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What Is the Impact of Liver Function to Predict Mortality in Patients with Severe Aortic Stenosis and Reduced Ejection Fraction?

Ciddi Aort Darlığı ve Azalmış Ejeksiyon Fraksiyonu Olan Hastalarda Mortaliteyi Tahmin Etmede Karaciğer Fonksiyonunun Etkisi Nedir?

ABSTRACT

Background: Liver is one of the target organs in patients with symptomatic severe aortic stenosis and reduced ejection fraction. We aimed to evaluate the prognostic impact of liver function reserve as assessed by albumin-bilirubin score on 30-day and 1-year mortality and rehospitalization at 1 year in patients with severe symptomatic aortic stenosis and reduced ejection fraction undergoing transcatheter aortic valve implantation.

Methods: The patients with severe symptomatic aortic stenosis and reduced ejection fraction who were hospitalized between 2013 and 2021 were included in this single-center retrospective study. Preoperative bilirubin and albumin levels were used for albumin-bilirubin score calculation as in the original report. The total primary outcomes were defined as 30-day and 1-year all-cause mortality and hospitalization for decompensated heart failure within 1 year. Two groups were generated based on albumin-bilirubin score scores: high (>−2.25) and low (≤−2.25) albumin-bilirubin score groups.

Results: A total of 77 patients (49 male) were included in the study. and 29 (37.7%) patients died within 1 year of follow-up with 17 corresponding to 30-day mortality. There was no difference between high and low albumin-bilirubin score groups in terms of length of hospital stay, postprocedural complications, and re-hospitalization within 1 year, while 30-day mortality (50.0% vs. 4.3%, $P < 0.0001$) and 1-year mortality (80.0% vs. 10.6%, $P < 0.0001$) were significantly higher in the high albumin-bilirubin score group. Hence, total primary outcomes (86.7% vs. 44.7%, $P < 0.0001$) were significantly higher in the high albumin-bilirubin score group.

Conclusion: High albumin-bilirubin score (> -2.25) was found as an independent risk factor associated with 30-day and 1-year mortality and total primary outcomes. The results of this study suggest that preprocedural assessment of the albumin-bilirubin score gives additional information to stratify of patients with severe symptomatic aortic stenosis with reduced ejection fraction.

Keywords: Albumin-bilirubin score, albumin, aortic stenosis, bilirubin, transcatheter aortic valve implantation

ÖZET

Amaç: Karaciğer, düşük ejeksiyon fraksiyonlu (EF) aort darlığı (AD) hastalarında hedef organlardan biridir. Bu çalışmada, transkateter aort kapağı implantasyonu (TAVİ) uygulanan düşük EF'li AD hastalarında, karaciğer fonksiyonlarının 30 günlük, 1 yıllık mortalite ve 1 yılda tekrar hastaneye yatış üzerine olan etkisini değerlendirmeyi amaçladık.

Yöntem: Bu tek merkezli, retrospektif çalışmaya 2013-2021 yılları arasında hastaneye yatırılan düşük EF'li ciddi AD tanısı ile TAVİ uygulanan hastalar dahil edildi. Karaciğer fonksiyonu albumin-bilirubin (ALBI) skoru ile değerlendirildi. ALBI hesaplaması için orijinal rapordaki gibi TAVİ öncesi bilirubin ve albümin seviyeleri kullanıldı. Birincil sonuçlar 30 günlük, 1 yıllık tüm nedenlere bağlı mortalite ve 1 yıl içinde dekompanze kalp yetersizliği nedeniyle hastaneye yatış olarak tanımlandı. ALBI puanlarına göre yüksek (> −2,25) ve düşük (≤ −2,25) olarak 2 grup oluşturuldu.

Bulgular: Toplam 77 hasta (49 erkek) dahil edildi, 1 yıllık izlem süresinde 17'si ilk 30 günde olmak üzere toplam 29 (%37,7) hasta öldü. Gruplar arasında hastanede kalış süresi, işlem sonrası komplikasyonlar ve 1-yıl içinde yeniden hastane yatışı açısından fark bulunmazken, 30 günlük mortalite (%50'ye karşı %4,3, $P < 0,0001$) ve 1 yıllık mortalite (%80,0'a karşı %10,6, $P < 0,0001$) yüksek ALBI grubunda anlamlı olarak daha yüksekti. Yüksek ALBI grubunda toplam birincil sonlanım noktaları (%86,7'ye karşı %44,7, $P < 0,0001$) anlamlı olarak yüksek saptandı.

