CHEST

Critical Care Ultrasonography Differentiates ARDS, Pulmonary Edema, and Other Causes in the Early Course of Acute Hypoxemic Respiratory Failure

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BACKGROUND: Pathogenic causes of acute hypoxemic respiratory failure (AHRF) can be difficult to identify at early clinical presentation. We evaluated the diagnostic utility of combined cardiac and thoracic critical care ultrasonography (CCUS).

METHODS: Adult patients in the ICU were prospectively enrolled from January through September 2010 with a Pao_2/Fio_2 ratio <300 on arterial blood gas (ABG) analysis within 6 h of a new hypoxemic event or the ICU admission. Focused cardiac and thoracic CCUS was conducted within 6 h of ABG testing. Causes of AHRF were categorized into cardiogenic pulmonary edema (CPE), ARDS, and miscellaneous causes after reviewing the hospitalization course in electronic medical records.

RESULTS: One hundred thirty-four patients were enrolled (median Pao_2/Fio_2 ratio, 191; interquartile range, 122-253). Fifty-nine patients (44%) received a diagnosis of CPE; 42 (31%), ARDS; and 33 (25%), miscellaneous cause. Analysis of CCUS findings showed that a low B-line ratio (proportion of chest zones with positive B-lines relative to all zones examined) was predictive of miscellaneous cause vs CPE or ARDS (receiver operating characteristic area under the curve [AUC], 0.82; 95% CI, 0.75-0.88). For further differentiation of CPE from ARDS, left-sided pleural effusion (>20 mm), moderately or severely decreased left ventricular function, and a large inferior vena cava minimal diameter (>23 mm) were predictive of CPE (AUC, 0.79; 95% CI, 0.70-0.87).

CONCLUSIONS: Combined cardiac and thoracic CCUS assists in early bedside differential diagnosis of ARDS, CPE, and other causes of AHRF. CHEST 2015; 148(4):912-918

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ABBREVIATIONS: ABG = arterial blood gas; AHRF = acute hypoxemic respiratory failure; AUC = area under the curve; CCUS = critical care ultrasonography; CPE = cardiogenic pulmonary edema; EMR = electronic medical record; IVC = inferior vena cava; LV = left ventricular

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Acute hypoxemic respiratory failure (AHRF) is a commonly encountered condition in the ICU.[1] The pathogenesis of AHRF can be classified into neuromuscular in origin; acute and chronic obstructive airway disease; alveolar processes, such as cardiogenic pulmonary edema (CPE) and noncardiogenic pulmonary edema; and vascular diseases, such as pulmonary embolism.[2] Although early recognition and treatment of a specific cause of AHRF are paramount, diagnosis can be challenging in the early stage of illness.

Critical care ultrasonography (CCUS) has been gaining attention because of its noninvasiveness and absence of radiation exposure. Several studies have reported on the value of thoracic CCUS to assist physicians in differentiating alveolar processes from other causes of AHRF in the ED and prehospital settings.[3-7] For intensivists, CCUS is beneficial in identifying a component of CPE or noncardiogenic pulmonary edema, such as ARDS, among the various AHRF etiologic factors secondary to alveolar processes. A previous study identified key thoracic CCUS findings that could help in discerning cardiogenic edema from noncardiogenic edema,[3] but other studies have suggested that using thoracic CCUS alone is limited in differentiating between the two types.[4,8,9] Although basic cardiac CCUS is helpful in the global assessment of left ventricular (LV) systolic fraction,[10,11] CPE can occur with preserved LV systolic fraction in approximately one-half of patients.[12]

Physicians routinely perform cardiopulmonary physical examinations in daily practice, and a recent prospective study demonstrated the potential of the integrated use of cardiac and thoracic CCUS in the diagnosis of AHRF.[13] Understanding CCUS as a screening tool to enhance the physical examination and not as a definitive diagnostic modality, we aimed to evaluate the diagnostic utility of combined cardiac and thoracic CCUS in identifying causes of AHRF in the early course of critical illness.

