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Pentraxin 3 genotyping in relation to serum levels of pentraxin 3 in patients with acute ST-segment elevation myocardial infarction

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ABSTRACT

Objective: The aim of the study was to investigate the association of serum Pentraxin 3 and genotyping with the risk of developing AMI and its severity.
Patients and methods: Fifty patients admitted to the coronary care unit presented with STEMI (acute ST segment myocardial infarction) at the Cardiology Department, Menoufia University Hospital in the period from October 2014 to April 2015 and another 20 subjects age- and gender-matched were taken as the control group. All patients and control groups were subjected to the following: Full history taking, complete clinical examination. ECG and echocardiography and Laboratory investigation including: estimation of lipid profile, urea and creatinine, CKMB, troponin I, serum pentraxin 3 and Genotyping of pentraxin 3 A/G SNP (rs2305619).
Results: The patients with myocardial infarction had significantly higher levels of pentraxin 3 than the controls. The cut-off values for PTX3 and troponin I were 4.35 ng/ml and 0.34 μg/l respectively. Pentraxin 3 showed the highest diagnostic accuracy of coronary artery disease (96%), with sensitivity (96%) and specificity (95%). The highest serum pentraxin 3 levels were in the AA mutant homozygous type.
Conclusion: PTX3 is one of the earliest biomarkers for detecting acute coronary syndrome. rs2305619 AA genotyping of the pentraxin 3 gene might be a candidate risk factor for development of coronary artery disease, presumably by increased pentraxin 3 levels.

1. Introduction

Cardiovascular disease is the leading cause of mortality in many countries, accounting for 16.7 million deaths each year [1,2]. Coronary artery disease (CAD) and cerebrovascular disease are the most common forms of cardiovascular disease, and they have severe consequences both for the individual person and society. Their underlying pathological process is atherosclerosis, a slowly progressing chronic disorder of large and medium-sized arteries [3].

For many years it was believed that atherosclerosis was merely passive accumulation of cholesterol in the vessel wall. Today, the picture is much more complex, with atherosclerosis being thought of as a chronic inflammatory disease [4].

Pentraxins form a superfamily of acute phase proteins with a distinctive multimeric organization. On the basis of the primary structure of the composing protomers, pentraxins are divided into two groups: short and long pentraxins. C-reactive protein (CRP) and serum amyloid P (SAP) components are typical short pentraxins and they represent the main acute phase reactants in humans and mice, respectively [5]. Pentraxin 3(PTX3) is the prototypic long pentraxin, a subfamily of pentraxins that are characterized by the presence of a long N-terminal domain, unrelated to other known proteins, associated with a C-terminal pentraxin-like domain. This last domain is 200 amino acids long and it contains the conserved 8 amino acid-long pentraxin signature [6].

In humans, PTX3 plasma levels predict 3-month mortality in patients with AMI [7] and increased tissue and plasma levels of PTX3 were also found in patients with non-rheumatic aortic valve stenosis, suggesting a role as a diagnostic and prognostic biomarker [8].

A number of evidences point to PTX3 as a useful marker of vascular integrity, including the observations that high levels of PTX3 are seen in the heart and vascular cells in response to inflammatory signals and ox-LDL and the protein is present in atherosclerotic lesions [9].

The aim of this study was to detect if there is an association of pentraxin 3 genotyping and pentraxin 3 plasma levels with the risk of developing and severity of AMI in Egyptian patients.

2. Subjects

This study was conducted on 70 subjects. They were categorized into Group 1 (patients): Composed of fifty patients with an established diagnosis of STEMI presented to the Cardiology Department, Menoufia University Hospital in the period from October 2014 to April 2015.

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Their diagnosis was based on clinical examination, laboratory tests, ECG and echocardiography. Quantitative evaluation of the severity of coronary artery stenosis by angiography was according to the standard criterion recommended by the American Heart Association [10]. Group 2 (control): Included 20 apparently healthy subjects serving as a control group.

Exclusion criteria include all patients who had acute non-ST segment elevation myocardial infarction (NSTEMI); valvular heart disease; heart failure; hepatic or renal dysfunction; evidence of active infective, or neoplastic conditions; chronic inflammatory diseases.

All patients and control groups were subjected to the following: Full history taking, complete clinical examination, ECG and echocardiography and laboratory investigation including: estimation of lipid profile, urea and creatinine, CKMB, troponin I, serum pentraxin 3 and genotyping of pentraxin 3 A/G SNP (rs2305619).

A written consent was obtained from each individual and the protocol was approved by the ethical committee of the Menoufia Faculty of Medicine and follows the Declaration of Helsinki.

