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Lustosa, R.P.; Fortuni, F.; Bijl, P. van der; Mahdiui, M. el; Montero Cabezas, J.M.; Kostyukevich, M.V.; ... ; Bax, J.J.

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# Changes in Global Left Ventricular Myocardial Work Indices and Stunning Detection 3 Months After ST-Segment Elevation Myocardial Infarction



Rodolfo P. Lustosa, MD<sup>a</sup>, Federico Fortuni, MD<sup>a,b</sup>, Pieter van der Bijl, MD<sup>a</sup>, Mohammed El. Mahdiui, MD<sup>a</sup>, Jose M. Montero-Cabezas, MD<sup>a</sup>, Marina V. Kostyukevich, MD<sup>a</sup>, Juhani Knuuti, MD<sup>c</sup>, Nina Ajmone Marsan, MD<sup>a</sup>, Victoria Delgado, MD<sup>a</sup>, and Jeroen J. Bax, MD<sup>a,d,\*</sup>

**Global left ventricular (LV) myocardial work (MW) indices (GLVMWI) are derived from speckle tracking echocardiographic strain data in combination with non-invasive blood pressure measurements. Changes in global work index (GWI), global constructive work (GCW), global wasted work (GWW) and global work efficiency (GWE) after ST-segment elevation myocardial infarction (STEMI) have not been explored. The aim of present study was to assess the evolution of GLVMWI in STEMI patients from baseline (index infarct) to 3 months' follow-up. Three-hundred and fifty patients (265 men; mean age 61 ± 10 years) with STEMI treated with primary percutaneous coronary intervention (PCI) and guideline-based medical therapy were retrospectively evaluated. Clinical variables, conventional echocardiographic measures and GLVMWI were recorded at baseline within 48 hours post-primary PCI and 3 months' follow-up. LV ejection fraction (from 54 ± 10% to 57 ± 10%,  $p < 0.001$ ), GWI (from 1449 ± 451 mm Hg% to 1953 ± 492 mm Hg%,  $p < 0.001$ ), GCW (from 1624 ± 519 mm Hg% to 2228 ± 563 mm Hg%,  $p < 0.001$ ) and GWE (from 93% (interquartile range (IQR) 86%-95%) to 95% (IQR 91%-96%),  $p < 0.001$ ) improved significantly at 3 months' follow-up with no significant difference in GWW (from 101 mm Hg% (IQR 63-155 mm Hg%) to 96 mm Hg% (IQR 64-155 mm Hg%);  $p = 0.535$ ). On multivariable linear regression analysis, lower values of troponin T at baseline, increase in systolic blood pressure and improvement in LV global longitudinal strain were independently associated with higher GWI and GCW at 3 months' follow-up. In conclusion, the evolution of GWI, GCW and GWE in STEMI patients may reflect myocardial stunning, whereas the stability in GWW may reflect permanent myocardial damage and the development of non-viable scar tissue. © 2021 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>) (Am J Cardiol 2021;157:15–21)**

## Introduction

Advances in the treatment of ST-segment elevation myocardial infarction (STEMI) significantly improved the prognosis of STEMI patients.<sup>1</sup> However, after myocardial reperfusion, regional myocardial function recovery could be delayed due to myocardial stunning,<sup>2</sup> leading to transient left ventricular (LV) dysfunction with (partial) recovery of function usually within 3 to 6 months after STEMI.<sup>3</sup> Various imaging techniques have been used to detect myocardial stunning (viability) after myocardial infarction.<sup>4,5</sup> Recently, global LV myocardial work (MW) indices (GLVMWI)<sup>6</sup> have been applied to STEMI patients<sup>7</sup> to

evaluate LV systolic function (and relate to myocardial glucose metabolism<sup>6</sup>). The changes in GLVMWI between the index event and follow-up after STEMI have not been extensively investigated and may provide further insights into the use of echocardiography to predict LV functional recovery after STEMI. The aim of the present study was to evaluate the evolution of GLVMWI in patients with STEMI from baseline to 3 months follow-up.

