Diagnosing Acute Heart Failure in Patients With Undifferentiated Dyspnea: A Lung and Cardiac Ultrasound (LuCUS) Protocol

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Abstract

Objective: The primary goal of this study was to determine accuracy for diagnosing acutely decompensated heart failure (ADHF) in the undifferentiated dyspneic ED patient using a Lung and Cardiac Ultrasound (LuCUS) protocol. Secondary objectives were to determine if ultrasound findings acutely change management and if findings are more accurate than clinical gestalt.

Methods: This was a prospective, observational study of adult patients presenting to the ED with undifferentiated dyspnea. Intervention consisted of a twelve-view LuCUS protocol performed by experienced emergency physician (EP) sonographers. The primary objective was measured by comparing ultrasound findings to final diagnosis independently determined by two blinded physicians. Acute treatment changes based on ultrasound findings were tracked in real time through a standardized data collection form.

Results: We analyzed data on 99 patients; 36% had a final diagnosis of ADHF. The overall sensitivity, specificity, positive and negative likelihood ratios of the LuCUS protocol were 83% (67-93 95% confidence interval [CI]), 83% (70-91 CI), 4.8 (2.7-8.3 CI) and 0.20 (0.09 – 0.42 CI), respectively. 47% of patients had changes in acute management, and 42% had changes in acute treatment. Observed agreement for the LuCUS protocol was 93% between coinvestigators. Overall, accuracy improved by 20% (83% vs 63%, 8-31 CI of the difference) over clinical gestalt alone.

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Conclusion: The LuCUS protocol may accurately identify ADHF and may acutely improve clinical management in dyspneic ED patients. This protocol has improved diagnostic accuracy over clinical gestalt alone.

INTRODUCTION

Dyspnea, one of the most common complaints evaluated in the emergency department (ED), has multiple and varied etiologies. In the United States, with five million people carrying a diagnosis of heart failure, and an additional 650 thousand diagnosed annually, patients with acute decompensated heart failure (ADHF) account for many of the presentations of acute dyspnea seen in EDs today.[1] Early diagnosis and goal-directed therapies are necessary for these patients in order to increase the efficacy and appropriateness of management, avoid unnecessary and potentially harmful interventions, as well as avoid delays in care. For example, the use of inhaled bronchodilators, in patients with undifferentiated dyspnea later found to have ADHF, is associated with worse outcomes.[2] Traditional work up for ADHF, using chest radiography and serum brain natriuretic peptide, is not always diagnostic or helpful in elucidating the cause of dyspnea and has an overall diagnostic accuracy of only 65%.[3-7]

Bedside ultrasonography may play a role in the management of patients with undifferentiated dyspnea by allowing early diagnosis of ADHF or by identifying alternative etiologies. Multiple prior studies have attempted to differentiate ADHF by using lung ultrasound alone to detect pulmonary edema, which appears as diffuse B-lines, also termed alveolar interstitial syndrome (AIS).[3,5,6,8-11] This finding on bedside ultrasound is highly sensitive for ADHF,[3,9-13] but lacks specificity as diffuse B-lines can be seen in a number of conditions including but not limited to, ADHF, non-cardiogenic pulmonary edema, bilateral pneumonia/pneumonitis, and lung cancer.[3,8,10,14]

Collapsibility and diameter variation with inspiration of the inferior vena cava (IVC) has been extensively studied independently of lung ultrasound.[1,15,16] Smaller variations in IVC diameter reflect elevated central venous pressure, a finding with a high sensitivity for detection of ADHF.[1] However, this finding also lacks specificity as

elevated central venous pressure can be seen in cardiac tamponade, pulmonary embolism, and valvular heart disease.[1]

Kajimoto et al were the first to assess lung, cardiac and IVC ultrasound to differentiate ADHF from other causes of dyspnea.[17] They found their scanning protocol to be highly sensitive and specific for diagnosing ADHF when performed by cardiology, and more accurate than lung ultrasound alone. Anderson et al later used a protocol similar to the Kajimoto study and found a specificity of 100% for diagnosing ADHF.[18] Our study is similar to these two prior studies in that we also used a scanning protocol, composed of lung, cardiac and IVC ultrasound, to diagnose ADHF. However, our study is the first to evaluate the direct impact of ultrasound findings on acute management of dyspneic patients. Also, we chose to evaluate for the presence of pleural effusions, the presence of diastolic cardiac dysfunction, and patients previously treated (within 30 minutes) for ADHF. We chose to include these additional elements in an effort to improve sensitivity for detecting ADHF and allow greater real world application.

The primary aim of this study was to determine the sensitivity, specificity and likelihood ratios for diagnosing ADHF in the undifferentiated dyspneic ED patient using a twelve-view Lung and Cardiac Ultrasound (LuCUS) protocol. Our secondary aims were to determine if ultrasound findings acutely change management and if these findings were more accurate then clinical gestalt alone. We hypothesize that the use of this diagnostic protocol will increase accuracy for diagnosing ADHF and acutely improve clinical management.

