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Assessment of the Diagnostic Accuracy of C-Reactive Protein and Pentraxin3 in Acute Coronary Syndrome Compared with Cardiac Troponin-1

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Abstract

High levels of pentraxin3 reflect severity of coronary lesions as measured by coronary angiography, very low levels of serum pentraxin 3 could exclude presence of risk for those patients completely so, it is considered agood negative test. We aimed to assess the diagnostic accuracy of C-reactive protein and pentraxin3 in acute coronary syndrome compared with cardiac troponin-1 Methods: A cohort study was conducted on 100 patients and were divided into:NSTE-ACS (NSTEMI and UA) included 70 patients. Non-ACS (SCAD and non-cardiac) included 30 patients. Laboratory investigations were done . Resting 12 leads surface Electrocardiogram (ECG) was done. Echocardiography to assess the left ventricular systolic function was done. By dividing our study populations into 4 groups NSTEMI, UA, SCAD and Non-ACS (non-cardiac),There was highly statistical significant difference regarding hs-CRP, CTnI and PX3. There was statistical significant difference regarding LVEF between group I & III, I & IV, II & III and II & IV. The best cut-off value considering the diagnostic accuracy of PX3 in prediction of acute coronary syndrome is 1.6 with 94.3% sensitivity and 60% specificity, for CTnI is 0.055 with 78.6% sensitivity and 53.3% specificity. Elevated levels of hs-CRP and serum PTX3 in the early hours clearly shows that they can be used as novel markers in the diagnosis of ACS. Their estimation in the early hours of ACS aid in the diagnosis and management of ACS.

1. Introduction

Atherosclerosis is an inflammatory disease characterized by vascular inflammation and a systemic inflammatory state. Inflammation is involved in all stages of atherothrombosis, from the induction of endothelial dysfunction to plaque formation, plaque destabilization, and subsequent thrombosis [1].

The levels of systemic inflammatory biomarkers, including C-reactive protein (CRP) and tumor necrosis factor α (TNFα), are related to the severity of cardiovascular disease. These biomarkers predict future cardiovascular events in patients with cardiovascular disease, as well as in apparently healthy individuals. The role of systemic inflammation in atherosclerosis has not yet fully been elucidated. Systemic inflammation may be secondary to vascular inflammation and/or underlying cardiovascular risk factors [2].

Pentraxin 3 (PTX3) is a newly discovered marker of the acute-phase inflammatory response, and plays an important role in innate immunity. Similar to CRP, PTX3 belongs to the PTX protein family [3].

High levels of pentraxin3 reflect severity of coronary lesions as measured by coronary angiography, very low levels of serum pentraxin 3 could exclude presence of risk for those patients completely so, it is considered agood negative test [4].

The aim of the study is to assess the diagnostic accuracy of C-reactive protein and pentraxin3 in acute coronary syndrome compared with cardiac troponin-1.

2. Patient and method

The present study is a cohort study and was conducted on 100 patients admitted to Helwan and Banha University emergency department.

Our Patients were divided into:

NSTE-ACS (NSTEMI and UA) included 70 patients.

Non-ACS (SCAD and non-cardiac) included 30 patients.

Inclusion criteria was Patients with chest pain in addition to renal impairment and other comorbidities (HCV, stroke) are included in our study.

Exclusion criteria was Patients with STEMI, Patients with systolic dysfunction, Nonspecific conditions (eg pericarditis and pulmonary embolism)

An informed written consent was obtained from all subjects. The study protocol was approved by the Ethical Review Committee.

All subjects included in the study were subjected to the following:

Complete history taking (Age, Sex, Risk factors history (hypertension, diabetes, dyslipidemia, smoking, BMI and family history), Previous MI, Previous PCI, Previous bypass surgery, Cerebrovascular disease, Peripheral arterial disease.

Clinical examination was done for all patients including vital signs (heart rate, blood pressure, respiratory rate and temperature), neck veins and cardiac auscultation. Clinical manifestation of heart failure, pulmonary hypertension and systemic hypertension.

Laboratory investigations included (CBC, Renal function, liver function, lipid profile, Electrolytes, Hs-CRP, CTnI, PX3)

→ From every patient (within 6 hours of presentation) a venous sample was withdrawn to determine Hs-CRP, Tpn-I and arterial sample for PX3.

Resting 12 leads surface Electrocardiogram (ECG): Analysed paying special interest for QRS complex, ST segment and T wave changes. Echocardiography to assess the left ventricular systolic function was done.

