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Global left ventricular myocardial work efficiency and Long-term prognosis in patients after ST-segment-elevation myocardial infarction

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ORIGINAL ARTICLE

Global Left Ventricular Myocardial Work Efficiency and Long-Term Prognosis in Patients After ST-Segment–Elevation Myocardial Infarction

BACKGROUND: Left ventricular (LV) global longitudinal strain has demonstrated incremental prognostic value over LV ejection fraction in patients with ST-segment–elevation myocardial infarction. However, LV global longitudinal strain does not take into consideration the effect of afterload. Novel speckle-tracking echocardiographic indices of myocardial work integrate blood pressure measurements (afterload) with LV global longitudinal strain. The present study aimed to investigate the prognostic value of global LV myocardial work efficiency (GLVMWE; reflecting LV performance) obtained from pressure-strain loops with echocardiography in patients with ST-segment–elevation myocardial infarction.

METHODS: A total of 507 ST-segment–elevation myocardial infarction patients (mean age, 61 ± 11 years; 76% men) were retrospectively analyzed. LV ejection fraction and GLVMWE were measured by transthoracic echocardiography within 48 hours of admission. GLVMWE was defined as the ratio of constructive work divided by the sum of constructive and wasted work in all LV segments and expressed as a percentage. Spline curve analysis was used to define the association between reduced GLVMWE and all-cause death.

RESULTS: After a median follow-up of 80 months (interquartile range, 67–97 months), 40 (8%) patients died. Patients with reduced GLVMWE (<86%) showed higher cumulative rates of all-cause mortality (17.5% versus 4.7%; log-rank $P < 0.001$) in comparison with patients with preserved GLVMWE ($\geq 86\%$). Reduced GLVMWE (<86%) showed an independent association with all-cause mortality (hazard ratio, 3.167 [95% CI, 1.679–5.972]; $P < 0.001$).

CONCLUSIONS: Reduced GLVMWE (<86%) measured by transthoracic echocardiography within 48 hours of admission in ST-segment–elevation myocardial infarction patients is associated with worse long-term survival.

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CLINICAL PERSPECTIVE

Left ventricular (LV) ejection fraction and LV global longitudinal strain have prognostic value in patients with ST-segment–elevation myocardial infarction. However, LV ejection fraction and LV global longitudinal strain are influenced by loading conditions. Novel speckle-tracking echocardiographic indices of myocardial work integrate blood pressure measurements (afterload) with LV global longitudinal strain. Global LV myocardial work efficiency obtained from echocardiography-derived pressure-strain loops takes into account the afterload and reflects the LV performance. In the current study, 507 ST-segment–elevation myocardial infarction patients were retrospectively analyzed and global LV myocardial work efficiency was measured by transthoracic echocardiography within 48 hours of admission. Reduced global LV myocardial work efficiency (<86%) in patients with ST-segment–elevation myocardial infarction was independently associated with worse long-term prognosis.

Ischemic heart disease remains as an important cause of death worldwide,¹ and patients with acute myocardial infarction face a substantial risk of additional cardiovascular events, including heart failure.² Infarct size and left ventricular (LV) dilation and dysfunction increase the risk of heart failure and cardiovascular mortality.³ In clinical practice, assessment of LV systolic function with LV ejection fraction (EF) remains as a widely recognized prognostic marker.⁴ However, its limitations are well known (ie, limited reproducibility and geometric assumptions).⁵

Recently, 2-dimensional speckle-tracking echocardiography–derived LV global longitudinal strain (GLS) has demonstrated incremental value over LV EF to predict prognosis after ST-segment–elevation myocardial infarction (STEMI).^{6,7} However, both LV EF and LV GLS are load-dependent parameters, and their assessment is influenced by heart rate and systolic blood pressure, which have also been associated with outcomes after STEMI.^{8–10}

The assessment of myocardial work indices based on 2-dimensional speckle-tracking echocardiography takes into consideration the loading conditions by integrating blood pressure measurements to generate a pressure-strain curve.¹¹ Specifically, global LV myocardial work efficiency (GLVMWE), which combines the measurement of constructive and wasted work, provides information on global LV performance. However, the association of this novel parameter with outcomes after STEMI has not been studied. The purpose of this study was to investigate the prognostic value of GLVMWE, obtained

from pressure-strain loops with echocardiography, in patients with STEMI.

METHODS

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Patient Population

A total of 507 patients with STEMI admitted to the Leiden University Medical Center (Leiden, the Netherlands) and treated with primary percutaneous coronary intervention between August 2011 and November 2015 were identified and included in this retrospective analysis. Patients known with severe valvular heart disease and prior cardiac surgery before the index event were excluded, as well as patients without noninvasively measured blood pressure data at the time of echocardiography.

