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Research Article

Does the Modified Glasgow Prognostic Score be a Predictive Parameter for Right Ventricular Systolic Dysfunction in Patients with Acute Decompensated Heart Failure?

Mustafa Kaplangoray,[1] Kenan Toprak[2]

[1]Department of Cardiology, Bilecik Şeyh Edebali University, Bilecik, Türkiye
[2]Department of Cardiology, Harran University Faculty of Medicine, Şanlıurfa, Türkiye

Abstract

Objectives: Right ventricular sistolic dysfunction (RHF) is associated with a poor prognosis in paients with acute decompensated heart failure (ADHF), regardless of the degree of left ventricular (LV) dysfunction. As previously shown, cachexia in heart failure is associated with right ventricular (RV) dysfunction rather than LV impairment. Modified Glasgow prognostic score (mGPS), which is calculated based on serum albumin (SA) and C-reactive protein (CRP) levels, is associated with inflammatory and nutritional status. Aims of this study was to investigate the relationship between mGPS and RV functions in patients with ADHF.

Methods: We prospectively enrolled 122 ADHF consecutive patients with reduced LV ejection fraction (LVEF <%35). RHF was determined according to RV fractional area change (RV FAC). Patients with RVFAC <35 % were considered as biventricular heart failure (BHF) and those with RVFAC ≥35% were considered as isolated left heart failure (isolated-LHF). mGPS was scored as 0, 1 or 2 according to CRP and SA levels.

Results: Compared to isolated-LHF patients, mGPS, B-type natriuretic peptide (BNP), CRP, systolic pulmonary artery pressure (SPAP), mitral E/Em were higher, while SA, hemoglobin, tricuspid annular plane systolic excursion (TAPSE) and RVFAC were lower in BHF patients (p<0.05). Correlation analysis showed a significantly correlation of mGPS with RHF (r=-0.424, p<0.001). Logistic analysis showed mGPS [OR:1.098 (1.027-1.179), p=0.012] was an independent predictive factor for RHF.

Conclusion: mGPS is an important independent predictor of RV dysfunction in patients with ADHF.

Keywords: Right ventricular systolic dysfunction, heart failure, modified Glasgow prognostic score, echocardiograpy

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All forms of heart failure (HF) are among the major causes of cardiovascular-related mortality and morbidity.End-stage heart failure still has a high morbidity and mortality rate despite advances in its treatment.[1] In contrast to what was believed in the past, recent studies have shown that the right ventricle (RV) is more than a passive conduit and that optimal function of the RV plays an important role in global cardiac function.It is also known that right heart ventricular systolic dysfunction (RHF) is an independent factor for mortality in patients with HF.[2] Although many factors are involved in the etiology of RHF, the major cause is left ventricular (LV) dysfunction. Edema in the intestinal region which develops secondary to RHF and venous congestion is known to play a role in malnutrition in these patients.[3]

Address for correspondence: Mustafa Kaplangoray, MD. Department of Cardiology, Bilecik Şeyh Edebali University, Bilecik, Türkiye
Phone: +90 532 394 56 38 **E-mail:** mkaplangoray@gmail.com

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Malnutrition has been shown to be associated with prognosis in cardiovascular patients such as acute coronary syndrome[4] and HF,[5] reflecting the general condition of patients. The catabolic process, the presence of malnutrition and the inflationary state in HF patients cause high levels of C-reactive protein (CRP) in these patients. Increased CRP level has been shown to be associated with increased morbidity and mortality in this patient group independent of the etiology of HF.[6] The modified Glasgow prognostic score (mGPS), related to inflammatory and nutritional status and calculated based on serum albumin (SA) and CRP levels, has been shown to be associated with prognosis in HF patients with low and preserved LV ejection fraction (LVEF) in previous studies.[7,8] However, to the best of our knowledge, there are no studies investigating the relationship between mGPS and RHF in patients with acute decompensated chronic heart failure (ADHF) and this relationship was investigated in our study.

Methods

Patient Population

This prospective cross-sectional study enrolled 122 consecutive patients who were in New York Heart Association (NYHA) functional class 3 or 4 and were hospitalized with a diagnosis of ADHF due to reduced LVEF. The diagnosis of ADHF was based on complaints associated with HF, presence of HF findings on physical examination, presence of congestion on chest radiography and LVEF <35% on echocardiography. Indications for hospitalization were determined by the attending physician blinded to the study design and protocol. According to echocardiography performed immediately after admission, patients were divided into two groups: those with right ventricular fractional area change (RVFAC) below 35% [biventricular heart failure (BHF)] and those without [isolated left heart failure (isolated-LHF)].[9] Exclusion criteria were myocardial infarction within 90 days, coronary artery bypass graft surgery, percutaneous coronary intervention or pacemaker implantation within the last 30 days, known infiltrative, hypertrophic or congenital heart disease, acute or chronic infection, autoimmune disease, chronic renal (eGFR less than 60 mL/min/1. 73 m^2 or dialysis) or hepatic insufficiency [aspartate transaminase (AST) or alanine transaminase (ALT) values 3 times higher than normal values], malignancy and recent major surgery.