## Methods

Patients admitted with STEMI treated with primary percutaneous coronary intervention (PCI) at Leiden University Medical Center, The Netherlands are included in an ongoing registry.<sup>8</sup> All patients were treated according to contemporary guidelines.<sup>1,9</sup> Patients underwent 2-dimensional (2D) echocardiography within 48 hours of admission and at 3 months' follow-up. Clinical and echocardiographic data were collected during the first year after STEMI in the departmental Cardiology Information System (EPD-Vision: Leiden University Medical Center, Leiden, The Netherlands) and echocardiographic database, respectively. All data were retrospectively analyzed. A total of 350 patients from September 2012 to November 2015 were analyzed, and

<sup>a</sup>Department of Cardiology, Heart Lung Center, Leiden University Medical Center, Leiden, The Netherlands; <sup>b</sup>Department of Cardiology, San Giovanni Battista Hospital, Foligno, Italy; <sup>c</sup>Department of Clinical Physiology, Nuclear Medicine and PET, Turku University Hospital and Turku PET Centre, University of Turku, Turku, Finland; and <sup>d</sup>Turku Heart Center, University of Turku and Turku University Hospital, Turku, Finland. Manuscript received April 10, 2021; revised manuscript received and accepted July 8, 2021.

See page 20 for disclosure information.

\*Corresponding author: Tel: +31 71 526 20 20; fax: +31 71 526 6809.

E-mail address: [j.j.bax@lumc.nl](mailto:j.j.bax@lumc.nl) (J.J. Bax).

Table 1  
Baseline clinical characteristics of the study population

Variable	n = 350
Age (years)	61 ± 10
Men	265 (75.7%)
Killip classification I	323 (92.3%)
Symptom onset to balloon time (min)	163 (113 to 260)
Peak Creatine Phosphokinase value (U/L)	1115 (548 to 2516)
Peak Troponin T (μg/L)	2.91 (1.36 to 6.62)
Hypertension	134 (38.3%)
Diabetes mellitus	19 (5.4%)
Dyslipidemia	65 (18.6%)
Smoker	151 (43.1%)
Family history of coronary artery disease	151 (43.1%)
Previous myocardial infarction	5 (1.4%)
Multivessel coronary disease	184 (52.6%)
Left anterior descending coronary artery cul- prit vessel	164 (46.9%)
Other culprit vessel locations	186 (53.1%)
Atrial fibrillation	2 (0.6%)
Thrombolysis in myocardial infarction (TIMI) Flow Grade <3	18 (5.1%)
Medication use	
Aspirin	349 (99.7%)
P2Y12 inhibitor	350 (100%)
β-blocker	336 (96%)
Statin	350 (100%)
Angiotensin-converting-enzyme inhibitor or Angiotensin receptor blocker	343 (98%)

Data are presented as mean ± SD, n(%), or median (25th to 75th percentile).

echocardiographic data acquired with either E9 or E95 GE Healthcare ultrasound systems (General Electric Vingmed Ultrasound, Horten, Norway) as well as simultaneous measurement of blood pressure to allow assessment of GLVMWI. Patients with known severe valvular disease and previous cardiac surgery before the index event were excluded. For retrospective analysis of clinically acquired data, the institutional review board waived the need for patient written informed consent.

Images were obtained in patients at rest in the left lateral decubitus position using commercially available ultrasound

systems (E9 or E95, General Electric Vingmed Ultrasound, Horten, Norway) equipped with M5S transducers. Standard M-mode and 2D, color, pulsed wave and continuous wave Doppler images of the parasternal, apical and subcostal views were acquired and saved in cine-loop format. Echocardiographic data were analyzed offline using EchoPac version 203 software (General Electric Vingmed Ultrasound, Horten, Norway). The LV end-diastolic volume (LVEDV) and end-systolic volume (LVESV) were assessed from the apical 4- and 2-chamber views using the Simpson's biplane method, and the LV ejection fraction (EF) was calculated.<sup>10</sup> To quantify LV global longitudinal strain (GLS), 2D-speckle tracking analyses were performed offline on standard routine grayscale images of the 4-, 2-chamber, and long-axis apical views as previously described.<sup>11</sup> LV GLS was derived with dedicated software (General Electric Vingmed Ultrasound, Horten, Norway) and presented as the average peak systolic strain of three apical views in a 17-segment model.

