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LEADING ARTICLE

Lung ultrasound in patients with decompensated heart failure with preserved or reduced left ventricular ejection fraction: a prospective study

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Objective. *To estimate the prognostic value of left ventricular ejection fraction (LVEF) and B-lines (lung ultrasound) in patients with decompensated heart failure (DHF).*

Material and methods.*162 patients with DHF underwent routine physical examination and 8-zone scanning lung ultrasound (66 % men, average age 68 ± 12 years, 97 % with arterial hypertension, 44 % with myocardial infarction, 60 % with atrial fibrillation, ejection fraction (EF) 40 ± 14 %, EF <40 %, 46 %, NT-proBNP 4246 (1741; 6837) pg/ml)*

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during admission and discharge. The sum of B-lines ≤5 was considered normal, 6–15, 16–30 and > 30 — mild, moderate and severe pulmonary congestion, respectively.

Results. *LVEF ≥ 50 % was detected in 49 of 162 (30.2 %) patients with DHF on admission, EF 40–49 % — in 38 (23.5 %), EF <40 % — in 75 (46.3 %). 31 % of patients had mild pulmonary congestion during initial lung ultrasound, 68 % — severe.*

By the time of discharge 33, 15 and 4 % of patients had mild, moderate and severe pulmonary congestion, respectively. During multivariate regression analysis, which included sex, age, functional class of HF and swelling of jugular veins by the time of discharge, the sum of B-lines ≥5 was independently associated with increased all-cause mortality (hazard ratio (HR) 2.86 with 95 % CI 1,15–7,13, p = 0.024) during one year of follow-up after discharge and the sum of B-lines ≥15 — with a high probability of HF readmission (HR 2.83, CI 1,41–5,67, p = 0,003). There was no significant correlation between LVEF, all-cause mortality (HR 0.72, 95 % CI) 0.61–1.41, p = 0.880) and HF readmission (HR 0.52, CI 0.24–1.09, p = 0.169) during one year of follow-up after discharge.

Conclusion. *Heart failure hospitalization is associated with poor long-term prognosis and an increased cardiovascular risk, regardless of LVEF. Lung ultrasound may be a simple, available non-invasive method for assessing the severity of pulmonary congestion, control its progression and may have prognostic value in patients with DHF.*

Keywords: *decompensated heart failure, left ventricular ejection fraction, B-lines, prognosis.*

Conflicts of interest: nothing to declare.

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Introduction

Pulmonary congestion is one of the most common cause of admission in patients with HF. Persistent clinical symptoms and signs of pulmonary congestion during discharge and outpatient examination are strong predictors of adverse outcomes. Clinical and radiological symptoms and signs of minor pulmonary congestion can be less obvious than severe congestion. One of the strongest markers of the severity and prognosis of pulmonary congestion is the concentration of NTproBNP, especially during discharge or outpatient examination, when patients are taking stable doses of diuretics [1].

It is remarkable that increased level of NTproBNP can be also observed in patients with DHF, heart rhythm disturbances, renal dysfunction, and obesity. Guidelines for the management of heart failure recommend to use ultrasound to assess ventricular function, valvular pathology, pulmonary artery pressure, collapse of the inferior vena cava, and, finally, to examine lungs, especially in patients with DHF (class IIb, level of evidence: C) [2].

Complex use of biomarkers and heart and lung ultrasound allows to assess pathophysiology and etiology of heart failure, as well as the severity of congestion [3]. B-lines that can be seen during lung ultrasound are artifacts caused by the accumulation of extravascular fluid. The number of B-lines correlates with the severity of pulmonary edema [4]. Lung ultrasound is simple, accurate, fast, and affordable method to assess pulmonary stasis and detect interstitial lung disease [5].

Even though the detection of B-lines increases diagnostic accuracy, its relationship with other non-invasive markers of lung congestion haven't been studied yet, especially in patients with HF depending on the left ventricular ejection fraction (LVEF). LVEF has been used for the stratification of patients with HF for a long time, but it is relatively subjective.