Patients were treated according to the institutional STEMI protocol,¹² which provides a clinical framework for optimal guideline-based medical therapy and standardized outpatient follow-up.^{1,13} During invasive coronary angiography, the culprit vessel was identified and multivessel disease was defined as ≥ 1 vessel with $>50\%$ luminal stenosis. Guideline-directed medical therapy was initiated during hospitalization, and echocardiography was performed within 48 hours of admission after primary percutaneous coronary intervention. Clinical and echocardiographic data were retrospectively analyzed in the departmental cardiology information system (EPD-Vision) and echocardiographic database, respectively. The Global Registry of Acute Coronary Events (GRACE) risk score¹⁴ was calculated for all population, which includes the following variables: age, heart rate, systolic blood pressure, Killip class, cardiac arrest on admission, ST-segment deviation, creatinine level, and cardiac enzyme levels. For retrospective analysis of clinically acquired data, the institutional review board waived the need for patient written informed consent.

Conventional Analysis of Echocardiographic Data

Transthoracic echocardiography was performed in patients at rest in the left lateral decubitus position using a commercially available ultrasound system (Vivid 7, Vivid E9, or E95; GE Vingmed Ultrasound, Horten, Norway) equipped with an M5S transducer. Standard M-mode, 2-dimensional, color, pulsed, and continuous-wave Doppler images were acquired, and all images were analyzed offline using the EchoPac, version 203, software (GE Vingmed Ultrasound). The LV EF and LV end-diastolic and end-systolic volumes were calculated in the 4- and 2-chamber apical views using the Simpson biplane method.¹⁵

Analysis of LV GLS was performed on standard routine gray-scale images in the apical 2-, 4-, and long-axis views, with a frame rate ≥ 40 frames/s. LV GLS was calculated by the software (GE Vingmed Ultrasound) as the average peak systolic strain of 3 apical views and presented in a 17-segment model. The value of LV GS is presented in absolute values.

Calculation of GLVMWE

Calculation of GLVMWE was performed using a commercially available software package (EchoPac, version 203, software;

GE Medical Systems, Horten, Norway). As reported by Russell et al,¹¹ GLVMWE was measured from pressure-strain loop areas, which were constructed from noninvasive estimation of peak LV pressure using patients' brachial cuff blood pressure recordings (which assumes that peak systolic LV pressure is equal to peak arterial pressure) combined with speckle-tracking echocardiographic strain data.

After calculating LV GLS and introducing the values of brachial blood pressure, the opening and closing time points of the aortic and mitral valves were identified from the apical 3-chamber or parasternal long-axis views. An LV pressure-strain curve was then constructed from LV GLS data of the entire cardiac cycle, according to the duration of isovolumic relaxation and contraction, ejection, and filling phases defined by timing of the aortic and mitral valve opening and closing events on 2-dimensional echocardiography, as well as noninvasive blood pressure values.

LV myocardial work was calculated as the product of the rate of segmental shortening and instantaneous LV pressure. LV myocardial work is a measure of instantaneous power, which was integrated over time to obtain myocardial work as a function of time. Constructive work was defined as cardiac work performed during shortening of a myocardial segment in systole or during lengthening in isovolumic relaxation, whereas wasted work was defined as work performed by a segment during lengthening in systole or during shortening against a closed aortic valve in isovolumic relaxation. The ratio of the constructive work in all LV segments, divided by the sum of constructive and wasted work in all LV segments, defines GLVMWE and is expressed as a percentage. Therefore, GLVMWE is an estimate of the mechanical performance and energy utilization of the LV that takes into consideration the loading conditions (Figure 1).

Follow-Up

Patients were followed up at the outpatient clinic according to the institutional protocol.¹² The primary end point was all-cause mortality. Mortality data after discharge were collected through municipal civil registries or by reviewing medical records. Follow-up data were available for all study patients.

Statistical Analysis

Categorical data are presented as frequencies and percentages and compared with the χ^2 test. Continuous data are presented as mean \pm SD or median and interquartile range, as appropriate. Comparisons between patients with preserved GLVMWE versus patients with reduced GLVMWE were analyzed by the Student *t* test (if normally distributed) or the Mann-Whitney *U* test (if not normally distributed). To evaluate the change in hazard ratio for all-cause mortality across a range of values of GLVMWE (as a continuous variable), spline curve analysis was performed. A cutoff value of GLVMWE to define reduced and preserved GLVMWE was derived from the spline curve (ie, when the hazard ratio of the lower limit of the 95% CI was ≥ 1). The cumulative event-free survival was calculated based on Kaplan-Meier analysis and compared between groups with a log-rank test. The association of clinical and echocardiographic variables (including GLVMWE) with all-cause mortality was tested using Cox proportional hazard regression

