Usefulness of admission gamma-glutamyltransferase level for predicting new-onset heart failure in patients with acute coronary syndrome with left ventricular systolic dysfunction

Gama-glutamil transferaz enziminin akut koroner sendroma bağlı sol venrikül sistolik fonksiyon bozukluğu gelişen hastalarda yeni başlangıçlı kalp yetersizliğini öngörmede yararı

Savaş Sarıkaya, M.D., Gülay Aydın, M.D.,[#] Hasan Yücel, M.D.,[#] Hakkı Kaya, M.D.,[#] Kutay Yıldırımlı, M.D.,[#] Ahmet Başaran, M.D.,[#] Ali Zorlu, M.D.,[#] Şafak Şahin, M.D.,[*] Lütfü Akyol, M.D.,[†] Musa Bulut, M.D.[‡]

Department of Cardiology, Bozok University and Cumhuriyet University Faculty of Medicine, Yozgat;
[#]Department of Cardiology, Cumhuriyet University Faculty of Medicine, Sivas;
[*]Department of Internal Medicine, Gaziosmanpaşa University Faculty of Medicine, Tokat;
[†]Department of Internal Medicine, Bozok University Faculty of Medicine, Yozgat;
[‡]Department of Cardiology, Universal Malatya Hospital, Malatya

ABSTRACT

Objectives: Our aim was to determine whether there is a relationship between admission gamma-glutamyltransferase (GGT) and subsequent heart failure hospitalizations in patients with acute coronary syndrome.

Study design: We selected 123 patients with newly diagnosed acute coronary syndrome of ejection fraction (EF) <45%. Patients were followed 15±10 months, and the relationship between admission GGT level and hospitalization because of heart failure during the follow-up was examined.

Results: Twenty-three (18.7%) patients were hospitalized during the follow-up of 15±10 months. Receiver operating characteristic (ROC) curve analysis showed that the cut-off point of admission GGT related to predict hospitalization was 49 IU/L, with a sensitivity of 81.7% and specificity of 65.2%. Increased GGT >49 IU/L on admission, presence of hypertension and hyperlipidemia, left ventricular ejection fraction (LVEF), right ventricular dysfunction, moderate-to-severe mitral regurgitation, alanine aminotransferase level, and antiplatelet agent usage were found to have prognostic significance in univariate Cox proportional hazards analysis. In multivariate Cox proportional-hazards model, increased GGT >49 IU/L on admission (hazard ratio [HR] 2.663, p=0.047), presence of hypertension (HR 4.107, p=0.007), and LVEF (HR 0.911, p=0.002) were found to be independent factors to predict new-onset heart failure requiring hospitalization.

Conclusion: Hospitalization in heart failure was associated with increased admission GGT levels. Increased admission GGT level in acute coronary syndrome with heart failure should be monitored closely and treated aggressively.

ÖZET

Amaç: Çalışmamızın amacı akut koroner sendrom nedeniyle hastaneye kabul sırasındaki gama-glutamil transferaz (GGT) düzeyleri ile kalp yetersizliği nedeniyle hastaneye yatışlar arasında ilişki olup olmadığını araştırmaktır.

Çalışma planı: Çalışmaya akut koroner sendrom ile başvurup ejeksiyon fraksiyonu (EF) %45'in altında olan 123 hasta alındı. Hastalar 15±10 ay takip edildi. Hastaların kabul sırasındaki GGT düzeyleri ile izleme süresinde kalp yetersizliği nedeniyle hastaneye yatışları arasındaki ilişki incelendi.

Bulgular: İzleme süresi olan 15±10 ay içinde 23 hasta (%18.7) kalp yetersizliğine bağlı olarak hastaneye yatırıldı. ROC (receiver operating characteristics) eğrisi analizi yöntemi ile hastaneye yatışı öngördüren GGT kesim değeri 49 IU/L olarak saptandı (%81.7 duyarlılık ve %65.2 özgüllük). Tek değişkenli Cox orantısal risk analizinde, GGT düzeyinin >49 IU/L olması, hipertansiyon ve hiperlipidemi, sol ventrikül ejeksiyon fraksiyonu (SVEF), orta-ciddi mitral yetersizliği varlığı, alanin aminotransferaz seviyesi ve antitrombosit ilaç kullanımı anlamlı bulundu. Çok değişkenli Cox orantısal risk modelinde, kalp yetersizliği nedeniyle hastaneye yatış ile ilişkili bağımsız risk faktörleri olarak ilk kabul sırasında GGT >49 olması (risk oranı [RO] 2.663, p=0.047), hipertansiyon varlığı (RO 4.107, p=0.007) ve SVEF (RO 0.911, p=0.002) parametreleri saptandı.

