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Lung Ultrasound and Echocardiographic Parameters as Predictors of Cardiovascular Events in Heart Failure Patients with Preserved and Reduced Ejection Fraction

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Abstract

Background: Pulmonary congestion is associated with an increased risk for adverse outcomes and mortality in heart failure (HF) patients, whether with preserved or reduced ejection fraction including mild reduced EF (HFpEF or HFrEF including HFmrEF). Lung ultrasound has been described as more sensitive for detecting pulmonary congestion compared to traditional imaging. Herein, we investigated the role of lung ultrasound as a predictor for outcomes in Egyptian HF patients.

Methods: Eighty HF were enrolled in our prospective trial, and they were divided into two groups; HFrEF (50 cases) and HFpEF (30 cases). Echocardiography was performed at patient admission, while lung ultrasound was done at admission and before discharge. Ultrasonographic findings were correlated with three-month outcomes.

Results: The number of B-lines expressed a significant rise in HFrEF patients only in Zone 1, and that was evident on admission and before discharge. Nonetheless, the remaining lung zones had comparable B-lines between HFrEF and HFpEF patients. The three-month follow-up revealed the incidence of decompensated HF in 22% and 16.7% of HFrEF and HFpEF patients, respectively ($p = 0.564$). Only one patient died in the HFrEF group (2%). Having B-lines ≥ 30 at admission was associated with a significant increase in the incidence of decompensation in the short term ($p < 0.001$), and that was evident in both groups.

Conclusion: Lung ultrasound could be used as a valid tool for the assessment of lung congestion in HF patients, with a strong correlation between increased admission B-lines and the incidence of short-term decompensation.

Keywords: Heart failure; Lung ultrasound; Predictors; Outcomes.

Introduction

Heart failure (HF) is a complex clinical entity defined as the inability of the heart to meet the metabolic demands of the human body. It occurs usually secondary to structural or functional cardiac disorders that induce impairment of cardiac filling during diastole or blood ejection during systole **[1, 2]**. That problem affects about 26 million individuals around the globe **[3]**, forming a significant financial and healthcare burden in many countries **[3, 4]**.

In Egypt, cardiovascular disease has remained the main cause of premature mortality since the end of the previous century. According to a recent epidemiological report, cardiovascular disease accounted for about half of overall mortality in the Egyptian population **[5]**. Although the prevalence of HF reaches about 2% of the Arab population in the Middle East, the exact epidemiology of HF in Egypt is still lacking **[6]**.

According to the ejection fraction (EF), HF secondary to left ventricular (LV) dysfunction could be classified as heart failure with either preserved or reduced EF including mid reduced EF. The former term is used when EF ≥ 50%. Otherwise, the latter term is used **[7]**. Whatever the type, HF is associated with a significant decline in the individual's functional capacity and increases the risk of mortality. Proper disease management and identification of the predictors of mortality in such patients are crucial for cardiologists to enhance patient outcomes **[8, 9]**.

Lung congestion is one of the main manifestations of HF, and it carries an increased risk of hospitalization and mortality in these patients **[10]**. Although lung congestion could be assessed by clinical examination (auscultation) and chest x-ray, both techniques have evident drawbacks. Clinical examination is of low sensitivity, whereas a normal chest x-ray does not exclude the presence of congestion **[11]**.

Lung ultrasonography has emerged as a fast, safe, reliable, and simple quantitative technique for the assessment of lung congestion **[12]**. B-lines, detected on lung ultrasound, appear secondary to extravascular lung water, and they have a strong correlation with other clinical and radiological indices of lung congestion **[11, 13]**.

According to our literature research, little has been published regarding the applicability of lung ultrasound in the diagnosis of lung congestion and its correlation with outcomes in HF patients in the Egyptian setting. That is why we conducted the present trial to investigate the role of lung ultrasound as a predictor for outcomes in patients with HF, whether HFrEF or HFpEF.