Approximately half of patients with HF have reduced LVEF <40 % (HFrEF) and > 50 % — preserved LVEF (HFpEF) [2]. Patients with heart failure with midrange LVEF from 40 to 49 % (HFmrEF) are at the «gray zone» and require additional studies to assess clinical picture, hemodynamics, laboratory and echocardiography (EchoCG) data. A meta-analysis that included 606.762 patients with HF showed that patients with HFmrEF have a lower all-cause mortality compared with HFrEF [RR 0.9; 95 % CI = 0.85–0.94, p <0.001] [6].

It is also remarkable that patients with HFrEF have higher rate of non-cardiological mortality compared with HFmrEF (RR, 1.31; 95 % CI 1.22–1.41, p <0.001).

At the same time, there is evidence of adverse long-term outcomes of pulmonary congestion ultrasound signs during discharge in patients with decompensated and stable HF [7]. There haven't been any prospective studies of pulmonary congestion prognostic value and its relationship with LVEF among Russian population in patients with HF.

The objective of this study was to assess the prognostic value of LVEF and pulmonary congestion, evaluated using lung ultrasound in three subgroups of patients with DHF.

Materials and methods

162 patients with DHF were included into the prospective single-center observational study (66% of men, average age 68 ± 12 years, arterial hypertension 97%, myocardial infarction 44%, atrial fibrillation 60%, ejection fraction (EF) 40 ± 14%, EF <40%, 46%, NT-proBNP 4246 (1741; 6837) pg / ml) (Table 1). Inclusion criteria were: a rapid increase of symptoms and/or signs of HF, structural and functional changes of the heart, and an increased NT-proBNP in patients with acute HF. Exclusion criteria were: acute coronary syndrome, terminal stage of chronic kidney disease, severe anemia, primary pulmonary pathology (pneumonia, COPD or chronic BA and severe hydrothorax requiring thoracentesis).

Table 1. **Clinical and demographic characteristics of patients (n=162)**

Parameter	Value
Sex (m/w), n (%)	107 (66)/ 55 (34)
Age, years (M±SD)	68±12
The duration of HF, years (Me (IQR))	2 (0,3;5)
HF functional class, NYHA, n (%) I II III IV	3 (2) 3 (2) 78 (48) 78 (48)
Left ventricular ejection fraction (EF), % (M±SD)	40±14
NT-proBNP, pg/ml (Me (IQR))	4246 (1741; 6837)

Comment: HF — heart failure

All patients underwent standard physical examination during admission and discharge (Table 2). Dyspnea at rest and on exertion, orthopnea, moist bubbling rales and jugular veins distention were the main symptoms and signs of pulmonary congestion.

Echocardiography and lung ultrasound (MicroMaxx SONOSITE) were performed during the first 12 hours of admission, according to the recommendations [8, 9]. Systolic and diastolic volumes and LVEF were determined by Simpson method in two- and four-chamber positions. Patients were divided into three groups depending on LVEF (PV> 50%; PV 40–49%; PV <40%).

The number of B-lines in each zone were counted using abdominal probe of lung ultrasound in eight zones of chest anterolateral surfaces. B-lines are reverberation artifacts shaped as laser beams arising from the pleural line to the screen edge [10, 11]. Over 5 B-lines can serve as a sign of pulmonary congestion: minor (6–15 B-lines), moderate (16–30 B-lines) and severe (≥30 B-lines) [10]. Residual pulmonary congestion was diagnosed if clinical and/or ultrasound signs of pulmonary congestion were presented during discharge.

The outcomes (all-cause mortality and readmission with DHF) were estimated after 1,3,6,12 months after discharge by phone calls.

The study complies the Declaration of Helsinki and was approved by the Ethical Committee of the RUDN Medical Institute (Peoples' Friendship University of Russia). All participants gave written informed consent.

Statistical data processing was performed using the STATISTICA 8.0 (Statsoft) software and SPSS 22.0. Quantitative variables were described as arithmetic mean (M) and standard deviation of mean (SD) (in case of normal distribution) or as median (Me) and interquartile range (IQR) (in case of asymmetric distribution). The significance of differences between quantitative variables of the groups was evaluated using the Mann-Whitney U-test. Qualitative variables

