Journal of Pharmaceutical Research International

33(52A): 199-205, 2021; Article no.JPRI.77076
ISSN: 2456-9119
(Past name: British Journal of Pharmaceutical Research, Past ISSN: 2231-2919, NLM ID: 101631759)

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

Mahir Abdulkadhum Khudhair Alzughaibi [a*#], Ammar Waheeb Obeiad [b†], Nassar Abdalaema Abdalhadi Mera [b‡] and Mohammed Sadeq Hamzah Al-Ruwaiee [c]

[a] Department of Anesthesia Techniques, Al-Hilla University College, Babylon, Iraq.
[b] Department of Internal Medicine, Merjan Teaching Hospital, Babylon, Iraq.
[c] Department of Pharmacology and Toxicology, College of Pharmacy, University of Babylon, Babylon, Iraq.

Authors' contributions

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

Article Information

DOI: 10.9734/JPRI/2021/v33i52A33576
Editor(s):
(1) Dr. Takashi Ikeno, National Institute of Mental Health, National Center of Neurology and Psychiatry, Japan.
Reviewers:
(1) Ingrid Prkacin, University of Zagreb, Croatia.
(2) Abdel-Zaher, Assiut University, Egypt.
Complete Peer review History, details of the editor(s), Reviewers and additional Reviewers are available here: https://www.sdiarticle5.com/review-history/77076

Original Research Article

Received 12 September 2021
Accepted 25 November 2021
Published 29 November 2021

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.

[#] F.I.C.M.S (Med.) Internist;
[†] F.I.C.M.S (Path.clinical biochemistry);
[‡] C.A.B.M, F.I.C.M.S, Endocrinologist and Internist;
[d] B.S. Pharma.
**Corresponding author: E-mail: mahieralzughaibi@yahoo.com;*

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 isoform 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/5thAMIs 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 99thpercentiles, 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-23for Windows.

3. RESULTS

3.1 Subjects' Characteristics (Table 1)

The mean age of participants was 67.5years (31-5years), the men were dominant 76.2%, while the mean BMI was 26.3 kg/m^2. The incidence of diabetes mellitus (DM) and hypertension were 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/m^2, 42.1±0.4, and 10.3±0.3 individually. Biochemical serum analysis revealed mean creatinine, urea, sugar, and STI values were79.8±4.2mmol/l, 15.9±1.7mmol/l, 10.9±0.9mmol/l, and 7.9±0.6ng/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 1. Demographic characteristics of the studied subjects

	Minimum	Maximum	Mean± SD
Age	31	95	67.5±0.9
Male sex (N %)	180 (76.2)		
Hypertension (N %)	114 (48.3)		
Diabetes mellitus (N %)	104 (44.1)		
Current smokers (N %)		58 (24.6)	
BMI (kg/m^2)	17.9	51.9	26.9±7.7
Packed Cells Volume	30.0	54.0	42.1±0.4
Leukocytes Count x 10^3	4.0	25.2	10.3±0.3
S. Creatinine (mmol/l)	3.5	569.0	79.8±4.2
Bl. Urea (mmol/l)	2.8	124.0	15.9±1.7
Random/Fasting BS	3.3	154.0	10.9±0.9
S. Troponin I (ng/ml)	0.09	38.0	7.9±0.6

Table 2. Gender variation of the risk factors among the studied subjects

		Sex		Total	Significance
		Females	Males		
Diabetes mellitus	Non- Diabetic	32 (24)	100 (75%)	132	0.47
	Diabetic	24 (23.1)	80 (76.9)	104	
Total		56 (23.7)	180 (76.3)	236	
Hypertension	Non-Hypertensive	16 (13.1)	106 (86.9)	122	0.001
	Hypertensive	40 (35.1)	74 (64.9)	114	
Total		56 (23.7)	180 (76.3)	236	
Smoking	Nonsmokers	34 (43.6)	44 (56.4)	78	0.001
	Ex-smokers	10 (10)	90 (90)	100	
	Smokers	12 (20.7)	46 (79.3)	58	
Total		56 (23.7)	180 (67.3)	236	
BMI		21.8 ± 2.6	29.3 ± (7.8)		0.001

Table 3. Gender variation of the study variables

	Sex	Mean± SE	Significance
Age/years	M	58.7±0.9	0.12
	F	61.9±1.9	
Packed Cells Volume	M	42.8±0.4	0.001
	F	40.0±0.6	
Leukocytes Count x 10^3	M	10.5±0.3	0.2
	F	9.6±0.5	
S. Creatinine	M	80.2±5.3	0.87
	F	78.6±4.9	
Bl. Urea	M	17.6±2.1	0.01
	F	10.3±1.9	
F/RBS	M	9.6±0.4	0.16
	F	11.0±3.8	
S. Troponin I	M	8.8±0.6	0.001
	F	4.9±0.9	

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. RECOMMEDATIONS

- 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

1. Nilgun IIB, Selcuk O, Fatma N, et al. Effect of age and gender differences on high sensitive troponin T measurement in the diagnosis of acute myocardial infarction. J Lab Med, 2019; 43(1):35–40.
2. Maki Alhindi MJ, Thekra Abid Jaber Al-kashwan, Ahmed Sudan, Saja Ahmed Abdul-Razzaq, On Admission Levels of High Sensitive C-Reactive Protein as A Biomarker in Acute Myocardial Infarction: A Case-Control Study. Indian Journal of Public Health Research & Development, 2019;10(4):5.
3. Al-Mumin A., A.-H.H., Hyperuricemia has a Deleterious Role in Patients with Acute Coronary Syndrome Presented with Poor Oral Hygiene. International Journal of Pharmaceutical Research, 2020;7.
4. Al-Saad RS, Shareef F, et al. Is There Any Association Between Highly Sensitive C-reactive Protein And Dental-Status In Ischemic Heart Diseases? A Comparative Study. Biochem. Cell. Arch. 2020;20(2): 6069-6075.
5. Saheb AAA, MJM, Combined Assessments of Multi-panel Biomarkers for Diagnostic Performance in Coronary Artery Disease: Case-Control Analysis. Sys Rev Pharm, 2020; 11(6):7.
6. Asseel K, Shaker RA-S, Raad Jasim, Hayder Abdul-Amir Makki Al-Hindy, Biochemical Significance of Cystatin-C and High Sensitive CRP in Patients with Acute Coronary Syndrome; any Clinical Correlation with Diagnosis and Ejection Fraction. Sys Rev Pharm, 2020;11(3):8.