3. Methods

5 ml of venous blood was collected from all subjects included in this study by venipuncture from the cubital vein, and was collected as follows: 2.5 ml was collected into EDTA containing tubes, for genotyping of the *pentraxin 3* gene. 2.5 ml was collected in another vacutainer tube (with no additives), centrifuged at 3000 rpm for 10 min then the sera were separated into several aliquots for colorimetric determination of serum urea [11] and creatinine [12]. Quantitative determination of total creatine kinase (CK) and CKMB levels in the serum using a commercial kit was supplied by Bio System Spain [13]. Determination of total cholesterol and triacylglycerides (TG) was done using colorimetric enzymatic method. HDLc was measured by the precipitation of chylomicrons, VLDL, and LDL by adding phosphotungstic acid and magnesium ions to the samples. Centrifugation leaves only the HDL in the supernatant, their cholesterol content is determined enzymatically [14]. LDLc was calculated if TG <400 mg/dl by the formula of Friedewald et al. [15]. Enzyme linked immunosorbant assay (ELISA) was used for the quantitative determination of serum troponin I [16] and pentraxin 3 [17].

3.1. Pentraxin 3 genotyping

Genomic DNA was extracted from whole blood using the Gene JET Whole Blood Genomic DNA Purification Mini Kit (Thermo Scientific, Vilnius, Lithuania).

Pentraxin 3 rs2305619 was genotyped using the TaqMan allelic discrimination assay technique that detects variants of a single nucleic acid sequence. The presence of two primer/probe pairs in each reaction allows genotyping of the two possible variants at the SNP site in a target template sequence. The actual quantity of the target sequence is not determined. The allelic discrimination assay classifies unknown samples as follows: [1] Homozygotes (samples with only allele 1 or allele 2). [2] Heterozygotes (samples with both allele 1 and allele 2).

Using the Maxima Probe qPCR Master Mix (2×), primers and probes were purchased from Applied Bio System. According to Sébastien et al. [18] the forward primer was 5′-CATCCCACTGAGGACCGTAAG-3′, and the reverse primer was 5′-GGTGGATATGTAGTCAGGGTTAGC-3′. Probes: allele G, 5′-FAM CTTTAACTGTTTCTCTGCTAACCCT TBHQ-3′, and allele A, 5′-VIC CCATCCCACTGAGGACCGTAAGTTC-BHQ-3′. The genotyping reaction mix was prepared by mixing 12.5 μl master mix, 1.25 of the genotyping assay mix (probe & primers) and 6.25 μl of DNAse-free water. For each unknown reaction, 5 μl (0.1 μg/μl) of genomic DNA template was added and for the negative control reaction, 5 μl of DNAse-free water was added.

The cycling parameters were set as follows: initial denaturation step at 95 °C for 10 min, 40 cycles of denaturation at 94 °C for 15 s, annealing/collection at 50 °C for 60 s, and extension at 72 °C for 2 min, and a final extension step at 72 °C for 3 min using 7500 Real-Time PCR System (Applied Bio System Co. Ltd., San Francisco Bay Area, USA). Then the results were analyzed as in Fig. 1. See Figs. 2 and 3

4. Statistical analysis

Student's t-test was used for comparison between groups of quantitative variables. Mann–Whitney test (U) was used as a test of significance for comparison between two groups not normally distributed having quantitative variables. Kruskal–Wallis test was used as a test of significance for comparison between more than two groups not normally distributed having quantitative variables. Chi-squared test (χ^2) was used to study the association between two qualitative variables. Fisher's exact test was used for 2 × 2 tables when the expected cell count of more than 25% of cases was less than 5. Receiver-operating characteristic (ROC) curve was used to determine cutoff points, sensitivity and specificity for quantitative variables of interest and 2 × 2 tables were used for the calculation of PPV, NPV and diagnostic accuracy. Spearman correlation coefficient test (r-test) is a test of significance used to study the correlation between nonparametric quantitative variables. Correlation coefficient test (r-test) results may be positive (+) correlation or negative (−) correlation. It is used to quantify the strength of the linear relationship between two variables. Odds ratio: describes the probability that people who are exposed to a certain factor will have a disease compared to people who are not exposed to the factor and obtained by regression analysis. P value of >0.05 was considered statistically insignificant. P value of ≤0.05 was considered statistically significant. P value of ≤0.001 was considered statistically highly significant.

5. Results

There is a significant statistical difference between the two studied groups regarding heart rate and ejection fraction, while non-significant difference as regards other clinical data, medical history, age and gender (Table 1). See Table 2

There is a significant difference among the two studied groups regarding total cholesterol, triglyceride, LDL, HDL, CK-MB, troponin I and serum pentraxin 3, while there was non significant difference regarding blood urea and serum creatinine (Table 3). There is a significant statistical difference as regards pentraxin 3 genotype distribution in comparing the two studied groups with increased frequency of the AA and AG genotypes and A allele in the patient group and increased GG genotype frequency in the control group. The results showed that the AG genotype of pentraxin 3 increases the risk of coronary artery disease by 5.14 fold and AA genotype increases the risk by 4.82 fold, while the A allele increases the same risk by 2.3 fold (Table 4).