Sonuç: Akut koroner sendromlu hastalarda kabul GGT düzeyleri takipte kalp yetersizliğine bağlı hastaneye yatışlar ile ilişkilidir. Bu hastalar daha yakın takip edilmeli ve tedavileri optimal düzeyde ayarlanmalıdır.

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Correspondence: Dr. Savaş Sarıkaya. Bozok Üniversitesi Tıp Fakültesi, Kardiyoloji Anabilim Dalı, 66000 Yozgat.
Tel: +90 354 - 212 70 60 e-mail: cardiology58@gmail.com

Heart failure (HF) is an important problem of public health worldwide and is associated with significant morbidity and mortality. In addition to the traditional ones, different types of biomarkers, such as systemic inflammation and metabolism, were shown to be associated with disease severity and disease progression.[1]

Gamma-glutamyltransferase (GGT) is a second-generation enzymatic liver function test, and it was used initially as a sensitive indicator of alcohol ingestion and hepatobiliary dysfunction.[2] It is found not only in the liver but also in the kidney and vascular epithelium, as well as in the extracellular fluid, attached to albumin carrier molecules and lipoproteins.[3-5] It may also play a role in oxidative stress in accompaniment with glutathione metabolism, and has a possible role as a proatherogenic marker because of its indirect relationship in the biochemical steps to low-density lipoprotein cholesterol oxidation.[2]

Recent studies have reported that serum GGT, which is an inexpensive and easily accessible laboratory test, is a predictor for incident cardiovascular diseases, and is associated with prognosis in cardiopulmonary disorders such as coronary artery disease, acute myocardial infarction, HF, and acute pulmonary embolism.[6-21] However, the prognostic significance of GGT in patients presenting with acute coronary syndrome (ACS) with left ventricular systolic dysfunction (LVSD) has not been searched yet. We hypothesized that increased admission serum GGT activity may be associated with future acute HF in ACS patients with LVSD.

PATIENTS AND METHODS

Study population

A total of 247 consecutive patients who presented with their first ACS were considered for enrollment. Patients who had no previous history of myocardial infarction or other cardiac diseases and who were not on any medications were selected. Patients with alcohol usage, malignancy, hepatobiliary pathology, and acute inflammatory diseases were excluded. Of these patients, echocardiographic examination at the index admission, which yielded low ejection fraction (EF <45%), was available in 123 patients with ACS. Finally, 123 ACS patients who presented with an initial reduced left ventricular systolic function (EF <45%) were enrolled into the study. Of these 123 patients, 75 presented with ST-segment elevation myocardial infarction (STEMI), 33 with non-ST-segment elevation myocardial infarction (NSTEMI), and 15 with unstable angina pectoris (USAP). These patients were followed-up for 15±10 months after discharge, based on the endpoints of rehospitalization with acute HF with regard to the initial admission serum GGT activity. The diagnosis of acute HF was based on the existence of novel symptoms or characteristic clinical signs and the evidence of left ventricular dysfunction, determined by echocardiography. The study was approved by the local ethics committee. Informed consent was obtained from all patients.

Abbreviations:

ACS	*Acute coronary syndrome*
AUC	*Area under the curve*
EF	*Ejection fraction*
GGT	*Gamma-glutamyltransferase*
HF	*Heart failure*
LVSD	*Left ventricular systolic dysfunction*
NSTEMI	*Non-ST-segment elevation myocardial infarction*
ROC	*Receiver operating characteristic*
STEMI	*ST-segment elevation myocardial infarction*
USAP	*Unstable angina pectoris*