Materials and Methods

Patient Enrollment

We conducted a prospective study in an academic teaching hospital from January 4 through October 23, 2010. Arterial blood gas (ABG) testing of patients admitted to the ICU was electronically screened between 8:00 AM and 5:00 PM on weekdays. Patients were eligible for participation in the study if (1) they had received a new diagnosis of AHRF or were admitted to the ICU with the diagnosis of AHRF, (2) ABG testing was ordered within 6 h of diagnosis of AHRF or ICU admission, or (3) ABG testing showed a Pao_2/Fio_2 ratio <300. Patients were excluded from the study if (1) an ICU provider declined bedside CCUS, (2) CCUS examination was deemed to interfere with patient care, (3) a sonographer was not available within 6 h after ABG testing, or (4) a previous ABG report during the same hospitalization met the criterion of Pao_2/Fio_2 ratio <300. Verbal consent was obtained from either the patients or their surrogates. This study was approved by the Mayo Clinic Institutional Review Board (IRB No. 09-004897).

CCUS Examination

Cardiac and thoracic CCUS was performed within 6 h of ABG testing. Duration of CCUS examination was limited to 10 min. A portable ICU-based ultrasonography machine (M-turbo with P21× phased-array transducer; FUJIFILM SonoSite, Inc) was used at the bedside to conduct thoracic CCUS followed by cardiac CCUS. Details of the examination are discussed in e-Appendix 1 and Figure 1. At each examination window, 6- to 10-s video clips were saved for offline image interpretation.

Interpretation

Board-certified radiologists and cardiologists reviewed thoracic and cardiac CCUS images, respectively. Patient clinical data were masked to the reviewers. Details of interpretation and definitions of CCUS findings are shown in e-Appendix 1 and Figure 1.

Etiologic Factors of AHRF and Data Collection

Two investigators to whom the CCUS image interpretation was masked (R. H. and J. S.) reviewed the electronic medical record (EMR) to classify the causes of AHRF into three groups: CPE, bilateral noncardiogenic pulmonary edema (ARDS), and other causes (miscellaneous). A patient with both CPE and ARDS was categorized into the CPE group. The diagnosis of ARDS was based on the definition published from the American-European Consensus Conference on ARDS.[14] For differing diagnoses between the two reviewers, a third physician reviewed the EMR to make the final diagnosis. The reviewers had access to the clinical tests ordered as part of patient care, such as echocardiography, chest radiograph, and CT scan, during the course of the patient's ICU stay. In addition to the diagnosis, the following data were extracted from the EMR: age, sex, Pao_2/Fio_2 ratio on ABG measurements, pro-brain natriuretic peptide value, peak troponin value, lactate value, leukocyte count, creatinine value, use of mechanical ventilation, and use of vasoactive or inotropic agents.

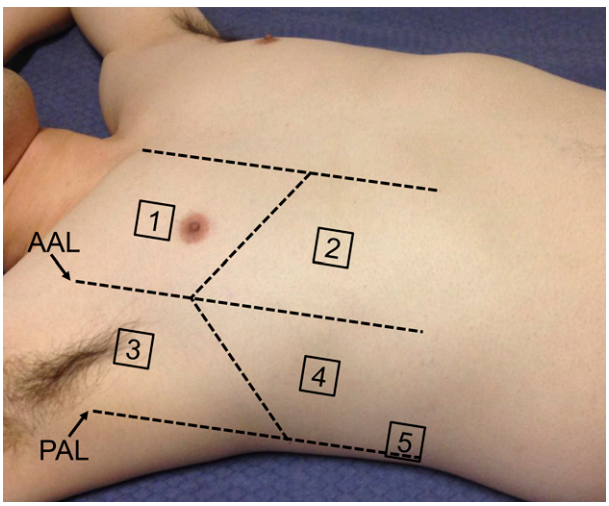

Figure 1 – *Thoracic critical care ultrasonography (CCUS) transducer application points. Range of points is 1 to 5. AAL = anterior axillary line; PAL = posterior axillary line. (The patient provided written consent for the use of this photograph.)*

Statistical Analysis

For statistical analysis, SAS 9.2 (SAS Institute Inc) and R version 3.0.2 software (The R Foundation) were used. The κ value was calculated to evaluate concordance of clinical diagnoses of AHRF between the two EMR reviewers. The lasso model of penalized logistic regression was performed to differentiate miscellaneous cause from CPE and ARDS and, subsequently, CPE from ARDS.[15] Ten-fold cross-validation was used to determine the optimal penalty for model selection. An optimal cut point was determined for pleural effusion and inferior vena cava (IVC) variables with classification and regression trees software using the rpart package.[16] IVC variables were categorized into three groups because of multiple missing variables: above an optimal cut point, below an optimal cut point, and missing IVC measurement. Receiver operating characteristic area under the curve (AUC) was computed to evaluate model discrimination. A weighted scorecard was produced on the basis of the optimal penalized logistic regression model.[15] Kruskal-Wallis test, χ^2 test, or Fisher exact test was used to compare variables among patients with CPE, ARDS, and miscellaneous causes. $P < .05$ was considered statistically significant.

