doppler, and pulmonary vein Doppler measurements, and for hemodynamic measurements were a family of pressures and a family of heart rate, cardiac output, and systemic vascular resistance index. Scatterplots were produced relating each parameter and PCWP for each study including a line of best fit.

To assess the role of the echocardiography outcomes as diagnostic tests, contingency tables were created at various PCWP cutoff values between 14 and 18 mmHg. The sensitivity, specificity, and area under the receiver operator characteristic curve were calculated for each echocardiography parameter.

Inter- and intraobserver variability was assessed for the key primary Doppler measurements by measuring the mean difference and limits of agreement (±2 SDs of the difference). We considered the agreement between observers to be acceptable if the limits of agreement were less than 30% of the mean value of the variable being measured.

Results

Twenty-seven patients were included, 24 males and 3 females, with a mean age of 63 ± 10.5 (44 to 85). Seven patients had an ejection fraction (EF) below 50%.

Visual assessment of QQ plots of all parameters indicated that the assumption of normality was satisfied, aside from some evidence of skewness for E/e′ septal. The mean ± SD and pairwise comparison of all spectral Doppler parameters for the echocardiographic studies are presented in table 1.

After induction of anesthesia, and using TTE, the E, A, a′ (septal), and S peak velocities were reduced. Compared with postinduction TTE, the A and a′ (lateral) peak velocities measured with TEE were significantly reduced, and E/A increased.

When comparing changes across all studies, significant differences were found for E, A, E/A, DT, E/e′ (lateral), a′ (lateral), and pulmonary S and D measurements. There were no significant differences across all studies for e′ and S/D ratio.

Hemodynamic parameters for each study are shown in table 2. The PCWP and mean pulmonary artery pressures did not change significantly over all studies, whereas the other measurements did. After induction of anesthesia, the central venous pressure and diastolic and systolic pulmonary artery pressures significantly increased, whereas the mean systemic arterial pressure and cardiac index decreased. The PCWP, systemic vascular resistance index, and heart rate did not change.

The Pearson correlation coefficients for the relationship between the echocardiography measurements and PCWP are shown in the appendix and stratified for normal *versus* reduced EF according to the ASE guidelines for chamber quantification.[13] The strongest correlations were observed in the pre-An TTE study in patients with reduced EF for E ($r = 0.89$, $P = 0.006$), DT ($r = -0.80$, $P = 0.030$), E/e′ lateral ($r = 0.83$, $P = 0.020$), E/e′ septal ($r = 0.96$, $P = 0.001$), D ($r = 0.89$, $P = 0.008$), and S/D ($r = -0.91$, $P = 0.004$). The only other significant correlation with r greater than 0.8 was in the reduced EF group in the graft harvest study for E ($r = 0.91$, $P = 0.011$).The data and line of best fit determined using simple linear regression analysis for mitral E wave velocity, early mitral inflow DT, ratios of E/A, lateral and septal wall E/e′, and S/D are shown in figure 1.

Based on the mixed model and considering the fixed factor of time of study, there was a significant difference in E between the graft harvest and pre-An TTE studies ($P = 0.03$), and in E/A between the postcardiopulmonary bypass TEE and the pre-An TTE studies ($P = 0.001$). All other echocardiography parameters were consistent over the five studies. Considering the interaction of time of study and PCWP on the relationship between Doppler parameters,

Table 1. Comparison of Diastolic Doppler Measurements of Transthoracic and Transesophageal Echocardiography for Each Study Time

