



● *Original Contribution*

EARLY POINT-OF-CARE ULTRASOUND ASSESSMENT FOR MEDICAL PATIENTS REDUCES TIME TO APPROPRIATE TREATMENT: A PILOT RANDOMIZED CONTROLLED TRIAL

Yael Ben-Baruch Golan,^{*} Re'em Sadeh,^{†,§} Yuval Mizrakli,^{†,§} Tali Shafat,^{*,†} Iftach Sagy,^{*,†} Tzachi Slutsky,^{†,¶} Sergio L. Kobal,^{†,||} Victor Novack,^{*,†,§} and Lior Fuchs^{*,†}

^{*} Internal Medicine Division, Soroka University Medical Center, Beer-Sheva, Israel; [†] Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer-Sheva, Israel; [§] Clinical Research Center, Soroka University Medical Center, Beer-Sheva, Israel; [¶] Emergency Department, Soroka University Medical Center, Beer-Sheva, Israel; and ^{||} Cardiology Department, Soroka University Medical Center, Beer-Sheva, Israel

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Abstract—Numerous studies emphasize the diagnostic importance of point-of-care ultrasound (POCUS), but the level of evidence remains low as most data are gathered from observational studies. We conducted a pilot, randomized controlled trial to evaluate the effect of POCUS exam on medical patient's management and clinical outcomes. Patients presenting with chest pain or dyspnea were enrolled and randomly allocated to an early POCUS scan group and a control group. POCUS assessment, within 24 h of internal ward admission, was conducted only for the intervention group. The primary outcome was time to correct diagnosis. Secondary outcomes included time to appropriate treatment, POCUS-related rate of primary diagnosis alteration and new clinically relevant findings and time to hospital discharge. Sixty patients were enrolled. Thirty patients were randomly allocated to each study arm. The POCUS exam revealed clinically relevant findings among 79% of patients and led to alteration of the primary diagnosis among 28% of patients. Time to appropriate treatment was significantly shorter among patients in the POCUS group compared with the control group (median time of 5 h [95% confidence interval: 0.5–9] vs. 24 h [95% CI: 19–29] $p=0.014$). The time needed to achieve correct diagnosis by the primary team was shorter in the POCUS group compared with the control group, yet it did not reach statistical significance (median time of 24 h [95% CI: 18–30] vs. 48 h [95% CI: 20–76], $p=0.12$). These results indicate that POCUS assessment conducted early among patients with dyspnea or chest pain improves diagnostic accuracy and shortens significantly the time to appropriate treatment. (E-mail: golany860@gmail.com) © 2020 World Federation for Ultrasound in Medicine & Biology. All rights reserved.

Key Words: Point-of-care ultrasound, Internal medicine, Clinical management, Chest pain, Dyspnea.

INTRODUCTION

Point-of-care ultrasound (POCUS) is a rapidly evolving concept in which portable ultrasonography is used in a focused manner at the patient's bedside, thus providing information that is immediately integrated into clinical assessment and patient management (Spencer et al. 2001; Kobal et al. 2004; Moore and Copel 2011; Narasimhan et al. 2016).

Because of its applicability to a wide range of specific pathologies, POCUS has proven to be an effective tool that narrows differential diagnosis among patients presenting with chest pain and dyspnea (Laursen et al.

2013; Al Deeb et al. 2014; Pivetta et al. 2015; Lamsam et al. 2018; Buhumaid et al. 2019), helping to achieve the correct diagnosis faster (Laursen et al. 2014). Similar results were obtained in patients presenting to the emergency department (ED) with hypotension where POCUS assessment reduced diagnostic uncertainty and affected acute medical management (Shokoohi et al. 2015).

Although POCUS has been found to be effective in the diagnostic evaluation of patients, the level of evidence, originating primarily from observational studies, remains low (Moore 2015). A literature search revealed no previous prospective randomized control studies that measured the effect of POCUS assessment on management and clinical outcomes of medical patients.

Therefore, in this pilot, randomized controlled trial we sought to evaluate the effect of POCUS exam

Address correspondence to: Yael Ben Baruch Golan, Soroka University Medical Center POB 151, Beer-Sheva, Israel. E-mail: golany860@gmail.com

integrated early into the evaluation of medical patients admitted to the internal medicine ward.

METHODS

Setting and study population

This study was designed as a pilot, single-center, prospective, randomized controlled trial, performed at Soroka University Medical Center, a 1200-bed university-affiliated referral center in southern Israel, serving a population of nearly 1 million people. During the study year (2015–2017), POCUS capabilities were not prevalent in the medical center. Patients were not routinely assessed with this modality either in the ED or in the internal wards.

Patient enrollment took place between August 2015 and November 2017 at seven different general internal medicine wards, each containing 38–46 admission beds.

The study was approved by the hospital ethics research committee. The clinical trials registration number is NCT02436317. All patients provided written informed consent before random allocation to groups.

