

Impact of serial cardiopulmonary point-of-care ultrasound exams in patients with acute dyspnoea: a randomised, controlled trial

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To cite: Arvig MD, Lassen AT, Gæde PH, et al. Emerg Med J Epub ahead of print: [please include Day Month Year]. doi:10.1136/ emermed-2022-212694 ABSTRACT

Background Serial point-of-care ultrasound (PoCUS) can potentially improve acute patient care through treatment adjusted to the dynamic ultrasound findings. The objective was to investigate if treatment guided by monitoring patients with acute dyspnoea with serial cardiopulmonary PoCUS and usual care could reduce the severity of dyspnoea compared with usual care alone.

Methods This was a randomised, controlled, blindedoutcome trial conducted in three EDs in Denmark between 9 October 2019 and 26 May 2021. Patients aged \geq 18 years admitted with a primary complaint of dyspnoea were allocated 1:1 with block randomisation to usual care, which included a single cardiopulmonary PoCUS within 1 hour of arrival (control group) or usual care (including a PoCUS within 1 hour of arrival) plus two additional PoCUS performed at 2 hours interval from the initial PoCUS (serial ultrasound group). The primary outcome was a reduction of dyspnoea measured on a verbal dyspnoea scale (VDS) from 0 to 10 recorded at inclusion and after 2, 4 and 5 hours.

Results There were 206 patients recruited, 102 in the serial ultrasound group and 104 in the control group, all of whom had complete follow-up. The mean difference in VDS between patients in the serial ultrasound and the control group was -1.09 (95% CI -1.51 to -0.66) and -1.66 (95% CI -2.09 to -1.23) after 4 and 5 hours, respectively. The effect was more pronounced in patients with a presumptive diagnosis of acute heart failure (AHF). A larger proportion of patients received diuretics in the serial ultrasound group.

Conclusion Therapy guided by serial cardiopulmonary PoCUS may, together with usual care, facilitate greater improvement in the severity of dyspnoea, especially in patients with AHF compared with usual care with a single PoCUS in the ED. Serial PoCUS should therefore be considered for routine use to aid the physician in stabilising the patient faster.

Trial registration number NCT04091334.

INTRODUCTION Background

Patients with acute dyspnoea constitute a large proportion of adult patients admitted to an ED.¹ Dyspnoea can be caused by different conditions, for example, acute heart failure (AHF), chronic obstructive lung disease exacerbation and pneumonia.² The subjective feeling of dyspnoea causes

WHAT IS ALREADY KNOWN ON THIS TOPIC

- ⇒ Cardiopulmonary point-of-care ultrasound (PoCUS) can be used to diagnose patients with acute dyspnoea.
- ⇒ It is not known if treatment guided by serial cardiopulmonary PoCUS can result in a faster improvement in patient-reported dyspnoea.

WHAT THIS STUDY ADDS

- ⇒ In this randomised study, patients with dyspnoea managed with serial PoCUS, together with usual care, had a greater reduction in selfreported severity of dyspnoea within 5 hours from arrival at an ED compared with those receiving a single ultrasound.
- \Rightarrow The difference was more pronounced in those patients with acute heart failure.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Monitoring patients with dyspnoea presenting to the ED with serial PoCUS should be considered to facilitate faster relief of symptoms.

a range of unpleasant sensations, for example, anxiety, air hunger and chest discomfort, and is an essential patient-reported outcome.³ Furthermore, patients admitted with dyspnoea have high mortality compared with patients with other complaints.⁴

Point-of-care ultrasound (PoCUS) has been used to diagnose the underlying aetiologies of dyspnoea in ED patients for several years. The utilisation of PoCUS of the heart, lungs and the legs' deep veins has improved the diagnostic accuracy in patients with dyspnoea from about 60% to 90% when done within 4 hours from arrival.⁵ However, subsequent monitoring is often done with just a combination of the trajectories of symptoms, vital signs and medical tests. The benefit of adding serial PoCUS to reassessment has the potential to improve the diagnostic accuracy and monitoring of the severity of certain conditions because of the dynamic nature of some ultrasound parameters. In particular, B-lines, which can be seen in the loss of peripheral lung aeration, for example, in cardiogenic and noncardiogenic pulmonary oedema, and pneumonia,