	Time of Echocardiography Study							
	Before	After Anesthesia and Mechanical Ventilation				During Surgery	After Surgery	
Echocardiographic Variable	Pre-An TTE	Post-An TTE	*P′* Pre-An TTE *vs.* Post-An TTE	Post-An TEE	*P′* Post-An TTE *vs.* Post-An TEE	Graft Harvest TEE	Post-CPB TEE	*P* Overall Effect of Time
E (cm/s)	73.0 ± 26.3	61.8 ± 17.2	0.004*	59.8 ± 20.3	0.99	58.9 ± 20.9	67.0 ± 18.5	<0.001*
A (cm/s)	69.4 ± 22.5	54.2 ± 20.2	0.005*	42.5 ± 19.9	0.005*	44.9 ± 18.9	37.6 ± 15.81	<0.001*
E/A ratio	1.2 ± 0.3	1.3 ± 0.6	0.279	1.7 ± 1.3	0.004*	1.4 ± 0.57	1.9 ± 0.9	<0.001*
A duration (ms)	163.7 ± 24.5	156.7 ± 28.1	0.376	155.6 ± 22.6	0.948	166.4 ± 23.1	151.1 ± 23.2	0.426
DT (ms)	200.2 ± 47.1	227 ± 44	0.072	207.3 ± 48.7	0.42	211.8 ± 58.7	179.6 ± 39.5	0.004*
e′ lateral (cm/s)	9.2 ± 2.5	8.5 ± 2.3	0.620	8.6 ± 2.2	0.513	8.7 ± 2.2	8.8 ± 2.5	0.724
e′ septal (cm/s)	6.8 ± 1.7	6.6 ± 1.7	0.403					
E/ e′ lateral	8.4 ± 3.9	8.1 ± 3.4	0.798	7.8 ± 3.9	0.746	7.2 ± 3.3	8.4 ± 3.8	0.038*
E/ e′ septal	11.3 ± 5.2	10.1 ± 4.4	0.275					
a′ lateral (cm/s)	8.5 ± 2.2	8.1 ± 2.5	0.616	6.6 ± 1.91	0.009*	7.5 ± 2	5.3 ± 2.1	<0.001*
a′ septal (cm/s)	7.8 ± 1.9	6.8 ± 2.1	0.024*					
PV S (cm/s)	41.7 ± 13.6	33.3 ± 6.3	0.048*	33.1 ± 11.5	0.644	33.5 ± 14.3	41.2 ± 16.7	0.023*
PV D (cm/s)	37.2 ± 14.7	32.2 ± 8	0.116	31.7 ± 15.5	0.99	32.0 ± 15.4	43.1 ± 16.3	0.001*
PV S/D ratio	1.2 ± 0.3	1.1 ± 0.3	0.268	1.2 ± 0.4	0.597	1.2 ± 0.5	1.0 ± 0.3	0.113

Data are presented as mean ± SD.

P overall effect of time is a comparison across all time periods. The *P* values given for the pairwise comparisons are based on a linear mixed model with a Ryan–Holm–Bonferroni correction. *$P < 0.05$ or $P' < 0.05$.

A = late mitral inflow peak velocity; a′ = atrial peak myocardial annular tissue velocity; D = diastolic pulmonary vein velocity; DT = deceleration time; E = early mitral inflow peak velocity; e′ = early peak mitral annular tissue velocity; graft harvest TEE = the measurement performed during harvest of coronary grafts; post-An TEE = the first TEE measurement performed after induction of anesthesia; post-An TTE = the TTE study performed after induction of anesthesia; post-CPB TEE = performed after separation from cardiopulmonary bypass; pre-An TTE = the preanesthetic measurement; PV = pulmonary vein; S = systolic pulmonary vein velocity; TEE = transesophageal echocardiography; TTE = transthoracic.

Table 2. Pulmonary Artery Catheter Hemodynamic Measurements for Each Measurement Period

