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A prospective cohort study of thoracic ultrasound in acute respiratory failure: the C_3PO protocol

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Summary

Objectives: This study was performed to assess the clinical utility of a standardised thoracic ultrasound examination when added to standard care in patients with acute respiratory failure admitted to an intermediate care unit. This study aimed to assess the impact on clinical diagnosis, clinician confidence and management. Ultrasound has been shown to have utility in patients admitted to intensive care and emergency; however, utility in a ward setting is unknown. Design: Prospective cohort study.

Setting: Tertiary hospital in Melbourne, Australia.

Participants: 50 patients with acute respiratory failure requiring admission to an intermediate care unit.

Main outcome measures: (1) Change in clinical diagnosis or additional clinical diagnosis following thoracic ultrasound. (2) Change in diagnostic confidence following thoracic ultrasound. (3) Change to management following thoracic ultrasound.

Results: In 34% of patients, ultrasound detected unexpected findings that changed or added to the clinical diagnosis. Diagnostic confidence was increased in 44%, and the treating clinician altered the management plan in 30% as a result of the ultrasound. Ultrasound was particularly useful in clarifying the diagnosis in patients with multiple initial diagnoses, reducing to a single diagnosis in 69%.

Conclusions: Thoracic ultrasound has clinical utility in nonintubated adults with acute respiratory failure managed outside intensive care settings. It changed aetiological diagnosis, increases diagnostic confidence and altered clinical management in one out of three patients scanned. Our results suggest extended utility of thoracic ultrasound in acute respiratory failure to a broader context outside the intensive care unit population.

Keywords

ultrasound, acute respiratory failure, pneumonia, pleural effusion, interstitial syndrome, cardiac failure, pulmonary oedema, critical care

Background

Acute respiratory failure is common and lifethreatening,¹ with numerous potential underlying aetiologies, often in patients with extensive medical co-morbidities.²

Critically ill patients with acute respiratory failure may be managed in intensive care units, either for mechanical ventilation or multi-organ support, or in carefully supervised ward settings.

Determining the cause of acute respiratory failure can be challenging. Frequently, patients are unable to be safely transferred for computed tomography imaging, echocardiography or other departmental imaging. Portable chest X-ray is usually feasible, but often provides suboptimal images due to limited patient cooperation and projection issues. In the intensive care unit setting, thoracic ultrasound has an increasingly recognised role as an alternative to portable chest X-ray and has a range of applications that are directly relevant to identifying the aetiology of respiratory failure.^{4–9} Ultrasound is feasible and effective in the diagnosis and management of pleural effusion,^{10–12} as well as having robust diagnostic accuracy for pulmonary interstitial oedema,^{13–15} pneumonia,^{16,17} and the detection of fluid overload.18,19

We tested the hypothesis that thoracic ultrasound in acute respiratory failure in patients admitted to an intermediate-care unit would assist in diagnosing the cause of respiratory failure and impact patient management. We prospectively evaluated the outcome of thoracic ultrasound, employing a standardised imaging protocol that was added to standard care.

Methods

Population

This study was conducted within a single respiratory care unit (RCU) at a tertiary hospital in Melbourne, Australia. The unit consists of a four-bed ward annexe capable of delivering non-invasive ventilation and high-flow oxygen therapy with a 1:2 nursing

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ratio. RCU admission criteria include acute or incipient respiratory failure from any cause, monitoring of patients with sleep disordered breathing or monitoring of acute severe asthma. All patients admitted with respiratory failure to the RCU from 12 p.m. on a Sunday to 12 p.m. on Friday (to allow scanning within 24 h on weekdays only) were considered for inclusion over a nine-month period. Respiratory failure was defined as hypoxaemia on pulse oximetry (resting oxygen saturations below 90% or a greater than 4% reduction in saturations on baseline support in patients with chronic respiratory failure) or acute hypercapnia (PaCO₂ greater than 45 mmHg with arterial acidaemia defined as pH < 7.35). Ultrasound was implemented on the basis of available literature supporting its use in this context. Approval was given to audit outcomes by the Royal Melbourne Hospital Human Research and Ethics Committee (OA2014048).

