



ORIGINAL ARTICLE

Diagnostic Performance of Point of Care Ultrasound Compared to Chest X-Ray in Patients with Hypoxia at a Teaching Hospital Emergency Department in Uganda

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ABSTRACT

Background: Hypoxia is a common presentation in the Emergency Department (ED) worldwide. It affects 9–12% of hospitalized adults in Sub-Saharan Africa. Timely diagnosis of the multiple causes such as pneumonia, heart failure among others is challenging. Chest X-Ray (CXR), one of the most utilized imaging modalities has many limitations, and the gold standard (Computed Tomography scan) is inaccessible. Point of care ultrasound (PoCUS) is more available and increasingly being used, however little is known of its performance in resource limited EDs. The study aimed to assess the diagnostic performance of PoCUS compared with CXR in identifying the causes of hypoxia in the medical ED.

Methods: 49 adults presenting with hypoxia ($SpO_2 \leq 88\%$) in the medical ED were evaluated. Ultrasound of the lungs and heart (PoCUS) was done, then CXR obtained. Lung ultrasound (LUS) was compared with CXR (first reference standard). Chest X-Ray and PoCUS were each compared to the physician diagnosis (second reference standard) to determine agreement using an acceptable disagreement cut-off of 15%.

Results: 31% more abnormalities were identified by LUS than CXR. Lung ultrasound findings agreed with CXR in 86% of the participants with moderate reliability ($\kappa=0.75$). There was no significant difference between the actual findings of the two tests ($X^2=2$, $p=0.1$). Using the second reference, 82% of the CXRs were similar with weak reliability ($\kappa=0.5$) compared to 98% of PoCUS findings with strong reliability ($\kappa=0.9$). Compared to PoCUS, CXRs significantly differed from the physician diagnosis ($X^2=0.85$, $p=0.38$ vs $X^2=8.5$, $p=0.004$ respectively).

Conclusion: Overall, PoCUS was not inferior to CXR when compared to final physician diagnosis in identifying causes of hypoxia, and LUS and CXR had comparable performance. Significantly more abnormalities were identified on PoCUS and it demonstrated better agreement and strong reliability with the physician diagnosis than CXR. We recommend PoCUS use in patients with hypoxia attending resource limited in- and pre-hospital settings.

African relevance

- Hypoxia is a common presentation with many differential diagnoses in the ED.
- Investigative challenges in the ED often lead to missed or delayed diagnoses
- Point of care ultrasound can be safely and promptly performed at the patients' bedside in to quicken management in resource limited settings.

Introduction

Hypoxia presents in 9–12% of hospitalized adults in Sub-Saharan Africa and has multiple causes ([1,2]). Immediate diagnosis remains a challenge yet timely management is key to avert unfavorable outcomes. Hypoxia can be diagnosed by Arterial Blood Gas (ABGs) or pulse oximetry. The latter is simple and more readily available especially in limited resource settings ([3,4]). Similarly, identification of the causes of hypoxia in these settings relies heavily on clinical examination and Chest X-Ray (CXR) (5, 6).

Although CXR is one of the most utilized imaging modalities, it has many limitations including a low validity, and a high inter- and intra-

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rather variability. It also misses over 50% of the causes of hypoxia. That said, CXR performs well in identifying pleural effusions, pneumothoraces and Acute Decompensated Heart Failure (ADHF) [6–10].

These limitations result in the need for advanced tests like Computed Tomography scans (CT) and echocardiography which are not readily accessible in most resource limited Emergency Departments (EDs). To solve this, Point of Care Ultrasound (PoCUS) is increasingly being used as an added diagnostic modality especially in hypoxia [11,12]. Point of care ultrasound is performed and interpreted by the treating clinician during a patient encounter to guide evaluation and management. In this study PoCUS comprised lung ultrasound (LUS), cardiac and inferior vena cava ultrasound (CUS and IVC). Lung ultrasound was performed on each hemi-thorax in five zones; one posteriorly with the patient upright, and two in anterior and axillary zones with the patient 30–45° [13].

