

E/e' as a Predictor of Short-Term Survival Following ST-Elevation Myocardial Infarction

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Received 15 May 2015; accepted 16 November 2015; published 19 November 2015

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Abstract

Background: We examined the usefulness of tissue Doppler imaging in evaluating the diastolic dysfunction and assessed the prognostic value of ratio between early mitral inflow velocity and mitral annular early diastolic velocity (E/e') in unselected patients with acute ST-elevation myocardial infarction (STEMI). **Methods:** Patients presenting with acute STEMI at Osmania General Hospital, Hyderabad, India between January-2012 and June-2012 were examined in this study. All patients underwent echocardiographic examination comprising Doppler assessment of transmitral flow velocities (peak E-wave velocity) and Doppler tissue imaging of the medial mitral valve annulus (e'). All patients were followed up for 6 months and all-cause mortality was measured as the study endpoint. Role of E/e' ratio as a predictor of survival after acute STEMI was evaluated by a comparative analysis of patients with E/e' ≤ 15 and >15 . **Results:** A total of 50 patients with acute STEMI (mean age: 52.2 ± 13.2 years; 80% males) were analyzed in this study. Of them, 23 (46%) patients had an E/e' >15 . Clinical parameters such as Killip class ≥ 2 as well as left ventricular ejection fraction of $<40\%$ were significantly associated with E/e' >15 . Five (10%) patients died during the 6-month follow-up period. All deaths occurred among patients from the E/e' >15 group, indicating that E/e' is an effective predictor of overall survival. **Conclusion:** E/e' ratio was identified as a strong predictor of survival after acute myocardial infarction and can be suitable for risk-stratification of patients in this setting. Further studies are warranted to substantiate the findings.

Keywords

ST-Elevated Myocardial Infarction, Echocardiography, Transmitral Flow Velocity, Medial Mitral Valve Annulus, E/e' Ratio, Survival

1. Introduction

Coronary artery disease is the leading cause of morbidity and mortality worldwide, and acute myocardial infarction is the most common mode of its presentation [1]. In patients with myocardial infarction, measurement of left ventricular diastolic dysfunction is important in decision-making and predicting the mortality because it is associated with progressive left ventricular dilatation, development of heart failure, and cardiac death [2]. Although invasive cardiac catheterization is the gold standard to measure left ventricular filling, it carries the risk of subsequent complications [3]. In this regard, echocardiography using tissue Doppler imaging has emerged as a valuable non-invasive tool, with similar predictive value as compared to cardiac catheterization [3] [4]. Doppler tissue imaging of mitral valve annulus appears to be particularly useful, and reduced early mitral annulus velocity (e') indicates impaired myocardial relaxation [2]. In addition, the ratio of early transmitral flow velocity (E) to early diastolic septal mitral annulus velocity (E/e') correlates well with left ventricular diastolic dysfunction [5] [6]. The prognostic value of $E/e' > 15$ following myocardial infarction has been evaluated previously in a study by Hillis *et al.* [2]. They indicated that E/e' is a powerful predictor of survival after acute myocardial infarction. Subsequently, E/e' ratio has become central in the guidelines for left ventricular diastolic evaluation [7]. However, till date no study from India has substantiated the prognostic value of E/e' following myocardial infarction. In these lines, we examined the usefulness of tissue Doppler imaging in evaluating the diastolic dysfunction and assessed the prognostic value of E/e' in unselected patients with acute ST-elevation myocardial infarction (STEMI).

2. Methods

2.1. Study Population

In this prospective cohort study, patients presenting with acute STEMI with or without thrombolysis at Osmania General Hospital, Hyderabad, India between January-2012 and June-2012 were examined. Patients with NSTEMI, unstable angina, or post-infarction angina and patients presenting after more than 7 days of onset of myocardial infarction were excluded.

