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Tissue Doppler Imaging in the Estimation of Intracardiac Filling Pressure in Decompensated Patients With Advanced Systolic Heart Failure

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Background—The ratio of early transmitral velocity to tissue Doppler mitral annular early diastolic velocity (E/Ea) has been correlated with pulmonary capillary wedge pressure (PCWP) in a wide variety of cardiac conditions. The objective of this study was to determine the reliability of mitral E/Ea for predicting PCWP in patients admitted for advanced decompensated heart failure.

Methods and Results—Prospective consecutive patients with advanced decompensated heart failure (ejection fraction ≤30%, New York Heart Association class III to IV symptoms) underwent simultaneous echocardiographic and hemodynamic evaluation on admission and after 48 hours of intensive medical therapy. A total of 106 patients were included (mean age, 57±12 years; ejection fraction, 24±8%; PCWP, 21±7 mm Hg; mitral E/Ea ratio, 20±12). No correlation was found between mitral E/Ea ratio and PCWP, particularly in those with larger left ventricular volumes, more impaired cardiac indexes, and the presence of cardiac resynchronization therapy. Overall, the mitral E/Ea ratio was similar among patients with PCWP >18 and ≤18 mm Hg, and sensitivity and specificity for mitral E/Ea ratio >15 to identify a PCWP >18 mm Hg were 66% and 50%, respectively. Contrary to prior reports, we did not observe any direct association between changes in PCWP and changes in mitral E/Ea ratio.

Conclusion—In decompensated patients with advanced systolic heart failure, tissue Doppler–derived mitral E/Ea ratio may not be as reliable in predicting intracardiac filling pressures, particularly in those with larger LV volumes, more impaired cardiac indices, and the presence of cardiac resynchronization therapy. **(*Circulation*. 2009;119:62-70.)**

Key Words: diastole ■ echocardiography ■ heart failure ■ hemodynamics ■ remodeling

Invasively measured pulmonary capillary wedge pressure (PCWP) has been widely used as a surrogate for left ventricular (LV) filling pressure and is directly associated with functional capacity and prognosis in patients with heart failure.[1–3] However, given the cost, potential complications, and lack of demonstrable benefits in routine use, hemodynamic assessment via pulmonary artery catheters has decreased substantially over the last decade.[4–6]

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Conventional echocardiography plays a critical role in the management of heart failure in that it serves as a noninvasive bedside tool to determine abnormalities in cardiac structure and performance. Transmitral flow velocity curves and other Doppler variables have been used as noninvasive estimates of intracardiac filling pressures, albeit with limitations. In particular, the ratio of early transmitral velocity to tissue Doppler mitral annular early diastolic velocity (E/Ea) has been shown to correlate with PCWP in a wide range of cardiac patients.[7–13] However, although some smaller studies have included patients with depressed LV systolic function, none has included patients admitted with advanced heart failure and extensive reverse remodeling.[14–19] Therefore, the primary goal of our study was to examine the relationship between mitral E/Ea and hemodynamic measurements in patients with advanced decompensated heart failure (ADHF), a patient cohort in which hemodynamic assessment is often considered. We further aimed to explore the potential clinical utility of serial mitral E/Ea assessment in estimating changes in intracardiac filling pressures in response to intensive medical therapy in the ADHF setting.

Methods

Study Population

We prospectively enrolled consecutive patients ≥18 years of age with symptomatic chronic (>6 months) heart failure who underwent a right heart catheterization because of concerns about hemodynamic derangements at the Cleveland Clinic heart failure intensive care unit between September 15, 2006, and October 15, 2007. Inclusion

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criteria included markedly impaired systolic LV function defined by LV ejection fraction ≤30% and New York Heart Association class III to IV symptoms. Patients on artificial ventilation, those who had undergone aortic and/or mitral valve repair or prosthesis, and cardiac transplantation patients were excluded. A previous cardiac resynchronization therapy with defibrillator (CRT-D) implantation was not an exclusion criterion, and all data provided in the Results for patients previously implanted with a CRT-D device were collected with the device on. The Cleveland Clinic Institutional Review Board approved this research project, and informed consent was prospectively obtained in all subjects.

Hemodynamic Study Design

Hemodynamic and echocardiographic data were simultaneously collected at baseline (within 12 hours of admission) and at follow-up (after 48 hours of intensive medical therapy) if the pulmonary artery catheter was still in place. Hemodynamic data, including systemic blood pressure, central venous pressure, and PCWP (wedge position was verified by fluoroscopy and phasic changes in pressure waveforms), represent the average of 5 cycles with balanced transducers (0 level at the midaxillary line). Central venous pressure and PCWP were assessed at end expiration with a balloon-tipped catheter at steady state with the patient in a supine position by an investigator unaware of the echocardiographic measurements. Cardiac index was determined with the Fick equation through sampling of a mixed central venous blood gas taken in the pulmonary artery while assuming standard metabolic rates.

The hemodynamic goals and pharmacological approach to intravenous therapy in the specialized heart failure intensive care unit have been previously described.[20] Briefly, optimal hemodynamic response was defined as a decrease in PCWP ≤18 mm Hg, a decrease in central venous pressure to ≤8 mm Hg, and an improvement in cardiac index to ≥2.2 $L \cdot {}^{-1}min \cdot m^{-2}$ while maintaining mean arterial pressure >65 mm Hg. To achieve the hemodynamic goals, most patients were treated with intravenous loop diuretics combined with vasodilators and/or inotropic agents while previous therapies were continued or intensified with angiotensin-converting enzyme inhibitors, antiadrenergic blockers, aldosterone receptor antagonists, and other vasodilators as indicated and as tolerated.

