

## CLINICAL STUDY

# Comparison of pentraxin-3 and ischemia-modified albumin with troponin in early diagnosis of acute coronary syndrome

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**ABSTRACT**

**INTRODUCTION:** In this study, our aim was to evaluate clinical utilities of Pentraxin 3 (PTX3) and Ischemia-modified Albumin (IMA) in diagnosis of acute coronary syndrome (ACS) and compare these two biomarkers with a conventional diagnostic marker, cardiac troponin I (cTnI).

**MATERIALS AND METHODS:** Sixty adult patients with ACS diagnosis were involved into this prospective study. Additionally, 20 healthy subjects were determined as control group (Group IV). Patients were divided into 3 groups as follows: Patients with Acute Myocardial Infarction (STEMI Group, n=20, Group I), patients without ST elevation but with elevated cTnI levels (NSTEMI Group, n=20, Group II), and patients with unstable angina pectoris (USAP Group, n=20, Group III). Blood measurements were obtained for each marker at admission and in the 4th hour.

**RESULTS:** Troponin level was significantly different between groups I and II at both admission and in the 4th hour. Additionally, PTX 3 level was significantly different at admission and 4th hour between groups II and III.

**CONCLUSION:** This study revealed that cTnI is the most sensitive test in ACS diagnosis at the admission to Emergency Department. Our results also revealed that PTX 3 may be a useful diagnostic tool for ACS at admission, however, IMA alone cannot be used for diagnosis of ACS. Similarly, in the 4th hour, cTnI was found to be the most useful marker in ACS diagnosis, however, PTX 3 and IMA were found to be inadequate for diagnosis of ACS (Tab. 3, Ref. 19). Text in PDF [www.elis.sk](http://www.elis.sk).

**KEY WORDS:** acute coronary syndrome, cardiac troponin i, ischemia-modified albumin, pentraxin 3, emergency department.

**Introduction**

Acute coronary syndrome (ACS) involves a broad spectrum of complaints from angina pectoris to irreversible myocardial damage resulting in acute myocardial infarction (AMI) (1). Recently, many potential biomarkers have been studied for the early and appropriate diagnosis of AMI. Cardiac troponin I (cTnI) and troponin T are commonly used for determining the extent of cardiac muscle injury in AMI. However, studies for novel early diagnostic biomarkers are still ongoing (2).

Ischemia-modified albumin (IMA) is a marker formed after damage in the N-terminal region of albumin. The causes of the increases in IMA have been shown to be endothelial or extracellular hypoxia, acidosis, and free oxygen radicals (34).

Similar to IMA, Pentraxin 3 (PTX 3) is known to be released as a specific response to vascular damage and PTX 3 levels are likely to be strongly related to later stages of atherosclerosis (5). In this article, our aim was to investigate the usefulness of IMA and PTX 3 in the early diagnosis of AMI and compare their utility with conventional marker, cTnI.

**Materials and methods**

After ethical approval form Local Ethics Committee, 60 adult patients with ACS diagnosis admitted to Coronary Intensive Care Unit were involved into this prospective study. Additionally, 20 healthy subjects formed a control group. Patients with ACS were divided into 3 groups as follows: Patients with AMI confirmed by ST elevation on serial electrocardiograms (ECGs) and cTnI measurements (STEMI Group, n = 20, Group I), patients without ST elevation but with elevated cTnI levels (NSTEMI Group, n = 20, Group II), and patients with unstable angina pectoris (USAP Group, n = 20, Group III). Control group was named as Group IV.

Patients with chronic obstructive pulmonary disease, renal failure, collagen tissue disease, vasculitis, depression, somatization disorder and patients with a medical history of coronary angiography, coronary by-pass and open heart surgery were excluded in order to avoid false positive cTnI levels.

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Blood samples of the patients were evaluated at admission and in the 4th hour of follow-up. Blood samples for IMA and PTX 3 were taken at admission and in the 4th and were centrifuged at 3500 rpm for 15 minutes, and serum samples were stored at  $-80^{\circ}\text{C}$  until analysis.

CK-MB and cTnI levels were measured in serum by Simens ADVIA Centaur Cp analyzers in emergency laboratory.

Serum PTX 3 level was measured by ELISA using a kit (USCN Life Science Inc. Cloud-Clone Corp. Houston, USA, Lot No: L140205003) and IMA was also measured by ELISA using a kit (Cusabio Biotech Co., Ltd. Wuhan, China, Lot No: W22169285). For this measurement, sandwich immunoassay technique was used.