2.2. Data Collection Statistical Analyses

Baseline characteristics and details of clinical presentation including the Killip-Kimball classification based on the first physical examination on admission, history and previous treatments were noted. All patients underwent echocardiographic examination comprising Doppler assessment of transmitral flow velocities and Doppler tissue imaging of the medial mitral valve annulus (Figure 1). Here, the left ventricular systolic function was measured

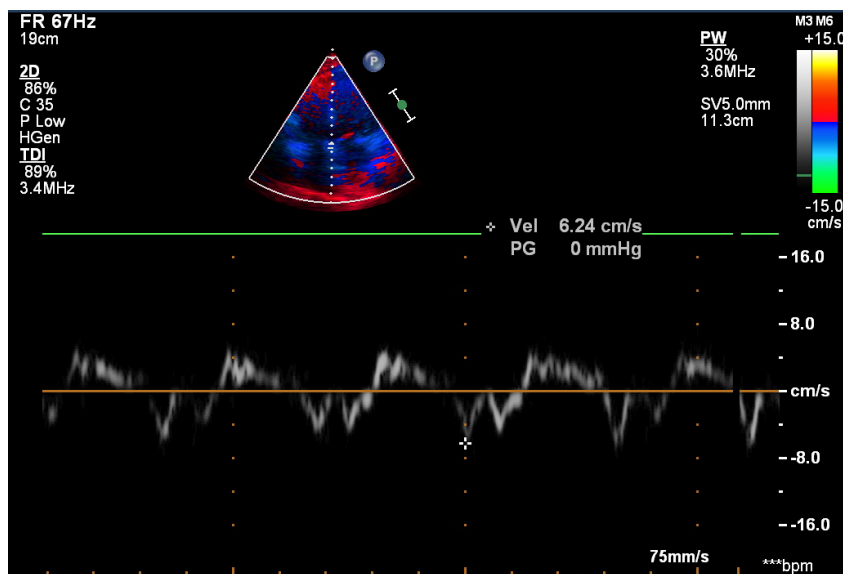


Figure 1. Tissue Doppler imaging of mitral annulus.

semi-quantitatively using a visually estimated left ventricular ejection fraction (LVEF). In addition, left ventricle dimensions, including and left ventricular end-systolic diameter (LVESD) and left ventricular end-diastolic diameter (LVESDD) were estimated. Mitral regurgitation was graded using color flow imaging. Mitral inflow was evaluated in the apical four-chamber view, using pulsed-wave Doppler echocardiography. Subsequently, peak E-wave and peak A-wave velocities were estimated from the mitral inflow profile. Tissue Doppler imaging of the mitral annulus was obtained from the apical four-chamber view to measure e' and a' . Further, the decision to treat with thrombolytic therapy was at the discretion of treating cardiologist. Severity of coronary artery disease was examined by elective coronary angiography. Subsequently, elective revascularization by PCI/CABG was performed. All patients were prospectively followed-up for 6 months to analyze patients' survival. All-cause death was estimated as the study end point.

Since E/e' ratio >15 is reported to be the best Doppler predictor of an elevated (>12 mm Hg) mean left ventricular diastolic pressure (mLVDP), clinical characteristics, echocardiographic characteristics, and survival outcomes were compared between patients with E/e' ratio >15 and patients with E/e' ratio ≤ 15 .

2.3. Statistical Analyses

The Statistical Package for Social Sciences (SPSS; Chicago, IL, USA) program, version 15 was used for statistical analysis. Continuous data are expressed as mean \pm standard deviation and are compared using the Mann Whitney U test. Categorical data are presented as frequencies and percentages and are compared using the Chi-square test or Fisher exact test. Correlations were calculated using the Spearman rho test and independent predictors of an elevated E/e' ratios were identified by regression analyses. Survival was plotted according to the Kaplan-Meier method, and mortality rates were compared using the log-rank test. P value of <0.05 was considered as statistically significant.

3. Results

3.1. Clinical Characteristics

A total of 50 patients, 40 males and 10 females, with acute STEMI were analyzed in this study. Baseline characteristics of overall patients, along with a comparative analysis of patients with $E/e' \leq 15$ and >15 are given in **Table 1**.

