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The TNF-inducible Gene 14 Protein (Pentraxin-3): Is it an Early Marker of Acute Myocardial Infarction?

Gholamhossein Hassanshahi[1,2*], **Ali Esmaeili Nadimi**[3,4], **Nicholas G Kounis**[5] **and Hossein Khorramdelazad**[1,2]

[1]*Molecular Medicine Research Center, Research Institute of Basic Medical Sciences, Rafsanjan University of Medical Sciences, Rafsanjan, Iran*

[2]*Department of Immunology, School of Medicine, Rafsanjan University of Medical Sciences, Rafsanjan, Iran*

[3]*Non-Communicable Diseases Research Center, Rafsanjan University of Medical Sciences, Rafsanjan, Iran*

[4]*Department of Cardiology, School of Medicine, Rafsanjan University of Medical Sciences, Rafsanjan, Iran*

[5]*Department of Cardiology, School of Medicine, University of Patras, Patras, Greece*

[*]**Corresponding author:** Gholamhossein Hassanshahi, Molecular Medicine Research Center, Rafsanjan University of Medical Sciences, Rafsanjan, Iran, Tel: +98 9021913002; E-mail: ghassanshahi@gmail.com

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Abstract

Background: The aim of this investigation was to explore whether serum levels of TNF-inducible gene 14 protein (TSG-14) which also known as pentraxin-3 are increased early in patients suffering from acute myocardial infarction (AMI).

Method: In this study TSG-14 serum levels were measured in 160 patients suffering from AMI and 140 age-matched normal subjects. In the patients with AMI, the average time between the onset of symptoms and the blood sampling was 5.9 ± 2.4 h.

Result: We did not observe any significance alteration in the circulatory levels of TSG-14 between the AMI patients and normal control group (1.86 ± 0.98 ng/mL *vs.* 1.1 ± 0.46 ng/mL; P=0.23).

Conclusion: Based on our findings, it appears that assessment of serum TSG-14 cannot be a valuable early biomarker in AMI.

Keywords: TSG-14; AMI; Biomarker

Introduction

It is well-evidenced that atherosclerosis is a chronic inflammatory disorder related to the arterial layers identified by progressive infiltration of immune cells including T-lymphocytes, macrophages along with smooth muscle cells, extracellular matrix cells, and also accretion of lipids [1]. Evidence showed that inflammation is associated with rupture of atherosclerotic plaques, which is a key factor in the pathogenesis and progression of AMI [2]. Immunological and biochemical indicators of myocardial injury have been profitable in the examination and monitoring of acute coronary syndrome (ACS) patients [3]. TNF-inducible gene 14 protein (TSG-14) structurally is associated with the classic pentraxin; nonetheless, it completely differs from its family in other points [4]. Several studies showed that TSG-14 is secreted by various cells such as neutrophils, monocytes/macrophages, and activated endothelial cells following stimulation by inflammatory cytokines including tumor necrosis factor-α and interleukin-1 which significantly expressed in atherosclerotic plaques. Foreign molecules recognized by TSG-14 and attachment of these molecules with TSG-1 are leading to activation of the lectin and classical complement pathways [5]. Evidence showed that in patients with ACS there was a significant elevation in TSG-14 serum levels [6,7], and the assessment of this marker has been suggested as a novel cardiac biomarker in patients with AMI [8]. Therefore, the purpose of this investigation was to explore fluctuations of serum TSG-14 levels in patients with AMI.

Materials and Methods

Subjects

In this study, 160 patients with ST-segment elevation myocardial infarction (MI) admitted to Ali-Ebn-Abitaleb hospital and also 140 non-AMI subjects were enrolled. The written information and consent forms were signed by the participants and approved by Rafsanjan University of Medical Sciences ethical committee. Attendants with advanced liver or end-stage renal disease, overt heart failure (stage C), and a history of surgery or major trauma within the previous month were excluded from the study. In addition, pregnancy, having an inflammatory disease, identified or suspected systemic thrombotic diseases (except for cases of coronary artery disease) were other exclusion indicators of this study [2].