3. Results

Patients with NSTE-ACS (NSTEMI and UA) considered the first group and patients with non-ACS

(SCAD and non-cardiac) considered the second one. Within 6 hours of presentation A venous sample was withdrawn to determine Hs-CRP, Tpn-I and PX3. Then, patients were devided into 4 subgroups (NSTEMI, UA, SCAD and Non-ACS (non-cardiac).

When comparing the four subgroups, the mean age was 55.36±8.1, 53.45±9.41, 53.78±6.38 and 60.17±7.22 respectively with non-significant difference between the two groups with p value 0.105. Meanwhile for gender there was also non-significant difference between the four groups with p value 0.784.

As regarding BMI, there was a statistically significant difference between group I when comparing with each of the other groups with p value ≤0.001. Also for dyslipidemia there was a statistically significant difference between group I when comparing with group III and IV with p value 0.046 with non-significant difference when comparing both subgroups of ACS with each other's.

As regarding smoking, HTN, DM and family history of heart disease, there was non-significant difference in between the four groups with p values 0.86, 0.35, 0.51 and 0.94 respectively

As regarding Killip calssification, 11 patients in group I, 10 in group II, 12 in group III and 9 in group IV had class I, 18 patients in group I, 12 in group II, 4 in group III and 2 in group IV had class II and 12 patients in group I, 7 in group II, 2 in group III and 1 in group IV had class III with a statistically significant difference in between the four groups with p value 0.022.

a: significant with ACS (NSTE1I), b: significant with ACS (UA), c: significant with Non-ACS (SCAD)

As regarding Hs-CRP, the median was 3.8 (0.7-8.2), 4.0 (1.9-6.9), 2.05 (0.7-3.9) and 1.05 (0.5-2.0) between the four groups with a high statistically significant difference between group I & III, I & IV, II & III, II& IV and III & IV with p value ≤0.001. Table 1

For CTnI, the median was 1.6 (0.8-3.2) 0.5, (0.01-0.13), 0.05 (0.01-0.1) and 0.06 (0.02-0.1) between the four groups with a high statistically significant difference between group I & II, I & III and I & IV with p value ≤0.001. Table 1

And finally for PX3, the median was 3.8 (1.7-6.9), 2.6 (1.3-5.7), 1.7 (0.6-2.6) and 1.0 (0.5-2.8) between the four groups with a high statistically significant difference between group I & II, I & III, I & IV, II & III and II& IV with p value ≤0.001Table (1).

Table (1) Hs-CRP, CTnI and PX3 in different groups.

Variables	ACS (NSTE1I) (n=41)	ACS (UA) (n=29)	Non-ACS (SCAD) (n=18)	Non-ACS (non-cardiac) (n=12)	Kruskil wallis test	P value
Hs-CRP	3.8 (0.7-8.2)	4.0 (1.9-6.9)	2.05 (0.7-3.9) [ab]	1.05 (0.5-2.0) [abc]	42.82	≤0.001*
CTnI	1.6 (0.8-3.2)	0.5 (0.01-0.13) [a]	0.05 (0.01-0.1) [a]	0.06 (0.02-0.1) [a]	72.26	≤0.001*
PX3	3.8 (1.7-6.9)	2.6 (1.3-5.7) [a]	1.7 (0.6-2.6) [ab]	1.0 (0.5-2.8) [ab]	47.65	≤0.001*

As regarding serum creatinine, the mean was 1.05±0.42, 1.09±0.42, 1.01±0.37 and 1.10±0.51 between the four subgroups with a statistically non-significant difference with p value 0.903.

Meanwhile, for LVEF, the mean was 52.63±6.34, 55.03±3.96, 58.28±5.47 and 58.42±4.81 between the four subgroups with a high statistically significant difference between group I & III, I & IV, II & III and II & IV with p value 0.001.

As regarding the outcome of the patients in the four groups, 7 patients in group I died, 4 in group II, 1 in group III and I in group IV died with non-significant difference with p value 0.702.

The best cut-off value considering the diagnostic accuracy of PX3 in prediction of acute coronary syndrome is 1.6 with 94.3% sensitivity and 60% specificity, for CTnI is 0.055 with 78.6% sensitivity and 53.3% specificity

As a conclusion, the best diagnostic accuracy in prediction of acute coronary syndrome was by PX3 (94.3%) followed by CTnI (78.6%).