The diagnostic accuracy of serum pentraxin 3 in the diagnosis of coronary artery disease is (96%), with sensitivity (96%), specificity (95%), positive predictive value (98%) and negative predictive value (90%) at the cutoff point of 4.35 IU/ml. The diagnostic accuracy of troponin I in the diagnosis of coronary artery disease is (80%), with sensitivity (82%), specificity (75%), positive predictive value (89%) and negative predictive value (63%) at the cutoff point of 0.34 IU/ml, while the diagnostic accuracy of combined serum pentraxin 3 and troponin I in the diagnosis of coronary artery disease is (82%), with sensitivity (95%), specificity (98%), positive predictive value (68%) and negative predictive value (86%) (Table 5).

There is a significant positive relationship between serum pentraxin 3 and age, LAD target vessel, % of occlusion and a significant negative relationship between serum pentraxin 3 levels and ejection fraction, while there is a non-significant relationship regarding other parameters (Table 6).

There is a significant positive correlation between serum pentraxin 3 and each of TG, LDL, CK-MB and troponin I, a significant negative

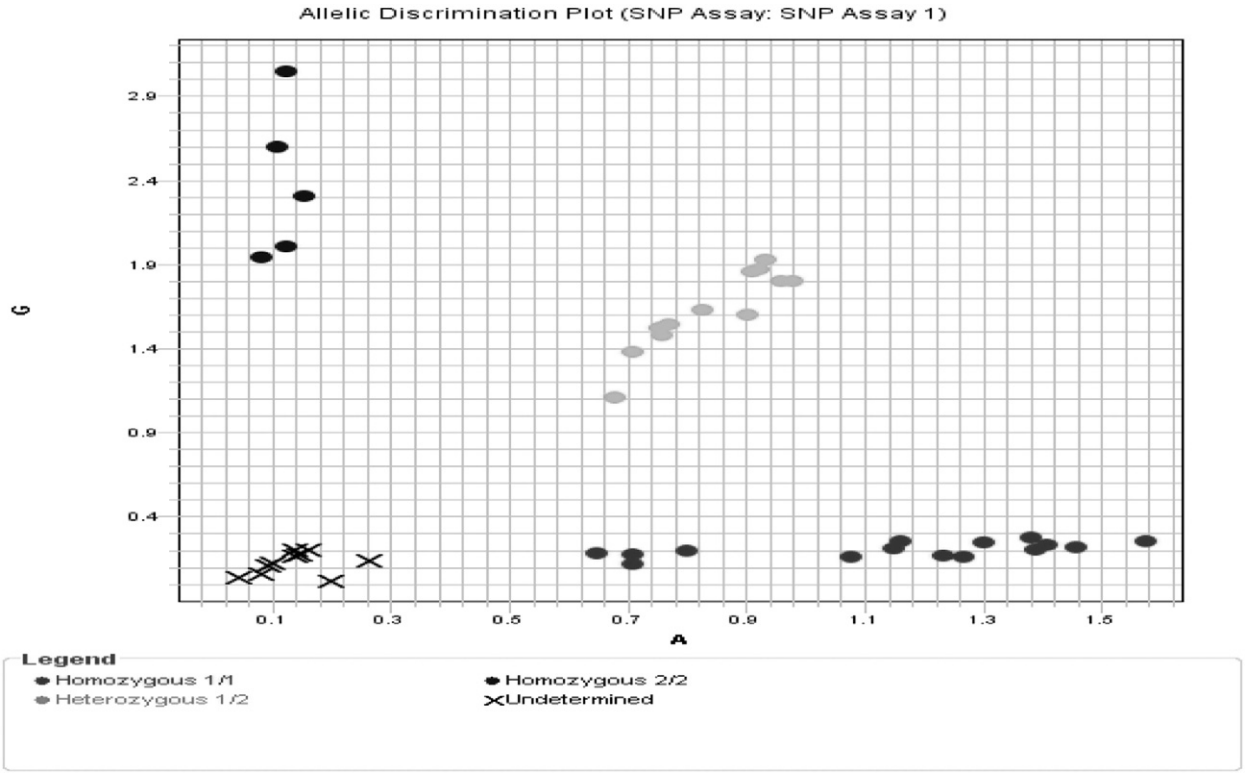

Fig. 1. Genotyping result: round black dots on the right lower region indicate (AA), gray dots on the centre indicate (AG) and black dots on the left upper region indicate (GG) genotyping of rs2305619 of pentraxin 3.

correlation between serum pentraxin 3 levels and HDL, while there is a non-significant relationship regarding other parameters (Table 7).

