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Original Article

Correlation between the Level of Creatinine, Serum Cardiac Troponines and Left Ventricle Function Tests in Patients with Chronic Renal Diseases without Acute Coronary Syndrome

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ABSTRACT

Background and Objectives*:* The aim of this study was to survey the relationship between the level of creatinine, cardiac troponins serum and the function of the left ventricle in patients with kidney insufficiency, without acute coronary syndrome.
Materials and Methods: The sample was 150 patients with nondialysis chronic kidney disease without acute coronary syndrome, hospitalized at Imam Khomeini Center through 2008-2009. All the patients had serum creatinine (cr) 1.5mg or greater and no symptoms of acute coronary syndrome in the first month. Serum Cr and troponin T and I were measured in blood samples and patients left ventricular function (LVEF) were estimated by echocardiography. Then based on the objectives, the findings were analyzed with SPSS soft ware.
Results: Serum troponin T levels were significantly higher in patients with greater Cr levels but there was no significant relationship between troponin I and Cr levels. Patients with greater degrees of LV dysfunction had significantly upper levels of troponin T(P=0.0001). In this category, patients with diabetes, old age, cigarette smokers, greater levels of Cr, advanced stages of chronic kidney disease and greater degrees of LV dysfunction showed significantly higher levels of troponin T(P =0.0001).
Conclusion: To identify chronic kidney disease patients at increased risk for cardiovascular events, serum troponin T can be used. In high-risk patients, the evaluation for cardiovascular diseases could be done earlier in the course of chronic kidney disease.

Keywords: Creatinine, Troponin-T, Troponin-I, Left Ventricular Dysfunction, Chronic Renal Failure

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Introduction

Heart and kidney have a hemodynamically close relationship. Cardiovascular diseases are the first reason of death in patients diagnosed with chronic kidney disease (CKD) (1). In addition, diseases such as myocardial, valvular, and fatal arrhythmic diseases occur more in such patients. Cardiovascular mortality in dialytic patients with End Stage of Renal Disease (ESRD) happens 10 to 20 times more than others (1). The Chronic Renal Deficiency (CRF) is defined using the amount of glumerolur filtration rate (GFR) and in different ranges.

Ejection fraction (EF) of the left ventricle is defined as the impulsive volume (which itself includes the diastolic end volume minus systolic end volume) divided by diastolic end volume multiplied by (times to) 100. The left ventricle function in different types of cardiac diseases, either in short or long time, enjoys a high prognostic value (2).

In patients with cardiac deficiency, T and I troponin molecules are released from myocytes due to the increase in heart's wall stress and subendocardial ischemia. In such patients, the high level of troponin could strongly predict the mortality (1). On the other hand, myopathy of skeleton muscles in these patients diagnosed with CFR could cause the increase in the level of Keratin kinase, myoglobin, and troponins in serum. In the absence of acute coronary syndrome symptoms, the level of T and I Cardiac troponin increase in Patients with CRF (2). In many studies, it is shown that it is possible to use the increased level of troponins to predict the fatality and future heart problems in those patients (3, 4). Some studies consider this increased level of I troponin, and some other both types of troponin useful for this purpose (5-13).

Having the high prevalence of cardiovascular problems in patients with CRF in mind and knowing that the mortality of heart problems has a direct relationship with the amount of left ventricle ejection fraction (LVEF), we studied the relation between the level of creatinine (Cr) and cardiac troponins and also its relation with the function of the left ventricle to choose these patients for early diagnostic studies and cures of their heart problems.

Materials and Methods

This study has been conducted using the cross-sectional method. The population under survey was 150 patients diagnosed with non-dialytic CRF and without acute coronary syndrome hospitalized at Imam Khomeini Hospital during the years 2008 and 2009.

Non-dyalitic CRF patients with the 1.5 mg/dl level of creatinine and more who did not have the symptoms of acute coronary syndrome in the month previous to the survey, were studied.

The dyalitic patients or those having the acute coronary syndrome symptoms in the past month were discarded from the research. Also those patients having significant disease in another organ such as lungs, gastrointestinal(GI) system and liver, skeleton muscles, urogenital system, etc (except for the cardiac ischemic disease like diabetes, blood pressure, hyperlipidemia, cigarette smoking, and any family history of cardiac ischemic disease) were omitted from the survey as well.

The blood sample from all those patients was taken for simultaneously examining creatinine, T, and I troponins. Then the patients' LVEF was estimated through echocardiography. Patients' information including gender, age, presence, or absence of risk factors of cardiovascular diseases such as diabetes, blood pressure, hyperlipidemia, cigarette smoking, any positive family history, and LVEF was also recorded in the questionnaire. After that through analyzing present data, presence, or absence of any relationship between the level of creatinine and cardiac troponins T and I and the level of troponins and

LVEF on the next grade was examined. Creatinine serum (estimation/examination/ measurement) was done using the enzymatic calorimetric system and without omitting any proteins and based on the JAFFE method by the JAFFE kit in Pars Azmoon Company. Cardiac troponins were examined in the system of enzyme immunoassay. I troponin was measured by the kit of Belgian Company of DGR and measurement of T troponin used the kit of German company of Roche.

