

# Modified Glasgow prognostic score predicts perioperative adverse events in elderly patients undergoing hip fracture surgery

Ahmet Emrah Acan<sup>1</sup>, Cem Yalin Kilinc<sup>2</sup>

<sup>1</sup>Balikesir University, Faculty of Medicine, Department of Orthopaedics and Traumatology, Balikesir, Turkey

<sup>2</sup>Mugla Sitki Kocman University, Faculty of Medicine, Department of Orthopaedics and Traumatology, Mugla, Turkey

Copyright © 2020 by authors and Annals of Medical Research Publishing Inc.

## Abstract

**Aim:** The association between modified Glasgow prognostic score (mGPS) and prognosis in patients undergoing hip fracture surgery (HFS) has not been studied. Therefore, we aimed to evaluate the predictive value of mGPS in outcomes of patients undergoing HFS.

**Material and Methods:** A total of 301 adult patients aged  $\geq 65$  years, undergoing HFS were included in this retrospective study. The mGPS was scored according to C-reactive protein (CRP) and albumin levels at enrolment. Patients with both elevated CRP ( $>1$  mg/dL) and hypoalbuminemia ( $<3.5$  g/dL) are given mGPS of 2, patients with serum CRP  $\leq 1$  g/dL with or without hypoalbuminemia received scores of 0. Patients with only elevated CRP levels received mGPS of 1. Primary outcome of the study was major perioperative adverse medical events defined as cardiovascular and noncardiovascular complications.

**Results:** A total of 38 patients (12.6%) experienced perioperative adverse medical events. Compared to patients without perioperative complications, patients with adverse events were more likely to have higher mGPS levels prior to surgery. Multivariate analysis showed that higher mGPS at presentation was an independent predictor of perioperative adverse medical events in patients undergoing HFS.

**Conclusion:** This is the first study which demonstrates that mGPS is a predictor of adverse events in patients with undergoing HFS.

**Keywords:** Modified glasgow prognostic score; hip fracture; surgery

## INTRODUCTION

There has been substantial growth in the number hip fracture surgeries (HFS) performed in the world over the last decades (1). Most of the patients undergoing HFS are elderly people who have various comorbidities resulting in several medical and surgical complications (2). Cardiopulmonary adverse events, pulmonary complications, gastrointestinal bleeding, and neurological alterations are the most common medical complications (3,4). These complications negatively impact outcomes, increase the length of stay and increase costs in HFS patients (3,4). Preoperative risk assessment has gained importance in recent years in patients undergoing HFS due to aging society. However, clinical and laboratory preoperative risk assessment of hip fracture patients is often complicated.

Since patients with hip fracture are older and have a high co-morbidity burden, malnutrition, inflammation, and immune dysfunction are expected to be common problems in these patients (5,6). Although malnutrition is associated with adverse outcomes in HFS patients, the significance of biomarkers of malnutrition or inflammation have not been well studied in HFS patients (7). The body mass index and serum albumin levels are often used as markers of malnutrition but previous data showed that they can be affected by many factors (8,9). To overcome these limitations, several objective nutritional indexes have been developed. The modified Glasgow prognostic score (mGPS) is based on serum albumin and C-reactive protein (CRP) concentrations which are measured as routine preoperative screening tests before HFS (10). Although Glasgow prognostic score was originally proposed to assess the risk in cancer patients undergoing

Received: 02.10.2019 Accepted: 09.12.2019 Available online: 19.02.2020

Corresponding Author: Ahmet Emrah Acan, Balikesir University, Faculty of Medicine, Department of Orthopaedics and Traumatology, Balikesir, Turkey E-mail: dremrahacan@hotmail.com

surgery, it has been used for predicting the outcome in other diseases like idiopathic pulmonary fibrosis, systemic lupus erythematosus, and inflammatory bowel diseases in recent years (11-14).

However, the importance of the assessment of immunonutritional status using mGPS in HFS patients remains unclear. Therefore, we aimed to evaluate the predictive value of mGPS for perioperative medical adverse events in patients with hip fracture.

## MATERIAL and METHODS

This is a single center, retrospective, and observational study included all patients aged 65 years or older who underwent HFS (hemiarthroplasty, total hip arthroplasty, hip screw or femoral nail) between January 2017, and May 2019 in our tertiary university hospital were eligible for the study.

