## Původní sdělení | Original research article

# Value of peri-procedural lung ultrasound in predicting heart failure or left ventricular systolic dysfunction within 3 months in STEMI patients undergoing primary PCI

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#### ARTICLE INFO

Article history: Submitted: 25. 2. 2024 Revised: 5. 1. 2025 Accepted: 5. 1. 2025

Klíčová slova: Infarkt myokardu Infarkt myokardu s elevacemi úseku ST Srdeční selhání Ultrazvukové vyšetření plic

#### **SOUHRN**

**Cíl:** Zjistit, zda by detekce subklinického městnání ultrazvukovým vyšetření plic (lung ultrasound, LUS) pacientů se STEMI mohla pomoci předpovědět rozvoj srdečního selhání a systolické, nebo diastolické dysfunkce levé komory.

Metody: Do studie bylo zařazeno 150 pacientů. U všech byla provedena úspěšná revaskularizace a při příjmu u nich nebylo z klinického hlediska přítomno srdeční selhání. Během prvních 24 hodin od příjmu u nich bylo provedeno LUS s 28 plicními body a byly spočítány B-linie. Pacienti byli rozděleni do dvou skupin: 64 pacientů do skupiny LUS pozitivní (se 6 nebo více B-liniemi) a 86 jedinců do skupiny LUS negativní; po tříměsíčním sledování byli vyšetřeni na přítomnost srdečního selhání stupně II nebo vyššího podle klasifikace NYHA, ejekční frakci (EF) ≤40%, a celková longitudinální deformace myokardu (global longitudinal strain, GLS) ≤−16 %.

**Výsledky:** K rozvoji klinického srdečního selhání došlo u většího počtu pacientů ve skupině LUS pozitivní (17 vs. 2 ve skupině LUS negativní; p < 0,01); totéž platilo pro EF  $\leq 40$  % (34 vs. 3; p < 0,01) i GLS  $\leq -16$  % (60 vs. 58; p < 0,01). Křivky operační charakteristiky přijímače (receiver-operating characteristic, ROC) prokázaly, že optimální mezní hodnota počtu B-linií pro predikci rozvoje klinického srdečního selhání i poruchy systolické funkce je 6 nebo více (senzitivita = 89,47 %, specificita = 64,62 %, resp. senzitivita = 91,89 %, specificita = 74,11 %). Analýza podskupin podle počáteční diagnózy prokázala, že predikční hodnota LUS byla statisticky významná pouze v případě STEMI přední stěny.

**Závěry:** Ultrazvukové vyšetření plic u pacientů se STEMI, provedené do 24 hodin od příjmu, dokáže předpovědět rozvoj klinického srdečního selhání nebo systolické dysfunkce do tří měsíců, zvláště v případě infarktu přední stěny.

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#### **ABSTRACT**

Aim: To see if the detection of subclinical congestion in STEMI patients by lung ultrasound (LUS) could be helpful in predicting the development of future heart failure, systolic dysfunction or diastolic dysfunction. **Methods:** 150 patients were included. All patients were successfully revascularized and were not suffering from clinical heart failure on admission. The patients had a 28-point LUS study within the first 24 hours of admission, and B-lines were counted. Patients were divided into two groups: 64 patients into the LUS positive group (with 6 or more B-lines) and 86 into the LUS negative group. They were followed-up after 3 months, looking for heart failure NYHA II or greater, ejection fraction (EF) ≤40%, and global longitudinal strain (GLS) <-16%.

**Results:** More patients from the LUS positive group developed clinical heart failure (17 vs 2 in the LUS negative group, p < 0.01), EF  $\leq 40\%$  (34 vs 3, p < 0.01), GLS  $\leq -16\%$  (60 vs 58, p < 0.01). Optimal cutoff derived from ROC curves revealed that the best B-line number cutoff to predict clinical heart failure as well as impaired systolic function was 6 or greater (sensitivity = 89.47%, specificity = 64.62% and sensitivity = 91.89%, specificity = 74.11%, respectively). Subgroup analysis by initial diagnosis revealed that the predictive power of LUS was significant only in anterior STEMI.