Results

Patient Characteristics

During the 9-month study, 241 adult patients in the ICU were screened for AHRF and a Pao_2/Fio_2 ratio < 300, and 134 were enrolled (Fig 2). Table 1 shows the patient characteristics at the time of ABG measurement. The median time delay from ABG testing to CCUS examination was 211 (interquartile range, 112-289) min. Fifty-nine patients were classified as having CPE, 42 as having ARDS, and 33 as having a miscellaneous cause. Seventeen of 59 patients (29%) in the CPE group had both CPE and ARDS. The κ value for the diagnoses between the two reviewers was 0.77 (95% CI, 0.66-0.88). The most common predisposing condition for the ARDS group was pneumonia (23 patients, 55%). In the miscellaneous group, unilateral pneumonia was most frequently seen (18 patients, 56%), followed by atelectasis (seven patients, 22%), exacerbation of chronic obstructive airway disease (four patients), pulmonary emboli (two patients), pneumothorax (one patient), and large malignant pleural effusion (one patient).

CCUS Variables

CCUS measurements and interpretation by diagnostic group (ie, CPE, ARDS, miscellaneous) are summarized in e-Table 1. Diastolic assessment, such as E/A or E/e′, was available in only 56% of patients and was not included in the multivariate analysis.

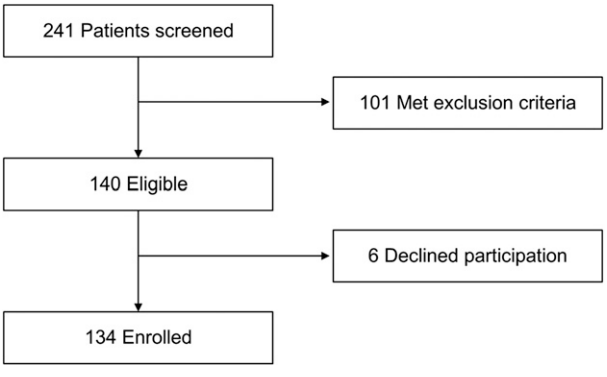

Figure 2 – *Flowchart of patient study enrollment.*

Multivariate Analysis

Penalized regression analysis with cross-validation was first conducted to differentiate the miscellaneous group from the CPE and ARDS groups. It identified a proportion of chest zones with positive B-lines relative to all zones examined (a B-line ratio) to be a significant variable (coefficient, −2.05). No other thoracic or cardiac CCUS finding was significant for differentiating miscellaneous causes from CPE and ARDS. The AUC of this prediction model was 0.82 (95% CI, 0.75-0.88) (Fig 3A).

Subsequently, penalized regression analysis was performed to differentiate CPE from ARDS among patients not given a miscellaneous cause diagnosis. The following CCUS variables were statistically significant as a prediction model for CPE: presence of left-sided pleural effusion > 20 mm in the left posterolateral zone (coefficient, 0.61), degree of LV systolic dysfunction (moderate or severe dysfunction) (coefficient, 0.49), and an IVC minimal diameter > 23 mm (coefficient, 0.43). Major valvular abnormalities, right ventricular systolic function and size, lung sliding, pleural assessment, or the presence of A-lines or C patterns was not significantly associated with the diagnosis of CPE. The AUC of this prediction model was 0.79 (95% CI, 0.70-0.87) (Fig 3B).

Simplified Scoring System for Clinical Use

To facilitate clinical use of this prediction model, we developed a simplified scoring system. For identifying the miscellaneous group, fewer than three (maximum of eight) chest zones with positive B-lines were associated with miscellaneous causes of AHRF (sensitivity, 97%; specificity, 53%). Table 2 shows the performance statistics for various score cut points. The AUC of this prediction model was 0.82 (95% CI, 0.75-0.88).