Patients who had a hip fracture due to high-energy trauma such as traffic accident were excluded and only hip fracture patients due to low-energy trauma were included. Patients who were treated conservatively and patients with an American Society of Anesthesiologists (ASA) classification of 5 were not included in this study. Patients with chronic inflammatory diseases which may influence the status of mGPS were also excluded from the study.

## Data collection

Patient demographic and clinical characteristics were obtained from patient medical records. Blood samples were obtained at admission to the hospital. Patients were classified into three groups according to mGPS; patients with both elevated CRP (>1 mg/dL) and hypoalbuminemia (<3.5 g/dL) were allocated a score of 2; patients with only CRP >1 mg/dL were allocated a score of 1; and patients with neither of these abnormalities were allocated a score of 0 (Table 1). The study was approved by local institutional review board.

**Table 1. Definition of modified Glasgow Prognostic Score**

Description	mGPS score
CRP ≤ 1g/dL and albumin ≥ 3.5 g/dL	0
CRP > 1g/dL (regardless of albumin level)	1
CRP > 1g/dL and albumin < 3.5 g/dL	2

**Abbreviations: CRP; C-reactive protein, mGPS; modified Glasgow Prognostic Score**

**Table 2. Comparison of patients who reached and did not reach the primary outcome**

	Without events (n = 263)	With events (n = 38)	p value
<b>Gender (female)</b>	195 (74.1)	28 (73.6)	0.356
<b>Age, years</b>	81.2±9.0	84.0±11.2	0.001
<b>Body mass index, kg/m<sup>2</sup></b>	27 ±9.5	28 ±9.4	0.136
<b>Smoking</b>	52 (19.8)	11 (28.9)	0.081
<b>Comorbidities</b>			
Hypertension	190 (72.2)	28 (73.7)	0.653
Diabetes mellitus	66 (25.1)	10 (26.3)	0.487
Chronic kidney disease	22 (8.4)	2 (5.3)	0.432
Coronary artery disease	60 (22.8)	8 (21.1)	0.165
Cerebrovascular disease	16 (6.1)	2 (5.2)	0.365
Chronic obstructive pulmonary disease	30 (11.4)	10 (26.3)	0.035
Atrial fibrillation	70 (26.7)	18 (47.3)	0.001
<b>Laboratory data</b>			
Fasting blood glucose, mg/dl	99 (90 – 155)	98 (92 – 152)	0.165
Serum creatinine, mg/dl	0.82 (0.7 – 1.0)	0.81 (0.7 – 1.1)	0.378
Hemoglobin, g/dl	12.2 (12.2 – 14.3)	12.7 (11.7 – 14.4)	0.652
Albumin, g/dl	3.6±0.64	3.2±0.52	0.032
C-reactive protein, mg/dL	2.2±3.1	4.5±5.4	0.004
<b>ASA physical status</b>	3.2±0.6	3.6±0.8	0.001
<b>Modified Glasgow prognostic score</b>	0.54 ± 0.63	1.12 ± 0.68	<0.001
<b>Length of stay (days)</b>	8.4 ± 9.3	11.4 ± 9.5	0.003

**Abbreviation: ASA, American Society of Anesthesiologists.**

**Data are presented as median with the first and third quartile (Q1 – Q3), number (%) or mean±SD**

## Study Outcomes

Primary outcome of the study was in-hospital major perioperative adverse medical events including cardiovascular and noncardiovascular complications, and secondary outcome was length of postoperative stay in hospital. Cardiovascular complications were defined as acute heart failure, death due to cardiac reasons, cardiac arrest, pulmonary embolism, severe arrhythmias, acute coronary syndrome, and ischemic stroke. Noncardiovascular complications were defined as pneumonia, respiratory failure, acute kidney injury, wound infection, bacteremia, and bleeding.

## Statistical analysis

All analyses were performed using SPSS software ver. 22.0 (IBM, Armonk, NY, USA). Multivariable analyses were performed to determine independent predictors of perioperative medical adverse events in patients undergoing HFS. The effectiveness of mGPS for predicting outcome was assessed by area under the receiver operating characteristic curves.

## RESULTS

A total of 360 patients underwent HFS in our institution during the study period. Preoperative CRP and/or albumin measurements were missing in 23 patients and these patients were excluded. Twenty patients were excluded because they were younger than 65 years of age, 11 patients were excluded due to concomitant diseases or use of immunosuppressive drugs, and 5 patients were excluded due to scored an ASA physical status 5 (Figure 1). Therefore, the final study population consisted of 301 patients (mean age  $83.4 \pm 9.8$  years, 74.1% female).