Transthoracic Echocardiography

A comprehensive 2-dimensional echocardiographic examination dedicated to research was performed with a commercially available system (Vingmed, System Seven, General Electric, Piscataway, NJ) by a single American Society of Echocardiography registered diagnostic cardiac sonographer (A.B.). Images were acquired in the left lateral decubitus position with a phased-array transducer in the standard parasternal and apical views. Standard 2-dimensional and Doppler data, triggered to the QRS complex, were digitally stored in a cine-loop format.

Echocardiographic Analysis

The analysis was performed offline by 2 independent investigators experienced in echocardiographic measurements who were blinded to hemodynamic data at the time of analysis. All reported echocardiographic measurements were averaged from 3 consecutive cycles. LV volumes, LV ejection fraction, mitral regurgitation, and left atrial maximum volume were assessed as recommended by the American Society of Echocardiography.[21] Mitral inflow was analyzed for peak E (early diastolic) and peak A (late diastolic) velocities, E/A ratio, and deceleration time of E velocity. Ea septal and lateral mitral annulus velocities were measured, and the dimensionless mitral E/Ea ratio for the septal and lateral annulus was calculated.[7,8,15] Interventricular mechanical dyssynchrony was assessed as the difference between the preejection intervals from the QRS onset to the beginning of ventricular ejection at the pulmonic and aortic valve levels using pulsed-wave Doppler and intraventricular mechanical dyssynchrony by the opposing wall time-to-peak myocardial velocity intervals in a 4-segment model with color tissue Doppler imaging.

To ensure optimal accuracy of the mitral E/Ea ratio in patients with advanced heart failure and possible regional wall motion abnormalities, all analyses provided are based on the mitral E/Ea ratio computed from the average of the septal and lateral Ea.[16] Pulsed-wave, not color, tissue Doppler imaging was used because temporal resolution is higher with pulsed-wave tissue Doppler imaging. Second, low-gain and filter settings were applied so that the onset of mitral Ea could be reliably identified. Third, the scale was adjusted as needed to range from −15 to 20 to 15 to 20 cm/s, and the sweep speed was set at 100 mm/s to achieve the optimal spectral display of myocardial velocities. Finally, identical R-R intervals (<5 ms) were chosen to minimize potential differences in diastolic time intervals and subsequent differences in interpretation at slightly different R-R cycle lengths.

Statistical Analysis

All data are expressed as mean±SD for continuous data and as a ratio for categorical data. Univariate comparisons of these variables were performed between baseline and follow-up variables and between patients with and without previous CRT-D implantation. Paired and unpaired *t* tests for continuous data and Spearman correlation coefficients were used for appropriate comparisons. Receiver-operating characteristic curves were constructed to determine optimal sensitivity and specificity for predicting PCWP >18 mm Hg with mitral E/Ea ratio. A PCWP of 18 mm Hg was chosen as the cutoff value because this was the target according to treatment protocol. On the basis of previous studies, a cutoff value for PCWP of 15 mm Hg also was analyzed. Statistical significance was set at a 2-tailed level of $P<0.05$. All analyses were performed with SPSS for Windows, release 13.0 (SPSS Inc, Chicago, Ill).

The authors had full access to and take full responsibility for the integrity of the data. All authors have read and agree to the manuscript as written.

Results

Patient Characteristics

A total of 110 patients met eligibility criteria during the study period. Four patients refused to be enrolled. Baseline characteristics and treatment of the final 106 patients enrolled during admission are summarized in Table 1. All patients (93% of whom were in sinus rhythm at the time of examination, 7% were in atrial fibrillation, and an additional 14% had a history of atrial fibrillation) were classified as New York Heart Association class III to IV with a mean LV ejection fraction of 24±8%. The median length of intensive medical therapy in the heart failure intensive care unit was 3.5 days. Fifty-one patients (49%) had a CRT-D device at the time of inclusion in our study, with overall baseline characteristics (except QRS width) and treatment patterns comparable to those of patients without previous CRT-D implantation.

Hemodynamic and Echocardiographic Measurements

Adequate mitral inflow, tissue Doppler signals, and hemodynamic variables were obtained in all patients. Table 2 presents the hemodynamic and echocardiographic measurements at the time of the baseline assessment for all patients stratified according to the presence or absence of CRT-D implantation. Overall, both patient groups had similar baseline hemodynamic derangements except for a higher heart rate in patients without CRT-D. Compared with those without CRT-D, patients with previous CRT-D implant had larger LV end-diastolic volumes and longer mitral deceleration times. Mitral Ea and E/Ea ratios for different annular regions were similar between those with and those without CRT-D. In addition,

