Role of plasma levels of CA-125 in predicting outcome of primary PCI after acute myocardial infarction in male patients

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Introduction
Cancer antigen 125 (CA-125) is a tumor marker of ovarian cancer, which has shown to be increased in different cardiovascular diseases. Although the prognostic role of CA-125 in heart failure and coronary heart disease is well-established, there is little known about its role in acute myocardial infarction (AMI). In this study we aimed to evaluate the serum levels of CA-125 in patients with AMI and its prognostic role in evaluating the in-hospital outcome of AMI.

Methods: We evaluated 120 male patients with AMI and 120 male normal subjects. CA-125 levels were measured upon the patient’s admission to hospital. The in-hospital major adverse cardiac events (MACE) and its predictors were also recorded for AMI patients.

Results: CA-125 levels were significantly higher in AMI patients compared to normal subjects (7.99±6.83 vs. 5.70±4.62, \(P=0.003\)). We found significant positive correlations between CA-125 levels with creatine kinase-MB (CKMB) (\(r=0.621, P<0.001\)) and CTnI (\(r=0.491, P<0.001\)). The in-hospital MACE was observed in 19 cases (15.8%). Patients with MACE had significantly higher value of CA-125, CKMB and CTnI and lower LVEF compared to patients without MACE. CKMB (OR=0.967, 95% CI [0.943-0.991], \(P=0.007\)) and CA-125 levels (OR=0.821, 95% CI [0.688-0.979], \(P=0.02\)) were independent predictors of MACE.

Conclusion: Serum CA-125 levels are significantly higher in male patients with AMI compared to normal subjects and have a significant role in predicting in-hospital MACE after AMI. In patients with higher CA-125 more aggressive treatment and close observation should be performed in order to reduce the possible adverse outcomes.

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including ovarian disease, to decrease the possible bias in CA-125 levels, we only recruited male subjects. Exclusion criteria were history of congenital heart disease, congestive heart failure (CHF), vascular or valvular disease, cardiomyopathy, left ventricular systolic dysfunction with non-ischemic causes, atrial fibrillation, previous STEMI, regional-wall motion abnormalities in non–infarct-related regions, previous coronary artery bypass grafting (CABG), pleural or pericardial effusion, ascites, active infection requiring intravenous antibiotics, chronic renal or liver disease, malignancy, hematological disorders.

Study sample was calculated \( n = 109 \) for each group using G*Power 3.1.3.9 software considering the effect size of \( d \geq 0.30 \) as statistically significant in a two-tailed test with \( \alpha = 0.05 \) and power of 0.95. In order to reach better results, we included 120 patients in each group.

Patients’ demographic, laboratory and clinical data were collected. All patients were classified by Killip classification 18 at the baseline. Left ventricular ejection fraction (LVEF) was measured by transthoracic echocardiography.

All patients underwent PCI and the in-hospital outcome and major adverse cardiac events (MACE) including cardiac and non-cardiac death, MI, HF and need for revascularization were recorded.

Blood samples were collected at the admission. Creatine kinase-MB (CKMB) was measured in three different periods and CTnI was measured twice and the peak CKMB and CTnI was included. CA-125 was measured with chemiluminescent enzyme immunoassay methods by using an Acculite CLIA, commercial kit (Monobind, USA). CA-125 normal level was 35 UI/mL.

**Data analysis**

All data were analyzed using SPSS statistics version 17.0. Numerical variables were expressed as mean ± standard deviation (SD), whereas categorical variables were expressed as percentage. The chi-square, Fisher exact test, Student’s \( t \) test and Mann-Whitney \( U \) test were used to compare findings between groups. Correlations were analyzed using the Pearson correlation. Logistic regression analysis was used to define predictors of in-hospital MACE. A \( P \) value <0.05 was considered statistically significant.

**Results**

Table 1 demonstrates demographic findings and CA-125 levels of patients and controls. Both groups were comparable regarding age and cardiovascular risk factors, while acute myocardial infarction (AMI) patients had significantly higher CA-125 levels.

Most patients were in Killips class I (110, 91.7%) and few were in Killips class II and III (6 [5%] and 4 [3.3%], respectively). Patients had mean LVEF of 42.29±9.52%. We found significant correlations between CA-125 levels with CKMB (\( r = 0.621, P < 0.001 \)) and CTnI (\( r = 0.491, P < 0.001 \)), while the correlations with other variables were not significant in patients with AMI.

