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Association Between Albumin-Bilirubin Score and Ventricular Arrhythmia in Patients with Heart Failure

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Abstract

Objectives: Heart failure (HF) is a serious disease associated with increased morbidity and mortality. Hepatic dysfunction secondary to hepatic congestion and ventricular arrhythmia (VA) are frequently observed in patients with HF. The albumin-bilirubin (ALBI) score, which predicts liver damage, is a parameter that has been used in patients with HF in recent years. In this study, we investigated the predictive value of the ALBI score in detecting VA in patients with HF.

Materials and Methods: This study was planned as a single-center retrospective study. The study included 150 consecutive HF patients with reduced ejection fraction who had an implantable cardioverter-defibrillator. The ALBI score was calculated using the following formula: [log10 TB (mg/dL) × 0.66] + [albumin (g/dL) × -0.085]. Patients were divided into two groups: those with and without VA. A receiver operator characteristic (ROC) curve analysis was used to define the cut-off level of the ALBI score to predict VA.

Results: The mean age of the group was 55.3±10.8 years, and 78.7% of the patients were male. 28 patients (18.7%) had VAs. Male gender and HF hospitalization in the previous year were more common in the arrhythmia group. ALBI score was higher in the arrhythmia group ($p<0.001$). Sacubitril-valsartan and digoxin use were higher in the arrhythmia group, whereas beta-blocker and statin use were higher in the non-arrhythmia group. In multivariate logistic regression analysis, the ALBI score was found to be an independent predictor of VA. Male gender, hospitalization in the previous year, sacubitril-valsartan use, and digoxin use were other independent predictors of VA. ALBI score at a cut-off point of

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-3.66, predicts ventricular tachycardia with 74% sensitivity and 70% specificity in ROC curve analysis (area under the curve=0.732, p<0.001).

Conclusion: The ALBI score is associated with VA in patients with HF. It can be easily assessed and used as a predictor of VA in this patient group.

Keywords: Albumin-bilirubin score, heart failure, ventricular arrhythmia

Introduction

Heart failure (HF) is one of the leading causes of hospitalization and mortality worldwide[1]. It is a clinical syndrome with a prevalence of 1-2% in the adult population[2]. The incidence of HF is increasing and continues to be an important public health problem. Despite advances in treatment, HF still has a high mortality rate[3]. Approximately half of HF patients have HF with reduced left ventricular ejection fraction (LVEF). Reduced LVEF is associated with a high risk of sudden death due to congestive HF and arrhythmia in patients with HF[4]. Ventricular arrhythmia (VA) is such an important cause of mortality in HF patients that almost 50% of mortality is due to fatal VA, including ventricular tachycardia (VT) and ventricular fibrillation (VF) in these patients[5]. Implantable cardioverter-defibrillator (ICD) implantation is a modality that has been shown to reduce morbidity and mortality in patients with reduced LVEF[6]. ICD detects the frequency of VA and provides therapy. However, feasible and cost-effective markers beyond LVEF are required to estimate the risk of VA.

It has been shown that HF is not a single organ failure, but many organs are involved and interact with each other, including the kidneys, brain, lungs, intestines, and liver[7]. Although the relationship between the heart and liver is increasingly recognized, its clinical and prognostic value remains unclear. Hepatic dysfunction occurs due to hepatic congestion and perfusion disorder and is associated with the severity of HF and poor prognosis[8,9]. Previous studies have evaluated the association between various liver function tests and HF[10,11]. However, no clinically applicable marker of liver dysfunction has been clearly defined. Recently, a new model for assessing liver function, the albumin-bilirubin (ALBI) score, has been developed[12]. It is a predictive liver dysfunction score that has been generally investigated in studies on the prognosis of primary liver pathologies[13,14]. However, there is no study on the relationship between the ALBI score and VA, which is an important cause of mortality and morbidity in HF patients. The ALBI score may be an appropriate scoring system to predict the severity of cardiohepatic syndrome and the risk of VA. In this study, we investigated the predictor of ALBI score in detecting VA in patients with HF.

