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Original Article

High-Sensitivity Modified Glasgow Prognostic Score For Predicting In-Hospital Mortality In Elderly Patients With Non-ST Elevation Myocardial Infarction

ST Yükselmesiz Miyokard Enfarktüslü Yaşlı Hastalarda Hastane İçi Mortaliteyi Öngörmek İçin Yüksek Duyarlıklı Modifiye Glasgow Prognostik Skoru

Lale Dinc Asarcikli*[1], Habibe Kafes[2], Burak Acar[3], Duygu Inan[4], Duygu Genc[4], Sennur Unal[1]

[1]Dr. Siyami Ersek Cardiovascular and Thoracic Surgery Research and Training Hospital, Department of Cardiology, Istanbul, Turkey.

[2]University of Health Sciences, Ankara City Hospital, Department of Cardiology, Ankara, Turkey

[3]Kocaeli University Faculty of Medicine, Department of Cardiology, Kocaeli, Turkey

[4]Basakşehir Cam and Sakura City Hospital, Department of Cardiology, Istanbul, Turkey

Abstract

Aim: Inflammation and malnutrition are poor prognostic markers in acute coronary syndromes. In this study, we aimed to investigate the association between high-sensitivity modified Glasgow prognostic score (HS-mGPS), derived from C-reactive protein and serum albumin levels, and in-hospital mortality of elderly patients with non-ST elevation myocardial infarction (NSTEMI).

Material and Methods: Included subjects were recruited from three different tertiary health centers. Totally, 282 eligible patients aged >65 years with diagnosis of NSTEMI were retrospectively enrolled. Global Registry of Acute Coronary Events (GRACE) risk score for in-hospital mortality and HS-mGPS was calculated for each patient. Subjects were categorized according to their inflammation-based scores ((high HS-mGPS group (HS-mGPS ≥1, n=124) vs. low HS-mGPS group (HS-mGPS =0, n=158)).

Results: Both groups were similar regarding admission blood pressure levels, coronary angiography findings, treatment modalities and GRACE scores. Patients with high HS-mGPS had higher admission heart rate and longer hospitalization duration compared to low HS-mGPS group. In-hospital mortality rates were higher in high HS-mGPS group compared to low HS-mGPS group (21.8% (n=27) vs. 3.2% (n=5), respectively, P<0.001). GRACE risk score (HR:1.037, 95% CI: 1.009-1.065, P=0.008) and HS-mGPS ≥1 (HR:4.602, 95% CI: 1.581-13.391, P=0.005) were independent predictors of in-hospital mortality. Furthermore, in hospital mortality in HS-mGPS group was significantly higher than low HS-mGPS group in the Kaplan–Meier curve analysis (log rank P < 0.001).

Conclusion: High HS-mGPS is independently associated with in-hospital mortality in elderly patients with NSTEMI. Using this inflammation-based simple score could help in more precise risk estimation of elderly patients in daily practice.

Keywords: acute coronary syndrome; albumin; C-reactive protein; elderly patients; Glasgow prognostic score; myocardial infarction.

Corresponding Author*: Lale Dinc Asarcikli, Dr. Siyami Ersek Cardiovascular and Thoracic Surgery Research and Training Hospital, Department of Cardiology, Istanbul, Turkey.
e-mail: mdlaledinc@gmail.com
ORCID: 0000-0002-7828-9487
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Öz

Amaç: Akut koroner sendromlarda inflamasyon ve malnütrisyon kötü prognostik belirteçlerdir. Bu çalışmada, ST yükselmesiz miyokard enfarktüslü (STYsizME) yaşlı hastalarda C-reaktif protein ve serum albümin düzeylerinden elde edilen yüksek duyarlıklı modifiye Glasgow prognostik skoru (HS-mGPS) ile hastane içi mortalite arasındaki ilişkiyi araştırmayı amaçladık.

Gereç ve Yöntemler: Çalışmaya dahil edilen hastalar üç farklı üçüncü basamak sağlık merkezinden alındı. 65 yaş üstü STYsizME tanısı almış 282 uygun hasta geriye dönük olarak kaydedildi. Hastane içi ölüm için GRACE risk skoru ve HS-mGPS her hasta için hesaplandı. Hastalar, inflamasyona dayalı skorlarına göre kategorize edildi (yüksek HS-mGPS grubu (HS-mGPS ≥1, n=124)' e karşın düşük HS-mGPS grubu (HS-mGPS =0, n=158).

