Prognostic Impact of Modified Glasgow Prognostic Score in Patients with Heart Failure with Mildly Reduced Ejection Fraction

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ABSTRACT

Introduction: Inflammation and malnutrition may trigger heart failure development and progression (HF). However, the relationship of the modified Glasgow prognostic score (mGPS), which is derived from C-reactive protein and albumin with mildly reduced ejection fraction HF (HFmrEF), is not well-known. We aimed to determine whether the modified Glasgow prognostic score (mGPS) is helpful for the prediction of all-cause mortality in patients with HFmrEF.

Patients and Methods: Patients with HFmrEF admitted to our outpatient clinic between January 2016 and January 2020 were enrolled. All-cause mortality was defined as the primary endpoint. The mGPS was calculated and, its association with overall survival was determined.

Results: Data were analyzed for 259 patients. The mGPS≤ 1 in 172 (66%), and 2 in 87 (34%) patients, respectively. Higher mGPS was related to worse results of routine biomarkers associated with prognosis, especially NT-proBNP [777 (112-4564) pg/mL vs. 350 (65-3521) pg/mL, respectively, p< 0.0001)]. In multivariable Cox model, NT-proBNP [1.83 (1.32-2.55), p< 0.0001], mGPS 2 vs. ≤1 [2.43 (1.2-4.93), p= 0.013], and coronary artery disease (CAD) [3.15 (1.46-6.82), p= 0.003] were found to be independently associated with all-cause mortality.

Conclusion: The immune-nutritional score mGPS predicts mortality during long-term follow-up of patients with HFmrEF. The mGPS might be used for risk status assessment of HFmrEF.

Key Words: Heart failure; ejection fraction

Hafif Düşük Ejeksiyon Fraksiyonlu Hastalarda Modifiye Glasgow Prognostik Skorunun Prognostik Gücü

ÖZET

Giriş: Enflamasyon ve malnütrisyon kalp yetersizliğinin hem ortaya çıkmasını hem de ilerlemesini tetikleyebilir (KY). Fakat, C-reaktif protein ve albüminden türetilmiş modifiye Glasgow Prognostik Skorunun (mGPS) Hafif Düşük Ejeksiyon Fraksiyonlu Kalp Yetersizliği (HDEF-KY) ile ilişkisi iyi bilinmemektedir. mGPS'unun, HDEF-KY'li hastalarda tüm nedenlere bağlı mortaliteyi öngörmede faydalı olup olmadığını araştırmayı amaçladık.

Hastalar ve Yöntem: Ocak 2016 ve Ocak 2020 arasında hastanemiz polikliniğine ayaktan başvuran HDEF-KY'li hastalar çalışmamıza dahil edildi. Tüm nedenlere bağlı ölüm primer sonlanım olarak tanımlandı. mGPS hesaplandı ve onun sağkalım ile ilişkisi belirlendi.

Bulgular: 259 hastanın verileri analiz edildi. 172 (66%) hastada mGPS≤ 1 iken 87 (34%) hastada mGPS 2'ydi. Yüksek mGPS özellikle NT-pro BNP [777 (112-4564) pg/mL kıyasla 350 (65-3521) pg/mL sırasıyla p< 0.0001)] olmak üzere prognozla ilişkili rutin biyobelirteçlerin daha kötü sonuçlarıyla ilişkiliydi. Çok değişkenli Cox modelinde, NT-proBNP [1.83 (1.32-2.55), p< 0.0001], mGPS 2'ye kıyasla ≤1 [2.43 (1.2-4.93), p= 0.013], ve koroner arter hastalığı [3.15 (1.46-6.82), p= 0.003]'nın tüm nedenlere bağlı ölümle bağımsız şekilde ilişkili olduğu saptandı.

Sonuç: Bir immün nütrisyonel skor olan mGPS HDEF-KY'li hastaların uzun dönem takibinde mortaliteyi öngördürür. mGPS, HDEF-KY'de risk durumu değerlendirmesinde kullanılabilir.