Patients and methods

The current prospective cross-sectional trial was conducted at Mansoura University Cardiology Department in collaboration with Damietta Cardiology and Gastroenterology Center over a two-year duration, from June 2020 to June 2022. The trial included 80 adult patients diagnosed with HF, whether new onset or worsening pre-existing chronic HF. We excluded patients with congenital heart disease, a previous lung lobectomy, significant pulmonary disease (asthma, COPD, etc.), a history of lung cancer, or a poor acoustic window on the echocardiographic assessment. We also excluded patients with atrial fibrillation (AF), as it decreases the accuracy of the cardiac doppler study.

All patients agreed to be enrolled in the study following their written approval, which explained the benefits of the trial. Then, they were subjected to the standard medical evaluation, which included taking their history in addition to a general and local cardiac examination. The diagnosis of HF was established when the patients fulfilled at least two of the following clinical or radiological parameters; shortness of breath, excessive tiredness, lower limb swelling, pulmonary rales, the third heart sound, distension of neck veins, hepatomegaly, and peripheral edema. An ECG was ordered for all patients to exclude the presence of AF.

The clinical congestion score was estimated for all patients depending on the presence of hepatomegaly, peripheral edema, the third heart sound, pulmonary rales, and distended neck veins. Every finding was given a score of 1 when detected, giving a maximum score of 5. That score was calculated at admission and before discharge.

The echocardiographic and tissue doppler studies were performed by an experienced cardiologist using a Vivid 9 ultrasound machine (General Electric, Norway) equipped with 1.7 – 4 MHz frequency transducer. The examination was performed when the patient was in the left lateral decubitus.

We began with the assessment of M-mode parameters in the parasternal long-axis view to measure ejection fraction (EF), aortic root dimension (Ao), left atrial dimension (LA), left ventricular (LV) end systolic and diastolic dimensions (LVESD and LVEDD), LV fractional shortening (FS), LV posterior wall thickness at end diastole (PWTd), and interventricular septum thickness at end diastole (IVSd).

That was followed by the assessment of 2-D echocardiographic parameters. Both the morphology and motion of the valves were assessed by the B-mode. The segmental wall motion was assessed in apical 4-chamber, 3-chamber, and 2-chamber views and left PSAX at mitral, papillary muscle, and apical levels. The Simpson method was used to estimate EF depending on LV end systolic and diastolic volumes (LVESV and LVEDV) in apical two- and four-chamber views.

Regarding doppler flow measurements, the mitral valve flow was assessed using pulsed wave doppler to measure early and late diastolic mitral flow and their ratios (E-velocity, A-velocity, and E/A ratio, respectively), and continuous wave doppler was used to assess flow across the tricuspid and aortic valves. The five-chamber view was used to obtain the isovolumetric relaxation time (IVRT), whereas the apical four-chamber view was used to assess the movement of the medial and lateral mitral annuli. Additionally, the tricuspid regurgitation signal was used to measure systolic pulmonary arterial pressure.

When it came to tissue doppler imaging, we used the four-chamber view to obtain mitral annulus systolic (S'), early (e'), and late (a') diastolic velocities, which were measured at the septal and lateral annuli. The mean of the previous measurements was used to calculate the E/e' ratio.

The diastolic pattern was classified as either restrictive (E/e’ ≥ 15, E/A > 1.5, IVRT < 70 msec, and deceleration time DT < 140 msec), impaired (E/e’< 15, E/A < 1, IVRT > 90 msec, and DT > 240 msec), or pseudonormal filling (E/e’ < 15, E/A 1-1.5, IVRT < 90 msec, and DT = 140-200 msec). In addition, LV filling pressure was classified as normal, gray zone, or elevated when the E/e’ ratio was ≤ 8, between 8 – 15, and ≥15, respectively. The included patients were classified according to their EF into two groups; the first included cases whose EF was < 50% (HFrEF) while the second included the remaining cases whose EF was 50% or more.

Lung ultrasound was performed using the same ultrasound device used for the echocardiographic examination. It was performed 12 hours following admission and before discharge. The sonographic assessment was performed when the patient was in a semi-recumbent position, and eight predefined anterior and lateral thoracic zones were examined for the number of B-lines in the parasternal, midclavicular, anterior, and mid-axillary lines.

