

https://dspace.org/

The utility of point of care ultrasonography driven by clinicians in the assessment and investigation of lung pathologies

Molepo, Samuel Ditau

2022
https://hdl.handle.net/10539/34731

Downloaded from a DSpace repository. https://dspace.org/

Submitted in fulfilment of the requirements for the degree Master in Medicine (MMed) Internal Medicine

The utility of point of care ultrasonography driven by clinicians in the assessment and investigation of lung pathologies

Candidate:
Dr Samuel Ditau Molepo
MBBCh (Wits), Dip HIV Man (SA)
Registrar: Department of Internal Medicine
University of the Witwatersrand, Johannesburg
0600849G

Supervisors:
Dr SA van Blydenstein
MBBCh (Wits), DCH, FCP (SA), Cert. Pulmonology (SA), MMed (Int. Med.)
Specialist Physician and Pulmonologist
Department of Internal Medicine
Chris Hani Baragwanath Academic Hospital
University of the Witwatersrand, Johannesburg

Dr Anita Graham
MBBCh (Wits), FCP (SA), Cert. Pulmonology (SA)
Specialist Physician and Pulmonologist
Helen Joseph Hospital
Department of Medicine and Pulmonology
University of the Witwatersrand, Johannesburg

Declaration

I, Samuel Ditau Molepo, declare that this research report is my own work which is being submitted for the degree Master of Medicine (in the submissible format with my protocol and an extended literature review) in the department of Internal Medicine at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at this or any other university.



……

11th day of May 2022

Acknowledgements
First and foremost, I thank my late parents, Grace and June Molepo for instilling a work ethic within me. My mother, herself an academic, believed in hard work and dedication to a cause. Even up to her death, she was always striving for her ultimate improvement.

I would also like to thank my 3 brothers and close friends for always providing unwavering emotional support. Throughout my career, you have had to take a backseat, all in the name of my academic advancement and the care of my patients. I shall cherish you always. A special thank you to Dr Lindokuhle Goqwana for her stern support, both academic and personal, and for always picking up the phone when I am in distress.

Lastly, I would like to thank my supervisors and teachers, Drs van Blydenstein and Graham, for believing in me enough to take this project. And, despite close deadlines, I hope to have made you proud.

Abstract

Background

Point of care ultrasonography (POCUS) is increasingly widespread in its use across most developed countries. In South Africa, it has been routinely used within emergency medicine and critical care medicine while its uptake in internal medicine has been slow.

Objectives

To describe the utility of point of care ultrasonography as used by the division of pulmonology in terms of its indications, findings, and safety profile.

Methods

A retrospective record review was undertaken of patients who underwent assessment with point of care thoracic ultrasonography at Helen Joseph Hospital by the division of pulmonology from 13 October 2017 to 31 July 2019.

Results

A total of 141 patients underwent thoracic POCUS of which 19.9% were for qualitative (imaging only) purposes, and 80.1% for interventional purposes. Of the interventional arm, the most common procedures were POCUS guided thoracocentesis followed by POCUS guided lung biopsies. The commonest cause of pleural effusions was found to be exudative pleural effusions that could not be further specified, while the commonest biopsy result was adenocarcinoma of the lung. The major complication rate was 0%, and minor complication rate was 12%.

Conclusion

There is a role for the expanded use of POCUS within internal medicine, specifically pulmonology. This study, although small, is in line with international literature that shows POCUS to be safe, cost effective, time saving and it can improve diagnostic accuracy.