Bulgular: Çalışma grupları arasında hastaneye yatış kan basıncı düzeyleri, koroner anjiyografi bulguları, tedavi modaliteleri ve GRACE skorları arasında fark yoktu. Yüksek HS-mGPS'li hastalar, düşük HS-mGPS grubuna kıyasla daha yüksek başvuru kalp hızına ve daha uzun hastanede kalış süresine sahipti. Hastane içi ölüm oranları yüksek HS-mGPS grubunda, düşük HS-mGPS grubuna kıyasla daha yüksekti (sırasıyla %21,8 (n=27)' e karşın %3,2 (n=5), P<0.001). GRACE risk skoru (HR:1,037, %95 GA: 1,009-1,065, P=0,008) ve HS-mGPS ≥1 (HR:4,602, %95 GA: 1,581-13,391, P=0,005) hastane içi mortalitenin bağımsız öngörücüleriydi. Bununla beraber Kaplan Meier analizinde HS-mGPS ≥1 grubunda hastane içi mortalite HS-mGPS =0 grubuna göre beirgin olarak daha yüksekti (long rank testinde P<0,001).

Sonuç: Yüksek HS-mGPS, STYsizME' lü yaşlı hastalarda hastane mortalitesi ile bağımsız olarak ilişkilidir. Hesaplaması basit olan bu inflamasyona dayalı skoru kullanmak, yaşlı hastalarda daha kesin risk tahminine yardımcı olabilir.

Anahtar kelimeler: akut koroner sendrom; albümin; C-reaktif protein; Glasgow Prognostik Skoru; miyokard enfarktüsü; yaşlı hastalar.

Introduction

The term "acute coronary syndrome" (ACS) refers to a wide range of cardiac entities, considering unstable angina pectoris, non-ST elevation myocardial infarction (NSTEMI), and ST elevation myocardial infarction (STEMI). Recently, incidence of ACS demonstrates a shift toward elder population [1]. Elder patients present unfavorable outcomes, due to several comorbidities, including chronic kidney disease, hypertension, anemia, cognitive impairment and frailty, [2]. Early risk stratification and prompt treatment are essential to prevent morbidity and mortality in ACS. Risk stratification strategies including Thrombolysis in Myocardial Infarction (TIMI) [3] and Global Registry of Acute Coronary Events (GRACE) scores, have been found to be associated with in-hospital mortality and major adverse cardiac events (MACE) [4]. Although these scores were well studied, they did not include inflammatory markers in scoring system.

The atherosclerotic process starts with infiltration of lipid-loaded macrophages and microinflammation in the arterial wall. More than half of patients with ACS have increased high-sensitivity C-reactive protein (hs-CRP) [5]. Inflammation plays a major role particular with plaque rupture in ACS pathophysiology. Inflammatory biomarkers such as fibrinogen, hs-CRP, [6]. CRP to albumin ratio, prognostic nutritional index was investigated in severity and risk stratification of patients with ACS [7, 8]. Serum CRP levels correlate with the degree of inflammation, which is associated with atherosclerotic plaque burden, endothelial dysfunction and prognosis of cardiovascular diseases [5]. Serum albumin levels represent both degree of nutritional status and inflammation as it has been known as negative acute phase reactant. On the other hand, albumin has a protective effect by anti-oxidant property, and has an antiplatelet effect by modulating arachidonic acid metabolism [9]. Modified Glasgow Prognostic Score (mGPS) is a simple inflammation-based risk score derived from albumin and CRP, that provides prognostic value in patients with malignancy [10], heart failure [11] and patients hospitalized in the coronary care unit [12]. High-sensitivity mGPS (HS-mGPS) is more sensitive than mGPS on the basis of prediction of prognosis in cancer patients [13].

Patients aged >65 years are characterized by calcific complex coronary anatomy and multiple comorbidities including frailty, which increases periprocedural complications. In elderly patients with acute MI, GPS has recently been found to be a good predictor of in-hospital mortality and MACE [7]. However, there is no evidence of an association between HS-mGPS and in-hospital mortality in elderly patients, particularly those with NSTEMI.