The mean age of overall patients was 52.2 ± 13.2 years. Of them, 23 (46%) patients had an $E/e' >15$. Patients with $E/e' >15$ were significantly older than patients with $E/e' \leq 15$ (57.65 ± 12.7 vs. 47.6 ± 12.0 years, $P = 0.012$). Further, diabetes mellitus ($n = 12$, 80%; $P = 0.002$), hypertension ($n = 18$, 58%; $P = 0.029$) were significantly more common among patients with $E/e' >15$. In addition, patients with $E/e' >15$ were significantly more

Table 1. Baseline clinical characteristics.

Characteristics	All patients (n = 50)	Patients with $E/e' \leq 15$ (n = 27)	Patients with $E/e' >15$ (n = 23)	P value
Age in years	52.2 ± 13.2	47.6 ± 12.0	57.65 ± 12.7	0.012
Age >45 years	26 (52%)	11 (42%)	15 (58%)	0.084
Male gender	40 (80%)	22 (55%)	18 (45%)	0.778
Hypertension	31 (62%)	13 (42%)	18 (58%)	0.029
Diabetes mellitus	15 (30%)	3 (20%)	12 (80%)	0.002
Smoker	23 (46%)	13 (56%)	10 (44%)	0.741
Killips class ≥ 2	14 (28%)	4 (28%)	10 (72%)	0.024
Anterior wall STEMI	33 (66%)	16 (48%)	17 (52%)	0.276
Posterior wall STEMI	3 (6%)	1 (33%)	2 (67%)	0.549
Thrombolytic therapy	24 (48%)	13 (54%)	11 (46%)	0.982

E, Early transmitral flow velocity; e' , Early diastolic septal mitral annulus velocity; STEMI, ST-elevation myocardial infarction.

likely to present with worse clinical profile, as determined by high frequency of the Killip class ≥ 2 on admission ($P = 0.024$). There were no differences in occurrence of AWTMI and requirement for inotropic support in both groups. There were moderate correlations between Killip class ≥ 2 E/e' ratio >15 (odds ratio: -2.93 ; $P = 0.025$). Treatment with thrombolytic therapy was similar in both groups.

3.2. Echocardiographic Characteristics

The echocardiographic characteristics for the entire study cohort along with a comparison of patients with E/e' ratio >15 and ≤ 15 are given in **Table 2**. Patients with an E/e' ratio >15 exhibited worse systolic function, as determined by the LVEF. Accordingly, the frequency of patients with LVEF $<55\%$ as well as LVEF $<40\%$ was significantly higher in E/e' >15 group, indicating more severe heart failure in patients with E/e' ratio >15 . LVEF $<40\%$ was also identified as an independent clinical predictor of E/e' ratio >15 (odds ratio: 6.6, 95% confidence interval: 1.1 to 20; $P = 0.01$). LVESD and LVESDD were comparable between two groups, while cases of E/A ratio >2 were non-significantly higher in the E/e' >15 group.

3.3. Angiographic Characteristics and In-Hospital Revascularization

Table 3 represents the angiographic characteristics and in-hospital revascularization for all patients' enrolled in

Table 2. Echocardiographic characteristics.

Characteristics	All patients (n = 50)	Patients with E/e' ≤ 15 (n = 27)	Patients with E/e' >15 (n = 23)	P value
LVEF (%)	51.4 \pm 11.1	54.1 \pm 11.2	48.3 10.3	0.045
LVEF $<55\%$	31 (62%)	13 (42%)	18 (58%)	0.029
LVEF $<40\%$	10 (20%)	2 (20%)	8 (80%)	0.016
LVESD (cm)	3.3 \pm 0.7	3.2 \pm 0.7	3.5 \pm 0.7	0.068
LVESDD (cm)	4.7 \pm 0.7	4.6 \pm 0.7	4.8 \pm 0.6	0.297
Peak E-wave velocity (cm/s)	93.2 \pm 20.1	82.4 \pm 19.8	106.0 \pm 10.8	<0.001
Peak A-wave velocity (cm/s)	64.6 \pm 21.7	64.7 \pm 19.5	64.4 \pm 24.5	0.823
E/A ratio	1.7 \pm 0.9	1.4 \pm 0.5	1.9 \pm 1.1	0.086
E/A ratio >2	11 (22%)	4 (36%)	7 (64%)	0.184
e' (cm/s)	7.2 \pm 2.6	8.8 \pm 2.4	5.3 \pm 1.1	<0.001
a' (cm/s)	8.4 \pm 2.1	9.2 \pm 1.8	7.6 \pm 2.5	0.076
E/e' ratio	14.7 \pm 7.1	9.5 \pm 2.0	20.8 \pm 5.9	<0.001
Mitral regurgitation	8 (16%)	2 (25%)	6 (75%)	0.072

