Coronary Artery Disease

Limited Efficacy of Myocardial Tissue Doppler for Predicting Left Ventricular Filling Pressure, Severe Pulmonary Edema, and Respiratory Failure in Acute Myocardial Infarction

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Background: Regional parameters such as E/e′ (ratio of early-diastolic mitral inflow velocity to early-diastolic mitral annular velocity) may not accurately reflect global left ventricular (LV) diastolic function in acute myocardial infarction (AMI), and the use of these parameters for predicting severe pulmonary edema and respiratory failure during acute phase of AMI is questionable.

Methods and Results: Four hundred patients with first AMI were catheterized for possible coronary intervention and measurement of LV filling pressure (LVFP). Although E/regional e′ correlated linearly with LVFP, it was not a sufficient correlation to identify an elevated LVFP in AMI. For purposes of assessing LVFP, average e′ was no better than regional e′. Regarding culprit lesions, the correlation between E/regional e′ and LVFP was weaker in the single left anterior descending artery (LAD)-culprit AMI than in any other culprit or in multiple- vessel disease. Comparisons of LV ejection fraction (LVEF) revealed weak correlations between LVFP and E/regional e′ in patients with LVEF of 45-55%. Severe pulmonary edema and respiratory failure were significantly associated with LVEF (for pulmonary edema, OR 0.944, 95% CI 0.908-0.982, p = 0.004; for respiratory failure, OR 0.95, 95% CI 0.910-0.993, p = 0.022) and LVFP (for pulmonary edema, OR 1.13, 95% CI 1.074-1.190, p < 0.0001; for respiratory failure, OR 1.077, 95% CI 1.021-1.135, p = 0.006). Although LVFP was an independent predictor of severe pulmonary edema and respiratory failure, E/e′ was a poor substitute for LVFP in terms of predictive power (all p > 0.05).

Conclusion: E/e′ has an imperfect efficacy for predicting LVFP, severe pulmonary edema and respiratory failure in the acute phase of AMI.

(Trial registry: ClinicalTrials.gov; No.: NCT01168609; URL: clinicaltrials.gov)

Key Words: Left ventricular filling pressure • Myocardial infarction • Pulmonary edema • Respiratory failure • E/e′ • Tissue Doppler

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INTRODUCTION

Diastolic dysfunction after acute myocardial infarction (AMI) has significant associations with adverse events and poor prognosis.[1-3] The E/e′ ratio (ratio of early-diastolic mitral inflow velocity to early-diastolic mitral annular velocity) is reportedly the most accurate noninvasive predictor of elevated left ventricular filling pressure (LVFP).[4] As a well-known characteristic of tis-

sue Doppler imaging (TDI), it provides regional data for systolic and diastolic function.[5-7] When E/e′ is used to assess disease entities with only regional defects such as ischemic heart disease,[8] regional parameters obtained by TDI may not reflect global LV function. Acute pulmonary edema is a relatively common complication of AMI. Although most patients with acute pulmonary edema respond well to medical therapy and coronary intervention, other subjects suffering hypoxemia require endotracheal intubation with mechanical ventilation. This high-risk group accounted for more than 50% of in-hospital mortality.[9] Given the limited value of E/e′ as an indicator of global LV function, this study evaluated the use of E/regional e′ for predicting LVFP, severe pulmonary edema and respiratory failure at the acute phase of AMI.

METHODS

Between July 2007 and November 2010, this study prospectively enrolled 524 consecutive patients admitted to Kaohsiung Veterans General Hospital due to their first AMI incident. All received emergent cardiac catheterization to attempt primary percutaneous coronary intervention (PCI). An AMI was defined using the European Society of Cardiology/American College of Cardiology guidelines.[10] Exclusion criteria were a history of previous myocardial infarction (MI), mitral regurgitation of more than moderate severity, rhythm other than sinus rhythm, a previous heart failure event requiring hospitalization, and inadequate image quality. Patients were also excluded if they presented with complete bundle branch block, preexcitation, moderate or large pericardial effusion, or post-MI ventricular septal defect with a bouncing motion of the interventricular septum, which could complicate TDI measurements. Thus, the final analysis included 400 patients. Another 45 patients who had positive results for the screening tests (treadmill, thallium scan, stress echocardiography, or 64-slice computed tomography angiography) but negative results for coronary angiography served as the control group. All patients gave written informed consent to participate in the study, and the study was approved by the ethics committee at this institute.