analysis. The hazard ratio and 95% CIs were calculated. The GRACE risk score¹⁴ was utilized to incorporate all important confounding variables into the multivariable analyses while avoiding model overfitting. To assess the incremental advantage of GLVMWE over baseline clinical characteristics, LV EF, and LV GLS for the risk of all-cause mortality, the change in χ^2 was assessed. The interobserver and intraobserver variability of GLVMWE was assessed in 20 randomly selected patients, and the intraclass correlation coefficients were calculated. All statistical analyses were performed with SPSS software, version 25.0 (IBM SPSS Statistics, for Windows, Armonk, NY), and R, version 3.6.2 (R Foundation for Statistical Computing, Vienna, Austria), and were 2 sided. *P*<0.05 was considered statistically significant.

RESULTS

Study Population and Clinical Characteristics

This retrospective study included 507 patients (384 men [76%]; mean age, 61 \pm 11 years) with STEMI (Table 1). The patient sample was divided according to the cutoff value of GLVMWE associated with an excess of mortality as assessed with spline curve analysis. After an initial plateau region until GLVMWE dropped below 90%, there was a substantial increase in hazard ratio for values of GLVMWE <86%. In addition, another plateau region was observed with values below 80%, where a further reduction in GLVMWE did not appear to substantially increase the risk of all-cause mortality (Figure 2). Based on this analysis, a GLVMWE value <86% was used to define a reduced GLVMWE and to dichotomize the population. The clinical characteristics of patients divided according to the presence of preserved ($\geq 86\%$) versus reduced (<86%) GLVMWE are summarized in Table 1. Reduced GLVMWE was observed in 126 patients (25%), with a median value of 81% (interquartile range, 77%–83%). Patients with reduced GLVMWE were significantly older, had a higher heart rate, had a higher GRACE risk score, and the left anterior descending coronary artery was the most frequently involved culprit vessel. The proportion of women was higher in the group of reduced GLVMWE versus the group with preserved GLVMWE (31% versus 22%, respectively). In addition, patients with reduced GLVMWE showed more myocardial damage based on significantly higher values of creatine phosphokinase and troponin T in comparison with patients with preserved GLVMWE.

The echocardiographic characteristics of the study population are shown in Table 2. In the overall population, the mean LV EF was 52 \pm 10% with a mean LV GLS of 15 \pm 4%. Patients with reduced GLVMWE had significantly larger LV end-systolic and end-diastolic volumes, significantly lower LV EF, and more impaired LV GLS as compared with patients with preserved GLVMWE.

