Serum gamma-glutamyltransferase and the burden of atherosclerosis in patients with acute coronary syndrome

Akut koroner sendromlu hastalarda serum gama-glutamiltransferaz düzeyi ve aterosklerozun yaygınlığı

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ABSTRACT

Objectives: We evaluated the relationship between serum gamma-glutamyltransferase (GGT) levels and the burden of atherosclerosis in patients with acute coronary syndrome (ACS).

Study design: This study involved 180 patients (139 male, 41 female; mean age 63±11 years) with the diagnosis of ACS (non-ST elevation myocardial infarction and unstable angina) who underwent coronary angiography on the first day after hospital admission. The burden of atherosclerosis was assessed by the number of involved vessels, and the Gensini and Syntax scores. Serum GGT levels were measured by enzymatic caloric test.

Results: Patients with high Syntax scores (≥33) were more frequently diabetic, hypertensive, and had higher GGT and creatinine levels compared to the patients with low Syntax scores (≤23). Similarly, patients with ≥3 diseased vessels were more frequently diabetic, hypertensive, and smokers. In addition, these patients were older and had higher serum glucose, urea and GGT levels. Correlation analysis revealed that the level of GGT was significantly associated with Gensini and Syntax scores, number of diseased vessels, and the number of critical lesions (r=0.378 p<0.001, r=0.301 p<0.001, r=0.159 p=0.036, r=0.355 p<0.001, respectively). Multivariate linear regression analysis demonstrated that increased GGT level was an independent risk factor for high Gensini and Syntax scores (p=0.029 and p=0.035, respectively), together with age (p=0.001 and p=0.002, respectively) and serum glucose levels (p=0.017 and p=0.012, respectively).

Conclusion: Serum GGT levels on admission are associated with increased burden of atherosclerosis in patients with ACS. This may account for the cardiovascular outcomes associated with increased GGT levels.

ÖZET

Amaç: Bu çalışmada, akut koroner sendromlu (AKS) hastalarda serum gama-glutamiltransferaz (GGT) düzeyi ile ateroskleroz yükü arasındaki ilişki araştırıldı.

Çalışma planı: Çalışmaya AKS (ST yükselmesi olmayan miyokart enfarktüsü veya kararsız anjina pektoris) tanısı ile kliniğe başvuran ve kabul edildikten sonraki ilk gün içinde koroner anjiyografi yapılan 180 hasta (139 erkek, 41 kadın; ort. yaş 63±11 yıl) alındı. Ateroskleroz yükü tutulan damar sayısı, Gensini skoru ve Syntax skoru ile değerlendirildi. Serum GGT düzeyi enzimatik kalorimetrik test ile ölçüldü.

Bulgular: Yüksek Syntax skoru olan hastalarda (≥33), düşük Syntax skoru (≤22) olan grup ile karşılaştırıldığında diyabetli ve hipertansiyonlu hasta oranı, serum GGT ve kreatinin düzeyleri daha yüksek bulundu. Benzer şekilde, ≥3 damar hastalığı olanlarda diyabetli, hipertansiyonlu ve sigara içen hasta oranı ile yaş, serum glukoz, üre ve GGT düzeyleri daha yüksekti. Korelasyon analizinde serum GGT düzeyleri, Gensini ve Syntax skorları ile, hasta damar sayısı ve kritik lezyon sayısı ile anlamlı ilişkili bulundu (sırasıyla, r=0.378 p<0.001, r=0.301 p<0.001, r=0.159 p=0.036, r=0.355 p<0.001). Çok değişkenli linear regresyon analizi, yüksek GGT düzeyinin yaş (sırasıyla, p=0.001 ve p=0.002) ve glukoz (sırasıyla, p=0.017 ve p=0.012) düzeyi ile birlikte Gensini ve Syntax skorları için (sırasıyla, p=0.029 ve p=0.035) bağımsız bir risk faktörü olduğunu gösterdi.

Sonuç: Akut koroner sendromlu hastalarda hastaneye yatış sırasında ölçülen serum GGT düzeyleri, aterosklerozun yaygınlığı ile ilişkilidir ve GGT yüksekliği ile birlikte görülen kardiyovasküler sonuçları açıklayabilir.