There is a significant statistical difference between the troponin I positive and negative cases at the samples taken before and after 2 h, while there was a non-significant statistical difference between the serum pentraxin 3 positive and negative cases at the samples taken before and after 2 h (Table 8).

There is a significant statistical difference between TC, TG, LDL and serum pentraxin 3 levels according to pentraxin 3 genotyping in the patient group, while there is no significant statistical difference regarding other parameters (Table 9).

Serum pentraxin 3 is the most significant independent risk factor followed by HDL, TG, pentraxin 3 AA genotypes, troponin I and total cholesterol, while LDL and CH-MB are not independent risk factors (Table 10).

6. Discussion

Inflammation plays a critical role in the development and progression of coronary heart disease (CHD), and increased local inflammation may induce plaque rupture, which has been acknowledged as the initial factor in acute coronary syndrome [19].

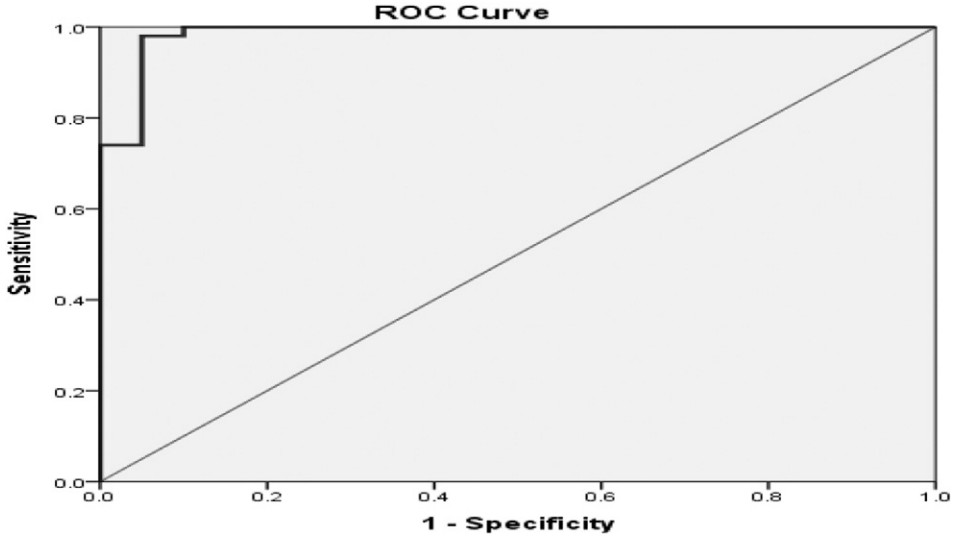

Fig. 2. ROC curve for detection of the best cutoff point of serum pentraxin 3 in cases of MI. The area under the curve was 0.986. There was a highly significant difference in the area under the curve (P value < 0.001) at 95% confidence interval = 0.96 to 1.00.

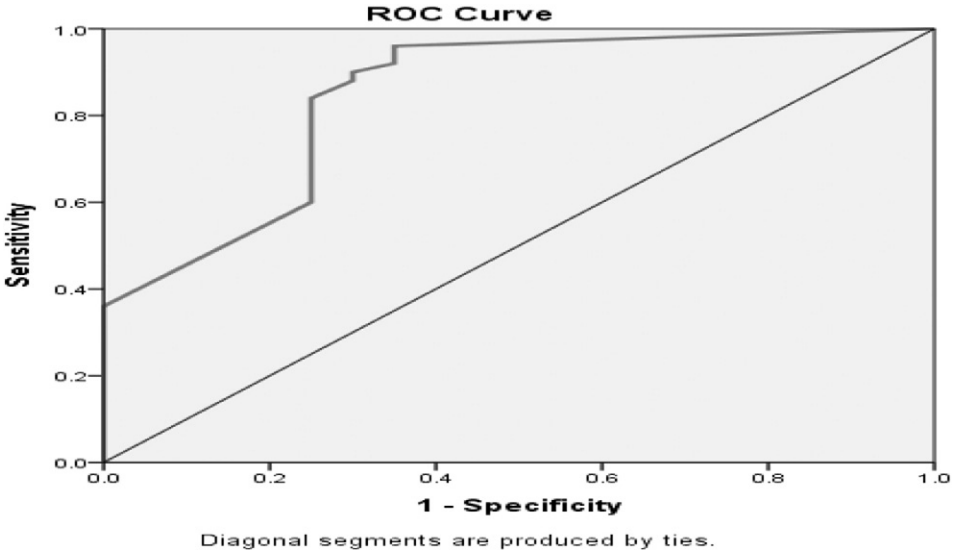

Fig. 3. ROC curve for detection of the best cutoff point of serum troponin I in cases of MI. The area under the curve was 0.846. There was a highly significant difference in the area under the curve (P value < 0.001) at 95% confidence interval = 0.739 to 0.952.

