Relation of Ratio of Left Ventricular Ejection Fraction to Left Ventricular End-Diastolic Pressure to Long-Term Prognosis After ST-Segment Elevation Acute Myocardial Infarction

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Risk stratification of patients with ST-segment elevation acute myocardial infarction (STEMI) is suboptimal. We assessed the prognostic value of the left ventricular ejection fraction to left ventricular end-diastolic pressure (LVEF/LVEDP) ratio in patients with STEMI who underwent primary percutaneous coronary intervention (PPCI). The study included 1,283 patients with STEMI. LVEF and LVEDP were measured at the time of PPCI. The primary outcome was 8-year cardiac mortality. Patients were divided into 3 groups: a group with a LVEF/LVEDP ratio within the first tertile (LVEF/LVEDP ratio < 2; n = 437 patients), a group with a LVEF/LVEDP ratio within the second tertile (LVEF/LVEDP ratio 2 to 3; n = 422 patients), and a group with a LVEF/LVEDP ratio within third tertile (LVEF/LVEDP ratio > 3; n = 424 patients). There were 109 cardiac deaths during the follow-up: 55 (17.1%), 36 (10.9%), and 18 (6.5%) deaths occurring in patients of the first, second, and third LVEF/LVEDP ratio tertiles, respectively (adjusted hazard ratio = 0.80, 95% confidence interval 0.66 to 0.97, p = 0.022 for 1 unit increment in the LVEF/LVEDP ratio). LVEF/LVEDP ratio (p = 0.035) but not LVEF (p = 0.290) or LVEDP (p = 0.145) alone improved the risk prediction of the models for cardiac mortality (p values show the difference in C-statistics between the models without and with LVEF/LVEDP ratio, LVEF or LVEDP). In conclusion, in patients with STEMI who underwent PPCI, a lower LVEF/LVEDP ratio was independently associated with increased risk of cardiac mortality up to 8 years after PPCI. The LVEF/LVEDP ratio, but not LVEF or LVEDP alone improved predictivity of multivariable models with respect to long-term cardiac mortality. **(Am J Cardiol 2019;123:199−205)**

Although survival after ST-segment elevation acute myocardial infarction (STEMI) has improved due to timely diagnosis and reperfusion, greater use of primary percutaneous coronary intervention (PPCI) and secondary prevention strategies, patients with STEMI remain at risk of adverse events both acutely and in the longer term. Left ventricular ejection fraction (LVEF) predicts prognosis after STEMI[1−4] and this metric has been extensively used to risk stratify patients after STEMI. However, LVEF has a moderate discriminatory power for mortality prediction[5,6] and has limitations including missing information on the left ventricular size and mass and diastolic function.[7] In a sizeable portion (34%) of patients with STEMI, LVEF measured at the time of hospital discharge may not reflect the efficacy of reperfusion because this index may be discordant with infarct size apparently due to stunned myocardium and compensatory hyperkinesia in acute phase of STEMI.[8,9] Left ventricular end-diastolic pressure (LVEDP) reflects ventricular compliance[10] and an elevated LVEDP is associated with increased risk of in-hospital and longer term mortality in STEMI patients.[11−13] We undertook this study to assess the association of the LVEF to LVEDP (LVEF/LVEDP) ratio with long-term mortality in patients with STEMI treated with PPCI. We hypothesized that LVEF/LVEDP ratio may be a better prognosticator than LVEF or LVEDP after STEMI.

Methods

This investigation represents a retrospective study of 1,283 patients with STEMI admitted from January 2002 to December 2007 in 2 university hospitals in Munich, Germany. All patients underwent PPCI. STEMI was diagnosed based on typical chest pain, electrocardiographic criteria, and elevation of cardiac biomarkers. The diagnosis was confirmed by angiography. Details of the source sample were provided in a previous study.[14] Patients who underwent conservative therapy (n = 112), thrombolysis (n = 35), coronary artery bypass surgery as primary reperfusion (n = 18) and those with mechanical failures to open the

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occluded arteries (n = 31), angiograms of poor quality (n = 86) or missing scintigraphic studies (n = 173) or LVEF or LVEDP measurements (n = 123) at the time of PPCI were excluded. The study compiles with the Declaration of Helsinki.