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Figure 1 Study design and flow. PoCUS, point-of-care ultrasound; US, ultrasound; VDS, verbal dyspnoea scale.

can resolve with treatment, especially in patients with heart failure.^{6 7} However, in our systematic review leading to this trial, no studies reported an effect of treatment guided by serial PoCUS on the severity of dyspnoea.⁶

The objective of this randomised, controlled trial was to investigate if therapy guided by monitoring adult ED patients with a primary complaint of dyspnoea using serial cardiopulmonary PoCUS in addition to usual care could reduce the severity of dyspnoea compared with treatment guided by usual care alone including a single POCUS exam.

METHODS

Study design and setting

We conducted a randomised, controlled and blinded-outcome trial in three EDs in Denmark between 9 October 2019 and 26 May 2021 (figure 1). The EDs provide 24-hour care and receive all acute medical and surgical patients referred from a general practitioner or as direct emergency admissions. In Denmark, healthcare is tax-funded and thereby provides equal access.

The study was prospectively registered at ClinicalTrials.gov (NCT04091334) and adhered to the Consolidated Standards of Reporting Trials guideline.^{8 9} The published protocol is provided in online supplemental appendix S1¹⁰ and protocol alterations in online supplemental appendix S2.

Selection of participants

Patients were recruited over 24 hours all days when an investigator was present in the ED during clinical duty. During the trial period of 595 days, patients were screened on 426 of the days (72%) and included over 159 days. Patients were eligible for inclusion if they: (1) arrived at the ED with a primary complaint of dyspnoea (confirmed by asking the patient on arrival); (2) were 18 years or older; (3) could provide informed consent and (4) the first evaluation of the patient including the first PoCUS exam could be done within 1 hour from arrival. No requirements regarding vital signs.

Exclusion criteria included: (1) trauma patients; (2) patients invasively ventilated within the first hour after arrival and (3) if an investigator was not present in the ED.

Randomisation and blinding

Patients in both groups were enrolled within 1 hour from arrival at the ED and received the same initial standard evaluation, including a PoCUS (figure 1). Patients were allocated on 1:1 ratio into the intervention or control group. Patients were randomised with Research Electronic Data Capture. Block randomisation was employed to ensure balance and reduce bias when assigning participants to different treatment groups.¹¹ The allocation sequence was concealed from the investigators. Randomisation was conducted after informed consent but before the patient's first examination. The investigators (MDA, SWG, HØP and GT) performed the screening, enrolment, all the examinations and treatment adjustments regardless of the study group. The investigators were all certified by the same PoCUS standards¹² and had similar working experience with PoCUS (about 5 years).

Intervention

In both groups, the initial assessment consisted of routine physical examination, medical history, measurement of vital signs, blood samples, ABG, CXR and PoCUS (figure 1). In the subsequent assessments of the patients 2, 4 and 5 hours from inclusion, usual care consisted of a clinical evaluation of the patients, including vital signs and VDS.

In the serial ultrasound group, usual care was supplemented by a lung ultrasound (LUS) and a focused cardiac ultrasound (FoCUS). LUS and FoCUS were performed according to international standards,¹³¹⁴ and a protocol developed for this trial (online supplemental appendix S3).¹⁰ LUS was performed with an 8-zone scanning protocol with the patient in a semi-supine position. The investigators looked for B-lines, pleural effusions, consolidations and the absence of lung sliding. In the FoCUS, the investigators assessed the right ventricle for dilatation, the function of the left ventricle, presence of pericardial effusion and calculating the inferior vena cava-collapsibility index (IVC-CI). The ultrasound was performed with a Venue (General Electric, Boston, Massachusetts, USA) or Sonosite X-Porte (FUJIFILM Sonosite, Bothell, Washington, USA) with a curvilinear probe (2-5 MHz and 1.4-5.7 MHz on the Sonosite and Venue, respectively) and a phased array probe (1-5 MHz and 1.1-4.7 MHz on the Sonosite and Venue, respectively). The investigators were instructed to adjust the treatment according to clinical parameters as per routine care as well as the serial ultrasound findings, for example, to give more diuretics if the clinical presentation and/or number of B-lines were the same or increased during the subsequent scans and a diagnosis of AHF was suspected (online supplemental appendix S1).