	Time of Echocardiography Study							
	Awake	After Anesthesia and Mechanical Ventilation				During Surgery	After Surgery	
Hemodynamic Parameters	Pre-An TTE	Post-An TTE	*P*′ Pre-An TTE *vs.* Post-An TTE	Post-An TEE	*P*′ Post-An TTE *vs.* Post-An TEE	Graft Harvest TEE	Post-CPB TEE	*P* Overall Effect of Time
Central venous pressure (mmHg)	5.8 ± 3.2	8.3 ± 2.5	<0.005*	8.5 ± 2.9	0.737	7.5 ± 3.7	8.7 ± 2.8	<0.001
Systemic mean arterial pressure (mmHg)	102.9 ± 20.9	83.3 ± 13.3	<0.006*	80.1 ± 14.1	0.714	77.8 ± 12	72.6 ± 9.4	<0.001
Hear rate (beats/min)	65 ± 10	63 ± 11	0.448	60 ± 13	0.714	62 ± 10	79 ± 7	<0.001
Pulmonary artery systolic pressure (mmHg)	29.4 ± 12.3	32.5 ± 8.3	0.042	30.8 ± 7.2	0.197	30.9 ± 7.7	28.1 ± 6	0.010
Pulmonary artery diastolic pressure (mmHg)	10.1 ± 6.4	12.5 ± 5.1	0.022	13.7 ± 4.1	0.995	13.4 ± 4.3	12.9 ± 3.9	0.001
Mean pulmonary artery pressure (mmHg)	18.3 ± 8.5	20.9 ± 5.6	0.108	19.6 ± 4.9	0.834	19.7 ± 5.8	19.5 ± 5.1	0.286
Cardiac index (l min^{-1} m^{-2})	3.0 ± 0.7	2.3 ± 0.7	0.003*	2.1 ± 0.6	0.108	2.2 ± 0.5	2.6 ± 0.5	<0.001
SVRI (dynes s^{-1} cm^{-5} m^{-2})	2,733 ± 833	2,810 ± 847	0.631	2,832 ± 841	0.539	2,753 ± 916	2,023 ± 398	<0.001
PCWP (mmHg)	12.9 ± 7.1	11.8 ± 5.3	0.315	13.1 ± 4.1	0.98	12.7 ± 5.3	12.2 ± 3.7	0.751

Data are presented as mean ± SD.

The *P* values given for the pairwise comparisons are based on a linear mixed model with a Ryan–Holm–Bonferroni correction. *$P < 0.05$ or $P' < 0.05$.

Graft harvest TEE = the measurement performed during harvest of coronary grafts; PCWP = pulmonary artery occlusion pressure; post-An TTE = the TTE study performed after induction of anesthesia; postanesthesia TEE = the first TEE measurement performed after induction of anesthesia; post-CPB TEE = performed after separation from cardiopulmonary bypass; pre-An TTE = the preanesthetic measurement; SVRI = systemic vascular resistance indexed to body surface area; TEE = transoesophageal echocardiography; TTE = transthoracic.

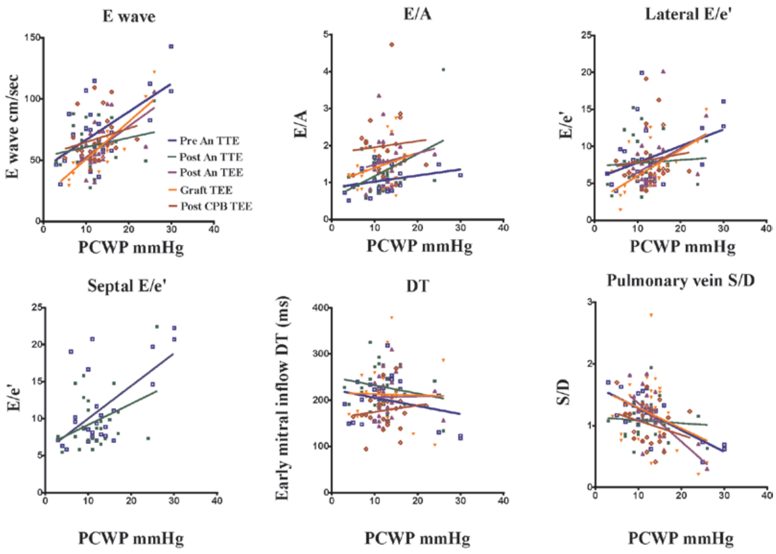

Fig. 1. Scatterplots indicating the relationship between pulmonary capillary wedge pressure (PCWP) and echocardiography variables across the times of study with individual lines of best fit. According to the linear mixed model results, the significant effects identified were (1) the effect of time of study on change in overall E wave between pre-An transthoracic echocardiography (TTE) and graft transesophageal echocardiography (TEE) ($P = 0.03$) and in E/A between pre-An and cardiopulmonary bypass (CPB) TEE ($P = 0.001$) and (2) the effect of interaction of time and PCWP on E wave between pre-An and post-An TTE ($P = 0.005$). A = late mitral inflow peak velocity; D = diastolic pulmonary vein velocity; DT = deceleration time; E = early mitral inflow peak velocity; e′ = early peak mitral annular tissue velocity; Graft TEE = the measurement performed during harvest of coronary grafts; post-An TEE = the first TEE measurement performed after induction of anesthesia; post-An TTE = the TTE study performed after induction of anesthesia; post-CPB TEE = performed after separation from cardiopulmonary bypass; pre-An TTE = the preanesthetic measurement; S = systolic pulmonary vein velocity.