It provides quicker diagnosis, safer interventions and monitoring without the risk of ionizing radiation. In some studies, PoCUS demonstrated better accuracy than CXR and was similar to chest CT for most causes of hypoxia [5,13–18].

A meta-analysis on accuracy of CXR and Lung Ultrasound (LUS) compared to chest CT recommended LUS as a first-line test for respiratory symptoms [6]. PoCUS was also recommended in the initial assessment of cardiovascular compromise and hypoxia [18–20]. In Tanzania, it changed the impression in up to 45% of cases [21]. In Rwanda, PoCUS improved diagnostic accuracy in over 50% of dyspneic patients and identified pneumonia and ADHF as the most frequent diagnoses [22]. Studies comparing LUS and CXR have produced variable findings [23–25]. However, agreement between LUS and final diagnosis was high compared to CXR and final diagnosis [10,26,27].

In Mbarara Regional Referral hospital (MRRH) ED, hypoxia and associated symptoms like dyspnea are common. Hypoxia accounts for 40% of presentations and significantly contributes to ED morbidity and mortality [28]. The limited accessibility to CXR and CT compounds this problem.

Even with the diagnostic challenges above, PoCUS use is currently on a “as needed” basis in these patients due to limited local evidence to support protocolized routine use. Documentation of the performance of PoCUS as diagnostic tool will increase routine use consequently hastening management of hypoxic patients.

We aimed to evaluate the diagnostic performance of PoCUS compared with CXR in identifying the causes of hypoxia among medical ED patients.

Methods

Study design, setting and duration

This was a cross-sectional study in MRRH, a public referral and teaching hospital serving over 4 million people. The ED admits approximately 30 patients per day

Data was collected over a nine-month period (January–September 2020) albeit with COVID-19 interruptions.

We hypothesized that there was no difference between LUS and CXR as well as CXR or PoCUS findings, and the physician diagnosis in identifying the causes of hypoxia. In this study, PoCUS comprised LUS, CUS and IVC assessments.

We included all consenting adults (≥18 years) with Oxygen Saturation (SPO2) of ≤88% on room air. We excluded those that required immediate mechanical ventilation or interventions such as thoracocentesis, thoracostomy or pericardiocentesis before PoCUS and CXR. Patients that died before study tests or did not have documented final physician diagnosis were excluded.

A sample size of 49 participants was used, assuming 15% disagreement between observers of CXR and LUS, or PoCUS/CXR and physician diagnosis from previous studies and unknown agreement coefficient

(Cohen Kappa statistic) [29] using the formula:

$$n = \frac{4\pi(1 - \pi_D)Z_{1-\alpha/2}^2}{W_D^2}$$

Where n = sample size, π_D = disagreement probability=15%, W_D (type II error)=0.2, $Z_{(1-\alpha/2)}^2$ = probability value in standard distribution table at a chosen significance level (Type I error α)= 0.05 and 95% Confidence level= 1.96.

Data collection procedure

Screening for eligibility and enrolment were done after patient admission to the medical ED. Assessment and management were according to the usual standard clinical practice. SPO2 was measured using a pulse oximeter (CONTEC-CMS50N) [30].

A SonoSite™ M-Turbo ultrasound machine with phased array (1–5 MHz), curvilinear (2–8Hz), and linear (7–13 MHz) probes was used by Emergency Medicine (EM) residents for PoCUS. The findings and diagnoses from PoCUS were noted in the chart and study tool. Videos were shared electronically and interpreted by two independent and blinded Emergency Physicians (EPs).

Within less than 24 hours of performing PoCUS, participants were transferred for CXR. CXRs were obtained using a manual Fujifilm x-ray machine [31]. The treating physicians interpreted the CXR (films) and noted their findings and diagnoses in the chart and study tool. Radiograph pictures were taken under the film viewer using a phone camera (8–12 megapixels) and shared for interpretation by two independent and blinded radiologists.

Physician diagnoses were derived from the chart, and these took into account physical examination, laboratory results, PoCUS, and CXR findings. These physicians were not blinded to test findings since they had been noted in the charts. LUS and CXR were compared as well as CXR and PoCUS findings with the physician diagnosis (See Supplementary Data B and E for findings used and Fig. 1 for systematic study flow).