**Conclusions:** LUS in STEMI patients, performed within 24 hours of admission, is able to predict the occurrence of clinical heart failure or systolic dysfunction at 3 months, especially in anterior infarctions.

Keywords:
Heart failure
Lung ultrasound
Myocardial infarction
ST-segment elevation myocardial
infarction

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DOI: 10.33678/cor.2025.006

#### Introduction

Heart failure is the most common complication of STEMI, and ischemic heart disease is the most prominent cause of heart failure.<sup>1</sup> The development of heart failure or asymptomatic systolic dysfunction after STEMI is associated with poorer in-hospital and long-term prognosis.<sup>2-8</sup>

In many cases, systolic dysfunction occurs after STEMI without necessarily becoming symptomatic. Lung ultrasound has been a very useful diagnostic tool in heart failure even in the pre-symptomatic phase, by detecting lung congestion at an early stage. 9,10 It also provides prognostic value and is useful in following-up treatment response. 11

We investigated the value of early lung ultrasound, conducted within 24 hours of the development of STEMI, in predicting the occurrence of clinical heart failure and systolic dysfunction within the next 3 months.

#### **Materials and methods**

This is a single-center, prospective cohort, non-consecutive study conducted in Cairo University Hospitals from March 2021 to February 2023. A total of 240 patients aged 18 years or older with ST-segment elevation myocardial infarction who have undergone successful primary PCI to the culprit lesion (defined as TIMI flow III at the end of the procedure in the infarct-related artery) were screened for inclusion, of which 150 made the final cut. Most of the rest of the patients were either lost in a follow-up or did not meet the inclusion criteria. Written informed consent was obtained from all participants.

We excluded patients younger than 18 years of age at enrollment, patients with heart failure Killip class II or greater on admission, patients with pre-existing left ventricular systolic dysfunction (LVEF  $\leq\!40\%$  or GLS  $\leq\!16\%$ , by history or previous documents if applicable), patients with history of CKD KDOQI  $\geq$  stage 3 and patients with interstitial lung disease that may confound the LUS findings. We also excluded patients who developed a non-transient confounding event that could precipitate heart failure or hemodynamic instability on its own and confound the results (e.g. failed primary PCI, stent thrombosis, mechanical complications such as ventricular septal rupture, acute

kidney injury, or resuscitated cardiac arrest). Transient events such as promptly cardioverted ventricular tachycardia were not counted as exclusion criteria.

All participants were managed according to the standard ACS protocol in Cairo University hospitals, while upholding the ethical standards of human experimentation in our institution.

#### On admission, the following data was collected:

- Patient history: Age, significant risk factors of atherosclerotic cardiovascular disease.
- Examination: Anthropometry, vital signs, signs of heart failure including jugular venous pressure, lung rales, lower limb edema and oxygen saturation on room air and signs of peripheral perfusion.
- 3. ECG on presentation.
- Procedural details: Infarct-related artery, presence of disease in other vessels, and the intervention done.

#### During hospital stay, the following was performed:

#### 1. Lung ultrasound

A 28-point lung ultrasound was performed within 24 hours of the primary PCI procedure, often shortly after returning to the CCU. The device used was a Philips EPIQ 7 ultrasound system and an X5 probe (1–5 MHz). The protocol used was the 28-point protocol, with scanning done in the 2nd, 3rd and 4th spaces bilaterally, and the 5th space on the right side only, in the parasternal, midclavicular, anterior axillary and mid-axillary lines as per the current consensus recommendations. B-lines, defined as vertical hyperechoic lines extending from the pleura to the bottom of the screen, moving with lung sliding, will be counted and totaled in all 28 zones (Fig. 1).

When B-lines are too many to the point where they coalesce together, the arc of the intercostal space that is in white relative to the width of the whole space is divided by 10 to obtain the number of B-lines (e.g. if 70% of the space is white, the number of B-lines is considered to be 7) (Fig. 2).

Other lung ultrasound findings such as the presence of pleural effusion were recorded as well, but were not specifically looked for beyond the scope of the 28-point study. All images will be digitally stored for offline analysis. The minimum number of B-lines considered significant was ≥5.