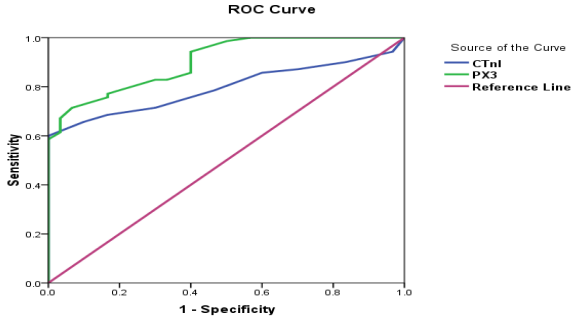

Fig (1) Receiver operating characteristics curve for diagnostic accuracy of CTnI and PX3 in prediction of ACS.

Positive significant correlation between PX3 and CTnI with p value 0.033, and r value 0.255. While there was a negative significant correlation between PX3 and LVEF with p value <0.001 and r value -0.459.

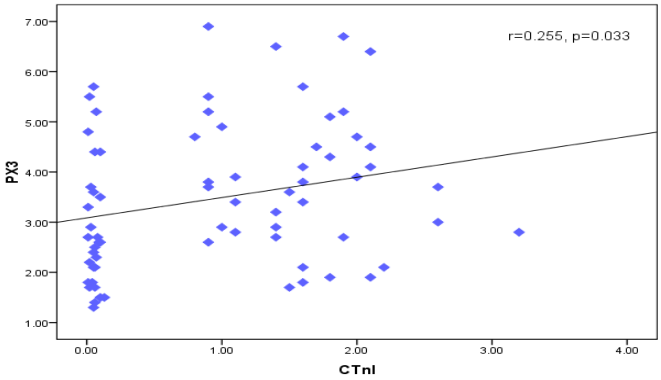

Fig (2) Scatter diagram for positive correlation between PX3 and CTnI

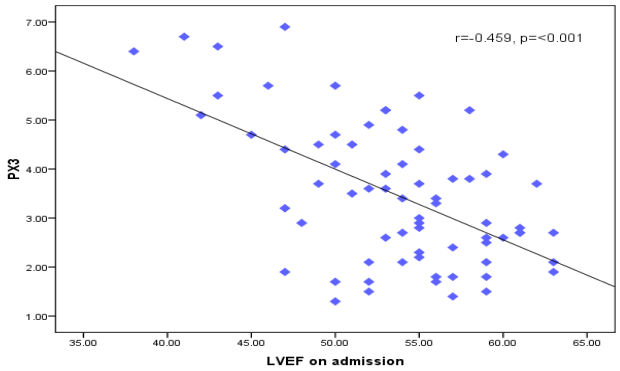

Fig (3) Scatter diagram negative correlation between PX3 and LVEF on admission

4. Discussion

Inflammation is central to the endothelial dysfunction that underlies vascular disease. Since atherosclerosis is an inflammatory process, several markers of inflammation have been evaluated for this purpose. Among them, high-sensitive C-reactive protein (hs-CRP) has emerged as the most important CV risk marker. More than a simple marker of inflammation, hs-CRP may influence vascular vulnerability directly through several mechanisms including, enhanced expression of adhesive molecules, reduced nitric oxide, increased expression of endothelial PAI-1 and altered LDL uptake by macrophages [5].

Pentraxin 3 (PTX3) is a newly discovered marker of the acute-phase inflammatory response, and plays an important role in innate immunity. Similar to CRP, PTX3 belongs to the PTX protein family[3].

The aim of our study is to assess the accuracy of serum pentraxin3 and Hs-CRP in diagnosis of ACS compared to cardiac troponin-I

This is a prospective Cohort study conducted on 100 subjects with sudden chest pain admitted to Helawn and Benha Cardiology department. Patients with NSTE-ACS (NSTEMI and UA) considered the first group and patients with non-ACS (SCAD and non-cardiac) considered the second one. Within 6 hours of presentation a venous sample was withdrawn to determine Hs-CRP, Tpn-I and PX3.

Regarding to age, the mean age was 54.57±8.69 years in ACS group and 56.33±7.33 years in Non-ACS group with non-significant difference between the two groups with p value 0.334. Regarding to gender there was 30 (42.9%) males and 40 (57.1%) females in ACS group while there was 15 (50%) males and 15 (50%) females in Non-ACS group with non-significant difference between the two groups with p value 0.511

This result was concordant with (6) in which there was (84.3%) were male and 11 (15.7%) were female in ACS patients and the mean age was 57.79±13.09. In the control group, 61.6% were male and 38.4% were female and the mean age was 57.08±10.76 years with no statistical significant difference between both groups.