Table 2. **Symptoms of congestion during admission and discharge**

Signs	Admission N=162	Discharge N=162	p
Dyspnea At rest, n (%) On exertion, n (%)	 54 (33,3) 162 (100)	 0 (0) 68 (41,9)	 <0,001 <0,001
Orthopnea, n (%)	127 (78,3)	31 (19,1)	<0,001
Rales, n (%)	141 (87,0)	21 (13)	<0,001
Jugular vein distension≥8 cm, n (%)	39 (24)	25 (15)	<0,001
Jugular vein distension, cm (Me (IQR))	7 (5;8)	5 (5;6)	<0,001
Hepatomegaly, n (%)	82 (50,6)	27 (17)	<0,001
The largest size of the liver, cm (M±SD)	10,9±2	9,2**±1,6**	<0,001
Ascites, n (%)	27 (16,6)	2 (1,2)	<0,001
Leg swelling, n (%)	150 (92,6)	53 (32,7)	<0,001

Comment: Data are presented as median, 25th and 75th percentile (Me (IQR)), arithmetic mean (M) and standard deviation of the mean (SD).

were represented by absolute (n) and relative (%) values. The significance of differences in different points of the same group was assessed using the Wilcoxon signed-rank test. The survival probability was estimated by Kaplan — Meyer survival curves and the comparison — using the log-rank test. The effect of pulmonary congestion on the risk of death or readmission with HF was assessed by one- and multivariate Cox's regression analysis. The p value = 0.05 was considered significant.

Results

During discharge 49 (30.2 %) patients had LVEF ≥50 %; 38 (23.5 %) — LVEF 40–49 %, 75 (46.3 %) — EF <40 % among 162 patients with DHF. Patients with LVEF <40 % had a higher level of NT-proBNP during admission, higher incidence of coronary artery disease (CAD), lower SBP, higher frequency of male patients compared with patients with EF> 40 % (Table 3).

Pulmonary congestion was mostly moderate and severe according to lung ultrasound: in 67 % of cases — severe, in 32 % — moderate, in 1 % — minor. During discharge there was the decrease in the frequency of severe pulmonary congestion — in 4 % of cases, frequency of moderate — in 15 %, of minor — in 33 %, and in 48 % of cases pulmonary congestion was absent according to the lung ultrasound (Fig. 1).

Patients during admission with severe pulmonary congestion did not differ from patients with non-severe form by clinical and demographic characteristics according to ultrasound, functional class of HF, LVEF and other structural and functional parameters of the myocardium, but had higher frequency of jugular vein distention, radiological signs of venous stasis in the lungs, and higher level of NT-proBNP (Table 4).

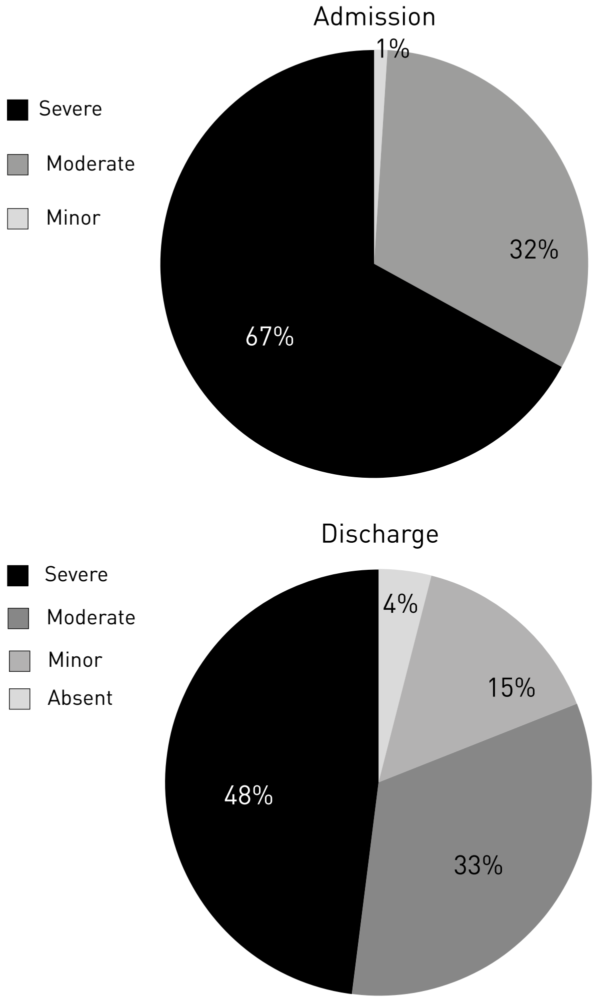

Figure 1. The dynamics of lung congestion according to lung ultrasound

Table 3. **Clinical and demographic characteristics of patients with DHF depending on LVEF**