The in-hospital MACE was observed in 19 cases (15.8%) including Re-MI in 6 cases, revascularization in 11 cases, CABG in 2 cases, cardiac death in 2 and overall death in 4 cases. Few patients had 2-3 complications during the hospital stay. There were no cases of major bleeding or stroke. There were also no cases of new onset atrial fibrillation or HF after MI during the hospital stay. Demographic and laboratory findings among patients with and without MACE were evaluated and there was significantly higher levels of CA-125, CKMB and CTnI and lower LVEF in patients with MACE compared to those without MACE (Table 2).

Significant findings were used in logistic regression analysis to find predictors of MACE (Table 3) and observed that only CKMB (OR=0.967, 95% CI [0.943-0.991], \( P = 0.007 \)) and CA-125 levels (OR=0.821, 95% CI [0.761-1.059], \( P = 0.02 \)) were independent predictors of MACE. In fact, lower levels of CKMB and CA-125 had protective effect in occurrence of MACE.

**Discussion**

The increased CA-125 levels have been reported in different cardiac pathologies including CHF, coronary heart disease (CHD), AF and valve disease such as aortic stenosis and mitral stenosis. 4-7,11,12 Although there are few reports, the increased CA-125 levels is also documented in AMI.7-9 In this prospective study, we observed that AMI patients compared to normal subjects had significantly higher levels of CA-125 levels. The outcome of AMI was poor in older patients and in those with lower LVEF. Higher levels of CA-125, CKMB and CTnI and lower LVEF were found in patients with MACE than without MACE, of which CKMB and CA-125 were independent predictors of MACE. Husser et al13 also reported that CA-125 levels before and after aortic valve implantation could independently predict death and MACE.

There are some possible mechanisms in which CA-125 could be increased in cardiac disease. The role of hemodynamic abnormalities and inflammatory
CA125- predictive role in AMI

Table 2. Demographic findings and laboratory findings of patients with and without MACE

|                   | MACE (n=19) | No MACE (n=101) | P value* |
|-------------------|-------------|-----------------|----------|
| Age (y)           | 60.1±9.43   | 56.2±8.50       | 0.07     |
| Hypertension      | 11 (57.9%)  | 49 (48.5%)      | 0.45     |
| Diabetes mellitus | 10 (52.6%)  | 45 (44.6%)      | 0.51     |
| Hyperlipidemia    | 7 (36.8%)   | 29 (28.7%)      | 0.47     |
| Smoking           | 3 (15.8%)   | 34 (33.7%)      | 0.12     |
| Familial history of CHD | 2 (10.5%) | 17 (16.8%)     | 0.49     |
| LVEF              | 38.1±10.16  | 43.0±6.24       | <0.001   |
| CA-125 (U/mL)     | 18.9±9.17   | 6.0±3.67        | <0.001   |
| CKMB              | 297.4±93.58 | 166.8±62.42     | <0.001   |
| CTnI              | 14.5±9.34   | 7.2±4.53        | <0.001   |

Abbreviations: MACE, major adverse cardiac events; CHD, coronary heart disease; LVEF, left ventricle ejection fraction; CKMB, creatine kinase-MB; CTnI, cardiac troponin I.
* P is two-sided significant. Student’s t test and Mann-Whitney U test are used.

Table 3. Logistic regression analysis to define predictors of MACE

| OR     | Lower limit | Upper limit | P Value* |
|--------|-------------|-------------|----------|
| LVEF   | 1.093       | 0.994       | 1.203    | 0.06     |
| CKMB   | 0.967       | 0.943       | 0.991    | 0.007    |
| CTnI   | 0.898       | 0.688       | 0.979    | 0.20     |
| CA-125 | 0.821       | 0.761       | 1.059    | 0.02     |

Abbreviations: OR, Odds ratio; LVEF, left ventricle ejection fraction; CKMB, creatine kinase-MB; CTnI, cardiac troponin I.
* P is two-sided significant.

Limitations
There were several limitations. This was a single center study that would limit to extend it to the general population. Also, the sample of patients and number of outcome, especially mortality rate were small. We did not recheck the CA-125 levels after the acute phase of the AMI to compare the possible changes in its levels and define its exact role in STEMI which could be another limitation of our study.

As in this study we excluded women from the study to reduce the possible effects of gender and women related disease on CA-125 levels, it could be concluded that there is higher CA-125 levels in male patients with AMI and have significant role in predicting in-hospital MACE after AMI. In patients with higher CA-125 more aggressive treatment and close observation should be performed in order to reduce the possible adverse outcomes.

Ethical approval
The Ethics committee of Tabriz University of Medical Sciences approved the study and in-formed consent were obtained from all participants.

Competing interests
None.

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