Figure 2 Consolidated Standards of Reporting Trials flow diagram.

Assessment

The patients' degree of dyspnoea was measured on enrolment, and then at 2, 4 and 5 hours after arrival. Dyspnoea was measured on a verbal dyspnoea scale (VDS) from 0 to 10, with 0 indicating no dyspnoea and 10 the worst dyspnoea imaginable. VDS is previously validated in the ED setting.^{15 16} Assessments of dyspnoea were made by healthcare professionals serving as outcome assessors who were blinded to the allocation and any interventions and approached the patient independently of the investigator.

The final hospital diagnosis was made by two independent physicians (CF and IRS) who audited the patients' records but were blinded to the allocation and the results of the additional ultrasound examinations done in the serial ultrasound group. Furthermore, these physicians were not involved in the enrolment process at any point. Disagreements were resolved by a third reviewer (SP). The audit was performed according to predefined diagnostic criteria (online supplemental appendix S4).

The intra-rater and inter-rater reliability of the PoCUS findings, including B-lines and IVC-CI, were estimated in a subsample of 25 randomly selected scans by an independent reviewer (H \emptyset P).¹⁷ ¹⁸ Furthermore, the overall quality of the clips was graded from 1 to 5, where 5 was best.¹⁹

Outcomes

The primary outcome was decreased dyspnoea on VDS evaluated at four different time points (figure 1). The secondary outcomes

were: (1) length of hospital stay (LOS); (2) the proportion of readmissions within 0–7 and 8–30 days from discharge date; (3) in-hospital mortality; (4) 0–7 days and 8–30 days mortality from admission date; (5) proportion of patients with a final ED diagnosis in agreement with the audit diagnosis; (6) IVC-CI correlated to vital signs and VDS; (7) B-line count correlated to vital signs and VDS; (8) the dynamic changes in IVC-CI between the PoCUS; (9) the dynamic changes in B-line count between the PoCUS; (10) medications and fluids administered in the groups; (11) proportions of differential diagnoses during the ED stay; (12) intra-rater and inter-rater reliability of the PoCUS findings and (13) image quality of the PoCUS.

Analysis

The sample size was based on a minimally clinically important difference of 1 point on VDS.^{20 21} The patients in the serial ultrasound group were expected to have a 2-point change in VDS compared with a 1-point change in the control group at the final evaluation of the patient in the ED. With a power of 80%, type 1 error of 5% and 10% dropouts, the sample size was calculated to be 206 patients.

The primary outcome was analysed using a mixed-effect model with a change from baseline VDS as the dependent variable. Factors assumed to have the same effect across many patients were baseline score in VDS, trial group, time points and interaction of trial group with time points. The individual patient was treated as the random effect. A subgroup analysis

Table 1	Baseline characteristics of patients in the serial ultrasound
and the co	ontrol group