Echocardiographic Examination

All patients underwent two-dimensional (2D), M-mode, pulsed-wave Doppler and pulsed-wave tissue Doppler echocardiography (TDI) evaluation through multiple acoustic windows in the lateral decubitus and supine position using a 3.5 MHz transducer with a Philips Envisor C echocardiograph (Philips Medical Systems, Andover, MA, USA) as recommended by ACC/AHA guidelines[10] by an experienced cardiologist blinded to study data and design. LVEF was calculated according to the modified Simpson method. LV diastolic function assessment was calculated according to the ratio of transmitral Doppler early filling velocity (E) to tissue Doppler early diastolic mitral annular velocity (Em). In addition, RVFAC, the tricuspid annular plane systolic excursion (TAPSE) and systolic pulmonary artery pressure (SPAP) measurements were also performed in all patients in line with the guidelines recommended.[9]

Analysis of mGPS and Other Laboratory Parameters

All patients were evaluated for BNP levels along with routine biochemistry and hemogram parameters on admission. The modified GPS score was calculated as score 0: SA level ≥3.5 g/dl and CRP ≤1 mg/dl, score 1: SA level ≥3.5 g/dl and CRP >1 mg/dl, score 2: SA level < 3.5 g/dl and CRP >1 mg/dl.[7]

Statistical Analysis

SPSS 24.0 version software package (Chicago, IL, USA) was used to analyze the data obtained. A p value <0.05 was accepted for statistical significance. Visual histogram and Kolmogorow-Smirnow test were used to determine whether the variables were normally distributed. Levene's test was used for homogeneity of variances. Mean±standard deviation was used for normally distributed continuous variables and median-interquartile ranges (25^{th}-75^{th} percentiles) were used for continuous variables that did not follow normal distribution. Categorical variables were expressed as percentages and Chi-square test was used for comparison. Student's t-test was used for the comparison of normally distributed continuous variables and Whitney U test was used for the comparison of variables that did not follow normal distribution. Spearman's correlation analysis was used to demonstrate the relationship between the modified GPS and echocardiographic and laboratory parameters. Logistic regression analysis was also performed to reveal independent predictors for BHF.

Results

A total of 122 patients, 66 with isolated-LHF and 56 with BHF, were included in the study. The mean age of the study population was 54.8±8.6 years and the male ratio was 57.4. Demographic, clinical and laboratory data at the time of admission are shown in Table 1. Compared to the isolated-LHF group, patients in the BHF group had higher BNP, CRP,

Table 1. Demographic, clinical, laboratory and hemodynamic data of the study population

	Isolated-LHF patients (n=66)	BHF patients group (n=56)	p
Demographics			
Age (year)	53.9±8	55.9±9	0.196
Male (%)	40 (60.6%)	30 (53.6%)	0.441
BMI (kg/m^2)	24.7±4	23.9±4	0.762
Medication usage			
ASA, n (%)	56 (84.8%)	50 (89.3%)	0.469
ACE-İ/ARB, n (%)	55 (83.4%)	47 (83.9%)	0.452
B-Blocker, n (%)	46 (69.7%)	40 (71.4%)	0.834
Aldosterone blocker, n (%)	28 (42.4%)	27 (48.2%)	0.522
Digoxin, n (%)	45 (68.2%)	40 (71.4%)	0.697
Diuretic, n (%)	40 (60%)	32 (61%)	0.898
Laboratory data			
BNP (pg/mL)	1122.9 (907-1242)	2292.6 (1803-2641)	<0.001
Albumin (g/dl)	3.8 (3.6-4.0)	3.6 (3.4-3.9)	0.044
C-reactive protein (mg/dL)	1.7 (0.8-2.1)	4.8 (2.5-6.9)	<0.001
Hemoglobin(g/dl)	11.7±0.9	10.8±0.7	<0.001
WBC (×10^3/µL)	7.7±2.4	7.9±2.5	0.614
Platelet (×10^3/µL)	246.4±97.9	259.7±108.5	0.476
BUN (mg/dl)	53±18	52±18	0.860
Creatinin (mg/dl)	1.05±0.2	1.04±0.2	0.882
Modified GPS			
0	30 (45.5%)	9 (16.1%)	<0.001
1	32 (48.5%)	30 (53.6%)	<0.001
2	4 (6.1%)	17 (30.4%)	<0.001
Echocardiographic variables			
LVEF (%)	26 (24-29)	25 (22-28)	0.099
SPAP (mmHg)	47.8 (42-52)	54.7 (52-59)	<0.001
RVFAC (%)	38.2 (36-40)	24.5 (21-28)	<0.001
TAPSE (mm)	18.8 (17-21)	10 (8.9-10)	<0.001
Mitral E/Em	13.9 (12-15)	16.9 (15-17)	<0.001