Demographic data were collected in all patients. Cardiovascular risk factors (arterial hypertension, hyperlipidemia, diabetes mellitus, and smoking) were defined according to the standard criteria. Congestive heart failure was graded according to the Killip's classification.[15]

Primary stenting (1,130 patients; 88%) and pre- and postprocedural care were performed as per routine practice. Before procedure, patients received 325 to 500 mg of aspirin intravenously and a loading dose of 600 mg of clopidogrel. Unfractionated heparin was used for periprocedural anticoagulation as per routine practice. After procedure, patients received dual antiplatelet therapy consisting of a thienopyridine (mostly clopidogrel, 75 mg per day for at least 6 months) and aspirin (200 mg per day continuously). Other medications were prescribed at the discretion of the treating physician.

LVEDP was measured using a fluid-filled pigtail catheter placed in the left ventricle. The global LVEF was measured on the left ventricular angiograms according to the method by Sandler and Dodge.[16] Both LVEDP and LVEF measurements were performed before reperfusion or intra-aortic balloon pump implantation. Epicardial blood flow in the infarct-related artery was quantified according to the Thrombolysis in Myocardial Infarction (TIMI) Group criteria.[17] Collateral circulation was graded according to the Rentrop classification.[18] Serum creatinine, C-reactive protein, creatine kinase myocardial band, and cardiac troponin T were measured using commercially available assays. Body mass index was calculated using the patient' weight and height measured during the hospital course. Glomerular filtration rate was estimated according to the Cockcroft-Gault formula.[19] Initial area at risk and infarct size were assessed with paired scintigraphic studies using 99mTc-sestamibi single-photon emission computed tomography imaging performed after admission and 7 to 14 days after the PPCI, as previously reported.[20] Scintigraphic examinations were performed in the setting of studies conducted to assess salvaging capacity of coronary stenting in patients with STEMI.[20]

The primary outcome was 8-year cardiac mortality. All-cause mortality was also assessed. Cardiac death was defined according to the Academic Research Consortium criteria.[21] Patients were visited by their physician or interviewed by telephone at 1 month, 6 months, 1 year, and yearly thereafter. The hospital records, death certificates, or telephone contact with the family physician or relatives of the patient, insurance companies, or registration of address office were used to obtain information with respect to patient's survival status. The follow-up information and the adjudication of the events were performed by personnel blinded to the patients' clinical data.

Patients are categorized in groups according to the LVEF/LVEDP ratio tertiles. The Kolmogorov-Smirnov test was used to assess the distribution pattern of the continuous data. Continuous data with skewed distribution were presented as median (with twenty-fifth and seventy-fifth percentiles) and compared with the Kruskal-Wallis rank sum test. Discrete data were presented as counts (percentages) and compared with the chi-square test. Correlation between LVEF/LVEDP ratio and other variables was performed using the Spearman's rank correlation test. Multiple linear regression model was used to assess correlates of LVEF/LVEDP ratio. Variables to be entered into the model were selected using the Least Absolute Shrinkage and Selection Operator regression method. The following variables were entered into the model: heart rate, baseline TIMI flow grade, body mass index, hypercholesterolemia, C-reactive protein, glomerular filtration rate, anterior infarct location, Killip's class, and initial area at risk. Survival analysis was performed with the Kaplan-Meier method and the comparison in groups was performed using the univariable Cox proportional hazard model. The multivariable Cox proportional hazard model was used to test the association between LVEF/LVEDP ratio and mortality. Variables entered into the model (selected using the Least Absolute Shrinkage and Selection Operator regression method) were LVEF/LVEDP ratio, infarct size, heart rate, postprocedural TIMI flow grade, age, gender, diabetes, arterial hypertension, current smoker, previous myocardial infarction, previous coronary artery bypass surgery, baseline C-reactive protein, glomerular filtration rate, Killip's class, time-to-admission interval, multivessel disease, collateral class and therapy at discharge (aspirin, angiotensin-converting enzyme inhibitors, β-blockers and statins). The C-statistic of multivariable Cox models of mortality without and with incorporation of LVEF/LVEDP ratio was calculated to assess whether adding LVEF/LVEDP ratio improves prediction of mortality. Bootstrapping method (400 samples) was used to calculate the CI of the C-statistic, enable comparison of C-statistics of different models, and assess the stability of the results. The statistical analysis was performed using the R 3.4.0 Statistical Package (The R foundation for Statistical Computing, Vienna, Austria). A 2-sided $p < 0.05$ was considered as significant.