Blood analysis

All of the blood samples were collected at the time of hospital admission before administration of any medications. In order to obtain serum, blood samples were centrifuged (5 mins at 2000 g) maximum 30 mins after blood collection, and kept at 80°C until examination. The average time between the onset of symptoms and the blood collection was 5.9 ± 2.4 h in AMI patients. A high-sensitivity quantitative ELISA

kit (HK347-Hycult Biotech, USA) was employed to measure serum levels of TSG-14. The intra-assay and inter-assay coefficients of variation were 3.4% and 5.8%, respectively. In addition, the detection limit of TSG-14 ELISA assay kit was 0.04 ng/mL. All other biochemistry indexes were measured by a biochemistry auto-analyzer (Hitachi 912, Roche, Germany) using standard methods in our laboratory unit of the biochemistry department.

Statistical analysis

SPSS software package version 18 (Chicago, USA) was employed for data analysis. All the categorical variables and quantitative variables were presented as percentages and mean ± SEM, respectively. The Kolmogorov-Smirnov test was used for normality of the data. Continuous variables between AMI patients and non-AMI subjects were assessed by an unpaired t-test. Multiple logistic regression test was also used to explore the associations between serum levels of TSG-14 with the risk of AMI. Adjusted P values of less than 0.05 were considered to be of statistical significance.

Results

Anthropometric parameters and biochemical indexes of AMI patients and control group are presented in Table 1. The risk factors for coronary artery disease were the same for both groups involved in the study. None of the participants in the study had a history of MI or other cardiovascular diseases. Our results showed that the serum levels of TSG-14 did not differ between the AMI patients and control group (1.86 ± 0.98 ng/mL **vs.** 1.1 ± 0.46 ng/mL; P=0.23) (Figure 1). As predictable, in AMI patients, CK-MB and troponin-I concentrations were significantly elevated in comparison with the control subjects. Data obtained from the age-adjusted logistic regression model for both genders showed that there was no significant relationship between circulatory levels of TSG-14 with the risk of AMI (Men: odds ratio, 1.00; 95% CI, 0.91-1.12 and women: odds ratio, 1.00; 95% CI, 0.90-1.07). Relative risks did not change following adjustment for total cholesterol concentration, blood pressure, smoking, and age. In addition, our findings showed that serum levels of TSG-14 were not associated to the CK-MB (r=0.06, P=0.65) and troponin I levels (r=0.04, P=0.79).

	Control n=140	AMI Patients N=160	P value
Age (years)	58.6 ± 7.1	60.1 ± 14.6	0.42
Men/women (n)	36/24	38/22	0.08
BMI (kg/m^2)	24.6 ± 5.21	26.4 ± 3.54	0.02
Smoking status (%)			
Never	45.6	45.2	0.32
Past	40.1	41.4	0.51
Current	14.3	14.4	0.69
TSG-14 (ng/mL)	1.1 ± 0.46	1.86 ± 0.98	0.23
Total cholesterol (mg/dL)	174.7 ± 15.9	286.1 ± 24.3	0.001
Triglyceride (mg/dL)	138.2 ± 29.1	207 ± 38.6	0.001
HDL (mg/dL)	44 ± 12.6	36 ± 17.7	0.001
LDL (mg/dL)	96 ± 24.8	126 ± 29.1	0.01
hsCRP (mg/L)	1.1 ± 0.58	7.4 ± 2.04	0.001
CK-MB(ng/mL)	5.1 ± 1.24	271 ± 39.7	0.01
troponin I (ng/mL)	0.12 ± 0.02	1.21 ± 0.35	0.04
Systolic BP (mmHg)	115.2 ± 5.8	139.6 ± 7.6	0.01

Table 1: Anthropometric parameters and biochemical indexes between AMI patients and healthy controls; Results are presented as frequencies, mean ± SD, or median (interquartile range) as appropriate.

