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Original Research Article

High Sensitive Troponin I and Troponin I in Myocardial Infarction

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ABSTRACT

Objective and study Design: To evaluate the role of high sensitive troponin I with sex specific threshold in men and women having MI and to compare them with complementary troponin I levels of single threshold.

Materials and Methods: Patients with signs and symptoms of chest pain diagnosed as MI patients by expert cardiologists based on history, levels of cardio specific and sensitive biomarkers and ECG changes formed the core of the study. Complementary troponin I and high sensitive troponin I was measured using chemiluminescence microparticle immunoassay using Architect i1000SR of Abbott.

Results: Complementary troponin assay with single threshold disproportionately underdiagnosed myocardial infarction in women and contributed to sex inequalities in treatment and its outcomes. High sensitive troponin assay identified the difference in the reference range for men and women .The incidence of MI in women with high sensitive troponin I is almost double as in conventional troponin I levels.

Conclusion: The present study highlights the importance of assaying high sensitive troponin I in women as an index which remained unrecognized so far with calamitous consequences.

Keywords: Myocardial Infarction, Troponin I, High sensitive Troponin I.

INTRODUCTION

Sophisticated biochemical markers have become increasingly important in the investigation of myocardial injury. It is 50 years since the first enzyme marker, viz serum glutamate oxaloacetate transaminase, has been reported to be an aid in the detection of myocardial injury. [1]

Over the ensuing 50 years there has been a progressive improvement in the tissue specificity of biomarkers and in their clinical specificity and sensitivity.

Biochemical markers now play an important role in the detection of disease risk stratification and monitoring of therapy.

The National Academy of Clinical Biochemists and the joint ESC /ACC committee for the redefinition of myocardial infarction (MI) have both recommended troponins as the markers of choice in the evaluation of acute MI because of their superior sensitivity and specificity when compared with other markers. [2] The analytical performance specified by both documents that the degree of imprecision (coefficient of variation) at 99th percentile

cut off point should be less than 10%.Unfortunately only a few recent assays can comply with this requirement ;the adoption of these recommendations have stimulated manufacturers of troponin assay kits to improve assay performance around the clinical cut off points. [3,4] Other organizations like National Institute of Clinical Excellence, ACC of American Association and ESC have also recommended troponins as biomarker in patients with MI. Increase in the level of Troponins reflected myocardial damage but not the extend of damage. The limit of detection is 28ng/L and the diagnostic threshold is 50ng/L.

Many inequalities manifest between men and women in the treatment and outcome of coronary syndrome with an increase in both early and late deaths in women. [5] Women with suspected AMI are less likely to have a timely diagnosis of MI probably due to atypical symptoms and less reliable findings in ECG. [6]

High sensitivity Troponin assay enables the measurement of troponin even in healthy people. This assay has identified important differences between the sexes with 99th percentile (upper limit), the levels being higher in men than in women. [7]

In the present study the effect of high sensitivity assay for cardiac Troponin I using sex specific diagnostic threshold on the incidence of MI is measured and the values are compared with the values of contemporary assay in men and women.

The universal definition of MI recognizes that reference value may differ for high sensitive troponin assay in men and women .These assays are available for clinical use and are recommended for the assessment of patients with suspected acute coronary syndrome. [8] More sensitive troponin assay improves the diagnosis of MI [8] and use of these assays has been associated with reduction in recurrent MI and subsequent death. [8, 9]

To ascertain the role of high sensitive troponin I in the diagnosis and treatment of MI in women contemporary troponin I and high sensitive troponin I have been measured in suspected cases of MI both in men and women in this study.

MATERIALS AND METHODS

Patients with signs and symptoms of chest pain diagnosed as MI patients by expert cardiologists based on history, levels of cardio specific and sensitive biomarkers and ECG changes formed the core of the study. Complementary troponin I and high sensitive troponin I are measured using chemiluminescence microparticle immunoassay using Architect i1000SR of Abbott.

RESULTS

A total of 860 patients who attended the OP/IP of SK Hospital are divided into two equal groups of 430 patients each .Troponin I is measured in one group by complementary assay and in the other group by high sensitive troponin I assay .Single threshold 0 >0.3 ng/ml is employed for complementary troponin I assay and sex specific thresholds of >15.6pg/ml for women and 34.2pg/ml for men with signs and symptoms of MI .The number of male and female patients are 240 and 190 respectively. In male patients complementary troponin I is positive in 76(32.1%) patients and only in 32 female patients troponin I is above the cut off level of 0.3ng/ml(16.58%). The results are presented in Table 1.

Table 1: Percentage of Male and Female MI patients based on complementary Troponin I levels

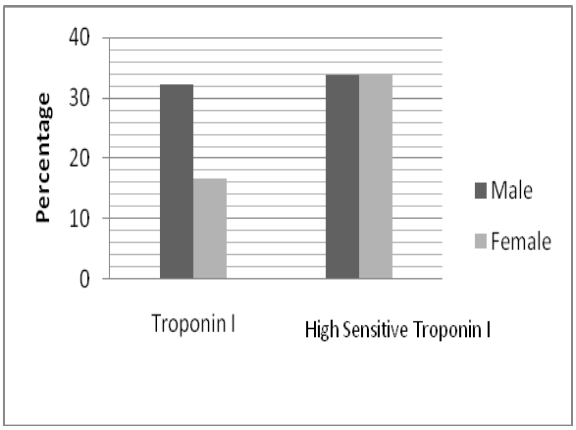
TOTAL	MEN			Women		
	Total	Positive	%	Total	Positive	%
430	240	76	32.1	190	32	16.58

In Table 2 using the sex specific threshold for men and women high sensitive troponin I is measured in the second group.