Results

The study included 1,283 patients with STEMI. The tertile values of LVEF/LVEDP ratio were used to divide patients into 3 groups: a group with LVEF/LVEDP ratio within the first tertile (LVEF/LVEDP ratio < 2; n = 437), a group with LVEF/LVEDP ratio within the second tertile (LVEF/LVEDP ratio 2 to 3; n = 422), and a group with LVEF/LVEDP ratio within third tertile (LVEF/LVEDP ratio > 3; n = 424). Baseline data are shown in Table 1. Previous myocardial infarction, peak creatine kinase myocardial band, peak cardiac troponin, C-reactive protein, infarct location, systolic blood pressure, diastolic blood pressure, heart rate, LVEF, LVEDP, Killip's class, proportion of patients with cardiogenic shock and aspirin prescription at discharge differed significantly in groups according to the LVEF/LVEDP ratio tertiles. Angiographic and procedural data are shown in Table 2. There were significant differences in the infarct-related coronary artery and baseline TIMI flow in groups according to the LVEF/LVEDP ratio tertiles. An intra-aortic balloon pump was implanted in 30 patients.

Table 1
Baseline data

Characteristic	LVEF/LVEDP ratio			p value
	Tertile 1 (n = 437)	Tertile 2 (n = 422)	Tertile 3 (n = 424)	
Age (years)	63 [52-72]	61 [52-72]	62 [54-71]	0.729
Women	101 (23%)	116 (27.5%)	95 (22%)	0.174
Body mass index (kg/m^2)	27 [24.5-29]	26 [24-28]	26 [24-29]	0.217
Type 2 diabetes mellitus	98 (22%)	74 (17.5%)	85 (20%)	0.201
On insulin therapy	15 (3%)	16 (4%)	16 (4%)	0.951
Arterial hypertension	308 (70.5%)	297 (70%)	295 (70%)	0.951
Current smoker	193 (44%)	186 (44%)	160 (38%)	0.093
Total cholesterol ($\geq$ 220 mg/dl)	241 (55%)	209 (49.5%)	218 (51%)	0.234
Previous myocardial infarction	68 (16%)	41 (10%)	42 (10%)	0.010
Previous coronary artery bypass surgery	17 (4%)	11 (3%)	13 (3%)	0.555
Peak troponin T (μg/L)	5.6 [2.5-10.8]	3.7 [2.0-6.0]	2.8 [1.25-4.9]	< 0.001
Peak creatine kinase myocardial band (U/L)	183 [75-382]	127 [70-258]	101 [52-187]	< 0.001
C-reactive protein (mg/L)	5.4 [0.3-12.5]	2.9 [0.0-8.0]	3.0 [0.0-10.0]	< 0.001
Glomerular filtration rate (ml/min)	84 [63-104]	84 [64-108]	86.5 [65-109]	0.552
Infarct location	271 (62%)	170 (40%)		< 0.001
Anterior	104 (24%)	195 (46%)	117 (28%)	
Posterior	62 (14%)	57 (14%)	230 (54%)	
Lateral			77 (18%)	
Systolic blood pressure (mm Hg)	131 [115-150]	130 [120-148]	130 [110-140]	0.012
Diastolic blood pressure (mm Hg)	75 [65-85]	70 [65-80]	70 [60-80]	< 0.001
