The Prognostic Role of Ultrasound Diagnostic Methods in the Comprehensive Assessment of Congestion in Patients with Acute Decompensation of Heart Failure

Zhanna D Kobalava[1], Tolkacheva Veronika Vladimirovna[1], Sarlykov Bekbolot Kanatbekovich[2], Rena Sh Aslanova[1], Lapshin Artem Alekseevich[1], Nazarov Ivan Sergeevich[1], Smirnov Ilya Pavlovich[1], Maria V Vatsik-Gorodetskaya[3], Ghazaal Alavi Tabatabaei[4], Ibrahim Al Zakwani[5,6], Mohammed Al Jarallah[7], Georgiana Luisa Baca[8], Peter A Brady[9], Rajesh Rajan[7] and Bhavesh Talera[10]

[1] Department of Internal Diseases with Courses of Cardiology and Functional Diagnostics, Peoples` Friendship University of Russia (RUDN University), Moscow, Russia

[2]Head of the Department of therapeutic disciplines IMFI Salymbekov University, 720054, 3 Fuchika street, Bishkek, Kyrgyzstan

[3]Deputy Chief Physician for Anesthesiology and Resuscitation of V. V. Vinogradov State Clinical Hospital, Vinogradov city clinical hospital, Moscow, Russian Federation, 117292, 61 Vavilova street, Moscow, Russia

[4] Isfahan Cardiovascular Research Center, Cardiovascular Research Institute, Isfahan University of Medical Sciences, Isfahan, Iran.

[5]Department of Pharmacology & Clinical Pharmacy, College of Medicine & Health Sciences, Sultan Qaboos University, Muscat, Oman

[6] Gulf Health Research, Muscat, Oman

[7] Department of Cardiology, Sabah Al Ahmed Cardiac Centre, Kuwait City, Kuwait

[8]Department of Intramural Research Program, Laboratory of Cardiovascular Science, National Institute on Aging, National Institutes of Health, Baltimore, MD, United States

[9] Department of Cardiology, Illinois Masonic Medical Center, Chicago, IL, USA

[10] Department of Internal Medicine, Ivy Superspeciality Hospital, Sector 71, Mohali, Chandigarh, India

Received: 12 September 2023

Accepted: 14 Jan 2024

***Corresponding author:** cardiology08@gmail.com

DOI 10.5001/omj.2024.65

Abstract

Objectives: To evaluate the prognostic value (total mortality + repeated hospitalization for HF) of ultrasound diagnostic methods in patients with acute decompensation of heart failure (ADHF), according to indirect elastometry performed upon discharge from the hospital in a comprehensive assessment of congestion in patients with on survival rates.

Methods: Ultrasound methods assessed were the number of B-lines, the presence of hepatic venous congestion according to the Venous Excess Ultrasound Score (VExUS) protocol and liver density. Clinical outcomes were assessed using a structured telephone survey method at 1,3,6,12 months after discharge. Combined overall mortality and readmission rates for HF were assessed. Threshold values were calculated for different methods for detecting congestion: the number of B lines according to ultrasound data> 5, liver density > 6.2 kPa.

Results: A total of 63 (30%) endpoints and 23 (11%) deaths were detected within 364 days (IQR from 197 to 365). Cox univariate regression analysis demonstrated independent prognostic value in relation to the total endpoint of all ultrasound methods for diagnosing congestion, such as lung ultrasound, ultrasound assessment of hepatic venous congestion according to the VExUS protocol, indirect elastometry. Cox multivariate regression analysis confirmed independent predictive significance for the potential endpoint risk for the following: liver density >6.2 kPa (HR 1,9 (95% CI 1,0 – 3,3); p=0,029), and hepatic venous congestion according to the VExUS protocol (HR 2.8 (95% CI 1,3

– 5,7); p=0,004). There was a significant increase in the risk of overall mortality and re-hospitalization in the presence of congestion, identified by liver fibroelastometry + lung ultrasound (HR 10,5 (95% CI 2,3 – 46,2); p = 0,002), according to ultrasound assessment of hepatic venous congestion according to the VExUS + lung ultrasound protocol (HR 16,7 (95% CI 3,9 – 70,7); p < 0.001), according to all three methods (HR 40,1 (95% CI 6,6 – 243,1); p < 0,001).