The optimal cut-off point of GGT (at which sensitivity and specificity would be maximal) for the prediction of HF-related rehospitalization was defined with receiver operating characteristic (ROC) curve analysis. Patients were categorized according to this GGT cut-off value. Group I consisted of patients with GGT ≤49 IU/L (n: 89) and Group II consisted of patients with GGT >49 IU/L (n: 34). A detailed history was obtained from patients, including history of hypertension and diabetes mellitus, cardiac rhythm, echocardiographic parameters such as right ventricular dilatation/hypokinesia, presence of pulmonary hypertension, mitral, aortic and tricuspid regurgitation, laboratory findings, and medication at discharge. Hypertension was defined as blood pressure ≥140/90 mmHg on more than two occasions during office measurements or receipt of antihypertensive treatment. Diabetes mellitus was defined as fasting blood glucose ≥126 mg/dL or receipt of antidiabetic treatment.

Measurements

Blood samples were drawn without stasis on admission. GGT activity was measured using a Beckman Coulter Synchron LX20 autoanalyzer with original kits. The laboratory reference limit differs significantly by sex and was set at 9-35 U/L for women and 9-40 U/L for men according to the test kit specification. All

other data including echocardiographic data, demographics and laboratory tests were obtained from the patients' files.

Echocardiographic evaluation

Echocardiographic examinations were performed in all patients within 24 hours of admission. All examinations were evaluated via Vivid 7 system (GE Healthcare; Wauwatosa, WI) in all participating centers using a 2.5–5-MHz probe. The modified Simpson method was used in EF calculations. Chamber sizes were defined according to recent guidelines.[22] Right ventricular dysfunction was defined as dilatation of the right ventricle (right ventricle dimension >3.4 cm at basal plane or >3.8 cm at midplane), combined with the presence of McConnell sign.[22,23] Valvular regurgitations were graded into two categories (moderate–to- severe versus non-moderate-to-severe) via a combination of color flow jet Doppler signal intensity and vena contracta width according to guideline recommendations.[24] Systolic pulmonary artery pressure was calculated as previously shown.[25]

Statistical analysis

Parametric data were expressed as mean ± standard deviation, nonparametric data as median (interquartile range) and categorical data as percentages. The Statistical Package for the Social Sciences (SPSS) 17.0 (SPSS, Inc.; Chicago, IL) was used to perform statistical procedures. Comparisons between groups of patients were made by use of chi-square or Fisher's exact test for categorical variables, independent samples t test for normally distributed continuous variables, and Mann-Whitney U test when the distribution was skewed. ROC curve analysis was performed to identify the optimal cut-off point of GGT (at which sensitivity and specificity would be maximal) for the prediction of new-onset (acute) HF-related rehospitalization. Area under the curve (AUC) was calculated as a measure of the accuracy of the tests. We compared the AUC with use of the Z test. Patients were categorized as having unchanged (Group I) or increased (Group II) GGT based on a cut-off value. Kaplan-Meier curves were used to display HF-related rehospitalization in two patient groups, defined as having unchanged (Group I) or increased (Group II) GGT, based on a cut-off value. A p value <0.05 was accepted as significant.

We used univariate Cox proportional-hazards analysis to quantify the association of variables with HF-related hospitalization. Variables found to be statistically significant ($p<0.25$) in univariate analysis were used in a multivariate Cox proportional-hazards model with backward stepwise method in order to determine the independent prognostic factors of HF-related rehospitalization in patients with ACS with reduced LVEF.

RESULTS

The mean age of the patients was 65±11 years (24% females, 76% males). Twenty- three (18.7%) patients were admitted to the hospital with acute decompensated HF during the follow-up.

Receiver operating characteristic (ROC) curve analysis of GGT is shown in Figure 1. According to the ROC curve analysis, the optimal cut-off value of GGT to predict HF-related rehospitalization was found as 49 IU/L, with 81.7% specificity, 65.2% sensitivity, 44.1% positive predictive value, and 91% negative predictive value (AUC 0.793, 95% confidence interval (CI): 0.693 to 0.893).