	Serial ultrasound group (n=102)		Control group (n=104)	
Sites				
Slagelse Hospital	102			101
Horsens Hospital	0			2
Zealand University Hospital	0			1
Patient characteristics				
Sex				
Female	42	(41.2)	52	(50.0)
Male	60	(58.8)	52	(50.0)
Age, years	76	(66–83)	76	(66–81)
BMI, mean, kg/m ²	26.6	(5.7)	27.5	(7.0)
Smoking status				
Never	25	(24.5)	20	(19.2)
Current	14	(13.7)	15	(14.4)
Previous	63	(61.8)	69	(66.3)
Medical history				
COPD	36	(35.3)	34	(32.7)
Asthma	18	(17.6)	7	(6.7)
Other lung disease	4	(3.9)	0	(0.0)
Chronic heart failure	28	(27.5)	19	(18.3)
Arterial hypertension	55	(53.9)	49	(47.1)
Coronary arterial disease	27	(26.5)	27	(26.0)
Thromboembolic disease	5	(4.9)	8	(7.7)
Stroke	13	(12.7)	17	(16.3)
Chronic kidney disease	5	(4.9)	9	(8.7)
Diabetes mellitus	21	(20.6)	16	(15.4)
Psychiatric disorder	13	(12.7)	14	(13.5)
Current or previous cancer	15	(14.7)	24	(23.1)
Dyslipidaemia	29	(28.4)	31	(29.8)
Atrial fibrillation/flutter	35	(34.3)	25	(24.0)
None	5	(4.9)	5	(4.8)
Others	70	(68.6)	75	(72.1)
Symptoms and physical examin	ation			
Chest pain	27	(26.5)	25	(24.0)
Cough	56	(54.9)	53	(51.0)
Sputum	34	(33.3)	36	(34.6)
Palpitations	19	(18.6)	13	(12.5)
RR, brpm	21	(18–23)	20	(18–23)
Oxygen saturation, %	95	(92–98)	96	(93–98)
Oxygen supply, L/min	1	(1–1)	1	(1–1)
Oxygen delivery method				
Nasal cannula	30	(29.4)	21	(20.2)
Mask	4	(3.9)	13	(12.5)
Other	2	(2.0)	1	(1.0)
Systolic blood pressure, mm Hg	138	(124–152)	136	(120–152)
Diastolic blood pressure, mm Hg	75	(64–90)	74	(65–85)
Heart rate, bpm	88	(76–105)	85	(74–103)
Temperature, °C	36.5	(36.5–37.3)	36.5	(36.5– 37.2)
Oedema				
None	65	(63.7)	69	(66.3)
One leg	2	(2.0)	0	(0.0)
Both legs	35	(34.3)	35	(33.7)
Focused lung ultrasound				Continued

Table 1 Continued

		Serial ultra (n=102)	erial ultrasound group n=102)		Control group (n=104)	
	B-lines present	87	(85.3)	77	(74.0)	
	Sum of B-lines in eight zones	5	(2–9)	2	(0–9)	
	Consolidation	38	(37.3)	29	(27.9)	
	Absence of lung sliding	1	(1.0)	2	(1.9)	
	Pleural effusion	46	(45.1)	29	(27.9)	
Focused cardiac ultrasound						
	Ejection fraction					
	Normal	50	(49.0)	58	(55.8)	
	Mild dysfunction	21	(20.6)	19	(18.3)	
	Moderate dysfunction	15	(14.7)	15	(14.4)	
	Severe dysfunction	14	(13.7)	7	(6.7)	
	Hyperdynamic	2	(2.0)	5	(4.8)	
	Pericardial effusion	1	(1.0)	2	(1.9)	
	Right ventricle dilatation	5	(4.9)	5	(4.8)	
	TAPSE, mm	20	(16–24)	20	(16–24)	
	IVC max diameter, mm	20	(20–20)	20	(10–20)	
	IVC min diameter, mm	10	(10–20)	10	(10–20)	
	IVC-CI, %	36	(25–56)	39	(23–61)	
Most common final ED diagnoses		S				
	Acute heart failure	41	(40.2%)	40	(38.5%)	
	Pneumonia	34	(33.3%)	28	(26.9%)	
	Exacerbation of COPD	22	(21.6%)	26	(25.0%)	

Data are n (%) or median (IQR), unless otherwise noted.

ARB, angiotensin receptor blocker; BMI, body mass index; brpm, breaths per minute; COPD, chronic obstructive pulmonary disease; IVC, inferior vena cava; NSAID, nonsteroidal anti-inflammatory drug; PPI, proton pump inhibitors; TAPSE, tricuspid annular plane systolic excursion.

of the patients with AHF was conducted because dynamic B-lines are mainly seen in this patient category. The proportion of different treatments provided in the two groups was examined to explain a possible effect of the serial ultrasound intervention.

For the secondary outcomes, the continuous variable (LOS) was compared with the Mood's median test and the categorical variables with the χ^2 test and supplemented with a two-sided significance level of 5% and a risk difference with 95% CI. A heatmap was used to visualise the correlations between B-lines, IVC-CI, VDS and vital signs. Box plots were employed to illustrate the variations in B-lines and IVC-CI. The proportion of ED diagnoses in agreement with the final hospital diagnoses was expressed as numbers and percentages. Inter-rater reliability between the presumptive diagnoses made by the investigator and the blinded audit was calculated with Cohen's kappa. Cohen's kappa was also used to calculate the intra-rater and inter-rater reliability of the ultrasound clips. Image quality was calculated as median.