there was a significant difference in the E wave velocity and PCWP relationship between pre- and postanesthesia TTE studies ($P = 0.005$) with a large overall range in linear regression slope ranging from −15.12 to 6.29. The overall difference in S/D for the fixed factor of time was not significant ($P = 0.052$), but there was a slight significant difference between pre- and postinduction TTE studies ($P = 0.032$). There were no significant differences between studies or in the relationship with PCWP for septal E/e′, lateral E/e′, or DT; these parameters were fairly constant across studies.

The sensitivity, specificity, and area under the curve (AUC) of the receiver operating characteristic curve for each echocardiography variable for the prediction of PCWP at thresholds of 14, 15, 16, 17, and 18 mmHg are shown in table 3. The E, septal e′ less than 8 cm/s, and lateral e′ less than 10 cm/s demonstrated high sensitivity but poor specificity and modest AUC values at all PCWP threshold values. The E/A, lateral E/e′, septal E/e′ (TTE only), and DT less than 160 ms showed good specificity, but poor sensitivity and modest AUC values. Of these measurements, the septal E/e′ had reasonable sensitivity for PCWP 18 mmHg or greater. The E/A, DT greater than 200 ms, and DT 160 to 200 ms showed poor sensitivity and specificity at all PCWP. The S/D less than 1 showed reasonable sensitivity and specificity for higher PCWP values. Of all the measurements, the best sensitivity, specificity, and AUC were for the fixed curve pattern of the interatrial septum, which improved as the PCWP cutoff increased, with AUC greater than 0.8 for PCWP 17 mmHg or greater and 0.98 for PCWP 18 mmHg or greater. The distribution of fixed curve and mid-systolic reversal patterns by PCWP is shown in figure 2. The fixed curve pattern occurring at PCWP less than 15 mmHg was seen during the graft harvest and postcardiopulmonary bypass studies.

The intraobserver variation for both observers and the interobserver variability showed acceptable agreement. The limits of agreement were less than 30% of the mean value for all comparisons, other than for pulmonary vein D wave, where the agreements were 30.54% for observer 1 and 30.68% for observer 2.

Discussion

The main finding of this study is that the correlation between Doppler parameters and PCWP is poor after induction of anesthesia, whether performed with TTE or TEE. Strong correlation was shown for some Doppler parameters in awake patients with a reduced EF using TTE, but not for patients with a normal EF. The correlations were lost after induction of anesthesia. There were no major changes in echocardiographic values postanesthesia with either TTE or TEE, indicating that the two modalities are largely equivalent. The ability of Doppler parameters to predict elevated PCWP was poor, with only S/D less than 1 demonstrating both reasonable sensitivity and specificity. A fixed curve pattern of the interatrial septum showed the best sensitivity and specificity of all measurements for higher PCWP values.

The ASE guidelines on the assessment of diastolic function[6] highlight the importance of estimating LAP, or the consequence of raised LAP, such as a dilated left atrium. These guidelines have been adopted in routine intraoperative practice despite inadequate validation of the accuracy of Doppler measurements to assess diastolic function and estimate PCWP in anesthetized patients. In this study, Doppler parameter correlations with PCWP were best for awake patients with reduced EF. Across all echocardiographic studies, there were few significant correlations. This is no doubt due in part to the small sample size for those with EF less than 50%. The highest correlation we found in the awake state was for septal E/e′, and this is consistent with previous data on estimation of LAP with Doppler in various cardiac conditions with reduced EF.[6,14–18] More recent studies validated this good correlation for a variety of TTE-derived Doppler parameters and PCWP in acute and advanced systolic heart failure, confirming TTE as a noninvasive tool for estimating PCWP.[19,20] We found that good correlation was lost after commencement of anesthesia and mechanical ventilation. There were no changes in septal and lateral mitral annular tissue Doppler parameters over any study, but significant change in mean E velocity and slope for E wave velocity during anesthesia was found when compared with preanesthesia. During the postcardiopulmonary bypass study higher mitral E wave velocity and pulmonary D wave were found. Although our data cannot determine the cause, this finding has been reported previously in anesthetized patients using TEE.[21]