Table 1
Demographic characteristics, medical history and clinical data of the two studied groups.

Demographic characteristics	Studied groups				Test of significance	P value
	Controls (n = 20)		Cases (n = 50)			
Age (years)						
Mean ± SD	54.96 ± 6.61		55.10 ± 8.17		t-test = 0.07	>0.05
Range	42.00–65.00		40.00–66.00			
HR (B/M)						
Mean ± SD	91.92 ± 15.64		75.55 ± 11.57		4.23	<0.001
Range	50.00–115.00		60.00–100.00			
SBP (mm Hg)						
Mean ± SD	129.10 ± 18.42		124.50 ± 16.69		0.97	>0.05
Range	100.00–180.00		100.00–160.00			
DBP (mm Hg)						
Mean ± SD	84.70 ± 11.71		83.50 ± 10.39		0.39	>0.05
Range	60.00–110.00		70.00–100.00			
Ejection fraction						
Mean ± SD	52.86 ± 6.18		60.00 ± 3.66		5.97	<0.001
Range	40.00–65.00		52.00–65.00			
	No.	%	No.	%		
Sex						
Male	33	66.0	12	60.0	$\chi^2 = 0.22$	>0.05
Female	17	34.0	8	40.0		
Smoking						
Positive	20	40.0	8	40.0	0.00	>0.05
Negative	30	60.0	12	60.0		
DM						
Positive	27	54.0	11	55.0	0.006	>0.05
Negative	23	46.0	9	45.0		
HTN						
Positive	15	30.0	6	30.0	0.00	>0.05
Negative	35	70.0	14	70.0		
Dyslipidemia						
Positive	20	40.0	8	40.0	0.00	>0.05
Negative	30	60.0	12	60.0		
FH of CAD						
Positive	10	20.0	4	20.0	0.00*	>0.05
Negative	40	80.0	16	80.0		

χ^2 = Chi square test. * Fisher's exact test.

Although PTX3 is in the same family with CRP (acute phase protein), its expression pattern is more tissue specific, especially in light of the fact that it is expressed in cells of the atherosclerotic plaque itself, and reflects active atherosclerosis [20].

Pathological study of the human coronary artery showed that immunoreactivity for PTX3 was quite sparse in lipid-rich lesions in fibro atheroma and areas with intra-plaque hemorrhage containing abundant PTX3 [21].

The PTX3 gene encodes for the long pentraxin PTX3, a molecule involved in the inflammatory response and associated with cardio- and atheroprotective functions. Data obtained in different in vivo models showed that PTX3 is involved in modulating inflammation in AMI and atherosclerosis [22].

Moreover, it represents a useful diagnostic and prognostic marker in cardiovascular pathology [9].

Table 2
Characteristics of the patient groups regarding angiography, pain sampling intervals and types of treatments.

Studied parameters	No.	%
Target vessels		
LAD	17	34.0
LCX	7	14.0
RCA	10	20.0
DIAG	9	18.0
RAM	4	8.0
OM	3	6.0
Site of the lesion		
Proximal	27	54.0
Middle	18	36.0
Distal	5	10.0
Therapy		
Thrombolytics	30	60
PPCI	20	40
% of occlusion		
Mean ± SD	89.20 ± 9.76	
Range	70.00–100.00	
Pain-sampling interval (hours)		
Mean ± SD	4.38 ± 1.46	
Range	1.30–6.00	

LAD: left anterior descending branch; LCX: left circumflex branch; DIAG: diagonal branch; RCA: right coronary artery branch.

Table 3
Statistical comparison of laboratory investigation among the two studied groups.

Laboratory parameters	Studied groups		Test of significance	P value
	Cases (n = 50)	Controls (n = 20)		
Serum creatinine (mg/dl)				
Mean ± SD	0.98 ± 0.21	1.06 ± 0.19	t = 1.51	>0.05
Range	0.65–1.48	0.60–1.35		
Blood urea (mg/dl)				
Mean ± SD	34.08 ± 15.44	36.74 ± 11.06	U = 1.69	>0.05
Range	18.00–115.00	19.00–66.00		
TC (mg/dl)				
Mean ± SD	174.53 ± 36.75	154.86 ± 10.97	t = 3.42	<0.001
Range	107.00–264.80	133.50–175.00		
TG (mg/dl)				
Mean ± SD	133.84 ± 17.83	106.20 ± 10.60	t = 7.98	<0.001
Range	100.00–170.00	92.00–129.00		
LDL (mg/dl)				
Mean ± SD	107.53 ± 38.57	85.37 ± 11.28	U = 2.74	<0.01
Range	33.34–200.00	65.50–108.60		
HDL (mg/dl)				
Mean ± SD	38.52 ± 4.94	48.25 ± 3.27	t = 9.61	<0.001
Range	30.00–48.00	42.00–55.00		
CK-MB (IU/ml)				
Mean ± SD	35.10 ± 14.49	16.35 ± 5.27	U = 5.75	<0.001
Range	12.00–72.00	6.00–28.00		
Troponin I (μg/l)				
Mean ± SD	0.62 ± 0.28	0.18 ± 0.27	U = 4.56	<0.001
Range	0.02–1.07	0.01–0.62		
Serum pentraxin 3 (ng/ml)				
Mean ± SD	10.12 ± 3.64	2.52 ± 1.73	U = 6.12	<0.001
Range	3.80–15.90	0.70–6.90		

t: t-test; U: Mann–Whitney test.

