Early predictors of left ventricular remodeling after primary percutaneous coronary intervention

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1. Introduction

Acute myocardial infarction (AMI) with its accompanying adverse sequelae, remains one of the most common causes of morbidity and mortality in the world. Reperfusion therapy is the most important therapy for treatment of AMI that reduces the infarct size and improves left ventricular (LV) function, both of which contribute to improved clinical outcome in AMI patients. Success of fibrinolytic therapy and recently of primary percutaneous coronary intervention (PPCI), has reduced AMI mortality. However, increased survival rate resulted in increased incidence of cardiovascular events mainly due to LV remodeling and congestive heart failure. Cardiac remodeling is a group of molecular, cellular and interstitial changes that clinically manifest as changes in geometry and function of the heart resulting from cardiac injury. Post-infarct ventricular remodeling develops in about 30% of patients with a history of MI. Ventricular remodeling is a predictor of heart failure and for this reason it assumes a negative prognostic value. The pathogenesis of LV remodeling after acute MI is multi-fac- torial that contribute at different stages from the time of coronary occlusion until the development of ventricular dilatation. There are clinical evidences that post-infarct remodeling can be prevented or in some cases reversed. Therapies with proven efficacy against post-infarct remodeling exist and research is bringing new discoveries in the pathogenesis of post-infarct remodeling into the field of clinical practice and therapy. For this reason, the battle of medicine against heart failure is against post-infarct remodeling which means that prevention is better than cure.

Infarct size, anterior location, the perfusion status of the infarct-related artery (IRA), a restricted pattern of LV filling and heart failure on admission have been identified as predictors of LV remodeling after MI in the thrombolysis era. Recently there has been increased interest in the prevalence of remodeling in the era of interventional cardiology. From a clinical point of view it is important to identify those patients at high risk for LV remodeling. The early identification of patients at a risk of LV remodeling may have important therapeutic implications. Factors predicting post-infarct LV remodeling after MI treated by PPCI remain to be clarified.

2. Material and methods

We conducted an observational cohort study included 152 patients diagnosed as acute STEMI and admitted in Coronary care unit (CCU) of Assiut University Hospital between January 1st 2016 and 30th September 2016. All patients were treated successfully with primary PCI within 12 h of onset of chest pain or up to 24 h of onset of chest pain if there were ongoing ischemia. We excluded patients with clinical manifestations of acute heart failure or cardiogenic shock at presentation, significant mitral regurgitation (≥2) or valve disease and patients with permanent pacemaker insertion. Detailed history was obtained from all patients including age, sex, cardiovascular risk factors (hypertension, diabetes mellitus, smoking and dyslipidemia) and onset of chest pain. 12 lead ECG was done to all patients within 10 min of arrival to emergency room (ER) and after primary PCI. Echocardiography: All patients were examined by transthoracic echocardiography within 24 h of admission and six months after discharge using Phillips ie33 ultrasound system device according to the following protocol:
LV volumes (LVEDV and LVESV) and ejection fraction (EF) were measured using modified Simpson’s method. Volume measurements are usually based on tracings of the blood-tissue interface in the apical four-chamber (A4C) and two-chamber (A2C) views. At the mitral valve level, the contour is closed by connecting the two opposite sections of the mitral ring with a straight line. The most commonly used method for 2D echocardiographic volume calculations is the biplane method of disk summation (modified Simpson’s rule). As shown in Fig. 1.

LV volume indices were calculated as follows:

\[ \text{LV volume indices} = \frac{\text{LV volumes}}{\text{Body surface area (BSA)}} \]

(1) Wall motion score index (WMSI) was calculated as follows:

The LV was divided according to a 17-segment model. A wall motion score was assigned to each segment to calculate the LV wall motion score index as the average of the scores of all segments visualized.

The following scoring system was used: normal or hyperkinetic scored (1), hypokinetic (reduced thickening) scored (2), akinetic (absent or negligible thickening, e.g. scar) scored (3), and dyskinetic (systolic thinning or stretching, e.g., aneurysm) scored (4).

\[ \text{WMSI} = \frac{\text{Sum of scores of all segments visualized}}{\text{Number of these segments}} \]  \hspace{1cm} (1)

(2) Pulsed wave (PW) Doppler of trans-mitral flow during diastole to assess LV diastolic filling pattern. The following variables were calculated at baseline:

Peak velocity of early rapid filling wave (E), peak velocity of atrial wave (A), peak E/A wave velocity ratio and Deceleration time (DT). Valsalva maneuver was done if needed to confirm grade of diastolic dysfunction.