Table 1. Demographics and Vital Statistics

	All Patients (n=106)	Patients Without CRT-D (n=55)	Patients With CRT-D (n=51)
Baseline characteristics			
Age, y	57±12	56±13	59±12
Men, %	76	72	78
Weight, kg	81±22	82±22	78±22
QRS width, ms	141±34	123±29	160±29*
Hypertension, %	58	56	60
Hyperlipidemia, %	59	59	63
Diabetes mellitus, %	32	34	27
Ischemic origin, %	42	44	39
LV ejection fraction, %	24±8	25±8	24±9
Hemoglobin, g/dL	11.7±2	11.7±2	11.8±2
Creatinine, mg/dL	1.8±1.1	1.7±0.7	1.9±1.3
BNP, pg/mL	1710±1406	1628±1247	1734±1386
Medical treatment during admission, %			
β-Blockers	58	54	62
ACE inhibitor/ARB	54	56	52
Spironolactone	44	39	48
Loop diuretic	85	84	78
Digoxin	22	17	24
Hydralazine	38	40	35
Isosorbide dinitrate	37	37	37
Inotropic drugs	35	38	32
Nitroprusside	41	44	40

BNP indicates brain natriuretic peptide; ACE, angiotensin-converting enzyme; and ARB, angiotensin receptor blocker. Values are mean±SD when appropriate.

*$P<0.01$ for comparison between patients with and patients without CRT-D.

Table 2. Initial Hemodynamic and Echocardiographic Measurements

	All Patients (n=106)	Patients Without CRT-D (n=55)	Patients With CRT-D (n=51)
Body mass index, kg/m^2	27±8	28±6	27±6
Heart rate, bpm	75±29	84±24	67±32*
MAP, mm Hg	75±11	76±13	74±9
CVP, mm Hg	12±7	13±6	11±8
MPA, mm Hg	34±11	34±11	36±10
PCWP, mm Hg	21±7	21±6	20±7
CI, L · min^{-1} · m^{-2}	2.1±0.7	2.0±0.7	2.1±0.8
LV mass, g	376±134	367±130	395±145
LV mass index, g/m^2	183±63	177±59	196±68
Left atrial volume, mL	92±38	89±39	96±38
Left atrial volume index, mL/m^2	45±16	43±17	47±14
LVEDV, mL	252±114	210±85	294±124*
LVEDV index, mL/m^2	124±57	104±45	142±62*
Mitral E velocity, cm/s	96±28	97±25	96±32
Mitral A velocity, cm/s	43±14	45±16	42±20
Mitral E/A	2.4±0.9	2.5±0.9	2.3±0.7
Mitral DT, ms	150±45	136±38	164±46*
Mitral Ea septal annulus, cm/s	5.1±2.8	4.9±2.1	5.2±3.2
Mitral E/Ea septal annulus	23±12	24±11	22±13
Mitral Ea lateral annulus, cm/s	7.4±4.6	7.2±3.1	7.5±5.8
Mitral E/Ea lateral annulus	17±11	17±10	17±12
Mitral Ea average, cm/s	6.1±3.6	5.9±2.5	6.3±4.4
Mitral E/Ea average	20±12	21±11	19±12

MAP indicates mean systemic arterial pressure; CVP, central venous pressure; MPA, mean pulmonary artery pressure; CI, cardiac index; LVEDV, LV end-diastolic volume; and DT, deceleration time. Values are mean±SD when appropriate.

*$P<0.01$ for comparison between patients with and patients without CRT-D.

septal and lateral Ea values for ischemic and idiopathic dilated cardiomyopathy patients were similar (5.1±3.2 versus 5.1±2.4 cm/s [$P=0.9$] and 7.5±5.7 versus 7.3±3.4 cm/s [$P=0.8$], respectively). Overall, 22% of patients had more than moderate mitral regurgitation at baseline. Compared with patients with mild or moderate mitral regurgitation, these patients had a nonsignificant trend toward higher PCWP and higher mitral E/Ea ratio. Finally, interventricular mechanical dyssynchrony and intraventricular mechanical dyssynchrony were only 19±26 and 36,38 ms, respectively.

The relationships between PCWP and different Doppler variables are shown in Table 3. A weak but statistically significant negative correlation was found between PCWP and mitral deceleration time, and a weak positive correlation was found between PCWP and mitral E velocity only in patients without previous CRT-D implantation. However, no correlation was observed between PCWP and mitral Ea in the septal annulus or lateral annulus or when averaged over both annular regions. Furthermore, the mitral E/Ea ratio (using all the definitions for Ea just mentioned) showed no significant correlation with PCWP. As illustrated in Figure 1, even an elevated mitral E/Ea ratio could be associated with a relatively low PCWP and vice versa. Interpretable pulmonary vein (PV) Doppler tracings were obtained in 66% of patients at baseline (systolic PV, 33±8 cm/s; diastolic PV, 56±19 cm/s; atrial PV, 27±9 cm/s). However, no significant correlation could be detected among PV Doppler tracings and PCWP (for systolic PV, $r=-0.01$; for diastolic PV, $r=0.1$; for systolic/diastolic PV, $r=-0.04$).

Only 53% of patients with a PCWP >18 mm Hg had a mitral E/Ea ratio >15. Figure 2 compares mean mitral E/Ea values in patients with PCWP >15 or 18 mm Hg and those with PCWP ≤15 or 18 mm Hg and stratified by the presence or absence of previous CRT-D implant. Overall, averaged mitral E/Ea ratio was similar among patients with normal versus elevated PCWP. Only patients without a previous CRT-D implant had a modestly (but significantly) higher mitral E/Ea ratio when PCWP >15 or 18 mm Hg.