Anahtar Kelimeler: Kalp yetersizliği; ejeksiyon fraksiyonu

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INTRODUCTION

Heart failure with mildly reduced ejection fraction (HFmrEF) is defined as HF with a left ventricular ejection fraction (LVEF) of 41 to 49%. It accounts for nearly 20-30% of the overall heart failure population[1]. As gaining popularity in HF subtypes, HFmrEF demonstrates intermediate characteristics between HFrEF and HFpEF. Whether HFmrEF represents a distinct subtype of HF or is a transitional stage between HFrEF and HFpEF remains controversial. The reason for identifying HFmrEF as a separate group is to stimulate researchers into the underlying characteristics and pathophysiology.

Recent data revealed that malnutrition is a significant poor prognostic factor for cardiovascular (CV) disease. Unlike other clinical variables, malnutrition has the advantage of being a modifiable risk factor. Nutritional status may be an indirect measure of inflammation[2]. There is evidence that inflammation may trigger the development and progression of heart failure[3,4]. Similarly, malnutrition was associated with adverse outcomes in patients with heart failure[5].

The immune-nutritional-based prognostic score, modified Glasgow prognostic score (mGPS), combining C-reactive protein and serum albumin concentration, provides valuable prognostic information for patients with cancer, recognizing the central role of inflammation and malnutrition in the course of malignancies[6]. This score reflects both the inflammatory status and the nutritional status. It is simple to measure, routinely available, and well-standardized[4]. There have been reports confirming the usefulness of the mGPS for predicting prognosis in patients with acute decompensated heart failure, patients with stable heart failure, and heart failure with preserved ejection fraction[4,7-9]. To our knowledge, no data exist on patients with HFmrEF.

In this study, we aimed to determine whether mGPS is helpful for the predictive value for all-cause mortality in patients with HFmrEF who was admitted to the cardiology outpatient unit.

PATIENTS and METHODS

Study Population

This retrospective cohort study included patients diagnosed with HFmrEF admitted to the outpatient clinic who were enrolled between 2016 and 2020. Patients were defined as HFmrEF according to current European Society of Cardiology guidelines[1]; patients with a left ventricular ejection fraction (LVEF) 41-49% who had heart failure symptoms and/or signs, who had elevated levels of natriuretic peptides [N-terminal pro-B-type natriuretic peptide (NT-pro-BNP) >125 pg/mL], and at least one additional echocardiographic criterion including relevant structural heart disease or diastolic dysfunction were enrolled. Inclusion criteria were the diagnosis of stable status, an age >18 years, and complete routine laboratory data for the index visit. Our study was a single-center, retrospective cohort study. The primary outcome of this study was all-cause mortality. The study was conducted following the ethical standards stated in the Declaration of Helsinki and was approved by the Local Ethics Committee (Registration number: 2021-92).

Data Collection and Laboratory Analysis

All consecutive outpatients with HFmrEF underwent comprehensive clinical evaluation, electrocardiography, and 2D transthoracic echocardiography. Patient characteristics, including age, gender, body mass index, comorbidities such as hypertension, diabetes mellitus and dyslipidemia, and medical therapy, were recorded from hospital databases. Patients with chronic inflammatory, or infectious disease, malignancy, taking immunosuppressive drugs or antibiotics/antiviral treatment, and having no laboratory data were excluded. Three hundred and fifty-four patients were evaluated; after excluding 95 patients, the final study sample was composed of 259 patients with HFmrHF. Blood samples were obtained at admission to the outpatient clinic to measure routine laboratory parameters, including NT-proBNP, CRP, and albumin levels. Death records were taken from the national health system database, telephone visits, or hospital databases (Figure 1).

Modified Glasgow Prognostic Score

The modified Glasgow prognostic score (mGPS) was described previously[3]. Briefly, patients were classified into three groups; patients with both elevated CRP (>1 mg/dL) and hypoalbuminemia (<3.5 g/dL) were classified to a score of two; patients with only CRP> 1 mg/dL were allocated a score of one; and patients without abnormalities in CRP and albumin levels, that is, CRP≤ 1 mg/dL and albumin≥ 3.5 g/dL, had 0 points allocated. The main feature of this modified score is that the mGPS defines normoalbuminemic patients without elevated CRP as having low risk (mGPS score 0).