ORIGINAL ARTICLE
KLİNİK ÇALIŞMA

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Sonuç: Yüksek ALBI skoru (> -2,25), yeniden hastaneye yatış, 30 günlük ve 1 yıllık mortalite ve toplam birincil sonlanım noktaları ile ilişkili bağımsız bir risk faktörü olarak bulundu. Bu çalışmanın sonuçları, karaciğer fonksiyonlarının ALBI skoru aracılığı ile değerlendirilmesinin ve toplam birincil sonlanım noktaları, düşük EF'li ciddi semptomatik AD olan hastaların sınıflandırılması için ek bilgi verdiğini düşündürmektedir.

Anahtar Kelimeler: Albümin-bilirubin skoru, albümin, aort darlığı, bilirubin, transkateter aort kapağı implantasyonu

Heart failure (HF) is one of the leading causes of death and, with aging population, it has become a significant public health problem. Besides that, aortic stenosis (AS) is the most common heart valve disease and the prognosis is poor in symptomatic patients. Surgical or transcatheter aortic valve implantation (TAVI) are the treatment options.[1,2] Symptoms may be a reason for reduced ejection fraction (EF) and those with reduced EF have poor prognosis. A cut-off value of 50% was accepted to differentiate between normal and reduced EF for patients with severe symptomatic AS, and those with left ventricular ejection fraction (LVEF) <50% were accepted as "reduced EF" according to the guidelines.[1] Furthermore, kidney, liver, and brain are the target organs in HF, and reduced perfusion may end up with organ dysfunction. Liver is one of the target organs impaired both via increased central venous pressure and decreased tissue perfusion. Also, the cardio-hepatic syndrome is associated with poor prognosis and high mortality in HF patients.[3]

Serum albumin and bilirubin concentrations are widely used markers to evaluate liver function. The nutritional intake, systemic inflammation, and colloid oncotic pressure determine serum albumin levels. Hypoalbuminemia is reported as a predictor of short-term mortality in acute HF.[4,5] On the other hand, raised serum bilirubin level is a marker of acute liver congestion and cholestasis. Elevated pulmonary capillary wedge pressure and central venous pressure were shown to be linked with elevated serum bilirubin levels, and moreover, a raised total bilirubin level was reported to be related with worse clinical outcomes in HF.[6-8] Serum bilirubin and albumin levels were used to generate albumin-bilirubin (ALBI) score to evaluate hepatic function in patients with hepatic disease.[9] The prognostic utility of ALBI score was reported in hepatocellular carcinoma patients and was shown as a useful tool to assess liver reserve function.[10] In addition, ALBI score was found as an independent predictor of in-hospital mortality in acute HF patients.[11] As far as we know, these widely used prognostic scoring system that was documented on admission has not yet been used for patients with severe AS and HF with reduced EF who have undergone TAVI.

The purpose of this study is to evaluate the prognostic impact of liver function as assessed by ALBI scores on 30-day and 1-year mortality and rehospitalization at 1 year in patients with severe symptomatic AS and reduced EF undergoing TAVI.

ABBREVIATIONS

AF	Atrial fibrillation
ALBI	Albumin-bilirubin score
ALT	Alanin transaminase
AS	Aortic stenosis
AST	Aspartat transaminase
AUC	Area under curve
BMI	Body mass index
CAD	Coronary artery disease
CI	Confidence interval
CVA	Cerebrovascular accident
DM	Diabetes mellitus
EF	Ejection fraction
Euro-SCORE	European System for CArdiac Operative Risk Evaluation
HF	Heart failure
HT	Hypertension
INR	International normalized ratio
LVEF	Left ventricular ejection fraction
MELD-XI	Model for End-Stage Liver Disease Excluding INR
NT-proBNP	N-terminal pro-B-type natriuretic peptide
NYHA	New York Heart Association
ROC	Receiver operating curve
SD	Standard deviation
TAVI	Transcatheter Aortic Valve Implantation

Materials and Methods

The patients with severe symptomatic AS and reduced EF who were hospitalized in our tertiary center between 2013 and 2021 were included in this single-center, retrospective study. Aortic stenosis and reduced EF diagnosis were based on recent guidelines.[1,12] Demographic, clinical, laboratory parameters, and details of the length of hospital stay were retrieved from the hospital database and patients' files. Patients with preoperative serum creatinine >2 mg/dL, albuminuria and chronic liver disease, albumin replacement therapy in the past 6 months, malignancy, and previous diagnosis of systemic inflammatory, hematologic, or autoimmune disease were excluded from the study. Patients with low-flow low-gradient AS were assessed with dobutamine stress echocardiography and those with a lack of contractile reserve were excluded from the study. Also, those with unavailable serum bilirubin or albumin levels were excluded. Cerebrovascular accident (CVA),[13] coronary artery disease (CAD),[14] hypertension (HT)[15] and diabetes mellitus (DM),[16] atrial fibrillation,[17] HF, and New York Heart Association (NYHA) classification[18] were described according to the established definitions. Transthoracic echocardiography data were retrieved from the hospital database (Vivid S70; GE Medical System, Horten, Norway). Left ventricular ejection fraction which was measured using Simpson's method was noted. Patients with low-flow low-gradient AS were evaluated by dobutamine stress echocardiography and the contractile reserve was determined.