Conclusions: Ultrasound diagnostic methods including the number of B-lines, presence of hepatic venous congestion according to the VExUS protocol and liver density according to indirect elastometry at discharge in patients with acute decompensation of heart failure (ADHF) has independent prognostic value.

Keywords: heart failure, congestion assessment, survival, prognosis, lung ultrasound, indirect fibroelastometry, hepatic venous congestion, VExUS protocol

Introduction

Acute decompensated heart failure (HF) is associated with high mortality and repeated hospitalization yet predictors of an unfavorable prognosis in these patients are lacking.[1,2] Disease progression leads dysfunction of internal organs due to hypoperfusion and systemic congestion; in this way HF is a multi-organ pathology. Systemic congestion is considered the main clinical feature of decompensation in HF,[3,4] the elimination of which is one of the main goals of therapy.[5] Recently, the prognostic value of an integral assessment using various modern methods of diagnosing stagnation, including ultrasound assessment methods, in patients hospitalized with acute decompensation of heart failure (ADHF) has been widely discussed.[6,7] Stratification of the risk of future cardiovascular events in patients with HF may help improve long-term outcomes by identifying high-risk patients and enhancing therapy in such patients.[8]

Acute and chronic decompensated HF may be accompanied by hepatic dysfunction, currently referred to as "cardio-hepatic syndrome" [9], with progressive development of liver fibrosis with declining synthetic function associated with a worsening prognosis.[10] A characteristic feature of cardio-hepatic syndrome is an increase in venous congestion, manifested by expansion of the hepatic and portal veins and a change in the shape of blood flow, that can be assesseed by ultrasound. One promising and informative method is a comprehensive sequential ultrasound assessment of venous congestion according to the Venous Excess Ultrasound Score (VExUS) protocol, which allows objective assessment the presence and severity of congestion with the study of port-hepatic Doppler waves in addition to measuring the diameter of the inferior vena cava.[11]

The the purpose of this study, therefore, was to evaluate the prognostic value including survival and re-hospitalization of ultrasound diagnostic methods including the number of B-lines using lung ultrasound, the presence of hepatic venous congestion according to the VExUS protocol and liver density according to indirect elastometry performed at the time of hospital discharge in patients with acute decompensated heart failure (ADHF).

Methods

Decompensation of HF was diagnosed on the basis of generally accepted criteria: the appearance or rapid aggravation of symptoms and signs of HF, which requires emergency hospitalization of the patient and intensive therapy in combination with objective signs of heart damage (systolic and/or diastolic dysfunction, left ventricular hypertrophy (LVH), LP enlargement according to echocardiography assesment) and an increase in NT levels-proBNP.[12]

The study did not include patients with acute coronary syndrome (ACS), lung diseases (exacerbation of COPD, BA), end-stage chronic kidney disease, malignant neoplasm, edematous syndrome of other etiology, primary liver pathology, acute hepatitis with increased transaminases (T.A.)> 5 upper limits of normal, alcoholic excess before hospitalization, severe cognitive deficit, immobilization and patients with the inability to perform Bioelectric Impedance Vector Analysis (BIVA) (amputation of limbs, ulcers or pronounced trophic changes on the skin of the limbs, the presence of metal implants and structures).

All patients signed an informed consent to participate in the study. The study was approved by the Ethics Committee of the Peoples' Friendship University of Russia (RUDN) Medical Institute (Protocol No. 26 of 18.02.21).

The clinical and demographic characteristics of patients are presented in Table 1. Among 207 patients, men and women were approximately equally represented (54.1% and 45.9%, respectively), the majority had a history of arterial hypertension (AH) (88.9%), coronary heart disease occurred in 49.3% of cases, type 2 diabetes mellitus 37.1%.

Table 1: Clinical and demographic characteristics of patients.