Ultrasound examination

Ultrasound was performed by MH, JG, LH, SJ or PW. All clinician sonographers attended the same thoracic ultrasound course to calibrate their technique and met level 1 requirements for Royal College of Radiology performance of ultrasound by non-radiologists.²⁰ Ultrasound was performed using a Sonosite NanoMaxx[®] portable ultrasound machine (SonoSite Inc, 2010, Bothell, WA, USA) within 24 h of admission to RCU.

Patients were examined in two positions: first seated and then semi-recumbent. A 5-2 MHz abdominal convex transducer was applied posteriorly and translated dorsal to ventral on both sides, parallel to the rib spaces. This was repeated anteriorly using a curvilinear 8-5 MHz transducer. Jugular venous height was measured with the patient positioned at a 45° incline using the 8-5 MHz probe. The collapse point of the internal jugular vein was taken to represent jugular venous pressure as previously described.¹⁸ Any difficulties with examination, and the resulting impact on examination completion, were recorded.

Ultrasound protocol: 'C₃PO'

Ultrasonographic findings were sought and interpreted using a novel integrated approach to sonographic findings, which was represented by the acronym C_3PO (see Table 1). This standardised protocol was developed by MH to provide a systematic approach tailored to this patient population. Each imaging component of this protocol was interpreted in keeping with the published literature.²¹

Three 'C's are assessed first.

The first 'C' stands for lung Comets (B-lines) indicating interstitial thickening (Figure 1). Comets may be diffuse or local, suggesting either pulmonary oedema/interstitial lung disease, or focal fibrosis or



Table	Ι.	Integrated	ultrasound	findings.
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	Pulmonary oedema/ILD	Biventricular failure	Pneumonia	Right heart failure	Predominant effusion	Normal exam
Comets	Diffuse	Diffuse	Focal	-	-	-
Consolidation	-	-	Focal	-	-	-
C VP (JVP) elevated	-	+	-	+	-	-
P leural effusion	-	±	±	±	+	-
O (zero) findings	-	-	-	-	-	Ventilatory failure/PE

Note. ILD: interstitial lung disease, PE: pulmonary embolus.

consolidation respectively.^{22,23} Comets were considered diffuse if seen in two or more intercostal spaces bilaterally, or local if not meeting this criteria.

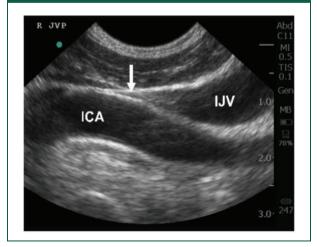
The second 'C' indicates sonographic Consolidation (Figure 2).²⁴ Adjunctive signs suggesting pneumonia were sought such as dynamic air bronchograms or associated pleural effusion.

The third **'C'** stands for elevated **'***C*entral venous pressure', defined as a taper point of the internal jugular vein at a level of greater than 3 cm above the manubrio-sternal joint (Figure 3). This correlates with both clinical assessment of the jugular venous pressure and invasive measurements of central venous pressure.¹⁸

Figure 2. Consolidation. Hyperechoic air bronchograms (bright branching pattern) with increased tissue density and serrated distal margin.



Figure 3. CVP - estimated internal jugular height. Arrow represents taper point of internal jugular vein; ICA: internal carotid artery; IJV: internal jugular vein.



'P' stands for *P*leural effusion, either in isolation or in combination with other findings.

'O' stands for 'O (Zero) findings', defined as absence of any positive findings. The significance of this null sonographic finding is analogous to a clear chest X-Ray in a patient with hypoxic respiratory failure, alerting the clinician to the important possibilities of either (i) vascular pathology, such as pulmonary embolism, or (ii) pure ventilatory failure due to airways disease (such as chronic obstructive pulmonary disease, COPD), muscle weakness or obesity hypoventilation.

Diaphragm movement was also examined on each side but not specifically mentioned in the report unless abnormal.

Study outcomes

Initial clinical diagnoses. Using all available diagnostic information, the treating team performed an initial clinical evaluation and documented their initial clinical diagnoses, findings on chest examination and chest X-ray interpretation, and whether diagnostic confidence on the basis of clinical assessment was low, intermediate or high.

Predicted ultrasound findings. Predicted ultrasound findings were then derived from the initial clinical diagnosis (for example, a patient with COPD and pneumonia would be expected to have ultrasound findings consistent with pneumonia).