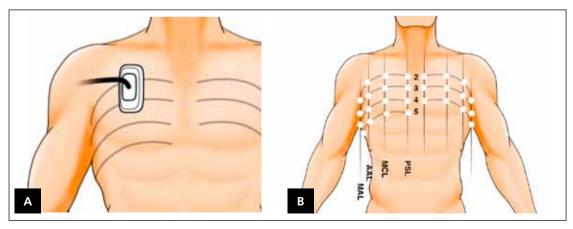


Fig. 1 – (A) Probe position relative to the ribs. (B) Sites that were scanned.



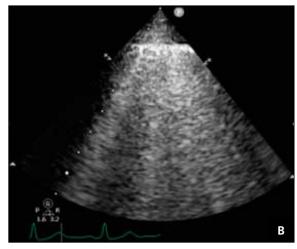


Fig. 2 – (A) Normal scan showing transverse A-lines. (B) Scan showing multiple vertical B-lines.

#### 2. Transthoracic echocardiography

Transthoracic echocardiography was performed in all subjects using a commercially available Philips EPIQ 7 ultrasound system and X5 probe. Important echocardiographic data required for management of the patient were recorded, including LV dimensions in the parasternal long axis view, systolic function using apical biplane Simpson's method whenever the image quality was sufficient and eyeballing whenever image quality was very poor, diastolic function using E and E' velocities, E/A and E/E' ratio, segmental wall motion abnormalities, left atrial volume using the biplane Simpson's method, valvular regurgitation, the presence of mechanical complications and right ventricular dimensions and TAPSE. All measurements were done as per ASE/EACVI guidance.

## During the follow-up visit 3 months later, the following data was collected:

#### 1. Clinical follow-up

This includes any cardiac symptoms, any new comorbidities, vital signs, JVP, lung rales and lower limb edema. Adherence to medications was also inquired about (defined as intake of appropriate doses of the prescribed drug in over 80% of the elapsed duration).

#### 2. Transthoracic echocardiography

Was performed again using the same devices. The data recorded in follow up included the same parameters recorded in the in-hospital echocardiogram, in addition to global longitudinal strain and left atrial volume using the apical biplane Simpson's method in end-systole. Imaging acquisition was done and offline analysis was performed using Philips Q-lab v10.0.

The primary outcome was determining the prognostic value of number of B-lines in LUS peri-primary PCI in predicting the development of systolic left ventricular dysfunction (defined as EF  $\leq$ 40% or GLS  $\geq$ -16%) within the 3-month follow up period.

Secondary outcomes were the development of clinical heart failure (as per the ESC definition mentioned previously), diastolic left ventricular dysfunction (grade II or above), and cardiovascular mortality within the same period.

#### Statistical analysis

Based on the study conducted by Xiao-Jun Ye et al.<sup>12</sup> and assuming that the number of B-lines in lung ultrasound could predict the occurrence of in-hospital as well as short-term left ventricular systolic dysfunction, with an intermediate effect size (0.15) and a probability significance of 0.05 and a power of 0.8, and using an online sample size calculator, the estimated minimum sample size is 84 patients. 150 patients were ultimately included in this study.

Analysis was done in the IBM Statistical Package for Social Sciences program (SPSS) version 24.0. Continuous data is displayed as mean ± standard deviation if the data is normally distributed, and as a median and interquartile range if not, while categorical data is displayed as an absolute number and a percentage. Comparison between continuous data was done using Student's unpaired ttest, while comparison between categorical data was done using a chi-square test.

When testing for correlation between two sets of continuous data, a scatter plot with a line of best fit was constructed when applicable, and the Pearson's product-moment correlation coefficient was calculated. For correlation between continuous data and categorical data, a one-way analysis-of-variance test was used. For correlation between two sets of categorical data, a chi-square test was used.

To determine the optimum sensitivity and specificity, ROC curves (sensitivity plotted against 1-specificity) were plotted using SPSS for each of the outcomes being examined. The uppermost, leftmost point corresponded to the cutoff with best sensitivity and specificity. To calculate positive predictive value and negative predictive value at a particular cutoff as well as their confidence intervals, an online calculator was used. For regression analysis, stepwise multiple linear regression analysis was performed when the dependent variable was continuous in nature, while logistical regression analysis was performed when the dependent variable was categorical in nature.