Patients aged ≥ 18 y were included if they were admitted to the internal ward for a respiratory or cardiovascular abnormality. Respiratory abnormality was defined if a patient was diagnosed with dyspnea, respiratory rate >22 breaths/min, any measured oxygen saturation $<90\%$ or new requirement for oxygen or non-invasive ventilation on internal ward admission. Cardiovascular abnormality was defined if the patient's primary complaint was chest pain or if the patient suffered from new or worsening peripheral edema or newly diagnosed electrocardiogram changes. Patients were excluded if they were admitted to the general internal medicine ward in the last 6 mo, had advanced end-stage cancer or were under palliative care, had an echocardiographic or POCUS study from the time of their admission to enrollment or were treated by a physician with POCUS capabilities. Research group members were not involved in the management of the enrolled patients before or after enrollment.

Patient assessment, screening and randomization

All patients included in the study completed a routine primary assessment conducted by ED physicians and by their internal ward physicians, all before POCUS assessment. This included medical history, physical examination, initial laboratory tests, electrocardiogram recording and other imaging studies, all according to standard medical assessment and by physicians' request. None of the patients received POCUS assessment before enrollment to the study.

Patients were screened for eligibility for the study within 24 h from hospital arrival. Eligible patients were enrolled and randomly allocated to the POCUS group or the control group. A computer-generated balanced successive block randomization (random block size 2–6)

was created using the WinPepi Etcetera Module, Version 3.26. Sealed envelopes were created for each participant before enrollment.

Point of care ultrasound assessment and reporting

Patients randomly allocated to the POCUS group underwent bedside focused sonographic assessment of the heart, lungs and inferior vena cava within 1 h from randomization and within 24 h from ward admission. The exam was conducted by L.F. and Y.B.B.G., after the primary team's first patient assessment. Both operators were qualified in focused sonography with practical experience >2 y and had performed more than 200 lung and cardiac focused ultrasound studies. All cardiac images were reviewed by author LF, who is certified by the American National Board of Echocardiography.

The exam was done according to our local point-of-care ultrasonography protocol (Supplementary Data, Appendix A, online only), which is based on accepted international POCUS guidelines (Mjølstad et al. 2012; Andersen et al. 2015). In short, the protocol includes (i) cardiac assessment using standard transthoracic echocardiography and inferior vena cava views evaluating ventricular and valvular function and abnormalities, volume status and presence of pericardial fluid; (ii) lung and pleural space assessment searching for B-lines, pleural effusion or signs of atelectasis or lung consolidation; and (iii) screening for peritoneal fluid.

Two ultrasound machines were used: a GE Vivid S70 D (GE Healthcare, Horten, Norway) with a Cardiac Sector Probe M5 Sc (active-matrix single-crystal phased-array probe) for the majority of cases and an Esaote MyLab 5 (Esaote, Naples, Italy) with cardiac phased-array probe PA121 for the remainder. Transthoracic echocardiography views were used with both 2-D and color Doppler imaging modalities for the examination.

The POCUS operators were not part of the internal ward medical team that took care of the patient and were blinded to the patients' management plan. During the study year, there were scarce POCUS capabilities among internal ward physicians in this medical center, enabling recruitment of patients naïve to early POCUS assessment.

On completion of the POCUS exam, a full report was completed and handed to the primary physician in the admitting internal ward. The same report was added to the patients' notes in the electronic medical record, visible to all teams caring for the patient. No diagnostic or treatment recommendations were given by the research team. Primary team exposure to the POCUS report was the only variable differing between the two study arms.

Patient data collection and expert review of files

After 1 y from enrollment, the following data were recorded with appropriate time stamp: baseline patient

characteristics, primary and final diagnosis given by the treating team, POCUS findings and diagnoses, imaging and diagnostic modalities used after enrollment, length of hospital stay (in hours), re-admission rate and mortality rates in 1 y.

Our two primary outcomes were time needed to achieve a correct primary diagnosis and time to appropriate treatment given to patients in both study arms. For this purpose, two independent, senior internal medicine experts, with >3 y of cardiac and lung POCUS qualification and experience, separately reviewed patients' medical records (including imaging modalities, consults and labs). The reviewers did not take part in research design or data collection and did not participate in the POCUS evaluation of the patients in the study.

On the basis of all available data, the reviewers' objectives were to determine the time when correct primary diagnosis could be achieved and the time it was achieved by the primary team (if it was achieved). Then, reviewers determined the exact time appropriate treatment was given (if such treatment was given).

Reviewers had to measure the rate of previously unknown, clinically relevant findings obtained with the POCUS scan. Clinically relevant findings were defined

as findings that may have potentially resulted in change of management or diagnostic measures. These findings are listed (under "conclusions") at the end of the POCUS exam report that was handed to the primary team (Supplementary Data, Appendix A, online only).

In cases where the reviewers disagreed, a third independent reviewer supported the decision of one of the evaluators or stated that the case was not clear. Rates of disagreement were documented.