Data management and analysis

Data was analyzed using Stata ver12, and the Standards of Reporting of Diagnostic Accuracy checklist (STARD) was used for completeness of reporting. Demographics, SPO2, comorbidities and presenting symptoms were summarized. Univariate analysis was done for continuous variables to derive the median and interquartile ranges. Categorization of CXR and PoCUS findings followed the features in **supplementary data B and E** [44,45]. Using 2×2 tables, performance of LUS was measured against CXR, and then CXR and PoCUS (LUS, CUS, IVC) measured against physician diagnoses to determine agreement.

Reliability between interpreters was determined using Cohen Kappa statistic graded as: none (0.0–0.2); Minimal (0.21–0.39); Weak (0.40–0.59); Moderate (0.60–0.79), Strong (0.8–0.9) and Perfect (>0.9). McNemar Chi-square (χ^2) was determined to test for differences between the LUS and CXR; then each of CXR and PoCUS with the physician diagnosis. We determined 95% confidence intervals for precision and used level of significance of 0.05.

Quality control: PoCUS was performed by certified level 1 and lung ultrasound users with at least 1 year of experience. Blinded radiologists and EPs provided independent interpretation of still images and videos respectively. Amidst disagreement between the primary (EM-residents and physicians) and secondary (Reviewers) reports, the latter were considered as final diagnoses. Patient data was shared only for independent review and patient care. Approval was sought from the University Research Ethics Committee.

Results

Forty-nine patients with a median age of 45 years were enrolled. Majority (55%) were female, and had a median SPO2 of 79%. Difficulty in breathing was the most frequent symptom (61%). Respiratory comorbidities included COPD, asthma, and TB, while cardiovascular disease