METHODS

Study Design and Setting

This was a prospective, observational study on the diagnostic performance of the LuCUS protocol to diagnose ADHF in ED patients with undifferentiated dyspnea. This study was conducted at an urban tertiary-care teaching hospital with over 120,000 annual ED visits and was approved by the Institutional Review Board.

Study Population

We enrolled a convenience sample of patients meeting the inclusion criteria: adult patients over 18-years-old and a primary complaint of undifferentiated dyspnea according to their treating clinician. We defined undifferentiated dyspnea as at least two possible etiologies in the differential diagnosis, and this did not have to include ADHF as a potential diagnosis. An example of differentiated dyspnea would include a patient with known heart failure not compliant with medications or diet restrictions. We excluded patients in whom the treating clinician was confident in their diagnosis after initial assessment, patients with an EKG showing ST segment elevation myocardial infarction, patients treated for ADHF with nitroglycerin, diuresis or positive pressure ventilation greater than 30 minutes prior to ultrasound, patients refusing consent, or patients having been enrolled in the study at a prior ED visit. Both research assistants and physicians identified study candidates through a standardized screening process. Research assistants enrolled patients when a study sonographer was available, typically Monday through Friday 8 AM to 5 PM. Patients consented to participate prior to enrollment in the study.

Intervention and Data Collection

After initial history, physical exam, and 12 lead electrocardiogram, but prior to ultrasound, treating clinicians were asked by a research assistant to rank ten possible etiologies of dyspnea in order of their likelihood (Table 1). Clinicians only had to rank two possible etiologies, but could rank up to ten diagnoses, including 'other' where they could write in an alternative diagnosis not included on the list. Treating clinicians included board certified Emergency Medicine physicians, Emergency Medicine residents (levels PGY 1-4), and third year Internal Medicine residents.

The LuCUS protocol was performed and interpreted by three investigators; an Emergency Medicine ultrasound director and two Emergency Medicine ultrasound fellows. All sonographers had greater than 1,000 previously performed ultrasounds, including lung and cardiac exams. All investigators were required to scan 5 patients at the bedside under the direct supervision of the principle investigator to ensure a standardized method of acquiring and interpreting images. Sonographers also spent 4 hours reviewing left ventricular function in the echocardiography reading room under the direction of a board certified cardiologist.

Sonographers were blinded to the treating clinician's initial assessment, patients'

comorbidities, and the results of lab tests or imaging studies performed during the patients' ED encounter.

The LuCUS Protocol

Each sonographer conducted a two-part scanning protocol using a Mindray M7 ultrasound machine. Patients were in a position of comfort, semi-recumbent, and as close to 30 degrees of head-elevation as possible.

The lung portion of the LuCUS exam interrogated four anterior/lateral lung zones in each hemi-thorax with a curvilinear probe.[14] Sonographers recorded the number of B-lines seen between two ribs in each lung zone. Greater than three B-lines in a rib space was considered a "B-profile". An exam that had at least two zones, in each hemi-thorax, with a B-profile was considered positive for diffuse B-lines or AIS.[4,19]

The cardiac portion of the LuCUS exam consisted of the following views:
1. Subxiphoid view: examined IVC diameter and collapsibility during inspiration in the long axis. The IVC diameter was measured two centimeters caudal to the hepatic vein inlet[20], using M mode with the cursor placed perpendicular to the IVC. An IVC with a maximal diameter ≥2 cm and < 50% collapse was considered plethoric. An IVC with a maximal diameter ≤ 2 cm and > 50% collapse was considered collapsible. Intermediate was defined as an IVC that did not fit either criteria.
2. Parasternal long and short-axis views: left ventricular ejection fraction was estimated visually in the parasternal long-axis view by wall contraction and thickening[21,22]. Ejection fraction was confirmed in the parasternal short-axis view at the level of the papillary muscles.

Unique elements of the of the LuCUS exam

1. Assessed for the presence of a pleural effusion in the mid-axillary line in the Extended Focused Assessment with Sonography in Trauma (EFAST)[23] position bilaterally.

2. Assessed diastolic function, in the apical four-chamber cardiac view, by measuring the ratio of the peak trans-mitral inflow velocity (E) to the average of the septal and lateral mitral annular velocities (e'^{Avg})—E/e'^{Avg}—obtained using pulsed-wave and tissue Doppler imaging (TDI), respectively. Diastolic function was graded as normal, indeterminate, impaired (grade 1), pseudo-normal (grade 2) or restrictive (grade 3)[22,24-26]. Criteria for detecting and grading diastolic dysfunction were pre-defined and developed using the recommendations of the American Society for Echocardiography (REF) in conjunction with a cardiologist board-certified in echocardiography.