2.1. The selected patients were categorized into two groups after 6 months of MI

- Group I (with LV remodeling):

  Patients with an increase in LVEDVI > 20% were considered to have LV remodeling.

  An arbitrary definition of ventricular remodeling, but widely adopted in follow-up studies,\textsuperscript{11,13,14} is an increase of at least 20% of LVEDV from the first post infarction imaging.

- Group II (without LV remodeling).

So, the percentage of patients who developed progressive LV remodeling after 6 months was detected.

Then the following factors and their influence on LV remodeling were evaluated in each group:

(A) Clinical: Age, Sex, Risk Factors (DM, HTN, Dyslipidemia, Smoking)

(B) ECG diagnosis and location of STEMI.

(C) Echocardiographic:

  - LVEDVI [ml/m\(^2\)]
  - LVESVI [ml/m\(^2\)]
  - Ejection fraction [%]
  - Wall motion score index (WMSI).
  - Grade of diastolic dysfunction.

(D) Angiographic:

  - IRA (LAD, LCX or RCA).
  - Number of vessels affected.
  - Thrombus aspiration.
  - Symptom to balloon time >4 h.
  - Stenting and type of the stent (DES or BMS).
  - Post PCI TIMI flow grade.

Informed consents were obtained from all participants after the explanation of all steps of the study. The ethical committee of Assiut Faculty of Medicine approved the study protocols.

3. Statistical analysis

All statistical analyses were carried out using Software Package for Social Sciences (SPSS) version 20.0. Categorical variables were described by number and percent (N, %) and continuous variables...
with an increase in LVEDVI > 20% who considered to have LV remodeling (Group I) were 49 (32.2%) while the other patients without LV remodeling were 103 (67.8%) (Group II).

Regarding demographic data: There was no significant statistical difference between the two groups (P value > 0.05) Table 1.

Regarding electrocardiographic data: Anterior MI was significantly more in group I (P < 0.00) while interophorosterior MI and inferior MI were significantly more in group II (P < 0.00) Table 2.

Regarding angiographic data: Significant difference between both groups noticed regarding IRA with significant affection of left anterior descending (LAD) artery in group I (P < 0.00) while significant affection of right coronary artery (RCA) and left circumflex (LCX) arteries in group II (P < 0.00). Other angiographic findings regarding number of vessels affected, use of thrombus aspiration, type of stent and post PCI TIMI grade had no significant statistical difference between both groups (P value in all >0.05) Table 3.

Regarding baseline echocardiographic data, group I had significantly higher LVEDVI, LVESVI and WMSI while, Ejection fraction and LVEF were significantly more in group II (51 ± 6.81 %) vs. (41.4 ± 6.59 %) (P value = 0.00) (Table 4).

Table 2

| ECG diagnosis                  | Group I (n = 49) | Group II (n = 103) | P value |
|-------------------------------|-----------------|--------------------|---------|
| Anterior MI                   | 44 (89.8 %)     | 46 (44.7 %)        | 0.00    |
| Extensive inferior MI         | 3 (6.1 %)       | 41 (39.8 %)        | 0.00    |
| Inferior MI                   | 2 (4.1 %)       | 16 (15.5 %)        | 0.00    |

Data was expressed in form of frequency (percentage). P value was considered of statistical significance if < 0.05. MI = Myocardial infarction.

Table 3

| Baseline angiographic findings of both groups. |
|-----------------------------------------------|
| Variables                                    | Group I (n = 49) | Group II (n = 103) | P value |
| Infarct related artery                        |                  |                    |         |
| Left anterior descending                      | 44 (89.8 %)      | 47 (45.6 %)        | 0.00    |
| Right coronary artery                         | 3 (6.1 %)        | 43 (41.7 %)        | 0.00    |
| Left circumflex artery                        | 2 (4.1 %)        | 13 (12.6 %)        | 0.00    |
| Number of vessels affected                    |                  |                    | 0.57    |
| Single vessel                                 | 30 (61.2 %)      | 54 (52.4 %)        |         |
| Two vessels                                   | 13 (26.5 %)      | 32 (31.1 %)        |         |
| Three vessels                                 | 6 (12.2 %)       | 17 (16.5 %)        |         |
| Thrombus aspiration                           | 10 (20.4 %)      | 21 (20.4 %)        | 0.89    |
| Yes                                          | 39 (79.6 %)      | 82 (79.6 %)        | 0.31    |
| No                                           | 1 (2%)           | 10 (9.7 %)         |         |
| Stenting                                      |                  |                    | 0.18    |
| Yes                                          | 48 (98 %)        | 93 (90.3 %)        |         |
| No                                           | 1 (2%)           | 10 (9.7 %)         |         |
| Symptoms to balloon time > 4 h               | 33 (67.3 %)      | 60 (58.3 %)        | 0.18    |
| Post PCI TIMI grade > 2                      | 46 (93.9 %)      | 100 (97.1 %)       | 0.29    |

P value was considered of statistical significance if <0.05.