Calculation of GLVMWI from noninvasive LV pressure-strain analysis along with its validation has been described previously.<sup>6,12</sup> GLVMWI was calculated using a vendor-specific module (EchoPac version 203 software, General Electric Medical Systems, Horten, Norway) combining LV GLS and noninvasively measured blood pressure. LV GLS was measured using 2D-speckle tracking echocardiography by manually tracing the LV endocardial border in the apical long-axis, 2- and 4-chamber views. Patients' brachial cuff blood pressure recordings were used to noninvasively estimate the diastolic and systolic LV pressures. The timings of mitral and aortic valve opening and closing were identified from the apical long-axis view to define the duration of the following cardiac cycle phases: isovolumic contraction, LV ejection, and isovolumic relaxation. The software then constructed a patient specific, non-invasive LV pressure-strain curve combining LV GLS data of the entire cardiac cycle, LV pressures and cardiac event durations. The following GLVMWI were calculated: GWI- defined as total work within the area of the LV pressure-strain loop from mitral valve closure to mitral valve opening; GCW- defined as the sum of the work performed during shortening in systole and the negative work during

Table 2  
Echocardiographic characteristics and myocardial work indices of the study population at baseline and follow-up

Variable	Baseline (n = 350)	Follow-up (n = 350)	p-value
Heart Rate (bpm)	73 ± 13	69 ± 13	<0.001
Systolic blood pressure (mm Hg)	123 ± 18	138 ± 18	<0.001
Diastolic blood pressure (mm Hg)	75 ± 12	81 ± 12	<0.001
Left ventricular end-systolic volume (ml)	39 (29 to 51)	36 (26 to 51)	0.032
Left ventricular end-diastolic volume (ml)	84 (68 to 105)	87 (69 to 110)	0.006
Left ventricular ejection fraction (%)	54 ± 10	57 ± 10	<0.001
Left ventricular global longitudinal strain (%)	-15 ± 4	-17 ± 3	<0.001
Global work index (mm Hg%)	1449 ± 451	1953 ± 492	<0.001
Global constructive work (mm Hg%)	1624 ± 519	2228 ± 563	<0.001
Global wasted work (mm Hg%)	101 (63 to 155)	96 (64 to 155)	0.535
Global work efficiency (%)	93 (86 to 95)	95 (91 to 96)	<0.001

Data are presented as mean ± SD or median (25th to 75th percentile).