Statistical Analysis

Statistical analyzes were performed using “rms”, “hmisc” and “survminer”, packages with R-software v.4.0 (R statistical, Vienna, Austria). The distribution of continuous variables was evaluated with the Shapiro-Wilk test. For descriptions, comparisons of baseline demographic, clinical, and laboratory characteristics, continuous variables were presented as a median and interquartile range because of non-normal distribution. In contrast, categorical variables were presented as counts and percentages. Mann-Whitney U test and Chi-square test or Fisher’s exact test were used to compare quantitative and categorical variables.

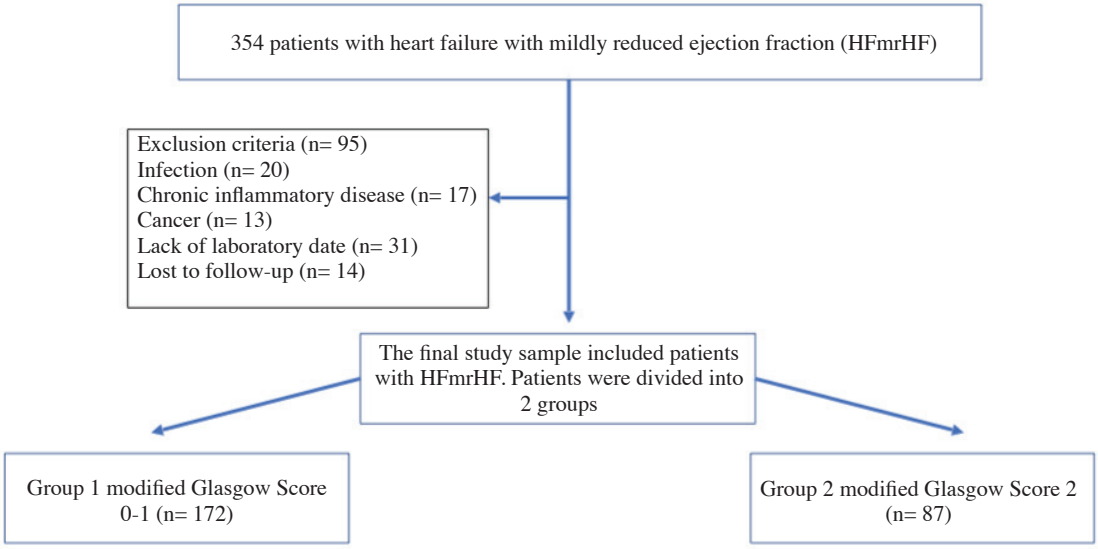

Figure 1. Consort flow diagram for inclusion and exclusion criteria.

All-cause death of the patients was the primary outcome of the present study. It is important that candidate predictors included in the model are pathophysiologically plausible and that their association with death has been demonstrated in previous studies[1,2,4,6]. As a result, we included nine candidate predictors in our Cox regression model. The predictors were age, creatinine, modified Glasgow prognostic score (0-1 vs. 2), hypertension, hemoglobin, NT-ProBNP, troponin, coronary artery disease, and NYHA class. Time-to-event data were assessed using Cox proportional univariate and multivariate regression methods to evaluate the relationship between death and predictors of death. Results of Cox regression were presented as Hazard ratio (HR) and confidence interval was 95%. Mortality was also assessed using the Kaplan-Meier curves with a log-rank test to compare mGPS 0_1 vs. 2 groups. The relative importance of any predictor in the Cox regression model was estimated by partial Chi-square value, which estimates the independent contribution of the predictor to the variance of the outcome. To assess the performance of the model, a calibration curve was used for the relationship between observed and predicted outcomes. All two-tailed p-values are considered statistically significant if $p< 0.05$.

RESULTS

A total of 259 patients [151 female (58.3%)] were included in the study. The patients were classified into two groups based on mGPS. The mGPS score was ≤1 in 172 (66%), 2 in 87 (34%) patients, respectively (Figure 1). During a median follow-up of 30 months [300 (40-1200 days)], a total of 55 patients (21.2%) died, and of these patients, 32 (36.7%) had an mGPS 2 on admission.