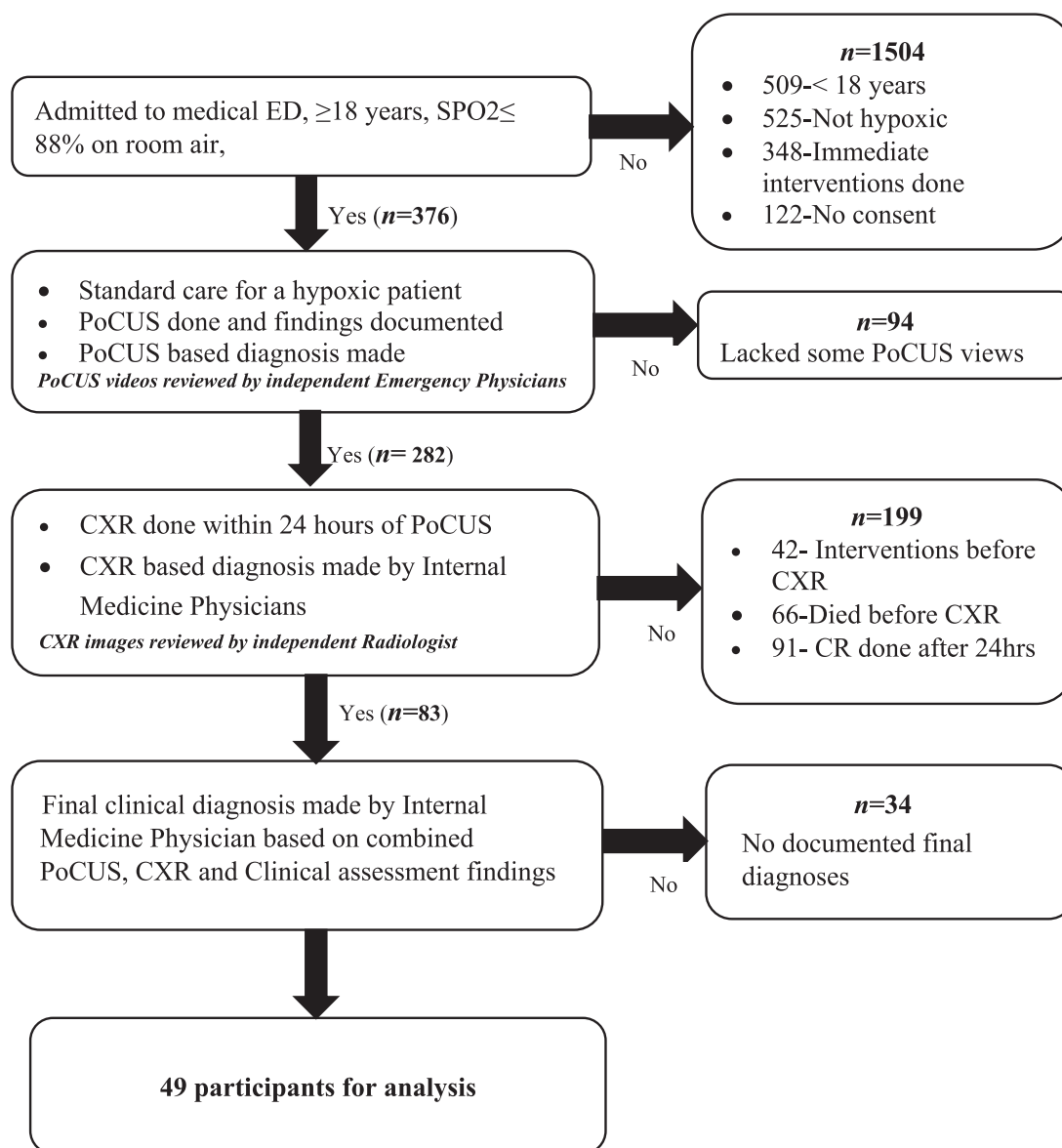


Fig. 1. Study Flow Chart.

included Acute Decompensated Heart Failure (ADHF), Ischemic Heart Disease and valvular disease. (See Table 1 for detailed baseline characteristics).

Comparison of LUS findings with chest X-Ray findings

Chest X-Ray (CXR) identified 41 (86%) while LUS found 46 (92%) abnormal findings. Pleural effusion, pneumonia and ADHF were the commonest patterns on both tests. LUS revealed 31% more abnormalities than CXR ($p < 0.001$).

Reliability between the observers and reviewers of the CXR was minimal ($K=0.23$) compared to that of PoCUS which was strong ($K=0.9$).

Of the 43 participants with abnormal CXRs, 37 (86% percent agreement) had similar abnormalities on LUS ($K = 0.75$, 95% CI: 0.55-0.95), best with pyopneumothorax and COPD, and worst with pneumonia. There was no statistical difference between diagnoses made by CXR and LUS ($X^2=2$, $p=0.1$) (see Table 2)

Chest X-Ray and physician diagnosis comparison

Pulmonary edema/ADHF (34%), pleural effusion (30%) and consolidation (32%) accounted for majority of physician diagnoses. Physician

diagnoses and CXR were similar in 40 participants (82% agreement, $K=0.5$, 95% CI: 0.2-0.8).

Chest X-Ray performed best with empyema (100%), pericardial and pleural effusion ($\geq 80\%$) and ADHF (71%) with strong to perfect reliability. There was a difference between the actual CXR and physician diagnoses ($X^2=8.5$, $p=0.004$). (See Table 3)

Cardiac ultrasound before PoCUS diagnoses were made

Twenty-six (53%) participants had cardiac abnormalities with good reliability ($K=0.77$, 95% CI: 0.69- 0.85). The top abnormalities were chamber dilatation (28%), pericardial effusion (16%), reduced LVEF (14%) and valvular abnormalities (12%).

Majority (43%) had full IVCs (volume overload), 22% flat IVCs (hypovolemia) and only 8% were normal with moderate reliability ($K=0.67$, 95% CI: 0.52-0.82). Majority (49%) of the participants with cardiac abnormalities had full IVCs.

POCUS versus physician diagnosis

Overall, PoCUS findings were similar in 48 (98%) participants with strong reliability (0.9, 95% CI: 0.7-1). For specific physician diag-

Table 1
Baseline characteristics.