Parameter	EF≥50 %	EF 40–49 %	EF<40 %	p
Age, years, (Me (IQR))	78 (69; 82)	70 (63; 77)	62 (57; 71)	0.015
Men, n (%)	24 (49)	20 (53)	62 (83)	0.001
AH, n (%)	49 (100)	37 (97)	71 (95)	0.240
CAD, n (%)	13 (27)	17 (45)	41 (55)	0.008
Dyslipidemia, n (%)	15 (31)	19 (50)	27 (36)	0.166
Type 2 DM, n (%)	19 (40)	15 (39)	28 (37)	0.972
AF, n (%)	26 (53)	22 (58)	49 (65)	0.379
HR, bpm, (Me (IQR))	80 (72; 100)	88 (80; 110)	98 (83; 120)	0.214
SBP, mmHg	150 (130; 170)	149 (130; 165)	130 (110; 150)	0.005
DBP, mmHg	80 (80;90)	80 (80;90)	80 (70;87)	0.148
RR per minute	23±2.8	23±3	23±3.7	0.296
Dyspnea at rest, n (%)	19 (39)	10 (26)	25 (33.3)	0.473
Orthopnea, n (%)	38 (78)	30 (79)	59 (79)	0.984
Rales, n (%)	42 (86)	33 (89)	66 (88)	0.932
Jugular vein distension ≥8 cm, n (%)	10 (20)	7 (18)	22 (29)	0.339
Jugular vein distension, cm, (Me (IQR))	5 (5; 7)	5 (5; 7)	6 (5; 8)	0.086
Hepatomegaly, n (%)	22 (45)	17 (45)	43 (57)	0.187
NT-proBNP during admission, pg/ml, (Me (IQR))	2521 (1390; 5092)	3298 (1621; 5520)	5039 (3139; 8131)	0.012
NT-proBNP during discharge, pg/ml, (Me (IQR))	1217 (644; 2524)	1842 (484; 5165)	3339 (1782; 6019)	0.139
Duration of admission, days.	9.4±3.5	9.6±2.2	9±3.8	0.056

Table 4. **Clinical and laboratory parameters depending on the presence of initial lung congestion during lung ultrasound**

Signs	Summary of B-lines ≤ 30 N=53	Summary of B-lines > 30 N=109	p
Men, n (%)	31 (58.5)	76 (70)	0.156
Age, years (M±SD)	68±11	69±13	0.633
HF functional class, NYHA, n (%) I II III IV	 0 (0) 1 (2) 23 (43) 29 (55)	 3 (2.7) 2 (1.8) 55 (50) 49 (45)	0.469
Ejection fraction, %	43.1±12.7	39±14	0.086
NT-proBNP, pg/ml (Me (IQR))	3328 (1439;4610)	4988 (2301;7134)	0.004
Symptoms and signs during admission			
Dyspnea at rest, n (%)	16 (30)	38 (35)	0.553
Dyspnea on exertion, n (%)	53 (100)	109 (100)	
Orthopnea, n (%)	43 (81)	84 (77)	0.555
Rales, n (%)	44 (83)	97 (89)	0.288
Jugular vein distension, cm (Me (IQR))	5.7±1.6	6.5±1.6	0.030
Hepatomegaly, n (%)	30 (56.6)	52 (48)	0.341
Ascites, n (%)	5 (9.4)	22 (20)	0.084
Leg swelling, n (%)	50 (94)	100 (92)	0.553
Hydrothorax, n (%)	23 (43.4)	54 (50)	0.253

Prognostic value of lung congestion according to lung ultrasound and LVEF in patients with decompensated heart failure

The median follow-up was 293 days. During this period, 30 (18.5%) patients died and 56 (35%) patients were readmitted due to DHF.

We used one-variative Cox regression analysis to assess the prognostic value and severity of pulmonary congestion and LVEF (Table 5, 6). We found that swollen jugular veins and pulmonary stasis detected using lung ultrasound are another signs of congestion during discharge associated with the risk of death.