Statistical analysis

Data are expressed as the mean \pm standard deviation, median and interquartile range or count and percentage. Continuous variables who met parametric test assumptions were compared with Student's *t*-test. For continuous variables with a non-normal distribution and for ordinal variables, comparisons were evaluated for significance with the use of the Mann–Whitney *U*-test. Categorical variables were compared using Pearson's χ^2 -test or Fisher's exact test, when appropriate. Time from admission to the reviewer's view of correct diagnosis and time to appropriate treatment were compared between the groups using the Kaplan–Meier method. The log rank test was used to assess the significance of

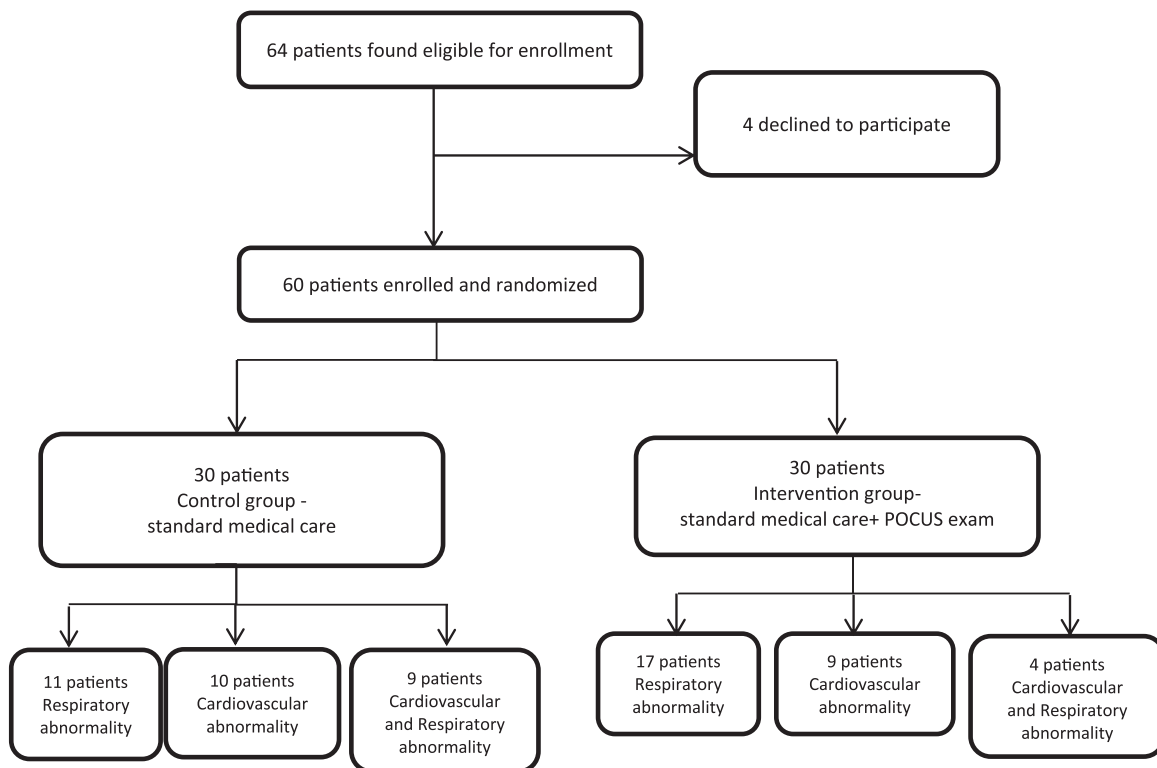


Fig. 1. Trial profile. Flow diagram of patient enrollment and randomization.

the difference in survival. Variables were considered significant at $p < 0.05$. Data were analyzed using SPSS Version 25 (IBM Corp., Armonk, NY, USA).

This was a pilot trial aimed at providing a better understanding of the study population and study groups. Therefore, the study comprised a total of 60 patients, 30 patients in the intervention group and an equal number in the control group. The results of this pilot trial can be used to design a larger clinical trial and to enable us to calculate the required sample size.

RESULTS

Study population

A total of 64 patients met inclusion criteria; 60 were included in the final analysis, and 30 patients were enrolled in each study arm. Only 4 patients declined to participate (Fig. 1).

The patients' baseline characteristics are outlined in Table 1. There were no significant differences between the two study groups with respect to age, sex, medical history and initial primary diagnosis. The mean age was 67.8 ± 15.3 y in both groups. There were 68% males, and hypertension was the most prevalent chronic disease among patients in both groups. Patients enrolled had chief complaints of chest pain (33%), dyspnea (45%) or both (22%).