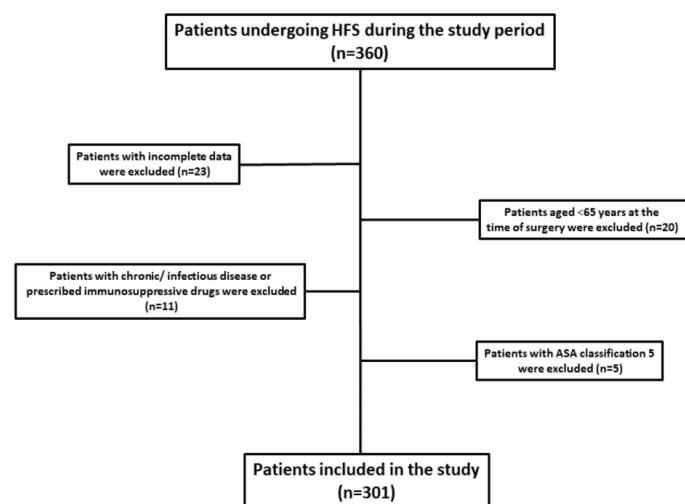


Figure 1. Flow chart of patients including exclusion criteria

A total of 38 patients (12.6%) experienced perioperative complications. Demographic, clinical, and laboratory characteristics of patients on admission who reached the endpoint relative to the rest of the cohort are shown in Table 2. Patients with perioperative complications were older, were more likely to be current smokers, had higher preoperative ASA scores, and had higher prevalence

of chronic obstructive pulmonary disease and atrial fibrillation at presentation compared to patients without perioperative complications. Patients with events had lower albumin, but higher CRP levels than those without events.

Postoperative length of stay was prolonged in patients who experienced perioperative complications ( $11.4 \pm 9.5$  vs  $8.4 \pm 9.3$  d,  $p = 0.003$ ). Patients with higher mGPS were more likely to experience complications than the patients with lower mGPS levels ( $1.12 \pm 0.68$  vs.  $0.54 \pm 0.63$ , respectively;  $p < 0.001$ ).

Table 3. Multivariate analysis for the prediction of primary composite endpoint

	Odds Ratio	95% CI	P
Age (per 1 y)	2.65	1.21-4.55	<0.01
ASA physical status	1.79	0.99-2.64	0.003
Modified Glasgow Prognostic Score	2.51	1.19-5.46	0.005
0	1		
1	2.32	1.25-4.87	0.01
2	3.76	2.11-5.55	<0.01

Abbreviation: ASA, American Society of Anesthesiologists

## Predicting clinical outcome

On univariate analyses, older age, higher ASA scores, presence of atrial fibrillation, higher CRP and mGPS but lower albumin levels at admission were significantly associated with perioperative adverse events. However, multivariate analyses showed that only age (OR: 2.65, 95% CI 1.21-4.55,  $p < 0.01$ ), ASA physical status (OR: 1.79; 95% CI, 0.99 to 2.64;  $p = 0.03$ ), mGPS 1 (OR: 2.32, 95% CI 1.25-4.87,  $p = 0.01$ ), mGPS 2 (OR: 3.76, 95% CI 2.11-5.55,  $p < 0.01$ ) were independently associated with adverse events (Table 3).

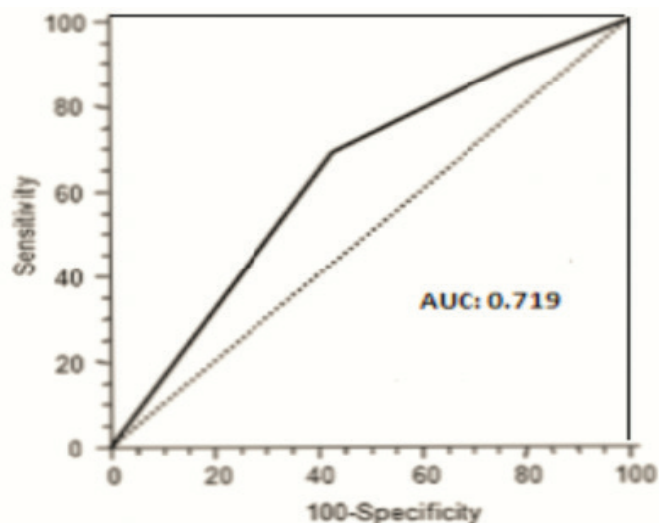


Figure 2. Receiver operating characteristic curves for mGPS in the prediction of perioperative medical complications following HFS. The area under the receiver operating characteristic curve (AUC) for mGPS was 0.719.