Patients with mGPS 2 on admission had a higher mortality rate than those with mGPS≤ 1. An mGPS score of two was associated with higher NT-proBNP levels [777 (112-4564) pg/mL vs. 350 (65-3521) pg/mL), respectively, $p< 0.0001$]. Patients with mGPS≤ 1 had higher frequency of DM compared to those with mGPS 2 [52 (30.2% vs. 14 (16.1%), $p= 0.014$]. There were no statistically significant differences in gender, smoking, hypertension, coronary artery disease, and chronic kidney disease between the two groups. Similarly, there were no statistically significant differences in troponin, MPV, and creatine levels among the two groups (Table 1).

In addition, the patients were compared according to their survival status. CAD [34 (69.4%) vs. 111 (52.9%), $p= 0.036$], smoking [20 (40.8 %) vs. 53 (25.2%), $p= 0.029$], NYHA class III [18 (36.7 %) vs. 35 (16.7%), $p< 0.001$], GWTG-HF risk score [31 (11-55) vs. 15 (11-45), $p< 0.001$], NT-proBNP [1352 (224-4451) pg/mL vs. 334 (66-4564) pg/mL, $p< 0.001$], and troponin [0.02 (0.01-2.1) ng/mL vs. 0.01 (0.01-2.1) ng/mL, $p= 0.003$)] levels were significantly higher in the deceased group (Table 2). Albumin, hemoglobin levels, and eGFR were significantly lower in the deceased group than that of survivors.

The relationship between nine candidate predictors and mGPS and death was examined in a model using both traditional univariable and multivariable Cox model analyses (Table 3). In multivariable Cox model, NT-proBNP (from 234 to 1255) [HR; 1.83 (1.32-2.55), $p< 0.001$], mGPS 2 vs. 0-1 [HR 2.43 (1.2-4.93), $p= 0.013$], and CAD [HR 3.15 (1.46-6.82), $p= 0.003$], were found to be independently associated with all-cause mortality, however, in multivariable model hypertension, age, hemoglobin, creatinine, and troponin levels and NYHA class were not associated with death (Table 3).

Table 1. Baseline characteristics of the total heart failure cohort with mid-range ejection fraction patients (n= 259) and according to mGPS groups

Variables	mGPS 0-1 (n= 172)	mGPS 2 (n= 87)	Overall (n= 259)	p
Age (years)	73 (52-94)	76 (50-94)	75 (50-94)	0.002
Gender (female)	92 (53.5%)	44 (50.6%)	136 (52.5%)	0.657
Ryhthm (AF)	82 (47.7%)	30 (34.5%)	112 (43.2%)	0.043
Smoking	49 (28.5%)	24 (27.6%)	73 (28.2%)	0.879
DM	52 (30.2%)	14 (16.1%)	66 (25.5%)	0.014
HT	120 (69.8%)	54 (62.1%)	174 (67.2%)	0.213
CAD	93 (54.1%)	52 (59.8%)	145 (56%)	0.383
CKD	2 (1.2 %)	7 (8%)	9 (3.5%)	0.004
NT-proBNP (pg/mL)	350 (65-3521)	777 (112-4564)	466 (65.8-4564)	<0.0001
Troponin T (ng/mL)	0.02 (0.01-2.1)	0.01 (0.001-2.1)	0.02 (0.01-2.1)	0.110
White Blood Cell	8.1 (4.4-32)	8.6 (5-22)	8.4 (4.4-32)	0.136
Hemoglobine	12.8 (7.5-16.5)	11.7 (8.8-15.8)	12.4 (7.5-16.5)	<0.001
MPV (fL)	9.9 (6.7-38.8)	10.3 (6.7-12)	9.9 (6.7-38.8)	0.219
Albumin (g/dL)	3.7 (2.9-4.5)	(2.9-3.99)	3.3 (0.4-3.2)	<0.001
Creatinine (mg/dL)	1.1 (0.4-1.9)	1 (0.6-3.2)	1 (0.4-3.2)	0.881
eGFR, mL/min/1.73 m^2	64.7 (27-146)	(19.2-135.7)	63.8 (19.2-135.7)	0.522
Crp (mg/dL)	1 (0.1-13.7)	1.7 (0.2-32.1)	1.1 (0.1-32.1)	<0.001
NYHA Class				
I	7 (4.1%)	3 (3.4%)	10 (3.9%)	
II	135 (78.5%)	61 (70.1%)	196 (75.7%)	0.240
III	30 (17.4%)	23 (26.4%)	53 (20.5%)	
GWTG-HF risk score	15 (11-55)	30 (11-55)	24 (11-55)	<0.001
Follow-up (days)	272 (60-1200)	300 (40-1180)	300 (40-1200)	0.250
Death	23 (13.3%)	32 (36.7%)	55 (21.2%)	<0.001