We identified poor correlation in patients with EF greater than 0.5 for early mitral inflow or E/A ratio and PCWP. This is consistent with similar findings in patients with ischemic heart disease.[22] The lack of correlation during anesthesia is consistent with recently published data by Kumar *et al.*,[23] who demonstrated poor correlation between E/e′ and PCWP before and after cardiopulmonary bypass during cardiac surgery. The Doppler parameters in their study only included E, e′, and E/ e′ratio with no pulmonary vein Doppler measurements. No prior TTE studies were conducted to allow comparison before and after anesthesia or of modality. In an earlier study by Kuecherer *et al.*,[24] examining the relationship between TEE-derived mitral inflow and pulmonary vein Doppler parameters and PCWP in cardiac surgery patients, good correlations were found for pulmonary vein systolic fraction but not mitral inflow. We did not measure the pulmonary vein systolic fraction, but there were reasonable correlations between S/D and PCWP with no overall change in S/D ratio across all studies in patients with less than 0.5 EF. However, no statistical association was found due to the inadequate number of patients in this subgroup. We have previously demonstrated that using TEE Doppler measurements to estimate PCWP is not sufficiently accurate to estimate PCWP, nor is the use of TTE-derived Doppler measurements on previously published TTE-derived formulas.[25]

Table 3. Sensitivity, Specificity, and Areas under Curve of Receiver Operating Characteristics (95% CI) to Assess the Ability of Echocardiography Results to Predict PCWP Levels

	PCWP ≥14			PCWP ≥15			PCWP ≥16			PCWP ≥17			PCWP ≥18		
Criteria	Sen (%)	Sp (%)	AUC ROC (95% CI)	Sen (%)	Sp (%)	AUC ROC (95% CI)	Sen (%)	Sp (%)	AUC ROC (95% CI)	Sen (%)	Sp (%)	AUC ROC (95% CI)	Sen (%)	Sp (%)	AUC ROC (95% CI)
E wave >50 (cm/s)	93	35	0.64 (0.42–0.76)	94	32	0.59 (0.39–0.75)	96	31	0.58 (0.37–0.75)	94	29	0.56 (0.33–0.76)	92	28	0.53 (0.28–0.76)
Mitral inflow E/A ≥2	21	90	0.56 (0.35–0.72)	18	88	0.54 (90.34–0.74)	17	87	0.55 (0.33–0.76)	12	86	0.56 (0.32–0.79)	17	87	0.58 (0.313–0.85)
E/A ≥1 to <2	49	49	0.54 (0.39–0.7)	64	48	0.53 (0.36–0.75)	58	51	0.56 (0.40–0.79)	62	51	0.55 (0.33–0.76)	50	50	0.48 (0.227–0.72)
E/A <1 and E> 50	14	87	0.48 (0.27–0.6)	9	85	0.46 (0.24–0.60)	4	85	0.41 (0.19–0.54)	0	85	0.37 (0.19–0.56)	0	85	0.37 (0.176–0.58)
Septal e′ <8 cm/s)	100	8	0.54 (0.36–0.71)	100	7	0.54 (0.35–0.72)	100	7	0.53 (0.34–0.73)	100	7	0.53 (0.32–0.74)	100	6	0.53 (0.299–0.77)
Lateral e′ <10 (cm/s)	72	29	0.46 (0.27–0.63)	81	31	0.52 (0.31–0.70)	75	29	0.51 (0.29–0.69)	81	30	0.51 (0.30–0.74)	75	29	0.47 (0.224–0.72)
Lateral E/e′ ≥12	21	85	0.55 (0.37–0.73)	27	86	0.58 (0.39–0.80)	33	87	0.6 (0.41–0.83)	31	85	0.6 (0.37–0.83)	42	85	0.67 (0.411–0.92)
Septal E/e′ ≥15	27	87	0.57 (0.31–0.67)	12	95	0.6 (0.30–0.70)	36	88	0.62 (0.30–0.71)	50	89	0.7 (0.29–0.75)	67	90	0.78 (0.286–0.80)
DT >200 (ms)	51	51	0.53 (0.30–0.66)	45	49	0.47 (0.22–0.62)	37	48	0.45 (0.19–0.59)	31	48	0.35 (0.11–0.53)	33	49	0.33 (0.07–0.54)
DT 160–200 (ms)	26	70	0.42 (0.27–0.62)	24	60	0.44 (0.27–0.65)	25	71	0.44 (0.27–0.66)	21	71	0.46 (0.27–0.70)	8	70	0.34 (0.19–0.63)
DT < 160 (ms)	21	84	0.57 (0.39–0.77)	27	85	0.6 (0.42–0.83)	37	86	0.62 (0.43–0.85)	44	86	0.7 (0.47–0.92)	58	86	0.73 (0.55–1)
PV S/D <1	53	77	0.69 (0.52–0.87)	64	77	0.7 (0.53–0.90)	71	75	0.74 (0.57–0.94)	75	73	0.74 (0.69–1)	83	72	0.78 (0.62–0.90)
Fixed curve IAS	33	98	0.65 (0.53–0.89)	39	98	0.68 (0.58–0.96)	54	98	0.76 (0.66–0.99)	81	98	0.89 (0.78–1)	100	97	0.98 (0.96–1)

