Smyrna Tıp Dergisi ***Araştırma Makalesi***

Analysis of the Predictive Value of Liver Function Tests in the Patients with Decompensated Heart Failure for Detecting the Early-Late Mortality

Dekompanse Kalp Yetersizliği Hastalarındaki Karaciğer Fonksiyon Testlerinin Erken ve Geç Dönem Mortalite ve Morbiditeyi Saptamada Öngörücü Değerinin Analizi

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Summary

Objective: To determine the predictive value of liver function tests in the patients with decompensated heart failure for predicting in-hospital and out-of-hospital mortality and morbidity.

Material and Methods: The files of the patients who were over the age of 18 and followed after hospitalization to Cardiology Clinic, Faculty of Medicine Hospital, Ondokuz Mayıs University between 01.01.2011 and 30.06.2013 with the diagnosis of decompensated heart failure. Patients were divided into the groups according to alanine aminotransferase (ALT) levels which is the more spesific determinant of liver cell necrosis and the association of it with other liver function tests was investigated.

Results: The average age of the patients included in the study was 67.6±11.6 years. The median of ALT, AST, direct bilirubin values of the patients was [24.4 (4.8-4533.0) U/L, 28.7 (9.2-7926.0) U/L, 0.22 (0.01-6.58) mg/dL respectively] and the average of albumin values was 3.8±0.5 mg/dL. Patients in group 4 with higher ALT levels were more hypotensive than other groups. It was detected that aspartate transaminase (AST) levels were higher, albumin levels were lower, direct bilurubine levels were higher, and hyponatremia was more common in the patients in group 4. Positive inotropic need, mechanical ventilation, ultrafiltration requirement, cardiac resynchronization therapy (CRT) need were found more in group 4. Of the patients in this group, hospitalization duration was longer, cardiac intensive care unite (CICU) needs were higher, and in-hospital mortality, total mortality and rehospitalization need were higher while there was no difference in out-of-hospital mortality. While cut-off value of ALT for in-hospital mortality was determined as 48.9 U/L with 86.4% sensitivity and 80.3% specificity, cut-off value of CICU hospitalization need was detected as 25.3 U/L with 71.7% sensitivity and 70.3% specificity. Considering the survival rates of the patients during one-year follow-up, the survival rate of group IV was lower with an average of 219 days.

Conclusion: It was detected that high level of ALT, which was measured during hospitalization to predict in-hospital mortality and morbidity of the patients hospitalized due to heart failure, to determine re-hospitalization needs due to heart failure and to evaluate their survival rates, was an important marker.

Key words: Alanine transferase, heart failure, in-hospital mortality, life rate analysis, liver function tests

Özet

Amaç: Dekompanse kalp yetersizliği hastalarındaki karaciğer fonksiyon testlerinin hastane içi ve hastane dışındaki, mortalite ve morbiditeyi göstermedeki öngörücü değeri araştırıldı.

Materyal ve Method: Bu çalışma Ondokuz Mayıs Üniversitesi Tıp Fakültesi Hastanesi Kardiyoloji Kliniği'ne 01/01/2011 ile 30/06/2013 tarihleri arasında dekompanse kalp yetmezliği tanısı ile yatışı yapılarak izlenen 18 yaş üstü hastaların dosyaları retrospektif olarak incelenerek yapıldı. Hastalar karaciğer hücre ölümünün daha spesifik göstergesi olan ALT değerlerine göre gruplara ayrıdı ve diğer karaciğer fonksiyon testleri ile ilişkisi araştırıldı.

Bulgular: Araştırmaya dahil edilen hastaların yaş ortalaması 67,6±11,6 yıldı. Hastaların ALT, AST, direk bilirubin değerleri ortancası [24,4 (4,8-4533,0) U/L, 28,7 (9,2-7926,0) U/L, 0,22 (0,01-6,58) mg/dl, sırasıyla]