Parameters	Value

Gender (male/female), n (%)	112 (54,1)/ 95 (45,9)
Age, years (M±SD)	70,7 ± 12,8
Systolic BP, mmHg (Me (IQR))	117 (106; 132)
Diastolic BP, mmHg (Me (IQR))	69 (62;77)
LVEF, % (Me (IQR))	44 (33; 55)
NT-proBNP, pg/ml (Me (IQR))	1076 (609; 2098)
Arterial hypertension, n (%)	184 (88,9%)
Coronary heart disease, n (%)	102 (49,3%)
History of myocardial infarction, n (%)	67 (32,4%)
Atrial fibrillation, n (%)	132 (63,8)
Type 2 diabetes mellitus, n (%)	77 (37,1)

The data is presented as median, 25th and 75th percentile (Me (IQR)) or the arithmetic mean (M) and the standard deviation of the mean (SD).

All patients underwent a standard physical examination at admission and at discharge, as well as laboratory and instrumental studies, including NT-proBNP, lung ultrasound, indirect liver fibroelastometry and Doppler ultrasound evaluation of hepatic venous congestion according to the VExUS protocol.

NT-proBNP in blood serum was determined by ELISA enzyme immunoassay using the NT-proBNP-ELISA-BEST test systems (Russia, Vector-Best CJSC). The accuracy of the test was 96.4% and is reliable.[12]

Upon discharge, ultrasound of both sides of the chest (Sonosite, convexic sensor) was performed in 8 areas (II and IV m/r between the parasternal and midclavicular lines and between the anterior and middle axillary lines). The number of B-lines was calculated, defined as vertical, hyperechoic reverberation artifacts from the pleural line to the bottom of the screen, moving synchronously with the movement of the lungs.

Indirect liver fibroelastometry was performed on the day of discharge using the FibroScan ® 502 touch device (Echosens, France) according to a standard technique in the projection of the right lobe of the liver at the level of 8 or 9 intercostal space along the anterior or median axillary line.[13] Studies with at least 10 and >60% of successful measurements were considered valid. The density (elasticity) of the liver in kilopascals (kPa) and the interquartile range in percent (%) were determined. The density quantitatively indicated the degree of fibrosis in this area of the liver parenchyma where the sensor was installed.

Ultrasound assessment of hepatic venous stagnation was carried out according to the VExUS protocol, on an expert-level device VIVID E-90 (GE, Healthcare) using abdominal and sector sensors, with an assessment of the diameter of the inferior vena cava, the shape of hepatic blood flows, portal in the mode of pulse-wave Dopplerography.[14] The study of Doppler curves was carried out on exhalation with simultaneous ECG registration on the monitor of the ultrasound machine. With a diameter of inferior vena cava ≥ 2.0 cm, according to the VExUS protocol, the shape of the blood flow of the port-hepatic veins was consistently evaluated. When constructing ROC curves for predicting outcomes (total mortality + re-hospitalization), the following threshold values of different methods for assessing congestion were identified, the number in the line >5 by lung ultrasound, the value of liver density >6.2 kPa

For hepatic vein Dopplerography, the systolic phase was normally of greater amplitude than the diastolic phase, while a decrease in systolic blood flow velocity was considered a minor deviation, and the presence of a reverse systolic phase was a pronounced deviation [Figure 1].