The measurement unit for Cr serum is mg/dl and for both T and I troponins is ng/ml. The normal laboratory level based on the kit used for T troponin is under 24 ng/ml and for I troponin is under 1.0 ng/ml. The reference domain for creatinine level in men is 0.7–1.4 mg/dl and in women is 0.6 –1.3 mg/dl. In echocardiography, LVEF was measured in biplane Simpson system.

The calculation method for the sample volume was based on a previous study (15). The prevalence of high level of troponin in non-dialytic CRF patients was about 59%. According to the following formula, the sample volume would be measured equal to 146 people. Our sample volume was assumed 150 people.

$$n = \frac{z^{2}_{1-\alpha/2} pq}{d^{2}}$$

α=0.05 $Z_{1-\alpha/2}$=1.961150776

d=0.08 n=146

P=0.59

This survey was conducted according to the principles of Helsinki declaration and moral checklist in research presented by the Deputy of Research in Tehran University of Medical Sciences in Tehran. Patients' consent to participation was considered fully; their information remained confidential and only used in clinical researches anonymously. All phases of the survey including paraclinical examinations and echocardiography are free of charge and no expense would be imposed on the patients.

After completing a special form for each patient, the related information would be entered into the SPSS for Windows 11.5 program to be analyzed. In order to review the relation between a quantitative variant in both groups, the *t*-test method and for the correlation, the Spearman roh method has been used. Statistical significant was set at $P<0.05$.

Results

In the population under survey, the average age of the patients was 52±17.3. The minimum age was 15 yr and the maximum was 90. From 150 people participating in the survey, 81 were male (54%) and the rest 69 were female (46%). Fifty-eight people from the whole 150 (8.7%) did not have HTN and 92 (61.3%) had it. 68.7% of cases were diabetic but the rest 47 (31.3%) were not. Ninety percent were cigarette smokers while the other 15 (10%) were not. 94.4% had the positive FH and the other 8 (%5.3) had negative FH. From all 150 patients, 120 (80%) were not diagnosed with HLP and 30 (20%) had it. The average level of Cr serum between the participants was 2.4±1.5 mg/dl, average level of T troponin of them was 33±67 ng/ml, and the average level of I troponin was 0.5 ± 2.3 ng/ml. The average of LVEF in the patients was also 55 ± 12.9 percent. The least amount of it was 20% and the most was 72%. There was a meaningful relationship between the serum level of creatinine and T cardiac troponin (P= 0.001).

A significant increase in the level of T troponin was also observed (P=0.0003). However, there was not a meaningful and significant relation between the levels of creatinine and I troponin (P= 0.883).

As the age of the patients increased the level of T troponin also increased in a significant way (P= 0.000) but no such meaningful relation existed between the age of the patients and the level of I troponin (P= 0.16).

The average of T troponin level in diabetic patients was 63.2 ng/ml and its level in non-diabetic ones was 20.6 ng/ml. the difference between the level of T troponin in these two groups was absolutely significant (*P*= 0.009).
For troponin I, the average level of it in diabetic patients was 0.20 ng/ml and in non-diabetic ones was 0.71 ng/ml. This difference in its level was not also of any significant meaning (*P*= 0.21).
In male patients, the average level of troponin T was 35.4 ng/ml and it was 32.4 ng/ml in female patients, which did not have a significant difference (*P*= 0.79). The average level of troponin I in male patients was 0.86 ng/ml and the same level in female ones was 0.19 ng/ml. Troponin I level in both groups also did not have a significant difference (*P*= 0.08).
The level of troponin T in patients with high blood pressure was 34.6 ng/ml and in those without it was 32.9 ng/ml. There was not a meaningful difference between the two (*P*= 0.881). The level of troponin I in high blood pressure patients was 0.37 ng/ml and its level in those who did not suffer from high blood pressure was 0.8 ng/ml. The level of troponin I did not have a meaningful difference as well (*P*= 0.24).
In patients with the positive family history, the average level of troponin T was 23.8 ng/ml and it was 34.5 ng/ml in patients with negative family history (of diseases) which did not have a significant difference (*P*= 0.66). The average level of troponin I in patients with the positive family history was 0.19 ng/ml and the same level in ones with negative family history was 0.65 ng/ml. Troponin I level in both groups also did not have a significant difference (*P*= 0.65).
The average of T troponin level in non-hyperlipidemic patients was 33.1 ng/ml and its level in hyperlipidemic ones was 37.1 ng/ml. the difference between the level of T troponin in these two groups was not significant (*P*= 0.70). For troponin I, the average level of it in non-hyperlipidemic patients was 0.65 ng/ml and in hyperlipidemic ones was 0.15 ng/ml. This difference in its level was not also of any significant meaning (*P*= 0.30).
The level of troponin T in smoking patients was 63.5 ng/ml and in those non-smokers was 30.6 ng/ml. This average level was not significantly higher among smokers (*P*= 0.001). The level of troponin I in smoking patients was 0.33 ng/ml and its level in non-smokers was 0.58 ng/ml. The level of troponin I did not have a meaningful difference (*P*= 0.876).
Reducing GFR, the level of troponin T increases (*P*= 0.02) but troponin I level does not have any connection with GFR amount (*P*= 0.39). The more the amount of GFR becomes, the less the level of troponin T would be. Troponin I level has no connection with the amount of GFR (*P*= 0.39).