albümin değerleri ortalaması 3,8±0,5 mg/dL'ydi. Yüksek ALT düzeyinin bulunduğu grup IV'teki hastalar diğer gruplara göre daha hipotansifti. Grup IV'teki hastalarda aspartat transaminaz (AST) seviyeleri daha yüksek, albumin seviyeleri daha düşük, direkt bilurubin seviyeleri daha yüksek ve hiponatremi daha yaygın saptandı. Grup 4'te pozitif inotrop gereksinimi, mekanik ventilasyon, ultrafiltrasyon ihtiyacı, resenkronizasyon tedavisi (CRT) gereksinimi daha fazla saptandı. Bu gruptaki hastaların hastane yatış süreleri daha uzun, koroner yoğun bakım ünitesi (KYBÜ) ihtiyaçları daha fazla,hastane içi ve total mortaliteleri daha fazla, rehospitalizasyon ihtiyacı daha fazla saptanırken , hastane dışı mortalitesinde fark saptanmadı. Hastane içi mortalite için ALT sınır değeri %86,4 sensivite, %80,3 spesifite ile 48,9 U/L saptanırken; KYBÜ yatış ihtiyacı için %71,7 sensivite, %70,3 spesifite ile 25,3 U/L saptandı. Hastaların 1 yıllık takiplerinde sağkalım hızlarına bakıldığında grup IV'ün sağ kalım hızı ortalama 219 gün ile daha düşük saptandı.

Sonuç: Kalp yetersizliği sebebi ile hastaneye yatırılan hastaların hastane içi mortalite ve morbiditelerini öngörmede, yeniden kalp yetersizliği nedeni ile hastaneye yatış ihtiyaçlarını belilemede ve sağ kalım hızlarını değerlendirmede yatış sırasında ölçülen ALT yüksekliğinin önemli bir belirteç olduğu saptanmıştır.

Anahtar kelimeler: Alanin transferaz, kalp yetersizliği, hastane içi mortalite, yaşam hızı analizi, karaciğer fonksiyon testleri

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Introduction

Heart failure is one of the diseases that cause death and disability the most in the world (1). Although important improvements have been made in this disease with the increase of modern treatments, the number of patients has gradually increased with the increase in the elderly population. Current treatment methods offer a wide range of options from lifestyle changes to artificial heart treatments. However, the question of how we should treat which patient at which stage is just as important.

The most important criterion in determining the prognosis of patients is definitely clinical evaluation. On the other hand, some quantitative measurements can assist the clinician during the prognosis and treatment phase. BNP and NT-proBNP measurements have become important markers guiding clinicians in the diagnosis of heart failure (2,3). Nowadays, new markers used for this purpose are tried and published every day. However, some of our classic tests still need to be interpreted more accurately. Hepatic cell injury can be a nonspecific condition that can accompany many diseases. But, the emergence of hepatic damage is a very strong determinant in terms of the importance of the problem (4). Although it has been shown with various reports that high level of transaminases increasing in the process of heart failure can provide information regarding the prognosis of the disease, most of these reports come from posthoc analysis of the studies that have not been performed for this purpose (5,6,7). In this study, it was aimed to test the importance of high level of transaminases in heart failure with short and long-term clinical results.

Material and Methods

Study population

This study is a retrospective case-control study. The hospitalizations to Cardiology Clinic, Faculty of Medicine Hospital, Ondokuz Mayıs University between 01.01.2011 and 30.06.2013 were scanned for the study. As a primary diagnosis in screening period, the patients with decompensated heart failure were included in the study. Primary pulmonary hypertension, pulmonary embolism, primary liver or biliary tract disease, previous history of viral hepatitis, acute myocardial infarction, cardiac tamponade, constructive pericarditis, advanced mitral valve stenosis, chronic obstructive pulmonary disease were determined as exclusion criteria.

The patients included in the study were divided into 4 groups based on their alanine aminotransferase (ALT) values. Patients were defined as group I with ALT values of 0-14.8 U/L, group II with ALT values of 14.9-24.2 U/L, group III with 24.4-46.1 U/L and group IV with ALT values of 48.7-4533 U/L.

Data analysis

The laboratory values, vital signs, clinical features, treatment regimens, hospitalization units and durations, electrocardiography (ECG) and echocardiography parameters of the patients included in the study after the exclusion phase were obtained from the local database, patient files and nurse observations.

The number of rehospitalization and death information of all patients for 12 months after hospitalization was evaluated through phone calls and Turkısh Republic The Provincial Population Directorate information system.

Laboratory analysis
Peripheral venous blood sampling was performed from all patients on the first day of hospitalization. ALT, aspartate aminotransferase (AST), albumin, direct bilurubine, total bilurubine values from the samples taken were measured by Roche Cobas 8000 modular analyzer (Series C701, Mannheim, Germany) in the biochemistry laboratory and prothrombin time was measured by SYSMEX CA-1500 coagulation device (Sysmex Corporation, Kobe, Japan).