### Statistical analysis

For statistical analyses, SPSS 17.0 programme was used. Data are presented as arithmetic mean  $\pm$  standard deviation and median (minimum–maximum) values. For evaluation of normality, Shapiro Wilk test was used. In comparison of groups, One Way ANOVA was used for normal distribution and Kruskal–Wallis variance analysis was used for non-normal distribution. For comparison of normally distributed two groups, Tukey was used for homogenous variance and Tamhane test was used for heterogeneous variance.

**Tab. 1. Groups according to demographic findings.**

Groups	Gender		Age $\pm$ SD
	Male	Female	
Group I	17 (85%)	3 (15%)	58.5 $\pm$ 19.1
Group II	15 (75%)	5 (25%)	63.6 $\pm$ 15.4
Group III	17 (85%)	3 (15%)	52.8 $\pm$ 13.3
Group IV	14 (70%)	6 (30%)	27.7 $\pm$ 9.5

For comparison of two normally distributed groups, Bonferroni corrected Mann Whitney U test was used. Pearson correlation test was performed to test correlation between normally distributed data and Spearman's correlation test was used for non-normally distributed data. Diagnostic values of the markers were evaluated by Receiver Operating Characteristic (ROC) Analysis and Area Under Curve (AUC).  $p < 0.05$  was considered statistically significant.

### Results

Demographical and laboratory findings of the groups are summarized in Tables 1 and 2. Troponin level was significantly different in groups I and II at both admission and the 4th hour when

**Tab. 2. Laboratory findings of the groups.**

Laboratory Findings (On admission)	Group I (n = 20)		Group II (n = 20)		Group III (n = 20)		Group IV (Controls) (n = 20)	
	Arithmetic Mean $\pm$ Standard Deviation	Median (Min–Max)						
White blood cell (3.7–9.7 thousand/uL)	12.4 $\pm$ 3.5	10.7 (8.3–17.5)	10.6 $\pm$ 3.2	10.7 (5.8–18.4)	9.2 $\pm$ 2.5	8.5 (4.6–13.6)	7.1 $\pm$ 1.5	6.7 (4.9–10.9)
Haemoglobin (13.3–17.2 g/dL)	14.36 $\pm$ 2.4	14.9 (9.3–17.2)	13.9 $\pm$ 2.0	14.4 (9.4–17.1)	14.4 $\pm$ 1.5	14.7 (12.0–17.6)	13.8 $\pm$ 1.6	13.7 (11.4–16.5)
Platelet (179–373 thousand/uL)	238.9 $\pm$ 50.2	239.5 (158.0–346.0)	240.8 $\pm$ 66.2	232.5 (161.0–394.0)	246.0 $\pm$ 112.7	224.5 (42.0–538.0)	249.5 $\pm$ 48.4	244.0 (180.0–342.0)
Glucose (70–110 mg/dL)	176.2 $\pm$ 84.8	136.0 (84.0–401.0)	155.4 $\pm$ 71.9	130.5 (84.0–380.0)	159.7 $\pm$ 86.3	122.0 (85.0–396.0)	94.9 $\pm$ 12.2	93.5 (72.0–121.0)
BUN (5–24 mg/dL)	17.8 $\pm$ 7.2	16.0 (9.0–44.0)	18.0 $\pm$ 4.7	17.0 (10.0–27.0)	19.4 $\pm$ 12.3	16.0 (8.0–63.0)	10.9 $\pm$ 3.3	10.0 (4.0–19.0)
Creatine (0.4–1.4 mg/dL)	0.9 $\pm$ 0.2	0.9 (0.5–1.5)	0.9 $\pm$ 0.2	0.9 (0.50–1.40)	0.9 $\pm$ 0.2	0.9 (0.6–1.4)	0.8 $\pm$ 0.2	0.9 (0.4–1.0)
AST (8–46 UL)	48.5 $\pm$ 37.8	34.0 (12.0–143.0)	56.30 $\pm$ 48.20	47.00 (22.0–233.0)	25.7 $\pm$ 12.8	22.5 (10.0–57.0)	18.95 $\pm$ 3.25	18.0 (14.0–26.0)
ALT (7–46 UL)	34.4 $\pm$ 14.5	32.0 (15.0–67.0)	30.6 $\pm$ 12.6	28.5 (14.0–64.0)	28.9 $\pm$ 21.6	22.5 (4.0–96.0)	19.7 $\pm$ 8.8	18.5 (11.0–43.0)
Creatin Kinase (35–195 UL)	339.6 $\pm$ 358.7	139.0 (71.0–1239.0)	428.9 $\pm$ 526.9	328.5 (39.9–2456.0)	218.3 $\pm$ 345.5	101.0 (34.0–1484.0)	171.2 $\pm$ 154.2	137.5 (64.0–796.0)
CK-MB (0–25 mg/dL)	48.3 $\pm$ 42.1	37.0 (2.0–200.0)	67.3 $\pm$ 99.8	40.0 (19.0–479.0)	25.6 $\pm$ 13.0	20.5 (3.0–51.0)	14.4 $\pm$ 1.31	14.0 (12.0–18.0)
Calcium (8.6–10.0 mg/dL)	9.42 $\pm$ 0.7	9.5 (7.9–11.1)	9.5 $\pm$ 0.5	9.40 (8.3–10.3)	9.8 $\pm$ 0.7	9.55 (8.8–11.6)	9.9 $\pm$ 0.6	9.8 (9.0–11.8)
Sodium (135–145 mEq/L)	138.8 $\pm$ 3.7	139.5 (132.0–145.0)	139.3 $\pm$ 2.8	139.0 (134.0–145.0)	139.6 $\pm$ 2.9	139.5 (134.0–145.0)	140.1 $\pm$ 1.5	140.0 (136.0–142.0)
Potassium (3.5–5.5 mEq/L)	4.0 $\pm$ 0.5	3.90 (3.3–5.3)	4.3 $\pm$ 0.5	4.2 (3.40–5.5)	4.3 $\pm$ 0.4	4.20 (3.70–4.90)	4.30 $\pm$ 0.34	4.23 (3.8–5.0)
Clor (99–110 mEq/L)	104.0 $\pm$ 4.2	105.0 (96.0–113.0)	105.9 $\pm$ 3.9	105.5 (97.0–115.0)	105.4 $\pm$ 3.9	106.0 (97.0–112.0)	104.0 $\pm$ 1.8	104.5 (101.0–107.0)