After LuCUS was completed, sonographers reported to the treating clinicians their leading diagnosis based on objective ultrasound findings. The treating clinician then re-ranked their differential diagnosis post-ultrasound on a standardized data collection form, eliminating any pathology no longer under consideration. They were also asked how the ultrasound findings would affect their management including changes in treatment, obtaining a new consult, admission to a different level of care, disposition, and overall confidence in their diagnosis. Ten percent of images were randomly selected for blind review by coinvestigators to assess the percentage of observed agreement. Approximately two-thirds of images were randomly selected for blind review by a cardiologist board-certified in echocardiography to assess inter-observer reliability for identifying and grading diastolic dysfunction.

Outcome Measures

Demographic information was collected including patient's age, gender and comorbidities. We also collected vital signs at presentation, admission diagnosis, cardiac biomarkers obtained in the ED and ED interventions. This information was abstracted by research assistants, trained in data abstraction according to recommendations from a previously published study.[27] Abstractors were blinded to ultrasound results and final discharge diagnosis.

ADHF was defined sonographically as a combination of the following findings:

1. A plethoric IVC *plus*
2. At least one B-profile bilaterally or any pleural effusion *plus*

3. Moderately to severely depressed left ventricular ejection fraction or grade 2 or 3 diastolic dysfunction.

For ultrasound findings suggesting alternative diagnoses like COPD/asthma, pneumonia, non-cardiogenic pulmonary edema, or normal, refer to Figure 1.

Final diagnosis was determined independently by two emergency physicians (KC, ST) through a rigorous chart review; this diagnosis served as our criterion standard. Chart reviewers followed previously published methods,[27] which included training, standardized data forms and periodic monitoring. They were not blinded to the study hypothesis, but they were blinded to the LuCUS protocol results. Chart reviewers assessed all cases and arrived at their final diagnosis after reviewing all labs, imaging studies, medications administered, consults obtained, comprehensive echocardiography results and discharge summaries from the index visit. Each review was performed independently and neither reviewer performed any of the ultrasounds for this study. If the reviewers disagreed, a third blinded reviewer made the decision on final diagnosis.

The impact of the LuCUS protocol was assessed in several ways. First, by determining whether there was a change in the top three etiologies in the differential diagnoses pre and post-ultrasound. Second, whether the top three etiologies in the differential diagnosis became more accurate in comparison to the patient's final diagnosis. Finally, whether the protocol has immediate clinical impact, as evidenced by improvement in acute disease-specific ED management and changes in the treating clinician's confidence in their admission diagnosis.

Data Analysis

A pilot study using the LuCUS protocol was conducted, enrolling twenty ED patients with undifferentiated dyspnea. Analysis of the pilot data showed LuCUS to be 25% more sensitive and 24% more specific for diagnosing ADHF than for patients in whom ultrasound was not used. From these results, we calculated based on a paired comparison, that a sample size of 96 patients would be needed to detect a 30% increase in accuracy with an α of 0.05 and a β of 0.20. Sensitivity, specificity, positive likelihood ratios and negative likelihood ratios were calculated and 95% confidence intervals (CIs) were derived using SPSS Statistics for Windows (IBM Corp Version 21.0, Armonk, NY). A sub-analysis (Table 3) was completed to see which variables, including B-lines, pleural

effusions, IVC assessment, and LV function, yielded the highest accuracy. Kappa and observed agreement were used to assess inter-rater reliability between coinvestigators' interpretations of images. Kappa was also used to assess agreement between EPs' and cardiology's grading of diastolic dysfunction.

RESULTS

Between December 2012 and July 2013, the LuCUS protocol was performed on 104 patients presenting to the ED with undifferentiated dyspnea. Demographic and clinical information are listed in Table 2. The flow of the study is presented in Figure 2. A total of five patients were excluded, in four patients the ultrasound was not feasible due to poor scanning windows and body habitus, and one patient dropped out of the study prior to completion of the ultrasound.

Overall, 36 out of 99 patients had a criterion standard diagnosis of ADHF, while 63 patients had an alterative final diagnosis. Sensitivity, specificity, accuracy, positive likelihood ratio and negative likelihood ratio of the LuCUS protocol are 83% (67-93 CI), 83% (70-91 CI), 83% (74-89 CI), 4.8 (2.7-8.3 CI) and 0.20 (0.09 – 0.42 CI), respectively. Observed agreement for the LuCUS protocol was 93% between coinvestigators, and κ = 0.82 (CI 0.70 – 0.95). Overall, accuracy improved by 20% (83% vs 63%, 8-31 CI of the difference) using the LuCUS protocol over clinical gestalt alone. Specificity improved by 39% (83 vs 44%, 22-51 CI of the difference) and sensitivity decreased by 11% (94 vs 83%, -4.4-26 CI of the difference) but this was not statistically significant. Clinicians felt more confident in their diagnosis after the LuCUS protocol in 92% of cases. Sensitivity and specificity for detecting diastolic dysfunction were 100% (95% CI 0.83-1.0) and 0.47 (95% CI 0.24-0.71), respectively. Agreement between EPs and cardiology had a weighted kappa of κ =0.51 (95% CI 0.35-0.66).