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Coronary artery disease (CAD) is the most common cause of mortality around the world.[1-3] Several risk factors have been defined as predictors of coronary atherosclerosis.[2-5] Previous reports demonstrated that serum gamma-glutamyltransferase (GGT) is an independent risk factor for the development of CAD and the morbidity and mortality associated with cardiovascular disease.[6-8] GGT activity has been observed in coronary atherosclerotic plaques.[9] In addition, serum GGT is an independent risk factor for diabetes mellitus, stroke and hypertension.[10,11]

The burden of atherosclerosis is strongly associated with cardiovascular prognosis in patients with acute coronary syndrome (ACS).[12] Therefore, prediction and diagnosis of the burden of atherosclerosis is critical in clinical practice. The aim of the current study was to evaluate the relationship between serum GGT and the burden of atherosclerosis in patients with ACS.

PATIENTS AND METHODS

Patients

The study involved 180 patients admitted to the hospital with ACS and who underwent coronary angiography. Patients with a history of prior myocardial infarction (MI), history of/detected renal disease, cerebrovascular event, peripheral arterial disease, percutaneous coronary intervention, or coronary bypass surgery were excluded. Other exclusion criteria were alcohol consumption and possible liver dysfunction defined as aspartate-aminotransferase (AST) or alanine-aminotransferase (ALT) levels >50 U/L.

Two study groups were established based on the diagnostic criteria of CAD: non-ST-segment elevation MI (non-STEMI) and unstable angina pectoris (USAP). Informed consent was obtained from all patients. The study was approved by our local ethical committee. All demographic and clinical data were collected prospectively.

Laboratory analysis

Fasting blood samples were drawn for the measurement of blood glucose, plasma total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, and plasma triglycerides (Thermo Scientific Konelab PRIME 60 Clinical Chemistry Analyzer, Helsinki, Finland) in all cases. Serum GGT levels were measured at 37ºC by enzymatic calorimetric test using a Roche/Hitachi analyzer (Mannheim, Germany).[7]

Abbreviations:

ACS	*Acute coronary syndrome*
BUN	*Blood urea nitrogen*
CAD	*Coronary artery disease*
GGT	*Gamma-glutamyltransferase*
MI	*Myocardial infarction*
USAP	*Unstable angina pectoris*

Coronary angiography

Quantitative coronary angiography was performed by two experienced interventional cardiologists who had no knowledge of the study design or the patient group designations. Gensini and Syntax scores were used to evaluate the grading and complexity of CAD.[13,14] For the Gensini score, the most severe stenosis in each of eight coronary segments (left anterior descending artery, main diagonal branch, first septal perforator, left circumflex artery, obtuse marginal and posterolateral vessels, right coronary artery, and main descending branch) was graded from 1 to 4 (1-49% lumen diameter reduction: 1 point, 50-74% stenosis: 2 points, 75-99% stenosis: 3 points, 100% occlusion: 4 points) for a total score between 0 and 32. Syntax score was calculated with Syntax score calculator 2.1 (www.syntaxscore.com). The Syntax score was classified as tertiles as follows: low Syntax score (≤22), intermediate Syntax score (23-32), and high Syntax score (≥33). The number of diseased vessel with >50% luminal stenosis was scored from 1 to 3 or more diseased vessels. Coronary stenotic lesions with >50% luminal stenosis were defined as critical lesions and vessels with <50% luminal stenosis were defined as non-critical lesions.

Statistical analysis

All analyses were performed using SPSS for Windows 16.0 (version 16.0, SPSS, Chicago, Illinois, USA). Quantitative variables were expressed as mean value ± SD for parametric variables, and median and minimum-maximum levels for non-parametric variables. Continuous variables were analyzed for normal distribution using the Kolmogorov-Smirnov test and analyzed for homogeneity using the Levene tests. Comparisons of parametric values among groups were performed by One-Way ANOVA. Comparisons of non-parametric values among groups were performed by the Kruskal Wallis test. Tukey HSD (for parametric variables) and Bonferroni adjustment Mann-Whitney U-test (for non-parametric variables) were used as a post hoc test for multiple comparisons between the groups.