Missing data were present in 6 out of 410 measurements of the IVC-CI and were only excluded in the analysis of the changes in IVC-CI during the ED stay.

All statistical analyses were performed with Stata V.17.0 (StataCorp, Texas, USA).

Patient and public involvement

Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.



Figure 3 Change in the primary outcome (VDS) between the two groups at the different time points. Data are mean (95% CI). *Inclusion: same standard diagnostics in both groups, including LUS and FoCUS. †2 hours: standard care in both groups. In the serial ultrasound group, an extra LUS and FoCUS. ‡4 hours: standard care in both groups. In the serial ultrasound group, an extra LUS and FoCUS. §5 hours: same standard care in both groups. No ultrasound examinations. FoCUS, focused cardiac ultrasound; LUS, lung ultrasound; VDS, verbal dyspnoea scale.

RESULTS

Characteristics of study subjects

Eligibility was assessed in 436 acute patients (figure 2). Of those, 206 (47%) patients were included and randomly assigned to the serial ultrasound group with 102 patients and the control group with 104 patients. The most common cause for patients not being included following assessment for study eligibility was absence of dyspnoea as the primary complaint during the screening of the patients. Most patients were enrolled and managed by two investigators in one ED (table 1).

The patients had a median age of 76 years, many were previous smokers and had chronic obstructive pulmonary disease or arterial hypertension as the most common comorbidities (table 1, online supplemental table S1). More patients in the serial ultrasound group had chronic heart failure. Besides dyspnoea, cough was the most common complaint. The patients had overall vital signs within normal levels.

One-third of patients had bilateral oedema of the legs. On the PoCUS, one-third had consolidations or pleural effusions. Nearly 80% had B-lines at arrival, and half had reduced ejection fraction. The proportion of pathological ultrasound findings was higher in the serial ultrasound group.

Main results

Patients in both groups experienced a decline in the severity of VDS (figure 3). At 4 and 5 hours from inclusion (measuring the effect of the first and the second extra PoCUS, respectively), the mean difference in VDS between the patients in the serial ultrasound and the control group was -1.09 (95% CI -1.51 to -0.66) and -1.66 (95% CI -2.09 to -1.23). In the planned subgroup analysis of the primary outcome in patients with a presumptive diagnosis of AHF, the difference in VDS at 4 and 5 hours were -1.52 (95% CI -2.52 to -0.78) and -1.97 (95% CI - 2.70 to -1.23) (figure 4, online supplemental figure S1). A larger proportion of patients received diuretics, inhaled beta2adrenergic agonists and oxygen in the serial ultrasound group (online supplemental table S2). However, the difference was only significant for diuretics, where patients in the serial group received a dose 6-8 times greater at 2 and 4 hours from inclusion compared with the control group.

No statistically significant differences were observed between the two groups regarding LOS, readmissions within 0-7 and 8-30 days, in-hospital mortality and 0-7 and 8-30 days mortality (table 2). The proportion of the final ED diagnoses in agreement with the audit diagnoses was higher in the serial ultrasound group (64% vs 59%), but the difference was not statistically significant. The final ED diagnoses of AHF were similar in the two groups (table 1) and with the audit diagnosis (online supplemental table S3). The overall agreement between the raters of the final audit diagnoses was 96% (kappa=0.69).

In the serial ultrasound group, the number of B-lines was nearly identical between the initial LUS and the second LUS but decreased at the final LUS exam (online supplemental figure S2A). In a subgroup of patients with a presumptive diagnosis of AHF, a similar pattern was found but with a higher median number of B-lines (online supplemental figure S2B). IVC-CI did not change between the scans (online supplemental figure S3) and there was no correlation between B-lines or IVC-CI and vital signs or VDS (online supplemental figures S4 and S5). The intra-rater and inter-rater reliability of the assessed ultrasound clips had an agreement of 96% (kappa=0.91) and 94% (kappa=0.87), respectively. Overall median image quality was 4.

DISCUSSION

This randomised trial assessed whether treatment guided by serial cardiopulmonary PoCUS in acute adult patients admitted with a primary complaint of dyspnoea could shorten the time to improvement in symptoms. We found that patients who underwent repeated PoCUS examinations had greater improvement in patient-reported dyspnoea than patients who had only a single PoCUS on arrival during their ED visit, with a larger statistically significant difference in those with AHF. The effect of serial PoCUS is likely due to the significantly greater use of diuretics in the serial ultrasound group.