Discussion

CRF in each phase is a major risk factor for cardiovascular diseases, which include coronary vessel disease, brain vessel disease, and peripheral vessel disease. Cardiovascular diseases are the first reason of death in chronic kidney disease patients. CRF intensifies Atherosclerosis and increases the probability of fatal diseases such as myocardial, valvular, and arrhythmic diseases. Cardiovascular diseases mortality increases significantly by the reduction of glomerular filtration to under 60ml/min/1.73m². This is related to Creatinine level of 1.5 mg/dl and more (2).
It is shown that in patients with CRF and without having the symptoms of acute coronary syndrome, the serum level of cardiac troponins T and I will increase. Since one of the diagnostic bases for acute [severe] heart attacks is serum biomarkers of troponins T and I, knowing the serum level of these biomarkers seems necessary(2,3).
Left ventricle malfunction results in reduction of cardiac output. Different studies have shown that this parameter either has a high prognostic value for different types of cardiac problems in short or long term (2). In Flisinski *et al.* study the population under survey was divided into three groups. First group was

composed of 10 young and healthy individuals without any chronic renal diseases, the second group contained 21 CRF patients in 2-3 phases, and in the third group, there were 30 patients who had dialysis for a long time. None of these patients had acute coronary syndrome symptoms. Serum level of troponin I was measured in all three groups. Comparing to control group serum level of troponin I in CRF patients was higher than the healthy ones. Serum level of troponin I in patients on the third group (dialytic ones) was obviously higher than the other two groups (12). However, there was no meaningful relation between the level of Cr serum and troponin I in our study.

In Bunet *et al.* study the serum level of troponin T and I in 105 dialytic patients without acute coronary syndrome symptoms was measured and these patients was followed for their clinical consequences in the next two years. The results of this following showed that the mortality is connected to the increased level of troponin T but not to the serum level of troponin I. it also showed that in dialytic patients without symptoms the serum level of troponin T has increased more comparing to the troponin I and therefore troponin I could be used for diagnosing the acute coronary syndrome in dialytic patients (13). It seems in our survey that troponin I is also more useful for diagnosing of the acute coronary syndrome in non-dialytic CRF patients.

Wrenn *et al*. completed a survey on 87 patients with Cr serum of 3 mg/dl and higher which showed that the increased level of troponin T in CRF patients was related to the high mortality of cardiovascular diseases (5).

The serum level of troponins T and I was measured in 98 dialytic CRF patients and other 103 patients who had done kidney transplant. In both groups of patients, the serum level of troponins T and I were reciprocal to the function of the kidney and the increased level of cardiac troponins is known as a very useful mean to define the risk of cardiovascular diseases in patients without any symptoms of such diseases (3).

In a similar study, on 222 non-dialytic CRF patients, the serum level of cardiac troponins was measured. This study shows that reducing the kidney function, the serum level of troponin T will show an obvious increase but no meaningful relation was found between the kidney function and the serum level of troponin I. It also showed that the increased troponin T would result in the reduction of survival in patients without any symptoms for cardiovascular diseases (14). The results of this study are very similar to ours.

In order for a preventive (precautionary) measure for a disease in a population to be more economical and also more individuals enjoy it, it is better to identify the high risk groups of patients rather than instead of a general group of patients and they would be considered for taking preventive (precautionary) measures. One of the cases, which are of a high prognostic value in this context, is cardiac troponins. In CRF patients, the high level of cardiac troponins would anticipate the probability of unpleasant cardiovascular incidents to happen in the future and the high mortality due to those incidents.

It seems that between two types of troponins T and I, the level of troponin T has a meaningful relationship with the increase of creatinine and the reduction of glomerular filtration. Therefore measuring troponin T could be used to identify the high-risk CRF patients for cardiovascular complications.

Conclusion

In the population of CRF patients, the diabetic, old, smoking patients, those with high level of creatinine or in advanced phases of renal failure, and low EF patients show a higher level of troponin T. therefore these people could be chosen as the target groups of high risk for measuring troponin T. identifying high risk people could help us to begin the diagnostic examinations for cardiovascular

problems earlier so that preventive and therapeutic measures could be taken in order to prevent or postpone the disease from progressing to the final phases.

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