Clinical characteristics and laboratory parameters with regard to the GGT cut-off value are presented in Table 1. Alanine aminotransferase, GGT and creatinine levels and acute HF- related rehospitalization rates were significantly different between the two groups ($p<0.05$), whereas, age, gender, presence of hypertension, diabetes mellitus and atrial fibrillation, medications, and other laboratory findings were not different between the two groups ($p>0.05$). Initial echocardiographic findings with regard to the GGT cut-off value are also presented in Table 1. Right ven-

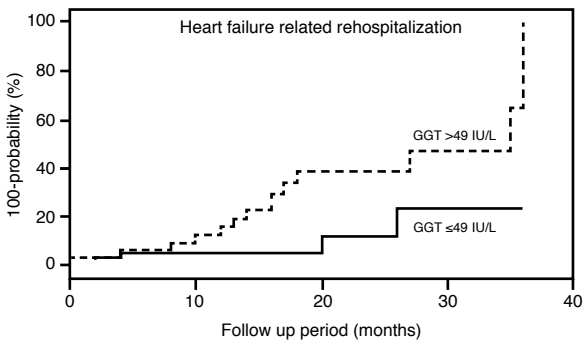

Figure 1. ROC curve for heart failure-related rehospitalization.

Table 1. Baseline characteristics of the study patients

	All patients	Gamma-glutamyltransferase		
		≤49 IU/L	>49 IU/L	p
	(n=123)	(n=89)	(n=34)	
Mean age (year)	65±11	64±10	67±10	0.234
Females	29 (24)	20 (21)	9 (27)	0.818
Presence of hypertension, n (%)	48 (39)	34 (38)	14 (41)	0.924
Presence of diabetes mellitus, n (%)	25 (20)	19 (21)	6 (18)	0.837
Atrial fibrillation, n (%)	11 (9)	6 (7)	5 (15)	0.166
STEMI, n (%)	75 (61)	55 (62)	20 (59)	0.924
Echocardiography at admission				
Left ventricular ejection fraction (%)	33±7	34±6	32±8	0.404
Right ventricular dysfunction, n (%)	14 (11)	4 (5)	10 (29)	**<0.001**
Moderate-to-severe tricuspid regurgitation, n (%)	12 (10)	5 (6)	7 (21)	0.019
Moderate-to-severe mitral regurgitation, n (%)	23 (29)	12 (14)	11 (32)	0.032
Moderate-to-severe aortic regurgitation, n (%)	3 (2)	3 (3)	0 (0)	0.560
Laboratory findings				
Gamma-glutamyltransferase (IU/L)	31 (18-53)	23 (17-35)	82.5 (58-107)	**<0.001**
Hemoglobin (g/dl)	14±2.1	14.1±2.0	13.9±2.6	0.330
Presence of anemia, n (%)	28 (24)	21 (24)	7 (22)	0.964
Creatinine (mg/dL)	1.1 (0.9-1.4)	1.0 (0.9-1.2)	1.25 (1.0-1.7)	0.008
Alanine aminotransferase (IU/L)	30 (18-52)	24 (17-43)	53.5 (34-107)	<0.001
Troponin I (ng/mL)	2.0 (0.25-11.5)	1.1 (0.20-13.4)	2.6 (0.25-9.0)	0.766
Medication at discharge				
Antiplatelet agents, n (%)	118 (96)	86 (97)	32 (94)	0.616
Beta-blockers, n (%)	105 (85)	76 (85)	29 (85)	**1.000**
ACE inhibitors/ARB, n (%)	97 (79)	73 (82)	24 (71)	0.253
Statins, n (%)	112 (91)	82 (92)	30 (88)	0.494
Aldosterone antagonist, n (%)	82 (67)	62 (70)	20 (59)	0.354
Primary endpoint				
Heart failure-related rehospitalization, n (%)	23 (18.7)	8 (9)	15 (44)	**<0.001**

ACE: Angiotensin-converting enzyme; ARB: Angiotensin receptor blocker; STEMI: ST-segment elevation myocardial infarction.

tricular dysfunction and moderate-to-severe tricuspid and mitral regurgitation were more frequent in the group with increased serum GGT activity.

Increased GGT >49 IU/L on admission, presence of hypertension and hyperlipidemia, LVEF, right ventricular dysfunction, moderate-to-severe mitral regurgitation, alanine aminotransferase level, and antiplatelet agent usage were found to have prognostic significance in univariate Cox proportional-hazards analysis (Table 2). In multivariate Cox proportional-hazards model with backward stepwise method, increased GGT >49 IU/L on admission (p=0.047, hazard ratio [HR] 2.663, 95% CI 1.012-7.007), presence of hypertension (p=0.007, HR 4.107, 95% CI 1.464-11.521), and LVEF (p=0.002, HR 0.911, 95% CI 0.858-0.966) were found to be independent factors to determine future acute HF requiring hospitalization (Table 3).