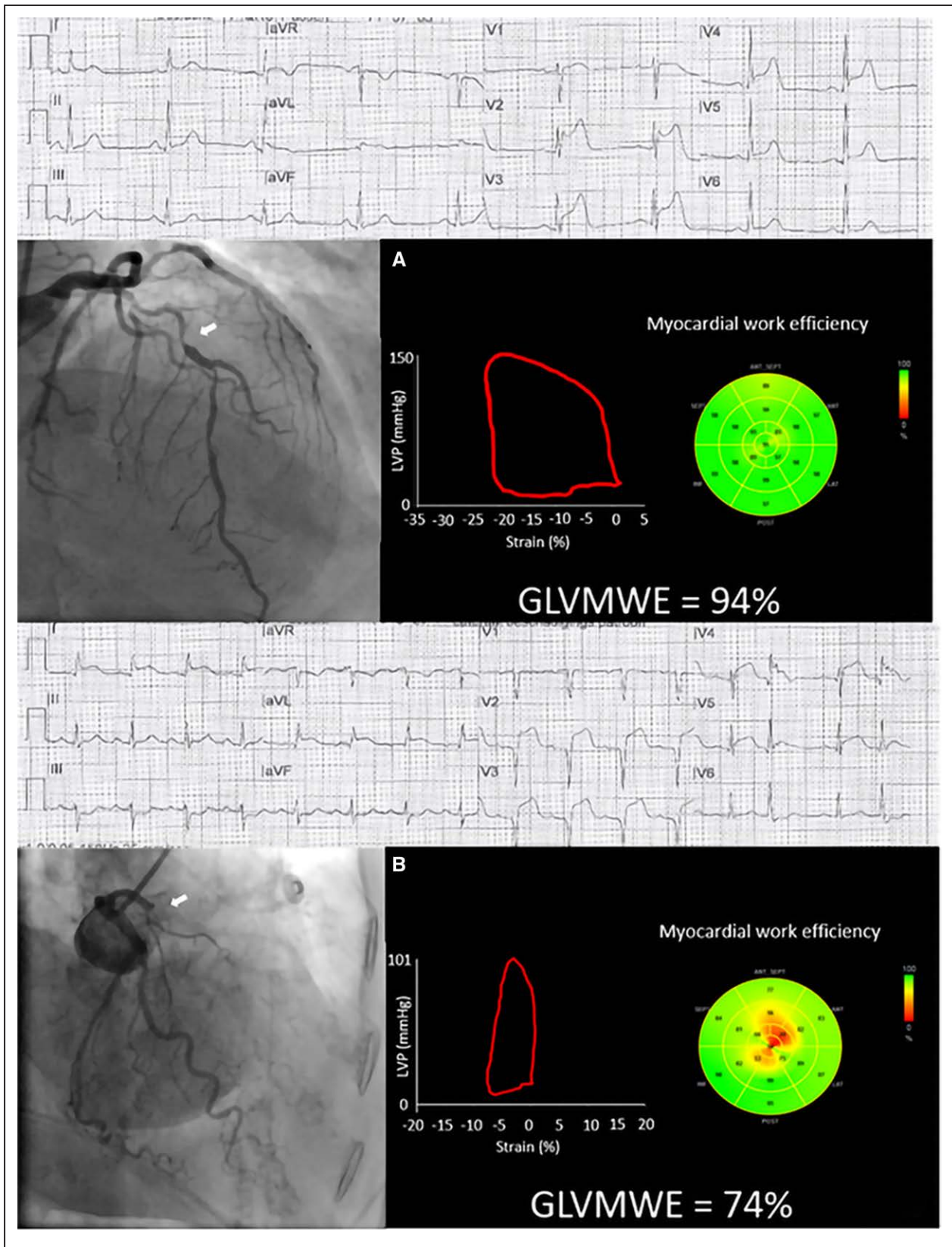


Figure 1. Calculation of global left ventricular myocardial work efficiency (GLVMWE). ECG showing anterior ST-segment–elevation myocardial infarction (STEMI), coronary angiography showing the left anterior descending (LAD) culprit vessel (white arrow), and left ventricular (LV) myocardial work efficiency bull’s-eye plots of STEMI patients with preserved GLVMWE ($\geq 86\%$; **A**) and reduced GLVMWE ($< 86\%$; **B**). Preserved segmental values of LV myocardial work efficiency are presented in green, and reduced segmental values of LV myocardial work efficiency are presented in yellow. Segmental values of LV myocardial work efficiency are expressed as a percentage. LVP indicates left ventricular pressure.

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Table 1. Clinical Characteristics

Variable	All patients (n=507)	Preserved GLVMWE (≥86%), n=381	Reduced GLVMWE (<86%), n=126	P value
Age, y	61±11	60±11	64±12	<0.001
Men, n (%)	384 (76)	297 (78)	87 (69)	0.043
Killip classification I, n (%)	477 (94)	360 (94)	117 (93)	0.501
Sinus rhythm, n (%)	502 (99)	378 (99)	124 (98)	0.431
Heart rate, bpm	73±12	71±12	78±13	<0.001
LBBB, n (%)	3 (0.6)	1 (0.3)	2 (1.6)	0.093
SBP, mmHg	122±18	122±18	124±21	0.332
DBP, mmHg	75±12	74±12	77±13	0.049
Symptom onset-to-balloon time, min	157 (106–255)	152 (104–233)	183 (114–334)	0.013
Peak CK value at baseline, U/L	1168 (562–2317)	1029 (498–1880)	2171 (950–3567)	<0.001
Peak troponin T at baseline, µg/L	3.01 (1.36–6.34)	2.54 (1.12–5.17)	5.71 (2.55–9.77)	<0.001
Creatinine level, µmol/L	76 (67–89)	77 (67–89)	74 (63–87)	0.164
eGFR, mL/min per 1.73 m ²	90 (76–100)	90 (77–100)	90 (72–97)	0.322
GRACE risk score (points)	113±24	111±22	120±27	0.001
Hypertension, n (%)	190 (38)	129 (34)	61 (49)	0.003
Diabetes, n (%)	31 (6)	19 (5)	12 (10)	0.067
Dyslipidemia, n (%)	89 (18)	64 (17)	25 (20)	0.466
Smoker, n (%)	224 (45)	174 (47)	50 (40)	0.203
Family history of CAD, n (%)	215 (44)	165 (45)	50 (41)	0.416
Previous myocardial infarction, n (%)	15 (3)	10 (3)	5 (4)	0.440
LAD STEMI, n (%)	236 (47)	133 (35)	103 (82)	<0.001
Other STEMI locations, n (%)	271 (53)	248 (65)	23 (18)	<0.001
Final TIMI flow ≤2, n (%)	24 (5)	18 (5)	6 (5)	0.986
Multivessel disease, n (%)	276 (54)	209 (55)	67 (53)	0.743
Aspirin, n (%)	506 (99)	381 (100)	125 (99)	0.082
P2Y12 inhibitors, n (%)	507 (100)	381 (100)	126 (100)	1.00
β-Blocker, n (%)	485 (96)	365 (96)	120 (95)	0.788
Statin, n (%)	506 (99)	381 (100)	125 (99)	0.082
ACE inhibitor or ARB, n (%)	495 (98)	371 (97)	124 (98)	0.507
Nitrates, n (%)	419 (83)	317 (83)	102 (81)	0.563