Table 1. Background characteristics of study population

Group	POCUS (n = 30)	Control (n = 30)	p Value
Age (y)	69.8 ± 14.5	65.7 ± 16.0	0.521
Female sex	10 (33.3%)	9 (30.0%)	1.0
Medical history			
Chronic obstructive pulmonary disease/asthma	7 (23.3%)	7 (23.3%)	1.0
Ischemic heart disease	11 (36.7%)	13 (43.3%)	0.598
Congestive heart failure	11 (36.7%)	9 (30.0%)	0.584
Hypertension	23 (76.7%)	21 (70.0%)	0.559
Cerebrovascular accident	5 (16.7%)	4 (13.3%)	1.0
Diabetes mellitus	14 (46.7%)	16 (53.3%)	0.606
Chronic kidney disease	9 (30.0%)	4 (13.3%)	0.117
Malignancy	3 (10.0%)	5 (16.7%)	0.706
Enrollment criteria			
Dyspnea	17 (56.7%)	11 (36.6%)	0.151
Chest pain	9 (30.0%)	10 (34.5%)	
Both	4 (13.3%)	9 (31.0%)	
Primary diagnosis by treating physician*			
Chronic obstructive pulmonary disease/asthma	4 (13.3%)	1 (3.3%)	0.353
Chest pain	8 (26.7%)	12 (40.0%)	0.273
Acute coronary syndrome	1 (3.3%)	3 (10.0%)	0.612
Congestive heart failure/pulmonary congestion	7 (23.3%)	7 (23.3%)	1.0
Other respiratory diagnosis	10 (33.3%)	11 (36.7%)	0.787
Other	2 (6.7%)	0 (0.0%)	0.492

POCUS = point-of-care ultrasound.

* Primary diagnosis given by treating physician before point-of-care ultrasound study.

Table 2. Point-of-care ultrasound findings*

Finding	POCUS group (n = 30)	
	Any findings	Previously unknown findings
Left ventricle dysfunction	5 (16.7%)	3 (10.0%)
Left ventricle hypertrophy	3 (10.0%)	1 (3.3%)
Elevated central venous pressure	4 (13.3%)	2 (6.7%)
Hypovolemia	1 (3.3%)	1 (3.3%)
Hyperdynamic heart	2 (6.7%)	1 (3.3%)
Valvulopathy	9 (30%)	5 (16.7%)
Moderate-size pleural effusion	5 (16.7%)	4 (13.3%)
Intraperitoneal fluid	1 (3.3%)	0 (0%)
Lung edema	4 (13.3%)	3 (10.0%)

* The scan was normal in five patients (16.7%). POCUS = point-of-care ultrasound.

POCUS findings and effect on diagnosis and management

Mean time from hospital admission to POCUS scan was 12 h, and all scans were completed within 24 h of hospital admission.

Overall, 22 of 30 patients had abnormal POCUS findings, which are detailed in Table 2. POCUS evaluation revealed left ventricle dysfunction among 16%, valvulopathy among 30% and lung edema among 13% of patients (Table 2).

As interpreted by the reviewers and outlined in Table 3, previously unknown clinically relevant findings were detected by POCUS exam among 79% of cases and POCUS findings that led to an additional diagnosis or alteration of previous diagnosis were obtained among 13.8% and 27.6% of patients, respectively. The added information from POCUS evaluation, as perceived by the reviewers, altered patient management in about a third of cases, by changing the treatment they received

Table 3. Point-of-care ultrasound effect on diagnosis and management in POCUS group (n = 30)

Did the exam provide new information?	
No	5 (17.2%)
Yes. New information WAS NOT clinically relevant to current admission	1 (3.4%)
Yes. New information WAS clinically relevant to current admission.	22 (75.9%)
Yes. New crucial information relevant for a life-threatening diagnosis	1 (3.4%)
Did the exam affect the primary diagnosis?	
No change	6 (20.7%)
Confirmation of the primary diagnosis	11 (37.9%)
Addition of another diagnosis	4 (13.8%)
Alteration of the primary diagnosis	8 (27.6%)
Did the exam alter management by:	
Medications	9 (31.0%)
Imaging studies	10 (34.5%)
Time of discharge	10 (34.5%)

POCUS = point-of-care ultrasound.

Table 4. Clinical case examples in which POCUS evaluation altered diagnosis and management