Fixed curve of the interatrial septum is where the septum remains bowed from left to right throughout the cardiac cycle.

A = late mitral inflow velocity; AUC = area under the curve; DT = deceleration time; E = early mitral inflow velocity; e′ = early mitral annular tissue velocity; IAS = interatrial septum; PCWP = pulmonary capillary wedge pressure mmHg; PV = pulmonary vein; ROC = receiver operating characteristic; Sen = sensitivity; Sp = specificity; S/D = systolic to diastolic pulmonary vein ratio.

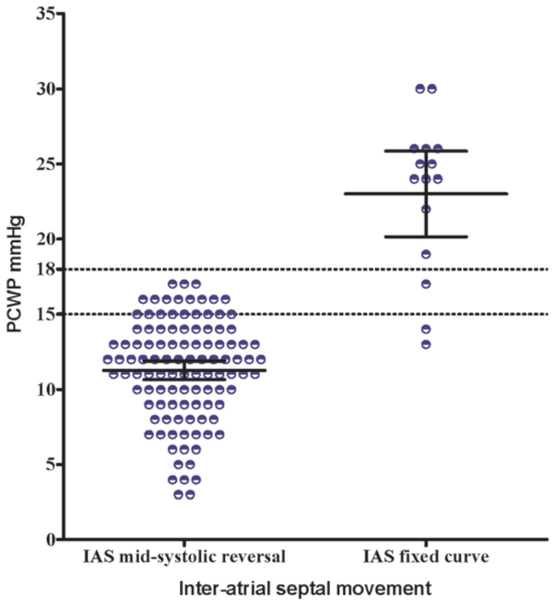

Fig. 2. Interatrial septal (IAS) movement patterns for all measurements across echocardiographic studies against pulmonary capillary wedge pressure (PCWP). The intervals, the mean, and 95% CI for PCWP. Mid-systolic reversal is the normal pattern where the septum changed direction and moved toward the left atrium during mid-systole, and fixed curve means that the IAS is bowed toward the right atrium throughout the cardiac cycle.

To be clinically useful, a measurement should have high sensitivity and specificity, and remain accurate over a wide range of hemodynamic conditions. Among the most commonly used Doppler parameters to estimate LAP is the E/e′ ratio. When assessing TTE-derived Doppler parameters in decompensated heart failure patients receiving various treatments, E/e′ has a high correlation with PCWP. E/e′ greater than 15 has been shown to be predictive of PCWP of 15 mmHg (sensitivity 89% and specificity 91%).[19] In patients with preserved left ventricular systolic function, Dokainish *et al.*[26] showed that a TTE-derived E/e′ ratio greater than 13 can predict left ventricular preatrial contraction pressure 15 mmHg or greater with a sensitivity of 70% and specificity of 93%. In this study, we found a similar specificity but significantly lower sensitivity at a PCWP cutoff of 15 mmHg. The sensitivity and specificity of septal E/e, which were measured by TTE only, were similar but only for PCWP 18 mmHg or greater (67% and 90%, respectively).

