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The Utility of Glasgow Prognostic Score as an Indicator of Mortality after Transcatheter Aortic Valve Implantation

Transkateter Aort Kapak İmplantasyonu Yapılan Hastalarda Mortalite Öngördürücüsü Olarak Glasgow Prognostik Skorunun Kullanımı

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Abstract

Aim: The Glasgow Prognostic Score (GPS) is a scoring system obtained by using inflammatory (C-reactive protein) and nutritional (albumin) parameters together, and it has been shown to have prognostic value in various cardiac pathologies in previous studies. In this study, we aimed to investigate the utility of the Glasgow Prognostic Score (GPS) in predicting 1-year mortality in patients who underwent transcatheter aortic valve implantation (TAVI).

Material and Method: Patients who underwent TAVI with the diagnosis of severe, symptomatic aortic stenosis in our hospital between 2013 and 2017 were included in this single center retrospective study. Demographic, clinical and laboratory data were obtained by reviewing patient files. GPS value was calculated by using C-reactive protein and albumin values which was obtained on admission. Two groups were formed as survivors and non-survivors according to 1-year mortality data.

Results: A total of 170 patients were included in this retrospective study and 59 patients constituted the non-survivors group. History of chronic obstructive pulmonary disease and cerebrovascular disease were higher in non-survivors' group. STS-TAVR, Euro SCORE II and GPS levels were also higher in non-survivors group. High GPS value calculated with pre-procedural data was determined as a predictor of 1-year mortality.

Conclusion: The Glasgow Prognostic Score allows the evaluation of inflammation and nutritional status together, is a practical method that can be obtained from routine laboratory parameters. It can be used as a predictor of mortality in patients undergoing TAVI. It can guide clinicians in taking preventive measures to reduce mortality before the procedure.

Keywords: Albumin; C-reactive protein, glasgow prognostic score, transcatheter aortic valve replacement

Öz

Amaç: Glasgow Prognostik Skoru (GPS) inflamatuar (C reaktif protein) ve nutrisyonel (albümin) parametrelerin birlikte kullanımı ile elde edilen bir skorlama sistemidir ve daha önce yapılan çalışmalarda çeşitli kardiyak patolojilerde prognostik değeri olduğu gösterilmiştir. Bu çalışmada, Transkateter aort kapak replasmanı (TAVR) yapılan hastalarda 1-yıllık mortaliteyi öngörmede Glasgow Prognostik Skoru (GPS)'nun kullanılabilirliğinin araştırılması amaçlanmıştır.

Gereç ve Yöntem: Hastanemizde, 2013-2017 yılları arasında ciddi, semptomatik aort darlığı tanısı ile TAVR uygulanan hastalar geriye dönük olarak çalışmaya dahil edilmiştir. Demografik, klinik ve laboratuvar verileri hasta dosyaları incelenerek elde edilmiştir. İşlem öncesi C-reaktif protein ve albumin değerleri kullanılarak GPS değeri hesaplanmıştır. Hastaların 1-yıllık mortalite verisine göre mortalite (+) ve mortalite (-) olmak üzere 2 grup oluşturulmuştur.

Bulgular: Bu çalışmaya toplam 170 hasta dahil edilmiş ve 59 hasta mortalite (+) grubu oluşturmuştur. Demografik verilerden kronik obstruktif akciğer hastalığı, serebrovasküler hastalık öyküsü olması, yüksek STS-TAVR, Euro SCORE II ve GPS mortalite grubunda daha yüksek saptanmıştır. İşlem öncesi verilerle hesaplanan GPS değerinin yüksek olması 1-yıllık mortalitenin öngördürücüsü olarak belirlenmiştir.

Sonuç: İnflamasyon ve nutrisyonel durumun birlikte değerlendirilmesine olanak sağlayan Glasgow Prognostik Skoru, rutin laboratuar tetkiklerinden elde edilebilen pratik bir yöntemdir. TAVR uygulanan hastalarda mortalite öngördürücüsü olarak kullanılabilir. İşlem öncesi mortaliteyi azaltabilmek yönünde koruyucu önlemlerin alınmasında klinisyenlere yol gösterebilir.