After miscellaneous causes were excluded, differentiation of CPE from ARDS was conducted with a 10-point scoring system. A base score of 3 was given to the patients for whom the miscellaneous cause was excluded. Left-sided pleural effusion > 20 mm was given 4 points; IVC minimal diameter ≤ 23 mm, −2 points; and moderate

TABLE 1] Characteristics of Patients With Acute Hypoxemic Respiratory Failure

Characteristic	Patients				*P* Value
	All (N = 134)	With CPE (n = 59, 44%)	With ARDS (n = 42, 31%)	With Miscellaneous Cause (n = 33, 25%)	
Male sex	79 (59)	30 (51)	28 (67)	21 (64)	.23
Age,[a] y	68 (55-77)	73 (62-80)	66.5 (52-73)	60 (49-70)	.01
Pao_2/FIo_2 ratio[a]	191 (123-252)	210 (130-249)	170 (111-214)	232 (158-272)	.04
Mechanical ventilation	70 (52)	30 (51)	25 (60)	15 (45)	.46
Noninvasive ventilation	25 (19)	14 (24)	4 (10)	7 (21)	.18
Vasoactive/inotropic agents	41 (31)	19 (32)	17 (40)	5 (15)	.06
Laboratory values					
Pro-BNP,[a] pg/mL (n = 40)	3,398 (854-11,039)	6,147 (2,764-24,072)	882 (311-3,581)	697 (216-2,905)	.002
Leukocyte count, No./nL (n = 134)	11.3 (7.5-15.8)	11.3 (8.1-15.7)	11.0 (6.3-15.3)	12.4 (7.6-16.7)	.66
Peak troponin T, ng/mL (n = 89)	0.6 (0.02-0.14)	0.08 (0.02-0.22)	0.04 (0.01-0.11)	0.03 (0.01-0.07)	.10
Lactate, nmol/L (n = 102)	1.70 (1.10-2.60)	1.80 (1.05-2.80)	1.7 (1.20-2.60)	1.50 (0.92-1.97)	.28
Creatinine,[a] mg/dL (n = 134)	1.2 (0.8-1.7)	1.4 (0.95-2.05)	1.1 (0.8-1.5)	0.8 (0.6-1.0)	< .001
CCUS examination					
Time from ABG testing, min	211.0 (112.2-289.8)	198.0 (125.5-262.0)	214.5 (106.0-291.8)	229.0 (113.0-296.0)	.71

Data are presented as No. (%) or median (interquartile range). ABG = arterial blood gas; CCUS = critical care ultrasonography; CPE = cardiogenic pulmonary edema; pro-BNP = pro-brain natriuretic peptide.
[a]Statistically significant by Kruskal-Wallis test.

or severe LV dysfunction, 3 points. This simplified scoring system had an AUC of 0.79 (95% CI, 0.70-0.87). Table 3 shows the performance statistics for each score cut point. A score ≤ 3 was specific for ARDS; a score ≥ 6 was highly specific for CPE (Fig 4).

Diastolic Assessment

Among the 101 patients with CPE or ARDS, 48 and 50 had E/A and E/e′ measurements, respectively. The R package part was used to identify the best partition points for E/A and E/e′ to separate patients with CPE from those with ARDS.[16] ARDS was predominantly seen when E/e′ ≤ 8.3; CPE was seen more when E/e′ ≥ 14.3. No pattern was observed using the E/A estimate.

Discussion

This study identified crucial cardiac and thoracic CCUS measurements for discerning causes of AHRF early in the course of critical illness. Lack of positive B-lines or a low B-line ratio in thoracic CCUS examination strongly suggested miscellaneous causes of AHRF. However, left-sided pleural effusion, moderate or severe LV dysfunction, and large IVC minimal diameter indicated CPE rather than ARDS. Both the penalized regression model and the simplified scoring system showed excellent AUCs.