Statistical analysis
Research data were uploaded to the computer and evaluated via SPSS (Statistical Package for Social Sciences for Windows v.22, SPSS Inc. Chicago, IL). Descriptive statistics were presented as mean (±), standard deviation, frequency distribution and percentage. In addition to descriptive statistics, chi-square test was applied. Binary comparisons were performed by applying Bonferroni correction in the variables found significant. The suitability of variables to normal distribution was examined using visual (histogram and probability graphs) and analytical methods (Kolmogorov-Smirnov / Shapiro-Wilk tests).

One-way variance analysis (One-way ANOVA) was used in statistical significance among the variables determined to conform to normal distribution as statistical method. The homogeneity of the variances was evaluated by Levene test. In cases where there was a significant difference between the groups, pairwise post-hoc comparisons were made using Tukey test. In cases where the variances were not homogeneous, comparisons between groups were analyzed with Welch ANOVA test. In cases where there was a significant difference between the groups, pairwise post-hoc comparisons were realized using Tamhane T2 test. The diagnostic value of ALT in predicting in-hospital mortality, out-of-hospital mortality, and 3 or more rehospitalizations was analyzed using Receiver Operating Characteristics (ROC) curve analysis. The sensitivity and specificity values of these cut-offs were calculated in the presence of significant cut-off values. The effects of the study groups on survival were analyzed using LogRank test. Survival rates were calculated using Kaplan-Meier survival analysis. Statistical significance level was accepted as $p<0.05$.

Results

Three hundred and one patients were included in the study after excluding those who met the exclusion criteria determined among patients hospitalized with decompensated heart failure between the dates we determined for the study. While the average age of the patients included in the study was 67.6±11.6 years, the median of ALT values was detected as 24.4 (4.8-4533.0) U/L. Age, hyperlipidemia, heart rate, ischemic etiology and CRT ratio were similar between the groups while hypertension, systolic blood pressure and NYHA degree were significantly different between the groups. Baseline demographic and clinical characteristics of the patients were shown in Table 1.

In comparison of the laboratory values between the groups, it was observed that serum sodium and albumin levels were lower whereas creatinine and direct bilirubin levels were higher in group IV with high ALT levels compared to other groups. In addition, wide QRS rate and LBBB rate were higher in group IV patients than the other groups (Table 2).

There were differences between the groups in terms of echocardiographic parameters. Especially, it was determined that EF value of group I was higher than the other three groups. However, there was no significant difference between the groups with respect to diastolic dysfunction rate (Table 2). On the other hand, the duration of hospitalization, intensive care need, in-hospital mortality, ventilator need, UF need and CRT need were found to be higher in group IV patients (Table 3).

Table 1. *Demographics and baseline clinical characteristics*

	Group 1 (0-14.8 U/L) (n=75)	**Group 2 (14.9-24.2 U/L) (n=75)**	**Group 3 (24.4-46.1 U/L) (n=75)**	**Group 4 (48.7-4533 U/L) (n=76)**	**p**
Age (years)	70.1 ± 11.6	68.6 ± 8.6	65.8 ± 12.8	66.1 ± 12.8	0.071
Men (n,%)	29 (39.2)[cd]	44 (57.9)	51 (67.1)	54 (72.0)	<0.001
Diabetes mellitus (n,%) (n=294)	22 (30.6)[b]	40 (52.6)	26 (35.6)	33 (45.2)	0.031
Hypertension (n,%) (n=294)	53 (74.6)	56 (75.7)	50 (66.7)	38 (51.4)[ab]	0.006
Hyperlipidemia (n,%) (n=293)	14 (20.0)	17 (23.3)	20 (28.2)	14 (20.0)	0.617
Systolic blood pressure (mmHg)	132.5±33.6	128.2±34.7[a]	119.7±21.7	108.6±31.7[ab]	<0.001
Heart rate (beat/min)	85.1±20.0	87.4±21.1	85.4±23.3	90.2±25.2	0.514
Etiology					
Ischemic (n,%)	39 (54.2)	48 (64.9)	47 (63.5)	42 (57.5)	0.509
Valvular disease (n,%)	8 (11.0)	11 (15.5)	15 (20.8)	21 (28.8)[a]	0.040
CRT (n,%)	1 (1.4)	5 (6.6)	8 (10.5)	9 (12)	0.066
NYHA (n,%)					<0.001
Class II 33 (11.3)	14 (19.2)	9 (12.2)	9 (12.2)	1 (1.4)[abc]	
Class III 162 (55.7)	41 (56.2)	51 (68.9)	51 (70.8)	19 (26.4)	
Class IV 96 (33.0)	18 (24.7)	14 (18.9)	12 (16.7)	52 (72.2)	
Hemoglobin (gr/dL)	11.5±1.6[bcd]	12.4±2.0	12.7±1.7	12.3±1.7	0.001
Na (mEq/L)	137.0±5.0	137.1±4.4	137.1±4.7	134.2±6.7[abc]	**0.002**
K (mEq/L)	4.4±0.7	4.4±0.7	4.4±0.5	4.5±0.7	0.783
Cr (mg/dl)	1.6±1.2[b]	1.2±0.4	1.3±0.5	1.6±0.7[bc]	**0.001**