Preoperative bilirubin and albumin levels were used for ALBI calculation as in the original report [$\log_{10}$ total bilirubin (mmol/L) $\times$ 0.66)]+[albumin(g/dL) $\times$ 0.085] (9). The patient population was separated into 2 groups: high ALBI (ALBI score > −2.25) and low ALBI (ALBI score ≤ −2.25) based on a mean score that was previously reported as a cut-off value for prognosis of HF patients.[19]

Transcatheter Aortic Valve Implantation Procedure

Transthoracic echocardiography was performed for each patient to determine valve morphology and disease severity as well as cardiac functions and calcification of the aortic valve. And also, multislice computed tomography was used to evaluate the aortic valve, aortic annulus, and the aorta anatomy besides the peripheral vascular anatomy and coronary ostium-annulus distance. Then, each patient was evaluated by our heart team to assess suitability for TAVI. Edwards SAPIEN XT valve (Edwards Lifesciences, Irvine, Calif, USA) balloon-expandable device (n=25), Medtronic CoreValve (MCV; Medtronic, Minneapolis, Minn, USA) self-expandable device (n=12), Portico valve [St. Jude Medical, St. Paul, Minn, USA] self-expandable device (n=24) and other balloon-expandable devices (n=16) were used for TAVI procedure. A vascular occlusion device (ProStar XL, Abbott Laboratories, North Chicago, Ill, USA) was used in eligible patients in terms of femoral artery diameter and anatomy. The surgical cutdown method was applied in patients who were unsuitable for using the iliac and femoral artery vascular closure device. All procedures were performed at the catheterization laboratory under conscious sedation with fluoroscopy guidance. After the procedures, the patients were taken to the intensive care unit and followed up with non-invasive tests (including transthoracic echocardiographic, electrocardiography, and laboratory tests).

A 30-day and 1-year mortality data and hospitalization for decompensated HF within 1 year were achieved using hospital records and the national health database system. The total primary outcomes were defined as 30-day and 1-year all-cause mortality and hospitalization for decompensated HF within 1 year.

The Human Studies and Research Committee of our institution approved the study and patient consent was waived accordingly (Approval No: 2022/11/06/027, Date: 16.11.2022).

Statistical Analysis

All statistical tests were conducted using the Statistical Package for the Social Sciences 22.0 (SPSS Inc., Chicago, Ill, USA). Continuous variables are expressed as mean ± SD, and categorical data are expressed as numbers (n) and percentages (%). The chi-square test was used to assess differences in categorical variables between groups. Student's *t*-test or Mann–Whitney *U* test was used to compare unpaired samples as needed. Variables having linear correlation were evaluated by using Pearson's correlation test and nonlinear variables were evaluated by using Spearman's correlation test. Logistic regression analysis was used to identify independent variables of 30-day and 1-year all-cause mortality and 1-year re-hospitalization. We also calculated the areas under the receiver operating curve (ROC) to assess the total sensitivity and specificity of ALBI to estimate outcomes. Groups were compared for all parameters with regard to ALBI score. The Kaplan–Meier test was used to evaluate the incidence of death after index event, and log-rank test was used to compare the difference in survival between groups. Significance was assumed at a 2-sided $P < 0.05$.

Results

A total of 87 patients were reviewed with the diagnosis of severe symptomatic AS and reduced EF (Figure 1). After exclusion of 10 patients who died during index hospitalization, as they may have been due to a procedural complication, a total of 77 patients were included in this study. The mean age was 76.3 ± 9.9 and 49 (63.6%) were male. Totally 29 (37.7%) patients died by the end of 1-year follow up with 17 corresponding to 30-day mortality. Two groups were generated based on ALBI scores: "high ALBI group" (n=30) and "low ALBI group" (n=47). Both groups were similar in terms of age, gender, body mass index (BMI), STS-TAVR score, and history of DM, HT, and CAD, while, advanced NYHA (83.3 vs. 53.2%, $P=0.007$), Euro SCORE II (24.8 ± 15.2 vs. 21.5 ± 15.9; $P=0.046$), history of atrial fibrillation (43.3% vs. 14.9%, $P=0.006$) were significantly higher in the high ALBI group. Regarding laboratory markers, troponin (Tn) [122.9 (12.0-2717.2) vs. 83.1 (7.8-1929.0); $P=0.041$], N terminal pro-B-type natriuretic peptide (NT-proBNP) [4790 (1703-25 600) vs. 3021 (2080-16 200); $P=0.038$], international normalized ratio (1.4 ± 0.4 vs. 1.1 ± 0.3; $P=0.002$), and ALBI [−1.9 (−0.85 to −2.24) vs. −2.6 (−2.27 to −4.6); $P < 0.0001$] levels were significantly higher in high ALBI group. When echocardiography parameters were examined, patients in high ALBI group were found to have significantly higher pulmonary artery pressure (47.8 ± 13.6 vs. 40.4 ± 11.8; $P=0.001$) and moderate-to-severe mitral regurgitation (66.7% vs. 42.6%, $P=0.039$). There was no difference between the high and low ALBI groups