Heart rate (beats/min)	79 [70-90]	76 [66-86]	70 [64-82]	< 0.001
Left ventricular end-diastolic pressure (mm Hg)	27 [24-30]	20 [19-22]	14 [11-16]	< 0.001
Left ventricular ejection fraction (%)	40 [32-45]	50 [45-55]	57 [51-63]	< 0.001
LVEF/LVEDP ratio	1.5 [1.2-1.8]	2.3 [2.1-2.7]	4.0 [3.4-4.8]	< 0.001
Killip's class				< 0.001
I	265 (60%)	316 (75%)	352 (83%)	
II	112 (26%)	78 (18%)	57 (13%)	
III	26 (6%)	12 (3%)	8 (2%)	
IV	34 (8%)	16 (4%)	7 (2%)	
With cardiogenic shock	34 (8%)	16 (4%)	7 (2%)	< 0.001
Time-to-admission interval (hours)	4.5 [2-9]	4 [2-9.5]	4 [2-10]	0.477
Door-to-balloon time (hours)	1.2 [0.8-1.7]	1.3 [0.9-1.7]	1.2 [0.9-1.8]	0.924
Therapy at discharge				
Aspirin	429 (98%)	418 (99%)	424 (100%)	0.020
Thienopyridines	437 (100%)	420 (99.5%)	424 (100%)	0.687
Statins	409 (94%)	402 (95%)	402 (95%)	0.536
Beta-blocking agents	423 (97%)	414 (98%)	414 (98%)	0.256
Angiotensin-converting enzyme inhibitors	403 (92%)	401 (95%)	397 (94%)	0.244

Data are median [twenty-fifth; seventy-fifth percentiles] or number of patients (%). LVEDP = left ventricular end-diastolic pressure; LVEF = left ventricular ejection fraction.

In patients with LVEF/LVEDP ratio in the first, second, and third tertiles, the initial area at risk was 40.0% (25.0% to 56.0%), 19.7% (12.0% to 33.0%), and 15.0% (7.0% to 26.0%) of the left ventricle, respectively ($p < 0.001$); infarct size in the 7 to 14 days scintigraphy was 22.0% (9.0% to 36.0%), 8.0% (2.0% to 18.0%), and 5.0% (1.0% to 12.0%) of the left ventricle, respectively ($p < 0.001$). LVEF/LVEDP ratio correlated with the initial perfusion defect ($R = -0.49$; $p < 0.001$) and infarct size ($R = -0.436$; $p < 0.001$). Expectedly, there was a strong correlation between LVEF/LVEDP ratio and its integers, LVEF ($R = 0.701$; $p < 0.001$) or LVEDP ($R = -0.871$; $p < 0.001$). There was an inverse correlation between LVEF and LVEDP ($R = -0.331$; $p < 0.001$).

Correlates of LVEF/LVEDP ratio were assessed using the multiple linear regression model (see methods for variables that were entered into the model). Higher heart rate ($p < 0.001$), lower baseline TIMI flow ($p < 0.001$), previous myocardial infarction ($p < 0.001$), higher C-reactive protein ($p = 0.003$), lower glomerular filtration rate ($p = 0.010$), anterior infarct location ($p < 0.001$), higher Killip's class ($p < 0.001$), and larger initial perfusion defect ($p < 0.001$) correlated independently with a lower LVEF/LVEDP ratio.