CRT. cardiac resynchronization therapy; NYHA. new york heart association ; [a]p<0.001 in comparison with group 1 ; [b]p<0.001 in comparison with group 2 ; [c]p<0.001 in comparison with group 3 ; [d]p<0.001 in comparison with group 4

Table 2. *Hepatic, electrocardiographic and echocardiographic parameters of the patients*

	Group 1 (0-14.8 U/L) (n=75)	**Group 2 (14.9-24.2 U/L) (n=75)**	**Group 3 (24.4-46.1 U/L) (n=75)**	**Group 4 (48.7-4533 U/L) (n=76)**	**p**
Hepatic parameters					
AST (U/L)	19.0 (9.2-63)[bcd]	25.8 (14-111)[cd]	31.6 (15-190.4)[d]	101 (21-7926)	**<0.001**
Albumin (g/dl)	3.7±0.5	3.8±0.3	3.8±0.6	3.6±0.5[bc]	**0.025**
Total bilirubin (mg/dl)	0.8±0.5	1.0±1.2	1.0±0.8	1.2±0.9	0.066
Direct bilirubin (mg/dl)	0.2±0.2	0.3±0.8	0.3±0.4	0.5±0.5[a]	**0.035**
Prothrombin time (sec)	14.5±4.2	13.7±2.9	14.3±6.1	15.9±5.1	0.192
Electrocardiographic parameters					
QRS >120ms (%)	18 (25.7)	26 (35.6)	24 (34.8)	45 (63.4)[abc]	**<0.001**
Atrial fibrillation (%)	36 (50.7)	30 (41.7)	32 (45.7)	26 (36.1)	0.343
LBBB (%)	12 (17.1)	20 (27.4)	19 (27.5)	38 (52.8)[abc]	**<0.001**
Echocardiographic parameters					
Ejection fraction (%)	44.2±12.2[bcd]	38.1±10.5	38.0±10.8	33.3±11.3[b]	**<0.001**
Diast. dysfunction (n, %)	34 (49.3)	28 (40.0)	31 (43.7)	35 (49.3)	0.624
LVEDd (mm)	53.5±9.3	56.6±9.5	56.3±9.7	59.8±11.9[a]	**0.004**
LVESs (mm)	40.2±10.5	43.9±10.1	43.7±10.6	47.9±13.5[a]	**0.001**
LV hypertrophy (n, %)	50 (68.5)	54 (73.0)	44 (59.5)	43 (58.9)	0.199
Mitral valve dysfunction	8 (11.0)	8 (11.3)	14 (19.4)	19 (26.0)	0.060
Aortic valve dysfunction	0 (0)	3 (4.2)	0 (0)	3 (4.1)	0.104

AST. aspartate aminotransferase; LBBB. Left bundle branch block; LVEDd. Left ventricular end diastolic diameter; LVESD. Left ventricular end systolic diameter; LV. Left ventricle.

