INTRODUCTION

Urgent reperfusion and aggressive anti-thrombotic therapy have dramatically improved the prognosis of patients with ST-segment elevation myocardial infarction (STEMI) (Schmidt, Jacobsen, Lash, Bøtker, & Sørensen, 2012). Thanks to this modern management, increasingly more patients leave the hospital with only modest reduction of their left ventricular (LV) systolic function as assessed by LV ejection fraction (LVEF). However, not all patients with normal LVEF post-STEMI have a favorable prognosis. Therefore, using relatively simple tools that could identify high-risk patients among those with apparently low risk for major adverse cardiac events (MACEs) is of particular interest.

ST segment resolution (STR) is a simple, rapid and noninvasive method for assessment of quality of reperfusion therapy in the...
setting of STEMI (Schröder et al., 1994). Although successful recanalization of epicardial vessels in STEMI is a necessary condition, it’s the microvascular not the epicardial flow that best determines prognosis and correlates with outcome. Fortunately, STR reflects myocardial rather than epicardial flow, hence it provides prognostic information beyond that provided by any other tool including coronary angiogram itself (Santoro et al., 1998). Many studies have shown a strong and consistent relationship between degree of STR and subsequent MACEs including mortality (deLemos & Braunwald, 2001). Regarding STR assessment methods, single lead STR (percentage of ST recovery in only the single lead showing maximum elevation) is reported to be superior, less time-consuming and more convenient than sum STR (percentage of recovery after measuring ST elevation from all leads related to infarct location; Zeymer et al., 2005) with no convincing evidence from literature to support the notion that continuous ST monitoring provides more accurate prognostic information than static ECG analysis (Schröder, Zeymer, Wegscheider, & Schröder, 2004).

The first month after STEMI is the most vulnerable period, during which critical management decisions that have a huge impact on long-term prognosis are taken, so identification of high risk patients should take place during this period and should be based on solid data focusing not only on the long term but also on short term outcome. Thus, we thought that it may be of considerable interest to explore the impact of STR on 30-day outcome among apparently low-risk patients with successful reperfusion and preserved LVEF following STEMI.

2 | METHODS

2.1 | Study design

In the period from January to July 2017, we conducted a single-center prospective observational study that included 110 consecutive patients admitted with a diagnosis of STEMI to coronary care unit at Benha University Hospital, Egypt who were successfully re-perfused (either by fibrinolytic therapy using streptokinase “SK” or primary percutaneous coronary interventions “PPCI”) and had normal LVEF (≥50%) by conventional echocardiography before discharge. STEMI was defined as chest pain typical for myocardial infarction of at least 30 min duration and less than 6 hr, new ST segment elevation in two contiguous leads with the cut-off points ≥0.2 mV in men or ≥0.15 mV in women in leads V2–V3 and/or ≥0.1 mV in other leads on the 12-lead ECG. Successful reperfusion was defined as disappearance or improvement of chest pain combined with resolution of ST-segment elevation by ≥50% in the single lead with maximum elevation on baseline ECG 90 min of starting SK infusion or shortly after PPCI that restores TIMI-II to III flow without inaprocedural complications. All patients provided informed consent and the study was approved by the local ethics committee at our institution. Key exclusion criteria included: patients less than 18 years old, those with missed MIs who did not receive any reperfusion, those who did not meet criteria for successful reperfusion, those with depressed LVEF (<50%) at discharge, those with noncardiac diseases that limit life expectancy and patients unable to give informed consent. Moreover, patients with poor technical ECG quality that hampers proper STR assessment were excluded from final analysis.

2.2 | Measurement of ST resolution
ST segment deviation was analyzed by a single investigator blinded to clinical data with lens intensified calipers to the nearest of 0.025 mV 20 ms after the end of QRS complex with the TP segment as reference baseline from leads I, aVL, and V1–V6 for anterior infarction, leads II, III, and AVF for inferior infarction and leads I, aVL, V5 and V6 for lateral infarction. Patients with bundle branch block who had clear ischemic ST segment elevation were included into the analysis (Sgarbossa et al., 1996). Calibration is 1 mV = 10 mm. As in previous studies (Schröder, Zeymer, Wegscheider, & Neuhaus, 1999), a time window of 70–110 min was allowed for the 90-min ECG recording. Single lead STR was measured by the ST segment deviation on the single ECG lead which showed maximum deviation at baseline 90 min after start of SK infusion or shortly after end of PPCI. Resolution was expressed as percentage from baseline.