B-lines were defined as vertical hyperechoic laser-like reverberations extending from the pleura down to the edge of the screen and moving synchronously with respiratory movements. The number of B-lines in each zone was calculated.

A follow-up, in the form of a one-page questionnaire, was performed after a minimum of 3 months following patient discharge. Follow-up information was gathered by reviewing the patient's hospital record, by speaking with patients themselves, or by contacting the patients' family or family doctor. The cardiovascular events were defined as hospitalization for decompensated HF, cardiac dysrhythmias, or mortality due to cardiac-related causes.

The SPSS software for MacOS (version 26) was used for tabulation and analysis of the collected data. Categorical data were presented as numbers and percentages and compared between groups using the Chi-square test. Quantitative variables were presented as means and standard deviations (compared using the Student-t test) or medians and ranges (compared using the Mann-Whitney test). Numerical variables within the same group were compared using the Wilcoxon signed rank test over time intervals. The correlation between the numerical variables was performed using the Spearman correlation. Any p-value less than 0.05 was considered statistically significant.

Results

We enrolled 50 patients with HFrEF in addition to 30 ones with HFpEF. Patients in the HFrEF group had a mean age of 58.16 years, compared to 61.56 for patients in the HFpEF group. Men represented 78% and 80% of patients in the HFrEF and HFpEF groups, respectively. The remaining participants were women. The previous two parameters were statistically comparable between the two groups ($p = 0.071$ and 0.832, respectively). Additionally, the prevalence of medical comorbidities and smoking was not significantly different between the two groups ($p > 0.05$), as shown in Table 1.

Table (1): Demographic data and medical comorbidities in the study groups.

Demographic data	HFrEF group (n=50)	HFpEF group (n=30)	Test of significance	P value
Age (years)				
Mean ± SD	58.16±7.45	61.56±9.00	t=1.83	0.071
Min-Max	42.00-73.00	43.00-78.00		

Gender **-Male** **-Female**	 39 (78.0%) 11 (22.0%)	 24 (80.0%) 6 (20.0%)	 $\chi^2=0.045$	 0.832
Hypertension	41 (82.0%)	25 (83.3%)	$\chi^2=0.023$	0.879
Diabetes mellitus	17 (34.0%)	5 (16.7%)	$\chi^2=2.825$	0.093
Smoking	27 (54.0%)	17 (56.7%)	$\chi^2=0.054$	0.816

Lung congestion score had a median value of 3 in both study groups at admission, which decreased to 0 at the time of discharge. Both groups showed a marked decline in that parameter on discharge compared to the corresponding admission values ($p < 0.05$) (Table 2).

Table (2): Lung congestion scores at admission and before discharge.

Congestion score	HFrEF group (n=50)	HFpEF group (n=30)	Test of significance	P value
Congestion score at admission	3.0 (2.0- 5.0)	3.0 (2.0- 5.0)	Z=0.221	0.825
Congestion score at discharge	0.0 (0.0- 2.0)	0.0 (0.0- 2.0)	Z=1.55	0.120
Wilcoxon signed rank test	6.38	4.89	-	-
P value	≤0.001	≤0.001	-	-

Echocardiographic assessment revealed significant differences between the two groups. Patients in the HFrEF group showed a significant decline in LVEDV, EF, E, E/A, e', TR velocity, and LA volume, while having higher LVESV, DT, and IVRT compared to patients in the HFpEF group. Nonetheless, A and E/e' had statistically comparable values between the two groups, as illustrated in Table 3.

Table (3): Echocardiographic parameters in the two groups.