Variables determined to fit to normal distribution were presented as mean ± SD, and those not fitting were presented as median (min-max).

ap<0.001 in comparison with Group 1; bp<0.001 in comparison with Group 2; cp<0.001 in comparison with Group 3; dp<0.001 in comparison with Group 4

Table 3. *Clinical results of the patients in-hospital and 12-month follow-up*

	Group 1 (0-14.8 U/L) (n=75)	**Group 2 (14.9-24.2 U/L) (n=75)**	**Group 3 (24.4-46.1 U/L) (n=75)**	**Group 4 (48.7-4533 U/L) (n=76)**	**P**
In-hospital					
Hospitalization (days)	7.5±4.7	6.7±2.6	7.3±4.4	11.3±8.0[abc]	**<0.001**
IC need (%)	9 (12.2)	13 (17.1)	17 (22.4)	53 (70.7)[abc]	**<0.001**
IC hospitalization (days)	3.1±2.0	2.6±1.9	3.5±2.5	5.6±6.3	0.129
In-hospitak mortality (%)	1 (1.3)	1 (1.3)	1 (1.3)	19 (25.3)[abc]	**<0.001**
Positive inotropic need (%)	13 (17.6)	11 (14.5)	15 (19.7)	56 (74.7)[abc]	**<0.001**
MV need (%)	1 (1.4)	1 (1.3)	2 (2.6)	17 (22.7)[abc]	**<0.001**
UF need (%)	0 (0)	1 (1.3)	1 (1.3)	7 (9.3)[a]	**0.003**
CRT need (%)	10 (13.5)	2 (2.6)	5 (6.6)	12 (16.0)[b]	**0.020**
Revascularization (%)	5 (6.8)	7 (9.2)	6 (7.9)	7 (9.3)	0.933

ap<0.001 in comparison with Group 1; bp<0.001 in comparison with Group 2; cp<0.001 in comparison with Group 3; dp<0.001 in comparison with Group 4

There was no difference between the medical treatments (ACE / ARB, beta-blocker, diuretics, MRAs, digoxin, anti-platelet, anti-coagulans and statins) of the patients included in the study.

A total of 88 deaths occurred during in-hospital and 12-month follow-up period in our study. Of these, 11 were group 1, 19 were group 2, 18 were group 3 and 40 were group 4 (p<0.001). The probability of one-year survival was 85% in group 1, 75% in group 2, 76% in group 3 and 46% in group 4 (p<0.001). The average life span of group 4 patients was significantly found lower than the other groups. The average life expectancy was 219 days in group 4, 309 days in group 3, 320 in group 2 and 334 days in group 1 (p<0.001). In addition, the number of rehospitalizations of group 4 patients at 12 months of follow-up was higher than the other groups (Table 4)

Table 4. *Comparison of 12-month follow-up between ALT groups*

	Group I (0-14.8 U/L) (n=75)	**Group II (14.9-24.2 U/L) (n=75)**	**Group III (24.4-46.1 U/L) (n=75)**	**Group IV (48.7-4533 U/L) (n=76)**	**p**
Rehospitalization Need (%)	22 (45.8)	24 (54.5)	31 (66.0)	30 (56.6)	0.268
The Number of Rehospitalization	1.55±0.67	1,54±0.83	1,84±0.96	2.67±1.84[ab]	**0.002**
Out-of-Hospital Mortality (%)	10 (13.5)	18 (23.7)	17 (22.4)	21 (28.0)	0.185
Total Mortality (%)	11 (14.9)	19 (25.0)	18 (23.7)	40 (53.3)[abc]	**<0.001**

[a]p<0.001 in comparison with group 1; [b]p<0.001 in comparison with group 2; [c]p<0.001 in comparison with group 3; [d]p<0.001 in comparison with group 4

It was observed that serum ALT cut-off value of 48.9 U/L had 86.4% sensitivity and 80.3% specificity for in-hospital mortality as a result of the evaluation realized by ROC analysis. It was detected that serum ALT cut-off value of 25.3 U/L had 71.7% sensitivity and 70.3% specificity in terms of the need for hospitalization in the intensive care unit (Table 5).

Table 5. *Determination of ALT cut-off values in terms of in-hospital mortality and the need for hospitalization to CICU*

	ALT Cut-off Value	**Sensitivity (%)**	**Specificity (%)**
In-hospital mortality	48.9	86.4	80.3
Hospitalization to CICU	25.3	71.7	70.3

Discussion

The importance of secondary hepatic dysfunction due to heart failure has been shown in previous studies (6,7,8,9). However, these studies may not reflect real-life data because they are mostly post-hoc analyzes of large studies.