The Pearson test was used for correlation of parametric variables and the Spearman test was used for non-parametric variables. Multivariate linear regression analysis was performed to evaluate the effects of the variables on the Gensini score and Syntax score. A two-tailed $p<0.05$ was considered significant.

RESULTS

Relationships between Syntax score and clinical and laboratory findings are shown in Table 1. Compared to the low Syntax group, age and glucose levels were higher and hemoglobin levels were lower in intermediate Syntax group. In addition, there were more diabetic and hypertensive patients and fewer smoking patients in the intermediate Syntax score group. Compared to the low Syntax score group, levels of GGT and creatinine were higher in high Syntax score group. Finally, the number of diabetic and hypertensive patients was greater in the high Syntax score group (Table 1).

Baseline clinical characteristics of the study population according to the angiographic findings are shown in Table 2. One, two, and three or more diseased vessels were detected in 46 (25.6%), 52 (28.9%), and 82 (45.6%) patients, respectively. Age and serum GGT, serum glucose, and blood urea nitrogen (BUN) levels were increased in patients with two and three or more diseased vessels compared to patients with one diseased vessel (Table 2). Additionally, the number of patients with diabetes, hyperten-

Table 1. Relation between Syntax score and clinical and laboratory findings

	Low Syntax score (n=119)			Intermediate Syntax score (n=39)			High Syntax score (n=22)			*p*
	n	%	Mean±SD	n	%	Mean±SD	n	%	Mean±SD	
Age (years)			61±12			66±7			65±8	**0.015**[a]
Gender (male)	93	78.2		25	64.1		21	95.5		0.018
Smoking	69	58.0		14	35.9		15	68.2		**0.021**[a]
Diabetes	4	3.4		8	20.5		5	22.7		**<0.001**[a,b]
Hypertension	5	4.2		10	25.6		6	27.3		**<0.001**[a,b]
Systolic BP (mmHg)			112.7±11.5			112.6±15.3			117.9±12.6	0.399
Diastolic BP (mmHg)			70.0±10.1			72.6±13.9			77.0±12.8	0.123
GGT (U/L)			26.7±17.0			31.3±17.2			35.5±17.3	**0.016**[b]
AST (U/L)			27.3±8.3			27.2±10.3			28.5±6.5	0.907
ALT (U/L)			23.4±10.0			22.1±9.5			25.9±8.0	0.452
Total protein (g/dl)			6.5±0.6			6.7±0.6			6.4±0.6	0.249
Albumin (g/dl)			3.7±0.4			3.6±0.4			3.7±0.4	0.960
WBC (cell/mm^{3}x10^5)			9.9±3.2			10.2±2.7			9.1±2.5	0.441
Hemoglobin (g/dl)			14.3±1.9			13.3±2.3			14.4±1.5	**0.019**[a]
Glucose (mg/dl)	108 (55-435)			150 (62-463)			138 (73-372)			**0.001**[a]
BUN (mg/dl)			17.8±5.9			20.1±7.0			19.8±6.9	0.089
Creatinine (mg/dl)			0.9±0.2			0.9±0.2			1.0±0.2	**0.058**[b]
Total cholesterol (mg/dl)	183.9 (77-335)			181.1 (119-295)			178.5 (104-258)			0.828
LDL-C (mg/dl)	119.3 (25-259)			114.5 (39-194)			119.2 (65-183)			0.725
HDL-C (mg/dl)			36.4±10.3			37.4±10.5			33.7±7.6	0.395
Triglycerides (mg/dl)	138 (42-360)			143 (41-342)			116 (35-314)			0.450
USAP	47	39.5		16	41.0		8	36.4		0.939
Non-STEMI	72	60.5		23	59.0		14	63.6		0.939

[a]Significant difference between low and intermediate Syntax scores; [b]Significant difference between low and high Syntax scores; BP: Blood pressure; GGT: Gamma-glutamyltransferase; AST: Aspartate-aminotransferase; ALT: Alanine-aminotransferase; WBC: White blood cell; BUN: Blood urea nitrogen; LDL-C: Low density lipoprotein cholesterol; HDL-C: High density lipoprotein cholesterol; USAP: Unstable angina pectoris; STEMI: ST-elevation myocardial infarction.

