Gender-Related Differences of Cardiac Troponin-I Levels in Patients with Acute Myocardial Infarction at Time of Acute Chest Pain

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Authors’ contributions
This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Background: Cardiac Troponins-I (CTNI) are myoregulatory polypeptides that control the actin-myosin interface, considered specific to cardiomyocytes. Age and sex variances in the extent of CTNI levels have arisen a recent debatable emphasis. Existing revisions do not display a reliable clinical power of sex-specific CTNI 99th centiles, which actually might mirror procedural aspects. Nevertheless, from a biochemical viewpoint, the trends of sex-specific CTNI 99th centiles seem sensible for the ruling-in of acute myocardial infarction AMI. Vulnerable females may be missed when applying the male sex-specific threshold.
This study aimed to determine whether gender differences in CTNI exist in patients with AMI presented with chest pain.

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Methodology: The study was a cross-sectional, single-center, included 236-patients with AMI diagnosis by cardiologists at Merjan teaching hospital during the period from April to July 2020 from patients attending the hospital for cardiac consultation complaining of acute chest pain suggestive of AMI. Blood analysis had initiated at the time of admission included serum creatinine, blood urea, R/FBS, WBCs, PCV, and serum CTNI. A p-value below 0.05 specifies statistical significance. All statistical bioanalyses had performed by IBM-SPSS, version-25 for Windows.

Results: The mean age of participants was 67.5 years, the men were dominant 76.2%. The incidence of DM and hypertension were significantly high and 24.5% of the patients were current smokers. Biochemical serum analysis revealed mean creatinine, urea, sugar, and STI values were 79.8±4.2 mmol/l, 15.9±1.7 mmol/l, 10.9±0.9 mmol/l, and 7.9±0.6 ng/ml separately. Both hypertension and smoking were significantly (p-0.001) more among males compared to the females, which is not the case for the prevalence of DM. The males were heavier significantly than females (p-0.001). Almost, there was no impact of gender on most of the other study variables other than serum TNI levels, which were significantly higher among the males (p-0.001).

Conclusion: In patients with AMI presented with acute chest pain, the routine of CTNI in the diagnosis of AMI is based on the patient’s gender. The application of gender-dependent cutoff levels for CTNI analyses appears to be highly suggested.

Keywords: Acute myocardial infarction; troponin; chest pain.

1. INTRODUCTION

Cardiac Troponins-I (CTNI) are myoregulatory polypeptides that control the actin-myosin interface, considered specific to cardiomyocytes because no other isof orm of this portion has even been found in other muscular tissue. CTNI is independently measured by monoclonal antibodies in biochemical assays specific (nearly entirely) to cardiomyocyte damage. Hence, they are considered as gold-standard biomarkers of cardiac injury and are indorsed by contemporary guidelines for detecting AMI and myocardial damage [1,2].

Acute myocardial infarction (AMI) is the principal etiology of mortality worldwide [3-7], and death for females in the USA is approximately 1 in every 4 women deaths [8]. A current revision verified that the typical CTNI criterion unable to distinguish one/500AMI in women [9-11].

Age and alterations in the extent of CTNI concentrations have arisen as a new debatable emphasis [12,13]. Researches on experimental animals had revealed higher serum CTNI in males in comparison to females of the identical species [14]. Similar works exposed that women with AMI frequently have lower CTNI levels compared with men [15]. Existing revisions do not display a reliable clinical power of sex-specific CTNI 99th-percentiles, which actually might mirror procedural features [1]. Nevertheless, from a pathophysiological aspect, the trends of sex-specific CTNI 99th centiles seem sensible for the including of AMI [15]. Generally, these data propose that vulnerable females may be missed when applying a male sex-specific threshold. Thus, those females with classical TNI levels standards of AMI have developed a greater extent of cardiac injury [8].

In the existing work, our objective was to determine whether gender differences in CTNI exist in patients with acute myocardial infarction presenting with chest pain.