Values are mean±SD or median (IQR). ACE indicates angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; CAD, coronary artery disease; CK, creatine phosphokinase; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; GLVMWE, global left ventricular myocardial work efficiency; GRACE, Global Registry of Acute Coronary Events; LAD, left anterior descending artery; LBBB, left bundle branch block; SBP, systolic blood pressure; STEMI, ST-segment-elevation myocardial infarction; and TIMI, thrombolysis in myocardial infarction.

Survival Analysis

After a median follow-up of 80 months (interquartile range, 67–97 months), 40 (8%) patients died. The Kaplan-Meier curves for all-cause mortality are shown in Figure 3. Patients with reduced GLVMWE showed higher cumulative event rates at 80 months (17.5% versus 4.7%; log-rank $P<0.001$) versus patients with preserved GLVMWE. The univariable and multivariable Cox regression analyses were constructed with variables known to be associated with outcomes in STEMI patients (Table 3). In univariable analysis, age, Killip class ≥II, heart rate, diabetes, higher creatinine levels, higher peak troponin T levels, higher GRACE risk score, lower

LV EF, impaired LV GLS, and GLVMWE <86% were significantly associated with all-cause mortality. On multivariable Cox regression analysis, higher GRACE risk score, diabetes, and GLVMWE <86% were independently associated with all-cause mortality. Furthermore, GLVMWE <86% demonstrated incremental prognostic value over baseline clinical characteristics and LV EF and LV GLS (Figure 4). The increment in χ^2 was higher when adding GLVMWE than when adding LVGLS (Figure 4). When performing the Cox regression analyses with GLVMWE as continuous variable, more impaired GLVMWE was associated with worse outcomes (Table 1 in the [Data Supplement](#)). Due to the limited number

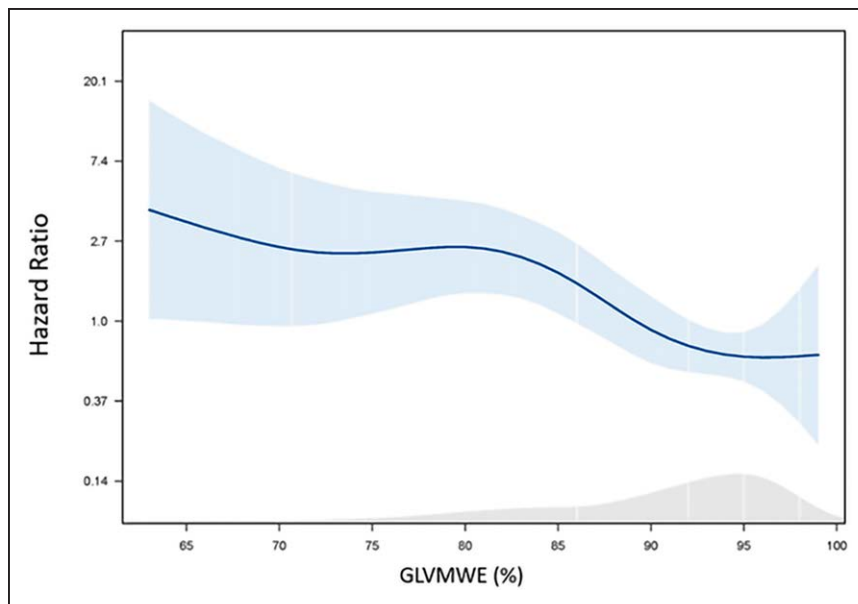


Figure 2. Spline curve for baseline global left ventricular myocardial work efficiency (GLVMWE) vs hazard ratio of all-cause mortality in patients after ST-segment-elevation myocardial infarction.

The spline curve demonstrates the hazard ratio change for all-cause mortality across a range of values of GLVMWE. The density plot beneath the curve demonstrates the distribution of the study population according to the values of GLVMWE.

of events during follow-up, other multivariable models were constructed including a maximum of 4 variables each time (Table II in the [Data Supplement](#)). In all the models, a GLVMWE <86% was significantly associated with all-cause mortality.