The effect of treatment guided by serial ultrasounds was a reduction in VDS by 1.23 after 4 hours from inclusion and a further reduction by 0.68 after 5 hours. A carry-over effect might explain the smaller improvement between hours 4 and 5 besides the patient being more stabilised in the later phase. The overall effect was primarily driven by the effect of PoCUS in patients with AHF, which might be due to the underlying cause of the B-lines found in these patients, contrary to B-lines found in other conditions, for example, pneumonia. The effect can partly be explained by the increasing amount of diuretics administered in the serial ultrasound group.



Figure 4 Change in the primary outcome (VDS) in patients with (A) and without a presumptive diagnosis of AHF (B). *Inclusion: same standard diagnostics in both groups, including LUS and FoCUS. †2 hours: standard care in both groups. In the serial ultrasound group, an extra LUS and FoCUS. †4 hours: standard care in both groups. In the serial ultrasound group, an extra LUS and FoCUS. §5 hours: same standard care in both groups. No ultrasound examinations. AHF, acute heart failure; FoCUS, focused cardiac ultrasound; LUS, lung ultrasound; VDS, verbal dyspnoea scale.

We found no difference in LOS, readmissions or short-term mortality between groups receiving a single or serial POCUS exam. Previous studies conducted in a similar setting using only a single PoCUS exam have yielded the same results.^{5 22} To further elucidate the potential impact of PoCUS performed within the first hours in the ED on patient prognosis, larger-scale studies are needed. However, it is noteworthy that if the final PoCUS exam is conducted prior to discharge in patients with AHF, it influences mortality and readmission rates.^{23 24}

The diagnostic accuracy of PoCUS was not significantly higher in the serial PoCUS group, presumably because an initial PoCUS was done in both groups. Still, the number of differential diagnoses was lower in the serial PoCUS group indicating that PoCUS might help the clinician to refine and narrow the diagnostic possibilities. However, we observed a lower overall agreement rate of 64% in our study compared with higher agreement rates of 79%–88% reported in comparable studies.⁵ ²² This discrepancy could be attributed to differences in the audit process. In our study, we used the final ED diagnosis made by the treating investigator, whereas the other studies relied on the final diagnosis recorded in the medical journal.

Two smaller studies limited to patients with AHF have found a correlation between B-lines and RR or VDS.²⁵ ²⁶ Although this intuitively makes sense, we found no correlation between

Secondary outcomes in serial ultrasound and the control group								
	Serial ultrasound group (n=102)		Control group (n=104)		Risk difference (95% CI)	P value		
Length of hospital stay, days	4	(1–7)	3	(0–6)	3.9 (–9.8 to 17.5)	0.58		
Readmissions								
0–7 days	15	(14.7)	10	(9.6)	5.1 (-3.8 to 14.0)	0.26		
8–30 days	15	(14.7)	7	(6.7)	8.0 (-0.4 to 16.4)	0.06		
In-hospital mortality	4	(3.9)	4	(3.8)	0.1 (-5.2 to 5.4)	0.98		
Mortality								
0–7 days	2	(2.0)	3	(2.9)	-0.9 (-5.1 to 3.3)	0.67		
8–30 days	2	(2.0)	2	(1.9)	0.0 (-3.7 to 3.8)	0.98		
No. of correct final ED diagnoses	64	(62.7)	59	(56.7)	6.0 (-7.4 to 19.4)	0.38		
Data are n (%) or median (IQR).								

the number of B-lines or IVC-CI and vital signs or VDS, so the patients' vital signs and clinical status do not necessarily mirror the dynamic parameters on the PoCUS or in VDS. This means that the clinician cannot solely rely on the vital signs to determine whom to re-scan.