LHF: Left ventricular heart failure; BHF: Biventricular heart failure; BMI: Body mass index; ACE-I/ARB: Angiotensin converting enzyme inhibitor/Angiotensin receptor blocker; BNP: B-type natriuretic peptide; WBC: White blood cell count; BUN: Blood Urea Nitrogen; GPS: Glasgow prognostic score; LVEF: Left ventricular ejection fraction; SPAP: Systolic pulmonary artery pressure; RVFAC: Right ventricle fractional area change; TAPSE: Tricuspid annular plane systolic excursion; E/Em: ratio of transmitral Doppler early filling velocity to tissue Doppler early diastolic mitral annular velocity.

SPAP, Mitral E/Em ratio and lower SA level, hemoglobin, TAPSE and RVFAC values. The prevalence of mGPS 1 (53.6 vs 48.5 %) and mGPS 2 (30.4 vs 6.1 %) was significantly higher in the BHF group (p<0.05). The results of Spearman's correlation analysis between modified GPS and right ventricular echocardiographic parameters and BNP are presented in Table 2. Based on this analysis, mGPS was moderately significantly correlated with RVFAC (r=-0.424, p<0.001), TAPSE (r=-0.366, p<0.001), and BNP (r=0.363, p<0.001), whereas a low significant correlation was observed with SPAP (r=0.278, p=0.002). Logistic regression analysis showed that BNP [odds ratio (OR): 1.098 confidence interval % (CI): 1.027-1.179, p=0.009] mGPS (OR: 0.948, CI: 0.907-0.999, p=0.012) SPAP (OR: 0.637, CI: 0.505-1. 071, p=0.044), TAPSE (OR: 0.190, CI: 0.039-0.922, p: 0.039) and mitral E/Em (OR: 0.637, CI: 0.412-1.067, p=0.049) were independent predictive factors for BHF (Table 3).

Table 2. Spearman correlation coefficient analysis of mGPS with right ventricular echocardiography parameters and BNP

	Spearman r	p
RVFAC	-0.424	<0.001
SPAP	0.278	0.002
TAPSE	-.366	<0.001
BNP	0.363	<0.001

BNP: B-type natriuretic peptide; mGPS: Modified Glasgow Prognostic Score; SPAP: Systolic pulmonary artery pressure; TAPSE: Tricuspid annular plane systolic excursion; RVFAC: Right ventricle fractional area change.

Table 3. Univariate and multivariate logistic regression analysis of the association between the RHF and multiple parameters

	Univariate analysis		Multivariate analysis	
Variables	**OR (95% CI)**	**p**	**OR (95% CI)**	**p**
BNP	1.006 (1.004-1.007)	<0.001	1.098 (1.027-1.179)	0.009
Albumin	0.234 (0.063-0.878)	0.031	-	
C-reactive protein	2.169 (1.662-2.832)	<0.001	-	
Hemoglobin	0.981 (0.951-1.034)	0.234	1.171 (0.278-3.955)	0.830
Modified GPS	3.620 (1.936-6.767)	<0.001	0.948 (0.907-0.999)	0.012
LVEF (%)	0.942 (0.861-1.030)	0.190	0.819 (0.540-1.242)	0.346
SPAP (mmHg)	1.187 (1.105-1.275)	<0.001	0.637 (0.505-1.071)	0.044
TAPSE (mm)	0.468 (0.364-0.602)	<0.001	0.190 (0.039-0.922)	0.039
Mitral E/Em	1.848 (1.444-2.364)	<0.001	0.637 (0.412-1.067)	0.049

BHF: Biventricular heart failure; BNP: B-type natriuretic peptide; GPS: Glasgow prognostic score; LVEF: Left ventricular ejection fraction; SPAP: Systolic pulmonary artery pressure; TAPSE: Tricuspid annular plane systolic excursion; E/Em: ratio of transmitral Doppler early filling velocity to tissue Doppler early diastolic mitral annular velocity.