In Figure 2, we also demonstrated the probability of future hospitalization acute HF in a patient with ACS over time, based on the GGT cut-off value.

Table 2. Univariate analysis of heart failure-related rehospitalization in patients with acute coronary syndrome with left ventricular systolic dysfunction

	Univariate		
	p	HR	(95% CI)
Gamma-glutamyl transferase >49 IU/L	**0.009**	3.222	1341-7.744
Baseline characteristics			
Age (year)	0.504	1.015	0.971-1.058
Gender	0.395	1.565	0.558-4.393
Presence of hypertension	0.015	3.038	1.237-7.459
Presence of diabetes mellitus	0.834	0.899	0.331-2.444
Presence of hyperlipidemia	0.104	3.366	0.778-14.559
Atrial fibrillation	0.499	1.592	0.413-6.140
STEMI	0.779	1.135	0.470-2.740
Echocardiography at admission			
Left ventricular ejection fraction (%)	**<0.001**	0.895	0.844-0.949
Right ventricular dysfunction	0.058	0.399	0.154-1.033
Moderate-to-severe tricuspid regurgitation	0.649	0.775	0.258-2.326
Moderate-to-severe mitral regurgitation	0.022	0.337	0.133-0.855
Moderate-to-severe aortic regurgitation	0.400	0.420	0.056-3.172
Laboratory findings			
Creatinine (mg/dL)	0.402	1.054	0.932-1.191
Alanine aminotransferase (IU/L)	**0.004**	1.007	1.002-1.011
Troponin I (ng/mL)	0.279	1.010	0.992-1.029
Presence of anemia	0.310	0.608	0.233-1.587
Medication at discharge			
Antiplatelet agents	0.142	0.196	0.022-1.730
Beta-blockers	0.378	1.581	0.571-4.377
ACE inhibitors/ARB	0.581	0.745	0.263-2.117
Statins	0.334	1.831	0.536-6.256
Aldosterone antagonist	0.824	0.905	0.375-2.181

ACE: Angiotensin-converting enzyme; ARB: Angiotensin receptor blocker; CI: Confidence interval; HR: Hazard ratio; STEMI: ST-segment elevation myocardial infarction.

DISCUSSION

The present study demonstrated that elevated serum GGT level on admission was significantly and independently associated with the risk of acute HF development in ACS patients with LVSD.

Wannamethee et al.[26] found that increased serum GGT levels were associated with cardiac mortality. This finding triggered the studies focusing on the usefulness of GGT as a predictor of cardiovascular diseases.[6-21] For the time being, this laboratory test has been searched by many groups regarding its suitability as a significant predictor for cardiometabolic diseases. Serum GGT was found to be a risk factor for cardiovascular mortality by the Vorarlberg Health Monitoring and Promotion Program Study Group.[7] Lee et al.[11] demonstrated that serum GGT also predicted cardiovascular mortality in those aged less than 70 years. In addition, it was found to predict non-fatal myocardial infarction and fatal coronary heart disease among 28,838 middle-aged men and women.[6] Fraser et al.,[12] in a recent meta-analysis of fully adjusted results of 10 prospective studies, described that

Table 3. Multivariate Cox proportional-hazards analysis of heart failure-related rehospitalization in patients with acute coronary syndrome with left ventricular dysfunction