Findings with a two-tailed *p*-value of <0.05 were considered statistically significant.

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#### **Results**

Out of the included 150 patients, 64 had 6 or more total B-lines on presentation on LUS "LUS positive", while the remaining 86 did not "LUS negative". The cutoff was selected in concordance with the HFA position paper on diuretics released in 2019. The baseline characteristics of the included patients, as well as patients in each group are presented in **Table 1**.

Five patients in the study had history of previous acute coronary syndrome; 3 in the LUS positive group and 2 in the LUS negative group. Five patients had previous CCS (by history or tests), 2 in the LUS positive group, and 3 in the other group (one of which had an old coronary

bypass surgery). All of these patients who had history of previous coronary artery disease had normal EF before their presentation to our center in older echocardiograms (Table 2).

There was a statistically significant difference in initial presentation between LUS positive and LUS negative groups, with the majority of the patients in the former group presenting with anterior or anterolateral STEMI, while the majority of the patients in the latter group presented with inferior, inferolateral, posterior or lateral STEMI. Mirroring the skew in diagnosis seen between both groups, over 85% of the patients in the LUS positive group had PCI to the LAD or LM vessels. On the other hand, over half of the patients in the LUS negative group had PCI to the LCx or RCA.

Table 1 – Baseline characteristics of the included patients					
	Total	LUS positive (n = 64)	LUS negative (n = 86)	<i>p</i> -value	
Patient characteristics					
Age mean ± SD	53.32 ± 11.24 y	51.93 ± 12.04 y	54.36 ± 10.56 y	0.201	
Male	120 (80%)	50 (78%)	70 (81%)	0.620	
Diabetes mellitus	60 (40%)	23 (36%)	37 (43%)	0.381	
Hypertension	48 (32%)	17 (27%)	31 (36%)	0.218	
Cigarette smoking	83 (55%)	31 (49%)	52 (63%)	0.143	
FH of premature ASCVD	8 (5%)	5 (8%)	3 (4%)	0.243	
Obesity (BMI ≥30)	24 (16%)	13 (20%)	11 (13%)	0.214	

ASCVD – atherosclerotic cardiovascular disease; BMI – body mass index; FH – family history; LUS – lung ultrasound; y – years.

Table 2 – Findings on initial presentation in the included patients				
	LUS positive (n = 64)	LUS negative (n = 86)	<i>p</i> -value	
Initial diagnosis				
Anterior STEMI	32 (50%)	26 (31%)	0.014	
Anterolateral STEMI	25 (40%)	3 (3%)	<0.01	
Inferior STEMI	5 (6%)	32 (37%)	<0.01	
Inferoposterior STEMI	1 (2%)	11 (13%)	0.012	
Isolated posterior STEMI	0	5 (6%)	0.050	
Lateral STEMI	0	9 (10%)	<0.01	
LM equivalent	1 (2%)	0	0.245	
Chest pain duration mean ± SD	15.18 ± 16.32 hours	7.76 ± 8.29 hours	0.013	
Clinical data				
SBP mean ± SD	139.32 ± 67.70 mmHg	142.39 ± 73.00 mmHg	0.252	
DBP mean ± SD	88.86 ± 42.95 mmHg	89.35 ± 45.31 mmHg	0.446	
Pulse mean ± SD	104.02 ± 50.56 bpm	90.00 ± 45.87 bpm	<0.01	
Procedural details: Culprit vessel PCI				
LM or LM-LAD	4 (6%)	0	0.019	
LAD or branches	52 (81%)	29 (34%)	<0.01	
LCx or branches	4 (6%)	32 (37%)	<0.01	
RCA or branches	4 (6%)	25 (29%)	<0.01	

DBP – diastolic blood pressure; LUS – lung ultrasound; PCI – percutaneous coronary intervention; SBP – systolic blood pressure; STEMI – ST-segment elevation myocardial infarction.

