International Journal of Psychosocial Rehabilitation, Vol.24, Issue 09, 2020
ISSN: 1475-7192

The relationship between Calcitonin and Creatine kinase levels in sera of newly diagnosed Iraqi patients with coronary artery disease

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Abstract:

One of the most serious heart diseases and May lead to sudden cardiac death is the coronary artery disease (CAD). Meanwhile, CAD diagnoses are very expensive and time-consuming. The propose of this work was to evaluate the levels of calcitonin (CT) and serum creatine kinase (CK) in newly diagnosed CAD patients. This study was conducted on 54 patients with CAD disease, including (23 female and 31 male), with age for male patients (56.61 ± 9.71) and (56.27 ± 9.22) for female patients, in addition to 54 healthy volunteers, including (23 females and 31 males) groups of matched control. After obtaining serum samples from separate patient and control groups, the measuring values for CK and CT were done using ELISA method and the data of analysis was carried out using the SPSS. The results of the study showed statistically high significant serum CK activities (660.24 ± 27.275), (653.18 ± 34.747) in male and female patients respectively, compared to the control group (69.19 ± 8.299), (89.54 ± 10.998), respectively. Similarly, there was a significant increase in the level of CT in the male patients as compared to female patients as it was as mean± SD (10.48 ± 0.375), (9.56 ± 0.453), respectively. When compared to the control males and females, the mean was ± SD (8.82 ± 0.389), (8.44 ± 0.434), respectively. There was also a negative association between CT and CK (r = -0.065) in females and a positive relationship (r = 0.294) in males, both of which were unimportant. There was a negative relationship between CT and age, in both patient groups, when compared with the other group (control). In regard to the relationship between CK and age, the positive relationship (r = 0.034) had a negative correlation, in males (r = -0.178) and in females, when compared to the control groups. Age and gender variables and family history of diabetes were taken into account and it was found that the difference is significant between the two groups. Because the relationship of serum levels CT and CK with CAD severity is unknown, the case presented here highlights the importance of serum CT and serum CK levels in differential diagnosis of coronary disease (CAD).

Key Words: *Coronary artery disease, Calcitonin, Creatine kinase, Gender.*

Abbreviations and Acronyms: CHD: coronary heart disease, CT: Calcitonin, CK: Creatine kinase, CAD: Coronary artery disease.

Introduction:

Cardiovascular disorders that lead to heart failure, coronary artery disease (CAD), cardiac arrest are the cause of sudden death by cardiovascular disease [1], and CAD is one of the important contributors to one of four cardiovascular diseases (CVD) [2]. The transmission of large-scale epidemics and environmental pollutants such as arsenic in groundwater or

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particles in the air, or specific weaknesses in genetic makeup or metabolism, may play an important role in causing disease [3]. A barrier on blood flow to the heart created by CAD can be diagnosed depending on patient clinical data such as age, gender, blood pressure, random blood sugar, and smoking habit, as well also symptoms must be identified by ECG [4]. Calcitonin (CT) is a 32-producing amino acid peptide hormone produced by thyroid C cells. There are negative reactions between blood calcium and computed tomography. High calcium in the blood triggers a computerized tomography scan, which later affects the kidneys and bones and reduces calcium in the blood [5]. Moreover, when concentrations are high, computerized tomography increases urinary phosphorous and calcium excretion [6]. Creatine kinase (CK) as a cardiac sign depends on its relatively high concentration in the heart muscle (> 20%) compared to typical skeletal muscles (1-2%) [7]. The amount of CK in the heart muscle is 10- 30% of the total enzyme amount. Therefore, these higher levels of CK in the heart may be caused by ischemic stress. Currently, CK is still considered to be the best biochemical indicator when diagnosing a heart attack. For instance, CK levels were found to be significantly higher in the myocardium than in experimental animals and the human cardiac muscle with CAD, aortic stenosis, or heart failure, compared to normal [8]. This is because this enzyme is not found extensively in the tissues outside the heart, as it is considered a specific indicator inside the heart. It is also worth noting that CK sometimes increases in conditions other than cardiac arrest [9]. From previous studies it was found that women are more likely to develop ischemic heart disease at an advanced age with more associated diseases when compared to males. Despite correcting the risk factors, women experience much worse outcomes, even if there is no coronary artery occlusion disease. While most of the recommendations applied to women are mostly drawn from male data, further study of gender differences may lead to approaches that may ultimately reduce inequalities in treating ischemic heart disease in women [10-13]. Thus, the aim of this work is to appreciate CK and CT levels in sera of Iraqi patients with CAD in association with this disease, in addition to gender difference and its relation coefficient with the above disease. According to the information obtained in our research from the literature, we noted that this study is the first attempt to assess the activity of the enzyme and the hormonal focus in this common disease.