According to multivariate Cox regression analysis (including gender, age, EF, functional class of HF and jugular vein distention during discharge), > 5 B-lines during discharge were independently associated with a higher probability of 12-month all-cause mortality (RR 2.86 95% CI 1.15–7.13, p = 0.024).

According to similar to Cox multivariate regression analysis, >15 B-lines were independently associated with higher probability of readmission due to heart failure during one-year follow-up (RR 2.83, 95% CI 1.41–5.67, p = 0.003) after the adjustment by age, gender, functional class of HF and the presence of jugular vein distention during discharge. We did not find any reliable associations of readmission and all-cause mortality with LVEF regardless of its level (Fig. 2-4).

Table 5. **Cox proportional-hazards regression one-variative model for lung congestion parameters, estimated by different methods for all-cause mortality in patients with HF**

Parameter	RR	95% CI	p
Admission			
Dyspnea at rest	0.63	0.30–1.30	0.218
Orthopnea	0.55	0.19–1.58	0.268
Rales	0.44	0.10–1.87	0.271
Jugular vein distension	0.61	0.28–1.30	0.206
Congestion on X-Ray	0.89	0.39–2.01	0.785
Hydrothorax	0.59	0.28–1.26	0.177
The summary of B-lines during admission	1.72	0.75–3.94	0.172
>30 B-lines during admission	1.70	0.73–3.98	0.215
EF <40%	1.1	0.58–2.43	0.638
EF 40–49%	0.7	0.30–2.04	0.633
EF ≥ 50%	0.8	0.38–2.00	0.757
Discharge			
Dyspnea on exertion	0.60	0.29–1.24	0.172
Orthopnea	0.57	0.25–1.28	0.173
Rales	0.88	0.30–2.52	0.814
Jugular vein distension	3.00	1.36–6.58	0.006
The summary of B-lines during discharge	1.05	1.02–1.09	0.001
>5 B-lines during discharge	3.94	1.68–9.21	0.002
>15 B-lines during discharge	2.44	1.11–5.36	0.026

Table 6. **Cox proportional-hazards regression model for lung congestion parameters, estimated by different methods for the risk of readmission in patients with HF**

Parameter	RR	CI	p
Admission			
Dyspnea at rest	0,60	0,35–1,02	0,061
Orthopnea	0,61	0,29–1,30	0,205
Rales	0,69	0,29–1,62	0,405
Jugular vein distension	0,73	0,41–1,31	0,300
Congestion on X-Ray	0,81	0,41–1,58	0,539
Hydrothorax	0,47	0,47–1,41	0,473
The summary of B-lines during admission	0,85	0,51–1,42	0,546
>30 B-lines during admission	0,88	0,49–1,58	0,678
EF <40%	1,5	0,93–2,68	0,087
EF 40–49%	0,5	0,24–1,09	0,086
EF ≥ 50%	0,7	0,39–1,30	0,276
Discharge			
Dyspnea on exertion	0,93	0,55–1,58	0,806
Orthopnea	0,75	0,35–1,58	0,451
rales	0,68	0,33–1,40	0,304
Jugular vein distension	0,54	0,28–1,03	0,065
The summary of B-lines during discharge	0,79	0,46–1,34	0,387
>5 B-lines during discharge	1,44	1,07–1,94	0,015
>15 B-lines during discharge	0,74	0,44–1,26	0,276
Dyspnea at rest	2,67	1,47–4,83	<0,001