Doppler parameters obtained with TEE in sedated intensive care patients correlate well with simultaneously measured PCWP.[27–30] Vignon *et al.*[29] prospectively evaluated TEE in intensive care unit patients with acute respiratory distress syndrome and found significantly higher correlations of Doppler parameters and PCWP in patients with systolic failure than in patients with preserved systolic function. They showed that an E/e′ 8 mmHg or less had a sensitivity of 83% and a specificity of 88% to predict PCWP 18 mmHg or less. Bouhemad *et al.*[27] also demonstrated that TEE-derived E/e′ predicts PCWP 13 mmHg or greater (AUC, 0.97), but the limits of agreement were wide, ranging from −4 to +5 mmHg.

The echocardiography parameter with the best sensitivity and specificity was the fixed curve pattern of the interatrial septum. This improved as the PCWP increased and was a very good predictor of PCWP 17 mmHg or greater.

By convention, raised LAP is defined as LAP or by its surrogate such as PCWP as greater than 15 mmHg. Importantly, the predictive power was good for both awake and anesthetized patients. According to Royse *et al.*,[11] the mean (95% CIs) of PCWP for the fixed curve interatrial septal pattern was 18.1 (16.7 to 19.6 mmHg) and 13.2 for mid-systolic reversal pattern (12.5 to 13.8 mmHg), indicating that there was a physiological range of PCWP that produced the interatrial septal patterns and a likely crossover of patterns around a strict cutoff definition for raised LAP. Kusumoto *et al.*,[31] using TEE in anesthetized patients, found that the mid-systolic reversal pattern occurred in 64 of 72 episodes when the PCWP was 15 mmHg or less, but in only 2 of 40 episodes where PCWP greater than 15 mmHg. They found similar sensitivity and specificity to our study (sensitivity 0.89 and specificity 0.95). They found that the shape and movement of the interatrial septum were dependent on the transatrial pressure gradient. LAP is normally higher than the right atrial pressure, except when increased venous return during expiration (mechanical ventilation) transiently raised the right atrial pressure more than the left, causing the reversal of movement during mid-systole. The shape and movement of the interatrial septum are easy to identify with both TTE and TEE and could be a promising method for identifying raised LAP.

Study Limitations

Raised LAP is a key finding in significant diastolic dysfunction. However, in this study, direct measurement of LAP was not ethical or feasible and PCWP was used as a surrogate, which has recognized limitations in accuracy. Inaccuracy of PCWP due to variability in difference in height of the pressure transducer with the left atrium was reduced by locating the anterior roof of the left atrium with TTE rather than estimating it from surface landmarks. Patients with mitral disease and atrial fibrillation were excluded as these conditions are known to interfere with accuracy of diastolic assessment. The number of patients with reduced EF was small. It is possible that with a larger sample size, the correlations at study time other than the preanesthetic TTE may have been better. However, despite small numbers, the correlations for some Doppler parameters were reasonable in the low EF group before anesthesia. A possible reason for the lack of correlation of Doppler measurements and PCWP is the rapidly changing hemodynamic conditions caused by commencement of anesthesia and mechanical ventilation, sternal retraction, and inflammatory response from surgery and cardiopulmonary bypass. This may have been contributed by differing anesthesia techniques and hemodynamic management by different anesthesiologists. In intensive care unit patients, a possible reason that Doppler measurements predicted PCWP may have been that the hemodynamic conditions were more stable.

Conclusions

Doppler assessment of PCWP was neither sensitive nor specific enough to be clinically useful in anesthetized and mechanically ventilated patients requiring cardiac surgery. The fixed curve pattern of the interatrial septum was the best predictor of raised PCWP only when the PCWP 17 mmHg or greater.

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Competing Interests

The authors declare no competing interests.

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Appendix. Pearson Correlation of Echocardiography Measurements and Pulmonary Artery Wedge Pressures Stratified by EF ≥50% and <50%