Table 3 – In-hospital events in each group			
	LUS positive (n = 64)	LUS negative (n = 86)	<i>p</i> -value
In-hospital heart failure	6 (10%)	0	<0.01
Clinical lung congestion requiring the use of intravenous diuretics	4 (6%)	0	0.019
Cardiogenic shock	2 (3%)	0	0.094
Arrhythmias			
Complete heart block	1 (2%)	0	0.245
Ventricular tachycardia	1 (2%)	3 (3%)	0.469
Atrial fibrillation	0	1 (1%)	0.386
In-hospital mortality	1 (2%)	0	0.245
In-hospital echocardiogram			
Ejection fraction mean ± SD	44.90 ± 7.04%	53.40 ± 8.20%	<0.01
Grade II diastolic dysfunction or more	20 (31%)	33 (38%)	0.465
Mural thrombus	5 (8%)	3 (4%)	0.244

LUS - lung ultrasound.

Table 4 – Summary of the follow-up visit findings in each group				
	LUS positive (n = 63)	LUS negative (n = 86)	<i>p</i> -value	
Clinical heart failure	19 (30%)	2 (2%)	<0.01	
NYHA II	17 (27%)	2 (2%)	<0.01	
NYHA class III+	2 (3%)	0	0.346	
Patient compliance	35 (56%)	51 (59%)	0.690	
Echocardiographic data: Systolic function				
Ejection fraction ≤40%	34 (55%)	3 (4%)	<0.01	
	41.08 ± 4.74%	55.22 ± 8.26%		
Global longitudinal strain ≤–16%	60 (96%)	58 (67%)	<0.01	
	-12.31 ± 1.24%	-15.24 ± 1.91%		
Echocardiographic data: Diastolic function				
Grade II diastolic dysfunction or more	25	28	0.469	
Left atrial volume index	36.41 ± 15.94 ml/m <sup>2</sup>	29.38 ± 11.88 ml/m <sup>2</sup>	<0.01	
Average E/E'	13.24 ± 7.16	9.06 ± 4.25	<0.01	

LUS – lung ultrasound; NYHA – New York Heart Association.

#### In-hospital events

More patients in the LUS positive group ultimately developed in-hospital acute heart failure (6 patients versus none in the LUS negative group, *p*-value = 0.003), mostly lung congestion requiring eventual in-hospital IV diuretic use (**Table 3**).

However, this statistical significance could not be demonstrated in cardiogenic shock specifically due to the low event count.

There was a statistically significant difference in the mean ejection fraction during hospitalization between both groups, with the LUS positive group being lower. However, there was no statistically significant difference between both groups in terms of number of patients with grade II diastolic dysfunction or more in-hospital.

#### Follow-up visit

Nineteen patients from the LUS positive group developed exertional dyspnea at 3 months, as opposed to only two in the LUS negative group (Table 4). Most of the patients had dyspnea NYHA class II. Only two patients developed dyspnea NYHA III; both were in the LUS positive group.

ROC curves were plotted to identify the best B-line cutoff that provided the highest sensitivity and specificity for impaired ejection fraction. The best cutoff to predict an impaired ejection fraction was  $\geq 6$  lines (which was what we used in this study) with an area under the ROC curve of 0.92. The sensitivity and specificity of  $\geq 6$  lines is displayed in **Table 5**, **Figure 3**.

Using the follow-up data, an evaluation of LUS as a diagnostic test was done by calculating the sensitivity,

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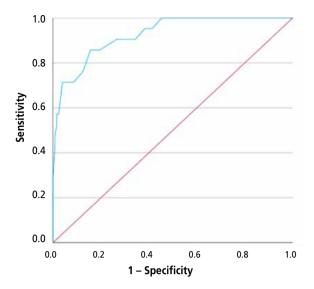


Fig. 3 – ROC curve for number of B-lines sensitivity and specificity in predicting clinical heart failure.

specificity, PPV and NPV to detect clinical heart failure or systolic dysfunction by ejection fraction or global longitudinal strain. LUS demonstrated a high sensitivity and high negative predictive value in predicting the occurrence of clinical heart failure or an ejection fraction ≤40%. For global longitudinal strain, LUS demonstrated a low sensitivity but high specificity in detection of impaired GLS in this subset of patients (Table 5).