Before catheterization, all patients received 300 mg of aspirin and 300 mg of clopidogrel. Patients were subjected to diagnostic coronary angiography via a femoral approach after intravenous injection of unfractionated 7500 U heparin. Forty-eight cases required coronary artery bypass grafting (CABG) with/without other repair procedures. The remaining patients were treated successfully by primary PCI and stenting. Nine of the 48 CABG patients had initially received primary PCI, but were treated by CABG later due to severe multiple-vessel disease or late-onset mechanical complications (ventricular septal rupture or cardiac rupture). Coronary angioplasty and stenting were performed only for the culprit lesion using standard techniques. All patients were subdivided according to their culprit lesions rather than the location of ST segment change, since some cases of AMI in the circumflex (LCX) territory lacked ST elevation of the lateral wall, and ST elevation over the inferoposterior area could be induced by the right coronary artery (RCA) or LCX.[11] Single-vessel disease was defined as no other stenosis exceeding 70% over non-culprit vascular territories. Otherwise, all others were classified as multiple-vessel disease.

The measurements of LVFP were performed via a fluid-filled pig-tail catheter placed into the LV after coronary angiography if PCI was not indicated, or after primary PCI (no case received left ventriculography). The fourth intercostal space in the mid-axillary line was used as the zero level. The LVFP was continuously recorded (50 mm/s) by a 6-F pigtail catheter placed at the mid-LV cavity using fluoroscopic screening. Digital records of rapid acquisition LV pressure tracings were recorded. Measurements were made offline. Measured pressure recordings included LV systolic pressure and LV pre-A wave pressure, which was defined as the pressure at the onset of atrial contraction. The average of LV pre-A wave pressure over 5 cardiac cycles was used as LVFP.[12,13] Any ectopic or post-ectopic beats were disregarded. LVFP was considered elevated when the averaged value exceeded 15 mmHg.

Echocardiography (iE33 system; Philips Medical Systems, Andover, Massachusetts, USA) was performed immediately after LVFP measurements were obtained, while patients were still in the catheterization laboratory. Slight adjustments were made in patient position to optimize acquisition of apical windows. The time interval between invasive LVFP measurements and echocardiography was less than 30 minutes. Left ventricular

ejection fraction (LVEF) was calculated using Simpson's method for biplane images. Mitral inflow was assessed by pulsed-wave Doppler echocardiography, and the E-, A-wave velocities, and E-deceleration time were measured. Pulsed-wave TDI was performed using spectral pulsed Doppler signal filters, by adjusting the Nyquist limit to 15 to 20 cm/s and using the minimum optimal gain. In the apical views, a pulsed-wave Doppler sample volume was placed at the level of the mitral annulus over the septal, anterior, lateral, and inferior borders. Pulsed-wave TDI results were characterized by a myocardial systolic wave (s′) and 2 diastolic waves: early (e′) and atrial contraction (a′). The pulsed-wave TDI tracing was recorded at a sweep speed of 100 mm/s and was used for offline calculations. The average e′ of septal and lateral mitral annulus was chosen to estimate LVFP by the E/e′ method.[14,15] Due to ethical concerns, all echocardiograms were performed immediately after coronary catheterization with/without primary PCI and LVFP measurements. The time required for echocardiography was 14 ± 5 minutes. No complications occurred during LVFP or echocardiographic measurements of the patients.

Pulmonary edema was diagnosed when the patient had severe dyspnea, rales covering both lung fields, and typical findings on a chest radiography. Frank pulmonary edema with rales covering more than one-half of the lung field, and the need of at least a non-rebreathing mask to maintain O_2 saturation was classified as severe pulmonary edema.

The SPSS software was used for all statistical analyses. All continuous variables were presented as means ± standard deviation. Analysis of variance and a post hoc test for unpaired data were performed to evaluate significant group differences. These differences were considered statistically significant if the p value was < 0.05. Comparison of clinical characteristics was performed by chi-square analysis for categorical variables, and simple correlation and linear regression were used when appropriate. Patients were subdivided into 4 groups according to their left ventricular systolic function. Patients with LVEF > 55% were classified as normal systolic function, LVEF between 55% and 45% as mild systolic dysfunction, LVEF between 45% and 35% as moderate systolic dysfunction, and LVEF less than 35% as severe LV systolic dysfunction. Subgroups were compared in terms of LV systolic function and culprit lesion to test for correlations between LVFP and E/e′. Receiver-Operating Characteristic (ROC) curves were constructed to determine sensitivity and specificity for predicting elevated LVFP (> 15 mmHg) using an optimal cut-off value for E/e′. Potential predictors of severe pulmonary edema and respiratory failure were evaluated by multivariate logistic regression. The potential predictors were selected by univariate analyses and then by entry and retention in the model set at a significant level of 0.05. Multivariate logistic regression was repeated after replacing LVFP with E/e′ to test the hypothesized efficacy of E/e′ for clinical use as an indicator of LVFP and as a non-invasive prognostic indicator of AMI.