Clinical diagnosis	Ultrasound findings	Impact on management
77-y-old man with a history of chronic ischemic heart disease admitted with dyspnea: Team could not decide between a respiratory tract infection or pulmonary congestion	Normal scan revealed no signs of pulmonary congestion and a normal ventricular function	Diuretics were stopped; a formal echo that was ordered was canceled; patient was discharged earlier
68-y-old woman with cardiovascular risk factors admitted for chest pain: Initial diagnosis was unstable angina	Normal heart scan; no regional wall hypokinesis	In this case there was no effect on management; the patient underwent PCI—normal coronary arteries were imaged
83-y-old woman with restrictive lung disease and hypertension admitted for dyspnea: Diuretics were prescribed for suspected pulmonary congestion	Mild LVH, mild AR, normal left ventricular function, no signs of pulmonary congestion or pleural effusion	Diuretic dosage was decreased significantly; chronic lung disease was diagnosed as reason for dyspnea; and patient was discharged earlier
79-y-old man with history of ischemic heart disease and multiple cardiovascular risk factors admitted for pulmonary congestion	Significant AS; severe LVH with normal ventricular function; bilateral moderate-sized pleural effusion	A formal echo was ordered confirming severe AS
87-y-old man with medical history of heavy smoking and multiple cardiovascular risk factors, admitted for dyspnea and cough: Team considered chronic lung disease exacerbation or pulmonary congestion	Mild LVH with segmental inferolateral hypokinesis, signs of pulmonary congestion—B-lines and moderate-sized pleural effusion, high CVP	Treatment for CHF was tailored and coronary ischemia was investigated
82-y-old man, smoker, CVS risk factors, admitted for chest pain and dyspnea with rapid atrial fibrillation	Overt signs of pulmonary congestion and heart failure: multiple B-lines, high CVP and large right pleural effusion	Treatment for CHF was tailored and diuretics were initiated
67-y-old man, smoker, with history of ischemic heart disease and CVS risk factors. Admitted owing to dyspnea, initial diagnosis was pulmonary congestion	Normal heart and lung scan	Diuretics were stopped; patient underwent pulmonary focused evaluation—HRCT, pulmonary function tests; diagnosis was changed to COPD exacerbation and he received steroids and bronchodilators
37-y-old man with a medical history consistent with pericarditis 1 y before admission, admitted for chest pain with suspected recurrent pericarditis versus pleurisy	Normal heart and lung scan with no pericardial or pleural effusion	Patient was discharged earlier with recommendation for peptic ulcer disease workup
72-y-old man with a medical history consistent with COPD, CIHD, moderate AS, admitted for dyspnea initially diagnosed as COPD exacerbation	Severe AS, severe LVH with normal ventricular function; no pulmonary congestion	Cardiac consult was ordered; patient was evaluated for severe AS

AR = aortic regurgitation; AS = aortic stenosis; CHF = congestive heart failure; CIHD = chronic ischemic heart disease; COPD = chronic obstructive pulmonary disease; CVP = central venous pressure; CVS = cardiovascular system; HRCT = high-resolution computed tomography; LVH = left ventricular hypertrophy; PCI = percutaneous coronary intervention; POCUS = point-of-care ultrasound.

(31%) or the imaging studies they underwent (34%) or by influencing time to their discharge from the hospital (34.5%).

In Table 4, we describe 9 clinical cases that emphasize POCUS exam-related alterations of primary diagnosis and management. In 5 patients, different and more appropriate treatment was given, and in 3 patients, other studies were cancelled, leading to early discharge.

POCUS effect on clinical outcomes

Equal rates of correct diagnosis were achieved by the primary team in both study arms (80.0% vs. 73.3%, $p = 0.543$, intervention group vs. control group, respectively) (Supplementary Data, Appendix B, Table B.1, online only). Survival analysis revealed that time needed to achieve a correct diagnosis (as determined by the reviewers) was shorter in the POCUS group than the control group (median time = 24 h [95% confidence interval: 18–30 h] vs. 48 h [20–76 h], $p = 0.12$; Fig. 2), but it did not reach statistical significance.

A higher percentage of patients received appropriate treatment in the POCUS group compared with the control group (83.3% vs. 63.3%, $p = 0.08$; Supplementary Data, Appendix B, Table B.1, online only). Time to appropriate treatment was about 20 h shorter among patients who underwent early POCUS scan as opposed to patients in the control group (median time of 5 h [95% confidence interval: 0.5–9 h] vs. 24 h [19–29 h], $p = 0.014$) (Fig. 3).

Fewer patients post-POCUS scan were sent for chest X-ray compared with control group patients (16.7% vs. 36.7% respectively, p value = 0.08). Hospital length of stay was not different between the two study arms as were re-hospitalization rate in 30 d and mortality rate in 1 y (Supplementary Data, Appendix B, Table B.1, online only).

In 90 of 330 (27%) reviewed items (Supplementary Data, Appendix B, online only) there were disagreements between the reviewers. In all of these cases, the third reviewer approved the decision of one of the two reviewers.

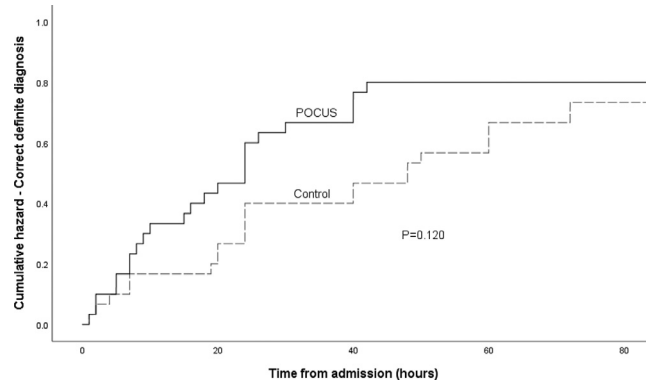


Fig. 2. Time from admission to correct diagnosis. Kaplan–Meier cumulative hazard curves for time to correct diagnosis for the point of care ultrasound (POCUS) group versus control.