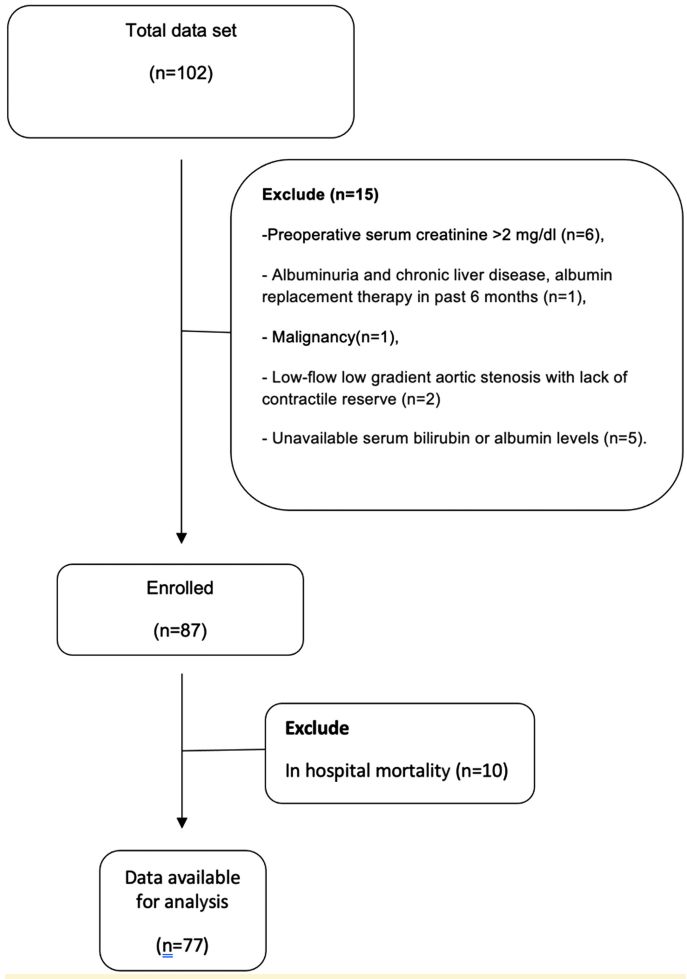

Figure 1. Selection of the study population.