Characteristic		Median (Interquartile range)	N=49 (%)
Age	Years	45 (30-60)	
Sex	Female		27 (55)
SPO2 (%)	Overall	79 (77-85)	
Associated symptoms	Difficulty in breathing (total)		30 (61)
	Difficulty in breathing only		4 (8)
	Difficulty in breathing with cough		9 (18)
	Difficulty in breathing with body swelling		5 (10)
	Difficulty in breathing with chest pain		7 (14)
	Cough with chest pain		2 (4)
	Cough with body swelling		4 (8)
	Difficulty in breathing with easy fatigability		5 (10)
	Fever with other symptoms,		5 (10)
	Altered mental state/seizures		4 (8)
	Others		5 (10)
Comorbidities	Respiratory disease		6 (12)
	Cardiac disease		6 (12)
	Hypertension		5 (10)
	Renal disease Liver disease		3 (6)
	Mental illness (Para-suicide, alcohol use)		2 (4)
	Diabetes Mellitus		4 (8)
			4 (8)
	Malignancy, UGIB, SCD		4 (8)
	None		15 (30)
HIV status	Negative		41 (84)
Smoking	No		43 (88)

Table 2
LUS compared with the CXR findings.

Diagnoses	CXRAbnormalities No (%)	LUSAbnormalities No (%)	Pvalue	LUS- CXRagreement (%)	X ² (Pvalue)
Participants	43 (86%)	46 (92)			
ADHF (pulmonary edema)	8 (16)	17 (35)	0.044	5 (63)	1.32 (0.25)
Chronic lung disease	5 (10)	6 (12)	1.264	4 (80)	0 (1)
Pleural effusion	17 (35)	21 (43)	0.498	8 (47)	0.39 (0.53)
Consolidation/ Pneumonia	10 (20)	17 (35)	0.120	4 (40)	2.88 (0.09)
	3 (6)	4 (8)	0.983	3 (100)	0 (1)
Pyopneumothorax/empyema					
COPD/Asthma	1 (2)	4 (8)	0.121	1 (100)	1 (0.32)
Lobar collapse	7 (14)	6 (12)	1.384	5 (71)	6 (0.01)
Lung mass/TB	10 (20)	9 (18)	0.242	8 (80)	8 (0.32)
Total observations (n)	61	80	0.001	37 (86)	2 (0.1)

Table 3
CXR and PoCUS findings compared with the physician diagnosis.

Physician Diagnoses	Total diagnosesn (%)	CXRfindings (%)	Difference between CXR and physician diagnoses [X ² (P value)]	PoCUS Findings (%)	Difference between PoCUS and physician diagnoses: X ² (P value)
ADHF (pulmonary edema)	17 (34)	12 (71)	0.1(0.72)	12 (71)	0.25 (0.61)
Right heart failure (RHF)	5(10)	0 (0)	5 (0.03)	4 (80)	0.11 (0.74)
COPD	4 (8)	1 (25)	4.5 (0.03)	1 (25)	2.67 (0.01)
Consolidation/ pneumonia	16 (32)	9 (56)	2 (0.16)	11 (69)	0.5 (0.48)
Possible TB	12 (24)	5 (42)	1 (0.31)	9 (75)	0.04 (0.83)
Chronic lung disease	3(6)	2 (67)	7 (0.08)	3 (83)	0.5 (0.48)
Pleural effusion	15 (30)	12 (80)	0.03 (0.85)	12 (80)	0 (1)
Pyopneumothorax/ empyema	3 (6)	3 (100)	0 (1)	3 (100)	0 (1)
Lung mass	1 (2)	5 (100)	2 (0.1)	1 (100)	0 (1)
Pericardial effusion	7 (14)	6 (86)	7 (0.01)	7 (100)	0 (1)
Total observations(n)	49	40 (82)	8.5 (0.004)	48 (98)	0.85 (0.38)

noses, PoCUS performed best with pericardial effusion, lung mass and Empyema, and worst with COPD.

All diagnoses had moderate to perfect reliability between interpreters. Except for COPD, there was no significant difference between the actual PoCUS and physician diagnoses ($X = 0.85$, $p0.38$) (See Table 3).