Anahtar Kelimeler: Albümin, C-reaktif protein, glasgow prognostik skoru, transkateter aort kapak replasmanı

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INTRODUCTION

Aortic stenosis (AS) prevalence is increasing in developed countries and it is still the most common valvular disease.[1,2] Although the patients may stay asymptomatic, the prognosis is poor in symptomatic patients and need to be treated. Surgical or transcatheter aortic valve implantation (TAVI) are treatment options. TAVI is found non-inferior to surgical aortic valve replacement (SAVR) and superior to medical therapy in randomized clinical trials.[3-5] TAVI is especially recommended for older (≥75 years) and high-risk patients according to STS (Society of Thoracic Surgeons) and Euro SCORE (European System for Cardiac Operative Risk Evaluation>8%).[1] Although, STS and Euro SCORE include most of the comorbidities, they do not take into account the functional decline typical of elderly patients. Besides the benefit on mortality, quality of life and symptom status of the patients were demonstrated to be improved after TAVI.[6,7] Various studies have developed to define new parameters associated with increased early and late mortality rates.[8,9]

Aortic stenosis is defined as a degenerative process however, the role of inflammation and oxidative stress iin the progression of aortic stenosis progression is established.[10] The inflammatory process followed by endothelial dysfunction and lipid infiltration are the initiators for the progression of aortic stenosis.[11,12] Glasgow prognostic score (GPS), includes C-reactive protein (CRP) and albumin levels as variables and , is one of the validated prognostic risk scores in cancer patients. [13] Moreover, it has been studied in various fields of cardiac disorders and studies have indicated that GPS can be used as a prognostic tool for determining survival in heart failure as well as mortality in acute coronary syndromes.[14,15]

MATERIAL AND METHOD

This study was approved by Ethical Committee of Bağcılar Training and Research Hospital (Date: 05/07/2022 Number: 2022/07/01/001). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

The patients with severe symptomatic AS who were treated by TAVI between 2013 and 2017 were included in this retrospectively designed, single center study. The decision was based on the consensus of the heart team due to patients' high surgical risk.

Pre-, peri- and postoperative data were retrieved from hospital database and patients' files. Demographic, clinical, laboratory parameters and details of length of hospital stay were noted for each patient. Patiensts were evaluated according to the European System for Cardiac Operative Risk Evaluation II (Euro SCORE II) and Society of Thoracic Surgeons- Transcatheter Aortic Valve Replacement (STS-TAVR) scoring system.[16,17] Patients with preoperative serum creatinine >2 mg/dl albuminuria and chronic liver disease, albumin replacement therapy in past 6 months, malignancy, endocrinologic disorders (hypo/hyperthyroidism), previous diagnosis of systemic inflammatory, hematologic or autoimmune disease, active infection were excluded from the study. Also, those with unavailable serum CRP or albumin levels were excluded. Preoperative CRP and albumin levels were used for GPS calculation (https://www.mdcalc.com/glasgow-prognostic-score). An increased CRP value (>10 mg/L) or a low albumin value (<3.5 g/dL) were defined as 1 point each to define GPS. The patient had a score of 0 if both parameters were normal whereas, 1 if one of them was abnormal and 2 if both parameters were abnormal.[18]

Mortality data within 1-year follow-up was achieved using hospital records and national health database system. We sought to asses if GPS has a predictive value for mortality in patients undergoing TAVI.

Statistical Analyses

The Statistical Package for the Social Sciences 25.0 (SPSS Inc., Chicago, IL, USA) was used for statistical analyses. The normality of the data was analyzed by Kolmogorov-Smirnov test. Categorical data was stated as percentages and continuous data are stated as mean ± SD. The differences in categorical variables between groups was tested by Chi-square test. Student's t- or Mann Whitney U test was used to compare unpaired samples as needed. Independent variables of 30-day and 1-year mortality were identified by binary logistic regression analysis. The diagnostic accuracy of GPS for TAVI mortality was evaluated by receiver operating characteristic (ROC) curve analyses. A 2-sided $p<0.05$ was regarded as significant.

RESULTS

A total of 170 patients (84 male, 86 female) were included. Mean age of all included patients was 78.4±7.1. Two groups generated according to 1-year mortality and 59 patients were formed non-survivor group. There was no difference between groups regarding body mass index, age, gender, history of malignancy, diabetes mellitus (DM), hyperlipidemia (HL), coronary artery disease, hypertension (HT), smoking status and atrial fibrillation. Chronic obstructive pulmonary disease (72.8% vs. 49.5%, p=0.003), peripheral artery disease (45.7% vs. 31.5%, p=0.048), history of previous cerebrovascular accident (22% vs. 3.6%, p<0.0001) were found to be higher in non-survivor group. Moreover, patients were in advanced NYHA class in non-survivors when compared to survivors' group (64.4% vs. 32.4%, p<0.0001). Urea (50.8±19.8 vs 60.9±36.8; p=0.021), STS TAVR score [8.4 (7.4-11.0) vs 14.5 (9.7-17.2-10.1); p<0.0001], and Euro SCORE II [13.4 (6.2-15.1) vs 16.1(7.9-27.9); p<0.0001] were significantly higher in non-survivors. There were 100 patients in low (GPS=0) and 70 patients in high GPS groups (GPS≥1). The non-survivor patients had significantly higher GPS when compared to survivors' group (p=0.021). Remarkably, the non-survivor patients

had lower left ventricular ejection fraction than survivors (49.6±11.7 vs 54.4±9.5; p=0.004). There were no significant differences in terms of left ventricular end-diastolic and left atrial diameters and pulmonary artery pressure between groups. Preoperative medication such as statin, ACEİ/ARB, β blockers, antiaggregant and anti-coagulant usage were similar between groups, whereas calcium channel blockers usage was more common in survivors' group. All demographic, clinical and laboratory variables of patients are presented in detail in **Table 1**.