Table 1. The Demographic, Biochemical, and Clinical Data of All Groups

Variables	All n=77	Group 1 ALBI Score > −2.25 n=30	Group 2 ALBI Score ≤ −2.25 n=47	*P*
Clinical characteristics and comorbidities				
Age (years)	76.3 ± 9.9	77.4 ± 12.5	75.5 ± 7.9	0.406
Male, n (%)	49 (63.6)	18 (60.0)	31 (65.9)	0.596
BMI (kg/m^2)	27.6 ± 4.1	28.5 ± 4.5	27.1 ± 3.8	0.143
NYHA III/IV, n (%)	50 (64.9)	25 (83.3)	25 (53.2)	**0.007**
HT, n (%)	62 (80.5)	27 (90.0)	35 (74.5)	0.093
DM, n (%)	30 (39.0)	10 (33.3)	20 (42.6)	0.418
CAD, n (%)	62 (80.5)	26 (86.7)	36 (76.6)	0.277
EuroSCORE II	22.8 ± 15.6	24.8 ± 15.2	21.5 ± 15.9	**0.046**
STS TAVR	12.1 ± 4.2	13.1 ± 5.1	11.6 ± 3.6	0.067
Atrial fibrillation, n (%)	20 (26.0)	13 (43.3)	7 (14.9)	**0.006**
Echocardiography				
Left ventricular ejection fraction (pre-operative) (%)	38.6 ± 9.1	38.8 ± 8.6	38.4 ± 9.5	0.866
Left ventricular end-diastolic diameter (mm)	52.8 ± 6.6	53.8 ± 6.8	52.2 ± 6.4	0.306
Left ventricular end-systolic diameter (mm)	44.0 ± 7.5	44.8 ± 8.1	43.5 ± 7.1	0.437
Left atrıum diameter, (mm)	44.0 ± 5.6	45.4 ± 5.1	43.1 ± 5.7	0.072
Pulmonary artery systolic pressure (mmHg)	43.1 ± 14.1	47.8 ± 13.6	40.4 ± 11.8	**0.001**
Mitral regurgitation (moderate-severe), n (%)	40 (51.9)	20 (66.7)	20 (42.6)	**0.039**
Aortic peak gradient (mmHg)	75.8 ± 16.6	75.6 ± 19.1	75.9 ± 14.9	0.925
Aortic mean gradient, (mmHg)	44.9 ± 9.1	45.1 ± 10.7	44.8 ± 7.9	0.902
Aortic valve area (cm^2)	0.8 ± 0.1	0.8 ± 0.1	0.8 ± 0.1	0.879
Laboratory parameters				
Hemoglobin,(g/dl)	11.5 ± 1.6	11.4 ± 1.8	11.6 ± 1.6	0.511
BUN (mg/dL)	61.3 ± 31.4	61.1 ± 35.1	61.4 ± 29.2	0.961
Creatinine (mg/dL)	1.2 ± 0.8	1.2 ± 0.6	1.1 ± 0.3	0.783
GFR ml/min/1.73 m^2	60.1 ± 21.6	58.9 ± 21.1	60.8 ± 22.1	0.719
Sodium (mmol/L)	137.6 ± 4.5	137.4 ± 4.9	137.8 ± 4.2	0.692
Uric acid (mg/dL)	7.1 ± 2.3	6.7 ± 2.3	7.3 ± 2.4	0.304
ProBNP (pg/mL)	3021 (1703-25 600)	4790 (1703-25 600)	3021 (2080-16 200)	**0.038**
Troponin (pg/mL)	109.9 (7.8-27 17.2)	122.9 (12.0-27 17.2)	83.1 (7.8-1929.0)	**0.041**
ALT (U/L)	14.0 (4.0-108)	15.7 (6.0-60.0)	13.0 (4.0-108.0)	0.692
AST (U/L)	26.9 ± 16.9	27.5 ± 17.1	26.5 ± 17.1	0.791
TSH (μIU/mL)	1.8 (0.04-11.4)	1.7 (0.07-11.5)	1.9 (0.4-9.6)	0.774
International Normalized Ratio	1.3 ± 0.4	1.4 ± 0.4	1.1 ± 0.3	**0.002**
ALBI	-2.5 (-0.85 - -4.6)	-1.9 (-0.85 - -2.24)	-2.6 (-2.27 - -4.6)	**<0.0001**
Outcomes				
Length of hospital stay, days	14.1 ± 8.8	14.1 ± 9.9	14.1 ± 8.2	0.973
Rehospitalization, n (%)	35 (45.5)	16 (53.3)	19 (40.4)	0.267
Mortality				
30-day	17 (22.1)	15 (50.0)	2 (4.3)	**<0.0001**
1-year	29 (37.7)	24 (80.0)	5 (10.6)	**<0.0001**
Total primary outcome, n (%)	47 (61.1)	26 (86.7)	21 (44.7)	**<0.0001**
Paravalvular aortic regurgitation, n (%) (postoperative) (more than mild)	7 (9.1)	3 (10)	4 (8.5)	0.562
Left ventricular ejection fraction (%) (postoperative)	42.2 ± 9.7	41.5 ± 8.7	42.6 ± 10.4	0.623
Permanent pacemaker requirement, n (%)	6 (7.8)	4 (13.3)	2 (4.3)	0.156

ALBI, albumin-bilirubin score; BMI, body mass index; BUN, blood unit nitrogen; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; CRP, C-reactive protein; CVA, cerebrovascular accident; DM, diabetes mellitus; EuroSCORE, European System for Cardiac Operative Risk Evaluation; GFR, glomerular filtration rate; HT, hypertension; LDH, lactate dehydrogenase; NYHA, New York Heart Association; Pro-BNP, pro-brain natriuretic peptide. STS, Society of Thoracic Surgeons.