Discussion

The study compared PoCUS and CXR findings with the physician diagnoses in hypoxic patients. The methodology was based on FDA recommendations for diagnostic accuracy studies [32], particularly useful in settings with inaccessible gold standard tests. Overall, PoCUS had similar diagnostic performance to CXR, as based on an acceptable percent disagreement of 15%.

LUS and CXR (reference) comparison

Lung Ultrasound (LUS) identified more abnormalities when compared with CXR. LUS and CXR findings agreed in 86% of the participants similar to other studies [23,25,33]. Although the most common abnormalities detected by both tests were pulmonary edema, pleural effusions and pneumonia, LUS diagnosed fewer of these than CXR, which is in contrast to previous studies [34,35].

The findings could be because LUS was interpreted using multiple views of saved videos while CXR interpretation relied only one view (PA or AP) of film images, and the higher sensitivity and specificity of LUS than CXR. Since LUS looked at ten lung chest regions, it detected even small abnormalities compared to the six routine lung zones of CXR interpretation. Pulmonary edema was the only cause where LUS performed significantly better than CXR as in several studies [7,15,20]. However, it had weak reliability possibly from confusion with other conditions that appear the same on LUS.

Based on the acceptable percent disagreement, LUS and CXR agreed in half of the study diagnoses. Some LUS features may be used for different causes of hypoxia often leading to misclassification, over or underdiagnosis (See Supplementary Data B). For example, pulmonary edema and CLD, and pneumothorax and COPD were possibly misreported depending on the user. Pulmonary edema occurs with a thin smooth pleural line while CLD with a thick uneven pleural line [36]. In assessing for pneumothorax and COPD, there was lack of reports on A-lines and the lung point which improve specificity of either in this study. However, there was correct identification of lack of pleural sliding required for quick diagnosis & management of a non-ventilating lung as may occur when both conditions are advanced [27].

LUS and CXR findings agreed in 86% of the participants similar to other studies [23,25,33]. Although the most common abnormalities detected by both tests were pulmonary edema, pleural effusions and pneumonia, LUS diagnosed fewer of these than CXR, which is in contrast to previous studies [34,35].

Chest radiography performed better in identifying lung collapse contrary to previous reports(25), similarly explained by “misclassification” as consolidation since they appear similar on LUS. Lobar collapse was more readily identified on CXR using lung volume loss and lack of air bronchograms. Dynamic or static air bronchograms which are specific for pneumonic consolidation and collapse respectively ensure specificity of the two pathologies [37], however these were not reported, emphasizing user-dependent PoCUS interpretation. Lung ultrasound identified fewer patients with malignancy/TB basing on variable diagnostic features, thus further exploration in a bigger and homogenous study population is recommended.

The study tests having differed in 14% participants confirms the need for a proper gold standard test in any accuracy study to act as a tie-breaker for differing findings. This is key despite the fact that there was no significant difference when the patterns by both tests were analyzed.

Based on this analysis however, the hypothesis that LUS is similar to and could replace CXR in hypoxia, was proven, but needs further sensitivity studies in our setting.

CXR and PoCUS compared with physician diagnoses (reference)

Overall, 82% (weak reliability) CXR findings versus 98% (strong reliability) PoCUS (lung and cardiac) findings were similar to physician diagnoses, proving our hypothesis. Specific CXR findings significantly differed from the physician diagnoses which was in contrast to PoCUS findings. Using our 20% disagreement cut off, CXR specifically agreed with only four of ten physician diagnoses, yet PoCUS agreed with six including CLD and Right Heart Failure (RHF). Our findings are similar to previous reports on CXR [9] and PoCUS [26,27] accuracy. Added to standard care, PoCUS improved diagnostic accuracy [7,21,22,34,38,39], however, most of these studies did not include CXR since chest CT scan was available. In our study, physicians were more likely to use PoCUS findings compared to CXR because it provided more observations, emphasizing usefulness of PoCUS as a diagnostic for hypoxic patients. We recommend further research on how PoCUS influences physician diagnosis as our study did not focus on this.