This study has a few notable points compared with previous literature. First, we aimed to identify important ultrasonographic features using both cardiac and thoracic CCUS. Previous reports showed a diagnostic use of thoracic CCUS alone to differentiate alveolar processes (CPE, ARDS, or pneumonia) from nonalveolar causes, such as airway obstructive disease (asthma and COPD) and vascular disorders (pulmonary embolus).[3,5,6] Whereas one study identified fundamental thoracic CCUS findings that could help to discern cardiogenic from noncardiogenic edema,[3] other studies suggested the limitation on thoracic CCUS alone in differentiating between the two.[4,8,9] Use of echocardiography for diagnosis and prognosis of

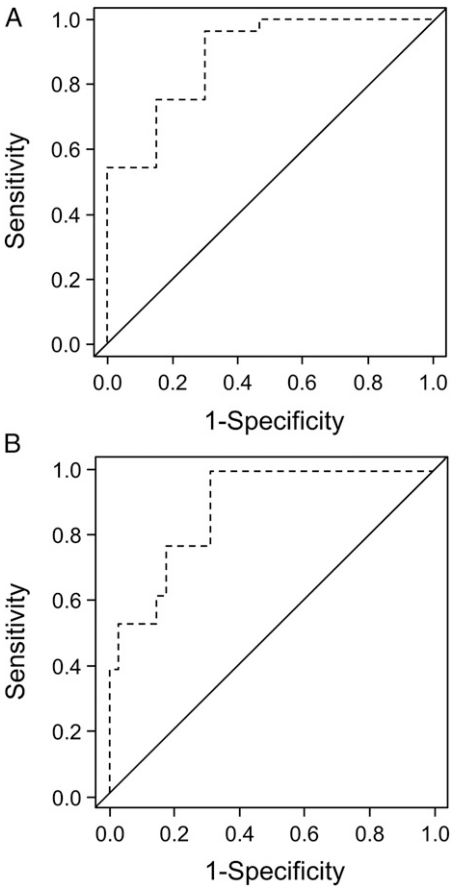

Figure 3 – *Receiver operating characteristic curve for differentiation among the groups. A, Differentiation of the miscellaneous group from the ARDS and cardiogenic pulmonary edema (CPE) groups (area under the curve, 0.82; 95% CI, 0.75-0.88). B, Differentiation of the CPE group from the ARDS group (area under the curve, 0.79; 95% CI, 0.70-0.87).*

heart failure has been reported[17-19]; however, investigators have recognized that CPE can occur with preserved LV systolic function in approximately one-half of patients.[12]

Given the intricate interaction between the cardiac and respiratory systems, it is natural to hypothesize that combining cardiac and thoracic components of CCUS would further improve CCUS diagnostic utility. In fact, a recent prospective study demonstrated that the integrated use of cardiac and thoracic CCUS is more accurate than thoracic CCUS alone in diagnosing CPE and pneumonia.[13] The present study not only proves this hypothesis but also provides physiologically plausible results. Positive B-lines in chest zones theoretically correspond to the rales heard in lung auscultation. If rales are not heard in most of the lung fields, a bilateral alveolar process, such as CPE or ARDS, is unlikely in patients with AHRF. The presence of left-sided pleural effusion corresponds to the dullness to percussion at the base of the left lung. LV systolic dysfunction corresponds to hearing a third heart sound, and the large IVC minimal diameter corresponds to a distended internal jugular vein. These physical examination findings are well known for CPE.[20] In consideration of the high noise level in the ICU,[21] the CCUS examination plays an adjunctive role to the conventional physical examination.

TABLE 2] Sensitivity and Specificity of Various Cut Points: Differentiation of the Miscellaneous Group From the ARDS and CPE Groups

No. Chest Zones With Positive B-Lines	Statistical Characteristic	
	Sensitivity (95% CI)	Specificity (95% CI)
0	0.55 (0.36-0.72)	0.85 (0.77-0.91)
1	0.76 (0.58-0.89)	0.70 (0.60-0.79)
2	0.97 (0.84-1.00)	0.53 (0.43-0.63)
3	1.00 (0.89-1.00)	0.42 (0.32-0.52)
4	1.00 (0.89-1.00)	0.31 (0.22-0.41)
5	1.00 (0.89-1.00)	0.18 (0.11-0.27)
6	1.00 (0.89-1.00)	0.09 (0.04-0.16)
7	1.00 (0.89-1.00)	0.05 (0.02-0.11)
8	1.00 (0.89-1.00)	0.00 (0.00-0.03)

See Table 1 legend for expansion of abbreviation.