Binary regression analysis was performed to determine independent risk factors for 1-year mortality and STS TAVR and history of previous CVA [p<0.0001; β: 2.708, OR (95% CI): 1.547-4.740) and p=0.014; β: 0.048, OR (95% CI): 0.004-0.537), respectively] were found as independent risk factors for 1-year mortality.

Table 1. Comparison of demographic, clinical and laboratory parameters between groups according to 1-year mortality.

Variables	All (n=170)	Survivors (111)	Non-survivors (59)	p
Age (years)	78.4±7.1	77.9±7.1	79.5±7	0.169
Gender Male, n (%) Female, n (%)	 84 (49.4) 86 (50.6)	 49 (44.1) 62 (55.8)	 35 (59.3) 24 (40.6)	0.76
NYHA III/IV	74 (43.5)	36 (32.4)	38 (64.4)	<0.0001
Body Mass Index	26.7 (24.5-30.6)	26.9 (24.4-30.2)	26.7 (25.227.8)	0.232
Coronary Artery Disease, n (%)	137 (80.6)	85 (62)	52 (88.1)	0.51
Hypertension, n (%)	126 (74.1)	84 (75.6)	42 (71.1)	0.323
Chronic obstructive pulmonary disease, n (%)	98 (57.6)	55 (49.5)	43 (72.8)	0.003
Diabetes mellitus, n (%)	80 (47.1)	50 (45)	30 (50.8)	0.288
Peripheric Artery Disease, n (%)	62 (36.5)	35 (31.5)	27 (45.7)	0.048
Hyperlipidemia, n (%)	119 (70)	79 (71.2)	40 (67.8)	0.726
Cerebrovascular accident, n (%)	17 (10)	4 (3.6)	13 (22)	<0.0001
Malignancy, n(%)	29 (17.1)	19 (17.1)	10 (16.9)	0.579
Smoking, n (%)	86 (50,6)	52 (47.3)	34 (57.6)	0.259
Atrial fibrillation, n (%)	32 (18.8)	17 (15.7)	15 (25.4)	0.152
Urea, (mg/dl)	54.3±27.3	50.8±19.8	60.9±36.8	0.021
Creatinine, (mg/dl)	1.07±0.6	1.02±0.6	1.17±0.5	0.113
Sodium (mEq/L)	139.9±3.7	139.2±3.6	138.5±3.9	0.256
Glomerular Filtration Rate (ml/min/1.73m2)	63.1±19.5	66.1±18.3	57.6±20.6	0.007
Hemoglobin, (g/dl)	11.5±1.9	11.6±2.02	11.4±1.8	0.382
Hematocrit, (%)	36.2±5.5	34.4±5.5	35.8±5.4	0.470
White Blood Cell Count (103 /µl)	7.15 (3.37-15.2)	7.3 (3.5-8.0)	7.1 (3.4-15.2)	0.326
Platelet (103/L)	231.27±81.9	237±86	220±73	0.211
STS-TAVR	8.7 (7.4-17.2)	8.4 (7.4-11.0)	14.5 (9.7-17.2)	0.0001
Euro SCORE II	14.3 (6.2-27.9)	13.4 (6.2-15.1)	16.1 (7.9-27.9)	0.0001
Glasgow Prognostic Score GPS=0 GPS≥1	 100 (58.8) 70 (41.2)	 72 (64.9) 39 (35.1)	 28 (47.5) 31 (52.5)	0.021
Intensive care unit stay (days)	4.8±4.2	2.4±1.5	5.8±3.2	0.007
Left Ventricular Ejection Fraction (%)	52.7±10.5	54.4±9.5	49.6±11.7	0.004
Left Ventricular End-Diastolic Diameter (mm)	55±4.8	53±5.5	59±7.2	0.495
Left atrial diameter (mm)	4.3±0.5	4.2±0.46	4.3±0.61	0.167
Aortic valve area (mm2)	0.75±0.13	0.79±0.12	0.73±0.12	0.035
Maximum Aortic gradient (mmHg)	81.9±18.9	81.9±18.9	81.8±19	0.981
Mean Aortic Gradient (mmHg)	48.1±10.8	48.0±10.9	48.4±10.5	0.837
Pulmonary artery Pressure (Systolic) (mmHg)	39.6±12.9	38.7±11.8	41±14.9	0.283
Balloon valvuloplasty (pre-TAVR), n(%)	99 (58.2)	65 (58.6)	34 (57.6)	0.517
Balloon valvuloplasty (post-TAVR), n(%)	24 (14.1)	16 (14.4)	8 (13.6)	0.538
Preoperative treatment, n (%) Statins ß-blockers Calcium channel blocker ACEI/ARB Anti-coagulant Anti-aggregant	 71 (41.8) 113 (66.5) 52 (30.6) 124 (72.9) 21 (12.4) 131 (77.1)	 47 (42.3) 74 (66.7) 40 (36) 79 (71.2) 14 (12.6) 91 (81.9)	 24 (40.7) 39 (66.1) 12 (20.3) 45 (76.2) 7 (11.8) 40 (67.8)	 0.871 0.536 0.037 0.587 0.549 0.054