**Tab. 3. Comparison of the markers on admission and in the 4th hour.**

Biomarker	Group I (n = 20)		Group II (n = 20)		Group III (n = 20)		Control (n = 20)		P value
	Arithmetic Mean±Standard Deviation	Median (Min–Max)	Arithmetic Mean±Standard Deviation	Median (Min–Max)	Arithmetic Mean±Standard Deviation	Median (Min–Max)	Arithmetic Mean±Standard Deviation	Median (Min–Max)	
cTnI (ng/ml) (On admission)	0.9±2.4	0.2 (0.1–8.5)	2.5±3.6	1.0 (0.1–15.4)	0.01±0.0	0.01 (0.01–0.01)	0.01±0.0	0.01 (0.01–0.01)	p<0.001
cTnI (ng/ml) (4.hour)	3.3±4.2	0.9 (0.1–1.1)	3.6±4.6	1.9 (0.1–9.2)	0.01±0.0	0.01 (0.01–0.1)	0.01±0.0	0.01 (0.01–0.01)	p<0.001
PTX-3 (ng/ml) (On admission)	7.2±4.7	6.9 (1.0–5.6)	8.9±5.1	9.6 (1.3–6.6)	5.4±3.5	4.4 (0.8–2.4)	1.3±0.5	1.3 (0.2–1.9)	p<0.001
PTX-3 (ng/ml) (4.hour)	3.3±4.2	6.5 (0.4–4.9)	11.3±4.6	12.9 (2.5–8.9)	7.7±2.8	7.6 (1.6–2.3)	1.5±0.6	1.5 (0.3–2.1)	p>0.05!!
IMA (IU/ml) (On admission)	18.6±12.2	13.7 (8.2–8.7)	16.5±5.2	15.6 (8.2–9.8)	21.2±16.6	15.3 (6.2–7.3)	9.9±1.8	9.7 (3.8–7.2)	p<0.001
IMA (IU/ml) (4.hour)	16.5±8.3	13.54 (2.1–9.3)	15.6±4.7	14.7 (8.1–8.8)	15.9±7.9	12.9 (0.7–7.5)	9.7±1.7	9.6 (3.6–7.1)	p<0.001

compared to other groups ( $p < 0.001$ ). Also, PTX 3 level was significantly different at admission and 4th hour in group II when compared to other groups ( $p < 0.05$ ). Statistical significance could not be shown for the differences between groups with respect to other biomarkers ( $p > 0.05$ ).

Comparisons between the groups in respect to biochemical markers are summarized in Table 3.

ROC analysis was performed for biomarkers. AUC value for troponin at admission was found to be 0.863 (95% CI: 0.771–0.954) ( $p < 0.05$ ). ROC analysis for troponin in the 4th hour revealed an AUC of 1.000 (95% CI: 1.000–1.000) ( $p < 0.05$ ).