Material and Method

The study included 108 volunteers ages ranged between (37-73) and (40-74) years for males and females, respectively. Patient group (P group), was a 54 selected men and women suffering from CAD; categorized as 23 female and 31 male patients, and a healthy control group (C group), (n = 54) with matched ages with the first group. As for indicators of coronary artery diseases, steps were depended on symptoms such as risk factors, and the appropriate non-seasonal test results (echocardiography due to dopamine and positive stress in cardiac, not normal, assured by during the stress test such as directed). In formation on age, height, comorbidities, body weight, current drug treatment, smoking state, and gender were collected before angiography was performed from separate charts in the electronic database of hospitals. Exclusion criteria include smokers, and patients with cancer, autoimmune diseases, liver disorders, inflammatory diseases, infections, blood diseases, and kidney dysfunction. A blood sample was collected in normal tubes and for about10 minutes at 25^0C until a clot formation. After centrifugation at (3000 rpm) for 10 minutes. Serum samples were kept at -20 ° C to determine CK and CT levels using the ELISA group, according to the Manufactures Protocol (demeditec REF: DEKAP0421) / Germany, and at the same time Creatin kinase (IU / L) was measured using a fully automated spindle. This study protocol has been approved by the Ethics Committee of the College of Science / University of Baghdad.

Statistical analysis

Based on gender ,the studied groups were divided into 2 subgroups. The data of this study are presented as mean ± standard Error (SE), specified by ANOVA test. The relation of correlation for calcitonin and creatine kinase with age was performed by Pearson correlation test, (r value as a coefficient), the account (p <0.05) of the result was counted to be statistically significant. Data was analyzed using SPSS 23.0.

Results

Blood samples were used to appreciate the alteration in CK and CT levels in classified patients with CAD (group P), and in (group C) as shown in Table 1.

Table (1): Distribution of subjects according to the healthy status and gender.

parameters	Male (n=31) Patient Mean±SEM	Male(n=31) Control Mean±SEM	Female(n=23) Patient Mean±SEM	Female(n=23) Control Mean±SEM	p-value
Age (year)	56.56±1.480	56.79±3.292	56.27±1.965	56.50±3.246	0.285
Calcitonin (pg/ml)	10.48±0.375	8.82±0.389	9.56±0.453	8.44±0.434	0.057*
Creatin kinase (IU/L)	660.24±27.275	69.19±8.299	653.18±34.747	89.54±10.998	0.000**

***: Significant using ANOVA test at p <0.05level of significance, **: p < 0.01 level of high significance**

The results indicate very significant (p <0.01) increase in the mean ± SE of CK and CT in male and female patient groups when compared to group C (69.19 ± 8.299, 89.54 ± 10.998, respectively)); as well group P CK (660.24 ± 27.275, 653.18 ± 34.747, respectively); and P group CT (10.48 ± 0.375, 9.56 ± 0.453, respectively). The mean (±SEM) values of serum CT, and CK concentrations and p-value in control and CAD patients were in figure (1). Comparison of female and male CK concentrations. According to Box-and-whisker the results showed that CK mass (creatine kinase-isoenzyme MB mass) for males were significantly different from those for females ($p < 0.0001$, Mann-Whitney test).