Table 2. Baseline clinical characteristics of the study population according to the angiographic findings

	1 vessel (n=46)			2 vessels (n=52)			≥3 vessels (n=82)			*p*
	n	%	Mean±SD	n	%	Mean±SD	n	%	Mean±SD	
AGGT (U/L)			19.3±10.5			27.7±14.0			34.7±20.4	**<0.001**[b]
Age (years)			58±13			62±10			65±9	**0.003**[b]
Gender (male)	38	82.6		43	82.7		58	70.7		0.165
Smoking	32	69.6		31	59.6		35	42.7		**0.009**[b]
Diabetes	1	2.2		2	3.8		14	17.1		**0.006**b
Hypertension	1	2.2		4	7.7		16	19.5		**0.008**[b]
Systolic BP (mmHg)			111.9±10.8			114.6±12.1			114.2±13.9	0.718
Diastolic BP (mmHg)			70.1±9.6			70.4±11.2			73.5±12.9	0.456
Hemoglobin (g/dl)			14.2±2.0			14.3±1.8			13.8±2.1	0.416
WBC (cell/mm^{3}x105)			9.3±3.4			10.2±2.6			9.9±3.0	0.335
Glucose (mg/dl)	102 (58-318)			108 (57-239)			140 (55-463)			**0.001**[b]
BUN (mg/dl)			16.3±5.1			18.3±5.8			19.9±7.0	**0.009**[b]
Creatinine (mg/dl)			0.9±0.2			0.9±0.2			1.0±0.2	0.062
Total cholesterol (mg/dl)			176.7±31.2			191.0±45.6			180.7±44.8	0.209
LDL-C (mg/dl)			114.1±26.0			125.5±38.0			115.8±38.1	0.203
HDL-C (mg/dl)			36.5±10.8			36.2±11.8			36.3±9.3	0.987
Triglycerides (mg/dl)	134.2 (42-347)			133.9 (41-360)			141.0 (35-342)			0.852
Total protein (g/dl)			6.5±0.5			6.4±0.6			6.6±0.6	0.162
Albumin (g/dl)			3.7±0.4			3.7±0.4			3.6±0.4	0.700
AST (U/L)			26.4±9.4			27.1±7.6			28.5±8.4	0.527
ALT (U/L)			22.4±9.1			22.6±9.5			24.6±10.3	0.393

[a]Significant difference between 1 and 2 vessel disease; [b]Significant difference between 1 and 3 or more vessel disease. GGT: Gamma-glutamyltransferase; BP: Blood pressure; WBC: White blood cell; BUN: Blood urea nitrogen; LDL-C: Low density lipoprotein cholesterol; HDL-C: High density lipoprotein cholesterol; AST: Aspartate-aminotransferase; ALT: Alanine-aminotransferase.

sion, and smoking history was among the patients with multivessel disease.

Correlation analysis revealed that the level of GGT was associated with Gensini and Syntax scores (r=0.378, p<0.001 and r=0.301, p<0.001, respectively) (Figure 1), number of diseased vessel (r=0.355 p<0.001) (Figure 2), and number of critical lesions (for >70%, r=0.159 and p=0.036). Gensini score was associated with serum levels of GGT (r=0.378, p<0.001), BUN (r=0.167, p=0.028), creatinine (r=0.266, p<0.001), glucose (r=0.234, p=0.002) and age (r=0.208, p=0.006). Syntax score was significantly correlated with GGT (r=0.301, p<0.001), age (r=0.231, p=0.002), creatinine (r=0.195, p=0.009), diastolic blood pressure (r=0.263, p=0.013), BUN (r=0.213, p=0.004), and glucose (r=0.307, p<0.001).

Multivariate linear regression analysis demonstrated that increased GGT level was an independent risk factor for Gensini and Syntax scores (β=0.244, p=0.029 and β=0.227, p=0.035, respectively), together with age (p=0.001 and, p=0.002, respectively) and glucose (p=0.017 and p=0.012, respectively) (Table 3).