2.3 | Echocardiographic measurements
All patients had echocardiographic study within 48 hr of admission and repeated at 30 days after discharge. All exams were performed by an experienced operator blinded to follow-up data. Transthoracic echocardiography examination was performed using commercially available ultrasound system (Philips EPIQ7 Ultrasound System) equipped with 3.5 MHz phased-array transducer. The image was obtained at held end-expiration. LVEF was calculated using the Simpson’s biplane method in accordance with the European Association of Echocardiography and the American Society of Echocardiography recommendations (Lang et al., 2005).

2.4 | Study protocol and endpoints
Based on the percent of ST segment resolution using single-lead STR method for assessment, patients were divided into two groups:

- Group (I): those with complete STR; defined as ≥70% STR.
- Group (II): those with partial STR; defined as 50%–70% STR.

Both groups were followed-up and the study endpoint was a composite of cardiovascular mortality, re-hospitalization for heart failure (HF), and urgent revascularization at 30 days from hospital discharge. Hospitalization for HF was defined as hospitalization due to dyspnea with objective signs of pulmonary congestion and treatment with intravenous diuretics. Verification of HF hospitalization was done by an independent reviewer blinded to echocardiographic data related to index MI. Information on mortality was obtained from hospital records and classified as cardiovascular and noncardiovascular.
2.5 Statistical analysis

Data management and statistical analysis was performed using SPSS software version 23. Numerical data were summarized using means and standard deviations. Categorical data were summarized as numbers and percentages. For numerical variables, comparisons between two groups were done using independent t-test for normally distributed variables or Mann–Whitney U test for non-normally distributed variables. For categorical variables, differences were analyzed with chi square test or fisher exact test when appropriate. Kaplan–Meier curve was drawn to estimate probability of MACE over 1 month, log rank test was used to compare probabilities in two groups. Logistic regression analysis was done for prediction of risk of MACE. Odds ratio with 95% Confidence interval were calculated. All p-values were two-sided. p-values < 0.05 were considered significant.

3 RESULTS

3.1 Study population

The mean age was 58.8 ± 14 years, 58% were males, 27% had diabetes mellitus, 33% were hypertensives, 39% were smokers, 23% were obese, 20% had known dyslipidemia, 16% had family history of premature coronary artery disease (CAD), 17% had past history of CAD, and 10% had history of previous coronary interventions. Between groups analysis did not reveal significant differences in baseline characteristics (Table 1).

3.2 STEMI

Fifty-nine patients (53.6%) had anterior STEMI, 39 patients (35.4%) had inferior STEMI, and 12 patients (10.9%) had lateral STEMI. Eighty-seven patients (79.1%) were reperfused using fibrinolytic therapy (Streptokinase, 1.5 million units over 60 min) and 23 patients (20.9%) underwent PPCI. We found no significant difference in time to peak CK-MB levels when comparing those reperfused by fibrinolysis and those reperfused by PPCI (21.4 ± 2.7 vs. 20.7 ± 2.9 hr, respectively, \( p = 0.263 \)). The mean total ischemic time for entire population was 203.3 ± 45.3 min and the mean door-to-reperfusion time (device or needle) was 44.1 ± 20.3 min. There was no statistically significant difference regarding location of STEMI, reperfusion strategy (SK vs. PPCI), total ischemic time, time to peak CK-MB levels, or door-to-reperfusion time between groups (Table 2).

3.3 In-hospital outcome

In-hospital MACEs were reported in 13 patients (11.8%) in the form of four patients with heart failure, three patients had reinfarction, one patients had ischemic stroke, and five patients had resuscitated cardiac arrest. No between groups significant difference regarding in-hospital MACEs were reported.