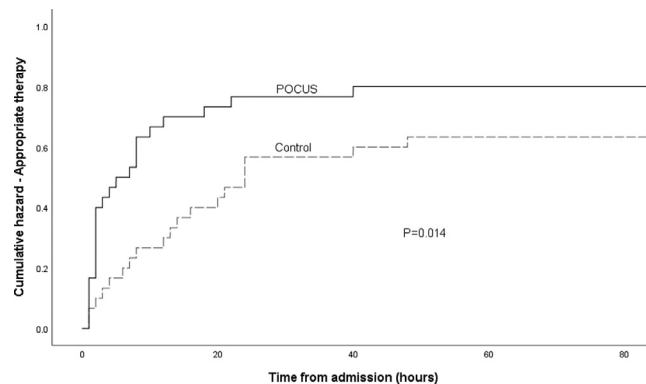


Fig. 3. Time from admission to appropriate treatment. Kaplan–Meier cumulative hazard curves for time to appropriate treatment for the point-of-care ultrasound (POCUS) group versus control.

DISCUSSION

The presented study, to the best of our knowledge, is the first randomized controlled trial to investigate the effect of early POCUS assessment on diagnosis, management and clinical outcomes among patients admitted to a general internal medicine ward with chest pain or dyspnea. Early POCUS assessment was the only different intervention between the study groups.

We have found that POCUS assessment, integrated early into the routine care of these patients, led to significantly shorter times to appropriate treatment. The median time to appropriate treatment was shortened by 19 h in patients who underwent a POCUS scan compared with those who did not. This time gap may have a significant effect on patient outcomes, as was described previously among patients with acute decompensated heart failure (Maisel et al. 2008) and chronic obstructive pulmonary disease exacerbations (Wilkinson et al. 2004).

Trends toward reduction of time to correct diagnosis and higher rate of appropriate therapy were apparent in patients in the POCUS group versus control group, yet

these findings did not reach statistical significance, probably because of the small sample size in our study.

We assume that the earlier appropriate treatment received by the POCUS group is responsible for the shorter time to correct diagnosis that was measured in the POCUS group compared with the control group.

These results reinforce the findings from another large observational study conducted by Zanobetti et al. (2017), which reported a shorter time to diagnosis among dyspneic patients when evaluated by POCUS compared with those not evaluated by POCUS at the time of diagnosis. We add to the current available literature by providing evidence, derived from randomized controlled trial, of a direct effect of POCUS on time to appropriate therapy.

Early POCUS exams led to the discovery of new or clinically relevant findings among 79% of the patients. Furthermore, a change in the final diagnosis occurred in 27% of the patients, and an additional diagnosis was given for 14% of patients. Previous studies described the effect of POCUS assessment on diagnostic accuracy (Mjølstad et al. 2012; Laursen et al. 2014; Andersen

et al. 2015) with different rates of diagnosis alteration (19%–24%), probably because of the different experience of the POCUS operators (Bobbia *et al.* 2015). All of these studies were not designed to show effect on treatment. We have found, beyond the diagnostic benefit, a management change in about a third of intervention group patients (Table 3).

Our present, small-sample pilot study, which enrolled patients with very short total admission times, failed to detect an impact of POCUS assessment on hospital length of stay, mortality or re-hospitalization rates. POCUS assessment may influence hospitalization time to both directions. Early diagnosis and treatment can shorten hospitalization time, but new pathologic findings may lead to further investigations that can prolong hospitalization.

A recent randomized controlled trial comparing the effects of POCUS combined with standard care as opposed to standard care alone in patients presenting to the ED with undifferentiated hypotension did not reveal a benefit in length of stay or survival (Atkinson *et al.* 2018). Other studies have reported that in heart failure patients, the presence of sonographic pulmonary B-lines as a sign of pulmonary congestion may be used as a monitor to guide diuretic therapy and reduce hospitalization time (Mozzini *et al.* 2018), as well as to predict re-hospitalization and mortality when evaluated at discharge (Gargani *et al.* 2015; Cogliati *et al.* 2016). One study found that POCUS utilization in critically ill patients can shorten duration of mechanical ventilation and length of stay in the intensive care unit (Chen *et al.* 2018). Yet, it is still unknown whether these results are applicable to the general and diverse medical patient populations.

We believe that earlier and correct diagnosis leads to earlier appropriate management, and should result in significant effects on prognosis and mortality. Therefore, larger randomized controlled trials should prove these assumptions.

Our study has limitations. First, as a pilot study, our research was done at a single center and on a relatively small number of patients. This could affect some of our results and their statistical significance as well as generalizability. Second, only two physicians conducted the POCUS assessments. Nevertheless, the fact that both were internal medicine physicians (neither cardiologists nor radiologists) proves that the use of POCUS as an effective diagnostic tool is feasible when used by a well-trained physician.

In this study, we chose to measure clinical outcomes such as correct diagnosis and treatment by assigning expert physicians in internal medicine to review patients' charts. We preferred this method over self-reporting of the treating physicians because we believe it

resulted in a more objective evaluation of the true effect of POCUS on the patient population. Nevertheless, some important limitations to our study are derived from this methodology. First, the reviewers were not explicitly blinded to the POCUS results. Second, the information on patients' charts may be subject to personal interpretation; therefore, disagreements were seen between the reviewers. We used a third reviewer to overcome this problem. Finally, there was no follow-up of patients after discharge to ensure the decisions made by the reviewers were correct.