Patients were followed up to 8 years. Cardiac deaths (countwithKaplan-Meierestimatesinparentheses)occurredin109 patients: 55 (17.1%), 36 (10.9%), and 18 (6.5%) of these occurring in patients in the first to third LVEF/LVEDP ratio tertiles, respectively (unadjusted hazard ratio [HR] 0.57, 95% confidence interval [CI] 0.44 to 0.73, $p < 0.001$ for 1 tertile increment in the LVEF/LVEDP ratio; Figure 1). All-cause deaths occurred in 160 patients: 81 (24.5%), 47 (14.2%), and 32 (11.0%) of these occurring in patients in the first to third LVEF/LVEDP ratio tertiles, respectively; unadjusted HR 0.60 (0.49 to 0.74), $p < 0.001$ for 1 tertile increment in the LVEF/LVEDP ratio.

Table 2
Angiographic and procedural data

Characteristic	LVEF/LVEDP ratio			p value
	Tertile 1 (n = 437)	Tertile 2 (n = 422)	Tertile 3 (n = 424)	
Number of narrowed coronary arteries				0.149
1	144 (33%)	163 (39%)	146 (34%)	
2	126 (29%)	128 (30%)	139 (33%)	
3	167 (38%)	131 (31%)	139 (33%)	
Multivessel coronary disease	293 (67%)	259 (61%)	278 (66%)	0.198
Infarct-related coronary artery				< 0.001
Left main	3 (1%)	0 (0%)	1 (0.2%)	
Left anterior descending	274 (62%)	176 (41%)	123 (29%)	
Left circumflex	69 (16%)	62 (15%)	90 (21%)	
Right	84 (19%)	177 (42%)	203 (48%)	
Venous bypass graft	7 (2%)	7 (2%)	7 (2%)	
Collateral class*				0.468
0	316 (72%)	306 (72.5%)	314 (74%)	
1	78 (18%)	70 (16.5%)	61 (14%)	
2	35 (8%)	29 (7%)	32 (8%)	
3	8 (2%)	17 (4%)	16 (4%)	
Preinterventional Thrombolysis in Myocardial Infarction flow grade*				< 0.001
0	235 (54%)	188 (44%)	176 (42%)	
1	56 (13%)	47 (11%)	42 (10%)	
2	96 (22%)	100 (24%)	108 (25%)	
3	50 (11%)	87 (21%)	97 (23%)	
Postinterventional Thrombolysis in Myocardial Infarction flow grade				0.502
0	5 (1%)	7 (2%)	6 (1.5%)	
1	14 (3%)	9 (2%)	13 (3%)	
2	49 (11%)	33 (8%)	34 (8%)	
3	369 (85%)	373 (88%)	371 (87.5%)	
Type of intervention				0.144
Stenting	388 (89%)	379 (90%)	363 (86%)	
Balloon angioplasty	49 (11%)	43 (10%)	61 (14%)	

Data are number of patients (%). LVEDP = left ventricular end-diastolic pressure; LVEF = left ventricular ejection fraction.
* Available in 1,282 patients.

To obtain a more detailed view of the relation between the LVEF/LVEDP ratio and the risk of mortality, a decile-based analysis was performed. The analysis showed that for a LVEF/LVEDP ratio < 1.3, the rates of cardiac and all-cause mortality were 19.2% and 27.7% whereas for a LVEF/LVEDP ratio > 4.6, the risk of cardiac and all-cause mortality was 2.4% and 8.7%, respectively (Figure 2).