Actual ultrasound findings. Following ultrasound:

- 1. If predicted ultrasound findings were demonstrated, the clinical diagnosis was considered confirmed by sonography.
- 2. If predicted ultrasound findings were not seen, the clinical diagnosis was considered unconfirmed by sonography.
- 3. If unexpected new ultrasound findings were encountered, alternative diagnoses were offered.

Measuring clinical utility. The ultrasound findings and alternative diagnosis (or diagnoses) were presented to the treating team who were then surveyed regarding:

- 1. Change in clinical diagnosis or if additional diagnosis had been made
- 2. Change in diagnostic confidence
- 3. Change to management (major or minor)

Changes to management were deemed minor if there was a change in dose or route of medication, and major if new medication was added, medication was ceased, or further investigations or invasive procedures were undertaken.

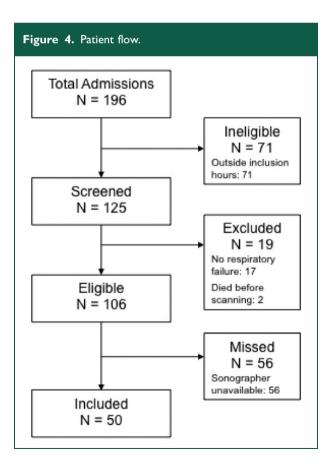
Data analysis

Data were collated using Microsoft Excel (Version 14.5.2, 2010; Microsoft Corporation, Redmond, WA, USA) and data analysed using IBM SPSS (Version 22.0, 2013; IBM Corporation, Armonk, NY, USA). Proportions were compared using two-tailed Z-test for proportions, with p < 0.05 considered significant. Descriptive data are presented as mean \pm standard deviation unless otherwise specified.

Results

Included patients

A total of 196 patients were admitted to the RCU between 1 January and 30 September 2011 (Figure 4); 71 were admitted outside inclusion hours, and 19 were excluded due to lack of acute respiratory failure (n=17) as defined or the patient dying before ultrasound was performed (n=2). A sonographer was unavailable for 56 subjects within 24 h of



admission ('missed'). Those missed were similar to those who were scanned.

All patients underwent chest X-ray on admission. Admission arterial blood gas was performed in 48 (96%), and the remaining 2 being stepped-down from intensive care. In-hospital mortality was 7/50 (14%).

The ultrasound examination was completed per protocol in 47/50 patients; the posterior chest could not be examined in 3 patients (too unwell – 2 patients and spinal precautions – 1 patient). Mean ultrasound duration was $20.5 \pm 6 \text{ min}$ (including introduction, performance of ultrasound, documentation and clean-up).

Changes in clinical diagnosis

Initial clinical diagnoses. The range of clinical diagnoses was broad, with the most common diagnosis being pneumonia (n = 13), followed by exacerbations of airways disease (n = 7) and biventricular heart failure (n = 7) (Table 2).

Predicted ultrasound findings. Based on the initial clinical diagnoses, 34 patients were predicted to have single ultrasound findings (Figure 5(a)) and 16 predicted to have multiple findings (Figure 5(b)).

Actual ultrasound findings. The actual ultrasound findings detected are shown in Figure 5(a) and (b).

Predicted findings confirmed. Ultrasound findings predicted by the initial diagnosis were sonographically confirmed in 33/50 patients.

New findings detected. The initial diagnosis was unconfirmed in 17/50 (34%) cases. In all cases, a new or additional ultrasound finding was detected, equating to an additional diagnosis for every three ultrasound scans performed.

Reducing diagnoses. In the 16 patients where multiple findings were predicted, ultrasound was able to simplify to a single ultrasound finding (and single clinical diagnosis) on 11 occasions (69% of cases).

Actual changes to final clinical diagnoses. Overall, clinicians described ultrasound as altering the final clinical diagnosis in 5/50 cases (10%) and providing an additional diagnosis (in conjunction with primary clinical diagnosis) in a further 12/50 cases (24%).