AF: Atrial fibrillation, DM: Diabetes mellitus, HT: Hypertension, CAD: Coronary artery disease, CKD: Chronic kidney disease, NT-proBNP: N-terminal prohormone of brain natriuretic peptide, eGFR: Estimated glomerular filtration rate, WBC: White blood cell, Hgb: Hemoglobin, MPV: Mean platelet volume, CRP: C-reactive protein, M-GPS: Modified Glasgow prognostic score, GWTG-HF: Get with the guidelines-heart failure, NYHA: The New York Heart Association functional class.

Three separate models for predicting all-cause mortality after the addition of albumin, CRP, and mGPS indices to the baseline model were compared via the assessment of fit (likelihood ratio Chi-square) and discrimination (C-index) (Table 4). The likelihood ratios were higher when compared baseline model (8 parameters except for mGPS). Likelihood improved to 49.97, 44.57, 51.44 when albumin and CRP were added to the baseline model, respectively. When mGPS was added to the baseline model, C-index increased to 0.779, and the likelihood ratio increased to 51.44. The relative importance of each predictor in the Cox model is depicted in Figure 2. Analysis of death by using the Kaplan-Meier survival curve is demonstrated in Figure 3 among mGPS group 2 vs. ≤1 (log-rank test result p< 0.001). The model's prediction in 1000 days and estimate of calibration function was slightly nonlinear and slightly underestimated our Cox predictive model. The corrected calibration depicts relative agreement with the apparent calibration; in our calibration plot, the mean error and quantile of error were 0.051, 0.091, respectively (Figure 4).

DISCUSSION

To our knowledge, this is the first study to have applied mGPS in ambulatory patients with HFmrEF measured at outpatient clinics and predicted poor survival among patients with HFmrHF. According to this study, mGPS was predictive of the outcomes of patients with heart failure with mildly reduced ejection fraction, independently of NT-proBNP and other parameters.

Table 2. Demographic, clinical, laboratory characteristics according to survival status

	Alive (n= 210)	Death (n= 49)	p
Age (years)	74 (52-94)	75 (50-91)	0.241
Gender (female)	113 (53.8 %)	23 (46.9%)	0.386
Ryhthm (AF)	92 (43.8 %)	20 (40.8%)	0.029
Smoking	53 (25.2 %)	20 (40.8%)	0.029
DM	51 (24.3 %)	15 (30.6%)	0.360
HT	145 (69 %)	29 (59.2%)	0.185
CAD	111 (52.9 %)	34 (69.4 %)	0.036
CKD	6 (2.9%)	3 (6.1 %)	0.261
NT-proBNP (pg/mL)	334.4 (65.8-4564)	1352 (224.2-4451)	<0.001
Troponin (ng/mL)	0.01 (0.01-2.1)	0.02 (0.01-2.1)	0.002
WBC	8.3 (4.4-32)	8.4 (5.1-22)	0.126
Hgb	12.4 (7.5-16.5)	11.7 (9.7-14.3)	0.011
MPV(fL)	9.9 (6.7-38.8)	10.2 (7.5-38.8)	0.549
Albumin (g/dL)	3.6 (2.9-4.5)	3.4 (2.9-4)	<0.001
Creatinine (mg/dL)	1 (0.4-3.2)	1.1 (0.6-1.9)	0.138
eGFR, mL/min/1.73 m^2	64.8 (19.2-146)	61.4 (27.3-135.7)	0.099
CRP (mg/L)	1.1 (0.1-32.1)	1.3 (0.1-16.9)	0.457
NYHA Class			
I	10 (4.8%)	0 (0%)	
II	165 (78.6%)	31 (63.3%)	<0.001
III	35 (16.7%)	18 (36.7%)	
GWTG-HF risk score	15 (11-45)	31 (11-55)	<0.001
Follow-up (days)	300 (60-1200)	270 (40-940)	0.006

AF: Atrial fibrillation, DM: Diabetes mellitus, HT: Hypertension, CAD: Coronary artery disease, CKD: Chronic kidney disease, NT-proBNP: N-terminal prohormone of brain natriuretic peptide, WBC: White blood cell, Hgb: Hemoglobin, MPV: Mean platelet volume, eGFR: Estimated glomerular filtration rate, CRP: C-reactive protein, M-GPS: Modified Glasgow prognostic score, GWTG-HF: Get with the guidelines-heart failure, NYHA: The New York Heart Association functional class.