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ED physicians could incorporate serial PoCUS when handling patients with dyspnoea, especially patients suspected of fluid accumulations in the lungs. These patients could be identified upfront with PoCUS as part of a standard clinical evaluation. However, as the minimally clinically important difference for VDS is 1, which was achieved at the 2-hour evaluation, our trial suggests that only one extra PoCUS could be sufficient. Because only B-lines and not IVC change in the first couple of hours in the ED, the second PoCUS might be limited to a LUS. Although serial PoCUS is more time-consuming, the patients are, on the other hand, stabilised faster, thereby potentially resulting in early disposition.

Limitations

First, most patients were recruited only in one ED and by two investigators when they were present, which could influence external validity. However, baseline characteristics were similar to other comparable studies.^{2 27 28} Second, despite baseline characteristic imbalances with a higher proportion of patients with a history of heart failure in the serial ultrasound group, this should not influence the primary outcome because treatment decisions were based on the presumptive diagnoses, and the final ED diagnosis of AHF was similar in both groups. Third, we did not implement a precise algorithm for changes in the ultrasound parameters (B-line count and IVC-CI) that should trigger a specific treatment as it would have been too complex and does not reflect the reality and the setting where the emergency physician works. Fourth, the investigator and patients were not blinded to the intervention; hence an 'ultrasound assessment placebo effect' might have influenced the primary outcome in the serial PoCUS group because of the intervention itself and the more time spent on the patient. Still, randomisation was carried out before the first evaluation of the patients to avoid selection bias, and all patients had a PoCUS done despite allocation. The patients in the control group were also exposed to clinical judgement and subsequent treatment by the same investigator at matching time points as in the serial ultrasound group. Most importantly, the outcome assessors were blinded. Fifth, patients unable to consent were excluded which could introduce selection bias. But, with the chosen primary outcome, it was a prerequisite that the patients were mentally cable of assessing their dyspnoea on VDS, and another study from Denmark has shown that the

most acute patients constituted only approximately 6% of all patients with dyspnoea.²⁹

CONCLUSION

Our study establishes that serial cardiopulmonary PoCUS serves as an effective treatment guide for patients with dyspnoea, offering valuable support alongside standard care to alleviate the discomfort linked to dyspnoea. Notably, the observed impact is predominantly found in patients with AHF. These findings endorse the use of serial cardiopulmonary PoCUS as a beneficial tool in managing dyspnoea, with particular attention to patients with AHF.

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REFERENCES

- 1 Raven W, van den Hoven EMP, Gaakeer MI, et al. The association between presenting complaints and clinical outcomes in emergency department patients of different age categories. Eur J Emerg Med 2022;29:33–41.
- 2 Kelly AM, Keijzers G, Klim S, *et al*. An observational study of dyspnea in emergency departments: the Asia, Australia, and New Zealand dyspnea in emergency departments study (AANZDEM). *Acad Emerg Med* 2017;24:328–36.
- 3 Stoeckel MC, Esser RW, Gamer M, et al. Dyspnea catastrophizing and neural activations during the anticipation and perception of Dyspnea. *Psychophysiology* 2018;55.
- 4 Lindskou TA, Pilgaard L, Søvsø MB, et al. Symptom, diagnosis and mortality among respiratory emergency medical service patients. PLoS ONE 2019;14:e0213145.
- 5 Laursen CB, Sloth E, Lassen AT, et al. Point-of-care ultrasonography in patients admitted with respiratory symptoms: a single-blind, randomised controlled trial. Lancet Respir Med 2014;2:638–46.