Clinical Accuracy of Mitral E/Ea Ratio to Predict PCWP

As illustrated in Figure 3, sensitivity and specificity for mitral E/Ea ratio >15 to identify a PCWP >18 mm Hg were 66%

Table 3. Correlation Coefficients of Echocardiographic Variables With PCWP

	All Patients (n=106)	Patients Without CRT-D (n=55)	Patients With CRT-D (n=51)
LV mass	0.01	−0.11	0.22
LVEDV	−0.07	−0.12	0.03
Left atrial volume	0.04	0.05	−0.09
E velocity	0.28*	0.29*	0.17
E/A	0.24	0.47*	−0.06
DT	−0.27*	−0.25*	−0.21
Ea septal annulus	0.06	0.03	0.16
E/Ea septal annulus	0.18	0.27	0.10
Ea lateral annulus	0.03	−0.05	0.13
E/Ea lateral annulus	0.14	0.18	0.12
Ea average	0.02	−0.06	0.11
E/Ea average	0.18	0.23	0.11

LVEDV indicats LV end-diastolic volume; DT, deceleration time.
*$P \leq 0.01$.

and 50%. The predictive value was similar when patients with atrial fibrillation were excluded from the analysis. However, a mitral E/Ea ratio >15 provided better accuracy in predicting PCWP >18 mm Hg in patients without previous CRT-D implantation (sensitivity, 72%; specificity, 54%) than in patients with previous CRT-D implantation (sensitivity, 59%; specificity, 52%). Sensitivity and specificity of mitral E/Ea ratio >15 to predict a PCWP >15 mm Hg in patients without previous CRT-D implantation (sensitivity, 63%; specificity, 57%) and in patients with previous CRT-D implantation (sensitivity, 58%; specificity, 50%) were poorer.

To further analyze the potential importance of a cutoff value for mitral E/Ea ratio, patients were divided into 3 groups. In the patients with mitral E/Ea ratios <8, 8 to 15, and E/Ea >15, average PCWPs were similar (19±4, 19±7, and 20±6 mm Hg, respectively). We also tested a previously derived equation (PCWP=2+1.3 mitral E/Ea ratio) to predict measured PCWP in our study cohort, but no correlation was observed ($r=0.03$, P=NS).

Relation of Mitral E/Ea Ratio to Cardiac Structure and Performance

To better understand the lack of correlation between mitral E/Ea ratio and PCWP, echocardiographic and hemodynamic variables were compared between 2 groups according to the presence or absence of concordant mitral E/Ea ratio >15 and PCWP >18 mm Hg (Figure 4). Interestingly, the only variables that demonstrated statistically significant differences between concordant and discordant mitral E/Ea-PCWP measurements were LV end-diastolic volume and cardiac index. In particular, those with discordant mitral E/Ea-PCWP measurements had significantly larger LV volumes and lower cardiac indexes. Left atrial volume and severity of mitral regurgitation did not differ between groups.

Follow-Up Measures

Fifty-one patients (49%) underwent simultaneous Doppler and hemodynamic measurements at follow-up. The absolute change in mean PCWP levels ranged from −24 to 16 mm Hg. No correlation between absolute change in PCWP and change in mitral E/Ea ratio was observed (Figure 1).

Discussion

In the present study, we report for the first time the reliability of the mitral E/Ea ratio to estimate PCWP in a large, well-characterized "cold and wet" patient population admitted with decompensation from advanced systolic heart failure (LV ejection fraction ≤30%). Using simultaneously measured echocardiographic and invasive hemodynamic variables, we found the predictive value of baseline mitral E/Ea ratio in estimating PCWP in this population to be less robust than previously reported, especially in patients with CRT. Furthermore, we were unable to identify any reliable direct correlation between changes in mitral E/Ea ratio and PCWP. We further explored this complex relationship and observed the discordance of mitral E/Ea ratio and PCWP to be linked to larger LV dimensions, more impaired cardiac output, and the presence of CRT. With increasing acceptance of mitral E/Ea ratio as a surrogate measure of diastolic function and as a reliable estimate of intracardiac filling pressures, our observations provide an important refinement in the clinical interpretation of the mitral E/Ea ratio as it applies to patient

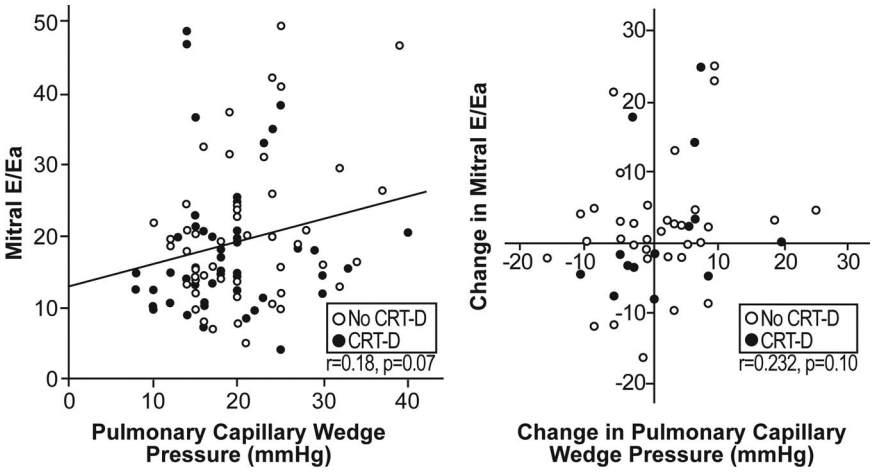

Figure 1. Relation between mitral E/Ea ratio and PCWP at baseline (top) and relation between changes (baseline to follow-up) in mitral E/Ea ratio and changes (baseline to follow-up) in PCWP (bottom).