Table 3. Cox proportional hazard, time fixed model for predicting death

Variables	Univariable Hazard Ratio and CI	p	Multivariable Hazard Ratio and CI	p
Hypertension	0.61 (0.34-1.08)	0.089	0.62 (0.32-1.19)	0.153
Age (increase from 65 to 82 years)	1.30 (0.84-2.02)	0.233	0.88 (0.54-1.45)	0.637
Hgb (increase from 11.2 to 13.8 gr/dL)	0.60 (0.40-0.89)	0.012	0.72 (0.45-1.16)	0.184
Creatinine (increase from 0.86 to 1.20 mg/dL)	1.17 (0.96-1.42)	0.108	0.85 (0.68-1.06)	0.162
NT-proBNP (increase from 234 to 1255 pg/mL)	1.95 (1.58-2.40)	<0.001	1.83 (1.32-2.55)	<0.001
mGPS score (2 vs. 0-1)	3.46 (1.94-6.17)	<0.001	2.43 (1.20-4.93)	0.013
Troponin (increase from 0.01 to 0.03 ng/mL)	1.02 (1.01-1.03)	0.001	0.99 (0.98-1.01)	0.846
CAD	1.91 (1.04-3.52)	0.036	3.15 (1.46-6.82)	0.003
NYHA class III vs. I and II	3.72 (2.05-6.75)	<0.001	0.92 (0.38-2.39)	0.865

Hgb: Hemoglobin, NT-proBNP: N-terminal prohormone of brain natriuretic peptide, mGPS: Modified Glasgow prognostic score, CI: Confidence interval, CAD: Coronary artery disease, M-GPS: Modified Glasgow prognostic score, NYHA: The New York Heart Association functional class.

Table 4. Model performance after the addition of albumin, Crp, and mGPS indexes to the baseline model for predicting all-cause mortality

	C-index	Likelihood ratio
Baseline model	0.766	44.56
Albumin model	0.769	49.97
Crp	0.777	44.57
mGPS model	0.779	51.44

Crp: C-reactive protein, mGPS: Modified Glasgow prognostic score
Baseline model: Hypertension, age, hemoglobin, creatinine, NT-proBNP, troponin, coronary artery disease, NYHA class.

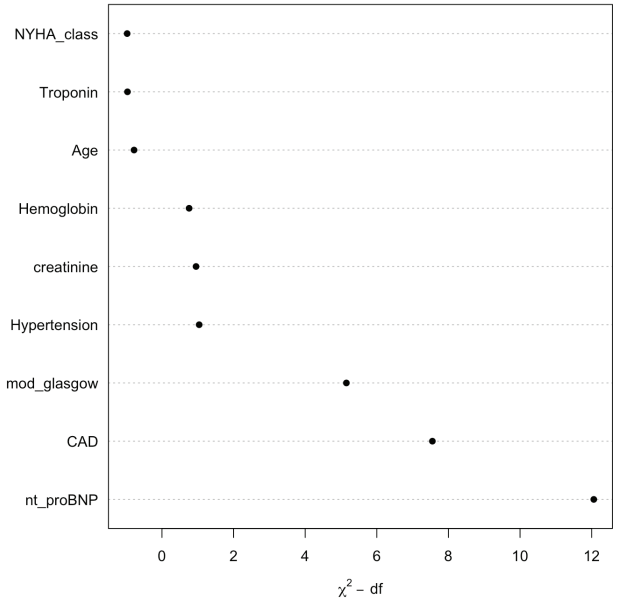

Figure 2. Relative importance of each predictor in the Cox regression model.