Reproducibility

Measurements of GLVMWE showed excellent intraobserver (intraclass correlation, 0.904 [95% CI, 0.777–0.961]; $P<0.001$) and interobserver agreement (intraclass correlation, 0.916 [95% CI, 0.801–0.966]; $P<0.001$).

DISCUSSION

The main findings of the present study can be summarized as follows: STEMI patients with reduced GLVMWE (<86%) showed more myocardial damage with higher values of creatine phosphokinase and troponin T, larger LV end-systolic and end-diastolic volumes, and a significantly lower LV EF with more impaired LV GLS as compared with their counterparts. In addition, reduced

GLVMWE was associated with worse long-term prognosis after STEMI.

Prognostic Implications of LV EF and LV GLS After Acute Myocardial Infarction

Current guidelines recommend routine echocardiography before discharge in all STEMI patients to assess LV EF and diastolic function, as well as other parameters that may influence outcomes such as wall motion score index and valvular heart disease.¹ Recent studies reported that LV GLS measured with echocardiography¹⁶ and cardiac magnetic resonance imaging¹⁷ predicts cardiovascular death after myocardial infarction and has incremental prognostic value over LV EF.¹⁸ However, similar to LV EF, LV GLS is also influenced (although to a lesser extent) by loading conditions, especially afterload.¹⁹ Noninvasive assessment of GLVMWE compared with standard parameters of LV function (ie, LV EF and LV GLS) integrates LV GLS, afterload, and isovolumic relaxation phase to provide a more comprehensive measure of LV myocardial performance. Moreover,

Table 2. Echocardiographic Characteristics of the Study Population at Baseline

Variable	All patients (n=507)	Preserved GLVMWE (≥86%) n=381	Reduced GLVMWE (<86%) n=126	P value
	LV end-systolic volume, mL	43 (32–57)	40 (30–52)	
LV end-diastolic volume, mL	89 (71–111)	88 (70–107)	95 (78–122)	0.003
LV EF, %	52±10	55±9	45±9	<0.001
Moderate mitral regurgitation, n (%)	32 (6)	22 (6)	10 (8)	0.379
LV GLS, %	15±4	16±3	10±3	<0.001
GLVMWE, %	92 (86–95)	94 (91–96)	81 (77–83)	<0.001

Values are mean±SD or median (IQR). LV GLS is presented as positive value. EF indicates ejection fraction; GLS, global longitudinal strain; GLVMWE, global left ventricular myocardial work efficiency; IQR, interquartile; and LV, left ventricle.