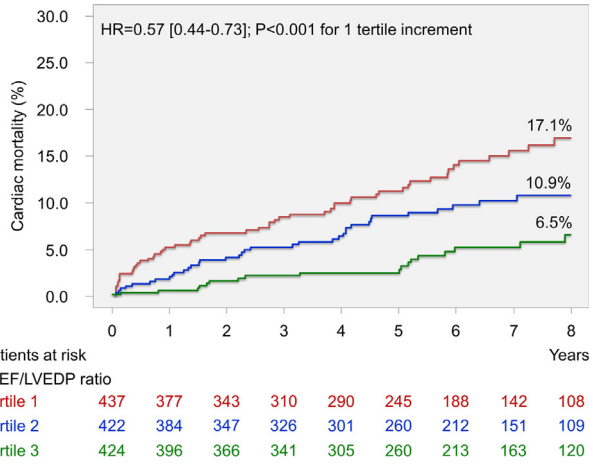


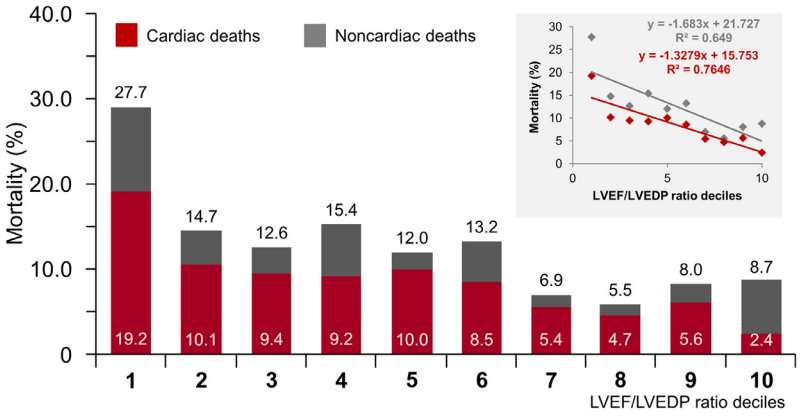
Figure 1. Kaplan-Meier curves of cardiac mortality according to tertiles of left ventricular ejection fraction (LVEF) to left ventricular end-diastolic pressure (LVEDP) ratio. HR = hazard ratio.

After adjustment, LVEF/LVEDP ratio was independently associated with the risk of 8-year cardiac mortality (adjusted HR 0.80 [0.66 to 0.97]; p = 0.022 for 1 unit increment in the LVEF/LVEDP ratio value). The results of the Cox proportional hazard model applied to assess the correlates of 8-year cardiac mortality are shown in Table 3. The association between LVEF/LVEDP ratio and all-cause mortality was attenuated after adjustment (adjusted HR 0.91 [0.79 to 1.04]; p = 0.180 for 1 unit increment in the LVEF/LVEDP ratio value).

The discrimination of the risk prediction for cardiac mortality was assessed by calculating the C-statistic of the Cox models without (with baseline variables only) and with inclusion of LVEF, LVEDP, or LVEF/LVEDP ratio (baseline variables plus LVEF, LVEDP, or LVEF/LVEDP ratio, respectively). The results are shown in Table 4. As seen, addition of LVEF/LVEDP ratio to baseline variables but not LVEF or LVEDP alone improved the discriminatory power of the model regarding prediction of cardiac mortality.

Discussion

The main findings of this study are as follows: first, in patients with STEMI who underwent PPCI, LVEF/LVEDP



LVEF/LVEDP ratio	0.3 to 1.3	>1.3 to 1.6	>1.6 to 1.9	>1.9 to 2.2	>2.2 to 2.5	>2.5 to 2.8	>2.8 to 3.2	>3.2 to 3.8	>3.8 to 4.6	>4.6 to 13.2
All-cause deaths	36	19	16	20	18	14	9	7	10	11
Cardiac deaths	25	13	12	12	15	9	7	6	7	3
Number of patients	131	129	127	130	150	106	130	128	125	127

Figure 2. Eight-year cardiac and all-cause mortality according to deciles of the LVEF/LVEDP ratio. Numbers on the top of the bars display all-cause mortality. Numbers within the red bars show cardiac mortality. The inset on the right upper corner represents the regression lines (and equations) for the association between the deciles of LVEF/LVEDP ratio and all-cause (gray squares) or cardiac (red squares) mortality. LVEDP = left ventricular end-diastolic pressure; LVEF = left ventricular ejection fraction. (Color version of figure is available online.)

ratio was independently associated with the risk for 8-year cardiac mortality. Second, LVEF/LVEDP ratio improved the risk prediction for cardiac mortality when added in multivariable models alongside cardiovascular risk factors and relevant clinical variables. Based on the values of C-statistic the LVEF/LVEDP ratio, but not LVEF or LVEDP alone improved the risk prediction for cardiac mortality up to 8 years after PPCI.