RESULTS

In the first 50 enrolled cases, mitral E velocities and TDI parameters for individual regions were measured independently by two different observers. Interobserver variability was calculated as the difference between the values obtained by the two observers divided by the mean. Interobserver difference and variability in mitral E velocity were 3.1 ± 5.8 cm/s and 4.2 ± 7.4%. Interobserver variabilities and differences were 2.7 ± 5.2% and 0.2 ± 0.4 cm/s for s′, 2.2 ± 5.1% and 0.2 ± 0.4 cm/s for e′, and 2.8 ± 5.6% and 0.3 ± 0.5 cm/s for a′, respectively.

When using average e′, septal, anterior and lateral e′ to assess the regression curve between LVFP and E/e′, linear regression analysis revealed acceptable fitness (correlation between LVFP and E/average e′: r square 0.377; correlation between LVFP and E/septal e′: r square 0.365; correlation between LVFP and E/anterior e′: r square 0.348; correlation between LVFP and E/lateral e′: r square 0.269; all $p < 0.0001$).

In AMI patients with single-vessel disease, the culprit lesions were in the LAD in 116 of the study subjects, in LCX in 40, and in RCA in 63. Table 1 shows the correlation between LVFP and E/regional e′ by ischemic territory. In patients with single-vessel disease, LVFP correlated with E/regional e′. In terms of ischemic territory, the association was weaker in the LAD-culprit subgroup than in other vessel-culprit subgroups. For assessing LVFP by E/regional e' method, average e′ was not superior to any regional e′.

Table 1. Pearson correlations between E/regional e′ and LVFP according to coronary vascular conditions

Coronary anatomy		Pearson correlation with LVFP									
		E/anterior e′		E/septal e′		E/lateral e′		E/inferior e′		E/average e′	
		Correlation	p value	Correlation	p value	Correlation	p value	Correlation	p value	Correlation	p value
Single-vessel disease	All (N = 219)	0.498	< 0.0001	0.53	< 0.0001	0.517	< 0.0001	0.577	< 0.0001	0.569	< 0.0001
	LAD (N = 116)	0.339	< 0.0001	0.351	< 0.0001	0.335	< 0.0001	0.35	< 0.0001	0.378	< 0.0001
	LCX (N = 40)	0.781	< 0.0001	0.777	< 0.0001	0.816	< 0.0001	0.779	< 0.0001	0.828	< 0.0001
	RCA (N = 63)	0.643	< 0.0001	0.634	< 0.0001	0.562	< 0.0001	0.784	< 0.0001	0.66	< 0.0001
Multiple-vessel disease	N = 181	0.666	< 0.0001	0.66	< 0.0001	0.49	< 0.0001	0.484	< 0.0001	0.618	< 0.0001
All cases	N = 400	0.59	< 0.0001	0.604	< 0.0001	0.519	< 0.0001	0.544	< 0.0001	0.614	< 0.0001

E, early-diastolic velocity of mitral inflow; e′, early-diastolic velocity of mitral annulus; LAD, left anterior descending artery; LCX, left circumflex artery; LVFP, left ventricular filling pressure; RCA, right coronary artery.

For further analysis, patients were subdivided by LVEF level (Table 2). Compared to patients in other subgroups, those with severe systolic dysfunction (LVEF < 35%) had higher heart rate, higher Killip classification, higher ratios of respiratory failure and heart failure, lower TDI parameters (s′, e′ and a′), and higher E/regional e′ and LVFP. In patients with mild systolic dysfunction (LVEF 45-55%), the correlation between LVFP and E/regional e′ was relatively weaker than in other subgroups (Table 3).

Septal, anterior, lateral, inferior, and average e′ of mitral annulus were used to identify LVFP exceeding 15 mmHg by E/e′ method, and cutoff points were assessed by ROC curve analysis. Use of regional e′ and average e′ in this equation revealed comparable capability for assessing high LVFP (> 15 mmHg): E/septal e′ > 12.5, area under the curve (AUC) 0.731, sensitivity 67%, specificity 63%; E/anterior e′ > 13.5, AUC 0.742, sensitivity 66%, specificity 67%; E/lateral e′ > 10.2, AUC 0.718, sensitivity 65%, specificity 64%; E/inferior e′ > 11, AUC 0.742, sensitivity 66%, specificity 67%; E/average e′ > 11.2, AUC 0.739, sensitivity 68%, specificity 67%; all p < 0.0001 (Figure 1).