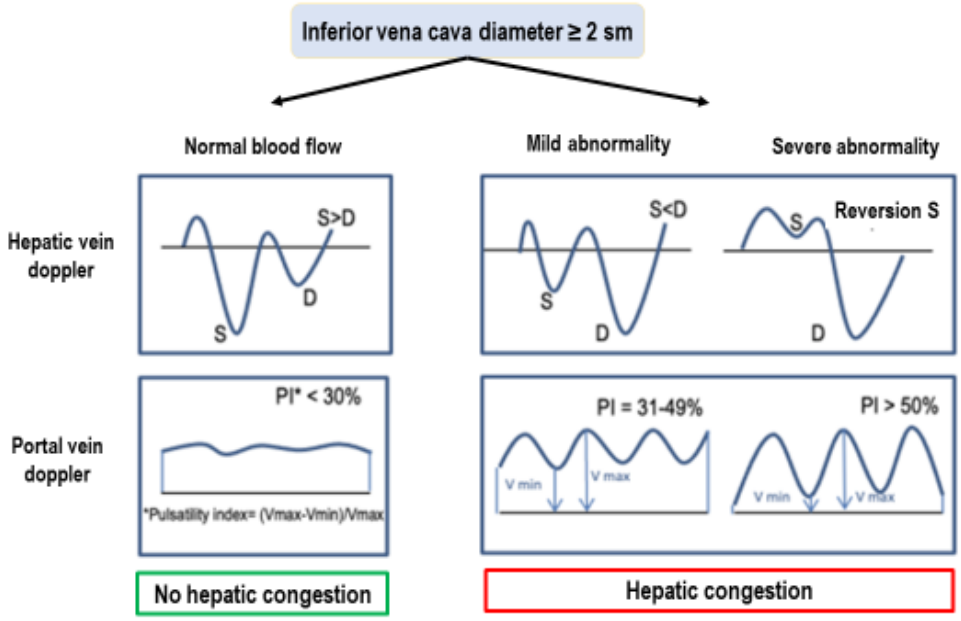

Figure 1: Assessment of hepatic venous congestion using Dopplerography.

Assessment of long-term clinical outcomes was carried out by a structured telephone survey 1, 3, 6, 12 months after discharge. Total mortality and the combined indicator of total mortality and repeated hospitalizations were evaluated as the end point.

Version 19.0 and SPSS (version 22.0) were used. Quantitative variables were described as the arithmetic mean (M) and the standard deviation of the mean (SD) (with a normal distribution) or as the median (Me) and interquartile range (IQR) (with an asymmetric distribution). The threshold survival values for each of the methods were determined by constructing ROC curves. P<0.05 was considered significant. To assess the prognostic significance of different methods for the risk of occurrence of variables of interest, single- and multi-factor models of Cox regression analysis were used. The variables included in the model were selected taking into account their significance. The probability of survival was estimated by the method of constructing Kaplan Meyer survival curves, the comparison was made using a lograng criterion.

Results

A total of 207 patients (54% men, average age 70.7±12.8 years) with chronic HF who were hospitalized for decompensation of HF were included.

Doppler curves of liver congestion according to the VExUS protocol persisted in 57 (28%) patients (Table 2).

Table 2: Characteristics of patients depending on the presence of hepatic congestion at discharge.

Parameters	**Total group, n=207**	**Congestion in hepatic veins (Inferior vena cava ≥2 cm) n= 57**	**No congestion in hepatic veins (Inferior vena cava <2 см) n= 150**	
Age, years	70,7 ± 12,8	71 ± 12,7	70,6 ± 12,9	0,876
Male, n (%)	112 (54,1%)	37 (64,9%)	75 (50%)	0,054
Coronary heart disease, n (%)	102 (49,3%)	31 (54,4%)	71 (47,3%)	0,387
History of myocardial infarction, n (%)	67 (32,4%)	19 (33,3%)	48 (32%)	0,902
Arterial hypertension, n (%)	184 (88,9%)	47 (82,5%)	137 (91,3%)	0,049

Type 2 diabetes mellitus, n (%)	69 (33,3%)	16 (28,1%)	53 (35,3%)	0,322
LVEF, %	44 (33; 55)	38 (30; 48,5)	48 (35; 55)	<0,001
NT-proBNP, pg/ml	1076 (609; 2098)	2077 (1442; 2795)	923 (451,7; 1640,7)	<0,001
Liver density, kPa	6,7 (5,0; 12,5)	15,5 (10,1; 25,5)	5,7 (4,4; 7,6)	<0,001
Ultrasound of the lungs (B lines)	9 (4; 18)	20 (13; 28)	7 (3; 12)	<0,001

The data is presented as median, 25th and 75th percentile (Me (IQR))

Table 3: Threshold values for predicting outcomes depending on the method.