Previous studies suggested an association between LVEF,[1–4] LVEDP,[11–13] or systolic blood pressure-to-LVEDP ratio[22,23] and prognosis after STEMI. This is the first study to assess the association between LVEF/LVEDP ratio and the risk of mortality in patients with STEMI after PPCI. The hypothesis that LVEF/LVEDP ratio may be superior to LVEF or LVEDP alone for risk prediction after STEMI is based on several lines of evidence: first, LVEF[1–4] and LVEDP[11–13] alone are independent correlates of a poor prognosis after STEMI; second, LVEF and LVEDP may reflect different aspects of cardiovascular risk and thus LVEF/LVEDP ratio may accumulate risk from both its components; third, there is only a weak inverse correlation between LVEF and LVEDP[12,13] and; fourth, combined use of an elevated LVEDP and reduced LVEF significantly improved risk prediction for major adverse cardiovascular events after STEMI.[24] These lines of evidence suggest that the LVEF/LVEDP ratio may absorb cardiovascular risk from different sources and thus it may be advantageous to its constituents as a mortality risk marker after STEMI.

LVEF/LVEDP ratio may be particularly a strong correlate of cardiac mortality after STEMI. First, there was a strong correlation between the LVEF/LVEDP ratio and its integers. Although mathematically expectable, the strong correlation between the LVEF/LVEDP ratio and its integers shows that LVEF and LVEDP are well represented by the ratio and that both of them insert in the ratio large and comparable amounts of the prognostic information. Second, the

Table 3
Results of Cox proportional hazard model applied to assess correlates of 8-year cardiac mortality

Variable*	Hazard ratio[95% confidence interval]	p value
LVEF/LVEDP ratio (for 1 unit increment)	0.80 [0.66-0.97]	0.022
Infarct size (for 5% of the left ventricle increment)	1.05 [1.01-1.11]	0.047
Postprocedural TIMI flow (for 1 grade increment)	0.84 [0.63-1.13]	0.265
Age (for 10-year increment)	1.59 [1.27-1.99]	< 0.001
Heart rate (for 10 beats increment)	1.06 [0.94-1.20]	0.319
Women	1.27 [0.82-1.96]	0.278
Diabetes mellitus	1.36 [0.91-2.09]	0.135
History of arterial hypertension	1.36 [0.80-2.32]	0.260
Current smoker	1.27 [0.80-2.01]	0.313
Previous myocardial infarction	1.71 [1.07-2.75]	0.025
Previous coronary artery bypass surgery	1.66 [0.78-3.51]	0.184
C-reactive protein (for 5 mg/L increment)	1.01 [0.98-1.04]	0.440
Glomerular filtration rate (30 ml/min decrement)	1.14 [0.87-1.49]	0.334
Killip's class (for 1 class increment)	1.42 [1.14-1.78]	0.002
Time-to-admission interval (for 1 hour increment)	1.02 [1.00-1.06]	0.082
Multivessel disease	1.30 [0.78-2.17]	0.318
Collateral class (for 1 class increment)	0.89 [0.68-1.17]	0.410
Therapy at discharge		
Aspirin	0.21 [0.08-0.61]	0.004
Angiotensin-converting enzyme inhibitors	0.44 [0.24-0.79]	0.006
Beta-blocking agents	0.44 [0.20-0.98]	0.044
Statins	0.42 [0.20-0.73]	0.002

LVEDP = left ventricular end-diastolic pressure; LVEF = left ventricular ejection; TIMI = Thrombolysis in Myocardial Infarction.

* Covariates in the multivariate model were selected using the Least Absolute Shrinkage and Selection Operator (LASSO) regression method.