Pre-Ultrasound (Clinical Gestalt)

ADHF was listed amongst the top three etiologies in the differential diagnosis in 69 (70%) out of 99 patients. Of these 69 patients, 34 (49%) had a criterion standard diagnosis of ADHF and 35 (51%) had an alternative diagnosis (Figure 3). Thus, the sensitivity and specificity of clinical gestalt was 94 and 44, respectively.

Post-Ultrasound (LuCUS Protocol)

ADHF was listed as one of the top three etiologies in the differential diagnosis in 41 (41%) out of 99 patients. Of these 41, 30 (73%) had a criterion standard diagnosis of ADHF and 11 (27%) had an alternative diagnosis (Figure 2).

Comparison of Pre to Post-Ultrasound

Of the initial 69 patients thought to have ADHF pre-ultrasound: 30 (43%) were found to have ADHF post-ultrasound and on final diagnosis; 4 (6%) were found to have a final diagnosis of ADHF but an alternative post-ultrasound diagnosis; 8 (12%) were found to have ADHF post-ultrasound but not on final diagnosis (Figure 3). Ultrasound correctly eliminated ADHF from the differential diagnosis in 27 (39%) patients who were found to have an alternative final diagnosis. No additional patients who were initially thought to have an alternative diagnosis pre-ultrasound were identified as having ADHF post-ultrasound.

Treatment prior to Ultrasound

Twelve patients were treated with positive pressure ventilation, nitroglycerin and/or furosemide prior to ultrasound, with an average of 21 minutes (range 3 to 30 minutes) between treatment and ultrasound. All 12 patients had a pre-ultrasound diagnosis of ADHF. Of these 12 patients, 9 (75%) were found to have ADHF post-ultrasound and on final diagnosis; 3 (25%) had an alternative final and post-ultrasound diagnosis - two had COPD, one had non-cardiogenic pulmonary edema.

Changes in Clinical Management based on Ultrasound

The LuCUS protocol led to seventy individual changes in management amongst 47 (47%) patients. This included 42 patients with a change in treatment plan, 12 patients with a change in disposition (e.g., admitted to a cardiology service versus medicine), 8 patients with a change in level of care (e.g. telemetry, ICU or catheterization lab), and 8 patients who received a new consult. Of the 42 patients with changes in treatment, 39 (93%) received correct disease-specific treatment (evidenced by concordance between post-ultrasound diagnosis and final diagnosis). In 3 of the 42 patients (7%), treatment changes were made based on ultrasound findings, but in these three the post-ultrasound diagnosis and final diagnosis differed. This included one patient with a final diagnosis of COPD where albuterol was initially discontinued as the patient was thought to have

ADHF post-ultrasound, and discontinuation of fluids in 2 patients felt to have non-cardiogenic pulmonary edema on ultrasound who were later found to have pneumonia and lung cancer as a final diagnosis, respectively.

Fifty-one out of 99 patients (51%) had a pre-ultrasound differential diagnosis that included both ADHF and COPD. Out of these 51 patients, 25 (49%) had changes in ED administered medications. These results are summarized in Table 4. As a result of the use of the LuCUS protocol, 24 out of 25 of these patients (96%) received correct disease-specific treatment (final diagnosis and post-ultrasound diagnosis were concordant). Only one patient, with both a pre-ultrasound and final diagnosis of COPD, incorrectly had albuterol discontinued as a result of the LuCUS protocol indicating ADHF.

The LuCUS protocol took an average total time of 12 minutes (SD 4 minutes) to complete; the lung portion took an average of 6 minutes, and the cardiac portion, including IVC, took 6 minutes. This time started when the first images were acquired.

DISCUSSION

Dyspnea is a common complaint in the ED and rapidly identifying the cause can pose a challenge for clinicians. In this study we found the LuCUS protocol improved diagnostic accuracy over clinical gestalt alone, including improved specificity, which was statistically significant. Clinical gestalt was more sensitive for the diagnosis of ADHF, but did not reach statistical significance. We believe clinical gestalt had such a high sensitivity due to ADHF being over-diagnosed. This is illustrated by the fact that over fifty percent of the patients thought to have ADHF based on clinical gestalt (pre-ultrasound) were ultimately found to have an alternative criterion standard diagnosis.

The LuCUS protocol had 6 false negative results. Two of these patients were thought to have atrial fibrillation as the primary etiology of dyspnea pre-ultrasound, the LuCUS protocol found a mixed diagnosis, which was defined as two etiologies contributing equally to the patient's clinical symptoms. In these two cases, ADHF was one of the two etiologies, so these ultrasounds were coded as a "mixed" diagnosis and not as ADHF alone. However, both of these patients were treated appropriately with diuresis. If these ultrasounds had been coded as ADHF instead of a mixed diagnosis, the sensitivity would have improved from 83 to 89% (75-95 CI).