DISCUSSION

We examined the level of serum GGT in patients with ACS to estimate the burden of atherosclerosis. Our findings indicate that high levels of GGT were associated with burden of atherosclerosis in patients with ACS.

To date, no studies were found that focus on an association between serum GGT activity and burden of atherosclerosis in patients with ACS. The results of studies in patients with CAD who underwent angiog-

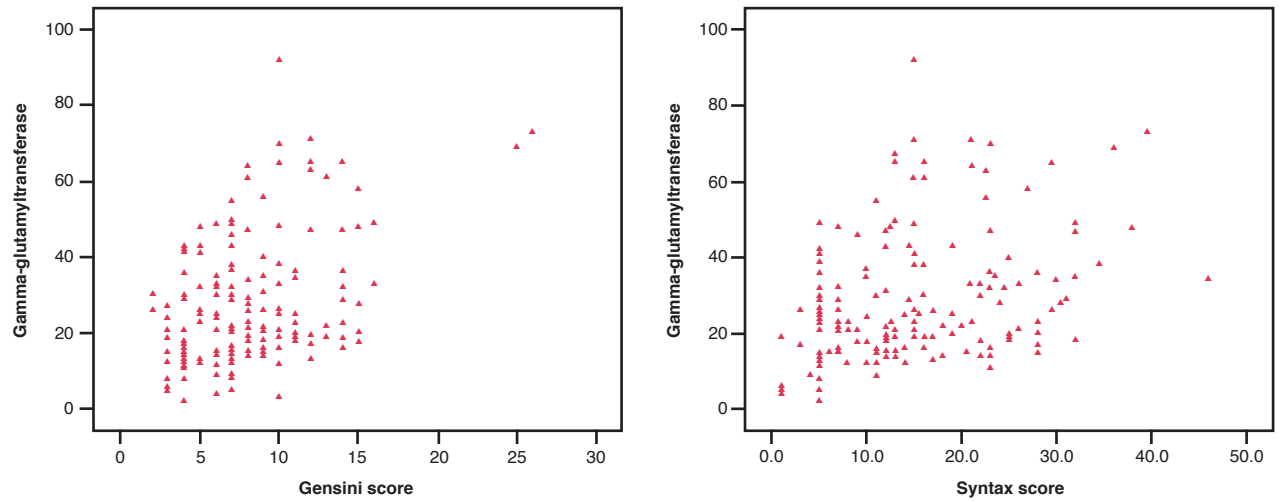

Figure 1. Graph of relation between levels of gamma-glutamyltransferase and Gensini and Syntax Scores.

raphy were controversial. Recently, Aksakal et al.[15] have reported that baseline serum GGT activity was independently associated with the complexity of the coronary lesions and all-cause mortality rate throughout long-term follow-up in patients with stable angina pectoris. Açikel et al.[16] found a significant relationship between serum GGT levels and CAD extent and severity assessed by Gensini scoring in patients who underwent coronary angiography, whereas Demircan et al.[17] observed no correlation between the number of affected vessels and GGT levels.

Elevated serum GGT concentration is an independent cardiac risk factor and predicts cardiovascular events, non-fatal MI, and cardiac mortality in unselected populations, in patients with history of MI, and in patients with ACS after adjusting for other known CAD risk factors as well as alcohol consumption.[6-8,18,19] In patients with stable CAD, serum GGT was associated with prognosis independent of a variety of established risk markers.[20] The underlying mechanisms linking GGT and cardiovascular mortality have not yet been clearly demonstrated. We suggested that high GGT levels were associated with burden of atherosclerosis and this may explain the cardiovascular outcomes associated with increased GGT levels.