- 6 Arvig MD, Laursen CB, Jacobsen N, et al. Monitoring patients with acute dyspnea with serial point-of-care ultrasound of the inferior vena cava (IVC) and the lungs (LUS): a systematic review. J Ultrasound 2022;25:547–61.
- 7 Dietrich CF, Mathis G, Blaivas M, et al. Lung B-line artefacts and their use. J Thorac Dis 2016;8:1356–65.
- 8 Moher D, Hopewell S, Schulz KF, et al. CONSORT 2010 explanation and elaboration: updated guidelines for reporting parallel group randomised trials. BMJ 2010;340:c869.
- 9 Zwarenstein M, Treweek S, Gagnier JJ, et al. Improving the reporting of pragmatic trials: an extension of the CONSORT statement. BMJ 2008;337:a2390.
- 10 Arvig MD, Lassen AT, Gæde PH, et al. Monitoring patients with acute dyspnoea with a serial focused ultrasound of the heart and the lungs (MODUS): a protocol for a multicentre, randomised, open-label, pragmatic and controlled trial. BMJ Open 2020;10:e034373.
- 11 Sealed Envelope. Create a blocked randomisation list. Available: https://www. sealedenvelope.com/simple-randomiser/v1/lists [Accessed 11 Feb 2022].
- 12 Laursen CB, Nielsen K, Riishede M, et al. A framework for implementation, education, research and clinical use of ultrasound in emergency departments by the Danish society for emergency medicine. Scand J Trauma Resusc Emerg Med 2014;22:25.
- 13 Via G, Hussain A, Wells M, et al. International evidence-based recommendations for focused cardiac ultrasound. J Am Soc Echocardiogr 2014;27:683.
- 14 Volpicelli G, Elbarbary M, Blaivas M, et al. International evidence-based recommendations for point-of-care lung ultrasound. Intensive Care Med 2012;38:577–91.
- 15 Saracino A, Weiland T, Dent A, et al. Validation of a verbal dyspnoea rating scale in the emergency department. *Emerg Med Australas* 2008;20:475–81.
- 16 Saracino A, Weiland TJ, Jolly B, et al. Verbal dyspnoea score predicts emergency department departure status in patients with shortness of breath. Emerg Med Australas 2010;22:21–9.
- 17 Bujang MA, Baharum N. Guidelines of the minimum sample size requirements for Kappa agreement test. *Ebph* 2017;14.
- 18 RANDOM.ORG. True random number service. Available: https://www.random.org/ [Accessed 11 Jan 2022].
- 19 Pietersen PI, Mikkelsen S, Lassen AT, et al. Quality of focused thoracic ultrasound performed by emergency medical technicians and paramedics in a prehospital setting: a feasibility study. Scand J Trauma Resusc Emerg Med 2021;29:40.
- 20 Pang PS, Lane KA, Tavares M, *et al*. Is there a clinically meaningful difference in patient reported dyspnea in acute heart failure? An analysis from URGENT dyspnea. *Heart & Lung* 2017;46:300–7.
- 21 Placido R, Gigaud C, Gayat E, et al. Assessment of dyspnoea in the emergency department by numeric and visual scales: a pilot study. Anaesth Crit Care Pain Med 2015;34:95–9.
- 22 Riishede M, Lassen AT, Baatrup G, et al. Point-of-care ultrasound of the heart and lungs in patients with respiratory failure: a pragmatic randomized controlled multicenter trial. Scand J Trauma Resusc Emerg Med 2021;29:60.
- 23 Platz E, Merz AA, Jhund PS, et al. Dynamic changes and prognostic value of pulmonary congestion by lung ultrasound in acute and chronic heart failure: a systematic review. *Eur J Heart Fail* 2017;19:1154–63.
- 24 Dubón-Peralta EE, Lorenzo-Villalba N, García-Klepzig JL, et al. Prognostic value of B lines detected with lung ultrasound in acute heart failure. A systematic review. J Clin Ultrasound 2022;50:273–83.
- 25 Martindale JL, Secko M, Kilpatrick JF, et al. Serial sonographic assessment of pulmonary edema in patients with hypertensive acute heart failure. J Ultrasound Med 2018;37:337–45.
- 26 Palazzuoli A, Ruocco G, Beltrami M, *et al*. Combined use of lung ultrasound, B-type natriuretic peptide, and echocardiography for outcome prediction in patients with acute HFrEF and HFpEF. *Clin Res Cardiol* 2018;107:586–96.
- 27 Beyer A, Lam V, Fagel B, et al. Undifferentiated dyspnea with point-of-care ultrasound, primary emergency physician compared with a dedicated emergency department ultrasound team. J Emerg Med 2021;61:278–92.
- 28 Stevens JP, Dechen T, Schwartzstein R, *et al.* Prevalence of dyspnea among hospitalized patients at the time of admission. *J Pain Symptom Manage* 2018;56:15–22.
- 29 Arvig MD, Mogensen CB, Skjøt-Arkil H, et al. Chief complaints, underlying diagnoses, and mortality in adult, non-trauma emergency department visits: a population-based, multicenter cohort study. West J Emerg Med 2022;23:855–63.