Echocardiography - Data	HFrEF group (n=50)	HFpEF group (n=30)	Test of significance	P value
EDV	134.40±2.42	145.60±10.78	t=7.08	≤0.001*
ESV	85.02±3.26	51.93±9.10	t=23.38	≤0.001*
EF	33.64±4.74	62.90±4.64	t=26.90	≤0.001*
E	0.69±0.29	1.08±0.28	t=5.81	≤0.001*
A	0.73±0.19	0.66±0.19	t=1.36	0.175
E/A	1.10±0.62	1.66±0.50	t=4.17	≤0.001*
e'	0.07±0.02	0.14±0.02	t=10.53	≤0.001*
E/e'	12.18±8.40	11.50±3.13	t=0.422	0.674
DT	209.22±52.80	164.07±21.12	t=4.46	≤0.001*
IVRT	82.06±14.81	77.30±9.25	t=1.58	0.118
TR velocity	2.84±0.45	3.21±0.33	t=3.83	≤0.001*
LA volume	74.32±8.19	82.10±5.45	t=4.61	≤0.001*

Admission lung ultrasonography showed a significant difference between the two groups only in zone 1 (p = 0.027), as the number of B-lines had a significant increase in patients with HFrEF (median = 3 vs. 2 in the other group). The number of B-lines within the remaining lung zones was comparable between the two groups. All in all, most patients had a B-line number less than 30 (78% and 80% of cases in the HFrEF and HFpEF groups, respectively (p = 0.832). The previous data is shown in Table 4.

Table (4): Admission lung ultrasound in the study groups.

Lung Ultrasound 12 h of admission	HFrEF group (n=50)	HFpEF group (n=30)	Test of significance	P value
Zone 1	3 (0.0- 7.0)	2 (0.0- 6.0)	Z=2.21	0.027*
Zone 2	2 (0.0- 6.0)	2 (0.0- 7.0)	Z=0.167	0.867

Zone 3	2 (0.0- 7.0)	2 (0.0- 7.0)	Z=0.48	0.631
Zone 4	1 (0.0- 5.0)	2 (0.0- 5.0)	Z=1.33	0.182
Zone 5	1 (0.0- 7.0)	1 (0.0- 5)	Z=0.12	0.904
Zone 6	2 (0.0- 7.0)	2 (0.0- 7.0)	Z=0.66	0.509
Zone 7	2 (0.0- 5.0)	2 (0.0- 5.0)	Z=0.005	0.996
Zone 8	1 (0.0- 6.0)	2 (0.0- 7.0)	Z=1.16	0.247
Total	12 (6.0- 41.0)	12.50 (7.0- 42)	Z=0.11	0.913
<30	39 (78.0%)	24 (80.0%)	χ^2 =0.045	0.832
≥30	11 (22.0%)	6 (20.0%)		

Lung ultrasound before patient discharge expressed no significant difference between the two groups in all lung zones, except for zone 1, which showed increased B-line numbers in association with HFrEF (p = 0.024) although both groups had the same median values (Table 5).

Table (5): Discharge lung ultrasound in the study groups.

Lung Ultrasound at discharge	**HFrEF group (n=50)**	**HFpEF group (n=30)**	**Test of significance**	**P value**
Zone 1	0.0 (0.0- 2.0)	0.0 (0.0- 1.0)	Z=2.25	0.024*
Zone 2	0.0 (0.0- 2.0)	0.0 (0.0- 1.0)	Z=0.644	0.520
Zone 3	0.0 (0.0- 1.0)	0.0 (0.0- 1.0)	Z=0.218	0.828
Zone 4	0.0 (0.0- 1.0)	0.0 (0.0- 1.0)	Z=0.151	0.880
Zone 5	0.0 (0.0- 1.0)	0.0 (0.0-0.0)	Z=1.78	0.075
Zone 6	0.0 (0.0- 1.0)	0.0 (0.0- 1.0)	Z=0.830	0.407
Zone 7	0.0 (0.0- 1.0)	0.0 (0.0-0.0)	Z=1.58	0.114
Zone 8	0.0 (0.0- 1.0)	0.0 (0.0- 1.0)	Z=0.305	0.761
Total	0.0 (0.0- 5.0)	0.0 (0.0- 3.0)	Z=1.81	0.070

Three-month outcomes did not differ between the two study groups. No patients developed cardiac dysrhythmia. Nevertheless, the incidence of decompensated HF was 22% and 16.7% in the HFrEF and HFpEF groups, respectively. In addition, only one patient died in the HFrEF group (2%) compared to no cases with HFpEF (Table 6).