2. METHODOLOGY

2.1 Methods and Subjects

The study was a cross-sectional, single-center, included 236-patients with a definite AMI diagnosis by cardiologists at Merjan teaching hospital during the period from April to July 2020 from patients attending the hospital for cardiac consultation complaining of acute chest pain suggestive of AMI. Those with symptom onset of more than 24hrs had been excluded.

The biochemical analysis had initiated at the time of admission where serum creatinine, R/FBS, and blood urea had completed based on local available conventional methods. CTNI had assessed by CALBIOTECH® ELISA assay kit. Hematological findings of WBCs and PCV were taken from patients’ archives. The whole biochemical analysis had finalized as quantified by the industrial conventions.

2.2 Statistical Analysis

Comparisons of continuous data (given as mean± SD) had finished by students’ t-tests for independent variables. A p-value of below 0.05 specifies statistical significance. All statistical
evaluations had made by SPSS, version-23 for Windows.

3. RESULTS

3.1 Subjects’ Characteristics (Table 1)

The mean age of participants was 67.5 years (31-5 years), the men were dominant 76.2%, while the mean BMI was 26.3 kg/m². The incidence of diabetes mellitus (DM) and hypertension was significantly high (48.3% and 44.1%) respectively. The current smokers represented 24.5% of the total. The mean BMI, PCV, WBC were 26.9±7.7 kg/m², 42.1±0.4, and 10.3±0.3 individually. Biochemical serum analysis revealed mean creatinine, urea, sugar, and STI values were 79.8±4.2 mmol/l, 15.9±1.7 mmol/l, 10.9±0.9 mmol/l, and 7.9±0.6 ng/ml separately.

3.2 Variation of the Risk Factors (Table 2)

Both hypertension and smoking were significantly (p<0.001) more among males compared to the females, which is not the case for the prevalence of DM. The males in this study were heavier significantly than females (p<0.001).

3.3 Gender Variation of the Study Variables (Table 3)

There was no impact of gender on most of the study variables other than PCV was less in females (p<0.01), and blood urea with serum TNI levels, which were significantly higher among the males (p<0.001).

4. DISCUSSION

The current research exposed that CTNI values were significantly lower in females compared to males amongst subjects diagnosed with AMI and presented with acute chest pain. The principles of "the universal definition of AMI analyses" are largely based on CTNI values. Even though the CTNI assays specify significant changes in the cutoff values in males compared to females, there was no agreement on the use of sex-specific limits of analytical decision [1]. Given that the absolute concentration of CTNI is persuasive in guiding therapeutic protocol, we recommend that lower CTNI may subsidize the application of less aggressive therapies in females.
Table 3. Gender variation of the study variables

<table>
<thead>
<tr>
<th></th>
<th>Sex</th>
<th>Mean± SE</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age/years</td>
<td>M</td>
<td>58.7±0.9</td>
<td>0.12</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>61.9±1.9</td>
<td></td>
</tr>
<tr>
<td>Packed Cells Volume</td>
<td>M</td>
<td>42.8±0.4</td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>40.0±0.6</td>
<td></td>
</tr>
<tr>
<td>Leukocytes Count x 10³</td>
<td>M</td>
<td>10.5±0.3</td>
<td>0.2</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>9.6±0.5</td>
<td></td>
</tr>
<tr>
<td>S. Creatinine</td>
<td>M</td>
<td>80.2±5.3</td>
<td>0.87</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>78.6±4.9</td>
<td></td>
</tr>
<tr>
<td>Bl. Urea</td>
<td>M</td>
<td>17.6±2.1</td>
<td>0.01</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>10.3±1.9</td>
<td></td>
</tr>
<tr>
<td>F/RBS</td>
<td>M</td>
<td>9.6±0.4</td>
<td>0.16</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>11.0±3.8</td>
<td></td>
</tr>
<tr>
<td>S. Troponin I</td>
<td>M</td>
<td>8.8±0.6</td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>4.9±0.9</td>
<td></td>
</tr>
</tbody>
</table>

The higher CTNI levels among males exposed by the present study agreed with several recent epidemiological and experimental researches [16]. In Asian and large American cohorts, the authors reported the same results of our study [17,18]. However, in another study, the authors did not observe a significant variation in the assay or specificity of serum CTNI by gender [19].