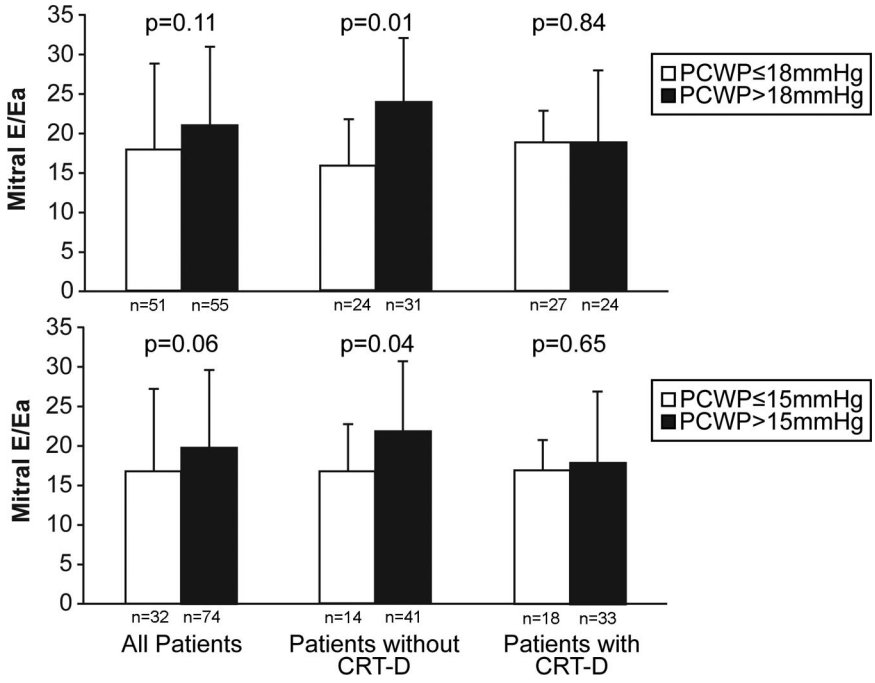

Figure 2. Mitral E/Ea ratio in all patients stratified to previous CRT-D implantation or not.

populations in which confounders such as alterations in myocardial structure, severity of systolic dysfunction, or the presence of synchronized pacing may influence its predictive value. Our data also caution against the use of serial mitral E/Ea assessment for titration of diuretic therapy in such conditions.

Conventional Doppler recording of mitral inflow velocities and PV velocities has been shown to be useful in estimating PCWP, although significant difficulties arise with alterations in loading conditions, mitral valve disease, aging, tachycardia, and atrial fibrillation.[22–26] Although LV filling is initiated and enhanced by augmentable myocardial relaxation in healthy individuals, it is driven by a high filling pressure in patients with heart failure because myocardial relaxation is reduced.[27] Our data corroborate these findings; we too found modest relations between PCWP and mitral inflow velocities and deceleration times in our study cohort. This relatively low correlation is an unexpected finding, probably attributable to the confounding effects of LV relaxation, LV stiffness, left atrial pressure, mitral valve function, and annular recoil in this advanced heart failure population, which affect mitral inflow velocities and deceleration times to a greater extent than in normal or less advanced heart failure patients. As a result, the mitral E and deceleration time, which are recorded in early diastole, are only very rough estimates of PCWP. To better account for relaxation, mitral annular velocity Ea has been shown to be less dependent on pressure gradients than blood flow.[27–29] As a consequence, the mitral E/Ea ratio,

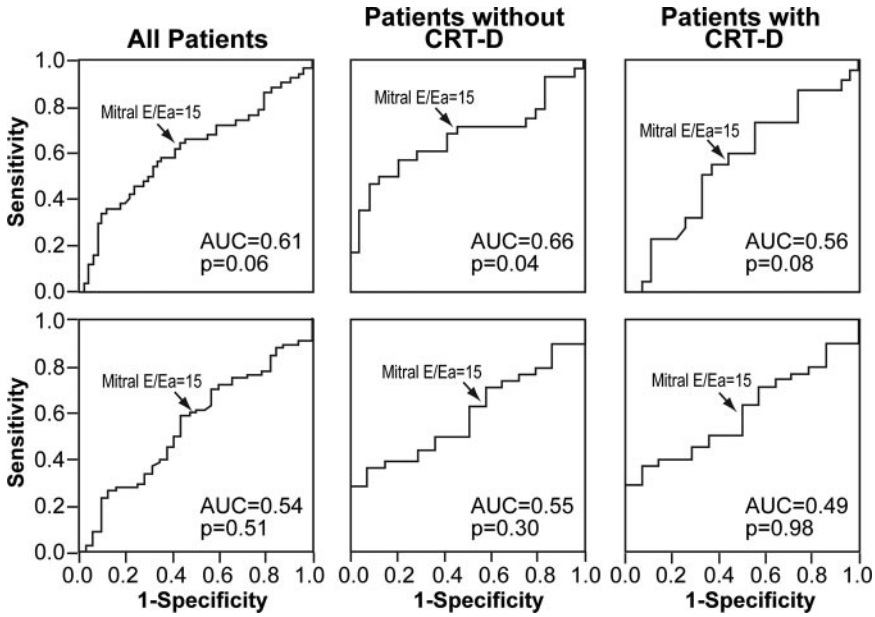

Figure 3. Receiver-operating characteristic curves for the prediction of PCWP >18 mm Hg (top) and >15 mm Hg (bottom) for mitral E/Ea ratio. AUC indicates area under curve.