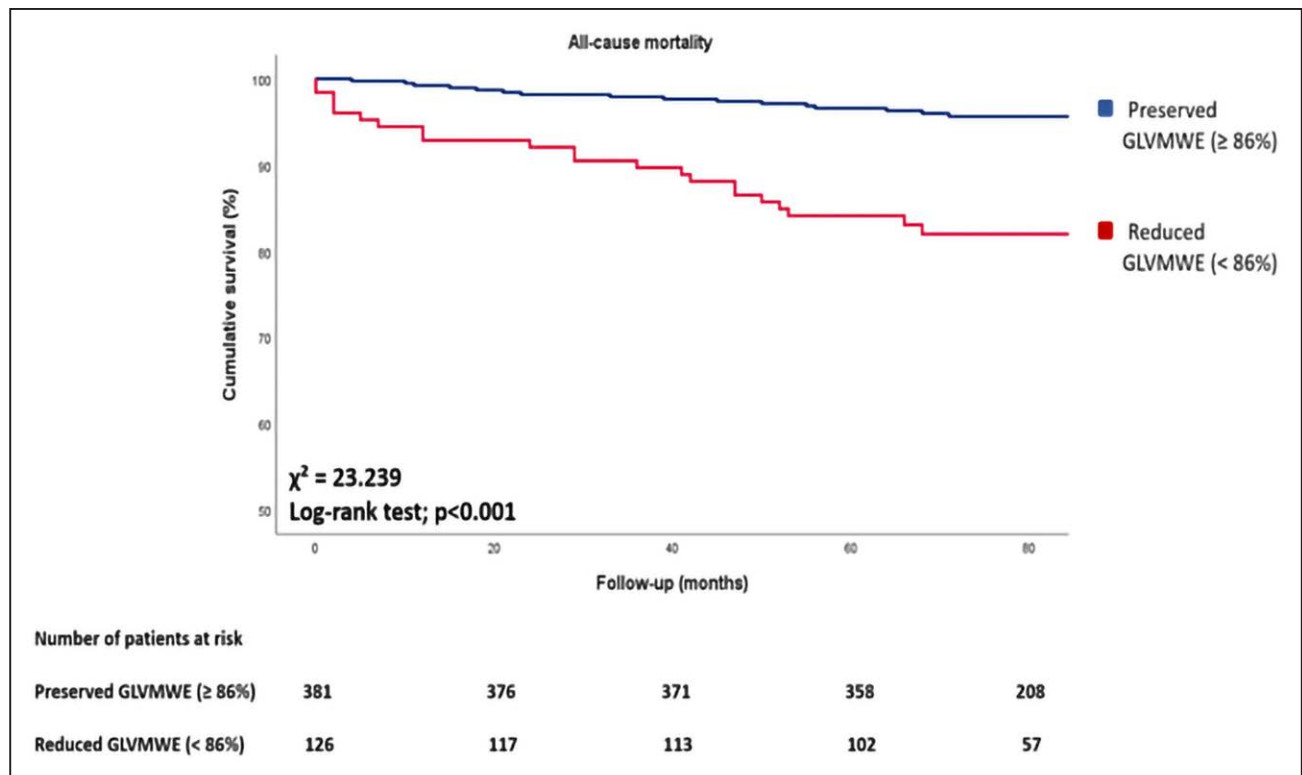


Figure 3. Survival analysis.

The Kaplan-Meier curves depicting time to cumulative survival in ST-segment-elevation myocardial infarction patients. Data are shown according to those with preserved and reduced global left ventricular myocardial work efficiency (GLVMWE).

it correlates with myocardial glucose metabolism assessed on ¹⁸F-fluorodeoxyglucose positron emission tomography, providing an estimate of LV myocardial

energetics.¹¹ The relation between GLVMWE measurement and STEMI was previously reported by El Mahdiui et al.²⁰ The authors found that STEMI patients showed

Table 3. Univariable and Multivariable Cox Regression Analysis for All-Cause Mortality

Univariable analysis				Multivariable analysis		
Variable	HR	95% CI	P value	HR	95% CI	P value
Age, y	1.067	1.036–1.100	<0.001			
Male gender	0.838	0.419–1.678	0.618			
Killip class ≥II	3.229	1.352–7.715	0.008			
Heart rate, bpm	1.025	1.002–1.049	0.035			
Systolic blood pressure, mmHg	0.998	0.980–1.015	0.778			
Symptom onset-to-balloon time, min	1.000	1.000–1.001	0.376			
Creatine phosphokinase, U/L	1.000	1.000–1.000	0.312			
Troponin T, μg/L	1.050	1.009–1.093	0.018			
Creatinine level, μmol/L	1.012	1.006–1.019	<0.001			
Diabetes	3.509	1.551–7.935	0.003	3.233	1.424–7.340	0.005
Left anterior descending as culprit artery	0.964	0.517–1.797	0.908			
Multivessel disease	1.586	0.828–3.036	0.164			
GRACE risk score (each 1-point increment)	1.031	1.019–1.043	<0.001	1.029	1.016–1.042	<0.001
LV EF (each 1% increment)	0.951	0.922–0.981	0.002			
LV GLS (each 1% increment)	0.870	0.804–0.942	0.001			
Baseline, GLVMWE <86%	4.109	2.202–7.665	<0.001	3.167	1.679–5.972	<0.001

LV GLS is presented as positive value. Therefore, more positive value, better function and better outcome. EF indicates ejection fraction; GLMWE, global left ventricular myocardial work efficiency; GLS, global longitudinal strain; GRACE, Global Registry of Acute Coronary Events; HR, hazard ratio; and LV, left ventricle.