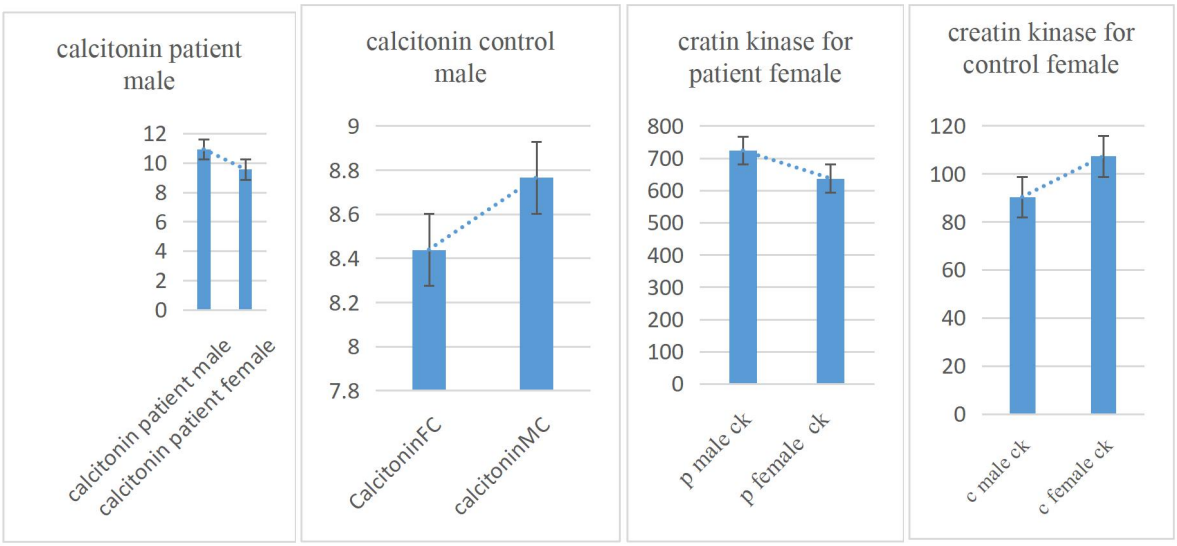

Figure 1. Comparison of female and male calcitonin, CK concentrations and age. Box-and-whisker representation of the results.

The data in Table (2) showed that the correlations between the vital signs factors with each of the sexes were evaluated as presented in both CK and CT were insignificant but the positive increase was associated with CT (r = 0.294) while negativity was associated with CK (r = -0.065) in a sick female patient with CAD.

Table 2. Correlation between different parameters in healthy and patient males and female.

	Female				Male			
	Patient		Healthy		Patient		Healthy	
	r	p-value	r	p-value	r	p-value	r	p-value

CT & Ck	-0.065	0.781	0.096	0.822	0.294	0.066	0.255	0.379
CT & age	-0.246	0.270	0.203	0.630	-0.013	0.935	0.019	0.948
Ck & age	-0.178	0.441	0.269	0.238	0.034	0.835	-0.023	0.889

The results are cleared in the next figures (2, 3, and 4), which show the relationship of calcitonin with creatine kinase in female (fig.2.A) and male (fig.2.B) coronary patients. In addition the correlation between calcitonin and age illustrated in (fig.3.A, B) for female and male respectively there was no significant correlation between calcitonin and age, meanwhile, there was no significant correlation between creatine kinase and age illustrated in (fig.4.A)for female and (fig.4.B) for male.

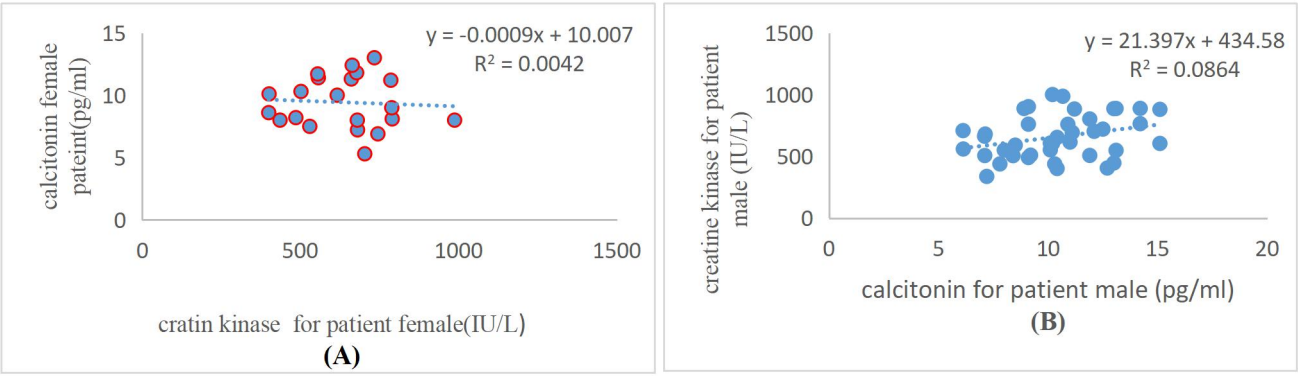

Figure 2 .Relation between calcitonin and creatine kinase in: (A) female patients, and (B) male patients.