Table (6): Three-month outcomes in the study groups.

Outcome	HFrEF group (n=50)	HFpEF group (n=30)	Test of significance	P value
Decompensated HF	11 (22.0%)	5 (16.7%)	χ^2 =0.333	0.564
Cardiac dysrhythmias	0 (0 %)	0 (0 %)	-	-
Death	1 (2.0%)	0 (0%)	FET	1.00

Patients with B-lines ≥ 30 at admission showed a significant increase in the incidence of decompensated HF in patients with HFrEF or HFpEF, as shown in Table 7.

Table (7): Association between admission lung ultrasound and decompensated HF.

	Lung Ultrasound 12 h of admission		Test of significance	P value
	B lines <30	**B lines ≥30**		
DHF in HFrEF group	2 (5.1%)	9 (81.8%)	χ^2 =29.4	≤0.001*
DHF in HFpEF group	0 (0%)	5 (83.3%)	χ^2 =24.0	≤0.001*

In the HFrEF group, the number of B-lines had a significant positive correlation with the lung congestion score at admission and before discharge. In the same group, admission B-lines were negatively correlated with EF, whereas discharge B-lines were positively correlated with TR velocity. In the HFpEF group, discharge B-lines were positively correlated with EF and discharge lung congestion score (Table 8).

Table (8): Correlation between lung ultrasound findings and echocardiographic parameters in patients with HFrEF and HFpEF.

	HFrEF group				**HFpEF group**			
	Admission lung ultrasound		Discharge lung ultrasound		Admission lung ultrasound		Discharge lung ultrasound	
	r	**p**	**r**	**p**	r	p	r	p
Congestion score at admission	0.562	**≤0.001***	0.583	**≤0.001***	0.285	0.126	0.356	0.053
Congestion score at discharge	0.510	**≤0.001***	0.577	**≤0.001***	0.345	0.062	0.508	**0.004**
EDV	-0.020	0.889	-0.080	0.581	0.011	0.955	-0.159	0.401
ESV	-0.017	0.909	0.024	0.869	-0.032	0.868	-0.105	0.579
EF	-0.374	**0.008***	-0.234	0.102	0.169	0.371	0.446	**0.014**
E	0.125	0.385	0.176	0.222	-0.185	0.327	-0.299	0.108
A	-0.160	0.267	-0.118	0.413	-0.239	0.203	-0.262	0.161
E/A	0.007	0.961	0.092	0.525	0.176	0.351	0.088	0.645
e'	-0.184	0.201	-0.137	0.342	-0.023	0.904	-0.002	0.990
E/e'	0.071	0.624	0.196	0.172	0.108	0.569	0.016	0.932
DT	-0.144	0.317	-0.197	0.171	0.164	0.385	-0.063	0.740
IVRT	-0.141	0.329	-0.186	0.197	0.093	0.625	0.129	0.497
TR velocity	0.164	0.254	0.351	**0.013***	0.047	0.806	0.276	0.140
LA volume	0.085	0.558	0.119	0.409	0.055	0.773	0.347	0.060

Discussion

Among different cardiology centers, HF still remains the most common cause of admission, and lung congestion is more likely to explain the admission of most rather than the decreased cardiac output **[11, 14]**. Lung congestion in HF patients requires accurate assessment as it is linked with worse cardiac outcomes. Both clinical assessment scores and chest radiography have their drawbacks, as they could miss cases of silent congestion **[15-18]**. Herein lies the importance of ultrasound as a sensitive and reliable tool that could be used to assess lung congestion. It could also be performed by the same echocardiography device available in most cardiology centers.

In this study, we investigated the role of lung ultrasound as a predictor for outcomes in patients with HF, whether HFrEF or HFpEF. First of all, the reader should notice that patients in both groups expressed a significant reduction in their clinical lung congestion score at discharge compared to their corresponding admission values, which indicates our proper management of such patients with marked resolution of their clinical manifestations indicating congestion.