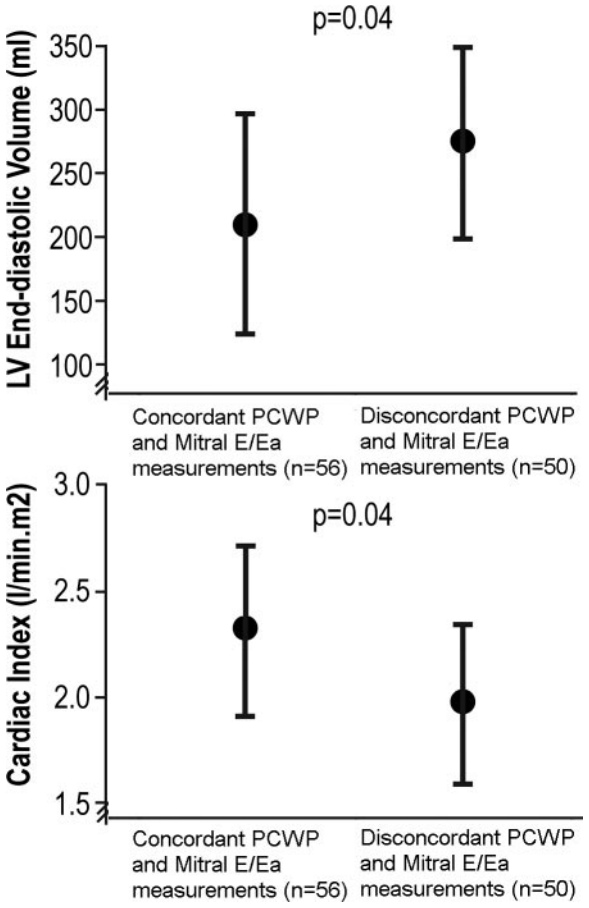

Figure 4. Relation of mitral E/Ea ratio and PCWP to LV end-diastolic volume and cardiac index. The *P* value represents the *t* test between concordant and discordant PCWP and mitral E/Ea ratio. Error bars represent SD.

which can be measured easily by standard equipment without extensive postprocessing, has been proposed as a surrogate for PCWP in patients with a variety of cardiac abnormalities, including diastolic heart failure, mitral valve disease, hypertrophic cardiomyopathy, atrial fibrillation, and sinus tachycardia.[7–13] The increasing acceptance is reflected by the endorsement of mitral E/Ea as a marker for LV filling pressure by a consensus statement from the European Society of Cardiology on the assessment of diastolic function.[30]

The sensitivity and specificity for the previously described cutoff value of mitral E/Ea >15 to detect elevated PCWP were far lower in our study population than described in prior studies, especially in those patients receiving CRT. However, it is important to emphasize that the profile of our patient population has important differences from those in several published reports that advocated mitral E/Ea ratio for the estimation of LV filling pressures in patients with depressed systolic function.[14–19] Not only was our sample size much larger, but our patient population by design experienced worsening of their clinical status just before evaluation and had significantly more cardiac dysfunction and LV remodeling (mean LV ejection fraction, 24±7%; mean cardiac index, 2.1±0.7 L · min^{-1} · m^{-2}; mean LV end-diastolic volume, 263±117 mL) than in prior studies. We also describe for the first time the impact of pacing on the accuracy of mitral E/Ea, as shown by the poorer correlation of this measure with PCWP in patients with biventricular pacing, although even without pacing we failed to find a robust relationship. To better illustrate the potential confounding aspects of this analysis, consider the 2 patients in Figure 5. The top tracing is for a patient with dilated cardiomyopathy presenting with low output in whom a high mitral E/Ea ratio (27.3 for septal Ea, 22.4 for lateral Ea, and 24.6 for the mean) is seen with a relatively low PCWP of 14 mm Hg. In contrast, the bottom tracing shows very elevated PCWP (23 mm Hg) in a patient with ischemic cardiomyopathy, CRT, low output, and relatively modest mitral E/Ea elevations (17.7 for septal Ea, 7.3 for lateral Ea, and 10.3 for the mean).

We did not confirm the previously reported finding that changes in the mitral E/Ea ratio track changes in PCWP in ADHF.[14] Patients with a reduction in mitral E/Ea could still have significantly elevated PCWP and vice versa at follow-up. Therefore, a potential reduction in mitral E/Ea during serial echocardiographic assessment should not be considered a surrogate for a drop in PCWP in advanced heart failure patients. Importantly, from the findings of our study, mitral E/Ea ratio should not be used as the only initial or continuing assessment of LV filling pressure to titrate diuretic therapy in the setting of decompensation or advanced systolic heart failure. Figure 6 illustrates a patient with dilated cardiomyopathy treated with loop diuretics and vasodilators in whom a fall in PCWP and an increase in cardiac index elicited a contradictory increase in mitral E/Ea. One issue here is the patient's tachycardia and low cardiac output, which cause a hyperdynamic state with increased movement and subsequent velocities of the lateral mitral annulus (high lateral E′). Furthermore, a patient's treatment may vary significantly over time, particularly in relation to the use of inotropic medications, which may have independent effects on annular motion. Clearly, many confounders may influence the predictive value of mitral E/Ea ratio.