Materials and Methods

Study Population

This study was planned as a single-center retrospective study. The study population consisted of 150 consecutive reduced LVEF (≤40%) HF patients who presented to the outpatient clinic between January 2022 and December 2022 and had previously had an ICD implanted. Clinically stable patients older than 18 years receiving optimal medical treatment recommended by the guidelines were included in the study. Patients with chronic liver disease, acute or chronic hepatitis, acute or chronic biliary tract disease, chronic kidney disease, collagen vascular disease, acute infection, malignancies in their medical records, and patients who underwent heart transplantation or had ventricular assist devices were excluded. The study protocol was approved by the Ankara Bilkent City Hospital No. 2 Medical Research Scientific and Ethical Evaluation Board (TABED) (approval no.: TABED 2-24-

02, date: 07.02.2024). All procedures were conducted in accordance with ethical rules and the principles of the Declaration of Helsinki.

Analysis of Patient Data and Laboratory Data

Patients' medical records were used to obtain data about the medical history of patients, including cardiovascular risk factors and demographic parameters. Venous blood samples were obtained at admission. Parameters such as complete blood count, creatinine, N-terminal pro-brain natriuretic peptide (NT-proBNP), alanine transaminase, aspartate transaminase, total bilirubin, lipid profile, electrolyte parameters, and albumin levels were recorded. Transthoracic echocardiography was performed, and the left LVEF was calculated using the modified Simpson's method. ICD control was routinely performed. The medications used by the patients were noted during the routine outpatient clinic visit.

Definitions

HF was identified as a known HF symptom affirmed with reduced LVEF. Arrhythmia included documented non-sustained and sustained VT and VF within the ICD control. Patients with fasting blood glucose >126 mg/dL, those with a documented diabetes mellitus (DM) diagnosis, or those who use insulin or oral antidiabetics at admission were considered diabetic. Hypertension (HT) was defined as current antihypertensive use or a systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg. Current tobacco users were defined as smokers.

The ALBI score was calculated using the following formula: [log10 TB (mg/dL) × 0.66] + [albumin (g/dL) × -0.085][12].

Statistical Analysis

SPSS Statistics version 24.0 for Windows (SPSS Inc, Chicago, IL) was used for statistical analysis. Data are presented as numbers, proportions, mean and standard deviation, or median and interquartile range. The Kolmogorov-Smirnov test was used to determine the distribution patterns. Student's t-test or Mann-Whitney U test was used as appropriate. Categorical variables were evaluated using the chi-square test. Receiver operating characteristic curve analysis was performed to determine the cut-off level of the ALBI score to predict the presence of VA. The association between VA and other variables was investigated using multivariate logistic regression analysis. Any variable with a p-value <0.2 in the univariate logistic regression analysis was included in the multivariate logistic regression model. A two-tailed p-value <0.05 was considered significant.

Results

A total of 150 patients were included in the study. Patients were divided into two groups: those with and without VA. 55.3 percent of the patients had an ischemic etiology. The mean age of the patients was 55.3 years, and 118 (78.7%) were male. The mean LVEF of the patients was 23.74%. VA was detected in 28 (18.7%) patients during a periodic ICD battery check. The baseline demographics and clinical and laboratory parameters are shown in Table 1. There was no significant difference in terms of age, HT, DM, smoking, previous coronary artery bypass graft surgery, atrial fibrillation, and New York Heart Association class between the two groups. Male gender and HF hospitalization in the previous year were more common in the arrhythmia group. Creatinine, ALBI score, sacubitril-valsartan, and digoxin use were higher in the arrhythmia group. In addition, sodium and low-density lipoprotein cholesterol levels were lower in this group. LVEF did not differ between groups. Beta blocker and statin use was higher in the non-arrhythmia group. No significant difference was found between the use of renin-angiotensin system inhibitors, namely angiotensin-converting enzyme inhibitors and angiotensin-II receptor blockers, mineralocorticoid receptor antagonists, and sodium-glucose cotransporter-2 inhibitors.