ROC analysis for PTX 3 at admission revealed an AUC of 0.661 (95% CI: 0.523–0.800) ( $p < 0.05$ ). AUC for PTX 3 in the 4th hour was found to be 0.563 (95% CI: 0.418–0.708) ( $p > 0.05$ ).

ROC analysis revealed AUC for IMA at admission and in the 4th hour as 0.479 (95% CI: 0.317–0.641) ( $p > 0.05$ ) and 0.554 (95% CI: 0.388–0.720) ( $p > 0.05$ ), respectively.

## Discussion

According to our results, cTnI is the most sensitive test in ACS diagnosis on admission to ED. Our results also revealed while PTX 3 may be a useful diagnostic tool for ACS on admission, IMA alone cannot be used for diagnosis of ACS. Similarly, in the 4th hour, cTnI was found to be the most useful marker in ACS diagnosis, however, PTX 3 and IMA were found to be insufficient for the diagnosis of ACS.

It is well-known in the literature that cardiac troponins play a critical role in the diagnosis of ACS and AMI. Troponin testing is performed widely in patients attending the Emergency Department (ED) for rapid evaluation and exclusion of multiple potential diagnoses simultaneously (6). A rise and/or fall in cardiac troponin with at least one value above the 99th centile of the upper reference limit in the context of symptoms or clinical evidence of AMI has recently been defined as NSTEMI (7). Cardiac troponin

remains the gold standard biomarker for the diagnostic evaluation of AMI (2). Compatible with the literature, in our study, cTnI was found to be the best diagnostic tool for ACS either on admission or in the 4th hour.

It was reported that PTX 3 was elevated in the acute phase of AMI and had prognostic significance in those patients (8). PTX 3 was also reported to reflect different aspects of atherosclerosis-related inflammation, however, the role of PTX 3 in atherosclerosis is not clear (5). Even though the discovery of PTX 3 in the myocardial tissue and the characterization of its role has led to proposing PTX 3 as an early indicator of irreversible myocyte injury in ischemic heart disease (9), plasma level of PTX 3 was reported to increase in patients with AMI after about 7 h from the onset of symptoms, with a decrease in baseline levels after three days (10, 11). In contrary, our results interestingly showed that PTX 3 level was elevated on admission which may be interpreted that PTX 3 is more useful as an early indicator of ACS. The early predictor role of PTX3 may be related to fact that PTX 3 is associated with plaque vulnerability which is the initial phase of AMI (12). In some conditions, PTX 3 may be used in differential diagnosis of NSTEMI and USAP where cTnI is not readily available. However, further studies are needed in this field.

During ischemia, the N-terminus of albumin is altered, possibly as the result of hypoxia, acidosis, free-radical injury, and energy-dependent membrane disruption, decreasing its binding capacity for metals (13, 14). There are numerous reports in the literature proposing IMA as a promising marker in ACS diagnosis (3). Sinha et al. reported that the sensitivity of IMA for the diagnosis of ACS is significantly greater than that of ECG and cardiac troponin, used alone or combined (15). However, Aggarwal et al. reported that the IMA assay is a sensitive but not very specific marker for the early detection of myocardial ischemia. IMA levels were found to be significantly higher in patients with chest pain with myocardial ischemia as compared to control groups. They also found that IMA levels were positively correlated with other

conventional markers of AMI such as CK-MB and troponin levels. They concluded that the use of IMA alone was not adequate as a marker in diagnosis of ACS and should be used in combination with other markers in order to increase its specificity (16). In our study, IMA was found to be useful neither in ACS diagnosis on admission nor in the 4th hour.

Our results revealed that IMA level correlated with creatine level compatible with the fact that IMA level is affected by renal function. In end-stage renal disease (ESRD) patients, serum IMA levels were found to be high because of anemia, leading to generalized hypoxia. In another study, Türedi et al. reported that IMA levels of ESRD patients, both pre and post-hemodialysis, were significantly higher than those of the control group (17, 18). However, another result of our study, correlation of WBC with IMA and PTX needs to be clarified. Previously, Baydin et al. reported that in patients with carbon monoxide poisoning, when hypoxic condition is causing damage to oxygen dependent tissues such as heart and brain, PTX3 and IMA were not superior to cTnI (19). Their results are in compliance with ours that these two markers cannot be used as independent predictors of ACS.

## Conclusion

Superiority of troponins, particularly cTnI, in the diagnosis of ACS is still accepted. Serum PTX 3 and IMA measurements alone do not reflect cardiovascular status of patients. PTX 3 may differentiate patients with NSTEMI and USAP. However, cTnI has advantage of being readily available in most of the EDs.

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