Serum GGT is a marker of alcohol intake but may also reflect oxidative stress and nonalcoholic fatty liver disease.[21-23] Serum GGT catalyzes the first step in the degradation of extracellular antioxidant glutathione, allowing for precursor amino acids to be re-utilized for intracellular glutathione synthesis.[23] It has been shown that the degradation of glutathione can play a pro-oxidant role in selected conditions, as well as production of reactive oxygen species.[24] Higher serum GGT was associated with both inflammation and oxidative stress, both of which are proposed as key mechanisms of atherosclerosis.[10] Specific pathogenetic mechanisms (from inflammation to lipid accumulation and oxidation within the plaque) likely contribute to the potential mechanism in atherosclerosis and plaque destabilization.[21] Serum GGT can trigger the oxidative stress within plaque and can contribute to the vulnerability and evolution of the plaques.[21]

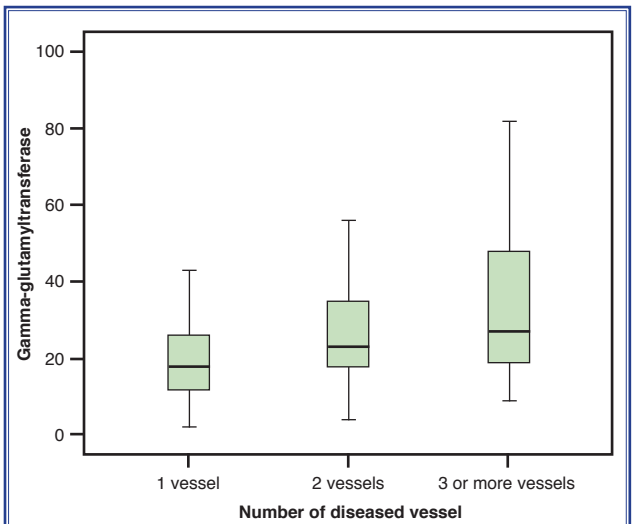

Figure 2. Graph of relation between levels of gamma-glutamyltransferase and number of diseased vessel.

Table 3. Multivariate analysis of determinants of Syntax and Gensini scores

	Gensini score			Syntax score		
Variables	β	*p*	Std. Error	β	*p*	Std. Error
Age	0.388	0.001	0.03	0.350	0.002	0.08
Gender	0.024	0.840	1.30	0.048	0.679	3.33
Hypertension	0.152	0.149	3.32	0.090	0.386	8.47
Smoking	0.024	0.833	0.87	-0.104	0.358	2.18
Dastolic BP	-0.008	0.942	0.03	0.138	0.189	0.08
GGT	0.244	0.029	0.03	0.227	0.035	0.07
Glucose	0.242	0.017	0.02	0.252	0.012	0.06
BUN	-0.038	0.745	0.08	-0.036	0.754	0.20
Creatinine	0.249	0.047	2.02	0.129	0.290	5.13

[a]Significant difference between 1 and 2 vessel disease; [b]Significant difference between 1 and 3 or more vessel disease. GGT: Gamma-glutamyltransferase; BP: Blood pressure; WBC: White blood cell; BUN: Blood urea nitrogen; LDL-C: Low density lipoprotein cholesterol; HDL-C: High density lipoprotein cholesterol; AST: Aspartate-aminotransferase; ALT: Alanine-aminotransferase.

Although the physiopathogenesis of the association between elevated GGT and burden of atherosclerosis is not completely understood, multiple mechanisms may be involved. Firstly, as we know, inflammatory process plays a key role in atherosclerosis, and serum GGT activity can serve as a proinflammatory protein in atherosclerosis.[25,26] Secondly, serum GGT can trigger progression and rupture of atherosclerotic plaques via LDL cholesterol oxidation.[21] Finally, serum GGT levels were positively associated with cardiac risk factors, which contribute to atherosclerotic processes, such as hypertension, diabetes, and metabolic syndrome.[27,28] In our study, patients with high GGT had high Gensini and Syntax scores and had greater numbers of critical lesions. Therefore, elevated serum GGT may indicate that patients with ACS had severe CAD and had a higher risk of acute coronary events due to increased burden of atherosclerosis. High levels of GGT can be used for predicting of high-risk patients.