E, Early transmitral flow velocity; A, Late transmitral flow velocity; e', Early diastolic septal mitral annulus velocity; a', Late diastolic septal mitral annulus velocity LVEF, Left ventricular ejection fraction; LVESD, Left ventricular end-systolic diameter; LVESDD, Left ventricular end-diastolic diameter.

Table 3. Angiographic characteristics, in-hospital revascularization, and survival outcomes.

Characteristics	All patients (n = 50)	Patients with E/e' ≤ 15 (n = 27)	Patients with E/e' >15 (n = 23)	P value
Angiographic characteristics				
Underwent coronary angiography	45 (90%)	26 (58%)	19 (42%)	0.108
Single-vessel disease	28 (56%)	18 (64%)	10 (36%)	0.099
Double-vessel disease	13 (26%)	8 (61%)	5 (39%)	0.526
Triple-vessel disease	4 (10%)	0 (0%)	4 (100%)	0.024
In-hospital revascularization				
PCI/CABG	9 (22%)	24 (%)	17 (%)	0.169
Survival outcomes				
Death	5 (12%)	0 (0%)	5 (100%)	0.011

E, Early transmitral flow velocity; e', Early diastolic septal mitral annulus velocity; PCI, Percutaneous coronary intervention; CABG, coronary artery bypass grafting.

the study. Four patients in $E/e' >15$ group and one patient in the $E/e' \leq 15$ group did not undergo coronary angiography. Single-vessel disease and double-vessel disease were non-significantly more frequent in the $E/e' \leq 15$ group while triple-vessel disease was significantly more frequent in the $E/e' >15$ group. Six patients from the $E/e' >15$ group and three patients from the $E/e' \leq 15$ group did not undergo PCI/CABG.

3.4. Survival Outcomes

Five (10%) patients died during the 6-month follow-up period (Table 3). All deaths occurred among patients from the $E/e' >15$ group, indicating that E/e' is an effective predictor of overall survival. The Kaplan-Meier analysis also substantiated the finding (Figure 2). The overall survival was 78.3% in $E/e' >15$ group compared to 100% in the $E/e' \leq 15$ group (log-rank $P = 0.011$).

4. Discussion

The echocardiogram is a standard tool in the management of patients with acute myocardial infarction. It is valuable in establishing the diagnosis, location, and extent of myocardial infarction [8] [9]. In the present study, the role of echocardiographic characteristics in providing prognostic information of survival following acute STEMI was assessed. We observed that the E/e' ratio was a strong predictor of survival after acute STEMI.

Earlier, Hillis *et al.* had conducted a study in similar lines [2]. They had found that E/e' was a powerful predictor of survival after acute myocardial infarction in 250 unselected patients followed up for a median duration of 13 months (risk ratio: 4.8; $p = 0.002$). Further, the prognostic value of E/e' was incremental to clinical factors and conventional echocardiographic parameters of left ventricular systolic and diastolic function [2]. Findings of the present study also substantiated the strong role E/e' in predicting the short-term survival in patients with acute STEMI. Notably, all deaths occurred exclusively in the $E/e' >15$ group. This can be interpreted as $E/e' \leq 15$ may have a strong association with survival, while the risk of all-cause death will be high in patients with $E/e' >15$ following STEMI. Obeidat *et al.* have also demonstrated the usefulness of echocardiographic predictors in prognosis of patients after first acute myocardial infarction [10].