Eleven patients had a false positive ultrasound. Of these 11 patients, 8 were thought to have a pre- and post-ultrasound diagnosis of ADHF, meaning they had both a clinical and sonographic appearance of ADHF and were treated as such. These 8 patients had final diagnoses that included renal failure with non-cardiogenic pulmonary edema, atrial fibrillation, pulmonary hypertension with interstitial lung disease, and sternal fracture with pulmonary contusion. There are several factors that could explain why these patients were found to be false positives. First, the etiology of their dyspnea on initial presentation may have been multifactorial, including, in addition to their final diagnosis, ADHF. This is supported by the fact that in all of these cases the patient had a history of ADHF and positive lung findings on ultrasound. Thus, their clinical and sonographic appearance is consistent with ADHF while the root cause of their dyspnea (at the index visit) is not related to their underlying cardiac condition. Second, since ADHF is a dynamic process, [28] it is possible these patients had evidence of ADHF in the ED and improved prior to admission after receiving proper treatment. These findings illustrate the limitations of the criterion standard used for diagnosing ADHF in this study. If, for example, these 8 patients truly had ADHF, the specificity would have improved from 83 to 95% (87-98 CI).

The LuCUS protocol had a large impact on acute clinical management, which is highly important as disease-specific therapies for acutely dyspneic patients improves outcomes[2]. Almost half of the patients enrolled had changes in ED-administered medications, changes in level of care and new consultations. Thirty-nine of 42 patients (93%) received correct disease-specific treatment. Only one patient had disease-specific treatment (albuterol) discontinued in error based on false positive ultrasound findings of ADHF.

In the subset of patients thought to have both ADHF and COPD pre-ultrasound, 24 out of 25 patients (96%) received correct disease-specific treatment post-ultrasound. Based on clinical gestalt, twelve out of these 25 patients (48%) were thought to have COPD and thus were treated with beta agonists and steroids; after LuCUS diagnosed ADHF, beta agonists were correctly discontinued. Final diagnosis confirmed that these patients had ADHF, not COPD.

This protocol not only differentiated patients with ADHF versus COPD, but it also identified alternative causes of dyspnea requiring very different treatment. For example, one patient thought to have ADHF based on clinical gestalt, was diagnosed post-ultrasound with a large pericardial effusion with early tamponade physiology and was taken immediately for drainage.

The findings of the LuCUS protocol are similar to other previous studies that investigated the utility of bedside ultrasound for diagnosing ADHF. However, there are several aspects of our study that make it unique. The study by Kajimoto et al[17] differs from ours in that their protocol was performed by trained cardiologists, thus limiting its utilization by EP's. Also, we included patients treated for ADHF prior to ultrasound to allow for better real-world application. The results of our study show that our protocol can be accurately applied in this subset of patients. We also evaluated the direct impact of ultrasound findings on acute management of dyspneic patients and found that the LuCUS protocol lead to correct disease-specific treatment in the vast majority of treated patients.

The LuCUS protocol utilized four unique elements that differ from prior protocols: (1) we included patients treated for ADHF before ultrasound, (2) we used bilateral B-profiles, rather than AIS, as a potential indicator of ADHF, (3) we evaluated for pleural effusions, and (4) we assessed and graded diastolic dysfunction.

We chose to include patients who had been treated less than 30 minutes prior to ultrasound as we thought this was more applicable to daily practice, as patients may be treated by EMS or other front-end providers prior to initial evaluation by an EP. We found in this subset of patients the LuCUS protocol to be 100% accurate. These results suggest that we can apply this protocol in patients who have been treated for heart failure within 30 minutes.

Using B-profiles and/or pleural effusions as potentially indicative of ADHF allowed us to apply our protocol to a much larger group of patients than previous similar studies. While it is well established that the presence of AIS is fairly sensitive for detecting ADHF,[3,8,10,14] it is possible to have ADHF without AIS. By using this definition, we found a bilateral B profile and ejection fraction <45% improved sensitivity

for detecting ADHF by 35% (69% vs 34%, 11-53 CI of the difference) compared to AIS with ejection fraction < 45%.

Although previous literature would support the conclusion that pleural effusions do not improve diagnostic performance,[10] we chose to include pleural effusions as part of the protocol, as we hypothesized that their inclusion may improve the protocol's overall accuracy, especially after commencement of treatment. We found the presence of a pleural effusion combined with an ejection fraction < 45% to be 98% specific for ADHF, with a positive likelihood ratio of 51.

Even though we were able to detect diastolic dysfunction 100% of the time, there was only moderate agreement between EPs and cardiology for grading the level of dysfunction. Its assessment in our study did not lead to substantive improvements in recognition of ADHF, as only 2 out of the 36 patients (5%) with a final diagnosis of ADHF had isolated diastolic dysfunction. However, we believe evaluation of diastolic function represents an area for future investigations as patients with isolated diastolic dysfunction will present to the ED in ADHF and are likely to benefit from early recognition of this as the etiology of their dyspnea.