Our study sample contained a larger number of patients admitted for dyspnea in the POCUS arm (56%) versus the control arm (36%). Although there was no statistical difference in patient characteristics between the two groups, it could have an effect on research outcomes in larger-sample studies.

The strength of our research relates to its design, as a randomized controlled trial, enrolling "real-world" internal medicine patients that represent the general medical population admitted. Because POCUS is becoming part of modern clinical assessment, such research, in which POCUS is not offered to half of the patients, is neither ethical nor feasible in many medical centers. In our medical center, at the time of the study, this modality was not utilized, enabling us to use such a design.

Another strength relates to the performance of the POCUS exam shortly after the first physician–patient encounter, augmenting the effect on management.

Finally, the novelty of this study relates to the focus of its primary outcome on clinical outcomes (time to treatment, change of management) and not on diagnostic values. a profoundly studied endpoint to date.

CONCLUSIONS

This is the first randomized controlled trial indicating that incorporation of the POCUS exam into the early diagnostic routine workup of patients admitted to the medical ward with chest pain or dyspnea reduces time to appropriate therapy. These results should be further investigated in larger prospective studies to strengthen the evidence that POCUS assessment affects clinical outcomes. Such findings will further expedite the integration of POCUS into the standard modern physical examination, especially in the setting of an internal medicine department.

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Conflict of interest disclosure—All authors report receiving a grant from General Electric Healthcare during the conduct of the study. L.F. reports personal fees from General Electric Healthcare—Point of Care

Ultrasound Division, outside the submitted work. V.N. reports personal fees from Cardiomed Consultants LLC, outside the submitted work.

SUPPLEMENTARY MATERIALS

Supplementary material associated with this article can be found in the online version at doi:[10.1016/j.ultrasmedbio.2020.03.023](https://doi.org/10.1016/j.ultrasmedbio.2020.03.023).