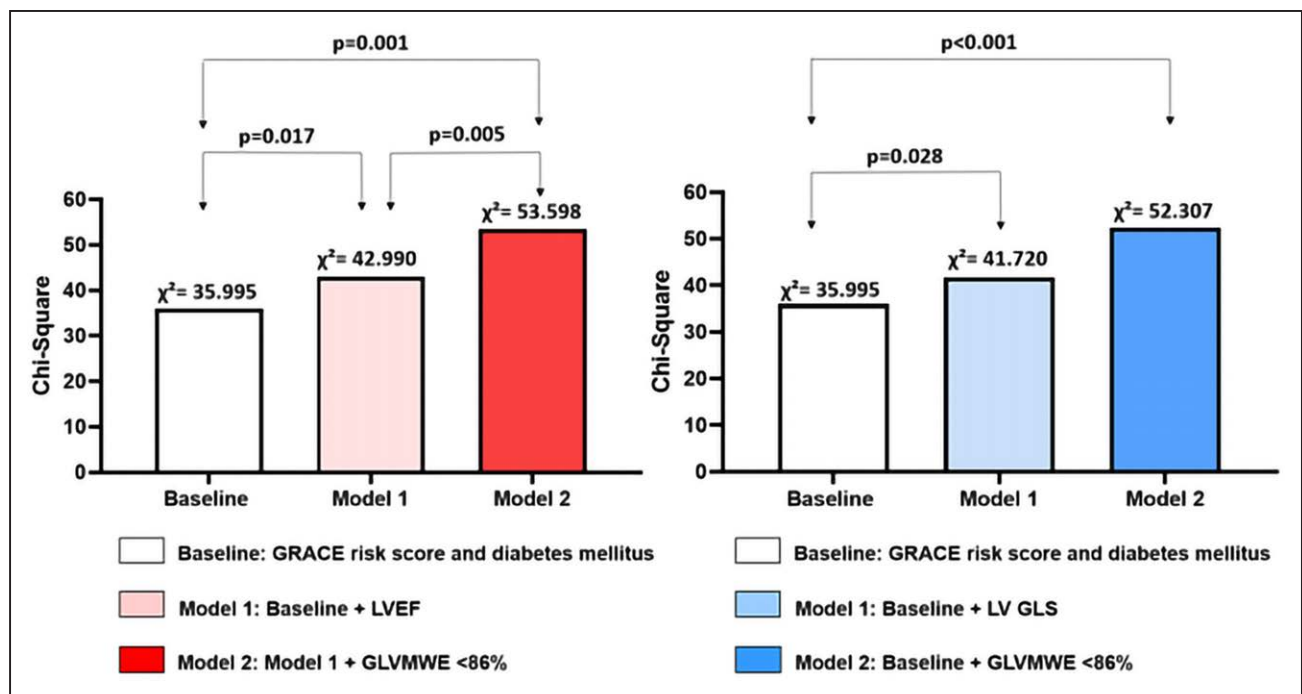


Figure 4. Incremental prognostic value of global left ventricular myocardial work efficiency (GLVMWE) in patients with ST-segment-elevation myocardial infarction.

The bar graphs show the χ^2 value for the three models associated with all-cause mortality. The baseline model includes global registry of acute coronary event (GRACE) risk score and diabetes. The addition of GLVMWE provides incremental prognostic information over the baseline model and models incorporating left ventricular ejection fraction (LV EF) and left ventricular global longitudinal strain (LV GLS).

lower values of GLVMWE in comparison with healthy subjects and patients with cardiovascular risk factors. In the current study, which included exclusively STEMI patients, those with reduced GLVMWE (<86%) showed evidence of more cardiac damage than STEMI patients with preserved GLVMWE (\geq 86%). Indeed, after STEMI, ischemia induces changes in myocardial metabolism, reducing ATP formation,²¹ leading to LV contractile dysfunction and reduced values of GLVMWE.

Prognostic Implications of GLVMWE After STEMI

Myocardial efficiency is related to the capacity of the heart to generate effective work based on hemodynamic parameters, oxygen consumption, and myocardial metabolism.²² At this moment, the prognostic implications of GLVMWE in patients with STEMI have not been explored. However, previous studies have related GLVMWE to prognosis in different populations. Kim et al²³ reported the prognostic value of invasive myocardial efficiency in 47 patients with dilated cardiomyopathy and demonstrated that patients with invasive myocardial efficiency below 11% showed worse prognosis. van der Bijl et al²⁴ analyzed the prognostic role of GLVMWE in 153 patients with heart failure with indication for cardiac resynchronization therapy. The authors demonstrated that a GLVMWE <75% measured before cardiac resynchronization therapy implantation was associated with a better

long-term outcome. The present study provides further evidence on the prognostic implications of GLVMWE in a large cohort of STEMI patients, showing that patients with reduced GLVMWE had worse prognosis at long-term follow-up. In addition, GLVMWE demonstrated incremental advantage over LV EF, and the change in χ^2 of the model was higher when adding GLVMWE than when adding LV GLS. Interestingly, higher values of GLVMWE were associated with better outcome, independent of other clinical parameters (Table I in the [Data Supplement](#)).

Study Limitations

This was a retrospective, single-center study, and prospective validation is needed. Moreover, the GLVMWE was evaluated in a registry of STEMI patients, and the clinical value of this index in other patient populations needs to be evaluated.

Conclusions

A reduced GLVMWE measured on transthoracic echocardiography within 48 hours of admission is associated with worse long-term survival in STEMI patients.

ARTICLE INFORMATION

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The Data Supplement is available at <https://www.ahajournals.org/doi/suppl/10.1161/CIRCIMAGING.120.012072>.

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Disclosures

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Supplemental Materials

Tables I and II

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