After adjustment for other co-variables, mGPS remained a significant prognostic factor ( $p < 0.001$ ). The receiver operating characteristic curve analysis revealed that area under the curve of mGPS in prediction of postoperative complications was 0.719 (Figure 2).

## DISCUSSION

To our knowledge, this is the first study to evaluate the predictive value of mGPS in HFS patients. Our study demonstrated that 12.6% of elderly patients who underwent HFS experienced perioperative medical adverse events and mGPS was an independent predictor of these complications. Patients with higher preoperative mGPS were at higher in-hospital risk of complications.

Several studies have reported the utility of prognostic risk scores, biomarkers, and nutritional indices for predicting prognosis following HFS (15-17). Objective tools and indices assessing the immunonutritional condition such as mGPS, prognostic nutritional index (PNI), and geriatric nutritional risk index (GNRI) have been developed and used to predict outcome in patients with various diseases (18,19).

However, prevalence of malnutrition and prognostic value of immunonutritional indices have not been well investigated in patients undergoing HFS. Malafarina et al. reviewed 44 studies including 26,281 patients (20). The prevalence of malnutrition was ranged from 18.7% to 45.7% according to the different nutritional assessment tools (20). The authors found that whatever the method used for the diagnosis of malnutrition, it was associated with an increased mortality (20).

Approximately one-third of the patients with hip fracture experience an infective complication during their hospital stay (21). Since age-related immune dysfunction is one of the most important reasons of these infections, preoperative analysis of immunological status before HFS is crucial. In a recent prospective study, Ren and colleagues examined the relationship between the CRP/PNI ratio and 1-year mortality in 80 elderly patients undergoing HFS (22). They showed that CRP/PNI was an important predictor of one-year mortality in HFS patients (22).

Glasgow Prognostic Score and mGPS have been used for predicting outcome of patients undergoing surgery for various tumors (23,24). However, the associations between mGPS and prognosis in HFS patients have never been studied. Since the mGPS reflects both the inflammatory and the nutritional status, it is assumed to be a predictor of outcomes in HFS in our study. Our results suggest that the addition of mGPS provided incremental prognostic value, and patients who had concomitant elevations of preoperative ASA physical status and mGPS were at high risk for complications. These results suggest that, mGPS could act as a tool to offer early identification of adverse events in patients following HFS.

## Study limitations

This study was performed at single center. The mGPS was measured at a single time point and the changes in mGPS were not examined. The current study examined in-hospital perioperative complications and the relationship between mGPS and long-term outcome was not investigated.

## CONCLUSION

In this pilot study, we provide first evidence that mGPS may become a novel biomarker for the risk stratification of HFS patients. Screening of immunonutritional status using mGPS may be helpful for the risk stratification of HFS patients. Larger prospective studies are needed to confirm these preliminary results.

*Competing interests: The authors declare that they have no competing interest.*

*Financial Disclosure: There are no financial supports.*

*Ethical approval: The study was approved by local institutional review board.*

*Ahmet Emrah Acan ORCID: 0000-0001-7116-8773*

*Cem Yalin Kilinc ORCID: 0000-0003-2568-0500*

## REFERENCES

1. Chen FP, Shyu YC, Fu TS, et al. Secular trends in incidence and recurrence rates of hip fracture: a nationwide population-based study. *Osteoporos Int* 2017;28:811-8.
2. Flikweert ER, Wendt KW, Diercks RL, et al. Complications after hip fracture surgery: are they preventable? *Eur J Trauma Emerg Surg* 2018;44:573-80.
3. Carpintero P, Caeiro JR, Carpintero R, Morales A, Silva S, Mesa M. Complications of hip fractures: A review. *World J Orthop* 2014;5:402-11.
4. Mak JC, Cameron ID, March LM. National Health and Medical Research Council. Evidence-based guidelines for the management of hip fractures in older persons: an update. *Med J Aust* 2010;192:37-41.
5. Bell JJ, Pulle RC, Crouch AM, et al. Impact of malnutrition on 12-month mortality following acute hip fracture. *ANZ J Surg* 2016;86:157-61.
6. Yoo JI, Ha YC, Choi H, et al. Malnutrition and chronic inflammation as risk factors for sarcopenia in elderly patients with hip fracture. *Asia Pac J Clin Nutr* 2018;27:527-32.
7. van Wissen J, van Stijn MF, Doodeman HJ, et al. Mini Nutritional Assessment and Mortality after Hip Fracture Surgery in the Elderly. *J Nutr Health Aging* 2016;20:964-8.
8. Aldebeyan S, Nooh A, Aoude A, et al. Hypoalbuminaemia-a marker of malnutrition and predictor of postoperative complications and mortality after hip fractures. *Injury* 2017;48:436-40.
9. Levitt DG, Levitt MD. Human serum albumin homeostasis: a new look at the roles of synthesis, catabolism, renal and gastrointestinal excretion, and