Table 4
C-statistic of the Cox proportional hazard models without and with inclusion of LVEF, LVEDP, and LVEF/LVEDP ratio

Model	C-statistic[95% confidence interval]	Delta C-statistic	p value
Baseline characteristics only	0.820 [0.777-0.862]	...	...
Baseline characteristics plus left ventricular ejection fraction	0.823 [0.781-0.864]	0.003 [-0.002-0.012]	0.290
Baseline characteristics plus left ventricular end-diastolic pressure	0.825 [0.781-0.866]	0.005 [-0.001-0.015]	0.145
Baseline characteristics plus LVEF/LVEDP ratio	0.827 [0.783-0.866]	0.007 [0.000-0.017]	0.035

LVEF = left ventricular ejection fraction; LVEDP = left ventricular end-diastolic pressure.

LVEF/LVEDP ratio correlated with some of the best known cardiac and noncardiac markers or conditions that signify a poor prognosis after STEMI including reduced blood flow in the infarct-related coronary artery, previous myocardial infarction and anterior wall infarction, severity of congestive heart failure and larger initial myocardial ischemia. All these conditions are known to correlate with the extent of myocardial damage (infarct size) in the setting of STEMI, which is a major determinant of subsequent prognosis.[25] LVEF/LVEDP ratio correlated independently with other prognostic markers including a higher heart rate, higher C-reactive protein level, and impaired renal function—all of which are known to portend a poor prognosis after STEMI. The close correlation between LVEF/LVEDP ratio and these conditions may explain why this metric was so strongly associated with the risk of mortality in patients with STEMI.

In the present study, 68% of deaths (109 of 160 deaths) were due to cardiac causes. This is in line with previous reports that patients with acute coronary syndromes die predominantly from cardiac causes.[26] Although, in univariable analysis, the association between LVEF/LVEDP ratio and the risk of all-cause mortality was significant (likely due to the dominant contribution of cardiac mortality in all but tenth decile of the LVEF/LVEDP ratio) the association was attenuated after adjustment in multivariable analysis. Based on these data, we hypothesize that LVEF/LVEDP ratio is a specific marker for cardiac mortality. The risk of mortality was highest in patients with a LVEF/LVEDP ratio of < 1.3. Considering the normal values for LVEDP (≤ 12 mm Hg) and LVEF ($\geq 55\%$), it is highly likely that such lower values of the LVEF/LVEDP ratio are obtained by abnormal values of both LVEF and LVEDP. On the other side of the LVEF/LVEDP ratio spectrum, patients with a LVEF/LVEDP ratio > 4.6 had the lowest rates of cardiac mortality. Again, it is likely that patients with a LVEF/LVEDP ratio value > 4.6 had at least 1 of the ratio components within the normal range and these patients were at the lowest risk of dying from cardiac causes.

The present study has several limitations. First, although coronary stents and antithrombotic therapy used were standard of care at the time of patients' recruitment, currently they are somewhat outdated. Second, in-hospital deaths were not included in the analysis because patients had to be alive at the time of scintigraphic imaging 7 to 14 days after PPCI.[20] However, considering the increased frequency of cardiogenic shock in patients with lower LVEF/LVEDP ratio values, the association with mortality could have been even stronger if these patients were included. Third, although C-statistic is the most thoroughly validated discriminatory test, it is conservative and clinical relevance of small but statistically significant increases in the C-statistic associated with incorporation of a given factor into the respective multivariable models remains unclear. Fourth, the follow-up was incomplete in some patients. Finally, the present study lacks a validation cohort in which the prognostic value of the LVEF/LVEDP ratio could have been validated. Although undesirable, we strongly believe that these limitations do not impact on the main findings of the study. It remains to be seen whether the findings of this study will foster the evaluation of left ventricular function and hemodynamic indexes as prognostic markers in the setting of PPCI.

Disclosures

The authors have no conflicts of interest to disclose.

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