The ALBI score at a cut-off point of -3.66, predicts VT with 74% sensitivity and 70% specificity in receiver operator characteristic curve analysis.

Table 1. Comparison of groups according to the baseline demographics and clinical and laboratory characteristics

Variables	Normal (n=122)	VT (n=28)	p-value
Age (years)	55.6±11.3	54.2±9.6	0.526
Male gender [n (%)]	92 (75.4)	26 (92.9)	**0.03**
Hypertension [n (%)]	55 (45.1)	11 (39.3)	0.367
Diabetes mellitus [n (%)]	57 (46.7)	13 (46.4)	0.573
Smoking [n (%)]	21 (17.2)	5 (17.9)	0.602
HF hospitalization in last year [n (%)]	22 (18.0)	20 (71.4)	**<0.001**
Previous CABG [n (%)]	24 (19.7)	8 (28.6)	0.214
Ischemic etiology in HF [n (%)]	67 (54.9)	16 (57.1)	0.456
Atrial fibrillation [n (%)]	38 (31.1)	9 (32.1)	0.484
NYHA Class	2.04±0.79	2.29±0.59	0.073
Hemoglobin (g/dL)	14.40±1.90	14.10±1.05	0.424
WBC (mcL)	8.15±1.72	8.17±1.76	0.846
Sodium (mEq/L)	139.21±6.97	128.81±13.22	**0.003**
Potassium (mEq/L)	4.38±0.49	4.38±0.46	0.981
Magnesium (mEq/L)	2.01±0.40	1.92±0.32	0.350
Calcium (mEq/L)	9.24±0.54	9.22±0.44	0.835
Glucose (mg/dL)	112.51±50.69	110.89±27.22	0.451
Creatinine (mg/dL)	1.02±0.24	1.18±0.39	**0.010**
AST (U/L)	30.01±19.22	29.8±21.22	0.455
ALT (U/L)	39.48±25.54	41.22±27.33	0.288
LDL-C (mg/dL)	95.42±56.21	82.33±20.21	**0.048**
HDL-C (mg/dL)	38.61±12.46	34.35±9.34	0.087
Triglyceride (mg/dL)	156.57±78.33	154.37±89.86	0.439
Albumin (g/dL)	4.36±0.55	4.23±0.48	0.116
Bilirubin (µmol/L)	15.39±8.22	15.55±7.45	0.488
ALBI score	-3.71±0.46	-3.44±0.36	**<0.001**
LVEF (%)	24.21±7.60	21.69±5.87	0.069
NT-pro BNP (ng/L)	2590±1720	2682±1674	0.650
TSH (mU/L)	2.41±2.03	2.40±1.31	0.981
Beta blocker [n (%)]	117 (95.9)	25 (89.3)	**0.034**
RAS blocker [n (%)]	96 (78.7)	21 (75.0)	0.418
Sacubitril-Valsartan [n (%)]	19 (15.6)	9 (32.1)	**0.044**
MRA [n (%)]	103 (84.4)	23 (82.1)	0.447
SGLT-2 inhibitors [n (%)]	65 (53.3)	15 (53.6)	1.000
Digoxin [n (%)]	21 (17.2)	11 (39.3)	**0.013**
Statin [n (%)]	66 (54.1)	8 (28.6)	**0.010**

HF: Heart failure, CABG: Coronary artery bypass graft surgery, NYHA: New York Heart Association, WBC: White blood cell, AST: Aspartate transaminase, ALT: Alanine transaminase, LDL-C: Low-density lipoprotein cholesterol, HDL-C: High-density lipoprotein cholesterol, ALBI: Albumin-bilirubin, LVEF: Left ventricular ejection fraction, NT-pro BNP: N-terminal pro–B-type natriuretic peptide, TSH: Thyroid stimulating hormone, RAS: Renin angiotensin system, MRA: Mineralocorticoid receptor antagonist, SGLT-2: Sodium-glucose transport protein-2

The area under the curve of the ALBI score in predicting VA was 0.732 [95% confidence interval (CI): 0.677-0.822; p<0.001] (Figure 1). Univariate and multivariate logistic regression analyses were performed to assess the independent predictors of VA. Variables with p<0.2 in univariate analysis were evaluated in multivariate logistic regression analysis (Table 2). In multivariate logistic regression analysis, the ALBI index was found to be an independent predictor of VA (hazard ratio: 1.43, CI: 1.12-2.22; p<0.001). Male gender, hospitalization for HF in the previous year, sacubitril-valsartan use, and digoxin use were other independent predictors of VA (Table 2).