The study aims to determine whether HS-mGPS is a predictor for the determination of major in-hospital adverse cardiac events in elderly patients hospitalized with NSTEMI.

Material and Methods

Study Population:

The present study was multi-center, retrospectively designed to evaluate the prognostic role of HS-mGPS in elderly hospitalized patients with NSTEMI. Patients were recruited from three tertiary hospitals (Dr. Siyami Ersek Cardiovascular Surgery Center, Kocaeli University Faculty of Medicine Hospital, Turkiye Yuksek Ihtisas Hospital) between January 2018 and January 2019. Hospitalized patients aged >65 years with NSTEMI according to standard definitions by European Society of Cardiology [14] were retrospectively screened. Of all screened elderly 628 consecutive patients, 346 patients (history of active malignancy and acute infection (n=52), connective tissue disorders, proteinuria, protein losing enteropathy (n=18), those not performed coronary angiography (n=142), those treated with emergency coronary artery bypass graft surgery (n=12), and patients with incomplete data in the hospital records (n=122)) were excluded from the study as presented with details in Figure 1. In total, eligible consecutive 282 elderly NSTEMI patients enrolled in the study.

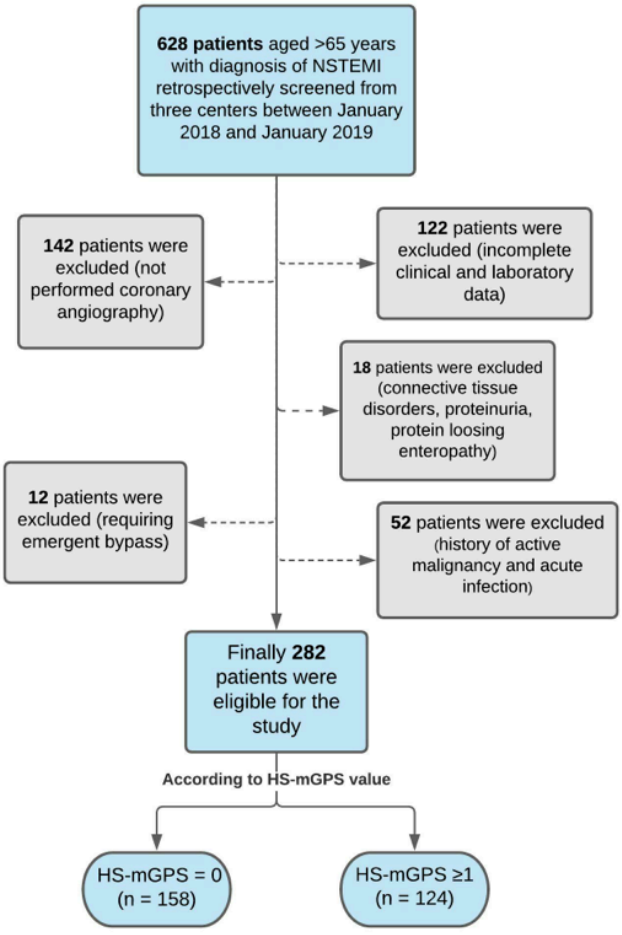

Figure 1: Flow chart of study population allocation. NSTEMI, non-ST elevation myocardial infarction; HS-mGPS, high-sensitivity modified Glasgow Prognostic Score.

Data collection:

Patients' demographic characteristics and related clinical information regarding laboratory values, medications, clinical follow-up data and in-hospital MACE (including cardiovascular death, ischemic cerebrovascular accident, and reinfarction) were obtained from the hospital's electronic database. The patient's laboratory data, left ventricular ejection fraction (LVEF), heart rate, and blood pressure were measured at the time of admission. All laboratory analyses were conducted using standard validated methods in each center's laboratory department. All blood tests, including lipid parameters, albumin and hs-CRP levels, were collected within the first 24 h of admission.

GRACE risk score for in-hospital mortality [4] and high-sensitivity modified Glasgow prognostic scores (HS-mGPS) [15] were calculated (0 points if CRP≤0.3g/dl, 1 point if CRP>0.3g/dl and Alb ≥3.5g/dl, 2 points if CRP>0.3g/dl and Alb<3.5g/dl) for each patient and the relationship between scores and in-hospital MACEs were analyzed. According to current guidelines, all patients were treated with standard care [14].