# Subgroup analysis according to the initial presentation

After performing subgroup analysis on follow-up data, the statistical significance of the difference between the LUS positive and LUS negative groups in clinical heart failure, ejection fraction ≤40 and global longitudinal strain ≥−16% at 3 months was carried over for anterior infarctions (including anterior, anterolateral, and anteroinferior infarctions), and lost for inferior infarctions (including inferior, inferolateral, and inferoposterior infarctions) (Table 6).

#### Correlation analysis

Pearson correlation analysis between the number of B-lines and ejection fraction  $\leq$  40%, global longitudinal strain  $\geq$  -16%, left atrial volume index and average E/E' ratio was done. The number of B-lines was strongly negatively correlated with the ejection fraction (r = -0.619, p < 0.01), and strongly positively correlated with the global longitudinal strain (r = 0.521, p < 0.01). It was also moderately positively correlated with the average E/E' ratio (r = 0.389, p < 0.01).

Table 5 – Sensitivity, specificity, positive predictive value, and negative predictive value of 6 or more B-lines in LUS in predicting various endpoints				
	Sensitivity	Specificity	PPV	NPV
Follow-up data				
Clinical HF	89.47%	64.62%	26.98%	97.67%
	95% CI: 66.8–98.7%	95% CI: 55.7–72.8%	95% CI: 21.8–32.8%	95% CI: 59.7–75.2%
EF ≤40%	91.89%	74.11%	53.97%	96.51%
	95% CI: 78.1–98.3%	95% CI: 65.0–81.9%	95% CI: 45.8–61.9%	95% CI: 90.3–98.8%
GLS ≤–16%	50.85%	90.32%	95.24%	32.56%
	95% CI: 41.5–60.2%	95% CI: 74.3–98.0%	95% CI: 87.1–98.4%	95% CI: 28.0–37.5%

CI – confidence interval; EF – ejection fraction; GLS – global longitudinal strain; HF – heart failure; NPV – negative predictive value; PPV – positive predictive value.

Table 6 – Subgroup analysis of the groups according to the initial diagnosis				
LUS positive – LUS negative	LUS positive	LUS negative	<i>p</i> -value	
Anterior STEMI	n = 57	n = 29		
Clinical heart failure	18 (32%)	2 (7%)	0.022	
Ejection fraction ≤40%	32 (56%)	2 (7%)	<0.01	
Global longitudinal strain ≥–16%	57 (100%)	25 (86%)	0.020	
Grade II diastolic dysfunction or more	20 (35%)	7 (24%)	0.430	
Inferior STEMI	n = 6	n = 43		
Clinical heart failure	1 (17%)	0	0.245	
Ejection fraction ≤40%	1 (17%)	0	0.245	
Global longitudinal strain ≥–16%	5 (83%)	22 (52%)	0.296	
Grade II diastolic dysfunction or more	4 (67%)	18 (42%)	0.480	

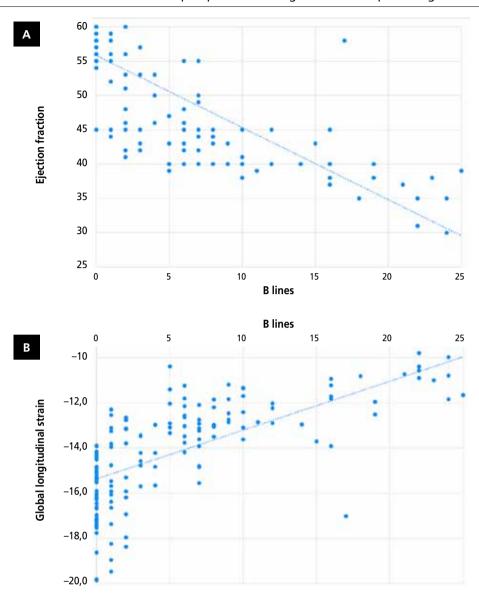


Fig. 4 – Scatter plots of number of B-lines against the ejection fraction (A) and global longitudinal strain (B).