Table 2: Percentage of Male and Female MI patients based on high sensitive Troponin I levels.

TOTAL	MEN			Women		
	Total	Positive	%	Total	Positive	%
430	240	81	33.75	190	64	33.64

Figure No. 1: High Sensitive Troponin I & Complementary Troponin I in MI Patients.



The levels were higher in 81 male (33.75 %) patients and 64 female (33.64 %) patients. The differences in the two groups are apparent in the histogram (Figure No: 1)

It is evident that the percentage of highsensitive troponin I positive cases are almost equal in men and women the percentage being 33.75 in men and 33.64 in women. Number of women with high sensitive troponin I levels is almost double compared to number of cases positive with complementary troponin I levels.

Troponin I and high sensitive troponin I are estimated in male and female MI patients.In male, Complementary troponin I varied between 0.3 ng/ml –50 ng/ml (Mean 1.6228). Under identical conditions in females the range of complementary Troponin I varied between 0.3 ng/ml-50ng/ml (Mean- 1.0822). High sensitive troponin I varied between 34.2 pg/ml to 50000pg/ml (Mean- 6603) in male and 15.6 pg/ml – 50000pg/ml (Mean- 2153) in women .The total no of patients in each group were equal 430 consisting of 230 males and 190 females.(Table 3)

Table 3: Levels Of Complementary And High Sensitive Troponin I In Male And Female Mi Patients

	n	ComplementaryTroponinI (ng/ml)			n	Highsensitive Troponin I (pg/ml)	
		Range(ng/ml)	Mean (ng/ml)			Range (pg/ml)	Mean (pg/ml)
Male	65	0.3- 50	1.6828	Male	81	34.2-50000	6003
Female	25	0.3- 50	1.0822	Female	64	15.6-50000	2153.3

The number of patients with complementary troponin I above the single threshold of 0.3 ng/ml is 65 males and 25 females. Based on sex specific threshold high sensitive troponin I am above 35.2pg/ml in 81 MI male patients and above >15.6 pg/ml is 64 females. The values varied over a wide range.

DISCUSSION

Major differences exist in the diagnosis and management of myocardial infarction in men and women presenting with suspected acute coronary syndrome. The measurement of high sensitive troponin suggested that the basis of contemporary analysis with a single diagnostic threshold >0.3 ng/mL disproportionately underdiagnose myocardial infarction in women and contribute to sex inequalities in treatment and outcomes. Although there is only a little effect on men, a high sensitive troponin assay with sex specific diagnostic threshold may double the diagnosis of MI in women and identify the high risk of reinfarction and death. Whether sex specific diagnostic thresholds will improve or not the outcome and tackling inequalities in the treatment of women with suspected acute coronary syndrome demands urgent attention. Sex differences in diagnostic

thresholds have been observed in other clinical trials also. [10]

When a comparison of complementary troponin I assay and high sensitive troponin assay is made in patients with suspected AMI, sex specific diagnostic threshold doubles the diagnosis of MI in women such that the proportion of men and women with a diagnosis of MI is now equal. Women identified with MI using only the high sensitive assay with sex specific diagnostics threshold have similar clinical characteristics and prognosis as women diagnosed with MI using the complementary assay .Women are less likely than men to be referred to a cardiologist to coronary angiography or revascularization or to receive secondary prevention. These inequalities are more pronounced in those women with MI who are not identified by the complementary assay. Women identified using the high sensitive troponin I assay with sex specific thresholds have the highest risk of death or recurrent MI suggesting that these women benefit the most from reclassification and treatment of MI. [11]

Men are twice as likely as women to have a diagnosis of MI, with single threshold of complementary assay. This is in agreement with several other clinical trials. [12] Historically this apparent under-diagnosis is attributed to difference in presentation with women likely to have typical symptoms and less reliable ECG changes. Troponin assay and use of sex specific diagnostic thresholds will definitely improve outcomes though better targeting of treatments for coronary artery diseases in women.

CONCLUSION

Coronary heart diseases remain the leading cause of mortality and morbidity all over the world. Many differences exist in the diagnosis, management and outcome in men and women with AMI. High sensitive troponin I assay identifies the difference in the reference range. [13] The explanation for the under diagnosis of MI in women could be the prevalent use of inappropriate diagnostic thresholds. Troponin concentration depends on left ventricular mass and women have less left ventricular mass than men. Hence it is justifiable to conclude that troponin levels are higher in men than in women. [14] This is true for other cardiac biomarker CK-MB also. Sex specific difference exists for cardiac biomarkers troponin I and CK-MB. Single diagnostic threshold for women and men leads to under diagnosis of MI in women and contributes to sex inequalities in treatment and outcomes. The present study suggests that differences in outcomes between men and women are due to sex difference in threshold and the clinical presentation of MI. Using the contemporary troponin assay with single threshold contributes to inequalities in the management and treatment of MI in women which can be overcome by high sensitive troponin I assay.

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