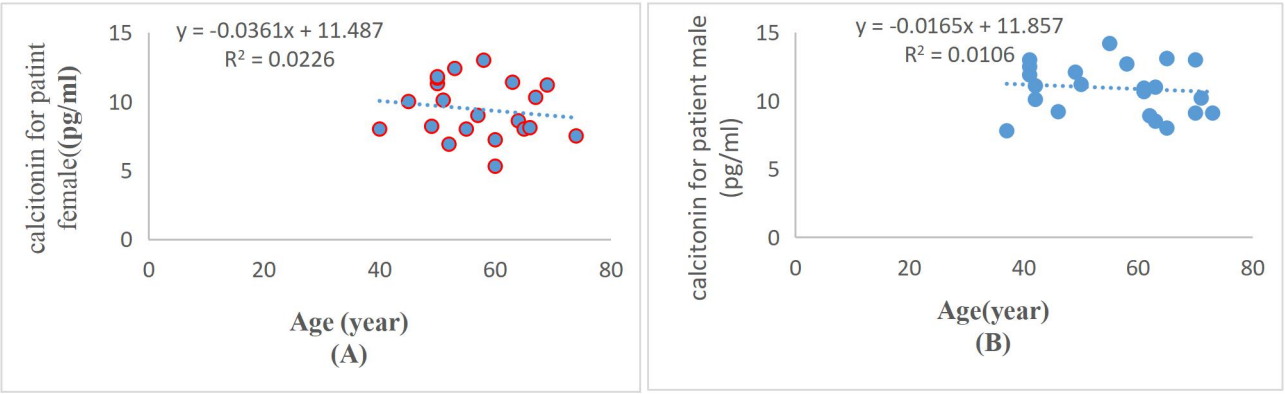

Figure 3.Relation between calcitonin and age in: (A) female patients, and (B) male patients.

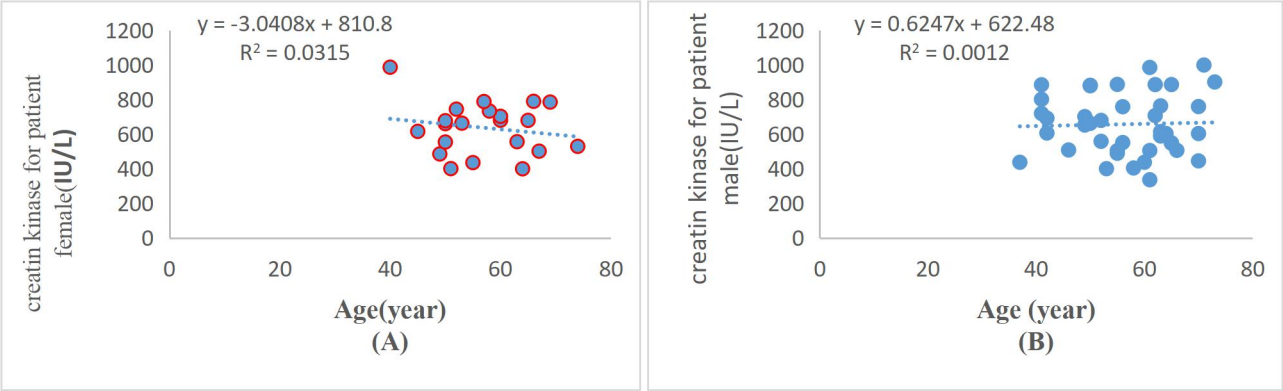

Figure 4.Relation between creatine kinase and age in: (A) female patients, and (B) male patients.