		p	HR	95.0% CI	
				Lower	Upper
Step 1	Gamma-glutamyltransferase >49 IU/L	0.096	2.613	0.844	8.090
	Presence of hyperlipidemia	0.961	1.042	0.202	5.376
	Presence of hypertension	0.008	4.473	1.490	13.431
	Left ventricular ejection fraction (%)	0.012	0.916	0.856	0.981
	Right ventricular dysfunction	0.220	2.362	0.599	9.317
	Moderate-to-severe mitral regurgitation	0.109	0.382	0.118	1.239
	Antiplatelet agents	0.220	0.247	0.027	2.304
	Alanine aminotransferase (IU/L)	0.573	1.002	0.995	1.009
Step 2	Gamma-glutamyltransferase >49 IU/L	0.087	2.629	0.870	7.944
	Presence of hypertension	0.008	4.477	1.492	13.434
	Left ventricular ejection fraction (%)	0.007	0.916	0.859	0.976
	Right ventricular dysfunction	0.219	2.365	0.600	9.327
	Moderate-to-severe mitral regurgitation	0.108	0.382	0.118	1.237
	Antiplatelet agents	0.220	0.247	0.027	2.302
	Alanine aminotransferase (IU/L)	0.571	1.002	0.995	1.009
Step 3	Gamma-glutamyltransferase >49 IU/L	0.066	2.759	0.935	8.140
	Presence of hypertension	0.008	4.236	1.454	12.343
	Left ventricular ejection fraction (%)	0.004	0.912	0.857	0.971
	Right ventricular dysfunction	0.225	2.366	0.588	9.514
	Moderate-to-severe mitral regurgitation	0.114	0.378	0.113	1.263
	Antiplatelet agents	0.220	0.250	0.027	2.286
Step 4	Gamma-glutamyltransferase >49 IU/L	0.145	2.141	0.769	5.958
	Presence of hypertension	0.011	3.829	1.360	10.786
	Left ventricular ejection fraction (%)	0.006	0.919	0.865	0.976
	Moderate-to-severe mitral regurgitation	0.234	0.499	0.159	1.568
	Antiplatelet agents	0.250	0.271	0.029	2.510
Step 5	Gamma-glutamyltransferase >49 IU/L	0.128	2.203	0.798	6.085
	Presence of hypertension	0.012	3.787	1.340	10.704
	Left ventricular ejection fraction (%)	0.005	0.918	0.864	0.975
	Moderate-to-severe mitral regurgitation	0.213	0.483	0.153	1.521
Step 6	Gamma-glutamyltransferase >49 IU/L	0.047	2.663	1.012	7.007
	Presence of hypertension	0.007	4.107	1.464	11.521
	Left ventricular ejection fraction (%)	0.002	0.911	0.858	0.966

Gamma-glutamyltransferase >49 IU/L, presence of hypertension and hyperlipidemia, left ventricular ejection fraction, right ventricular dysfunction, moderate-to-severe mitral regurgitation, alanine aminotransferase, and antiplatelet agent usage were entered into the multivariate Cox proportional-hazards model with backward stepwise method. CI: Confidence interval; HR: Hazard ratio.

a change in GGT of 1 U/L was associated with a 20% increase in the risk of coronary heart disease and a 54% increase in the risk of stroke. Serum GGT is also associated with coronary artery disease, acute myocardial infarction, diabetes mellitus, hypertension, and metabolic syndrome.[13-17] In addition, higher se-

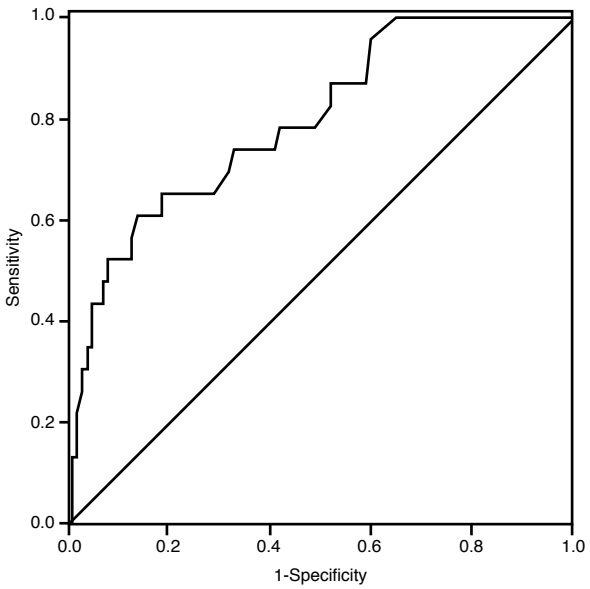

Figure 2. Kaplan-Meier curves for heart failure-related rehospitalization.

rum GGT concentrations were shown to be associated with greater risk of HF.[18,19] Wang et al.[19] showed that moderate-to-high levels of serum GGT were significantly associated with incident HF in males and females. Poelzl et al.[20] described the increased prevalence of elevated GGT in patients with chronic HF. They found the GGT levels to be associated with disease severity and increased GGT to be an independent predictor of death or heart transplantation. Finally, in addition to these studies, Zorlu et al.[21] showed that GGT was associated with impaired hemodynamics and can be used for risk stratification of patients with acute pulmonary embolism.