This study has shown that EP sonographers with extensive ultrasound experience can make an accurate diagnosis of ADHF, more accurate then clinical gestalt alone, and this in turn can improve patient care. Future directions for this research would include assessing a modified protocol with less experienced sonographers to further validate the results and to improve its generalizability.

LIMITATIONS

This study has several limitations that could limit its generalizability. We enrolled a convenience sample of patients at a single institution, which may have introduced selection bias, as one of the expert sonographers need to be available for enrollment. In addition, despite being powered to detect a clinically significant improvement in accuracy, the overall sample size was small.

The gold standard for diagnosing ADHF is comprehensive echocardiography in combination with clinical symptoms and therapeutic response. Due to limited resources, however, not all patients enrolled in the study had a comprehensive echocardiogram. If it

was performed, it was often not completed in a rapid manner, sometimes not occurring until days after admission, thereby limiting its utility as a gold standard. For our study, the gold standard was the final diagnosis determined by two independent expert reviewers; this model has served as criterion standard in multiple previous heart failure studies.[1,11,29-31] It is possible that results of the bedside ultrasound, directly or indirectly, were included in patients' ED chart and thus could act as a potential source of bias for the chart reviewers. However, our experience is that this is an infrequent practice at this institution and thus we feel the risk for bias is minimal. Also, BNP levels were not analyzed for this study as not enough patients had levels available, although it was not a requirement for enrollment as its use in the acute setting is not as well supported.[32]

Due to limitations imposed by the institutional review board, treating clinicians were not blinded to ultrasound results as the use of bedside sonography by EPs is considered standard care our institution. Thus, subsequent management may reflect results of the ultrasound and therefore the treatment record may not be independent of the diagnostic test, which may have influenced the chart reviewers' determination of final diagnosis. Furthermore, sonographers may have been biased as they could not be blinded to the physical appearance of patients. However, we believe that this would be of minimal significance as patients were covered, we did not perform a physical exam, and clinical gestalt, including physical assessment, has been proven to be unreliable for determining etiology of dyspnea.[18,33] Lastly, this study was designed as an expert-level study with future goals of prospective validation using less experienced sonographers.

CONCLUSIONS

In summary, our findings indicate that the LuCUS protocol, when performed by an experienced EP-sonographer in the assessment of ED patients with undifferentiated dyspnea, may accurately identify ADHF in dyspneic ED patients and increase the rate of correct, disease-specific treatment decisions.

This protocol has better diagnostic accuracy than clinical gestalt alone and increases physician confidence in their diagnosis.

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TABLES

Table 1. Dyspnea Differential Diagnosis

Acute Coronary Syndrome	Pleural effusion
Acutely Decompensated Heart Failure	Pneumonia
COPD/Asthma	Pulmonary Embolism
Lung Cancer	Mixed
Non-cardiogenic pulmonary edema	Other

Abbreviation: COPD=chronic obstructive pulmonary disease

Table 2. Patient Characteristics

	ADHF **n = 36**	**TOTAL** **n = 99**
Age, SD, Range	57±14, 34-91	56±13, 22-91
Male	23 (63.9)	55 (55.6)
Medical Comorbidities		
Congestive heart failure	23 (63.9)	40 (40.4)

	COPD	12 (33.3)	43 (43.4)
	Coronary artery disease	6 (16.7)	16 (16.2)
	Hypertension	30 (83)	68 (68.7)
	Lung cancer	1 (2.8)	10 (10.1)
	Diabetes	11 (30.6)	29 (29.3)
	Smoking	6 (16.7)	21 (21.2)
Vital Signs			
	Hypotension (SBP<100)	3 (8.3)	5 (5.0)
	Tachycardia (HR>100)	15(41.7)	36 (36.3)
	Tachypnea (RR>20)	16 (44.4)	44 (44.4)
	Fever (>100.4F)	0 (0)	0 (0)
	Hypoxia (<92%)	4 (11.1)	12 (33.3)
Disposition			
	ICU	3 (8.3)	9 (9.1)
	Catheterization Lab	0 (0)	1 (1)
	Floor	26 (72.2)	64 (64.6)
	Observation Unit	4 (11.1)	9 (9.1)
	Home	3 (8.3)	16 (16.2)
Final Diagnosis			
	ADHF	36 (36.3)	
	COPD	24 (24.2)	
	Pneumonia	10 (10.1)	
	Lung cancer	7 (7.1)	
	Pleural effusion	3 (3)	
	Non cardiogenic pulmonary edema	2 (2)	
	Pulmonary embolism	2 (2)	
	Acute coronary syndrome	1 (1)	
	Other	15 (15.1)	