Institutional local ethics committee approved the study protocol (05.07.2021, HNEAH-KAEK 2021/KK/191) in accordance with the principle of the Declaration of Helsinki.

Statistical analysis

Statistical analysis was performed using SPSS software version 20.0 (SPSS Inc., Chicago, IL). To determine normality, the Kolmogorov-Smirnov test was used. Non-normally distributed continuous variables were reported as median (interquartile range), normally distributed continuous data were reported as mean ± standard deviation. The numbers and percentages were used for categorical data. The student's t-test was used to analyze normally distributed continuous variables, while the Mann-Whitney-U test was used to analyze non-normally distributed and ordinal variables. A chi-square test was used to analyze categorical data. Cox proportional hazards regression models were used to estimate the univariate and multivariate associations between possible factors and in-hospital mortality. Variables that had P <0.05 in the univariate analysis were further analyzed with multivariate Cox regression model to identify significant variables (P <0.05) predictors of mortality. Kaplan–Meier survival analysis was used to calculate cumulative survival of MGPS and survival curves were compared using log-rank tests. A p value of 0.05 was considered statistically significant.

Table 1: Demographic, clinical and laboratory parameters of the study subjects according to HS-mPGS.				
Characteristics		HS-mGPS =0 (n=158)	HS-mGPS ≥1 (n=124)	P value
Age, years		72.2 ± 4.5	71.9 ± 4.7	0.604
Male gender, n		102 (64.6%)	65 (57.5%)	0.240
Diabetes mellitus, n		60 (38.0%)	51 (41.1%)	0.590
Hypertension, n		115 (72.8%)	91 (73.4%)	0.910
Chronic renal disease, n		8 (5.1%)	5(4.5%)	0.833
COPD, n		8 (5.1%)	11 (8.9%)	0.199
Smoking, n	none	79 (50.0%)	67 (54.0%)	0.083
	active	22 (13.9%)	26 (21.0%)	
	quitting	57 (36.1%)	31 (25.0%)	
Peripheral arterial disease, n		2 (1.3%)	4 (3.5%)	0.210
Hemoglobin, g/dL		13.2 ± 1.8	13.2 ± 1.6	0.873
WBC, ×103 µl		8.2 (9.7-6.9)	9.0 (10.6-7.3)	0.027
eGFR, ml/min/1.73m2,		71.7 (78.3-58.0)	70.8 (83.1-52.3)	0.646
LDL, mg/dL		115.1 ± 40.2	119.0 ± 35.9	0.438
Admission troponin, ng/ml		3.97 (5.0-0.5)	4.3 (9.3-2.0)	0.001
Continuous variables are either given as mean +/- SD or as median and IQR. SD, standard deviation; IQR, interquartile range; HS-mGPS, high-sensitivity modified Glasgow Prognostic Score; COPD, chronic obstructive pulmonary disease; WBC, white blood cell; eGFR, estimated glomerular filtration rate; LDL, low-density lipoprotein				

Results

The baseline demographic, clinical, and laboratory parameters of the study are summarized in Table 1. The subjects were categorized according to the HS-mGPS: HS-mGPS = 0 (n = 158, 56.0%) and HS-mGPS ≥1 (n = 124, 44.0%). Both groups were similar in terms of age, gender and comorbidities such as diabetes mellitus, hypertension, chronic renal disease and smoking status. Patients with high HS-mGPS had higher white blood cell (WBC) count, and higher admission troponin levels. Clinical findings and in-hospital outcomes of study subjects were presented in Table 2. Admission blood pressure levels, coronary angiography findings, treatment modalities and in-hospital GRACE scores were not different between study groups. Patients with high HS-mGPS had higher admission heart rate and longer hospitalization duration compared to the low HS-mGPS group.