We further highlight the complex relationships between cardiac structure and performance in that we observed that the discordance of mitral E/Ea and PCWP was linked to larger LV dimensions and more impaired cardiac output in patients with ADHF. The presence of more severe LV remodeling seems to indicate the presence of a "disconnect" between LV diastolic function and actual LV filling pressure in patients with ADHF, which limits the clinical utility of mitral E/Ea ratio in estimating filling pressures in patients admitted with ADHF. Conversely, the lack of a significant correlation between mitral E/Ea and PCWP in patients with ADHF can also be explained by the presence of a more pronounced, irreversible diastolic and systolic dysfunction. Patients with advanced heart failure often have severe LV fibrosis and impaired cardiac output, which could restrict systolic and subsequent early diastolic mitral annular motion so that the relationship between left atrial driving pressure (E) and LV relaxation kinetics (Ea) within the LV could become defective, resulting in discordance between echocardiographically measured mitral E/Ea ratio and invasively measured PCWP. In addition, both mitral E and Ea occur in early diastole and reflect a host of factors relating to recoil, suction, intraventricular pressure gradients, and the previous systolic

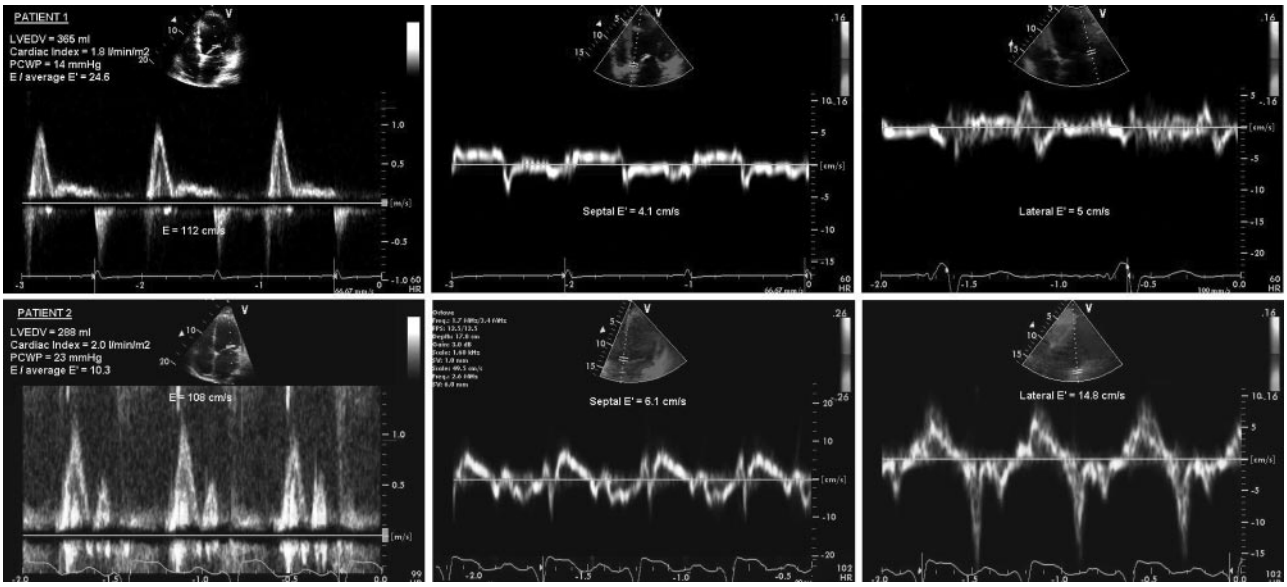

Figure 5. Example of 2 patients with discordant PCWP and mitral E/Ea ratio. Top, Patient with low PCWP and high mitral E/Ea ratio. Bottom, Patient with high PCWP and low mitral E/Ea. LVEDV indicates left ventricular end-diastolic volume.

contraction, whereas PCWP is a mean value of diastolic pressure. Therefore, it is not surprising that mitral E/Ea ratio is only a very rough measure of LV end-diastolic pressure. In other words, mitral E/Ea ratio has lower accuracy in assessing PCWP, especially at the more severe end of the heart failure syndrome spectrum, because E and Ea are probably altered by volume shifts to a different degree than in cases with less severe heart disease.

Study Limitations

No direct hemodynamic measurements of LV end-diastolic or left atrial pressure were performed, although PCWP is accepted as a well-validated surrogate considering the clinical condition of the patients and the need for serial monitoring.[1,31,32] Wedge position was verified by changes in pressure waveforms without fluoroscopic guidance or measured venous blood oxygen content with balloon inflation. To analyze cardiac output, a standard resting metabolic rate was assumed, but overall cardiac outputs assessed by the Fick equation were comparable to those assessed by the thermodilution technique. Regional wall motion abnormalities in severely dilated and/or ischemic ventricles might have altered Ea. However, instead of analyzing only the septal or lateral Ea, we also considered the average of both walls.[16] The exact mechanism through which CRT-D influences mitral E and Ea is not known, but pacing the heart leads to altered interventricular and intraventricular activation sequences with subsequent alterations in wall segmental loading and contraction,