Table 7 – Linear regressi	on analysis results			
	Unstandardized coefficient	Unstandardized coefficients		
	В	Standard error	Beta	<i>p</i> -value
<b>Ejection fraction at 3 mc</b> R = 0.845, R square = 0.7	onth follow-up visit 14, adjusted R square = 0.691			
Presentation HR	-0.105	0.035	-0.186	<0.01
In-hospital EF%	0.380	0.083	0.349	<0.01
Number of B-lines	-0.617	0.095	-0.483	<0.01
	n at 3 month follow-up visit 34, adjusted R square = 0.604			
Hypertension	-0.743	0.325	-0.164	0.025
Presentation HR	0.022	0.009	0.172	0.017
In-hospital EF%	-0.097	0.017	-0.244	<0.01
Number of B-lines	0.051	0.018	0.514	<0.01

EF – ejection fraction; HR – heart rate; STEMI – ST-segment elevation myocardial infarction.

However, no statistically significant correlation could be seen between the number of B-lines above 5 and the left atrial volume index (r = 0.217, p = 0.114) (Fig. 4).

#### Regression analysis

Stepwise multiple linear regression analysis was done to demonstrate the independent predictive ability of the number of B-lines in LUS. Out of age, diabetes, hypertension, smoking, heart rate on presentation, ejection fraction on presentation and B-lines on presentation, only the latter three demonstrated a statistically significant ability to independently predict the ejection fraction and global longitudinal strain at 3 months in our study. Hypertension was able to predict an impaired global longitudinal strain at 3 months, but not ejection fraction at 3 months (Table 7).

#### **Discussion**

In our study, there was an obvious, statistically significant association between a positive in-hospital LUS and the eventual development of in-hospital heart failure. Since B-lines are themselves markers of subclinical congestion, this conclusion is hardly surprising.

Aside from that, there was a common theme immediately apparent in the LUS positive group of patients even before they came in for their follow-up visit. Their chest pain to revascularization time was longer, they were more tachycardic, more often had anterior infarctions, and subsequently often had an LAD culprit. Their baseline systolic function measured in-hospital was also often worse. All of these characteristics are themselves established predictors of heart failure in STEMI patients.<sup>13</sup>

The differences in terms of the primary and secondary outcomes between the two groups in the follow-up visits could not be more discordant. Patients who had a positive LUS were much more likely to develop clinical heart failure and systolic dysfunction on follow-up. To take it a step further, there was evidence of a strong linear correlation between the number of B-lines above 5 inhospital and the ejection fraction and global longitudinal strain in the follow-up visit.

It seems however that this predictive ability only holds true for patients with anterior infarctions, and the difference between the two groups when examining other non-anterior infarctions was not statistically significant in our study.

The results were also less conclusive in terms of diastolic function. There was no statistically significant difference in the number of patients having grade 2 or higher diastolic dysfunction (diagnosed according to the ASE algorithm) between both groups. In terms of the individual components of the algorithm however, there was a statistically significant difference in the mean left atrial volume index and the mean average E/E' ratio between the two groups.

Regression analysis reinforced the predictive power of LUS in systolic dysfunction independent of other factors.

#### **Previous studies**

The studies examining the role of LUS in STEMI patients are relatively scarce, are mostly on a limited number of patients, and most of those focus on immediate outcomes (either in-hospital or within the first 30 days after discharge).

The largest study conducted on the matter was by Araiza et al in 2022, on 226 patients. <sup>14</sup> The investigative team performed a 4-point LUS during the first 24 hours of hospitalization. On 30-day follow-up, there was a statistically significant increase in the incidence of heart failure in the LUS positive group, similar to our findings. It has to be noted, however, that this study did not exclude patients with renal impairment or higher Killip classes.

The study with the longest follow-up was done by Xiao-Jun Ye et al in 2019. It enrolled a total of 102 STEMI patients. Interestingly, they were anterior STEMI patients; the exact subgroup where the results of our study were particularly relevant to. The investigators performed a 28-point LUS within 5 hours of admission, then monitored them for in-hospital heart failure. After discharge, rehospitalization for heart failure within two years was documented, unlike our study which monitored patients for a much shorter duration and for general (even mild) heart failure symptoms as opposed to only hospitalizations or cardiovascular events.