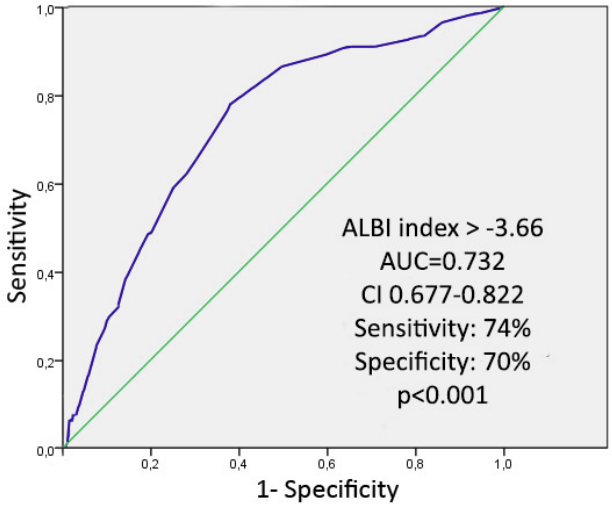

Figure 1. ROC curve ALBI
ROC: Receiver operator characteristic, ALBI: Albumin-bilirubin, AUC: Area under the curve, CI: Confidence interval

Discussion

This study analyzed the relationship between the ALBI score and VA in HF patients. The results showed that the ALBI score was independently associated with the development of VA in patients with HF. To the best of our knowledge, this is the first study to examine the relationship between ALBI score and VA in patients with HF.

HF is an important cause of morbidity and mortality caused by cardiac dysfunction, has structural and functional abnormalities, and has a higher incidence of arrhythmias than healthy people[15,16]. Data on the relationship between congestion and stage and arrhythmia frequency in patients with HF are limited. The use of ICD is widely used in patients with HF for arrhythmic events[6]. Because of its common use, it enables more detailed data

Table 2. Independent predictors of ventricular arrhythmia

Factor	Univariable		Multivariable	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Male gender	13.2 (2.11-28.22)	0.001	12.9 (1.24-26.61)	**0.001**
HF hospitalization in last year	32.23 (3.23-154.22)	0.001	24.46 (4.34-137.56)	**<0.001**
NYHA Class	1.77 (0.56-5.44)	0.288	-	-
Sodium	0.95 (0.89-1.22)	0.268	-	-
Creatinine	0.94 (0.066-13.63)	0.967	-	-
LDL-C	0.97 (0.094-1.105)	0.295	-	-
HDL-C	0.94 (0.87-1.127)	0.290	-	-
ALBI score	1.53 (1.32-2.11)	<0.001	1.43 (1.12-2.22)	**<0.001**
LVEF	1.12 (1.002-1.308)	0.04	1.066 (0.942-1.207)	**0.125**
Beta blocker	0.87 (0.67-1.25)	0.265	-	-
Sacubitril-Valsartan	3.53 (1.22-13.56)	0.03	2.56 (0.98-22.1)	**0.08**
Digoxin	2.55 (1.14-5.76)	0.008	2.12 (1.10-11.43)	**0.03**
Statin	0.65 (0.33-2.54)	0.256	-	-

HF: Heart failure, NYHA, New York Heart Association, LDL-C: Low-density lipoprotein cholesterol, HDL-C: High-density lipoprotein cholesterol, ALBI: Albumin-bilirubin, LVEF: Left ventricular ejection fraction, OR: Odds ratio, CI: Confidence interval

about arrhythmia to be recorded. Baman et al.[17] reported that frequent VAs cause left ventricular dysfunction. A previous study examined patients implanted with cardiac resynchronization therapy for HF[18]. Higher NT-proBNP levels and higher mortality rates were observed in the ALBI-positive group. However, no arrhythmia-related data were found. In our study, NT-proBNP was not an independent predictor of VA.