Changes in diagnostic confidence. Following ultrasound, there was an overall increase in clinician diagnostic confidence in 22/50 cases (44%). Clinician confidence increased more often when ultrasound findings

Demographic data					
Ν	50				
Age (mean \pm SD)	71 ± 13				
Gender	F = 20 (40%)				
PaCO ₂ mmHg at admission. Median (1st, 3rd Quartiles)	45 (35, 55)				
$PaCO_2 > 45 mmHg$	23/48 (48%)				
Chest computed tomography prior to admission	12 (24%)				
Transthoracic echocardiogram prior to admission	8 (16%)				
Initial clinical diagnosis(es)					
Single diagnosis:					
Exacerbation of COPD or asthma	7				
Left ventricular failure	5				
Pneumonia	13				
Right ventricular failure	I				
Interstitial lung disease	2				
Pulmonary embolism	I				
Other ^a	5				
Multiple diagnoses:					
LVF and RVF	7				
LVF, RVF and pneumonia	5				
LVF and pneumonia	I				
RVF and pneumonia	I				
Pneumonia and effusion	2				

 Table 2. Patient demographics, prior investigations, and initial clinical diagnoses.

^aDiagnoses were: hypoventilation (n = 4) and acute respiratory distress syndrome (ARDS) (n = 1).

SD: standard deviation; PaCO₂: partial pressure of arterial carbon dioxide; COPD: chronic obstructive lung disease; LVF: left ventricular failure; RVF: right ventricular failure.

confirmed the initial clinical diagnosis (18/33) than when new ultrasound findings were discovered which called into question the validity of the initial diagnosis (4/17), p = 0.036.

Changes in management. As a result of the ultrasound findings, patient management was modified in 15/50 cases, giving a 'number needed to scan' of 4. The most common clinical context for this occurring was in patients with crackles on chest auscultation and chest X-ray opacification, with management being altered on 10 occasions in this group (10/26 or 39%).

Patients who had multiple initial clinical diagnoses (and thus multiple predicted ultrasound findings – Figure 1(b)) were more likely to have a change in management following ultrasound scanning (8/16 patients, compared to 7/34 patients with a single diagnosis, p = 0.034).

Major management changes were made in six patients, comprising addition of medication (n=2), further investigations such as computed tomography scanning (n=2), or diaphragm screening with cessation of medication (n=1), or intercostal catheter insertion (n=1). Minor changes occurred in 9/15 patients, reflecting changes in dosage (n=6), route of medication administration (n=2) and a decision not to perform pleural aspiration (n=1).

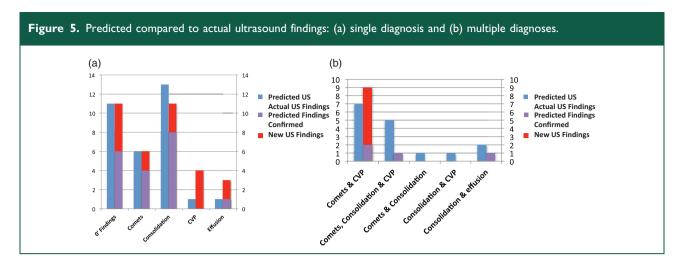
Influence of alternative imaging modalities. Twelve of 50 had undergone a computed tomography chest during the hospital admission prior to ultrasound examination, with a median time between computed tomography and ultrasound of 3.5 days (Quartiles: 1,8.5). Five patients had computed tomography within 48 h prior to RCU admission (recent computed tomography) and seven more than 48 h prior (remote computed tomography).

Having a computed tomography prior to ultrasound, recent or remote, did not change the likelihood of ultrasound changing diagnosis, diagnostic confidence or management.

Discussion

In this cohort of adults with acute respiratory failure managed in a specialised hospital ward, thoracic ultrasound was a useful adjunct to standard care. The C₃PO protocol, which was designed specifically for acute respiratory failure, appears feasible to perform and to have substantial clinical utility. On the basis of ultrasound findings, alternative clinical diagnoses were suggested in 34%, diagnostic confidence enhanced in 44% and management modified in 30% of cases.