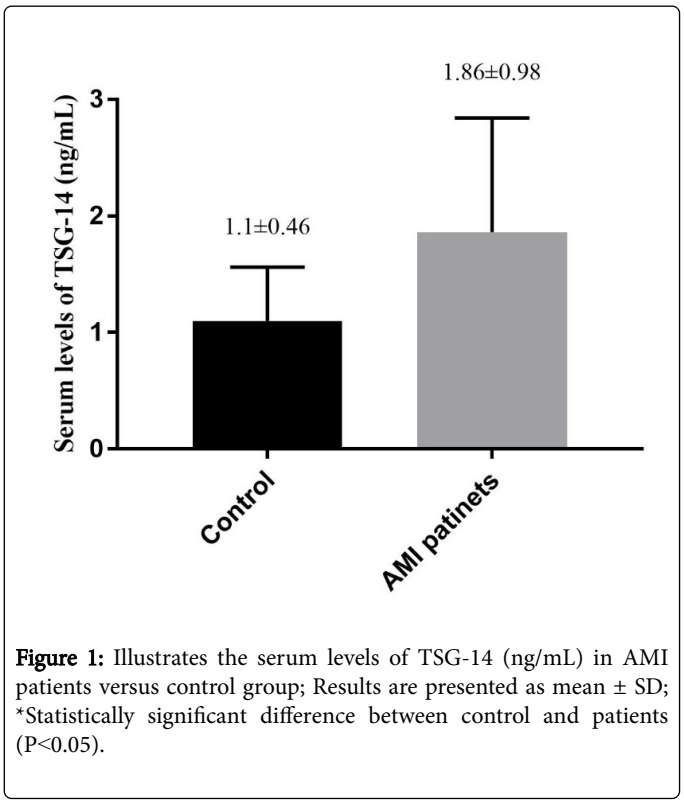

Figure 1: Illustrates the serum levels of TSG-14 (ng/mL) in AMI patients versus control group; Results are presented as mean ± SD; *Statistically significant difference between control and patients (P<0.05).

Discussion

Findings of this investigation showed that the serum level of TSG-14 could not be a potential early biomarker for AMI and also no significant correlation was observed between TSG-14 and troponin-I or CK-MB serum levels. Several previous studies reported that the circulatory levels of TSG-14 significantly elevated in patients with AMI [9]. Vengen et al. reported significantly higher levels of TSG-14 in youngest MI patients in comparison with controls. They suggested that TSG-14 and following complement-dependent inflammation are responsible for the development of cardiovascular disease [5]. A prognostic part of serum TSG-14 for short-term adverse cardiovascular events such as mortality in AMI was reported in recent investigations. For instance, Akgul et al. stated that acute ST-segment elevation myocardial infarction (STEMI) patients, there was a significant association between the serum level of TSG-14 and increased in-hospital cardiovascular mortality [10]. Altay et al. showed that TSG-14 is a novel and potential biomarker that may help to recognize high-risk AMI patients, who are potentially at risk of early

major adverse cardiovascular events including mortality in the long-term period [8]. However, the sample size in the mentioned study was lower than our work. It is notable that the lower limit of detection of used TSG-14 ELISA kit in our study was 0.04 ng/mL that was similar or less than different analytical kits and methods used in previous related studies [11,12]. Consistent with our study, Özer et al. showed that TSG-14 is not valuable biomarkers in the differential diagnosis and the determination of in-hospital mortality in ACS. In addition, the findings of the mentioned study confirmed that due to the differential diagnosis and the prediction of mortality, Troponin I and CK-MB are useful markers [13]. Barbati et al. in a study showed that polymorphisms of TSG-14 affecting plasma levels of TSG-14 and high circulatory levels of TSG-14 are not associated with the risk of AMI. They suggested that the TSG-14 concentration itself is unlikely to be even a modest causal factor for AMI. Findings of their study also confirmed that TSG-14 is a prognostic indicator after AMI [14]. In this study, the absence of a significant correlation may be due to sampling time, however, in Matsui et al. study patients were hospitalized within 24 h (mean of 7.5 h) after the onset of chest symptoms [6]. They reported that assessment of circulatory PTX3 levels may considerably surpass the early risk stratification of UA/NSTEMI patients. Furthermore, in a recent study concerning patients with diabetes mellitus type 2 (T2D), the number of diseased coronary artery vessels was positively correlated with TSG-14 and hemoglobin A1c (HbA1c), which might have clinical significance in assessing the severity of AMI in this kind of patients [15]. Expression and influence of TSG-14, HbA1c, and ApoA1/ApoB in the serum of patients with AMI combined with T2D [15].

Conclusion

In summary, our findings demonstrated that in AMI patients, TSG-14 serum concentrations could not be a valuable early biomarker. Further studies with larger sample size and more sensitive methods should be performed to explore the usefulness of TSG-14 circulatory levels as a biomarker in early diagnosis of AMI.

Compliance with Ethical Standards

Written informed consent was obtained from participants.

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Conflict of Interest

The authors declare that there is no conflict of interest regarding the publication of this article.

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