In present study, impaired LVEF was more common among patients with E/e' ratio >15 . Further, LVEF $<40\%$ was identified as an independent clinical predictor of E/e' ratio >15 . Further, a high frequency of the Killip class ≥ 2 on admission was also evident among patients with $E/e' >15$. Similar to the observations of present study, Hillis *et al.* also reported a significant association of Killip Class ≥ 2 and left ventricular ejection fraction $\leq 40\%$ with E/e' ratio >15 [2]. We also observed that all cases of triple-vessel diseases occurred in $E/e' >15$ group, indicating a trend of severe coronary artery disease in patients with $E/e' >15$.

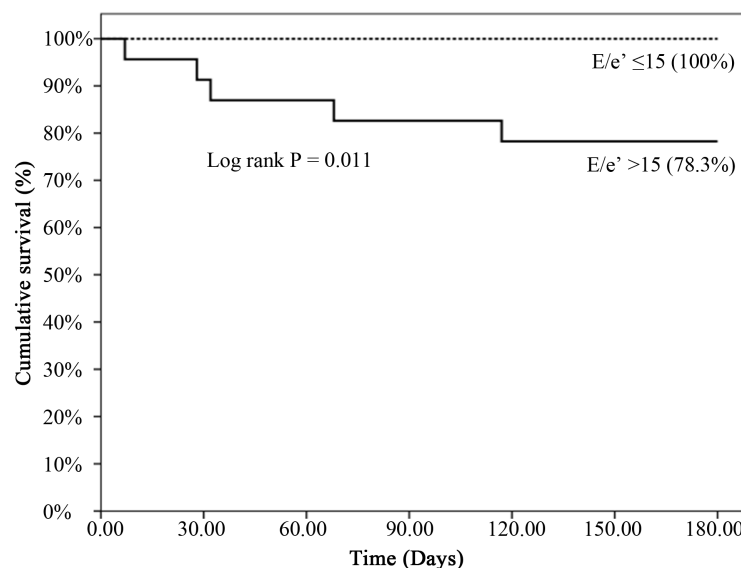


Figure 2. Kaplan-Meier plot of survival in STEMI patients stratified by $E/e' \leq 15$ and >15 .

Although the E/e' ratio is a robust marker in the prediction of left ventricular filling pressure, it is imperfect and should be interpreted with consideration of many situations such as severe mitral annular calcification, significant mitral stenosis, moderate-to-severe mitral regurgitation, severe left ventricular dysfunction, and hypertrophic cardiomyopathy. These conditions can be a source of misleading information in the setting of acute myocardial infarction [3].

Study Limitations

Our study has certain limitations: 1) the sample size is inadequate to draw conclusions in whole population; 2) echocardiographer was not blinded in this study, which might impact selection bias; 3) certain compounding factors like PCI/CABG and compliance of drug intake were not considered in the analysis, which might influence the study findings; 4) Since E/e' ratio reflects an instantaneous measure of left ventricular filling pressure, a single measurement may not convey maximal prognostic information as the left ventricular filling pressure may change over the course of the peri-infarct period; and 5) the follow-up period was only 6 months, which is not enough to draw significant conclusions of survival. We suggest that studies involving larger sample-size and long-term follow-up would offer necessary insights regarding the prognostic value of E/e' ratio. We are of opinion that echocardiographic estimation of E/e' can be used as a valuable bedside tool in the risk-stratification of the patients with acute myocardial infarction.

5. Conclusion

Findings of the present study suggest that an E/e' ratio >15 is a powerful predictor of decreased survival after acute STEMI. Further studies are warranted to substantiate the findings. However, we opine that measurement of E/e' may assist risk-stratification of patients in this setting.