	Measurement Period									
	Awake		After Anesthesia and Mechanical Ventilation				During Surgery		After Surgery	
	Pre-An TTE		Post-An TTE		Post-An TEE		Graft Harvest TEE		Post-CPB TEE	
Hemodynamic Parameters	EF ≥50%	EF <50%	EF ≥50%	EF <50%	EF ≥50%	EF <50%	EF ≥50%	EF <50%	EF ≥50%	EF <50%
E (cm/s)	0.31 (0.173)	0.89** (0.006)	−0.01 (0.991)	0.47 (0.346)	0.50* (0.027)	0.54 (0.262)	0.65* (0.002)*	0.91* (0.011)	0.17 (0.501	0.51 (0.294)
A (cm/s)	0.17 (0.470)	0.23 (0.658)	−0.08 (0.725)	−0.42 (0.401)	0.11 (0.654)	−0.5 (0.312)	0.24 (0.322)	−0.6 (0.402)	0.09 (0.723)	−0.84 (0.154)
E/A ratio	0.18 (0.43)	0.69 (0.129)	0.10 (0.665)	0.55 (0.248)	0.19 (0.419)	0.62 (0.187)	0.26 (0.272)	0.53 (0.470)	−0.17 (0.485)	0.59 (0.403)
A duration (ms)	0.43 (0.058)	−0.70 (0.183)	−0.17 (0.468)	0.82 (0.083)	0.11 (0.634)	0.6 (0.400)	0.22 (0.345)	0.55 (0.448)	−0.26 (0.294)	0.08 (0.916)
DT (ms)	0.53* (0.017)	−0.80* (0.03)	−0.10 (0.673)	−0.24 (0.695)	0.43 (0.062)	−0.18 (0.765)	−0.15 (0.536)	0.23 (0.662)	0.12 (0.629)	0.46 (0.353)
e′ lateral (cm/s)	0.31 (0.174)	0.01 (0.978)	0.06 (0.790)	0.14 (0.821)	0.79 (0.748)	−0.65 (0.349)	−0.01 (0.978)	−0.45 (0.703)	−0.29 (0.230)	−0.43 (0.563)
e′ septal (cm/s)	−0.01 (0.979)	−0.44 (0.312)	−0.34 (0.154)	−0.61 (0.199)						
E/ e′ lateral	0.14 (0.542)	0.83* (0.020)	−0.02 (0.944)	0.34 (0.502)	0.28 (0.239)	0.24 (0.644)	0.35 (0.140)	0.74 (0.090)	0.21 (0.410)	0.06 (0.902)
E/ e′ septal	0.01 (0.991)	0.96** (0.001)	0.06 (0.809)	0.42 (0.404)						
a′ lateral (cm/s)	0.31 (0.174)	−0.66 (0.100)	0.06 (0.789)	0.14 (0.821)	0.08 (0.746)	−0.65 (0.349)	−0.01 (0.978)	−0.45 (0.703)	0.29 (0.23)	−0.43 (0.563)
a′ septal (cm/s)	−0.31 (0.186)	−0.73 (0.061)	−0.34 (0.152)	−0.61 (0.199)						
PV S (cm/s)	−0.14 (0.542)	0.26 (0.564)	0.18 (0.459)	−0.11 (0.821)	0.25 (0.287)	−0.15 (0.774)	0.18 (0.449)	−0.5 (0.311)	−0.11 (0.648	−0.05 (0.933)
PV D (cm/s)	−0.01 (0.968)	0.89** (0.008)	0.12 (0.607)	−0.19 (0.717)	0.66** (0.002)	−0.07 (0.887)	0.14 (0.556)	0.8 (0.052)	−0.05 (0.819)	0.72 (0.170)
PV S/D ratio	−0.19 (0.423)	−0.91** (0.004)	0.24 (0.304)	−0.58 (0.221)	−0.35 (0.139)	−0.70 (0.117)	0.06 (0.784)	−0.64 (0.165)	−0.05 (0.826)	−0.8 (0.109)

Data are presented as correlation coefficient and *P* value.

* $P < 0.05$, ** $P < 0.01$.

A = late mitral inflow peak velocity; a′ = atrial peak myocardial annular tissue velocity; D = diastolic pulmonary vein velocity; DT = deceleration time; E = early mitral inflow peak velocity; e′ = early peak mitral annular tissue velocity; EF = ejection fraction; graft harvest TEE = the measurement performed during harvest of coronary grafts; post-An TEE = the first TEE measurement performed after induction of anesthesia; post-An TTE = the TTE study performed after induction of anesthesia; post-CPB TEE = performed after separation from cardiopulmonary bypass; pre-An TTE = the preanesthetic measurement; PV = pulmonary vein; S = systolic pulmonary vein velocity; TEE = transesophageal echocardiography; TTE = transthoracic.