Ye et al. found that a positive LUS study significantly predicted heart failure rehospitalization and all-cause mortality, although the cutoff for that was 18 B-lines. The investigators also found out that the predictive power of LUS could be improved further by adding E/E' measurements and NT-proBNP. We did not use biomarkers in our study.

In a study by He et al. published in 2022 that included 63 patients with acute myocardial infarction (as opposed to just STEMI patients), an 8-point LUS conducted during the first 24 hours was able to predict not only worsening heart failure as we had found out in our study, they also found out that it predicted rehospitalization and all-cause mortality at 30 days. 15

To the best of our knowledge, there are no published studies on the ability of LUS to predict systolic or diastolic dysfunction after a myocardial infarction.

The STEMI event itself represents the brunt of the hit on the myocardium, when transient factors such as myocardial stunning are present and not enough time is available for compensatory mechanisms to cope with the cardiac dysfunction that has happened.

The appearance of subclinical congestion early on could be interpreted as a marker that the cardiac dysfunction (whether systolic or diastolic) is significant enough to overwhelm the rest of the myocardium and elevate the left ventricular end diastolic pressure, and consequently lower the likelihood of the myocardium functioning as adequately in the future.<sup>16</sup>

One peculiar finding in our study is that congestion in LUS is more predictive of systolic dysfunction at 3 months (as defined before) than the ejection fraction on presentation. This is probably because as mentioned before, B-lines are a surrogate for left ventricular end diastolic pressure, which is influenced by systolic and diastolic

myocardial performance rather than just systolic. Since STEMI is a disease that affects systolic and diastolic function, not all future heart failure events can be accounted for by the admission ejection fraction alone, and LUS will be superior to it in that regard.

The biggest takeaway from this study is that LUS provides beneficial prognostic data at no extra cost, effort or time. It is performed at the end of the routine echocardiographic study that is done for all STEMI patients. It can help planning of investigations, medications and the frequency of follow-up visits.

#### **Study limitations**

The NYHA classification is entirely subjective and is subject to many confounding causes of dyspnea. The use of the Kansas City Cardiomyopathy Questionnaire or a 6-minute walk test may have been more accurate.

In many patients, a physical previous echocardiogram document was not always available and history alone may be very misleading.

Global longitudinal strain is highly influenced by the quality of the patient's echocardiographic windows.

The study was not blinded; the operator knew the results of the LUS during the follow-up visits of the patients.

The study was conducted in a single center and patients were selected non-consecutively. The sample size was limited; a larger study on a bigger sample size would be more suitably powered to detect statistically significant differences between the two arms in in-hospital cardiogenic shock, non-anterior STEMI patients, and diastolic dysfunction.

The exclusion criteria were quite exhaustive and excluded a large subset of STEMI patients, such as those with comorbidities or unsuccessful revascularization. These specific patients are the ones who may gain extra benefit from further risk assessment over stable, straightforward cases.

The study did not include the use of cardiac biomarkers such as NT-pro BNP.

#### Conclusion

LUS in STEMI patients, performed within 24 hours of admission, is able to predict the occurrence of clinical heart failure or systolic dysfunction at 3 months according to our study, especially in anterior infarctions.

#### **Acknowledgements**

The authors acknowledge Prof Dr Yasser Boghdady and Prof Dr Mohamed Seleem for their valuable comments and suggestions. We also acknowledge Prof Dr Magdy Abd El Hamid for his support throughout the research.

#### **Funding**

The authors declare that no funds, grants, or other support were received during the preparation of this manuscript.

#### **Ethical statement**

This is an observational study. The Cairo University Faculty of Medicine ethics committee has approved this research

on 19-08-2021 (Code: MD-220-2021). The work conforms to the standards currently applied to research methodology in Egypt.

#### Consent to participate

Informed written consent to participate in the research was obtained from all individual participants included in the study.

#### Consent to publish

Informed written consent to publish research results was obtained from all individual participants included in the study.

#### Availability of the data and material

The data is available upon reasonable request.

#### **Author contributions**

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Mohamed Abou El Ezz. The first draft of the manuscript was written by Mohamed Abou El Ezz, and Ahmed Talaat commented on the previous versions of the manuscript. All authors read and approved the final manuscript.

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