Values are mean ± standard deviation, number (%). Abbreviations: ADHF=acutely

decompensated heart failure; COPD=chronic obstructive pulmonary disease; ICU=intensive care unit

Table 3. Performance Characteristics for Diagnosing ADHF

		Sensitivity	Specificity	LR (+)	LR (-)
Clinical Gestalt (Pre-Ultrasound)		94.4 (81-98)	44.4 (33-56)	1.7	0.12
LuCUS (Post-Ultrasound)		83.3 (67-93)	82.5 (70-91)	4.8	0.20
	AIS and EF<45%	34.3 (21-51)	96.8 (89-99)	10.9	0.67
	B Profile and EF<45%	69.4 (53-82)	93.7 (84-97)	10.9	0.33
	Pleural effusion and EF<45%	79.4 (63-89)	98.4 (92-99)	51	0.21
	Plethoric IVC and EF<45%	70.6 (54-83)	81.5 (70-89)	3.8	0.36

Abbreviations: ADHF=acutely decompensated heart failure, EF=ejection fraction, IVC=inferior vena cava, LR=likelihood ratio

Table 4. Treatment changes in patients with Pre-Ultrasound Differential Diagnosis including both ADHF and COPD

Post (LuCUS) Diagnosis	Final Diagnosis	Treatment change
ADHF	ADHF	Discontinued albuterol
ADHF	ADHF, viral myocarditis	Discontinued albuterol
ADHF	ADHF	Discontinued albuterol
COPD	COPD	Discontinued diuresis
ADHF	ADHF	Discontinued albuterol
ADHF	COPD	Discontinued albuterol
ADHF+ACS	ADHF, A fib RVR	Started diuresis, stopped albuterol
COPD	COPD	Discontinued diuresis
ADHF	ADHF	Discontinued albuterol

NCPE+PNA	ARDS +PNA	Started IVF
Tamponade	Tamponade	Started IVF, Catheterization Lab
COPD	COPD	Discontinued diuresis
ADHF	ADHF	Discontinued albuterol
ADHF	ADHF	Discontinued albuterol
COPD	COPD	Discontinued diuresis
COPD	COPD	Discontinued diuresis
ADHF+ACS	ADHF, A fib RVR	Discontinued albuterol
COPD	COPD	Discontinued diuresis, Started albuterol
ADHF	ADHF	Discontinued albuterol
NCPE	Renal Failure	Dialysis
COPD +PNA	PNA	Discontinued diuresis
COPD	COPD	Discontinued diuresis
ADHF	ADHF	Discontinued albuterol
ADHF	ADHF	Discontinued albuterol
COPD	COPD	Discontinued diuresis

Abbreviations: ADHF=acutely decompensated heart failure; ARDS=acute respiratory distress; COPD=chronic obstructive pulmonary disease; NCPE=non cardiogenic pulmonary edema

FIGURE LEGENDS

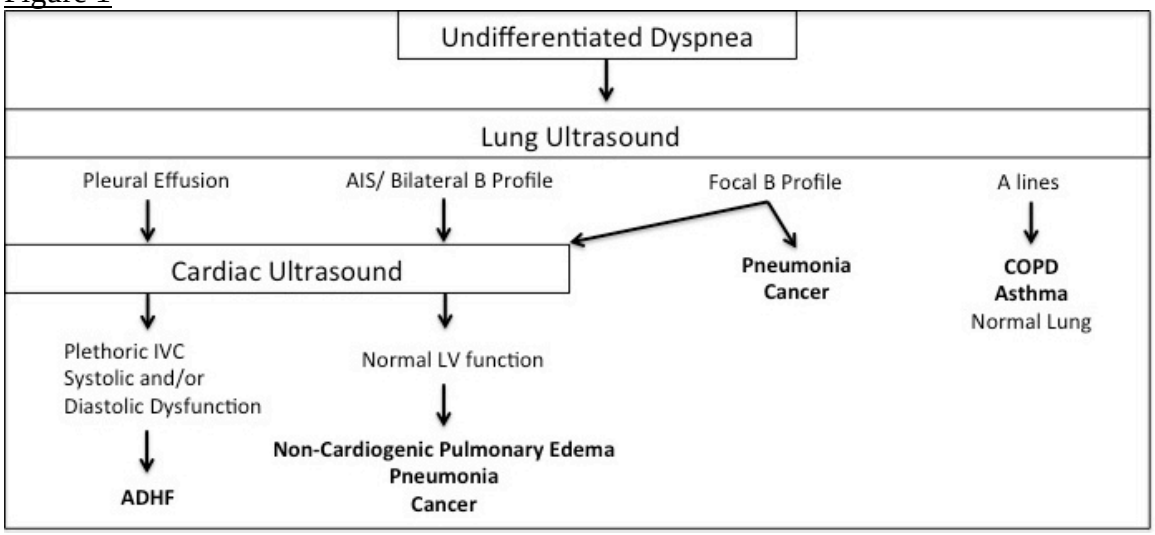
Figure 1: Algorithm for differentiating dyspnea using lung and cardiac ultrasound findings.