We did not also note any significant difference between HFrEF and HFpEF patients as regards the incidence of adverse cardiac events, including decompensation and cardiac-related death. Numerous previous studies have reported similar morbidity **[19-21]** and mortality rates **[22, 23]** between the previous two HF categories. However, Palazzuoli et al. reported a significant rise in cardiac adverse events in association with HFrEF (44% vs. 28% in HFpEF patients – $p = 0.04$) **[24]**.

Our study revealed almost no significant difference between HFrEF and HFpEF patients regarding the number of B-lines. This is in accordance with Gargani and his colleagues, who also noted that admission B-line numbers were comparable between HFrEF and HFpEF patients **[11]**. On the other hand, other authors highlighted the significant rise in the same parameter in association with HFrEF compared to HFpEF, and that significance was noted at admission and before discharge **[24]**.

Our trial showed that the increase in admission B-lines is markedly associated with a significant rise in the incidence of decompensation on three-month follow-up ($p < 0.001$ in both groups). It was previously reported that the severity of pulmonary congestion is associated with worse clinical outcomes in HF patients **[25-28]**. Therefore, it is reasonable to find the admission B-lines, the sonographic indicator of pulmonary congestion, strong predictors of worse outcomes in such patients **[12, 25]**.

Frassi and his colleagues reported that increased admission B-lines were associated with a two-fold rise in rehospitalization due to acute HF, myocardial infraction, and mortality (CI 1.1 – 3.4) **[26]**. Additionally, Platz et al. noted an increased six-month rehospitalization rate due to acute HF with the increased B-lines at admission (41% for patients with ≥3 lines, 19% for patients with 1 – 2 lines, and 14% in patients with no detected B-lines) **[12]**.

Moreover, other studies also showed that B-lines at discharge and their changes in relation to the baseline or admission values could also predict adverse outcomes in the same patients **[24, 29]**. Palazzuoli et al. reported that pre-discharge B-lines were stronger prognostic factors compared to admission B-lines. The authors attributed their finding to the fact that all patients are well-managed by medical treatment during admission, leading to a marked clinical improvement. Some patients, on the other hand, could still have subclinical congestion despite the clinical improvement, which poses a significant risk for rehospitalization due to cardiac adverse events **[24]**.

Our findings showed that admission B-lines were positively correlated with clinical lung congestion scores in HFrEF patients ($p < 0.001$). Similarly, Platz et al. reported that jugular venous distension, the third heart sound, lung crackles, and lower limb edema increased with the rise in B-line numbers **[12]**. All the previous parameters are included in the clinical congestion score, which confirms our findings. Additionally, Palazzuoli et al. reported a significant positive relationship between B-lines and clinical congestion score in HF patients ($r = 0.25$ – $p = 0.001$) **[24]**. Furthermore, Platz et al. found that the evidence of radiographic congestion on the chest x-ray increased significantly with the increase in B-lines ($p = 0.002$) **[29]**.

In the current study, admission B-lines had a significant negative correlation with EF, while they were positively correlated with TR velocity in HFrEF patients. In the same context, Gargani et al. reported that the same ultrasonographic parameters expressed a negative correlation with LVEF ($r = -0.32$) and a positive correlation with TR velocity ($r = 0.42$), and both correlations were statistically significant ($p < 0.001$) **[11]**.

We recommend using lung ultrasound in the initial assessment of HF patients for better assessment of lung congestion. Patients with more B-lines at admission should be closely monitored for early detection of cardiac adverse events.

Our trial has some limitations, manifested mainly in the relatively small patient sample as well as the lack of intermediate- and long-term follow-up.

Conclusion

Lung ultrasound could be used as a valid tool for the assessment of lung congestion in HF patients, with a strong correlation between increased admission B-lines and the incidence of short-term decompensation. Junior cardiologists should be well-trained to use that efficient tool alongside echocardiography to assess patients with HF.

Conflicts of interest: Nil.

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