There is growing evidence that revealed gender-related changes in plasma CTNI values owing to lower 99th URL standards in females than males [20]. It is expected that this difference in CTNI levels might be due to different cardiac mass [21], variability of cardiomyocyte renewal [22].

Preclinical and clinical studies have reported a lower prevalence of AMI in younger females compared to younger males, and in postmenopausal females under estrogen therapy versus those women who do not [23]. Estrogen might have a protective advantage against the progression of arteriosclerosis among females [24]. Females with bilateral oophorectomy are at higher risk of AMI that might be reduced by replacement with estrogen therapy [25].

A current survey confirmed intra-individual biochemical disparity of CTNI in healthy adults with those with chronic renal disorders is around 8-10%, while the inter-individual variation is around 3-times higher if assessed using a highly-sensitive technique [26]. These statistics open the inquiry on how to interpret variations greater than the limit of detection value, estimated by highly-sensitive assays, which still are within the 99th URL level in patients with AMI [22,27]. As well, the disparity in patients’ selection criteria (among the studies) regarding concomitant risk factors, including DM, arterial hypertension, overweight, and smoking habit which were relatively high in this study.

- Specially females with AMI often presenting with atypical manifestations like jaw pain or nausea compared with males, and are accompanied with atypical angina signs more often attributed to gastrointestinal before cardiac causes.
- The topic of gender effect in CTNI measurement in AMI is still indistinct and requires further studies.
- It is necessary to send a message to the physicians about this hot subject to prevent the risks of under-diagnosis of AMI in females.
- Fourthly, the present guiding principle have not yet acclaimed clear cut-off levels and algorithms for females.

5. CONCLUSION

This study underlines that in patients with AMI presented with acute chest pain, the routine of CTNI for the diagnosis of AMI is based on the patient's gender. Application of gender-dependent cutoff levels for CTNI analyses appears to be highly suggested but further investigations are desirable to estimate probable cutoff standards to adjust analytic precision of CTNI for males and females.

6. RECOMMENDATIONS

- Specially females with AMI often presenting with atypical manifestations like jaw pain or nausea compared with males,
and are accompanied with atypical angina signs more often attributed to gastrointestinal before cardiac causes.

- The topic of gender effect in CTNI measurement in AMI is still indistinct and requires further studies.

- It is necessary to send a message to the physicians about this hot subject to prevent the risks of under-diagnosis of AMI in females.

- Fourthly, the present guiding principle have not yet acclaimed clear cut-off levels and algorithms for females.

### 7. LIMITATIONS

Our study had some shortcomings. Firstly, somewhat small in size, and it is a single-center design. Secondly, the application of implements showing precise myocardial viability, for example, PET scan and/or Thallium scintigraphy would have been superior to the diagnostic tools applied in this study. Such an approach might reduce the risks of under or over-diagnosis of AMI female patients, and consequently, pointless treatments and/or coronary interventions.

Prolonged and large follow-up multi-center cohorts would better expose the clinical and prognostic significance of our outcomes, particularly if extended to include other biochemical changes like lipid profile, hypersensitive C-reactive protein, Troponin-T, atrial natriuretic peptides, D-dimers, and others that may clarify gender variations relating to the pathophysiological processes, risk stratification, and clinical responses in patients with AMI.

### DISCLAIMER

The products used for this research are commonly and predominantly used products in our area of research and country. There is no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by the personal efforts of the authors.

### CONSENT AND ETHICAL APPROVAL

Informed consent initially had been obtained from all patients (or attendants), and the whole work had been agreed upon by the local committee for research ethics at the hospital.

### COMPETING INTERESTS

Authors have declared that no competing interests exist.

### REFERENCES


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