Previous reports showed that there is a close relationship between serum GGT levels and other prognostic factors, such as hypertension, metabolic syndrome, diabetes, dyslipidemia, and smoking.[27-29] But we do not have clear information about the association between GGT and known ischemic heart disease risk factors. In our study, high levels of serum GGT were associated with hypertension (p=0.001) and diabetes (p=0.016). Of note is that our study had sufficient numbers of diabetic and hypertensive patients to assess the impact of diabetes on burden of atherosclerosis.

Limitations

First, the assessment of coronary angiographic findings was limited to visual interpretation and angiography is a technique that detects only major coronary arterial lesions. Second, no information was available regarding the severity or duration of hypertension and other cardiovascular disease risk factors. We also have no data available for medication use. Third, the small sample size is the most important limitation of the present study. However, our population contains homogeneous unselected ACS patients submitted to coronary angiography, which mirrors a real world scenario. Fourth, this study was not a follow-up study. Fifth, we did not evaluate an association between serum GGT and well-known risk scores (eg. GRACE).

In conclusion, high levels of serum GGT on admission were associated with burden of atherosclerosis in patients with ACS. As serum GGT is a cost effective and simple vascular risk marker, its routine measurement on admission may be helpful in determining high-risk patients in clinical practice.

Conflict-of-interest issues regarding the authorship or article: None declared

REFERENCES

1. Kaya MG, Uyarel H, Akpek M, Kalay N, Ergelen M, Ayhan E, et al. Prognostic value of uric acid in patients with ST-elevated myocardial infarction undergoing primary coronary