Second, we conducted bedside CCUS in a practical manner in which the examination was performed with an ICU-based portable ultrasound machine in ≤ 10 min. Important ultrasonography findings shown to be useful in this study are easy to be obtained and interpreted by intensivists who have undergone a structured ultrasonography

TABLE 3] Sensitivity and Specificity of Various Cut Points: Differentiation of the CPE Group From the ARDS Group

Simplified Prediction Score for CPE	Statistical Characteristic	
	Sensitivity (95% CI)	Specificity (95% CI)
1	1.00 (0.94-1.00)	0.00 (0.00-0.08)
3	0.77 (0.64-0.87)	0.69 (0.53-0.82)
4	0.61 (0.48-0.74)	0.83 (0.69-0.93)
5	0.53 (0.39-0.66)	0.86 (0.72-0.95)
6	0.39 (0.26-0.52)	0.98 (0.87-1.00)
7	0.30 (0.18-0.43)	1.00 (0.92-1.00)
8	0.11 (0.04-0.22)	1.00 (0.92-1.00)
10	0.04 (0.00-0.12)	1.00 (0.92-1.00)

See Table 1 legend for expansion of abbreviation.

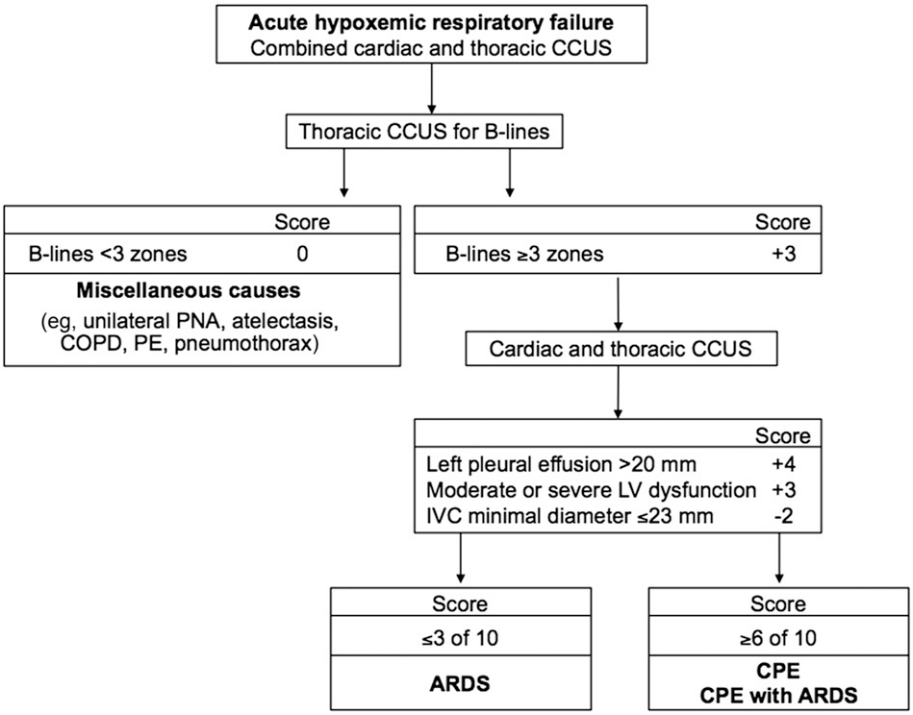

Figure 4 – *Cardiac and thoracic CCUS algorithm with a simplified scoring system. IVC = inferior vena cava; LV = left ventricular; PE = pulmonary embolism; PNA = pneumonia. See Figure 1 and 3 legends for expansion of other abbreviations.*

training session.[22,23] In addition, these examinations are within the scope of fundamental competency recommended for intensivists.[10] If the examination is limited to key measurements, no more than 5 min are needed to calculate the present simplified prediction scores.

Third, this study focused on the ICU setting, where early recognition of AHRF etiologic factors can be beneficial. Generally speaking, basic radiologic or laboratory information often is available before the ICU admission, and differentiating alveolar processes (CPE, ARDS, or unilateral pneumonia) from nonalveolar processes (neuromuscular disorder, chronic obstructive airway disease, or pulmonary embolus) is not particularly difficult for intensivists. Such differentiation often is made in the ED through laboratory and radiographic findings together with the BLUE (bedside lung ultrasonography in emergency) protocol suggested by Lichtenstein and Mezière.[5] Although emergency medicine physicians initiate a primary treatment of AHRF, intensivists need to provide specific management targeted for a cause of the AHRF. Differentiation between CPE and ARDS, although they may overlap, can be difficult in the early stage of critical illness.[24,25] A previous study has shown a decision support tool using such patient risk factors as age, alcohol abuse, chemotherapy, and oxygen saturation as measured by pulse oximetry/FIO_2 ratio.[26] According to the present study, CCUS examination is still beneficial when such information is not readily available at the bedside.