The main reason for the increase in hepatic transaminases due to heart failure is liver cell damage (8). Impairment of permeability in hepatocytes causes an increase in the serum level of intracellular enzymes such as AST and ALT (10). Moreover, chronic insufficiency of systemic perfusion causes malnutrition, fatty liver and liver fibrosis (11,12). This is also associated with a decrease in the synthesis ability of the liver and a decrease in serum albumin level. Impairment of cardiac function and secondary hepatic dysfunction causes an increase in AST, ALT as well as other hepatic markers such as GGT, alkalen phosphatase, bilirubin (6,7,13). Especially, the association of hepatic congestion with an increase in direct bilirubin has also been reported (8). In the study, AST and direct bilirubin levels were found higher while albumin levels were lower in group 4 patients.

In the study, it was observed that groups with high ALT levels were functionally worse. These patients stayed in the hospital for a longer time and the number of rehospitalizations was higher in the post-hospital period. Arruda LA et al. (12) reported that there was a significant increase in transaminase levels of the patients with NYHA IV heart failure although this increase didn't occur in NYHA II-III patients (14). Kubo et al. (13) examined the assocaition between liver functions and cardiac index and found that AST and ALT values were significantly higher in patients with cardiac index <1.5 L/min/m^2. The need for positive inotropic therapy, mechanical ventilation and ultrafiltration were found significantly higher in group 4 than in other groups in the study. This may be due to the fact that the patients in group 4 are more hypotensive at admission and their NYHA functional classes are worse. Similarly, the need for more support and device therapy was observed in the patients with high transaminases in post-hoc analysis of the RO-AHFS study (15).

In-hospital and one-year total mortalities were found higher in group 4 patients with very high ALT levels in the study. Out-of-hospital mortality was proportionally higher in group with high ALT level but no statistical significance was found. However, 19 (25.3%) of group 4 patients already died in the in-hospital period. More than a third of the remaining patients (36%) died in the post-hospital period. Therefore, statistical insignificance seems to be associated with low number of patients. Moreover, serum ALT cut-off value of 48.9 U/L was found to have 86.4% sensitivity and 80.3% specificity for in-hospital mortality as a result of the evaluation performed by ROC analysis in the study. Murin J et al. (16) detected that transaminase levels during hospitalization were higher in patients with mortality due to congestive heart failure. In a study in which Jan bigeus et al. (16) retrospectively evaluated 189 decompensated patients, a higher mortality rate was found at low albumin and high ALT levels at 180-day follow-up.

It was reported in the post-hoc analysis of SURVIVE study that increased transaminase level in patients with acute heart failure who should receive positive inotropic treatment was associated with both short (30 days) and long (180 days) mortality (9). There was no similar association between transaminase levels and mortality in the post-hoc analysis of CHARM study. The reasons for this may be the fact that patients with acute decompensated heart failure and symptomatic hypotension were excluded and only 2.6% of the patients had NYHA IV functional class in this study (6).

Heart failure is associated with both anatomical and electrical remodeling. Moreover, prolonged QRS duration and the presence of LBBB are associated with progression of heart failure and poor outcomes (17,18). It was detected in the study that group 4 patients with very high ALT levels had greater QRS duration and more LBBB. Similarly, it was observed that group 4 patients showed higher anatomic remodeling in terms of EF, LVEDd and LVESd. The association between transaminases and cardiac electrical remodeling has not been previously reported in the literature. However, it is not surprising that the progress in the stage of heart failure and the results of anatomical remodeling will lead to electrical remodeling.

Study Limitation

This study is a retrospective and single-center study. Therefore, the discrimination of secondary hepatic injury that accompanies heart failure from primary hepatic injury was realized only with retrospective file information. This may have prevented some patients with primary hepatic injury from being excluded in the study. On the other hand, hepatic injury was not evaluated by any imaging method. It was noticed that the information about alcohol use of the patients was quite insufficient in the file information.

Conclusion

Hospitalization duration, IC need, in-hospital mortality, positive inotropic need, cardiac resynchronization requirement, mechanical ventilation, ultrafiltration need and total mortality were found to be higher in the patients with very high ALT in the study. Some cut-off values found in the study can provide important information in terms of prognosis of the patients hospitalized with heart failure and may assist in the planning of recent treatments such as supportive treatments or transplantation that the patients may need.

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