Parameters	Threshold values	Sensitivity	Specificity	AUC	p
Ultrasound of the lungs (B lines)	>5	66,7	63,16	0,61	0,044
Liver density, kPa	>6,2	68,3	54,2	0,635	0,001

Median follow-up was 364 days (IQR from 197 to 365). 63 events (30%) were detected, including 23 deaths (11%). **Table 4**.

Table 4: Values of congestion markers in patients with ADHF depending on outcomes.

Parameters	All patients n=207	Patients without events n=144	Patients with events n=63	p
Ultrasound of the lungs (B lines)	9 (4; 18)	6,5 (3; 13)	18 (9; 26)	<0,001
Liver density, kPa	6,7 (5,0; 12,5)	6 (4,7; 10,2)	8,3 (5,9; 16)	<0,001
Number of patients with venous congestion, n (%)	57 (27%)	27 (18,8%)	30 (47,6%)	<0,001
NT-proBNP	1076 (609; 2098)	987 (512; 1974)	1548 (936; 2757)	<0,001

Univariate Cox regression analysis demonstrated independent prognostic value in relation to the total endpoint of all markers of congestion evaluated by different methods, such as lung ultrasound (HR 7 (95% CI 2.8 – 17.6); p<0.001), ultrasound evaluation of hepatic venous stagnation according to the VExUS protocol (HR 2.9 (95% CI 1.7 – 4.8); p<0.001), liver density index according to indirect elastometry (HR 2.2 (95% CI 1.3 – 3.8); p=0.003). Multivariate Cox regression analysis, retained prognostic significance with respect to adverse outcomes for liver density >6.2 kPa (HR 1.9 (95% CI 1.0 – 3.3); p=0.029) and hepatic venous congestion according to the VExUS protocol (HR 2.8 (95% CI 1.3 – 5.7); p=0.004).

By analyzing the Kaplan-Meyer survival curves, significant differences were apparent between groups depending on B line >5; [Figure 2]; liver density >6.2 kPa; [Figure 3] and hepatic venous congestion according to the VExUS protocol [Figure 4].

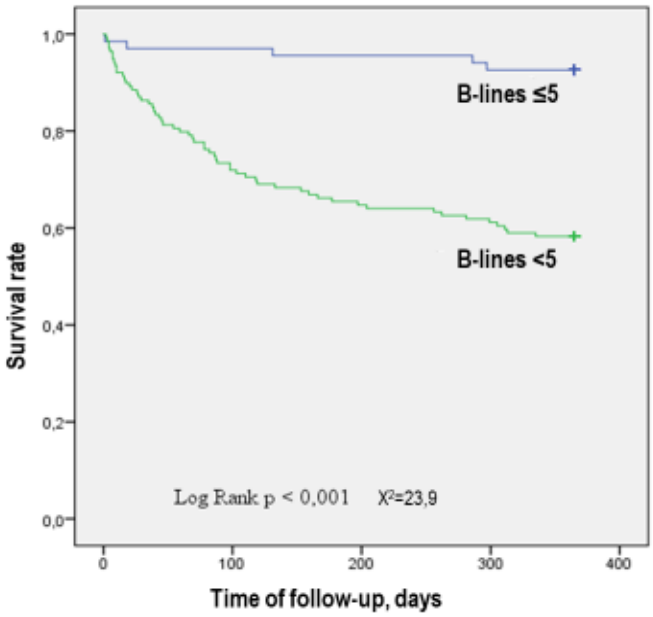

Figure 2: Kaplan-Meyer curves of cumulative probability of survival (total mortality+ re-hospitalization) depending on the presence of pulmonary congestion according to ultrasound data.