7. Hajir Karim Abdul-Husseein FSD, Ameera Jasim Al-Aaraji, Hayder Abdul-Amir Makki Al-Hindy, Mazin Jaafar Mousa, Biochemical causal-effect of circulatory uric acid, and HSCRP and their diagnostic correlation in admitted patients with ischemic heart diseases. Journal of Cardiovascular Disease Research 2020;11(2):25-31.
8. Sobhani K, et al. Sex differences in ischemic heart disease and heart failure biomarkers. Biology of sex differences, 2018;9(1):43-43.
9. Kaur S. High sensitivity cardiac troponin and the under-diagnosis of myocardial infarction in women: prospective cohort study. Ann Clin Biochem, 2015;52(Pt 5):622.
10. Hayder Abdul-Amir Maki Al-Hindi MJM, Thekra Abid Jaber Al-Kashwan, Ahmed Sudan, Saja Ahmed Abdul-Razzaq, Correlation of on Admission Levels of Serum Uric Acid with Acute Myocardial Infarction: Case: Control Study. Journal of Global Pharma Technology, 2019; 11(7):6.
11. Samer MM, Hayder AA, Mazin JM. C-Reactive Protein is Associated with the Severity of Periodontal Disease — An Observational Study Among Acute Myocardial Infarction Patients. Sys Rev Pharm 2020;11(10):252-257.
12. Dhulfiqar A, JR, AA Hayder, Obaide A., Cystatin-C in patients with acute coronary syndrome: Correlation with ventricular dysfunction, and affected coronary vessels. Journal of Contemporary Medical Sciences. 2020; 6(1).
13. Hayder Abdul- Amir Maki Al-hindi SFA-S, Basim MH Zwain, Thekra Abid Al-Kashwan Jaber, Relationship of Salivary & Plasma Troponin Levels of Patients with AMI in Merjan medical city of Babylon Province: Cross-Sectional Clinical Study. Al-Kufa University Journal for Biology, 2016;8(3):53-58.
14. Krintus M, et al., Defining normality in a European multinational cohort: Critical factors influencing the 99th percentile upper reference limit for high sensitivity cardiac troponin I. Int J Cardiol, 2015;187:256-63.
15. Eggers KM, Lindahl B. Impact of Sex on Cardiac Troponin Concentrations-A Critical Appraisal. Clin Chem. 2017;63(9):1457-1464.
16. Hussein AZB, Thekra A, Hayder A, Al-hamadawi ZA. Relationship of Periodontitis with Acute Myocardial Infarction: Case Control Study. Al-Kufa Univ J Biol; 2017.

    www.uokufa.edu.iq/journals/index.php./ajb/index.(Special is:57-68).
17. Aw TCPS, Tan SP. Measurement of cardiac troponin I in serum with a new high-sensitivity assay in a large multiethnic Asian cohort and the impact of gender. Clin Chim Acta, 2013;422: 26–8.
18. Gore MOSS, Defilippi CR, Nambi V, Christenson RH, Hashim IA, et al. Age- and sex-dependent upper reference limits for the high-sensitivity cardiac troponin T assay. J Am Coll Cardiol, 2014; 63: 1441–8.
19. Shoaibi ADR. Tavris, McNulty S. Gender differences in correlates of troponin assay in diagnosis of myocardial infarction. Transl Res, 2009;154(5): 250-6.
20. Clerico A, et al. Pathophysiological mechanisms determining sex differences in circulating levels of cardiac natriuretic peptides and cardiac troponins. 2019; 2019:4.
21. Kerkhof PLM, Peace RA, Macfarlane PW. Sex- and Age-Related Reference Values in Cardiology, with Annotations and Guidelines for Interpretation. Adv Exp Med Biol, 2018;1065:677-706.
22. Mair J, et al. How is cardiac troponin released from injured myocardium? Eur Heart J Acute Cardiovasc Care. 2018; 7(6):553-560.
23. Tan YC, et al. Gender differences in outcomes in patients with acute coronary syndrome in the current era: A review. Eur Heart J Acute Cardiovasc Care. 2016; 5(7):51-60.
24. Mendelsohn ME, Karas RH. The Protective Effects of Estrogen on the Cardiovascular System. 1999;340(23): 1801-1811.
25. Colditz GA, et al. Menopause and the risk of coronary heart disease in women. N Engl J Med. 1987;316(18): 1105-10.

26. Van der Linden, N., et al., Twenty-Four-Hour Biological Variation Profiles of Cardiac Troponin I in Individuals with or without Chronic Kidney Disease. Clin Chem. 2017;63(10):1655-1656.

27. Apple FS, et al. Cardiac Troponin Assays: Guide to Understanding Analytical Characteristics and Their Impact on Clinical Care. Clin Chem. 2017;63(1): 73-81.

Peer-review history:
The peer review history for this paper can be accessed here:
https://www.sdiarticle5.com/review-history/77076