Discussion

The data of the present study indicated that CK activity and CT concentration are changing. On the basis of these variation criteria and results, it seems appropriate to establish reference values for both CK and CT measurements in the sera of the studied groups. For the outlier of individual CK and CT differences Fig. (1). Generally, inter-individual variability of CK activity in the people is greater than previously proposed and that comparatively high levels frequently occur in varied subgroups [14]. Those and our findings are consistent with the existing knowledge that males have higher values than females. Table (1) shows a significant increase in the level of CK and CT in male and female. In table (2) correlations between factors of vital signs in each of the sexes were found and were evaluated. Both CK and CT were insignificant, but the positive increase was associated with CT, while negativity was associated with CK in sick female patients with CAD.

Secreted calcitonin by porous cells in the thyroid gland, which reduces calcium in the blood as well as phosphates mainly by inhibiting the activity of osteoarthritis in the bone. At high concentrations, CT increases the excretion of calcium and urinary phosphorous, most likely by working on nearby tubes, but this effect is not important ; physiologically [15]. Several studies have been carried on CT concentration; some authors have found associations between CT concentration and other factors associated with minerals metabolism , such as alkali phosphatase, serum calcium and parathyroid hormones (PTH), while others have not, as previously described by us and others [16, 17, 18, 19].

In Figure (1), comparison of female and male CK concentrations, Box-and-whisker representation of the results, CK mass = creatine kinase-isoenzyme MB mass, CK values for males were significantly different from those for females ($p < 0.0001$, Mann-Whitney test).

High blood CK usually means muscle damage causing muscles to release CK into the blood. The possible reasons for this may be that the heart is a muscle, so when it is destroy by a heart attack, CK is released into the blood. Meanwhile, CK-MB (a CK form) or a troponin test considered as the better blood tests for a heart attack [14].

Our study found that CT and CK were more in males than females and that they increased in patients with CAD when compared with the control group. This study is consistent with the study conducted by the obtained CK values was above 5.10 mg per ml suggested by the laboratory kit manufacturs. Therefore, resolution boundaries must be related to people and gender to prove the privacy of the used diagnostic tool, and to avoid mis-classification of patients [20].

From a previous study, significant relationship between CT and the severity of the CAD was found when it was adjusted only to metabolic metabolism criteria in addition to two factors are FGF 23, and fetuin A. Nevertheless , after the inclusion of risk factors Framingham, eGFR, and proteinuria, but this relationship did not statistical significance. In multivariate analysis, the study concluded that both FGF23 and fetuin play a role in large CAD severity predictions. Despite the risk factors [21].

Our study indicates a new relationship between CT and CK with CAD that was not in the last reported in either the all population or even in coronary kidney diseses patients. This finding seems surprising and even counter-intuitive, given the

physiological effects of CT. Despite many studies, but until now it has not been proven that CT has any major vascular effects in humans. However, it can prevent experimental induction of calcified plaque from atherosclerosis, by blocking the flow of calcium into the smooth vascular muscles of rabbits [22]. Still, it is difficult to explain the relationship between CT and CAD in the context of current knowledge.

It should also be noted that traditional risk factors such as aging, high blood pressure, smoking, diabetes, dyslipidemia, proteinuria, blood calcium levels and phosphate levels in the blood, have not predicted the seriousness of the Gensini score in the small study population. The role of CT in the preoperative evaluation will be very beneficial in planning operations, thus preventing potential secondary processes and eliminating the risk of additional diseases and deaths [23]. In addition to the increased oxidative stress that has already been mentioned, there is a number of other mechanisms through which obesity may affect the function of the coronary microvasculature. There may be a dilute expansion without mediating the coronary vessels with decreasing bioavailability of NO and changes in the cyclase-cGMP pathway without melting [24-26]. Aging can provide an additional risk factor for microvascular disease [27] where fibrosis plays an important role. Increasing CT secretion and the resulting hypocalcemia promotes to reduce stress response. Additionally, there is no noticeable increase in the level of computed tomography and reduction in calcium, except under long pressure [28].

Conclusion

In conclusion, our current study confirms the correlations of age, CT, CK with CAD and the difference in gender. Meanwhile, it creates CT as a new agent that may be involved in this process. The level of CT, and CK were important parameters to indicate the effect of the physiological and CAD role which means an increase in this parameter of increased calcium ion and thyroid hormone (PTH) effect. This discovery deserves further experimental and clinical exploration.

Conflicts of Interest

All authors declare no conflicts of interest.

Acknowledgments

We recognize all participating patients and healthy individuals, who helped give information and blood samples.

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