In our cohort, ultrasound confirmed the predicted sonographic findings and supported the initial diagnosis in 66% of cases. When the original diagnosis was not confirmed on ultrasound, an alternative diagnosis was always suggested by new ultrasound findings. A diagnostic change was suggested most frequently among patients with crackles on auscultation and



opacification on chest X-ray. This is a common clinical problem, whereby both pneumonia and left ventricular failure may result in similar clinical findings. Our data suggest ultrasound is highly effective at resolving this diagnostic dilemma, with recent literature supporting the notion that ultrasound is accurate in this context.¹⁴

When ultrasound supported the clinical diagnosis, i.e. confirming predicted findings and detecting no additional findings, significantly more clinicians indicated improved diagnostic confidence.

Management changed following ultrasound in 30% of cases, more frequently when there were multiple initial diagnoses, and also when ultrasound findings were discordant with the clinical impression.

Thoracic ultrasound has previously been examined in acute respiratory failure in intensive care settings.^{5,6,8} In that context and in expert hands, it appears to have a high diagnostic accuracy⁵ and significant utility.^{6,8} Our study extends those findings to patients with acute respiratory failure managed by respiratory physicians in an intermediate care setting. The incidence of acute respiratory failure *not* requiring intensive care unit or invasive ventilation is not well reported and difficult to estimate, but clinical experience suggests that this hospital cohort significantly outnumbers the intensive care unit cohort. Our results therefore suggest that ultrasound may be useful in a wider context than previously appreciated.

The context of our study also differs from previously reported intensive care cohorts in several important ways.

First, respiratory failure was less severe compared to intensive care cohorts^{5,7} as our patients did not require intubation and invasive mechanical ventilation. Intuitively, a less florid disease process may affect less lung parenchyma and thus be harder to detect on ultrasound. Second, our patients were complex and many had multiple diagnoses at both admission and discharge. Previous studies in intensive care unit settings have explicitly excluded⁶ such cases or reported their occurrence at a low frequency,⁵ yet our data suggest that these are exactly those patients who benefit most from ultrasound. When the clinician postulated multiple diagnoses in our cohort, ultrasound was able to simplify to a single process more than two thirds of the time.

Third, the causes of acute respiratory failure in our cohort were different to those of intensive care patients, with no cases of multi-organ failure or septic shock, and only one case of acute respiratory distress syndrome. Fourth, non-intubated patients such as those in our cohort are more likely to be semi-erect and tachypnoeic, making ultrasound more challenging to perform.

Finally, respiratory physicians as a craft group are generally less experienced in sonography than intensive care specialists. Additionally, previously published critical care studies have often augmented thoracic ultrasound with focused echocardiography,^{25,26} which we did not perform. It is therefore reassuring to find a similar utility for single modality thoracic ultrasound in our hands when compared to these intensive care unit protocols.

Limitations

This was a small prospective observational cohort study in a single centre and limitations of the study should be acknowledged. Patient sampling was nonconsecutive due to a weekday service and incomplete sonographer availability; however, the sample was representative of the typical RCU workload at this hospital. Patients were scanned up to 24h after RCU admission, and the time to ultrasound scanning varied between patients. This could have influenced the perceived utility of ultrasound. Lastly, we acknowledge that no diagnostic gold standard was available for the clinical diagnosis in our cohort; however, diagnostic uncertainty is common among patients with acute respiratory failure.²⁵ These findings require confirmation in larger prospective studies.

Conclusion

In adults with acute respiratory failure managed in an intermediate care setting, thoracic ultrasound performed by respiratory physicians may beneficial with regards to improving clinician confidence, altering diagnoses and changing management. We have demonstrated that the addition of thoracic ultrasound to standard care was able to influence these important outcomes with a relatively low 'number needed to scan' of three to four patients. Such an approach has the potential to aid timely commencement of appropriate care, although it comes at the cost of capital outlay, acquisition of expertise, and 20 min of sonography time per patient.

Declarations

Competing Interests: None declared.

Funding: None declared.

Ethics approval: Approval by Melbourne Health Research and Ethics Committee (HREC ID: QA2014048) as a low-risk study.

Guarantor: PW.

Contributorship: PW: Performed ultrasound examinations, participated in study coordination, collated and analysed data, drafted manuscript; SJ: Performed ultrasound examinations, helped draft manuscript; LH: Performed ultrasound examinations, helped draft manuscript; DS: Assisted in data analysis, helped draft manuscript; MH: Conceived of study, participated in design and coordination, performed ultrasound examinations, assisted in data analysis and helped draft manuscript. All authors read and approved final manuscript.

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