This study examined the role of PTX3 genetic variations and serum pentraxin 3 level in the susceptibility to AMI and also the possible effect of the rs2305619 SNPs on serum PTX3 levels.

This study showed that there was a significant statistical difference between patients with myocardial infarction and the control group as regards lipid profile, CKMB, troponin I and serum pentraxin 3 levels. This was in agreement with the several studies [23,24,25] which stated that the coronary artery disease group had significantly higher PTX-3 levels than the control group. This can be explained by, PTX-3 binds and inactivates fibroblast growth factor-2, an angiogenic growth factor responsible for smooth muscle proliferation in atherosclerosis or may be part of a protective mechanism in vascular repair [26]. Very high levels of PTX-3 may indicate a more severe vascular disease state, explaining its ability to detect increased risks for adverse outcomes [27].

PTX3 is rapidly induced in mouse and rat models of MI and is present in atherosclerotic lesions, inflammatory cytokines rapidly induce high levels of PTX3 expression in the heart, most prominently in heart endothelial cells [20]. In vitro, this prototypic long pentraxin is induced in endothelial cells, smooth muscle cells, and mononuclear phagocytes by primary inflammatory cytokines (IL-1, tumor necrosis factor) and oxidized LDL [28].

Table 4
Comparison between the two studied groups regarding pentraxin 3 genotyping.

Genotyping	Studied groups				χ^2 test	P value	OR (95% CI)
	Cases (n = 50)		Controls (n = 20)				
	No.	%	No.	%			
Allele frequency							
G	42	42.0	25	62.5			
A	58	58.0	15	37.5	4.81	0.03 S	2.30 (1.08–4.89)
Genotype							
GG	7	14.0	9	45.0			Reference
AG	28	56.0	7	35.0	6.70	0.009 S	5.14 (1.42–18.67)
AA	15	30.0	4	20.0	4.61	0.03 S	4.82 (1.10–21.19)

Table 6
Relationship between serum pentraxin 3 level and clinical data among the studied cases.

Studied parameters	N	Serum pentraxin 3 level (ng/ml)	Test of significance	P value
		Mean ± SD		
Age (years)	50	r = −0.46	Spearman's rho	0.001
Sex				
Male	33	10.55 ± 3.93	U = 0.97	>0.05
Female	17	9.55 ± 3.00		
Smoking				
Smoker	20	10.49 ± 4.24	U = 0.47	>0.05
Non-smoker	30	10.02 ± 3.25		
DM				
Positive	27	10.67 ± 3.47	U = 0.95	>0.05
Negative	23	9.66 ± 3.84		
HTN				
Positive	15	11.11 ± 4.27	U = 1.17	>0.05
Negative	35	9.82 ± 3.33		
Dyslipidemia				
Positive	20	10.22 ± 3.55	U = 0.01	>0.05
Negative	30	10.20 ± 3.76		
FH of CAD				
Positive	10	11.90 ± 3.14	U = 1.64	>0.05
Negative	40	9.79 ± 3.67		
HR	50	r = 0.11	Spearman's rho	>0.05
SBP	50	r = −0.07	Spearman's rho	>0.05
DBP	50	r = 0.11	Spearman's rho	>0.05
EF	50	r = −0.56	Spearman's rho	<0.001
Target vessel				
LAD	17	13.78 ± 1.78	K = 36.95	<0.001*
LCX	7	6.93 ± 1.32		
RCA	10	11.36 ± 2.84		
Diag	9	7.59 ± 1.68		
RAM	4	8.25 ± 1.53		
OM	3	4.30 ± 0.56		
Site of culprit lesion				
Proximal	27	10.22 ± 3.94	K = 0.78	>0.05
Middle	18	9.83 ± 3.71		
Distal	5	11.48 ± 0.89		
% of occlusion	50	r = 0.66	Spearman's rho	0.001

K=Kruskal-Wallis Test. * Post Hoc test for target vessel show.

Table 5
Clinical performance of serum pentraxin 3 and troponin I in cases with acute ST-segment elevation myocardial infarction.