Regarding to risk factors, Patients with increased risk factors are more prone to ACS. In our study there was increased risk factors (smoking, HTN, DM, dyslipidemia, family history and BMI) in ACS group.

Our study show that there was statistically significant difference between the two groups

regarding BMI and dyslipidemia with p value ≤0.001, 0.006 respectively as there were more dyslipidemic patients and increased BMI in ACS group.

As regarding smoking, HTN, DM and family history of heart disease, there was non-significant statistical difference between both groups with p values 0.422, 0.084, 0.628 and 0.532 respectively.

This was disconcordant with [7] in which there was statistical significant difference regarding DM, hypertension, dyslipidemia and smoking between both groups while there was no statistical significant difference regarding family history.

[8] stated that there was no statistically significant difference regarding DM, hypertension, dyslipidemia, family history while there was statistical significant difference regarding smoking.

In [9] there was no statistical significant difference between ACS group and non ACS group regarding to age, sex, DM, HTN, smoking, lipid profile and family history.

Markers of ACS

As regarding Hs-CRP, the median level was 3.9 (0.7-8.2) and 1.7 (0.5-3.9) between the two groups with a high statistically significant difference with p value ≤0.001.

For CTnI, the median level was 0.9 (0.01-3.2) and 0.05 (0.01-0.1) between the two groups with a high statistically significant difference with p value ≤0.001.

Our study showed that there was highly statistically significant difference with p value ≤0.001 between both groups regarding to Hs-CRP, CTnI and PX3 level. This was concordant with (10) in which there was statistical significant difference between both groups regarding CRP, troponin.

The present study results are comparable to the studies by M.D. Yuksel Cavusoglu [11] who demonstrated that the CRP concentrations in patients presenting with acute coronary syndromes, within 6 hours of onset of symptoms were significantly higher as compared to the Control Group. The inflammatory process has been shown to be one of the mechanisms causing plaque rupture leading to elevated CRP levels in less than 6 hours in patients with acute coronary syndrome.

In patients presented with ACS, hsCRP concentrations are more than 10-fold higher than in patients with stable coronary disease or no known coronary disease.

In M.Üstündağ [6] the median level of serum Pentraxin-3, ng/ml was 0.50±0.39 in control group and 1.73±0.82 in ACS group with p value <0.001 with highly statistical significant difference between both groups which is concordant with our study results.

V.Vuković-Dejanović [12] showed that increased circulating levels of PTX3 and hsCRP represent inflammatory markers of advanced atherosclerosis in patients with CAD, and both markers might be quantitative indicators of disease extent.

As regarding serum creatinine, the mean was 1.06±0.41 and 1.05±0.43 between the two groups with a statistically non-significant difference with p value 0.835. This was concordant with Huang et al, 2019 in which there was no statistical significant difference between ACS and Non ACS groups regarding creatinine. Regarding to LVEF, a high statistically significant difference between both groups with p value ≤0.001 as the mean LVEF was 53.63±5.57 in ACS group and 58.33±5.13 in Non-ACS group. This was concordant with, [13] in which there was significant difference regarding LVEF

G.Paramasivam [14] stated that there was no statistical significant difference regarding LVEF. It was 51 ± 10 in ACS group and 54 ± 11 in Non ACS group with p value 0.076 which is disconcordant with our study.

As regarding the outcome of the patients in the two groups, our study showed that 11 patients in ACS group and 2 in Non ACS group died with non-significant difference with p value 0.218. This was disconcordant with (15) in which Patients with ACS are at a higher risk for adverse outcomes as compared those with non ACS. They had significantly worse outcomes in terms of all-cause death and MACE.

When comparing the four subgroups, the mean age was 55.36±8.1, 53.45±9.41, 53.78±6.38 and 60.17±7.22 respectively with non-significant difference between the two groups with p value= 0.105. Meanwhile for gender there was also non-significant difference between the four groups with p value= 0.784.

In A.Qanitha [16] which assess the Predictors of medium-term mortality in patients hospitalised with coronary artery disease, there was statistical significant difference regarding age and sex.

As regarding BMI, there was a statistically significant difference between group I when comparing with each of the other groups with p value ≤0.001. Also for dyslipidemia there was a statistically significant difference between group I when comparing with group III and IV with p value 0.046 with non-significant difference when comparing both subgroups of ACS with each others.