3.4 Echocardiographic parameters

The baseline end-systolic volume (ESV) was 47.4 ± 18.5 ml, the baseline end-diastolic volume (EDV) was 107.4 ± 32.3 ml, the baseline LVEF was 55.7% ± 7.7% and the baseline tissue doppler E prime (TDE’) velocity at the medial mitral valve (MV) annulus was 8.89 ± 1.2 cm/s. Between groups analysis regarding baseline echocardiographic parameters is illustrated in Table 3. At 30-day follow-up, ESV significantly increased—compared to baseline—in group II (partial STR) more than group I (complete STR). Median percent change in group I and group II were 14.9 and 25, respectively. This difference was statistically significant (p value = 0.014). Similarly, EDV significantly increased—compared to baseline—in group II (partial STR) more than group I (complete STR). Median percent change in group I and group II were 11.1 and 16.2, respectively.

### TABLE 1 Baseline characteristics of study population

<table>
<thead>
<tr>
<th></th>
<th>Group I (N = 55)</th>
<th>Group II (N = 55)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>Mean ± SD</td>
<td>58.4 ± 14.9</td>
<td>59.1 ± 13.3</td>
</tr>
<tr>
<td>Gender</td>
<td>Male</td>
<td>33 (60.0)</td>
<td>31 (56.4)</td>
</tr>
<tr>
<td>DM</td>
<td>Yes</td>
<td>16 (29.1)</td>
<td>14 (25.5)</td>
</tr>
<tr>
<td>HTN</td>
<td>Yes</td>
<td>17 (30.9)</td>
<td>19 (34.5)</td>
</tr>
<tr>
<td>Smoking</td>
<td>Yes</td>
<td>20 (36.4)</td>
<td>23 (41.8)</td>
</tr>
<tr>
<td>Obesity</td>
<td>Yes</td>
<td>13 (23.6)</td>
<td>12 (21.8)</td>
</tr>
<tr>
<td>Known dyslipidemia</td>
<td>Yes</td>
<td>12 (21.8)</td>
<td>10 (18.2)</td>
</tr>
<tr>
<td>FH of premature CAD</td>
<td>Yes</td>
<td>8 (14.5)</td>
<td>9 (16.4)</td>
</tr>
<tr>
<td>PH of CAD</td>
<td>Yes</td>
<td>9 (16.4)</td>
<td>10 (18.2)</td>
</tr>
<tr>
<td>PH of coronary interventions</td>
<td>Yes</td>
<td>5 (9.1)</td>
<td>6 (10.9)</td>
</tr>
</tbody>
</table>

Note. CAD: Coronary artery disease; DM: diabetes mellitus; FH: family history; HTN: hypertension; PH: past history; SK: streptokinase; STEMI: St-elevation myocardial infarction.
This difference was statistically significant ($p$ value = 0.003). LVEF significantly decreased—compared to baseline—in group II (partial STR) more than group I (complete STR). Median percent change in group I and group II were −5 and −16, respectively. This difference was statistically significant ($p$ value < 0.001). TDE' velocity at medial MV annulus increased—compared to baseline—in group I (complete STR) more than group II (partial STR). Median percent change in group I and group II were 7.1 and 2.2, respectively. This difference was just borderline significant ($p$ value = 0.051) (Figure 1).

### Study endpoints

Thirty-day MACEs were reported in 24 patients (21.8%) of the whole population in the form of five deaths due to cardiovascular causes, 13 patients with re-hospitalization due to heart failure and six patients with urgent revascularization. The primary endpoint of combined MACEs occurred in seven patients (12.7%) of group I (complete STR) versus 17 patients (30.9%) of group II (partial STR) (Relative risk = 2.43, 95%CI = 1.1–5.4, $p$ = 0.021) using single lead STR method as the ECG indicator (Figure 2). This was driven by a statistically significant reduction in rates of re-hospitalization due to HF (three patients [5.5%] in group I vs. 10 patients [18.2%] in group II, $p$ = 0.03) (Table 4). A multivariate logistic regression analysis model using the occurrence of MACEs as a dependent factor showed incomplete STR to be a significant independent predictor for 30-dayMACEs (OR 3.25, 95% CI 1.2–8.83, $p$ = 0.02) even after adjustment for the location of infarction (anterior vs. non-anterior).