Table 4

| Baseline echocardiographic characteristics of all studied patients. |
|---------------------------------------------------------------------|
| Variables                                                           | Group I (n = 49) | Group II (n = 103) | P value |
| LVEDVI (ml/m²)                                                      | 62.75 ± 17.23   | 53.91 ± 14.97      | 0.01    |
| LVESVI (ml/m²)                                                     | 33.63 ± 11.21   | 25.39 ± 7.71       | 0.00    |
| Ejection fraction (%).                                             | 41.41 ± 6.59    | 51.68 ± 6.81       | 0.00    |
| Wall motion score index.                                           | 1.66 ± 0.19     | 1.28 ± 0.17        | 0.00    |
| Grade of diastolic dysfunction                                     |                  |                    | 0.46    |
| 1                                                                  | 32 (65.3 %)      | 65 (63.1 %)        |         |
| 2                                                                  | 17 (34.7 %)      | 38 (36.9 %)        |         |

P value was considered of statistical significance if < 0.05.
**Table 5**
Six month follow-up echocardiographic characteristics of all studied patients.

| Variables         | Group I (n = 49) | Group II (n = 103) | P value |
|-------------------|------------------|--------------------|---------|
| LVEDVI (mL/m²)   | 90.40 ± 17.69    | 55.18 ± 14.31      | 0.00    |
| LVESVI (mL/m²)   | 42.10 ± 12.39    | 26.06 ± 7.23       | 0.00    |
| Ejection fraction (%) | 36.18 ± 6.66    | 52.57 ± 6.38       | 0.00    |
| Wall motion score index | 1.67 ± 0.17     | 1.22 ± 0.14        | 0.00    |

P value was considered of statistical significance if <0.05.

**Discussion**

Despite the latest advances in AMI management, the post-infarct LV remodeling process that leads to CHF still represents a major problem. Over the past decades, scientists made substantial efforts to improve the understanding of this process by searching bad or good predictors and also risk factors which can be associated with this process.

Two-dimensional (2D) echocardiography is a widely available and well-established method for assessing LV remodeling. We used 2D echocardiography to assess LV volumes in patients treated by PPCI within 24 h of admission and 6 months after discharge.

In our study, percentage of patients who developed progressive LV remodeling after the first 6 months of AMI treated with PPCI was 32.2%. This was concordant with findings of Bolognese et al. who found that LV dilatation at 6 months with >20% increase in LVEDVI occurred in 30% of a group of 284 patients undergoing PPCI for AMI. Also, in accordance with findings of Loboz-Grudzień et al. who found that progressive LV dilatation had occurred in 24% of a group of 88 patients underwent PPCI for AMI. Also, a review article published 2011 in European heart journal stated that post-infarct ventricular remodeling develops in about 30% patients with a history of MI.

The early identification of patients at a risk of LV remodeling may have important therapeutic implications. So, we aimed to identify at discharge the clinical, angiographic and echocardiographic predictors of LV remodeling after PPCI in a group of STEMI patients.

**Regarding risk factors**, no significant difference between both groups regarding age, sex and risk factors. These findings are consistent with findings of Zaliaduonyte-Peksiene et al. and Loboz-Grudzień et al. who couldn't detect a clinical risk factor as a significant predictor of post-infarct LV remodeling. In contrast to findings of Pop et al. who studied predictors of post-infarct LV remodeling in a group of 105 STEMI patient treated by PPCI and found that risk factors correlated with post-infarct LV remodeling were female sex, smoking and dyslipidemia. This difference could be due to smaller sample size of Pop et al. study as they studied only 105 patients of whom there were only 27 females (12 females developed LV remodeling and 15 didn’t develop remodeling) this represented 52% in Group 1 vs. 18% in Group 2 (p < 0.00) and considered as significant predictor while in our study females were 33 (11 developed LV remodeling and 22 didn’t develop remodeling), but due to larger sample size this represented 22.4% in group 1 and 21.4% in group II (P = 0.51). Similarly regarding other risk factors as smoking and dyslipidemia, difference in results between our study and that of Pop et al. may be attributed to different sample size.