- the clinical value of serum albumin measurements. *Int J Gen Med.* 2016;9:229-55.
10. Petrelli F, Barni S, Coinu A, et al. The Modified Glasgow Prognostic Score and Survival in Colorectal Cancer: A Pooled Analysis of the Literature. *Rev Recent Clin Trials* 2015;10:135-41.
  11. McMillan DC. The systemic inflammation-based Glasgow Prognostic Score: a decade of experience in patients with cancer. *Cancer Treat Rev* 2013;39:534-40.
  12. Kang HS, Cho KW, Kwon SS, et al. Prognostic significance of Glasgow prognostic score in patients with acute exacerbation of idiopathic pulmonary fibrosis. *Respirology* 2018;23:206-12.
  13. Delcea C, Dima A, Jurcut C, et al. Utility of the Glasgow Prognostic Score in systemic lupus erythematosus, in a Single Center Cohort of 130 Patients. *Ann Rheum Dis* 2015;74:638.
  14. Zhao C, Ding C, Xie T, et al. Validation and optimization of the Systemic Inflammation-Based modified Glasgow Prognostic Score in predicting postoperative outcome of inflammatory bowel disease: preliminary data. *Sci Rep* 2018;8:747.
  15. Cenzer IS, Tang V, Boscardin WJ, et al. One-Year Mortality After Hip Fracture: Development and Validation of a Prognostic Index. *J Am Geriatr Soc* 2016;64:1863-8.
  16. Katsanos S, Mavrogenis AF, Kafkas N, et al. Cardiac Biomarkers Predict 1-Year Mortality in Elderly Patients Undergoing Hip Fracture Surgery. *Orthopedics.* 2017;40:417-24.
  17. Helminen H, Luukkaala T, Saarnio J, et al. Comparison of the Mini-Nutritional Assessment short and long form and serum albumin as prognostic indicators of hip fracture outcomes. *Injury* 2017;48:903-8.
  18. Shoji F. Clinical impact of preoperative immunonutritional status in patients undergoing surgical resection of lung cancer. *J Thorac Dis* 2019;11:408-12.
  19. Nakao M, Muramatsu H, Arakawa S, et al. Immunonutritional status and pulmonary cavitation in patients with tuberculosis: A revisit with an assessment of neutrophil/lymphocyte ratio. *Respir Investig* 2019;57:60-6.
  20. Malafarina V, Reginster JY, Cabrerizo S, et al. Nutritional Status and Nutritional Treatment Are Related to Outcomes and Mortality in Older Adults with Hip Fracture. *Nutrients* 2018;10:555.
  21. Southwell-Keely JP, Russo RR, March L, et al. Antibiotic prophylaxis in hip fracture surgery: a metaanalysis. *Clin Orthop Relat Res* 2004;419:179-84.
  22. Hanru Ren, Lianghao Wu, Wankun Hu, et al. Prognostic value of the c-reactive protein/prognostic nutritional index ratio after hip fracture surgery in the elderly population. *Oncotarget* 2017;8:61365-72.
  23. Lv Y, Pan Y, Dong C, et al. Modified Glasgow Prognostic Score at Recurrence Predicts Poor Survival in Resected Non-Small Cell Lung Cancer (NSCLC) Patients. *Med Sci Monit* 2017;23:3780-8.
  24. Zhang X, Chen X, Wu T, et al. Modified Glasgow prognostic score as a prognostic factor in gastric cancer patients: a systematic review and meta-analysis. *Int J Clin Exp Med* 2015;8:15222-9.