intervention. Am J Cardiol 2012;109:486-91. [CrossRef]
2. Hansson GK. Inflammation, atherosclerosis, and coronary artery disease. N Engl J Med 2005;352:1685-95. [CrossRef]
3. Goldberg RJ, Glatfelter K, Burbank-Schmidt E, Lessard D, Gore JM. Trends in community mortality due to coronary heart disease. Am Heart J 2006;151:501-7. [CrossRef]
4. Duran M, Kalay N, Akpek M, Orscelik O, Elcik D, Ocak A, et al. High levels of serum uric acid predict severity of coronary artery disease in patients with acute coronary syndrome. Angiology 2012;63:448-52. [CrossRef]
5. Libby P, Theroux P. Pathophysiology of coronary artery disease. Circulation 2005;111:3481-8. [CrossRef]
6. Emdin M, Passino C, Michelassi C, Titta F, L'abbate A, Donato L, et al. Prognostic value of serum gamma-glutamyl transferase activity after myocardial infarction. Eur Heart J 2001;22:1802-7. [CrossRef]
7. Ruttmann E, Brant LJ, Concin H, Diem G, Rapp K, Ulmer H; Vorarlberg Health Monitoring and Promotion Program Study Group. Gamma-glutamyltransferase as a risk factor for cardiovascular disease mortality: an epidemiological investigation in a cohort of 163,944 Austrian adults. Circulation 2005;112:2130-7. [CrossRef]
8. Wannamethee G, Ebrahim S, Shaper AG. Gamma-glutamyltransferase: determinants and association with mortality from ischemic heart disease and all causes. Am J Epidemiol 1995;142:699-708.
9. Paolicchi A, Emdin M, Ghliozeni E, Ciancia E, Passino C, Popoff G, et al. Images in cardiovascular medicine. Human atherosclerotic plaques contain gamma-glutamyl transpeptidase enzyme activity. Circulation 2004;109:1440. [CrossRef]
10. Lee DH, Jacobs DR Jr, Gross M, Kiefe CI, Roseman J, Lewis CE, et al. Gamma-glutamyltransferase is a predictor of incident diabetes and hypertension: the Coronary Artery Risk Development in Young Adults (CARDIA) Study. Clin Chem 2003;49:1358-66. [CrossRef]
11. Jousilahti P, Rastenyte D, Tuomilehto J. Serum gamma-glutamyl transferase, self-reported alcohol drinking, and the risk of stroke. Stroke 2000;31:1851-5. [CrossRef]
12. Huang G, Zhao JL, Du H, Lan XB, Yin YH. Coronary score adds prognostic information for patients with acute coronary syndrome. Circ J 2010;74:490-5. [CrossRef]
13. Gensini GG. A more meaningful scoring system for determining the severity of coronary heart disease. Am J Cardiol 1983;51:606. [CrossRef]
14. Serruys PW, Onuma Y, Garg S, Sarno G, van den Brand M, Kappetein AP, et al. Assessment of the SYNTAX score in the Syntax study. EuroIntervention 2009;5:50-6. [CrossRef]
15. Aksakal E, Tanboga IH, Kurt M, Kaygın MA, Kaya A, Isik T, et al. The relation of serum gamma-glutamyl transferase levels with coronary lesion complexity and long-term outcome in patients with stable coronary artery disease. Atherosclerosis 2012;221:596-601. [CrossRef]
16. Açikel M, Sunay S, Koplay M, Gündoğdu F, Karakelleoğlu S. Evaluation of ultrasonographic fatty liver and severity of coronary atherosclerosis, and obesity in patients undergoing coronary angiography. Anadolu Kardiyol Derg 2009;9:273-9.
17. Demircan S, Yazici M, Durna K, Kilicaslan F, Demir S, Pinar M, et al. The importance of gamma-glutamyltransferase activity in patients with coronary artery disease. Clin Cardiol 2009;32:220-5. [CrossRef]
18. Whitfield JB. Serum gamma-glutamyltransferase and risk of disease. Clin Chem 2007;53:1-2. [CrossRef]
19. Lee DS, Evans JC, Robins SJ, Wilson PW, Albano I, Fox CS, et al. Gamma glutamyl transferase and metabolic syndrome, cardiovascular disease, and mortality risk: the Framingham Heart Study. Arterioscler Thromb Vasc Biol 2007;27:127-33.
20. Breitling LP, Grandi NC, Hahmann H, Wüsten B, Rothenbacher D, Brenner H. Gamma-glutamyltransferase and prognosis in patients with stable coronary heart disease followed over 8 years. Atherosclerosis 2010;210:649-55. [CrossRef]
21. Emdin M, Pompella A, Paolicchi A. Gamma-glutamyltransferase, atherosclerosis, and cardiovascular disease: triggering oxidative stress within the plaque. Circulation 2005;112:2078-80. [CrossRef]
22. Lee DH, Blomhoff R, Jacobs DR Jr. Is serum gamma glutamyltransferase a marker of oxidative stress? Free Radic Res 2004;38:535-9. [CrossRef]
23. Whitfield JB. Gamma glutamyl transferase. Crit Rev Clin Lab Sci 2001;38:263-355. [CrossRef]
24. Paolicchi A, Minotti G, Tonarelli P, Tongiani R, De Cesare D, Mezzetti A, et al. Gamma-glutamyl transpeptidase-dependent iron reduction and LDL oxidation-a potential mechanism in atherosclerosis. J Investig Med 1999;47:151-60.
25. Libby P. Inflammation in atherosclerosis. Nature 2002;420:868-74. [CrossRef]
26. Lee DH, Jacobs DR Jr. Association between serum gamma-glutamyltransferase and C-reactive protein. Atherosclerosis 2005;178:327-30. [CrossRef]
27. Onat A, Can G, Örnek E, Çiçek G, Ayhan E, Doğan Y. Serum γ-glutamyltransferase: independent predictor of risk of diabetes, hypertension, metabolic syndrome, and coronary disease. Obesity (Silver Spring) 2012;20:842-8. [CrossRef]
28. Bozbaş H, Yıldırır A, Karaçağlar E, Demir O, Ulus T, Eroğlu S, et al. Increased serum gamma-glutamyltransferase activity in patients with metabolic syndrome. Turk Kardiyol Dern Ars 2011;39:122-8. [CrossRef]
29. Nikkari ST, Koivu TA, Kalela A, Strid N, Sundvall J, Poikolainen K, et al. Association of carbohydrate-deficient transferrin (CDT) and gamma-glutamyl-transferase (GGT) with serum lipid profile in the Finnish population. Atherosclerosis 2001;154:485-92. [CrossRef]

Key words: Acute coronary syndrome; atherosclerosis; biological markers/blood; coronary artery disease; hypertension/blood; multivariate analysis; gamma-glutamyltransferase/blood.

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