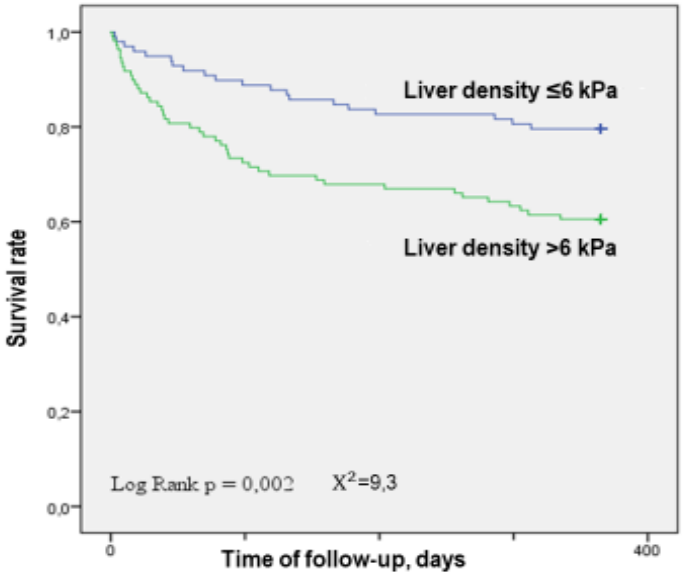

Figure 3: Kaplan-Meyer curves of cumulative probability of survival (total mortality+ re-hospitalization) depending on liver density according to indirect elastometry.

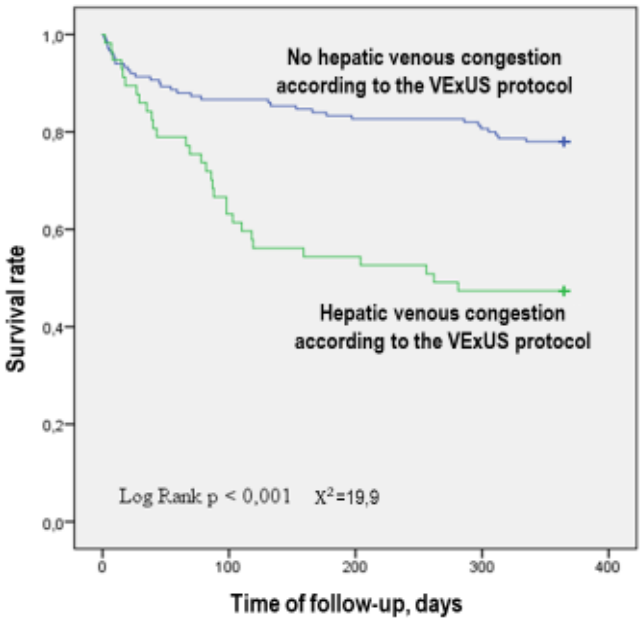

Figure 4: Kaplan-Meyer curves of cumulative survival probability (total mortality+ re-hospitalization) depending on the presence of hepatic venous congestion according to the VExUS protocol.

The Kaplan-Meyer curves of cumulative survival probability (total mortality+re-hospitalization) depending on the number of methods used to assess congestion are shown in Figure 5. A significant increase in the risk of overall mortality and re–hospitalization was found in association with congestion detected by liver lung ultrasound+ fibroelastometry (HR 10.5 (95% CI 2.3 - 46.2); p = 0.002), lung ultrasound + ultrasound of hepatic veins (HR 16.7 (95% CI 3.9 – 70.7); p < 0.001), and with all three methods (HR 40.1 (95% CI 6.6 – 243.1); p < 0.001).

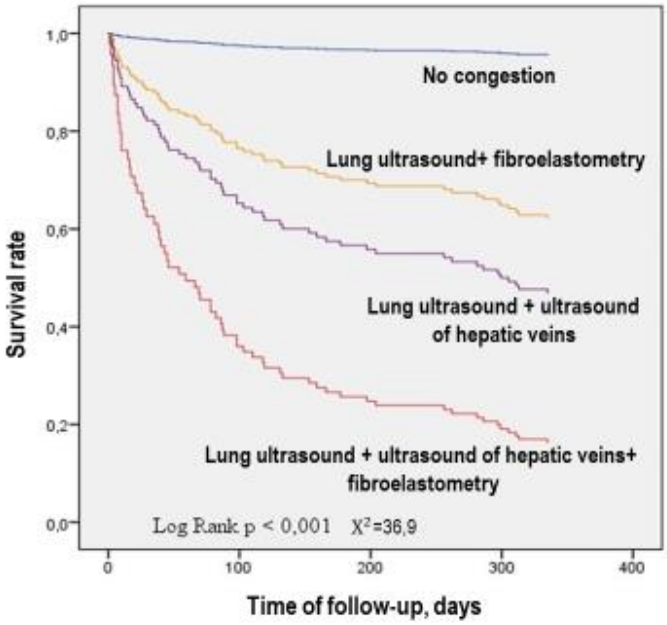

Figure 5: Kaplan-Meyer curves of cumulative survival probability (total mortality+ re-hospitalization) depending on the number of methods used to assess congestion.