This study has several limitations. First, not all eligible patients with AHRF were enrolled in the study because of a narrow enrollment window. When the CCUS examinations were deemed to interfere with patient care (ie, transportation, procedures, family discussion), the patient was not enrolled. Second, CCUS examination was performed only once per patient. A patient's cardiopulmonary conditions constantly change, especially for patients with CPE who tend to respond to medical therapy in a short period. In reality, the advantage of CCUS is its portability and repeatability, which makes it easier for intensivists to chart the trend of a patient's clinical condition and reach the correct diagnosis. The one-time CCUS examination in the present study might have led to an underestimation of its value and diagnostic accuracy. Third, not all patients underwent diastolic assessment because of time constraints and suboptimal image acquisition. Although diastolic assessment could further increase diagnostic accuracy, we believe that bedside cardiac and thoracic CCUS should be used as a quick screening tool to enhance the physical examination but not as a definitive diagnostic modality. Diastolic assessment should be performed with use of comprehensive echocardiography not with an ICU-based portable ultrasonography machine. Finally, we identified central ultrasonographic findings and created a prediction

model on the basis of a cohort at a single institution. This model needs to be validated in a larger cohort.

Conclusions

This study identified important cardiac and thoracic CCUS findings to differentiate causes of AHRF in adult patients in the ICU. Although the simplified prediction model may need to be prospectively validated in a large cohort, we show a valuable use of bedside-focused cardiac and thoracic CCUS to differentiate ARDS, CPE, and other causes of AHRF early in the course of critical illness.

Acknowledgments

Author contributions: H. S. had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis, including and especially any adverse effects. H. S. and O. G. contributed to the study design, data collection and analysis, interpretation of results, and writing and revision of the manuscript; L. A. S. contributed to the statistical analysis and revision of the manuscript; R. H., J. S., E. H. L., B. P. M., T.-E. C., and A. L. contributed to the data collection and analysis and revision of the manuscript; and S. V. M. contributed to the data collection and analysis, interpretation of results, and writing and revision of the manuscript.

Conflict of interest: L. A. S. is a stockholder in Johnson & Johnson Services, Inc, and Medtronic plc. None declared (H. S., R. H., J. S., E. H. L., B. P. M., T.-E. C., A. L., S. V. M., O. G.).

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Additional information: The e-Appendix and e-Table can be found in the Supplemental Materials section of the online article.