Cardiac marker	Optimal cutoff point	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	Diagnostic accuracy (95% CI)	DOR (95% CI)
Serum pentraxin 3 (ng/ml)	4.35 (ng/ml)	96% (85–99)	95% (73–99)	98% (88–99)	90% (68–98)	96% (87–99)	10.29 (2.75–38.46)
Troponin I (μg/l)	0.34 (μg/l)	82% (68–91)	75% (73–99)	89% (76–96)	63% (41–80)	80% (68–88)	2.38 (1.40–4.02)
Combined pentraxin & troponin	–	82% (68–91)	95% (73–100)	98% (86–100)	68% (48–83)	86% (75–93)	3.04 (1.77–5.21)

95% CI = 95% confidence interval; PPV = positive predictive value.
NPV = negative predictive value; DOR = diagnostic odds ratio.

Table 7
Correlation between serum pentraxin 3 level and laboratory parameters among the studied cases (n = 50).

Laboratory parameters	Serum pentraxin 3 (ng/ml)	
	r (correlation coefficient)	P value
Serum creatinine (mg/dl)	−0.02	>0.05
Blood urea (mg/dl)	−0.03	>0.05
TC (mg/dl)	0.14	>0.05
TG (mg/dl)	0.49	<0.001
LDL (mg/dl)	0.55	<0.01
HDL (mg/dl)	−0.46	<0.001
CK-MB (IU/ml)	0.51	<0.001
Troponin I (μg/l)	0.61	<0.001

r: Spearman correlation coefficient.

Table 8
Statistical comparison between cases with pain sample interval less than or equal to and more than 2 h as regards serum pentraxin 3 and troponin I levels.

Cardiac markers	Pain sampling interval among cases (n = 50)				Fisher's exact test	P value
	≤2 h (n = 8)		>2 h (n = 42)			
	No.	%	No.	%		
Serum Pentraxin 3						
Positive	8	100	40	95.2		
Negative	0	0.0	2	4.8	0.39	>0.05
Troponin I						
Positive	4	50.0	37	88.1		
Negative	4	50.0	5	11.9	4.28	<0.05

In this study a significant positive correlation of PTX3 concentrations has been found in association with age, but not with sex. This was in agreement with previous studies [29,30,31], while the study of Noriaki et al. [32] found no correlation between serum pentraxin 3 and age.

The results of this study showed that there was a linear relationship between PTX3 and, left anterior descending branch (LAD) target vessel affection and % of occlusion and a significant negative relationship between serum pentraxin 3 levels and ejection fraction.

Our results are matched with Hua et al. (2015) [33] who found that serum PTX3 was positively correlated with cardiac artery occlusion %. Also, other studies stated that PTX3 has the potential to be a more specific marker for the severity of CAD as measured by the Gensini score, than CRP [34,35,36].

The superior prognostic value of PTX-3 might result from a higher specificity of PTX-3 for localized inflammation and damage in the cardiovascular system [37]. A previous study has shown that PTX3 can predict 3-month mortality after AMI [7].

In the present study, the diagnostic accuracy of serum pentraxin 3 in the diagnosis of coronary artery disease is (96%), with sensitivity (96%), specificity (95%), positive predictive value (98%) and negative predictive value (90%) at the cutoff point of 4.35 IU/ml.

These results are in agreement with several studies which found that sensitivity and specificity of PTX3 for the diagnosis of ACS appear to be higher than other cardiac markers. The area under the curve (AUC) value for PTX3 was 0.920 [18,32]. It also matched with a study showing that sensitivity and specificity of PTX3 for the diagnosis of ACS appear to be higher than those of TnT with a sensitivity 98.5% and 94.4% and specificity 92.3% and 86.2 respectively [38].

PTX-3 seems to be a more specific and sensitive marker in cardiovascular diseases. Measurement of plasma PTX-3 represents a more effective means for early risk stratification compared to hs-CRP in patients with myocardial infarction [7] and chronic heart failure [39].

In the present study, serum pentraxin levels show more positive cases than troponin I with a pain sample interval less than 2 h. So, PTX-3 may be more valuable and beneficial in diagnosing ACS rather than other cardiac markers, particularly within the first two hours after the onset of chest pain.

This result also is in agreement with Peri et al. [29] who stated that in patients with acute myocardial infarction, PTX3 peaked in plasma sooner than other markers. The distribution of PTX3 plasma levels

Table 9
Comparison between different genotypes of pentraxin 3 among coronary artery disease patients regarding laboratory investigation.