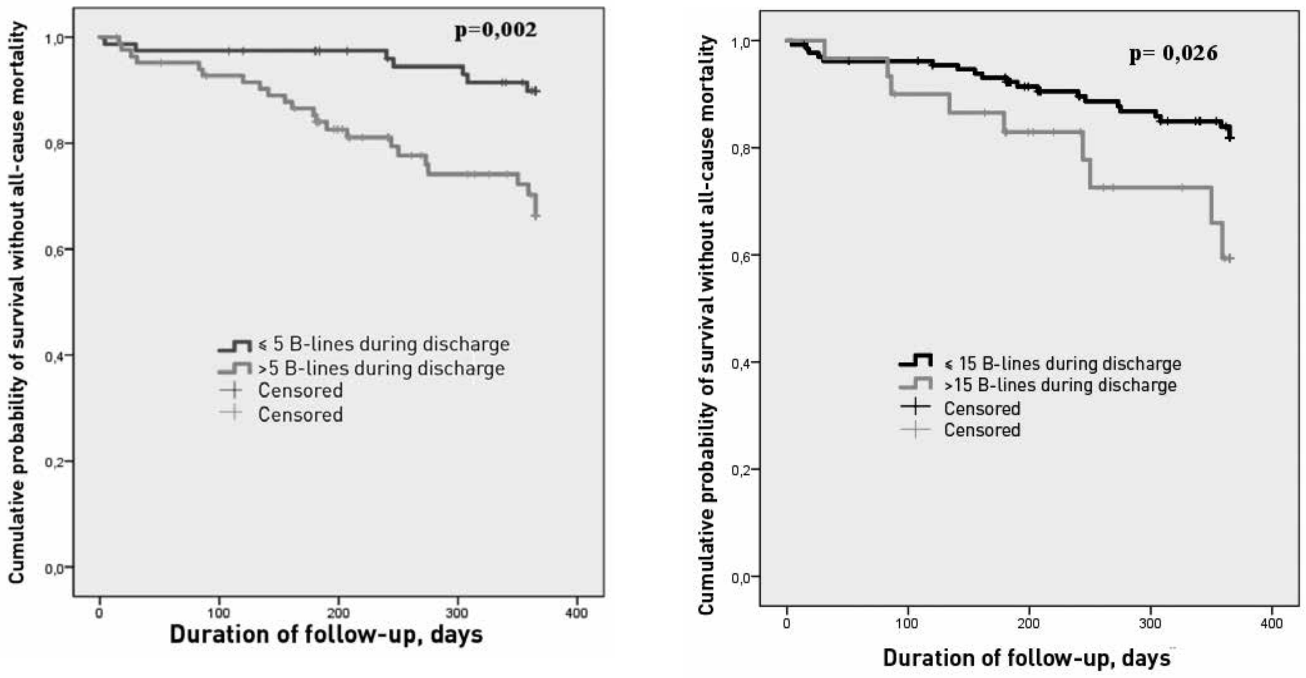

Figure 2. Kaplan Meier curves for cumulative probability of survival (without all-cause mortality) depending on the presence and severity of lung congestion according to lung ultrasound during discharge.