Table 2. Univariate and Multivariate Forward Stepwise Logistic Regression Analysis: Predictors of Total Primary Outcomes

	Univariate OR	95% CI	*P*	Multivariate OR	95% CI	*P*
Diabetes mellitus	0.513	0.132-1.027	0.124			
Previous CAD	1.396	1.017-2.489	**0.006**	1.610	1.125-2.695	**0.018**
Atrial fibrillation	1.189	1.013-2.459	**0.001**	1.370	1.082-3.457	**0.025**
Pulmonary artery systolic pressure	1.396	1.081-3.396	**0.040**	0.092	0.007-1.283	0.076
International normalized ratio	0.268	0.068-1.087	0.087			
ALBI	0.136	0.057-0.169	**<0.0001**	0.068	0.001-0.180	**0.002**

ALBI, albumin-bilirubin score; CAD, coronary artery disease; OR, odds ratio.

in terms of length of hospital stay, postprocedural complications (paravalvular aortic regurgitation more than mild degree, permanent pacemaker requirement), and re-hospitalization within 1 year. On the other hand, 30-day mortality (50.0% vs. 4.3%, $P < 0.0001$) and 1-year mortality (80.0% vs. 10.6%, $P < 0.0001$) were significantly higher in the high ALBI group. Hence, total primary outcomes (86.7% vs. 44.7%, $P < 0.0001$) were significantly higher in the high ALBI group. All demographical, clinical, and biochemical characteristics of the 2 groups are presented in detail in Table 1.

Univariate and multivariate logistic regression analyses were performed to further evaluate individual risk factors associated with outcomes. The ALBI score was found as an independent risk factor associated with 30-day mortality [$P=0.005$, β: 0.026 OR (95% CI): 0.013-0.331], 1-year mortality [$P=0.006$, β: 0.806, OR (95% CI): 0.707-0.893] and total primary outcomes [$P=0.002$, β: 0.068, OR (95% CI): 0.001-0.180] (Tables 2-4). History of CAD [$P=0.018$, β: 1.610, OR (95% CI): 1.125-2.695] and AF [$P = 0.025$, β: 1.370, OR (95% CI): 1.082-3.457] were found as independent predictors for total primary outcomes (Table 2). Being in AF rhythm [$P=0.031$, β: 1.304 OR (95% CI): 1.164-3.882], postoperative LVEF [$P=0.023$, β: 0.809, OR (95% CI): 0.675-0.971] and EuroSCORE II [$P=0.034$, β: 1.414, OR (95% CI): 1.015-3.682] were detected as independent predictors for 30-day mortality, as well (Table 3). Moreover, history of CAD [$P=0.016$, β: 1.248, OR (95% CI): 1.046-3.449], AF [$P=0.013$, β: 1.226, OR (95% CI): 1.049-2.404], advanced NYHA [$P=0.011$, β: 0.213, OR (95% CI): 0.049-0.378], and higher pulmonary artery pressure [$P=0.007$, β: 1.575, OR (95% CI): 1.194-1.769] were revealed as independent predictors for 1-year mortality by multivariate logistic regression analysis

Table 3. Univariate and Multivariate Forward Stepwise Logistic Regression Analysis: Predictors of 30-day Mortality

	Univariate OR	95% CI	*P*	Multivariate OR	95% CI	*P*
Atrial fibrillation	1.281	1.090-3.882	**0.020**	1.304	1.164-3.882	**0.031**
Previous CAD	0.482	0.098-2.383	0.371			
EuroSCORE II	1.022	1.001-3.061	**0.012**	1.414	1.015-3.682	**0.034**
Postoperative left ventricular ejection fraction	0.359	0.116-0.906	**0.015**	0.809	0.675-0.971	**0.023**
International normalized ratio	3.478	2.050-8.627	**0.007**	2.465	0.998-12.707	0.174
ALBI	0.010	0.001-0.105	**<0.0001**	0.026	0.013-0.331	**0.005**

ALBI, albumin-bilirubin score; CAD, coronary artery disease; OR, odds ratio.

Table 4. Univariate and Multivariate Forward Stepwise Logistic Regression Analysis: Predictors of 1-year Mortality

	Univariate OR	95% CI	*P*	Multivariate OR	95% CI	*P*
Previous CAD	1.346	1.089-2.351	**0.007**	1.248	1.046-3.449	**0.016**
Diabetes mellitus	1.722	1.327-2.689	**0.026**	1.357	0.991-3.721	0.306
Atrial fibrillation	1.210	1.071-1.622	**0.005**	1.226	1.049-2.404	**0.013**
NYHA III/IV	0.681	0.229-0.942	**0.007**	0.213	0.049-0.378	**0.011**
Pulmonary artery systolic pressure	2.384	1.048-2.982	**0.004**	1.575	1.194-1.769	**0.007**
Postoperative left ventricular ejection fraction	0.968	0.922-1.016	0.189			
ALBI	0.016	0.001-0.020	**<0.0001**	0.806	0.707-0.893	**0.006**

ALBI, albumin-bilirubin score; CAD, coronary artery disease; NYHA, New York Heart Association; OR, odds ratio.