Of the 400 patients, 85 (21.3%) had severe pulmonary edema; 59 (14.8%) had respiratory failure requiring mechanical ventilation. In univariate logistic analysis, age, gender, diabetes, Killip score, coronary status, infarct type, creatinine level, LVEF, LVFP, and E/average e′ were associated with both severe pulmonary edema and respiratory failure (all p < 0.05). In initial multivariate logistic analysis comprising all significant univariate factors except E/average e′, only LVEF and LVFP were independent predictors of severe pulmonary edema; however, diabetes, LVEF and LVFP were independent predictors of respiratory failure (Table 4). Another multivariate logistic regression model was constructed in which E/e′ was used instead of the invasive LVFP to reflect the current preference for LVFP in clinical practice. Unlike LVFP, E/e′ doesn't offer the predictive power of the presence of severe pulmonary edema and respiratory failure.

DISCUSSION

TDI provides information about regional myocardial systolic and diastolic function. TDI of mitral annulus is considered an accurate and reproducible measure of global LV systolic and diastolic function.[16-20] E/e′ reportedly correlates with pulmonary capillary wedge pressure and LVFP,[4,21,22] and it can be used to predict prognosis in patients with coronary artery disease,[23] chronic heart failure,[24] or in patients who have been intubated in an intensive care unit.[25] In a relatively healthy population with a low anticipated mortality rate, LVFP, as determined by cardiac catheterization and E/e′, is also an

Table 2. Comparison of patient characteristics and echocardiographic parameters according to left ventricular ejection fraction (LVEF)

Variable		Normal systolic function, LVEF ≥ 55% (n = 58)	Mild systolic dysfunction, 45% ≤ LVEF < 55% (n = 160)	Moderate systolic dysfunction, 35% ≤ LVEF < 45% (n = 132)	Severe systolic dysfunction, LVEF < 35% (n = 50)	p value
Sex (F/M)		14/44	31/129	24/108	7/43	0.142
Diabetes (%)		15 (26%)	54 (34%)	52 (39%)	24 (48%)	0.001
Hypertension (%)		30 (52%)	92 (58%)	77 (58%)	35 (70%)	0.001
Current Smoker (%)		34 (59%)	97 (61%)	78 (59%)	31 (62%)	0.367
Respiratory failure (%)		1 (2%)	20 (13%)	19 (14%)	19 (38%)	< 0.0001
IABP (%)		0 (0%)	0 (0%)	6 (5%)	10 (20%)	< 0.0001
Fluid supply (%) during PCI		0 (0%)	2 (1.3%)	1 (0.8%)	0 (0%)	0.832
Diuretic (%) during PCI		0 (0%)	0 (0%)	24 (18.2%)	16 (32%)	0.002
Age (years)		57 ± 13	64 ± 13	67 ± 15	67 ± 12	< 0.0001*†‡§
Creatinine > 1.5 mg/dL (%)		12 (21%)	28 (18%)	23 (17%)	8 (16%)	0.247
LDL-Cholesterol (mg/dL)		110 ± 29	114 ± 34	110 ± 37	115 ± 32	0.09
Heart rate (BPM)		70 ± 13	70 ± 12	79 ± 14	89 ± 14	< 0.0001†‡§‖#
Killip level (1-4)		1.3 ± 0.6	1.7 ± 0.8	2.1 ± 0.9	2.5 ± 0.8	< 0.0001*†‡§‖#
Peak creatinine kinase (U/L)		1272 ± 1273	2019 ± 1752	2647 ± 2496	2593 ± 2840	< 0.0001*†‡§
Mitral E velocity (cm/s)		71 ± 19	74 ± 21	75 ± 23	92 ± 25	< 0.0001‡‖#
Mitral A velocity (cm/s)		72 ± 19	78 ± 19	77 ± 25	66 ± 26	0.009‖#
Deceleration time (ms)		198 ± 47	198 ± 48	186 ± 55	156 ± 44	< 0.0001‡‖#
LV ejection fraction (%)		60.0 ± 3.5	50.2 ± 2.8	41.0 ± 2.7	31.1 ± 3.1	< 0.0001*†‡§‖#
Septal mitral annulus	s′ (cm/s)	7.4 ± 1.9	6.4 ± 1.5	5.6 ± 1.4	4.8 ± 1.3	< 0.0001*†‡§‖#
	e′ (cm/s)	7.0 ± 2.4	5.7 ± 1.8	5.0 ± 1.7	4.7 ± 2.0	< 0.0001*†‡§‖
	a′ (cm/s)	8.7 ± 1.8	7.8 ± 1.8	6.9 ± 1.8	5.9 ± 1.8	< 0.0001*†‡§‖#
Anterior mitral annulus	s′ (cm/s)	7.0 ± 1.9	6.1 ± 1.5	5.3 ± 1.4	4.5 ± 1.3	< 0.0001*†‡§‖#
	e′ (cm/s)	6.7 ± 2.4	5.5 ± 1.8	4.7 ± 1.7	4.4 ± 2.1	< 0.0001*†‡§‖
	a′ (cm/s)	8.5 ± 1.8	7.6 ± 1.8	6.7 ± 1.8	5.7 ± 1.7	< 0.0001*†‡§‖#
Lateral mitral annulus	s′ (cm/s)	9.0 ± 2.3	7.8 ± 2.1	6.8 ± 2.1	6.1 ± 2.2	< 0.0001*†‡§‖#
	e′ (cm/s)	8.6 ± 2.3	7.1 ± 2.5	6.6 ± 2.5	6.6 ± 2.8	< 0.0001*†‡
	a′ (cm/s)	10.1 ± 2.5	9.3 ± 2.4	8.3 ± 2.8	7.1 ± 2.7	< 0.0001†‡§‖#
Inferior mitral annulus	s′ (cm/s)	9.2 ± 2.0	7.9 ± 2.1	7.0 ± 2.0	6.4 ± 1.9	< 0.0001*†‡§‖
	e′ (cm/s)	8.0 ± 2.8	6.8 ± 2.4	6.0 ± 2.4	6.0 ± 2.3	< 0.0001*†‡§‖
	a′ (cm/s)	9.9 ± 2.7	9.1 ± 2.1	8.5 ± 2.6	7.7 ± 2.3	< 0.0001*†‡§‖#
Mitral E/Septal e′		11.1 ± 4.6	13.8 ± 4.7	16.3 ± 6.1	21.9 ± 8.2	< 0.0001*†‡§‖#
Mitral E/Anterior e′		11.9 ± 4.9	14.6 ± 5.1	17.6 ± 6.6	23.8 ± 8.7	< 0.0001*†‡§‖#
Mitral E/Lateral e′		9.5 ± 4.9	11.9 ± 6.4	13.1 ± 6.6	16.5 ± 8.1	< 0.0001*†‡‖#
Mitral E/Inferior e′		10.3 ± 4.9	11.8 ± 4.5	14.0 ± 6.1	15.8 ± 6.7	< 0.0001*†‡§‖
Mitral E/Average e′		10.1 ± 4.6	12.3 ± 4.6	14.1 ± 6.4	18.0 ± 6.7	< 0.0001*†‡§‖#
LVFP (mmHg)		14.5 ± 4.3	16.8 ± 5.0	20.8 ± 6.5	25.7 ± 6.4	< 0.0001*†‡§‖#