Laboratory parameters	Genotyping of cases (n = 50)			Kruskal–Wallis test	P value
	GG (n = 7)	AG (n = 28)	AA (n = 15)		
Serum creatinine (mg/dl)					
Mean ± SD	1.10 ± 0.22	0.97 ± 0.23	0.93 ± 0.16	2.69	>0.05
Range	0.80–1.33	0.58–1.48	0.56–1.20		
Blood urea (mg/dl)					
Mean ± SD	36.04 ± 11.69	36.61 ± 18.78	28.45 ± 6.84	4.25	>0.05
Range	20.00–50.00	18.00–115.00	19.00–40.00		
TC (mg/dl)					
Mean ± SD	184.83 ± 26.85	161.86 ± 34.71	193.37 ± 36.61	6.48	<0.05
Range	158.67–220.92	107.00–232.14	138.27–264.80		
TG (mg/dl)					
Mean ± SD	134.57 ± 21.99	128.25 ± 15.99	143.93 ± 15.48	7.24	<0.05
Range	100.00–160.00	100.00–160.00	120.00–170.00		
LDL (mg/dl)					
Mean ± SD	92.09 ± 24.78	96.71 ± 36.35	130.24 ± 36.55	6.79	<0.05
Range	49.80–153.32	33.34–174.34	72.27–200.00		
HDL (mg/dl)					
Mean ± SD	39.00 ± 3.56	39.57 ± 5.23	36.33 ± 4.47	3.98	>0.05
Range	33.00–43.00	30.00–48.00	30.00–43.00		
CK-MB (IU/ml)					
Mean ± SD	37.43 ± 15.49	34.75 ± 14.58	34.67 ± 14.79	0.05	>0.05
Range	21.00–59.00	12.00–72.00	18.00–70.00		
Serum pentraxin 3 (ng/ml)					
Mean ± SD	8.54 ± 3.32	9.48 ± 3.46	12.03 ± 3.93	6.19	<0.05
Range	4.20–12.50	4.50–15.70	6.60–15.90		
Troponin I (μg/l)					
Mean ± SD	0.57 ± 0.46	0.35 ± 0.23	0.32 ± 0.15	0.44	>0.05
Range	0.11–1.07	0.11–0.97	0.11–0.55		

Table 10
Multivariate analysis of risk factors of coronary artery disease.

Risk factors	OR (95% CI)	P value
TC (mg/dl)	1.28 (0.89–1.83)	<0.05
TG (mg/dl)	3.25 (1.09–9.67)	<0.01
LDL (mg/dl)	0.76 (0.46–1.26)	>0.05
HDL (mg/dl)	3.63 (1.76–7.45)	<0.01
CK-MB (IU/ml)	0.66 (0.43–1.0)	>0.05
Troponin I (μg/l)	1.55 (0.95–2.51)	<0.05
Serum pentraxin 3 (ng/ml)	5.61 (2.53–11.87)	<0.01
Genotype (AA vs. [AG + GG])	2.02 (1.22–3.35)	<0.01

Odds ratio (OR) at 95% confidence intervals (CI).

among different genotyping of pentraxin 3 showed that the carriers of the AA genotype at the rs2305619 SNP had the higher amount of PTX3 in the blood compared to the AG and GG carriers, while GG genotyping is associated with the lower value of plasma PTX3.

These results are matched with the study of Barbati et al. [24] who stated that carriers for AA rs2305619 (vs.AG and GG genotypes) had higher PTX3 levels, while GG genotyping has been previously associated with a protective effect against pulmonary tuberculosis in West Africans [40] and *Pseudomonas aeruginosa* colonization in Italian cystic fibrosis patients [41].

The mechanism by which PTX3 SNPs affect PTX3 plasma levels is still to be clarified but possibly the rs2305619 genetic variant is in linkage with a regulatory region, perhaps the PTX3 promoter. So, it could affect the binding of a transcription factor to its consensus binding site, modifying the PTX3 expression level. It cannot be completely ruled out that PTX3 SNPs are related to high plasma levels of a functionally less active protein [24].

This study showed that serum pentraxin 3 is the most significant independent risk factor for coronary artery disease. This matched with Norata et al. [9] who found that when pentraxin 3 was measured with established markers including CRP, NT-proBNP and troponin-T, it emerged as the only independent predictor of three-month mortality.

7. Conclusion

It can be concluded that diagnostic sensitivity and specificity of PTX3 for ACS, in the early stage, appear to be superior to those of troponin I, thus, indicating that PTX3 is one of the useful biomarkers for detecting ACS, alone or in combination with other biomarkers including Tn I. PTX3 is likely to be an earlier systemic inflammatory marker than troponin I.

rs2305619 in the *pentraxin3* gene might be a candidate risk factor for the development of coronary artery disease, presumably by increasing pentraxin 3 levels. Individuals carrying the A/A or AG genotype and the A allele of *pentraxin3* rs2305619 have an increased risk of developing coronary artery disease, whereas individuals carrying the GG genotype and the G allele have a protective effect for developing coronary artery disease. Further study is needed to investigate the larger sample size and the role of other SNPs of the pentraxin 3 gene in coronary artery disease.

Disclosures

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