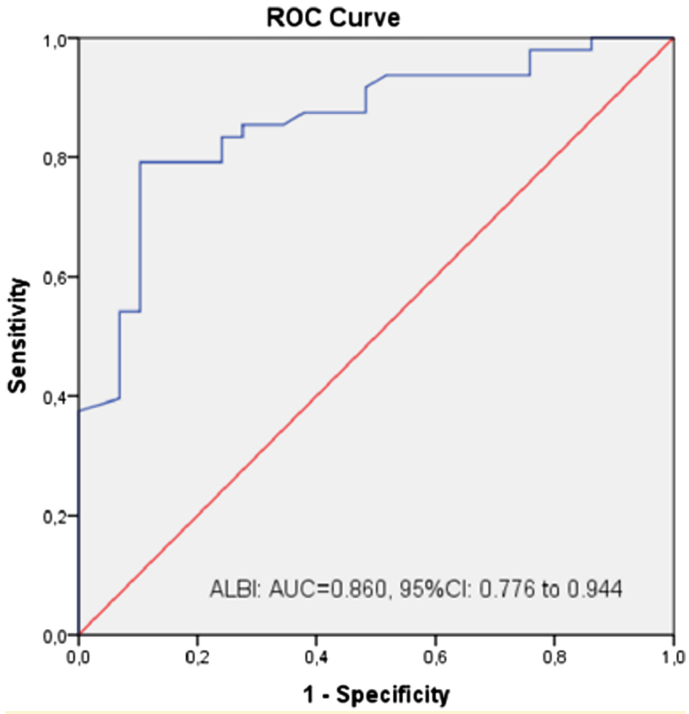

Figure 2. Albumin-bilirubin score for predicting 1-year mortality for patients with severe symptomatic aortic stenosis and reduced ejection fraction.

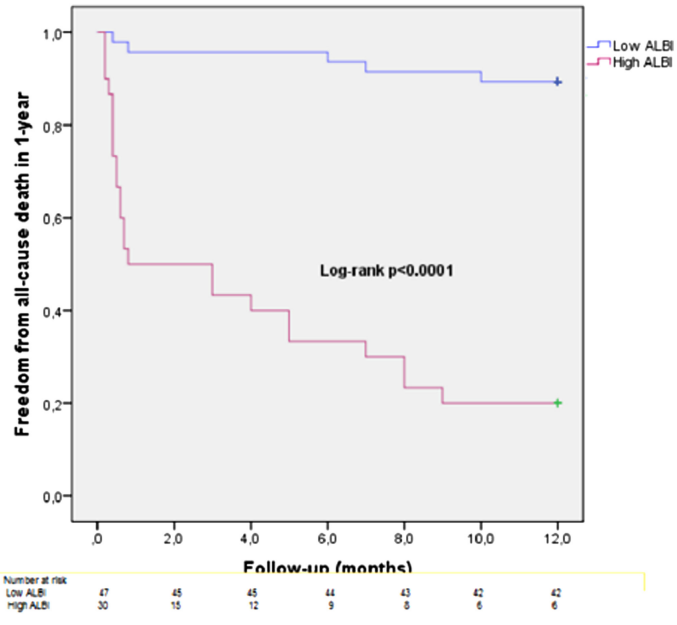

Figure 3. Kaplan–Meier curves for all-cause death during 1-year follow-up.

(Table 4). Receiver operating curve for accuracy of ALBI score for predicting 1-year mortality for patients with severe symptomatic AS and reduced EF is shown in Figure 2. The area under curve (AUC) for ALBI score was 0.792 [95% CI: 0.670-0.914] and a cut-off value of –2.06 for ALBI score was associated with 75.0% sensitivity and 70.6% specificity in prediction of 30-day mortality. Furthermore, a cut-off value of –2.02 for ALBI score was associated with 79.2% sensitivity and 74.6% specificity in prediction of 1-year mortality with an AUC of 0.860 [95% CI: 0.776-0.944]. High ALBI group was found to have higher 1-year mortality compared to low ALBI group (log rank: $P < 0.001$). Kaplan-Meier curves for all-cause death during 1-year follow-up are shown in Figure 3.

Discussion

In this study, we sought to assess if ALBI score could predict the clinical course of patients with severe symptomatic AS and reduced EF. Consequently, high ALBI score (> -2.25) was found as an independent risk factor associated with 30-day and 1-year mortality and total primary outcomes. The results of this study suggest that preprocedural assessment of the ALBI score gives additional information to stratify patients with severe symptomatic AS with reduced EF.