Analysis of variance in acute myocardial infarction patients; * normal systolic function versus mild systolic dysfunction, $p < 0.05$ in post hoc analysis; † normal systolic function versus moderate systolic dysfunction, $p < 0.05$ in post hoc analysis; ‡ normal systolic function versus severe systolic dysfunction, $p < 0.05$ in post hoc analysis; § mild systolic dysfunction versus moderate systolic dysfunction, $p < 0.05$ in post hoc analysis; ‖ mild systolic dysfunction versus severe systolic dysfunction, $p < 0.05$ in post hoc analysis; # moderate systolic dysfunction versus severe systolic dysfunction, $p < 0.05$ in post hoc analysis; a′, late-diastolic velocity of mitral annulus; e′, early-diastolic velocity of mitral annulus; IABP, intra-aortic balloon pump; LDL, low-density lipoprotein; LVFP, left ventricular filling pressure; PCI, percutaneous coronary intervention; s′, systolic velocity of mitral annulus.

Table 3. Pearson correlations between E/regional e′ and LVFP according to left ventricular systolic function

		Pearson correlation of LVFP									
		E/anterior e′		E/septal e′		E/lateral e′		E/inferior e′		E/average e′	
		Correlation	p value	Correlation	p value	Correlation	p value	Correlation	p value	Correlation	p value
Normal systolic function (LVEF ≥ 55%)	N = 58	0.518	< 0.0001	0.544	< 0.0001	0.626	< 0.0001	0.678	< 0.0001	0.598	< 0.0001
Mild systolic dysfunction (45% ≤ LVEF < 55%)	N = 160	0.371	< 0.0001	0.383	< 0.0001	0.419	< 0.0001	0.393	< 0.0001	0.446	< 0.0001
Moderate systolic dysfunction (35% ≤ LVEF < 45%)	N = 132	0.517	< 0.0001	0.553	< 0.0001	0.485	< 0.0001	0.523	< 0.0001	0.559	< 0.0001
Severe systolic dysfunction (LVEF < 35%)	N = 50	0.511	< 0.0001	0.629	< 0.0001	0.441	< 0.0001	0.418	< 0.0001	0.612	< 0.0001

LVEF, left ventricular ejection fraction; LVFP, left ventricular filling pressure.