Our study show that there was a statistically significant difference between group I when comparing with group III and IV regarding BMI and dyslipidemia with p value ≤0.001, 0.046 respectively and non-significant difference when comparing both subgroups of ACS with each others.

As regarding smoking, HTN, DM and family history of heart disease, there was no statistical significant difference in between the four groups with p values 0.86, 0.35, 0.51 and 0.94 respectively.

Compared with our study, In A.Qanitha [16], there was no statistical significant difference regarding DM, lipid profile and BMI while there was statistical significant difference regarding smoking, HTN and lipid profile.

In [17] there was statistical significant difference regarding age, hypertension and smoking while there was no statistical significant difference regarding DM, gender and hypercholesterolemia.

As regarding Hs-CRP, the median was 3.8 (0.7-8.2), 4.0 (1.9-6.9), 2.05 (0.7-3.9) and 1.05 (0.5-2.0) between the four groups with a high statistically significant difference between group I & III, I & IV, II & III, II& IV and III & IV with p value ≤0.001.

For CTnI, the median was 1.6 (0.8-3.2) 0.5, (0.01-0.13), 0.05 (0.01-0.1) and 0.06 (0.02-0.1) between the four groups with a high statistically significant difference between group I & II, I & III and I & IV with p value ≤0.001.

And finally for PX3, the median was 3.8 (1.7-6.9), 2.6 (1.3-5.7), 1.7 (0.6-2.6) and 1.0 (0.5-2.8) between the four groups with a high statistically significant difference between group I & II, I & III, I & IV, II & III and II& IV with p value ≤0.001.

This was concordant with [6] in ACS subtypes PTX-3 levels were considerably higher compared with the Non ACS group. Similarly, cTnI was significantly high only in the NSTEMI group.

There was statistical significant difference between all groups regarding the level of serum troponin and Pentraxin-3.

As regarding serum creatinine, the mean was 1.05±0.42, 1.09±0.42, 1.01±0.37 and 1.10±0.51 between the four subgroups with a statistically non-significant difference with p value 0.903. Meanwhile, for LVEF, the mean was 52.63±6.34, 55.03±3.96, 58.28±5.47 and 58.42±4.81 between the four subgroups with a high statistically significant difference between group I & III, I & IV, II & III and II & IV with p value 0.001.

In (8) LVEF was 53.30±11.38 in NSTEMI patients and 52.82 ±12.87 in Non ACS group. There was no statistical significant difference between between NSTEMI and control group.

As regarding the outcome of the patients in the four groups, 7 patients in group I died, 4 in group II, 1 in group III and I in group IV died with non-significant difference with p value 0.702.

In F.Fath-Ordoubadi [17] there was a statistically significant increase in cardiac death was observed in the NSTEMI group compared to the stable angina group. Similarly, a statistically significant increase in MACE was observed in the NSTEMI group compared to the stable angina group.

The best cut-off value considering the diagnostic accuracy of PX3 in prediction of acute coronary syndrome is 1.6 with 94.3% sensitivity and 60% specificity, for CTnI is 0.055 with 78.6% sensitivity and 53.3% specificity.

As a conclusion, the best diagnostic accuracy in prediction of acute coronary syndrome was by PX3 (94.3%) followed by CTnI (78.6%).

Our study show that there was a Positive significant correlation between PX3 and CTnI with p value 0.033. While there was a negative significant correlation between PX3 and LVEF with p value <0.001.

In M.Tomandlova [18] there was negative correlation between PTX3 levels was found with LVEF. While there was no correlation between PTX3 levels and CRP or between PTX3 levels and serum creatinine.

In S.Altay [19], PTX3 level was found to be significantly positively correlated with high sensitive C-reactive protein (hsCRP) (p=0.024) and troponin I (p=<0.001), and negatively correlated with LVEF (p=0.028).

High serum levels of pentraxin-3 in STEMI patients and its association with both LVEF support the concept that the magnitude of pentraxin-3 levels correlates to the severity of myocardium injury. This confirms the role of pentraxin-3 as a biomarker of ACS due to its local production and increased blood level after acute. Event [20].

5. Conclusion

Elevated levels of hs-CRP and serum PTX3 in the early hours clearly shows that they can be used as novel markers in the diagnosis of ACS. Their estimation in the early hours of ACS aid in the diagnosis and management of ACS.

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