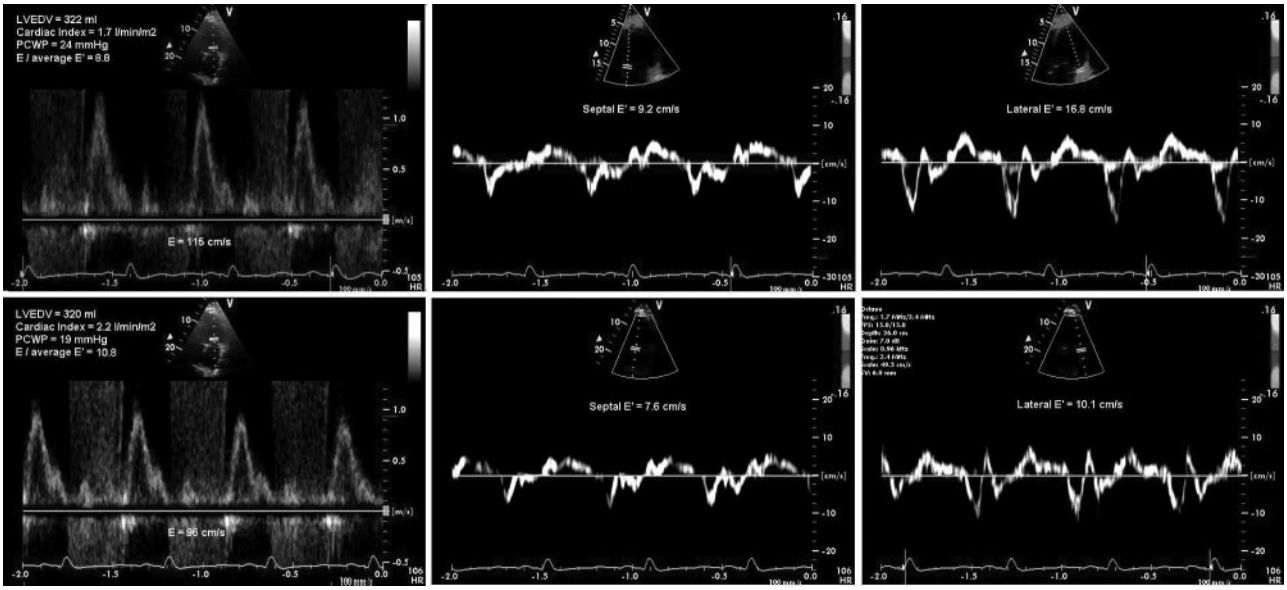

Figure 6. Example of changes in PCWP and mitral E/Ea in 1 patient from baseline (top) to follow-up (bottom). Note the discordant PCWP and mitral E/Ea ratio at baseline and at follow-up and the reduction in PCWP (−5 mm Hg), which is associated with an increase in mitral E/Ea ratio (2). LVEDV indicates left ventricular end-diastolic volume.

which probably influences Doppler parameters. Finally, the main aim of the study was to evaluate mitral E/Ea as a surrogate for PCWP, and we did not evaluate the reliability of combinations of different Doppler variables (including PV signals) in estimating LV filling pressures. Our data do not imply in any way that Doppler evaluation is not useful in ADHF but merely support the notion of a stepwise approach incorporating all available echocardiographic data.[11,16] We also did not evaluate the role of these measurements on the assessment of LV diastolic function of the failing myocardium. Although this is the largest reported cohort of patients with ADHF (especially with LV ejection fraction ≤30% and with serial measurements) and the sample size was substantially larger than in prior reports involving invasive hemodynamic validations, the sample size is still relatively small, notably for subgroup analyses.

Conclusions

In decompensated patients with advanced systolic heart failure, tissue Doppler–derived mitral E/Ea ratio alone may not be reliable in predicting intracardiac filling pressures, particularly in patients with larger LV volumes, more impaired cardiac indexes, and the presence of CRT. Our observations underscore a need for a refinement in the broad clinical use of the mitral E/Ea ratio to estimate filling pressures and caution against the direct inference of such relationships in patients in the decompensated state with significant LV systolic dysfunction, cardiac remodeling, or biventricular pacing.

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Disclosures

None.

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CLINICAL PERSPECTIVE

The ratio of early transmitral velocity to tissue Doppler mitral annular early diastolic velocity (E/Ea) has been correlated with pulmonary capillary wedge pressure in a wide variety of cardiac conditions. However, the reliability of the mitral E/Ea ratio for predicting pulmonary capillary wedge pressure in patients admitted for advanced decompensated heart failure is unknown. A total of 106 prospective consecutive patients with advanced decompensated heart failure (ejection fraction ≤30%, New Your Heart Association class III to IV symptoms) underwent simultaneous echocardiographic and hemodynamic evaluation on admission and after 48 hours of intensive medical therapy. We found the predictive value of baseline mitral E/Ea ratio in estimating pulmonary capillary wedge pressure to be less robust than previously reported, which appears to be related to larger left ventricular dimensions, more impaired cardiac output, and the presence of cardiac resynchronization therapy. In addition, no reliable direct correlation between baseline or changes in mitral E/Ea ratio and pulmonary capillary wedge pressure was found. Taken together, our observations provide an important refinement in the clinical interpretation of the mitral E/Ea ratio as it applies to patient populations in which important confounders such as alterations in myocardial structure, severity of systolic dysfunction, or the presence of synchronized pacing may pose challenges to the accurate prediction of left ventricular filling pressures.

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