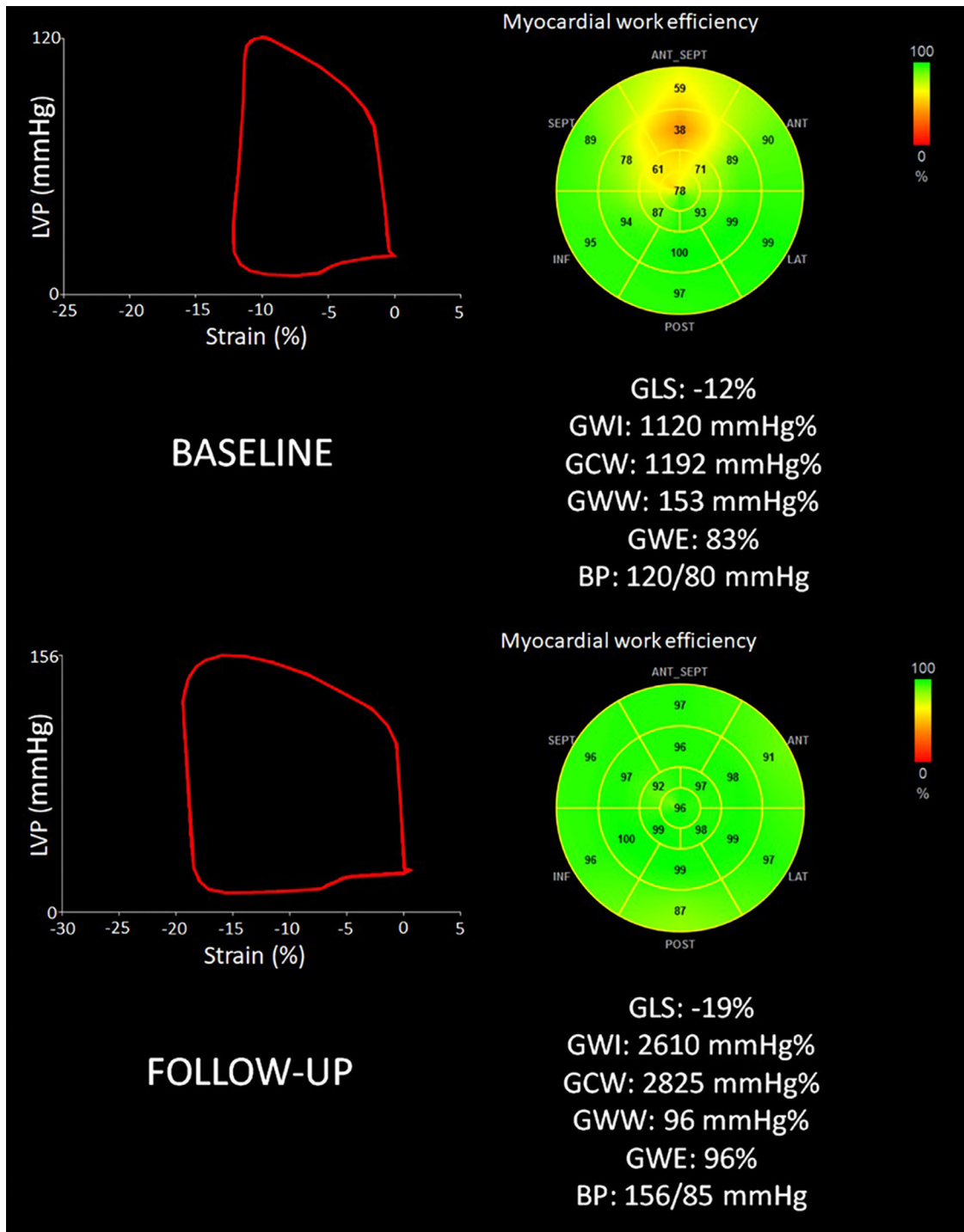


Figure 1. Calculation of global LV myocardial work indices. Myocardial work efficiency bull's-eye plots showing segmental work efficiency and global LV myocardial work indices at baseline and after 3 mo' follow-up of a patient with an anterior STEMI. LV GLS, GWI, GCW and GWE improved after 3 mo. Reduced segmental values of LV myocardial work efficiency are represented in yellow and preserved segmental values of LV myocardial work efficiency are represented in green. LV GLS and segmental values of LV work efficiency are expressed as a percentage. GWI, GCW and GWW are expressed as mm Hg%. BP = blood pressure; GCW = global constructive work; GLS = global longitudinal strain; GWE = global work efficiency; GWI = global work index; GWW = global wasted work; LV = left ventricular.

lengthening in isovolumic relaxation; GWW- defined as the sum of the negative work performed during lengthening in systole and the work performed during shortening in isovolumetric relaxation; and GWE- calculated as the sum of the

constructive work in all LV segments, divided by the sum of the constructive and wasted work in all LV segments.

Data analyses were performed using SPSS software version 25.0 (IBM SPSS Statistics for Windows. Armonk, NY).