Inflammation may play a significant role in the pathogenesis and progression of heart failure[10,11]. Elevated inflammatory markers in HFrEF correlate with disease severity and prognosis[12]. The causality between heart failure and the pro-inflammatory state is not clear. Either inflammation is a direct cause of HF, and its role in the pathogenesis or progression of HFrEF has significant therapeutic implications. If inflammation is predominantly a marker of the disease, it may help clarify those patients who would benefit from aggressive therapy[13]. However, there is evidence that an elevated inflammatory state is a marker of disease severity and may induce the onset and progression of heart failure. Heart failure may develop based on comorbidities associated with low-grade chronic inflammation such as obesity, diabetes, and predisposing substrates such as endothelial dysfunction or atherosclerosis[14].

Malnutrition is relatively frequent in patients with HF. Malnutrition is triggered by multiple factors such as anorexia, malabsorption secondary to intestinal edema, high energy demand, and cytokine-induced hypercatabolism. In addition to body weight or body mass index (BMI) to assess nutritional status, there are many surrogate markers of nutritional status, e.g., albumin, lymphocyte, total cholesterol, etc. Malnutrition and its advanced form of cardiac cachexia are associated with poor prognosis in HF[15-17].

The current evidence suggests that HFmrEF is characterized by mixed pathophysiology. In addition, the trajectory of LV systolic function, i.e., whether a patient develops mildly reduced EF as a result of worsening versus improving EF and cause of HF, is crucial[18-22]. The pooled data from four community-based longitudinal cohorts showed that biomarkers, such as natriuretic peptides, cystatin-C, and high sensitivity troponin predicted incident HFmrEF[23]. Besides, they demonstrated that all-cause mortality of HFmrEF was worse than that of HFpEF (50 vs. 39 events per 1000 person-years) but similar to that of HFrEF (46 events per 1000 person-years). Interestingly, while natriuretic peptides had a higher association with the incidence of HFrEF than HFmrEF, they did not differ in their association with the incidence of HFmrEF and HFpEF. Another study conducted by Chioncel et al.[24] found that mortality rates at one year were 8.8% in patients with HFrEF, 7.6% in patients with HFmrEF, and 6.4% in patients with HFpEF. All-cause mortality was 12.7% in our study.

The mGPS is used as a simple predictor of prognosis in cancer patients[6]. The components of the score are easy to measure and well-standardized. Like cancer, heart failure is a systemic disease that shares an activated inflammatory response and nutritional decline. The association between mGPS and prognosis in HF patients has been studied in acute heart failure, stable heart failure, and heart failure with preserved ejection fraction[4,7,8]. Still, the authors did not analyze the results separately in patients with HFmrEF. No data on HFmrEF patients can be found in the literature. In addition to these studies, our study showed that the increased inflammatory response and malnutrition are typical in all stages of heart failure. Screening of immune-nutritional status by mGPS may provide additional information in predicting the prognosis of heart failure patients. Furthermore, this study suggests that in addition to NT-proBNP, mGPS may provide additional prognostic value. Patients with HFmrEF who had combined elevations of NT-proBNP and mGPS were at exceptionally high risk for one-year mortality.

Our findings suggest that screening for inflammation and malnutrition in all patients with HFmrEF might determine patients at superior risk of adverse events. In patients with high mGPS scores, identification of malnutrition may guide interventions for improvement of prognosis. Consequently, choosing patients at exceptional mortality risk may enable rapid and