While PoCUS could pick up mild pathology, the accuracy of CXR improves with increasing severity and duration of illness such cardiac congestion. In pyo-pneumothorax, CXR performed excellently and this differed from studies where over 30% pneumothoraces were missed [10]. Our study participants were severely ill as showed by the median level of hypoxia (SPO of 79%), and therefore improved CXR performance in some diagnoses. Coexistence of pneumothorax together with pyo/hydrothorax provided obvious diagnostic signs like a meniscus, air-fluid level, pleura separation by hyperlucency, and opacity, making it easier to identify both pneumothorax and pleural effusion. The low utility and reliability of CXR in COPD is not different from what GELAW, 2015 reported [40].

That the PoCUS protocol in our study comprised multiple sites (lung, heart, IVC) explains the bigger number of observations and physiological causes similar to the physician diagnoses. The advantages of PoCUS over CXR were more evident in patients with shock, pericardial effusion and RHF where it allowed real-time assessment and test repetition at the bedside without worrying about deterioration during patient transfer for Chest X-Rays (CXR). It also enabled immediate interventions such as thoracentesis, pericardiocentesis, cautious fluid resuscitation and further tests like sample analysis. Whereas a clinician would use cardiomegaly a non-specific sign on CXR to diagnose pericardial effusion, CUS performed better at confirming presence, size and cardiac effect as observed here and in past studies [19]. European Respiratory Society reported lower accuracy on of CXR versus LUS alone or in combination with other sites [10].

Finally, the reliability between performers and reviewers of CXR was minimal compared to PoCUS (strong). This is because PoCUS has a steep learning curve [41,42] while CXR interpretation is affected by complex superimposition of anatomical structures causing a slow learning curve [10,43].

Limitations

Firstly, our study did not use the ideal reference test (chest CT scan) to determine accuracy. However, this was mitigated by using a second reference (physician diagnosis) as recommended by FDA diagnostic guidelines. Secondly, there was inclusion bias as the final diagnosis we used was based on the findings of both ultrasound and x-ray and not on an independent gold standard. However, the independent physicians' reviews provided for some mitigation of this bias.

Thirdly, PoCUS technique and interpretation are operator dependent, however, the EM residents were re-trained before the study to minimize interpretation variability. The study also had many exclusions (199). 157 of these were due to delayed X-ray tests following power outages complexities of transferring oxygen dependent patients. Lastly, the independent reviewers for CXR used pictures taken under a film

viewer while those for PoCUS used videos, which introduced interpretation bias. This bias was minimized by obtaining interpretations by treating physicians, using blinded specialists as reviewers, and determining interrater reliability.

Conclusion

Overall, the findings showed that PoCUS was not inferior to CXR when compared to final physician diagnosis in patients with hypoxia, and similarly, LUS and CXR had comparable performance. Both tests were similar in majority of the participants with moderate reliability. PoCUS demonstrated significantly more similarities with the physician diagnoses compared to CXR, and had strong reliability.

We recommend PoCUS as an alternative to CXR for patients with hypoxia in resource limited Emergency Departments (ED) and pre-hospital settings. Other ED clinicians should be trained in PoCUS provision since its findings are user dependent. This will reduce waiting time for chest x-rays, ensuring timely management of patients with hypoxia. Studies on sensitivity and specificity using the gold standard test in a larger population, and on influence of PoCUS on clinician diagnosis is recommended to overcome our study limitations.

Dissemination of results

Information relevant to patient care was informally shared with the treating clinicians immediately after PoCUS and CXR to guide diagnosis. The study findings were shared with Faculty of Medicine at MUST and MRRH Emergency Department clinicians through a formal presentation, and at the international conference on Emergency Medicine 2021.

Authors' contribution

Authors contributed as follows to the conception or design of the work; the acquisition, analysis, or interpretation of data; and drafting the work or revising it critically for important intellectual content: PMK contributed 50%; BKD 15%, DH 7.5%, AM 7.5%, HC, JAO, NLG, and OP 5% each. All authors approved the version to be published and agreed to be accountable for all aspects of the work.

Declaration of Competing Interest

The authors declared no conflicts of interest

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.afjem.2023.02.004.

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