Risk stratification is extremely crucial for ACS patients. The GRACE risk scoring system, an international registry including STEMI, NSTEMI and USAP, which was derived from clinical parameters at the time of hospitalization, was found to accurately predict mortality at six months. Parameters in this GRACE scoring system are age, history of congestive heart failure, history of myocardial infarction, elevated resting heart rate, low systolic blood pressure on arrival, ST-segment depression, elevated initial serum creatinine, and elevated cardiac enzymes in-hospital.[27] Among patients hospitalized for ACS, the subsequent development of HF portends a poor prognosis. The CARE trial found age and LVEF as the most important predictors of HF. Other predictors included diabetes, history of hypertension, previous myocardial infarction, and baseline heart rate. Furthermore, moderate exercise three or more times per week was independently associated with a 30% lower risk of HF.[28] In VALIANT, the most important predictors of HF were older age, antecedent diabetes, prior infarct before index myocardial infarction, and reduced renal function.[29]

Serum GGT also takes part in the cellular glutathione synthesis and thus the antioxidant defense system.[30,31] Increased serum GGT may reflect increased oxidative stress in humans.[32] It is also strongly related to systemic inflammation.[33] Oxidative stress and systemic inflammation are involved in ventricular remodelling and endothelial dysfunction, both of which contribute to progression of the HF syndrome.[1,34,35]

To identify patients who develop acute HF after ACS and to determine the specific therapy are of clinical importance. Hence, throughout this time, biomarkers that might predict future HF were a topic of focus. C-reactive protein was found to be an independent predictor of death and development of HF in patients with ACS in previous studies.[36,37] Furthermore, B-type natriuretic peptide (BNP) was also found to be a significant predictor.[38,39] Ess et al.[40] showed that GGT and total bilirubin were associated with disease severity in CHF. However, only GGT was independently associated with adverse outcome. New biomarkers that predict future cardiovascular events are still needed.

In our study, we found that the subsequent acute HF risk was increased with the increase in serum GGT. Patients with higher GGT also had more frequent pulmonary hypertension, right ventricular dilation/hypokinesia, moderate-to-severe tricuspid and mitral regurgitation, and higher alanine aminotransferase and creatinine levels at the first admission with ACS. Only lower LVEF, presence of hypertension and higher GGT levels were determined as independent predictors for subsequent acute HF in ACS patients by univariate and multivariate regression analyses. Previous studies pointed out the same findings about LVEF being a predictor for subsequent cardiac deterioration; however, the relation between increased GGT level at admission with ACS with subsequent hospitalization for acute HF seems to be a novel finding. Serum GGT may act as a simple and inexpensive biomarker for a

physician to predict the subsequent risk of HF in ACS patients. This would provide a more careful approach for critical patients during their follow-up.

Study limitations

Even though medications were generally similar after discharge, patients were not monitored for changes in medication and doses during the follow-up. Hence, this may constitute a potential confounder for the study results. In addition, though most of the documented risk factors were included in the analysis, the possibility of residual confounding factors that were not accounted for cannot be entirely excluded. We could not assess which patients underwent percutaneous coronary intervention or cardiac surgery or those on medical therapy. All procedures may affect EF and patient outcomes. Finally, data were derived from a moderate-sized population from a single center, and hence, larger and multi-centered studies are needed to draw certain conclusions.

In conclusion, to our knowledge, this is the first study to report an association between increased serum GGT activity in ACS patients and subsequent risk for acute HF. Further studies are necessary to evaluate the physiopathological role of serum GGT activity in these patients and GGT's overall importance and independence from previously accepted biomarkers and traditional risk factors used for predicting the development of acute HF. However, because of its widespread availability and inexpensive cost for screening, identifying higher than expected GGT levels in ACS patients should alert the physician to give particular attention to caring for these patients and assessing the appropriate aggressiveness of the therapy, with the hopeful outcome of preventing subsequent acute HF development.

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

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