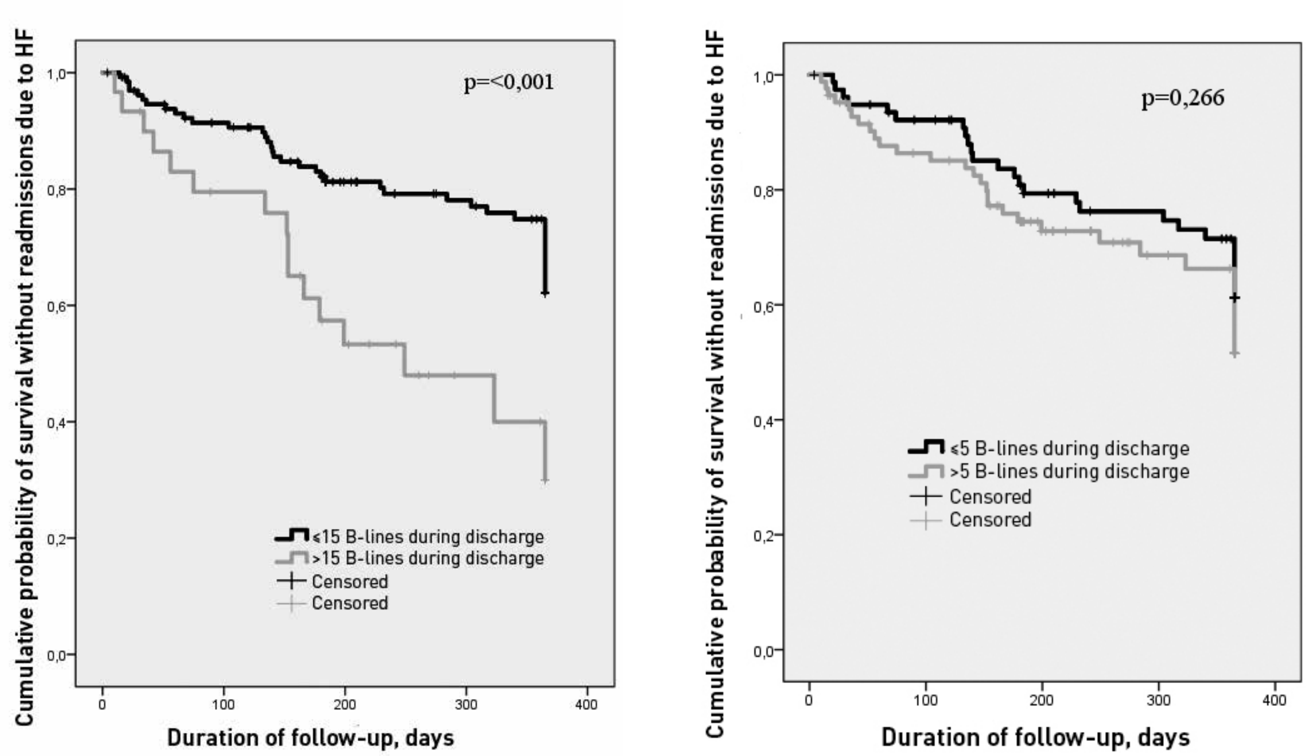

Figure 3. Kaplan Meier curves for cumulative probability of survival without readmissions due to HF depending on the presence and severity of lung congestion according to lung ultrasound during discharge.

Discussion

Chronic heart failure (CHF) is still one of the most common outcomes with poor prognosis of many cardiovascular diseases (CVD). According to epidemiological studies over 37.7 million people are affected by CHF in the world [12]. This chronic progressive disease is characterized by high mortality, high risk of complications and hospital admissions [13]. HF is classified by LVEF level that also defines the effectiveness of evidence-based therapy. According to the MAGGIC study, patients with HFmrEF have lower mortality rates compared with patients with HFrEF [14]. Even though some studies have shown that patients

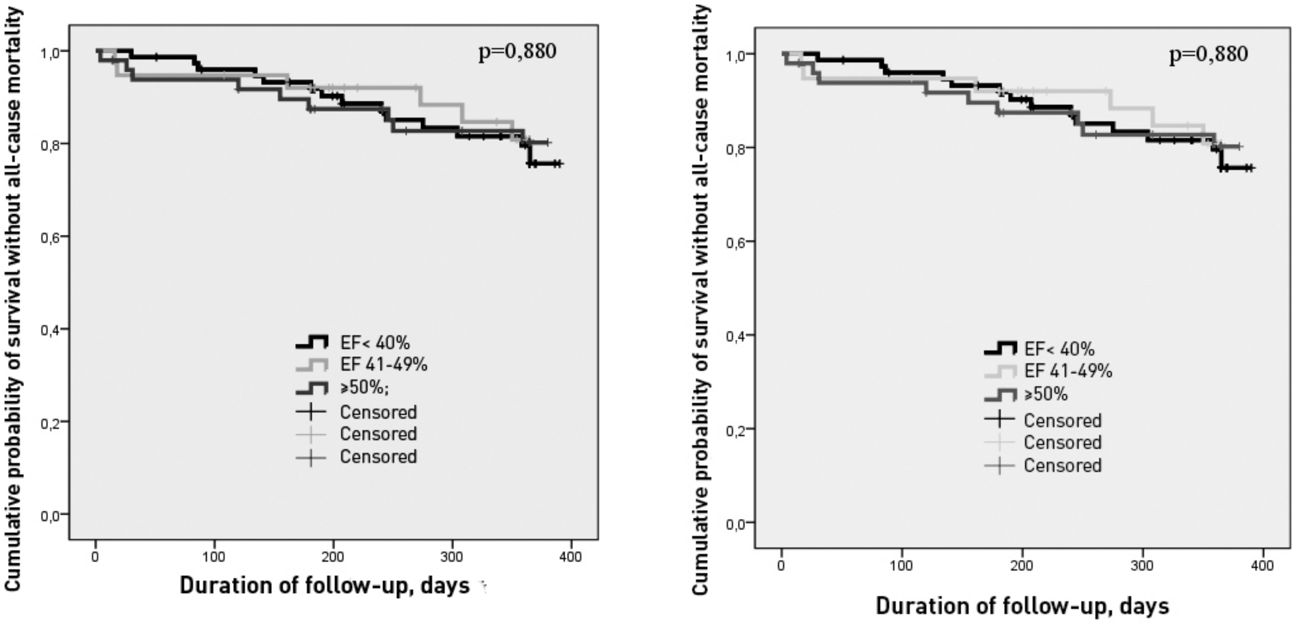

Figure 4. Kaplan Meier curves for cumulative probability of survival (without all-cause mortality) and without readmissions due to HF depending on the LVEF during discharge.

with HFmrEF have a significantly better prognosis compared with patients with HFrEF, other investigations established similar mortality and hospital admission rates [15–20].