### Discussion

Risk stratification of patients who recently sustained STEMI is a cornerstone step in management in order to implement secondary preventive measures that could improve short and long-term outcome. This task becomes more difficult among apparently low risk patients with successful reperfusion and preserved LVEF at hospital discharge. Moreover, most guideline-recommended therapeutic decisions such as use of angiotensin-converting enzyme inhibitors (ACEIs) (Pfeffer et al., 2003) and/or aldosterone antagonists (Pitt et al., 2003) are focused on those with impaired LVEF. Therefore, any novel measure for risk stratification after STEMI should be preferentially directed to those with preserved LVEF for whom treatment decisions are still ambiguous.

Based on these facts, and in a time of dizzying advances in diagnostic modalities, it is refreshing to see what a useful, simple, non-invasive, broadly accessible, easily repeatable and affordable tool the ECG is. The prognostic value of STR may be in part explained by the fact that it reflects myocardial rather than epicardial blood flow, and this has been demonstrated in several studies (van’t Hof, Liem, deBoer, & Zijlstra, 1997).

The present study done exclusively in patients with preserved LVEF following successful reperfusion of STEMI demonstrated that complete rather than partial STR allowed rapid risk assessment and predicted 30-day adverse outcome among patients with LVEF ≥ 50%. Additionally, complete STR provided independent information concerning combined endpoint of
cardiovascular mortality, re-hospitalization for heart failure and urgent revascularization.

A sub-analysis of the In Time-II study (Giugliano et al., 2001) showed that 30-day cardiovascular mortality was significantly different between low (1.2%), medium (3.6%) and high risk (10.3%) STR categories using single-lead STR method for assessment. Prasad et al. (2004) demonstrated that rates of 30-day mortality and 30-day combined MACEs were inversely related to the degree of STR (using single-lead STR method) in a group of patients undergoing PPCI for acute MI and that this relation was consistent across all age subgroups. Brodie et al. (2005) found that STR (complete vs. partial) using single-lead STR method for assessment correlated with in-hospital mortality (4.0% vs. 6.7%, $p = 0.005$), reinfarction (1.4% vs. 3.4%, $p = 0.01$), and late cardiac mortality (17% vs. 25%, $p < 0.0001$).

We showed a statistically significant reduction in rates of re-hospitalization for HF among those with complete versus partial STR, and this was accompanied by a statistically significant percent increase in ESV and EDV and percent decrease in EF. This is similar to Saran, Been, Furniss, Hawkins, and Reid (1990) and Andrews et al. (2000) who demonstrated that more complete STR is consistently associated with improved LV function and that the probability of congestive HF decreases in a stepwise fashion with greater degrees of STR.

The fact that reduction of 30-day combined MACEs in our study was driven by significant reduction in rehospitalization rates for HF and that differences in 30-day mortality between those with complete versus partial STR was nonsignificant could be explained by taking into account that our selected study population are already low-risk patients (successfully reperfused with normal LV systolic function) in addition to small sample size. However, the novelty of our study may stem from the idea that we did not examine the broad group of all patients who received reperfusion therapy for STEMI and instead of classifying them according to degree of STR into complete, partial, and absent irrespective to LVEF and success of reperfusion, we ought to focus selectively on those defined conventionally to have successful reperfusion (≥50% STR) and good LV function (LVEF ≥ 50%) after STEMI and then we reclassified them according to the degree of STR into complete (≥70%) and partial (50%-70%) hypothesizing that this classification may refine risk stratification process by allowing to pick up those with relatively higher risk among group of patients that has been always thought to have low risk for MACEs.

Two methods are now acceptable for assessment of ST deviation recovery; single-lead STR and max-STE (existing maximum ST-elevation that is present at a given time point in a single lead not compared to the baseline ECG; Schröder, 2004). A noteworthy point is that we used single-lead STR not max-STE as a measurement method to assess ST deviation recovery, despite the fact that max-STE method...
provides more predictive power for MACEs when compared with single-lead STR (Schröder, Wegscheider, Zeymer, Neuhaus, & Schröder, 2001). We thought that it may be more meaningful if we could prove the validity of our hypothesis using a less predictive but still acceptable method.

5 | CONCLUSION

Complete rather than partial STR predicts 30-day adverse outcome in patients with preserved LVEF following successful reperfusion of STEMI.

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CONFLICTS OF INTEREST

None declared.

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