Continuous data are presented as mean  $\pm$  SD or median with interquartile range (IQR) according to data distribution. Categorical data are presented as frequencies and percentages. Changes in continuous variables over time were compared with the paired Student's *t* test when variables were normally distributed or the Wilcoxon signed-rank test if non-normally distributed. To investigate the influence of various clinical and echocardiographic parameters on the values of GLVMWI at 3 months, univariate and multivariate linear regression analyses were performed. GLVMWI at 3 months was used as the dependent variable and changes in clinical variables (heart rate, systolic blood pressure and diastolic blood pressure), peak creatine phosphokinase (CK) and troponin T at baseline, changes in LV GLS and medications at discharge as independent variables. Potential confounders were identified based on the univariable linear regression analysis and those variables with a *p*-value < 0.05 were included in the multivariable models. All statistical tests were two-sided and a *p*-value < 0.05 was considered statistically significant.

## Results

This retrospective study included 350 patients (265 men (76%), mean age  $61 \pm 10$  years) with STEMI treated with primary PCI. Clinical characteristics of the overall population are shown in Table 1. At 3 months, patients had lower heart rates, and higher systolic and diastolic blood pressure as compared to baseline (Table 2).

The echocardiographic characteristics of the study population are shown in Table 2. At 3 months, there were

significant improvements in LVEF and LV GLS as compared to baseline. LVEDV significantly increased whereas no changes in LVESV were observed at 3 months follow-up.

The measurements of GLVMWI are shown in Table 2. In the overall study population, there were significant improvements in GWI, GCW and GWE whereas no changes in GWW were observed. Figure 1 and Figure 2 present the GLVMWI analysis at baseline and 3 months after STEMI and of the total population at baseline and 3 months' follow-up, respectively. Tables 3 and 4 summarize the uni- and multivariable analyses presenting the associates of GLVMWI at 3 months. After correcting for potential confounders identified based on the univariable linear regression analysis, lower values of peak troponin T at baseline were independently associated with higher GWI, GCW and GWE at 3 months, whereas higher values of troponin T were independently associated with higher GWW. Increase in systolic blood pressure was independently associated with higher GWI, GCW and GWW at 3 months and improvement in LV GLS was independently associated with higher GWI and GCW at 3 months.

## Discussion

The present study demonstrates that in patients with STEMI treated with primary PCI and optimal medical therapy, values of GWI, GCW and GWE significantly improved 3 months after STEMI, which may reflect the presence myocardial stunning. Interestingly, GWW did not