Table 2: Clinical characteristics and in-hospital outcomes of the patients.				
Characteristics		HS-mGPS =0 (n=158)	HS-mGPS ≥1 (n=124)	P value
In-hospital mortality, n		5 (3.2%)	27 (21.8%)	<0.001
Ischemic cerebrovascular accident, n		0 (0.0%)	2 (1.6%)	-
Reinfarction, n		0 (0.0%)	0 (0.0%)	-
Hospitalization time, days		5 (7-3)	6 (10-4)	<0.001
Diastolic blood pressure, mmHg		88 (96-78)	86 (97-78)	0.731
Systolic blood pressure, mmHg		156 ± 27	153.1 ± 27.8	0.266
Heart rate, beat per minute		80 (93-66)	86.5 (101.5-72)	0.048
In hospital GRACE risk score		116 (133-106)	123 (143-109)	0.053
Left ventricular ejection fraction, %		45.9 ± 10.0	46.4 ± 8.5	0.674
Treatment, n	Medical	46 (29.1%)	23 (18.5%)	0.080
	PCI	86(54.4%)	72 (58.1%)	
	CABG	26 (16.5%)	29 (23.4%)	
Three vessel diseases, n		33 (20.9)	34 (30.1%)	0.083
Left main disease, n		7 (4.4%)	7 (5.6%)	0.641
Continuous variables are either given as mean +/- SD or as median and IQR. HS-mGPS, high-sensitivity modified Glasgow Prognostic Score; GRACE, Global Registry of Acute Coronary Events; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grefting				

A total of 34 (12.0%) patients had in-hospital MACE, and 32 (11.4%) patients died during hospitalization. In-hospital mortality rates were 21.8% (n=27) in the high HS-mGPS group, whereas in-hospital mortality rates were 3.2% (n=5) in the low HS-mGPS group. Cerebrovascular accident was observed only in two patients (1.6%) with high HS-mGPS while no event was observed in the low HS-mGPS group. No reinfarction was observed in both groups.

Clinical parameters that reached clinical significance (P<0.05) at the univariate analysis were included in multivariate analysis, as shown in Table 3. The HS-mGPS≥1 (HR:4.602, 95% CI: 1.581-13.391, P=0.005) and GRACE risk score (HR:1.037, 95% CI: 1.009-1.065, P=0.008) were found to be independent predictors of in-hospital mortality in multivariate regression analysis. In hospital mortality in HS-mGPS group was significantly higher than low HS-mGPS group in the Kaplan–Meier curve analysis (log rank p < 0.001) (Figure 2).

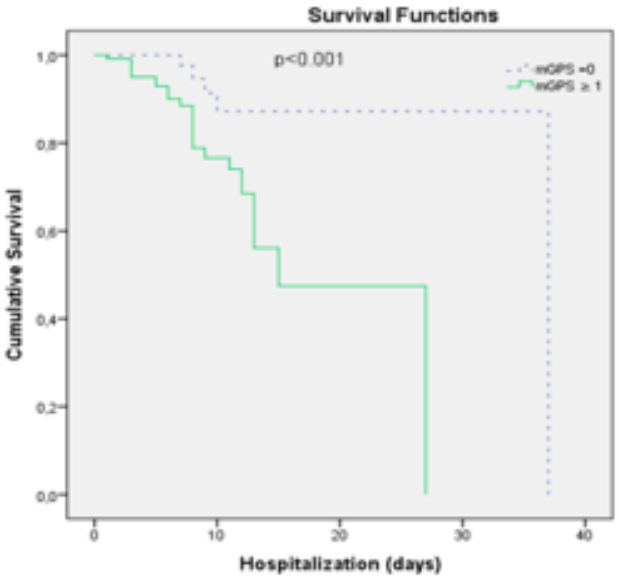

Figure 2: Kaplan–Meier curve analysis showed that in-hospital mortality in HS-mGPS group was significantly higher than low HS-mGPS (log rank P < 0.001).

Table 3: Cox regression analysis of mortality in hospital setting.

	Univariate			Multivariate		
Variables	HR	95% CI	P	HR	95% CI	P
Age	1.009	0.933-1.090	0.831			
LVEF	0.952	0.905-1.001	0.053			
HS-mGPS ≥1	5.434	1.891-15.618	0.002*	4.602	1.581-13.391	0.005
GRACE risk score	1.042	1.023-1.062	<0.001*	1.037	1.009-1.065	0.008
Male gender	3.308	0.966-11.332	0.057			
Systolic blood pressure	0.981	0.968-0.995	0.008*	0.993	0.976-1.009	0.378
Heart rate	1.016	1.003-1.028	0.012*	0.998	0.983-1.014	0.836
Treatment modality	0.827	0.445-1.539	0.550			
White blood cells	1.143	0.992-1.316	0.064			
Admission troponin	1.048	0.976-1.125	0.198			
eGFR	0.982	0.963-1.002	0.071			
LDL	1.014	0.999-1.029	0.072			