Although liver dysfunction is one of the most common complications in patients with HF, its clinical and prognostic utility is usually underscored. Cardiogenic liver injury may occur as a result of increased central venous pressure and passive congestion or decreased perfusion due to decreased cardiac output in HF patients. Cholestatic enzymes usually raise due to passive congestion and transaminases due to decreased perfusion; however, patients usually remain asymptomatic.[20] Serum total bilirubin is a marker of cholestasis and albumin is associated with central venous pressure in patients with HF, and the prognostic utility of ALBI in HF has been reported.[11,19] Albumin-bilirubin score was found as an independent predictor of in-hospital mortality in HF. Additionally, ALBI score was found to enhance diagnostic accuracy used in combination with NT-proBNP.[21] Heart failure and AS are conditions related with increased mortality and impaired vital organ functions. In this study, we used the ALBI score to conclude the liver function of patients with severe AS and reduced EF who underwent TAVI. The patients in high ALBI group found to have higher pulmonary artery systolic pressure, troponin, and NT-proBNP levels which might be a result of increased venous pressure due to reduced EF and AS. These are common cardiovascular risk factors related to mortality, and consequently, ALBI score can be used to assess the severity of liver impairment in HF patients and as a result ALBI score may provide additional information for mortality prediction. Model for End-Stage Liver Disease Excluding INR (MELD-XI) score was used to assess the impact of liver function on outcomes of patients who were treated by TAVI previously. A high MELD-XI score at baseline was an independent predictor for 2-year mortality.[22] Model for End-Stage Liver Disease Excluding INR score consists of serum bilirubin and creatinine levels. Similarly, ALBI was used to determine liver function in our study and was found as an independent predictor of 30-day and 1-year mortality in patients with severe AS and reduced EF who underwent TAVI. On the other hand, TAVI may improve liver function in severe AS and reduced EF patients by improving cardiac output and organ perfusion; however, our study was not designed to assess ALBI changes after successful TAVI.

The prognostic impact of liver function tests in HF patients was evaluated in previous studies. Reduced albumin and elevated

bilirubin, the aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels, were reported to be related with outcomes of HF patients.[6,8,23,24] Similarly, ALT and AST levels were higher and albumin levels were lower in high ALBI group in our study. Moreover, our patient population had milder elevation in ALT and AST levels; ALBI levels predicted mortality even in milder elevated transaminases levels. Transcatheter aortic valve implantation may improve liver perfusion by increasing cardiac output; our study was not designed to assess postprocedural levels. Considering the discriminative ability of ALBI score for prognosis, re-evaluation of ALBI after TAVI would give essential information. Our study population included higher risk patients while symptomatic AS and reduced EF patients are known to have high mortality risk. In this study, in-hospital deaths were excluded since TAVI-related complications might be associated with these events. Moreover, we found high ALBI score to be an independent predictor of 30-day and 1-year mortality in patients with severe symptomatic AS with reduced EF.

Both HF and AS are related with increased mortality and impaired vital organ functions.[25] Left ventricular systolic dysfunction was shown to be improved by surgical aortic valve replacement and associated with favorable clinical outcomes and reduced all-cause mortality.[26] Similarly, TAVI improved outcomes mainly in patients with moderate left ventricular systolic dysfunction.[27] Postprocedural left ventricular ejection fraction was found as an independent predictor of 30-day mortality according to our results in concordance with the literature.

Study Limitations

This study was retrospectively designed and performed in a single center with a small number of patients. The guideline-directed treatments are cornerstone of HF therapy. Since, the use of β-blockers and renin-angiotensin-aldosterone system inhibitors were similar between the groups in our study, we did not have data on drug doses, the length of drug use in targeted doses, and drug compliance, and those are the factors which may alter the study outcomes. The length of HF diagnosis and the impact of cardiac remodeling (e.g., rate of fibrosis) was not evaluated since this may impact the prognosis of patients. Larger and prospective studies are required to evaluate the relationship between ALBI score and outcomes for HF patients with severe symptomatic AS and reduced EF.

Conclusions

Our current study showed that ALBI score has effective discriminating power in determining 30-day and 1-year mortality of patients with severe AS and reduced EF which constitute a specific subgroup with high mortality rates. ALBI score, which provides information about liver fibrosis and fluid overload, was found as a marker of mortality and outcomes in patients with severe AS and reduced EF according to our findings.

Ethics Committee Approval: The Human Studies and Research Committee of Bağcılar Training and Research Hospital approved the study and patient consent was waived accordingly (Approval No: 2022/11/06/027, Date: 16.11.2022).

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