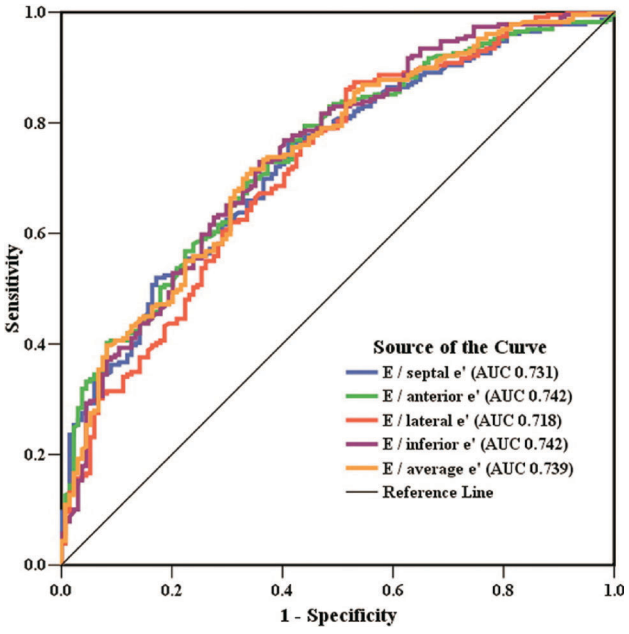

Figure 1. *ROC curves for LVFP > 15 mmHg.*

independent predictor of future heart failure.[26] As a well-known characteristic of TDI, it offers the systolic and diastolic function of the regional area. Therefore, while it is used for assessing global function of LV, it may be better suited for assessing conditions in which regional dysfunctions are concordant with global changes, such as dilated cardiomyopathy and post-remodeling status after AMI. In the current study, the correlation between E/regional e′ and LVFP was weaker in patients with mild LV systolic dysfunction than in other subgroups. This supports our hypothesis that, in the case of a regional condition parallel to a global condition, whether positive or negative, regional TDI parameters may provide a more accurate indication of global LV function.

Specifically, in AMI with single-vessel disease, s′ and e′ in all four locations of the mitral annuluses decreased globally in comparison with normal subjects, regardless of culprit lesion site (Table 5). Generally, MI in any region should affect TDI parameters in other regions, even in patients with single-vessel disease. This study revealed no evidence of hyperdynamic compensation in the non-ischemic regions of the LV. This may reflect early remodeling after AMI onset and may explain why regional TDI parameters, even those for sites other than the culprit site, predict global diastolic function and LVFP in AMI patients. However, because global reduction in e′ is not perfectly symmetrical, E/regional e′ has limited value for estimating LVFP in AMI patients.

Regardless of whether regional e′ or average e′ was

Table 4. Multivariate logistic analysis according to presence of either severe pulmonary edema or respiratory failure with ventilator

Characteristic	For severe pulmonary edema				For respiratory failure with ventilator			
	Odds ratio	95% CI	Wald X^2	p value	Odds ratio	95% CI	Wald X^2	p value
NSTEMI	1.313	0.966-1.785	3.034	0.082	1.192	0.866-1.642	1.158	0.282
Multi-vessel disease	0.973	0.734-1.290	0.036	0.85	1.076	0.786-1.474	0.209	0.648
Age (per 1 year increase)	1.013	0.991-1.035	1.301	0.254	1.023	0.997-1.049	3.104	0.078
Diabetes	1.12	0.609-2.059	0.133	0.716	2.301	1.191-4.445	6.146	0.013
Creatinine (per 1mg/dL increase)	1.019	0.852-1.220	0.044	0.835	1.054	0.884-1.257	0.341	0.599
Female gender	1.183	0.580-2.412	0.214	0.644	1.15	0.544-2.430	0.134	0.715
LVEF (per 1% increase)	0.944	0.908-0.982	8.37	0.004	0.95	0.910-0.993	5.271	0.022
LVFP (per 1 mmHg increase)	1.13	1.074-1.190	22.048	< 0.0001	1.077	1.021-1.135	7.503	0.006
Values obtained when using E/average e′ instead of LVFP								
NSTEMI	1.42	1.067-1.890	5.776	0.016	1.259	0.925-1.714	2.151	0.184
Multi-vessel disease	0.938	0.718-1.224	0.225	0.635	1.065	0.783-1.447	0.161	0.688
Age (per 1 year increase)	1.014	0.993-1.035	1.601	0.206	1.025	1.001-1.051	3.702	0.034
Diabetes	1.204	0.680-2.131	0.404	0.525	2.371	1.249-4.500	6.973	0.008
Creatinine (per 1mg/dL increase)	1.052	0.891-1.242	0.356	0.551	1.077	0.908-1.277	0.729	0.393
Female gender	1.278	0.643-2.541	0.49	0.484	1.263	0.598-2.669	0.374	0.541
LVEF (per 1% increase)	0.907	0.875-0.940	28.292	< 0.0001	0.926	0.890-0.964	14.248	< 0.0001
E/average e′ (per 1unit increase)	1.038	0.990-1.087	2.424	0.119	1.02	0.970-1.073	0.602	0.438