REFERENCES

- Al Deeb M, Barbic S, Featherstone R, Dankoff J, Barbic D. Point-of-care ultrasonography for the diagnosis of acute cardiogenic pulmonary edema in patients presenting with acute dyspnea: a systematic review and meta-analysis. *Acad Emerg Med* 2014;21:843–852.
- Andersen GN, Graven T, Skjetne K, Mjølstad OC, Kleinau JO, Olsen O, Haugen BO, Dalen H. Diagnostic influence of routine point-of-care pocket-size ultrasound examinations performed by medical residents. *J Ultrasound Med* 2015;34:627–636.
- Atkinson PR, Milne J, Diegelmann L, Lamprecht H, Stander M, Lussier D, Pham C, Henneberry R, Fraser JM, Howlett MK, Mekwan J, Ramrattan B, Middleton J, van Hoving DJ, Peach M, Taylor L, Dahn T, Hurley S, MacSween K, Richardson LR, Stoica G, Hunter S, Olszynski PA, Lewis DA. Does point-of-care ultrasonography improve clinical outcomes in emergency department patients with undifferentiated hypotension? An International Randomized Controlled Trial from the SHO-C-ED Investigators. *Ann Emerg Med* 2018;72:478–489.
- Bobbia X, Pradeilles C, Claret PG, Soullier C, Wagner P, Bodin Y, Roger C, Cayla G, Muller L, de La Coussaye JE. Does physician experience influence the interpretability of focused echocardiography images performed by a pocket device?. *Scand J Trauma Resusc Emerg Med* 2015;23:52.
- Buhmaid RE, Bourque JS-C, Shokoohi H, Ma IW, Longacre M, Liteplo AS. Integrating point-of-care ultrasound in the ED evaluation of patients presenting with chest pain and shortness of breath. *Am J Emerg Med* 2019;37:298–303.
- Chen Z, Hong Y, Dai J, Xing L. Incorporation of point-of-care ultrasound into morning round is associated with improvement in clinical outcomes in critically ill patients with sepsis. *J Clin Anesth* 2018;48:62–66.
- Cogliati C, Casazza G, Ceriani E, Torzillo D, Furlotti S, Bossi I, Vago T, Costantino G, Montano N. Lung ultrasound and short-term prognosis in heart failure patients. *Int J Cardiol* 2016;218:104–108.
- Gargani L, Pang PS, Frassi F, Miglioranza M, Dini F, Landi P, Picano E. Persistent pulmonary congestion before discharge predicts rehospitalization in heart failure: a lung ultrasound study. *Cardiovasc Ultrasound* 2015;13:40.
- Kobal SL, Atar S, Siegel RJ. Hand-carried ultrasound improves the bedside cardiovascular examination. *Chest* 2004;126:693–701.
- Lamsam L, Gharahbaghian L, Lobo V. Point-of-care ultrasonography for detecting the etiology of unexplained acute respiratory and chest complaints in the emergency department: A prospective analysis. *Cureus* 2018;10(8):e3218.
- Laursen CB, Sloth E, Lambrechtsen J, Lassen AT, Madsen PH, Henriksen DP, Davidsen JR, Rasmussen F. Focused sonography of the heart, lungs, and deep veins identifies missed life-threatening conditions in admitted patients with acute respiratory symptoms. *Chest* 2013;144:1868–1875.
- Laursen CB, Sloth E, Lassen AT, Christensen R, Lambrechtsen J, Madsen PH, Henriksen DP, Davidsen JR, Rasmussen F. Point-of-care ultrasonography in patients admitted with respiratory symptoms: a single-blind, randomised controlled trial. *Lancet Respir Med* 2014;2:638–646.
- Maisel AS, Peacock WF, McMullin N, Jessie R, Fonarow GC, Wynne J, Mills RM. Timing of immunoreactive B-type natriuretic peptide levels and treatment delay in acute decompensated heart failure: an ADHERE (Acute Decompensated Heart Failure National Registry) analysis. *J Am Coll Cardiol* 2008;52:534–540.
- Mjølstad OC, Dalen H, Graven T, Kleinau JO, Salvesen O, Haugen BO. Routinely adding ultrasound examinations by pocket-sized ultrasound devices improves inpatient diagnostics in a medical department. *Eur J Intern Med* 2012;23:185–191.
- Moore CL. Does ultrasound improve clinical outcomes?. *Prove it. Crit Care Med* 2015;43:2682–2683.
- Moore CL, Copel JA. Point-of-care ultrasonography. *N Engl J Med* 2011;364:749–757.
- Mozzini C, Di Dio Perna M, Pesce G, Garbin U, Fratta Pasini AM, Ticinesi A, Nouvenne A, Meschi T, Casadei A, Soresi M, Cominacini L. Lung ultrasound in internal medicine efficiently drives the management of patients with heart failure and speeds up the discharge time. *Intern Emerg Med* 2018;13:27–33.
- Narasimhan M, Koenig SJ, Mayo PH. A whole-body approach to point of care ultrasound. *Chest* 2016;150:772–776.
- Pivetta E, Goffi A, Lupia E, Tizzani M, Porrino G, Ferreri E, Volpicelli G, Balzaretto P, Banderali A, Iacobucci AJC, Locatelli S, Casoli G, Stone MB, Maule MM, Baldi I, Merletti F, Cibinel GA, Baron P, Battista S, Buonafede G, Busso V, Conterno A, Del Rizzo P, Ferrera P, Pecetto PF, Moiraghi C, Morello F, Steri F, Ciccone G, Calasso C, Caserta MA, Civita M, Condo C, D'Alessandro V, Del Colle S, Ferrero S, Griot G, Laurita E, Lazzeri A, Lo Curto F, Michelazzo M, Nicosia V, Palmari N, Ricchiardi A, Rolfo A, Ros-tagno R, Bar F, Boero E, Frascisco M, Micossi I, Mussa A, Stefanone V, Agricola R, Cordero G, Corradi F, Runzo C, Soragna A, Sciallo D, Vercillo D, Allione A, Artana N, Corsini F, Dutto L, Lauria G, Morgillo T, Tartaglino B, Bergandi D, Cassetta I, Masera C, Garrone M, Ghiselli G, Ausiello L, Barutta L, Bernardi E, Bono A, Forno D, Lamorte A, Lison D, Lorenzati B, Maggio E, Masi I, Maggiorotto M, Novelli G, Panero F, Perotto M, Ravazzoli M, Saglio E, Soardo F, Tizzani A, Tizzani P, Tullio M, Ulla M, Romagnoli E, SIMEU Group for Lung Ultrasound in the Emergency Department in Piedmont. Lung ultrasound-implemented diagnosis of acute decompensated heart failure in the ED. *Chest* 2015;148:202–210.
- Shokoohi H, Boniface KS, Pourmand A, Liu YT, Davison DL, Hawkins KD, Buhmaid RE, Salimian M, Yadav K. Bedside ultrasound reduces diagnostic uncertainty and guides resuscitation in patients with undifferentiated hypotension. *Crit Care Med* 2015;43:2562–2569.
- Spencer KT, Anderson AS, Bhargava A, Bales AC, Sorrentino M, Furlong K, Lang RM. Physician-performed point-of-care echocardiography using a laptop platform compared with physical examination in the cardiovascular patient. *J Am Coll Cardiol* 2001;37:2013–2018.
- Wilkinson TM, Donaldson GC, Hurst JR, Seemungal TA, Wedzicha JA. Early therapy improves outcomes of exacerbations of chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2004;169:1298–1303.
- Zanobetti M, Scorpiniti M, Gigli C, Nazerian P, Vanni S, Innocenti F, Stefanone VT, Savinelli C, Coppa A, Bigiarini S, Caldi F, Tassinari I, Conti A, Grifoni S, Pini R. Point-of-care ultrasonography for evaluation of acute dyspnea in the ED. *Chest* 2017;151:1295–1301.