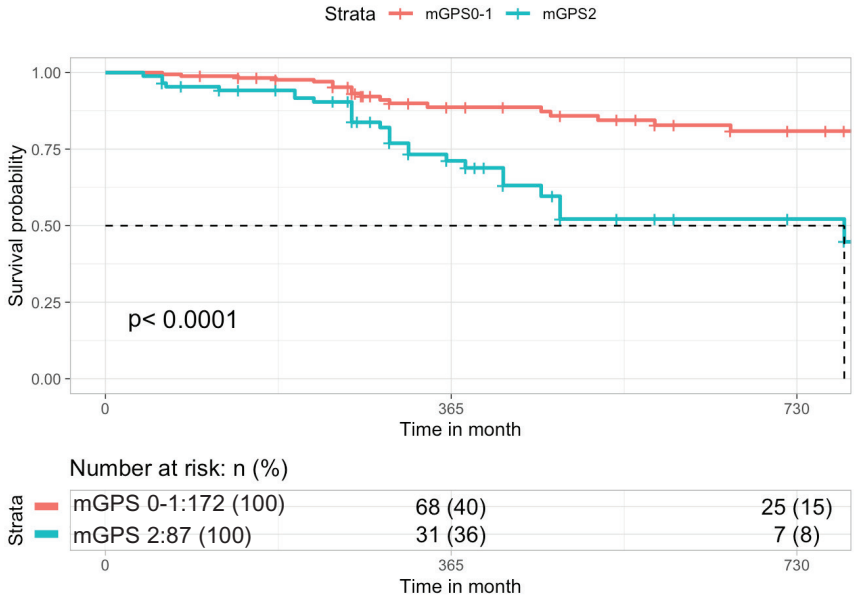

Figure 3. Analysis of death by using Kaplan-Meier curve depicted among mGPS (modified Glasgow prognostic score) Group 2 vs. ≤1 (p< 0.001).

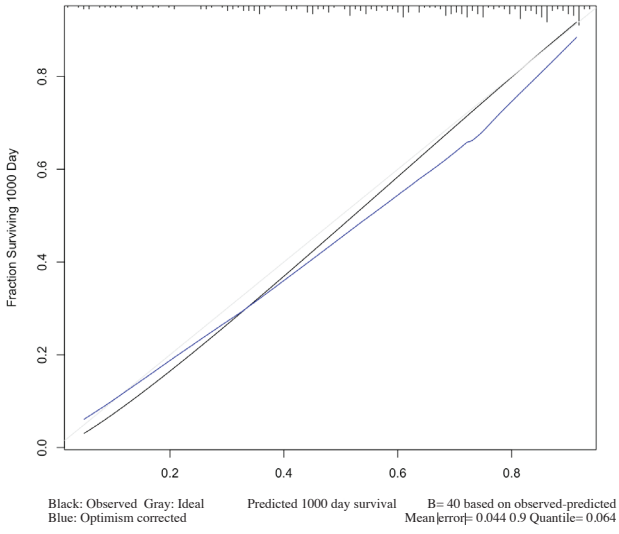

Figure 4. The model's prediction in 1000 days and estimate of calibration function was slightly nonlinear and slightly underestimated our Cox predictive model. The corrected calibration depicts relatively agreement with the apparent calibration; in our calibration plot, the mean error and quantile of error were 0.051, 0.091, respectively.

effective multidisciplinary collaboration involving dietary counseling, food/fluid enrichment, oral nutritional supplements, and educational interventions. However, there are numerous immune-nutritional screening tools but no guidelines on which to select for patients with all HF groups. Nevertheless, clinicians should notice the recent scientific proof to maintain practical and revealing nutrition guidance to patients for better survival.

Limitations

This study has been conducted in a single center. It was limited to the outpatient cardiology unit, and this study did not include hospitalized HFmrHF patients. Including only patients with laboratory data is another drawback of our study. Since our study was observational, the sample size may have limited the power to detect significant changes. Due to the nature of the regression analysis, an unmeasured confounder may exist that could be a significant predictor of death. Laboratory measurements were assessed only at a single time point, and serial follow-up measurements might provide further understanding. Not analyzing patients with HFpEF and HFrEF was another drawback of our study. Further prospective and multi-center studies are needed to determine the predictive value of mGPS in HFmrEF.

CONCLUSION

High mGPS, the immune-nutritional score, is an independent predictor of mortality during long-term follow-up in this newly described heart failure group. The mGPS, which combines CRP and serum albumin concentrations, helps predict all-cause mortality in ambulatory patients with HFmrEF. This study may provide a better understanding of the relationship between mid-range heart failure and immune-nutritional status.

Ethics Committee Approval: The approval for this study was obtained from Kocaeli Derince Training and Research Hospital Clinical Research Ethics Committee (Decision no: 2021-92, Date: 09.09.2021).

Informed Consent: This is retrospective study, we could not obtain written informed consent from the participants.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept/Design - TB, AK, MÇ; Analysis/Interpretation - TB, AİÇ, AK; Data Collection - FB, MÇ, NZB; Writing - FB, SK; Critical Revision - NZB, CK; Final Approval - CK, AİÇ, SK; Statistical Analysis - AK, MÇ; Overall Responsibility - FB.

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