HF is a systemic disease that negatively affects other organ systems because of the failure to function as a pump. In patients with HF, not only left but also right ventricular function is impaired[19]. Therefore, congestion is mainly associated with increased right heart diastolic pressures and related symptoms[20]. The major result of these symptoms is hepatic congestion[21]. Liver dysfunction is one of the most common complications in HF patients[22]. In recent years, prognostic and clinical evaluations have been performed using different liver function parameters in patients with HF. Liver function tests such as albumin, bilirubin, alanine aminotransferase, and aspartate aminotransferase have been used to predict the prognosis of HF[23,24]. In some studies, the severity of HF was correlated with total bilirubin and albumin levels[25]. It was found that both high total bilirubin and low serum albumin levels are associated with poor outcomes in HF patients[26,27]. In our study, patients were divided into two groups, with and without arrhythmia, and no significant difference was found between albumin and total bilirubin levels in both groups.

Bilirubin is a marker of serum cholestasis. Elevated bilirubin levels are associated with acute liver congestion. In a study, it was shown that bilirubin levels increased as cardiac output decreased[28]. In another study, high bilirubin levels increased mortality in patients with HT-related HF[29]. Albumin is the most abundant plasma protein in the body and indicates hepatocyte function. Plasma albumin levels are known to decrease in inflammatory conditions. The cause of hypoalbuminemia in patients with HF is hepatocyte damage due to both chronic inflammation and hepatic congestion[30]. Therefore, the more progressive the HF, the lower the albumin level. Low albumin levels are associated with chronic congestive hepatopathy and poor prognosis in patients with HF[8,30].

The ALBI score, which includes serum bilirubin and albumin levels, was developed to assess liver function and predict survival in patients with chronic liver disease. It is a cost-effective and simple method to predict liver function. It was first published in 2015 and has been widely used in clinical practice until today[12]. Studies have shown that the ALBI score can reliably predict the prognosis and survival of patients with liver disease[31]. The ALBI score also predicts left and right ventricular dysfunction and associated liver dysfunction in patients with HF. In a study of patients with HF with reduced LVEF, it was shown that the group with a high ALBI score had a more severe poor prognosis[2].

In another study, there are findings suggesting that liver disease is associated with VA. Non-alcoholic fatty liver disease was found to increase the risk of VA by 3.5-fold[32]. In the same study, it was also shown that elevated gamma-glutamyl transferase was independently associated with VA. Systemic inflammation, cardiac lipotoxicity, and oxidative stress in liver diseases may lead to structural, electrical, and autonomic remodeling, leading to arrhythmogenic damage in the heart[33].

There has been no study between the ALBI score, which is used as a marker of liver function, and arrhythmia in HF patients. Our study is the first to demonstrate this relationship. According to our study, a relationship was found between the ALBI score and VA.

Study Limitations

This study has several limitations. First, this study has a single center design and has included a limited number of patients. Second, this was a retrospective cross-sectional study. The results should be supported by future prospective studies.

Conclusion

This is the first cross-sectional study to show that the ALBI score is independently associated with an increased risk of ventricular arrhythmias in patients with HF. The ALBI score is a cost-effective and simple index. It may provide preventive treatment and close follow-up in this patient group.

Ethics

Ethics Committee Approval: The study protocol was approved by the Ankara Bilkent City Hospital No. 2 Medical Research Scientific and Ethical Evaluation Board (TABED) (approval no.: TABED 2-24-02, date: 07.02.2024).

Informed Consent: This study was planned as a single-center retrospective study.

Authorship Contributions

Concept: Özilhan MO, Açıkgöz SK, Design: Özilhan MO, Açıkgöz SK, Data Collection and/or Processing: Özilhan MO, Analysis and/or Interpretation: Açıkgöz SK, Literature Search: Özilhan MO, Writing: Özilhan MO, Açıkgöz SK.

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