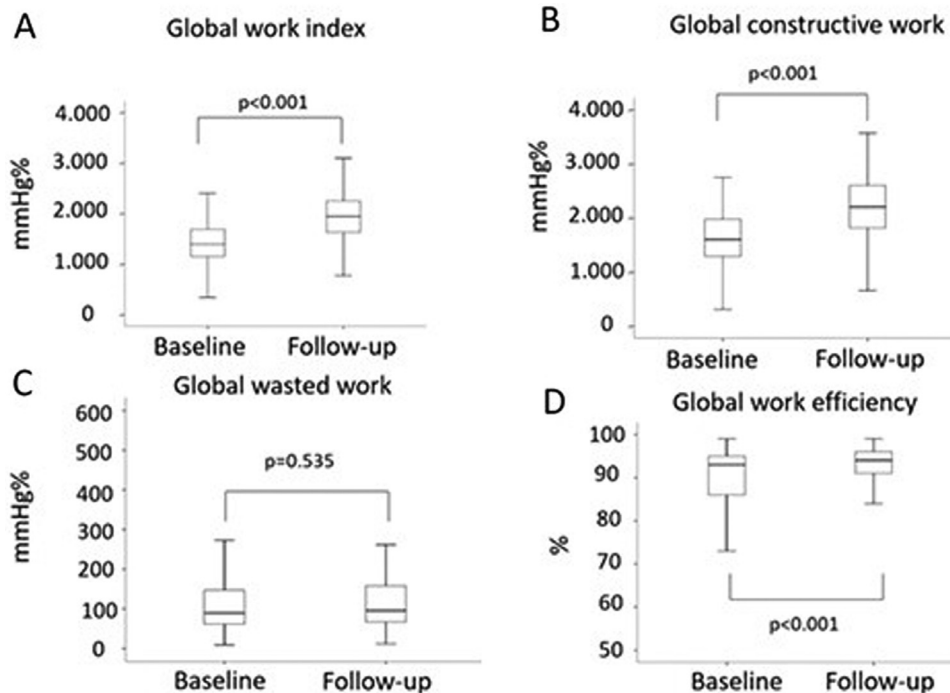


Figure 2. Changes in global LV global myocardial work indices after STEMI. The values of global LV myocardial work indices at baseline and 3 mo' follow-up is presented. At 3 mo, global work index (panel A), global constructive work (panel B) and global work efficiency (panel D) improved significantly whereas no changes in global wasted work (panel C) were observed. LV = left ventricular; STEMI = ST-segment elevation myocardial infarction. Data are presented as mean  $\pm$  SD or median (25th–75th percentile).

Table 3  
Univariable linear regression analysis of changes in global LV myocardial work indices from baseline to follow-up

Variable	Global work index at 3 mo $\beta$ coefficient (95% Confidence Interval)	Global constructive work at 3 mo $\beta$ coefficient (95% Confidence Interval)	Global wasted work at 3 mo $\beta$ coefficient (95% Confidence Interval)	Global work efficiency at 3 mo $\beta$ coefficient (95% Confidence Interval)
% Change Left Ventricular Global Longitudinal Strain	2.689 (1.128 to 4.251)	2.358 (0.562 to 4.155)	0.036 (-0.249 to 0.320)	0.008 (-0.009 to 0.025)
p-value	0.001	0.010	0.805	0.367
% Change Heart Rate	0.897 (-1.472 to 3.267)	1.864 (-0.840 to 4.568)	-0.036 (-0.461 to 0.389)	0.002 (-0.023 to 0.028)
p-value	0.457	0.176	0.869	0.857
% Change Systolic Blood Pressure	6.372 (3.722 to 9.022)	7.362 (4.335 to 10.389)	0.762 (0.278 to 1.245)	-0.018 (-0.047 to 0.012)
p-value	<0.001	<0.001	0.002	0.238
% Change Diastolic Blood Pressure	3.835 (1.382 to 6.287)	4.451 (1.650 to 7.253)	0.405 (-0.039 to 0.848)	-0.005 (-0.032 to 0.022)
p-value	0.002	0.002	0.073	0.700
Peak Creatine Phosphokinase value, U/L	-0.120 (-0.146 to -0.093)	-0.147 (-0.177 to -0.117)	0.012 (0.007 to 0.017)	-0.001 (-0.002 to -0.001)
p-value	<0.001	<0.001	<0.001	<0.001
Peak Troponin T, $\mu$ g/L	-40.170 (-48.870 to -31.471)	-49.178 (-58.948 to -39.409)	2.873 (1.165 to 4.581)	-0.452 (-0.546 to -0.358)
p-value	<0.001	<0.001	0.001	<0.001
Left Ventricular ejection fraction, %	19.082 (14.339 to 23.826)	22.361 (16.964 to 27.758)	-2.591 (-3.473 to -1.708)	0.219 (0.168 to 0.270)
p-value	<0.001	<0.001	<0.001	<0.001
$\beta$ -blocker at Discharge	123.857 (-140.316 to 388.031)	168.089 (-133.722 to 469.901)	47.485 (0.333 to 94.637)	-2.321 (-5.184 to 0.541)
p-value	0.357	0.274	0.048	0.112
Angiotensin-converting- enzyme inhibitor or Angiotensin receptor blocker at discharge	190.790 (-178.881 to 560.461)	249.499 (-172.859 to 671.856)	-9.534 (-75.896 to 56.829)	1.880 (-2.135 to 5.896)
p-value	0.311	0.246	0.778	0.358

Table 4  
Multivariable linear regression of changes in global LV myocardial work indices from baseline to follow-up