Discussion

The major finding of our study is that a comprehensive assessment of congestion at discharge can predict adverse events (survival and rehospitalization) in patients with ADHD at 1 year. In addition, individuals with congestion detected in both blood circulation and by each of the three methods (ultrasound of the lungs, ultrasound of the hepatic veins according to the VExUS protocol and liver fibroelastometry), had the worst prognosis.

In a previous studies, retention of B-lines is associated with increased risk of re- hospitalization for CHF at 3 and 6 months,[15] and patients with liver density >6.9 kPa were characterized by a higher frequency of death and repeated hospitalizations for HF (HR=3.57; 95% CI: 1.93–6.83; p<0.001).[16] In other studies, venous congestion according to the VExUS protocol, was associated with adverse outcomes including re-hospitalization for CHF, cardiovascular mortality and total mortality at 12-month follow-up.[11,17-19]

In our study, comprehensive assessment of congestion using a combination of hepatic vein ultrasound + lung ultrasound had the greatest prognostic significance (HR 16.7 (95% CI 3.9 – 70.7); p < 0.001), and not the combination of lung ultrasound + liver fibroelastometry (HR 10.5 (95% CI 2.3 – 46.2); p = 0.002), which according to the literature has the greatest prognostic significance.[20]

Conclusion

In patients with acute decompensated heart failure, comprehensive assessment of congestion prior to discharge using ultrasound of the lungs counting the sums of B-lines, assessment of hepatic veins according to the VExUS protocol and liver fibroelastometry is useful in predicting survival and re-hospitalization at 1 year.

Declaration

Conflict of interest. The authors declare the absence of obvious or potential conflicts of interest related to the publication of this article.

Source of financing. The authors state that they received no funding for the study.

Conformity with the principles of ethics. All patients signed an informed consent to participate in the study. The study was approved by the local Ethics Committee at RUDN University (Protocol No. 26 от 18.02.21).

References

1. O'Connor C, Fiuzat M, Mulder H, Coles A, Ahmad T, Ezekowitz JA, et al. Clinical factors related to morbidity and mortality in high-risk heart failure patients: the GUIDE-IT predictive model and risk score. Eur J Heart Fail 2019 Jun;21(6):770-778.

2. Wehbe RM, Khan SS, Shah SJ, Ahmad FS. Predicting high-risk patients and high-risk outcomes in heart failure. Heart Fail Clin 2020 Oct;16(4):387-407.

3. Harjola VP, Mullens W, Banaszewski M, Bauersachs J, Brunner-La Rocca HP, Chioncel O, et al. Organ dysfunction, injury and failure in acute heart failure: from pathophysiology to diagnosis and management. A review on behalf of the Acute Heart Failure Committee of the Heart Failure Association (HFA) of the European Society of Cardiology (ESC). Eur J Heart Fail 2017 Jul;19(7):821-836. .

4. Fudim M., Hernandez A.F., Felker G.M. Role of Volume Redistribution in the Congestion of Heart Failure. *J Am Heart Assoc*. 2017; 17; 6 (8): e006817. DOI:

5. Gheorghiade M, Follath F, Ponikowski P, Barsuk JH, Blair JE, Cleland JG, et al; European Society of Cardiology; European Society of Intensive Care Medicine. Assessing and grading congestion in acute heart failure: a scientific statement from the acute heart failure committee of the heart failure association of the European Society of Cardiology and endorsed by the European Society of Intensive Care Medicine. Eur J Heart Fail 2010 May;12(5):423-433. .