*All clinically relevant parameters were included in the model. Only parameters that reached statistical significance at univariable analysis were included in multivariate analysis. CI, confidence interval; HR, hazard ratio; LVEF, left ventricular ejection fraction; HS-mGPS, high-sensitivity modified Glasgow Prognostic Score; GRACE, Global Registry of Acute Coronary Events; eGFR, estimated glomerular filtration rate; LDL, low-density lipoprotein.

Discussion

This is the first study to examine the value of HS-mGPS, which reflects inflammation and nutritional status of the subject, for predicting in-hospital mortality of elderly patients with NSTEMI. In this study, we found that those with a higher HS-mGPS at admission had a higher rate of in-hospital mortality. Multivariate Cox regression analysis revealed that GRACE risk score and HS-mGPS ≥1 on admission were found to be independent predictors of in-hospital mortality.

As the population becomes aging, physicians are confronted with the growing number of elderly patients presenting with ACS. Atypical presentation and prehospital delay contribute late diagnosis of ACS in elderly population. Despite having more severe calcific coronary artery lesions than their younger counterparts, elderly patients are less likely to be treated with invasive strategies, and experience more adverse outcomes [15]. Frailty and malnutrition are prevalent in patients older than 65 years. Previous data have reported that frailty and

malnutrition was related to increased inflammatory markers like CRP and interleukin-6 (IL-6) as well as decreased serum albumin levels [16]. With these findings, we can speculate that elder subjects might have higher HS-mGPS. In individuals with ACS, both systemic inflammatory response and malnutrition are useful predictors of prognosis [17].

CRP, an acute phase protein, is the most preferred biomarker for inflammation and current findings have presented the relation of high CRP levels with poor outcomes in patients with ACS [18, 19]. Systemic inflammation contributes to the stability of atherosclerotic plaques and is a risk factor for atherosclerosis. Thrombotic products increase the production of IL-6 and CRP, which result in thrombosis and inflammation in ACS [20]. Additionally, serum albumin plays an antiaggregatory role by increasing prostaglandins. As a result, a decrease in albumin may result in an increase in blood viscosity [21]. For this reason, combination of CRP and serum albumin levels to compose the HS-mGPS may be able to predict the nutritional and inflammatory condition of a patient with ACS, which has already been known as prognostic marker for patients with ACS [22-24]. HS-mGPS is easier to calculate than GRACE and SYNTAX scores. Because the HS-mGPS depends on the levels of CRP and albumin in the peripheral blood. Although aforementioned scores were well studied, they did not consider the nutritional status of included individuals. To combine HS-mGPS with GRACE or SYNTAX scores will be useful for comprehensive evaluation of elderly patients with NSTEMI.

In elderly patients with NSTEMI, inflammatory response and inadequate protein or caloric intake results in hypoalbuminemia. A decrease in serum albumin levels has been linked to a poor prognosis in ACS in recent studies [25]. Serum albumin is an important parameter of the HS-mGPS, which is a marker of inflammation and nutrition status, which has been associated with prognosis of patients with ACS [24]. In a study, it was reported that there is a substantial link between having a higher GPS and having a higher mortality rate for patients with STEMI [23].

This study has a number of significant limitations. It was conducted retrospectively, and we solely assessed the patients' in-hospital outcomes. Long-term monitoring studies could provide a more comprehensive interpretation of the inflammation-based prognostic score's predictive value. In addition, only admission levels of CRP and serum albumin were assessed, although serial assessments of these parameters could give additional prognostic value. Finally, laboratory analyses were not performed in the core laboratory, they were performed in the laboratory of each center.

Conclusion

High HS-mGPS is independently associated with in-hospital mortality in elderly patients with NSTEMI. As a result, assessing patients' nutritional-inflammatory profile at the time of admission to the hospital can better determine in-hospital mortality in elderly patients with NSTEMI.

Declaration of conflict of interest

The authors received no financial support for the research and/or authorship of this article. There is no conflict of interest

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