**Regarding electrocardiographic data**, patients with anterior location of MI were at high risk for LV remodeling after AMI by univariate analysis, but in multivariate regression analysis it was not an independent predictor of LV remodeling. These findings are consistent with findings of Zaliaduonyte-Peksiene et al. Who studied the impact of clinical, echocardiographic parameters and polymorphism of angiotensinogen gene on LV remodeling after AMI in a group of 141 patients with first STEMI and found that anterior localization of the infarct was independent predictor of LV remodeling after AMI.

**Regarding angiographic data**, we found no significant difference between both groups regarding number of vessels affected, use of thrombus aspiration, type of stent used either BMS or DES and post PCI TIMI flow. But, regarding IRA, patients with LAD were at high risk for LV remodeling by univariate analysis and also an independent predictor by multivariate regression analysis. These findings are consistent with findings of Warren et al. who studied...
the time course of LV dilatation after MI and influence of IRA; they found that LV dilatation was more frequent and chronic dilatation significantly more marked (p < 0.01) in patients with LAD occlusion as compared with RCA occlusion. Also concordant with findings of Loboz-Grudzięń et al. who studied early predictors of adverse LV remodeling after PPCI in 88 patients with first STEMI and found that LAD as IRA was a significant predictor of LV remodeling by univariate regression analysis (P < 0.05). But regarding number of vessels affected, our findings are not consistent with findings of Bolognese et al. who studied LV remodeling after PPCI in 284 patients with AMI treated with PPCI and found that independent predictors of late (after 6 months) LV dilatation were high peak creatine kinase (CK) value and the presence of multi-vessel coronary artery disease (CAD). Also not consistent with findings of Pop et al. who studied predictors of post-infarct LV remodeling in a group of 105 STEMI patient treated by PPCI and found that the presence of multi-vessel coronary artery disease was a significant predictor of LV remodeling. It could be attributed to different sample size.

Regarding echocardiographic data, we found that baseline LVEDVI and LVESVI were significantly higher in patients who developed LV remodeling. But, neither LVEDVI nor LVESVI was a significant predictor of LV remodeling by univariate regression analysis.

Patients with baseline (at discharge) Low LVEF ≤45% and high WMSI > 1.5 were found to be at high risk for LV remodeling by univariate analysis.

Multivariate regression analysis showed that WMSI > 1.5 is an independent predictor of LV remodeling. Our findings were consistent with findings of Bolognese et al. who found that high WMSI independently predicted early LV dilatation. Also, consistent with findings of Loboz-Grudzięń et al. who also found that high WMSI > 1.5 is an independent predictor of LV remodeling after PPCI.

Our study showed no significant difference between both groups regarding grade of diastolic dysfunction. In contrast to our results, Cerisano et al. studied the relation between early assessment of Doppler-derived mitral deceleration time (DT), a measure of LV compliance and filling, and prediction of progressive LV dilatation after AMI and found that DT was the most powerful predictor of LVEDVI changes at 6 months (P = 0.02). Also inconsistent with findings of Loboz-Grudzięń et al. who found that restrictive pattern of LV filling is a significant predictor of LV remodeling. This difference may be attributed to smaller sample size of Loboz-Grudzięń et al. study who studied predictors of LV remodeling in 88 patients.

5. Study limitations

One limitation of our study is that echocardiographic assessment of global left ventricular systolic function is usually performed subjectively. Two-dimensional echocardiography does not offer very precise data about the ventricular volumes or the infarct size, it is better to be assessed by cardiac magnetic resonance imaging. Another limitation of our study was a lack of knowledge of late IRA patency. We were unable to perform coronary angiography at 6-month follow-up and thus cannot exclude the possibility that recurrent ischemia may have played a role in triggering the remodeling process. Also, we didn't evaluate myocardial perfusion after PPCI which may play an important role in development of LV remodeling.

6. Conclusion

Post-infarct LV remodeling occurred in 32.2% of studied patients. Patients with anterior location of MI, WMSI 1,5, LVEF ≤45% and LAD as IRA were considered at high risk for LV remodeling after PPCI. However, by multivariate regression analysis WMSI > 1.5 and LAD as IRA were only the independent predictors of LV remodeling after PPCI.

Conflicts of interest notification

The authors have no conflicts of interest to declare.

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