6. Kobalava ZhD, Tolkacheva VV, Sarlykov BK, Cabello FE, Bayarsaikhan M, Diane ML, et al. Integral assessment of congestion in patients with acute decompensated heart failure. Russian Journal of Cardiology 2022;27(2):4799. . in Russ.

7. Curbelo J, Rodriguez-Cortes P, Aguilera M, Gil-Martinez P, Martín D, Suarez Fernandez C. Comparison between inferior vena cava ultrasound, lung ultrasound, bioelectric impedance analysis, and natriuretic peptides in chronic heart failure. Curr Med Res Opin 2019 Apr;35(4):705-713. .

8. Omote K, Nagai T, Asakawa N, Kamiya K, Tokuda Y, Aikawa T, et al. Impact of admission liver stiffness on long-term clinical outcomes in patients with acute decompensated heart failure. Heart Vessels 2019 Jun;34(6):984-991. .

9. Poelzl G, Auer J. Cardiohepatic syndrome. Curr Heart Fail Rep 2015 Feb;12(1):68-78. .

10. Nikolaou M, Parissis J, Yilmaz MB, Seronde MF, Kivikko M, Laribi S, et al. Liver function abnormalities, clinical profile, and outcome in acute decompensated heart failure. Eur Heart J 2013 Mar;34(10):742-749. .

11. Beaubien-Souligny W, Rola P, Haycock K, Bouchard J, Lamarche Y, Spiegel R, et al. Quantifying systemic congestion with Point-Of-Care ultrasound: development of the venous excess ultrasound grading system. Ultrasound J 2020 Apr;12(1):16. .

12. Colom G, Salvador JP, Acosta G, Albericio F, Royo M, Marco MP. Competitive ELISA for N-terminal pro-brain natriuretic peptide (NT-proBNP) determination in human plasma. Analyst 2020 Oct;145(20):6719-6727. .

13. Foucher J, Chanteloup E, Vergniol J, Castéra L, Le Bail B, Adhoute X, et al. Diagnosis of cirrhosis by transient elastography (FibroScan): a prospective study. Gut 2006 Mar;55(3):403-408. .

14. Rola P, Miralles-Aguiar F, Argaiz E, Beaubien-Souligny W, Haycock K, Karimov T, et al. Clinical applications of the venous excess ultrasound (VExUS) score: conceptual review and case series. Ultrasound J 2021 Jun;13(1):32. .

15. Coiro S, Rossignol P, Ambrosio G, Carluccio E, Alunni G, Murrone A, et al. Prognostic value of residual pulmonary congestion at discharge assessed by lung ultrasound imaging in heart failure. Eur J Heart Fail 2015 Nov;17(11):1172-1181. .

16. Taniguchi T, Ohtani T, Kioka H, Tsukamoto Y, Onishi T, Nakamoto K, et al. Liver Stiffness Reflecting Right-Sided Filling Pressure Can Predict Adverse Outcomes in Patients With Heart Failure. JACC Cardiovasc Imaging 2019 Jun;12(6):955-964. .

17. Denault A, Couture EJ, De Medicis É, Shim JK, Mazzeffi M, Henderson RA, et al. Perioperative Doppler ultrasound assessment of portal vein flow pulsatility in high-risk cardiac surgery patients: a multicentre prospective cohort study. Br J Anaesth 2022 Nov;129(5):659-669. .

18. Rajan R, Al Jarallah M. New Prognostic Risk Calculator for Heart Failure. Oman Med J 2018 May;33(3):266-267. .

19. Al-Jarallah M, Rajan R, Al-Zakwani I, et al. Mortality and Morbidity in HFrEF, HFmrEF, and HFpEF Patients with Diabetes in the Middle East. Oman Med J. 2020;35(1):e99. Published 2020 Feb 18.

20. Kobalava Z, Tolkacheva V, Cabello Montoya F, Sarlykov B, Al-Jarallah M, Brady P, et al. Prognostic value of integral assessment of congestion in patients hospitalized with acute decompensated chronic heart failure: A single center study. Annals of Clinical Cardiology 2022;4(2):77-84. .