Discussion

This study investigated the relationship between mGPS and RHF in patients with ADHF and NYHA functional class 3 and 4 with an indication for hospitalization. RHF was diagnosed according to RVFAC. The reason for the use of RVFAC in this study is that RVFAC is a noninvasive, inexpensive and easily accessible imaging method that provides information about RV systolic functions and shows a good correlation between cardiac magnetic resonance imaging and RV ejection fraction values.[11]

Our study revealed that mGPS is an independent and important factor for RHF and we think this is an important result. These results of our study are in parallel with the results of Valentova et al.[12] Their study revealed the presence of significant RV systolic dysfunction in cachectic patients compared to non-cachectic patients with similar LVEF and NYHA class. Likewise, in our study, the prevalence of mGPS 1 and mGPS 2 was significantly higher in the BHF group compared to the isolated-LHF group.

Similar to HF, cancer is a systemic disease and progression of the disease is associated with an increased inflammatory response and nutritional impairment. Therefore, mGPS, which is accepted as an indicator of immuno-nutritional status, was first used in cancer patients and its relationship with prognosis has also been demonstrated.[13] Poor RV function is a strong predictor of morbidity and mortality in patients with LV systolic dysfunction.[14] RV dysfunction complicated with increased right atrial pressure is thought to lead to fluid retention characterized by edema in the peripheral and splanchnic regions and subsequent hepatic and intestinal system dysfunction.[15] Malabsorption caused by congestive hepatic and intestinal edema secondary to RHF leads to nutritional impairment and causes a decrease in SA level.[16] In addition, congestion in the intestinal wall leads to bacterial translocation and further increase in inflammation, which is already present in heart failure, and this leads to increased CRP levels as a laboratory counterpart.[17,18] In the light of these mechanisms, this study was designed and the mGPS of the patients in the BHF group was found to be higher in our study and these results support the mechanisms suggested above.

In addition, in this study, the BNP level of BHF patients was found to be higher than that of isolated-LHF patients and it was also demonstrated that BNP is an independent and important predictor factor for BHF. In parallel with these results of our study, Denis et al.[19] demonstrated that BNP levels were higher in patients with left heart failure accompanied by RHF compared to isolated-LHF patients. The source of release of BNP is myocytes within areas of fibrosis that develop after cardiomyopathy. When the thin RV wall is exposed to volume and pressure load, it is thought to hypertrophy and this is thought to lead to increased BNP release.[20]

TAPSE is a parameter frequently used in the assessment of right ventricular systolic function and correlates well with radionuclide-derived estimation of right ventricular ejection fraction.[21] In our study, TAPSE was shown to be an independent factor for RHF. Increased mitral E/Em ratio in left heart failure is thought to cause an increase in pulmonary artery pressure, which in turn leads to increased right ventricular afterload and eventually RHF.[8] In this study, SPAP and mitral E/Em were also shown to be independent predictive factors for RHF. In this study, mGPS was shown to be an independent and important predictor factor for RHF. In addition, a significant correlation between mGPS and echocardiographic and laboratory markers of RHF such as

RVFAC, SPAP, TAPSE and BNP was also demonstrated.

The most important limitation of this study is the small number of patients. Furthermore, another limitation is the lack of follow-up of RHF-related echocardiographic and laboratory parameters, including mGPS, during the treatment period in the patients included in the study and the lack of investigation of the effect of treatment on these parameters.

In conclusion, our findings indicated that in patients hospitalized for ADHF, LV dysfunction is accompanied by a significant proportion of RHF. Compared to patients with isolated-LHF, the frequency of mGPS 1 and mGPS 2 is higher in patients with BHF. In this study, mGPS was shown to be associated with echocardiographic and laboratory parameters favoring RHF. The mGPS calculated using routine laboratory parameters can be used as an auxiliary parameter to diagnose RHF, which is associated with mortality in left heart failure.

Disclosures

Ethics Committee Approval: The study protocol was approved by the Ethics Committee of Bilecik Şehyh Edebali University Faculty of Medicine in accordance with the Declaration of Helsinki. Informed written consent was obtained from all participants.

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Conflict of Interest: None declared.

Authorship Contributions: Concept – M.K.; Design – M.K, K.T.; Supervision – M.K.; Materials – M.K., K.T.; Data collection &/or processing – M.K., K.T.; Analysis and/or interpretation – M.K., K.T.; Literature – M.K.,K.T.; Writing – M.K.; Critical review – M.K.

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