References

1. Vincent J-L, Akça S, De Mendonça A, et al; SOFA Working Group. The epidemiology of acute respiratory failure in critically ill patients. *Chest*. 2002;121(5):1602-1609.
2. Mac Sweeney R, McAuley DF, Matthay MA. Acute lung failure. *Semin Respir Crit Care Med*. 2011;32(5):607-625.
3. Copetti R, Soldati G, Copetti P. Chest sonography: a useful tool to differentiate acute cardiogenic pulmonary edema from acute respiratory distress syndrome. *Cardiovasc Ultrasound*. 2008;6:16.
4. Gargani L, Frassi F, Soldati G, Tesorio P, Gheorghiade M, Picano E. Ultrasound lung comets for the differential diagnosis of acute cardiogenic dyspnoea: a comparison with natriuretic peptides. *Eur J Heart Fail*. 2008;10(1):70-77.
5. Lichtenstein DA, Mezière GA. Relevance of lung ultrasound in the diagnosis of acute respiratory failure: the BLUE protocol. *Chest*. 2008;134(1):117-125.
6. Prosen G, Klemen P, Štrnad M, Grmec S. Combination of lung ultrasound (a comet-tail sign) and N-terminal pro-brain natriuretic peptide in differentiating acute heart failure from chronic obstructive pulmonary disease and asthma as cause of acute dyspnea in prehospital emergency setting. *Crit Care*. 2011;15(2):R114.
7. Volpicelli G, Mussa A, Garofalo G, et al. Bedside lung ultrasound in the assessment of alveolar-interstitial syndrome. *Am J Emerg Med*. 2006;24(6):689-696.
8. Picano E, Frassi F, Agricola E, Gligorova S, Gargani L, Mottola G. Ultrasound lung comets: a clinically useful sign of extravascular lung water. *J Am Soc Echocardiogr*. 2006;19(3):356-363.
9. Volpicelli G, Elbarbary M, Blaivas M, et al; International Liaison Committee on Lung Ultrasound (ILC-LUS) for International Consensus Conference on Lung Ultrasound (ICC-LUS). International evidence-based recommendations for point-of-care lung ultrasound. *Intensive Care Med*. 2012;38(4):577-591.
10. Mayo PH, Beaulieu Y, Doelken P, et al. American College of Chest Physicians/La Société de Réanimation de Langue Française statement on competence in critical care ultrasonography. *Chest*. 2009;135(4):1050-1060.
11. Labovitz AJ, Noble VE, Bierig M, et al. Focused cardiac ultrasound in the emergent setting: a consensus statement of the American Society of Echocardiography and American College of Emergency Physicians. *J Am Soc Echocardiogr*. 2010;23(12):1225-1230.
12. Owan TE, Hodge DO, Herges RM, Jacobsen SJ, Roger VL, Redfield MM. Trends in prevalence and outcome of heart failure with preserved ejection fraction. *N Engl J Med*. 2006;355(3):251-259.
13. Bataille B, Riu B, Ferre F, et al. Integrated use of bedside lung ultrasound and echocardiography in acute respiratory failure: a prospective observational study in ICU. *Chest*. 2014;146(6):1586-1593.
14. Bernard GR, Artigas A, Brigham KL, et al; The American-European Consensus Conference on ARDS. The American-European Consensus Conference on ARDS. Definitions, mechanisms, relevant outcomes, and clinical trial coordination. *Am J Respir Crit Care Med*. 1994;149(3):818-824.
15. Friedman J, Hastie T, Tibshirani R. Regularization paths for generalized linear models via coordinate descent. *J Stat Softw*. 2010;33(1):1-22.
16. Therneau TM, Atkinson B. An introduction to recursive partitioning using the RPART routines. The Comprehensive R Archie Network website. http://cran.r-project.org/web/packages/rpart/vignettes/longintro.pdf. Accessed March 7, 2014.
17. Joseph MX, Disney PJ, Da Costa R, Hutchison SJ. Transthoracic echocardiography to identify or exclude cardiac cause of shock. *Chest*. 2004;126(5):1592-1597.
18. Slama M, Maizel J. Echocardiographic measurement of ventricular function. *Curr Opin Crit Care*. 2006;12(3):241-248.
19. Marum S, Price S. The use of echocardiography in the critically ill; the role of FADE (Fast Assessment Diagnostic Echocardiography) training. *Curr Cardiol Rev*. 2011;7(3):197-200.
20. Wang CS, FitzGerald JM, Schulzer M, Mak E, Ayas NT. Does this dyspneic patient in the emergency department have congestive heart failure? *JAMA*. 2005;294(15):1944-1956.
21. Christensen M. Noise levels in a general intensive care unit: a descriptive study. *Nurs Crit Care*. 2007;12(4):188-197.
22. Sekiguchi H, Bhagra A, Gajic O, Kashani KB. A general critical care ultrasonography workshop: results of a novel web-based learning program combined with simulation-based hands-on training. *J Crit Care*. 2013;28(2):217.e7-217.e12.
23. Sekiguchi H, Suzuki J, Gharacholou SM, et al. A novel multimedia workshop on portable cardiac critical care ultrasonography: a practical option for the busy intensivist. *Anaesth Intensive Care*. 2012;40(5):838-843.
24. Ware LB, Matthay MA. Clinical practice. Acute pulmonary edema. *N Engl J Med*. 2005;353(26):2788-2796.
25. Murray JF. Pulmonary edema: pathophysiology and diagnosis. *Int J Tuberc Lung Dis*. 2011;15(2):155-160.
26. Schmickl CN, Shahjehan K, Li G, et al. Decision support tool for early differential diagnosis of acute lung injury and cardiogenic pulmonary edema in medical critically ill patients. *Chest*. 2012;141(1):43-50.