NSTEMI, Non-ST segment elevation myocardial infarction; other abbreviations as given in Table 2.

Table 5. Summary of patient characteristics and echocardiographic parameters for three acute myocardial infarction (AMI) groups with single-vessel disease

Variable		Control (N = 45)	AMI with only LAD lesion (N = 116)	AMI with only LCX lesion (N = 40)	AMI with only RCA lesion (N = 63)
Fluid supply (%) during PCI			0 (0%)	0 (0%)	3 (4.8%)
Diuretic (%) during PCI			14 (12.1%)	2 (5%)	2 (3.2%)
Mitral E velocity (cm/s)		80 ± 36	70 ± 19	75 ± 21	80 ± 23
Mitral A velocity (cm/s)		75 ± 25	76 ± 20	78 ± 23	72 ± 19
Deceleration time (ms)		222 ± 61	186 ± 46	186 ± 48	183 ± 40
LV ejection fraction (%)		57 ± 8	45 ± 9	49 ± 7	50 ± 7
Septal mitral annulus	s′ (cm/s)	7.3 ± 1.6	6.3 ± 1.7	6.9 ± 2	6.5 ± 1.5
	e′ (cm/s)	6.6 ± 2.6	5.7 ± 2.0	6.2 ± 2.4	6.5 ± 2.1
	a′ (cm/s)	8.3 ± 2.3	7.8 ± 1.9	8.3 ± 2.2	8.1 ± 1.7
Anterior mitral annulus	s′ (cm/s)	7.1 ± 1.9	5.3 ± 1.7	6.8 ± 2.0	6.5 ± 1.5
	e′ (cm/s)	6.9 ± 2.0	4.8 ± 2.0	6.0 ± 2.4	6.4 ± 2.0
	a′ (cm/s)	8.4 ± 2.1	7.1 ± 1.9	8.3 ± 2.4	7.6 ± 1.7
Lateral mitral annulus	s′ (cm/s)	9.6 ± 2.3	7.9 ± 2.4	7.2 ± 2.2	8.3 ± 2.3
	e′ (cm/s)	8.3 ± 3.1	7.3 ± 2.8	7.0 ± 2.6	8.3 ± 2.8
	a′ (cm/s)	9.7 ± 2.9	9.4 ± 2.6	9.2 ± 2.9	9.1 ± 2.5
Inferior mitral annulus	s′ (cm/s)	8.9 ± 2.1	8.2 ± 2.1	8.0 ± 2.1	7.8 ± 2.1
	e′ (cm/s)	8.0 ± 2.5	7.0 ± 2.7	7.2 ± 3.2	7.4 ± 2.7
	a′ (cm/s)	9.4 ± 2.4	9.3 ± 2.4	9.3 ± 3.1	9.2 ± 2.8
Mitral E/Septal e′		12.6 ± 5.2	13.3 ± 5.1	14.1 ± 6.1	13.2 ± 4.4
Mitral E/Anterior e′		12.0 ± 5.4	17.1 ± 7.5	14.5 ± 7.2	13.2 ± 4.5
Mitral E/Lateral e′		10.5 ± 5.5	11.7 ± 5.9	12.0 ± 7.0	10.6 ± 5.3
Mitral E/Inferior e′		11.2 ± 7.3	11.7 ± 4.8	12.9 ± 7.0	11.9 ± 5.2
LVFP (mmHg)		12.1 ± 5.2	18.8 ± 5.6	17.4 ± 6.9	17.3 ± 5.5

Abbreviations as given in Table 2.