Variable	Global work index at 3 mo $\beta$ coefficient (95% Confidence Interval)	Global constructive work at 3 mo $\beta$ coefficient (95% Confidence Interval)	Global wasted work at 3 mo $\beta$ coefficient (95% Confidence Interval)
% Change Left Ventricular Global Longitudinal Strain	2.836 (1.485 to 4.187)	2.535 (1.010 to 4.060)	-
p-value	<0.001	0.001	-
% Change Systolic Blood Pressure	6.122 (2.897 to 9.347)	7.313 (3.672 to 10.954)	0.750 (0.273 to 1.226)
p-value	<0.001	<0.001	0.002
% Change Diastolic Blood Pressure	0.738 (-2.192 to 3.667)	0.698 (-2.609 to 4.006)	-
p-value	0.621	0.678	-
Peak Troponin T, $\mu\text{g/L}$	-42.356 (-50.517 to -34.194)	-51.486 (-60.700 to -42.271)	2.686 (1.002 to 4.370)
p-value	<0.001	<0.001	0.002
$\beta$ -blocker at Discharge	-	-	49.632 (3.598 to 95.666)
p-value	-	-	0.035

change at 3 months' follow-up, which may reflect the presence of scar tissue. Lower values of troponin T at baseline were independently associated with higher values of GWI and GCW and lower values of GWW 3 months after STEMI. Both improvement in LV GLS and changes in systolic blood pressure were independently associated with changes in GWI and GCW at 3 months' follow-up.

2D speckle tracking strain echocardiography has shown to be a useful tool to detect myocardial viability after myocardial infarction. Migrino et al<sup>13</sup> demonstrated in 21 patients with previous myocardial infarction that 2D-strain echocardiography can detect post-infarct myocardial viability. Another study<sup>14</sup> demonstrated that strain is useful to differentiate viable from infarcted, non-viable myocardium. Recently, Boe et al<sup>15</sup> showed in patients with NSTEMI that strain can be influenced by changes in afterload, and that MW analysis permits correction of LV GLS for afterload. Moreover GLVMWI correlated well with glucose myocardial metabolism as assessed by PET using FDG<sup>6</sup> which is considered the gold standard for myocardial viability.<sup>16</sup> Accordingly, the new parameters derived from MW analysis may be used to discriminate viable (stunned) myocardium from scar tissue in patients after STEMI. The presence of reduced values of GWI, GCW and GWE after STEMI has been demonstrated in previous studies. El Mahdiui et al<sup>17</sup> showed low values of GWE in STEMI patients treated with primary PCI, and Chan et al<sup>18</sup> demonstrated low values of GLVMWI in ischemic cardiomyopathy. Previous work<sup>19</sup> revealed that regional work can be reduced after coronary occlusion and may recover after reperfusion. Stunned myocardium can be related to low myocardial oxygen consumption and consequently impaired metabolism which can explain reduced values of myocardial work indices at the index event. These variables (potentially reflecting stunning) may recover within 3 to 6 months after the infarction, when stunning has resolved. The present study shows that lower values of troponin T at baseline were related with higher values of GWI, GCW and GWE at 3 months' follow-up, whereas higher values of troponin T were associated with worse GWW. This can be explained by the fact that myocardial necrosis leads to troponin release<sup>20</sup> which reflects

permanent myocardial damage and infarct size.<sup>21</sup> Moreover, GWW did not change between baseline and 3 months. Therefore, it may be hypothesized that GWI, GCW and GWE may (partially) reflect myocardial stunning and GWW can be useful to identify infarct size and may reflect myocardial damage at the time of STEMI. Further studies comparing GLVMWI with more accurate techniques to define infarct size and myocardium at risk would be needed to confirm this hypothesis. This is a single-center study with a retrospective design. Moreover, since late gadolinium contrast-enhanced cardiac magnetic resonance, SPECT or PET data were not available for most of the patients, myocardial work indices at baseline and 3 months' follow-up could not be directly compared to those modalities for viability assessment.

In conclusion, changes in GWI, GCW and GWE from baseline to 3 months after STEMI may reflect myocardial stunning whereas GWW may reflect irreversible myocardial damage (scar tissue).

## Disclosures

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