Figure 2: Patient flow through study, from enrollment to LuCUS (post-ultrasound) findings.

Figure 3: Patient flow through study, comparing clinical gestalt (pre-ultrasound) diagnosis to criterion standard diagnosis and LuCUS (post-ultrasound).

FIGURES

Figure 1



Abbreviations: ADHF=acutely decompensated heart failure, COPD=chronic obstructive pulmonary disease

Figure 2

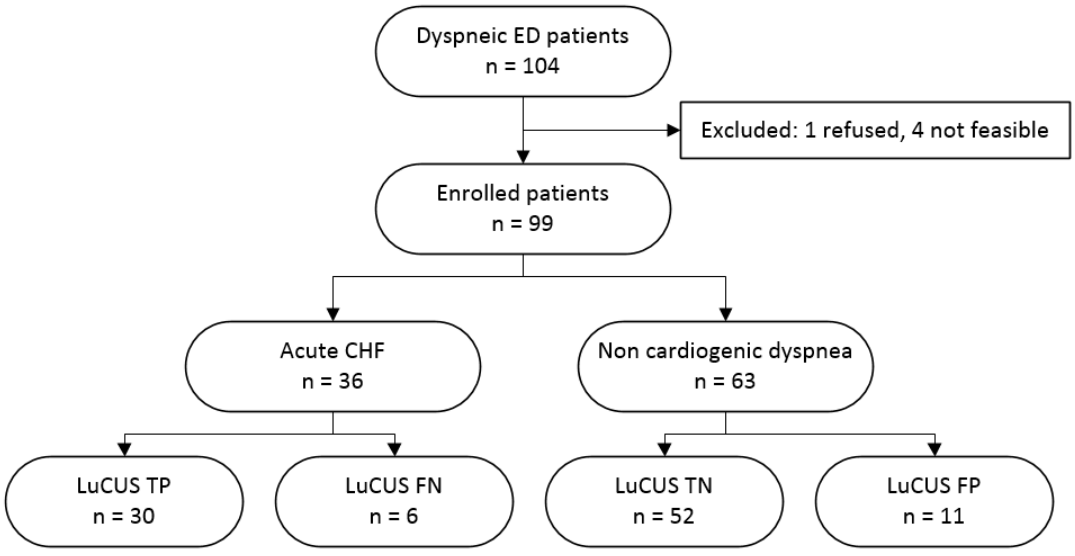
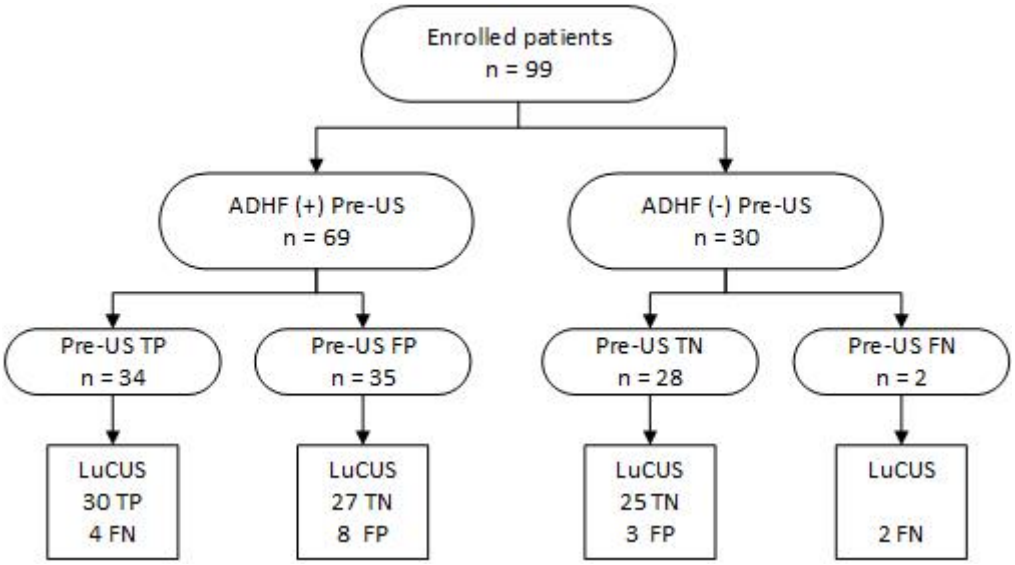


Figure 3


Enrolled patients
n = 99
ADHF (+) Pre-US
n = 69
ADHF (-) Pre-US
n = 30
Pre-US TP
n = 34
Pre-US FP
n = 35
Pre-US TN
n = 28
Pre-US FN
n = 2
LuCUS
30 TP
4 FN
LuCUS
27 TN
8 FP
LuCUS
25 TN
3 FP
LuCUS
2 FN