used to estimate LVFP > 15 mmHg in the AMI patients, both sensitivity and specificity were lower than 70%, and no single regional e′ proved superior in terms of predictive accuracy (Figure 1). Bivariate correlation analysis corresponding to culprit lesion revealed a much weaker relationship between E/regional e′ and LVFP in patients with a single LAD-culprit lesion than in other patient subgroups. Unfortunately, MI with single LAD-culprit lesion comprises 30-40% of primary PCI in our Catheterization laboratory. A possible reason why E/e′ is unsuitable for assessing LVFP in MI with a single culprit lesion in LAD is that the Doppler method tracks movement velocity and cannot separate active contraction from passive tethering. AMI in the LAD territory usually affects the mid-to-apical anterior and anteroseptal walls, with only minimal effect on basal segments. Thus, the septal mitral annulus where e′ is measured is not directly involved, and the TDI parameters reflect passive tethering. In contrast, MI in the LCX or RCA territories usually affects the basal segments and influences the mitral annulus motion detected by TDI. Second, the change of systolic function is relatively larger in single-vessel LAD-culprit MI than in single-vessel LCX- or RCA-culprit MI (LVEF 45% vs. 49% vs. 50%; Table 5). Thus, the discordance between infarct and non-infarct zones is larger in single-vessel LAD-culprit MI. This also suggests that the accuracy of regional TDI parameters for assessing global function is questionable in this condition.

Given that some earlier works have cast doubt on the accuracy of E/e′ in isolation for the prediction of LVFP,[27-30] the current study is the first large prospective investigation to assess the accuracy of E/e′ for estimating LVFP in AMI patients according to infarct zone, vascular status, and LVEF level. The finding that E/regional e′ is an unreliable indicator of LVFP substantially differs from those findings reported in previous articles.[4,21] A possible explanation is that our patient population was a homogenous group of AMI patients who had received primary PCI.

Although one year all-cause mortality of AMI is associated with high E/e′ (E/septal e′ > 15 or E/lateral e′ > 10) according to the reports of Hillis et al.[23] and Moller et al.,[31] few Medline-published articles have discussed the correlation between E/e′ and LVFP during the acute phase of AMI. Additionally, no article has reported the power of E/e′ to predict severe heart failure complicated with profound pulmonary edema and respiratory failure. Acute cardiogenic pulmonary edema in AMI results from increased LVFP associated with systolic and/or diastolic LV dysfunction. Elevated LVFP forces capillary fluid into the pulmonary interstitial and alveolar spaces. In AMI patients hospitalized in coronary care units, the mortality rate is 21-57% in those with pulmonary edema,[9,32-34] and 51-55% in those requiring mechanical ventilation after respiratory failure.[35] The current study showed that E/e′ is not a reliable independent predictor of severe pulmonary edema and respiratory failure. In daily practice, particularly in an intensive coronary care unit, estimated LVFP is crucial to guide treatment management, and the need for an accurate, non-invasive assessment tool to predict LVFP with accuracy is of paramount importance. Therefore, it is better to propose new methods for assessing global diastolic function for AMI patients.

This study had some limitations. First, in some cases, preload may have been altered by use of diuretics, inotropic drugs, fluid challenge or ventilators. Since mitral E is preload-dependent, this may have influenced the mitral E velocity and E/A ratios. However, this problem was unavoidable in this patient group. Second, the mitral E and A, as well as e′ and a′, became completely merged at heart rates > 110 bpm. Peak velocities of merging E and A waves were used as E velocities in 12 cases, and peak velocities of merging e′ and a′ were used as e′ velocities in 6 cases. Although actual velocities of E or e′ in sinus tachycardia could not be identified, Nagueh et al. reported that the peak velocities of merging mitral E and A wave substituted for E velocity were acceptable for assessing LVFP by E/e′.[36] Third, LVFP was measured using fluid-filled pig-tail catheters and was not obtained at end expiration since many patients could not tolerate holding their breath. Although micromanometer-tipped catheters would have been ideal, this would have limited our sample size. Furthermore, the method used to measure LVFP was the standard used in the clinical setting and has been well-validated.

CONCLUSION

In conclusion, the E/regional e′ has limited efficacy

for assessing LVFP in AMI patients because correlations are weak in patients with single LAD-culprit MI or mild systolic dysfunction. Moreover, for assessing LVFP, average e′ is not superior to septal, anterior, lateral, or inferior e′. Although LVFP correlates well with severe pulmonary edema and respiratory failure, the use of E/e′ to represent LVFP to help predict these two critical conditions in the multivariate analysis model is unreliable.

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