ACEI: Angiotensin converting enzyme inhibitor; ARB: Angiotensin receptor blocker; Euro SCORE: European System for Cardiac Operative Risk Evaluation; NYHA: New York Heart Association; STS: The Society of Thorasic Surgeons; TAVR: Transcatheter Aortic Valve Replacement

DISCUSSION

In this retrospective single center study, rate of in-hospital mortality was 8.8%, 30-day mortality was 11.8% and 1-year mortality was 34.1%. Higher pre-procedural GPS values were found to be associated with an increase in 1-year mortality, moreover high STS-TAVR score and history of previous CVA were found as independent predictors related with mortality.

Previous researchs have shown the role of Inflammation and endothelial injury in the pathophysiology and progression of aortic stenosis.[19,20] Also, studies revealed the mechanism at the cellular level and defined pathways which exhibited to contribute to the pathophysiology. The aortic valve cells were shown to become involved in the inflammatory environment by producing osteogenic protein.[21] The imbalance between pro- and anti-inflammatory status end-up with degradation of valvular structure and may fasten the progression of valvular pathology.

The scoring systems consist more than one variable to evaluate and concomitant use of these variables improve the diagnostic capacity in clinical practice. GPS, is a validated inflammatory risk score especially in malignancy and is reflecting both inflammatory and nutritional status. Its prognostic role has been studied in heart failure and acute coronary syndromes.[13-15] Prognostic nutritional index (PNI) is a scoring system consist of lymphocyte and albumin levels and is reflecting the inflammatory and nutritional status of patients similar to GPS. Higher PNI values were found to be related with higher short-term survival and lower complications after TAVI.[22] In our study, 30-day mortality was observed in 11.8% of patients and the rate of vascular surgery, acute heart failure and cerebrovascular accident was 15%, 18% and 1.7% respectively in mortality group. However, we couldn't detect a correlation between immune nutritional status as stated by the GPS score and 30-day mortality and rate of complications. In this cohort, patients with acute or chronic inflammatory diseases which may have affect CRP and albumin levels were excluded. Although, higher pre-procedural GPS values were found to be associated with an increase in 1-year mortality in our data, it is not identified as an independent predictor of 1-year mortality.

The validated risk scores for risk stratifying for TAVI are STS TAVR and Euro SCORE-II, which do not include variables such as nutritional status, frailty and inflammation. In patients who underwent TAVI with a diagnosis of severe symptomatic aortic stenosis, frailty is related with worse outcomes.[8] Hypoalbuminemia, is an important manifestation of frailty and shown to be linked with higher mortality rates in TAVI patients, as well.[23] In our study STS TAVR, Euro SCORE-II and GPS have been found to be associated with 1-year mortality. However, only the STS TAVR score was found as an independent predictor of 1-year mortality.

Small sample size, single-center experience and retrospective design are the limitations of this study. Since the use of TAVI is getting more common, the valve technology is improving. Our cohort consist of earlier periods of TAVI procedure including higher risk patients, this may be a reason for high rate of 1-year mortality.

CONCLUSION

Since TAVI is recommended for intermediate risk patients as well as high risk patients, managing complications and mortality is getting more precious. GPS value, which is a noninvasive, user-friendly score may support additive information to validated risk scores and may be used to determine the prognosis in this patient group. Further prospective studies in larger patient population may give more comprehensive information.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Bağcılar Training and Research Hospital Non-interventional Clinical Researches Ethics Committee (Date: 05/07/2022, Decision No: 2022/07/01/001).

Informed Consent: All patients signed the free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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