References

- [1] Gaziano, T.A., Bitton, A., Anand, S., Abrahams-Gessel, S. and Murphy, A. (2010) Growing Epidemic of Coronary Heart Disease in Low- and Middle-Income Countries. *Current Problems in Cardiology*, **35**, 72-115. <http://dx.doi.org/10.1016/j.cpcardiol.2009.10.002>
- [2] Hillis, G.S., Moller, J.E., Pellikka, P.A., Gersh, B.J., Wright, R.S., Ommen, S.R., Reeder, G.S. and Oh, J.K. (2004) Noninvasive Estimation of Left Ventricular Filling Pressure by E/e' Is a Powerful Predictor of Survival after Acute Myocardial Infarction. *Journal of the American College of Cardiology*, **43**, 360-367. <http://dx.doi.org/10.1016/j.jacc.2003.07.044>
- [3] Park, J.H. and Marwick, T.H. (2011) Use and Limitations of E/e' to Assess Left Ventricular Filling Pressure by Echocardiography. *Journal of Cardiovascular Ultrasound*, **19**, 169-173. <http://dx.doi.org/10.4250/jcu.2011.19.4.169>
- [4] Liang, H.Y., Cauduro, S.A., Pellikka, P.A., Bailey, K.R., Grossardt, B.R., Yang, E.H., Rihal, C., Seward, J.B., Miller, F.A. and Abraham, T.P. (2006) Comparison of Usefulness of Echocardiographic Doppler Variables to Left Ventricular End-Diastolic Pressure in Predicting Future Heart Failure Events. *American Journal of Cardiology*, **97**, 866-871. <http://dx.doi.org/10.1016/j.amjcard.2005.09.136>
- [5] Ommen, S.R., Nishimura, R.A., Appleton, C.P., Miller, F.A., Oh, J.K., Redfield, M.M. and Tajik, A.J. (2000) Clinical Utility of Doppler Echocardiography and Tissue Doppler Imaging in the Estimation of Left Ventricular Filling Pressures: A Comparative Simultaneous Doppler-Catheterization Study. *Circulation*, **102**, 1788-1794. <http://dx.doi.org/10.1161/01.CIR.102.15.1788>
- [6] Poulsen, S.H. (2001) Clinical Aspects of Left Ventricular Diastolic Function Assessed by Doppler Echocardiography Following Acute Myocardial Infarction. *Danish Medical Bulletin*, **48**, 199-210.
- [7] Nagueh, S.F., Appleton, C.P., Gillebert, T.C., Marino, P.N., Oh, J.K., Smiseth, O.A., Waggoner, A.D., Flachskampf, F.A., Pellikka, P.A. and Evangelisa, A. (2009) Recommendations for the Evaluation of Left Ventricular Diastolic Function by Echocardiography. *European Journal of Echocardiography*, **10**, 165-193. <http://dx.doi.org/10.1093/ejechocard/jep007>
- [8] Cerisano, G. and Bolognese, L. (2001) Echo-Doppler Evaluation of Left Ventricular Diastolic Dysfunction during Acute Myocardial Infarction: Methodological, Clinical and Prognostic Implications. *Italian Heart Journal*, **2**, 13-20.
- [9] Shanks, M., Ng, A.C., van de Veire, N.R., Antoni, M.L., Bertini, M., Delgado, V., Nucifora, G., Holman, E.R., Choy, J.B., Leung, D.Y., Schali, M.J. and Bax, J.J. (2010) Incremental Prognostic Value of Novel Left Ventricular Diastolic Indexes for Prediction of Clinical Outcome in Patients with ST-Elevation Myocardial Infarction. *American Journal of*

Cardiology, **105**, 592-597. <http://dx.doi.org/10.1016/j.amjcard.2009.10.039>

- [10] Obeidat, O., Alam, M., Divine, G.W., Khaja, F., Goldstein, S. and Sabbah, H. (2004) Echocardiographic Predictors of Prognosis after First Acute Myocardial Infarction. *American Journal of Cardiology*, **94**, 1278-1280. <http://dx.doi.org/10.1016/j.amjcard.2004.07.112>