Recently published data from GWTG-HF (Get with The Guidelines — HF) showed that patients with HFrEF and HFpEF have equally low survival rates during 1-month and 1-year follow-up after admission compared with patients with HFrEF. In addition, patients with HF, regardless of LVEF, have high 5-year mortality rate compared with admission index (75.4 %) [12].

In our study, 30.2 % of patients admitted due to DHF had LVEF ⩾50 %; 23.5 % — LVEF 40–49 %, 46.3 % of patients — LVEF <40 %. During the follow-up (median follow-up — 293 days) 18.5 % of patients died, 35 % were readmitted. However, we did not find the association between the level of LVEF and all-cause mortality level (RR 0.72, 95 % CI) 0.61–1.41, p = 0.880) during 1-year follow-up and with the probability of readmission due to HF (RR 0.52, CI 0.24–1.09, p = 0.169).

In the presented study, patients with DHF, were investigated with standard laboratory, clinical and instrumental methods, and underwent lung ultrasound to assess the frequency and dynamics of pulmonary congestion during admission and prognostic significance of residual pulmonary stasis. We found signs of pulmonary congestion according to clinical data and lung ultrasound in all patients during admission and in 87.7 % of cases, it was confirmed by lung radiography. We established the association between initially severe pulmonary congestion according to lung ultrasound with jugular vein distention, radiological signs of stasis, and significantly higher level of NT-proBNP. We also demonstrated high frequency of residual pulmonary stasis during discharge.

Randomized two-center study included 518 patients with acute respiratory failure (ARF) and demonstrated that lung ultrasound as part of routine screening examination during the diagnosis of DHF is superior to traditional physical examination, chest radiography, and NTproBNP laboratory test [21]. The accuracy of the HF diagnosis using lung ultrasound was significantly higher compared with physical examination (area under the curve [AUC] 0.95 versus 0.88, p <0.01) or its combination with X-ray examination and NTproBNP determination (AUC 0 95 versus 0.87, p <0.01). In contrast, lung radiography and NTproBNP determination was not superior to physical examination alone (AUC 0.87 and 0.85, respectively, p> 0.05). In addition, lung ultrasound was associated with decreased number of diagnostic errors by 7.98 cases compared with 2.24 cases per 100 patients using x-ray and NTproBNP [21]. The results of meta-analysis, which included 1827 patients with shortness of breath also showed higher sensitivity of lung ultrasound (88 %) compared with chest x-ray (73 %, p <0.001) with comparable specificity of the methods (90 %) [22].

Multivariate analysis showed that > 5 B-lines was independently associated with all-cause mortality. Patients with > 15 B-lines had higher risk of readmission due to CHF during 12-months follow-up.

The results of published studies also showed that B-lines allows to identify the risk group of adverse long-term outcomes in patients with HF at outpatient and inpatient levels. In outpatient study ⩾3 B-lines during ultrasound of 5 and 8 zones was associated with 4-fold risk of all-cause mortality and readmission due to HF during 6 months follow-up [23]. Other studies also showed that preservation of B-lines during discharge in patients admitted due to DHF is associated with the risk of readmission due to DHF during the next 3 and 6 months [24, 25, 26]. Thus, high frequency of pulmonary congestion detected by lung ultrasound and the possibility to monitor its dynamics, combined with prognostic significance, emphasize the need to include this method into the algorithm of investigation of patients with DHF during admission along with clinical, laboratory and other instrumental methods.

Conclusion

Heart failure hospitalization is associated with poor long-term prognosis and an increased cardiovascular risk, regardless of LVEF. Lung ultrasound may be a simple, available non-invasive method for assessing the severity of pulmonary congestion, control its progression and may have prognostic value in patients with DHF.

Conflict of interest: None declared.

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