Table of contents

Declaration....2
Acknowledgements....3
Abstract....4
Table of contents....5
List of tables and figures....6
List of abbreviations....7
Chapter 1: Protocol with extended literature review....8
1.1 Introduction....8
1.2 Research question and main objective....14
1.3 Hypothesis....14
1.4 Specific objectives....14
1.5 Methodology....14
1.6 Data collection....15
1.7 Data analysis....15
1.8 Funding....15
1.9 Ethics approval....15
1.10 Intention....15
1.11 Timeline....16
1.12 Limitations....16
1.13 References....17

Chapter 2: Submissible article.... 20
2.1 Background....21
2.2 Methodology and study population....21
2.3 Data analysis....22
2.4 Results....22
2.5 Discussion....27
2.6 Limitations....27
2.7 Conclusion....29
2.8 References....30

Chapter 3:
Appendices....31
3.1 Data collection form....31
3.2 Ethics clearance....32

List of Tables

Table 1. The demographics of patients undergoing thoracic POCUS……...22
Table 2. POCUS interventions performed, stratified by sex and HIV status..……..23
Table 3.1. Outcomes of diagnostic interventions…….…….……..…24
Table 3.2. Outcomes of thoracocentesis…….…..……..25
Table 3.3. Outcomes of POCUS guided transthoracic/pleural biopsies and procedural interventions…….....26
Table 3.4. Association between HIV status and diagnosis of infection or malignancy…….……...26
Table 4. Acute complications of ultrasound-guided procedures.. ..…….27

Graphs

Figure 1. The indications for thoracic POCUS……..…23

Abbreviations

ADA	Adenosine deaminase activity
ARDS	Acute respiratory distress syndrome
cm	Centimetres
COPD	Chronic obstructive pulmonary disease
CT	Computed tomography
eFAST	Extended focused assessment with sonography in trauma
EPCUS	Emergency point-of-care ultrasound
FASH	Focused assessment with sonography for HIV-associated TB
FAST	Focused assessment with sonography in trauma
FNA	Fine needle aspiration
HIV	Human immunodeficiency virus
HREC	Human Research Ethics Committee
ICD	Intercostal drain
ICU	Intensive care unit
IJ CVC	Internal jugular central venous catheter
IPC	Indwelling pleural catheter
mmHg	Millimetres of mercury
NHLS	National Health Laboratory Service
PCR	Polymerase chain reaction
PE	Pulmonary embolism
PFNA	Percutaneous fine needle aspiration
POCUS	Point of care ultrasonography
ROSE	Rapid on-site evaluation
RUSH	Rapid ultrasound in shock
SARS-Cov2	Severe adult respiratory syndrome coronavirus 2
SCC	Squamous cell carcinoma
Tat	Transactivator of transcription
TB	Tuberculosis
TIP30	Tat-interacting protein 30
TTFNA	Transthoracic fine-needle aspiration
UK	United Kingdom
USA	United States of America

Chapter 1: Protocol with extended literature review

1.1 Introduction

1.1.1 Historical background

Early concepts concerning ultrasonography are attributable to the Italian priest and physiologist Lazarro Spallanzani, (1729 - 1799) who was intrigued by the ability of bats to navigate in complete darkness. He experimented by blindfolding them to prove that their navigation was not based on sight, and also discovered that if their ears were occluded they could not navigate [1].

Ultrasound's first formal application was by Canadian inventor Reginald A. Fessenden who patented it in 1912 for localising icebergs following the Titanic shipwreck [1]. The term SONAR was thus coined from *SO*und *NA*vigation and *R*anging [1]. Its first medical use is credited to Karl Dussik, an Austrian Neurologist who is reported to have first used it transcranially to characterise and measure brain tumours in 1942 [1][2].

As ultrasound equipment became more compact and available, the concept of point of care ultrasonography (POCUS) began to emerge [3]. POCUS refers to ultrasonography brought to and performed at the patient's bedside with real-time results and/or intervention [3].

The earliest use of POCUS was in the setting of blunt trauma in the 1990's [4]. In the same decade United States trauma surgeons adopted the use of focused assessment with sonography in trauma (FAST) and later extended FAST (eFAST) [4]. FAST initially entailed the assessment of four abdominal quadrants as well as the pelvis, looking for free abdominal fluid as a marker for intraperitoneal bleeding. Its extension (eFAST) included thoracic assessment for haemo- and pneumothorax, as well as sub-xiphoid views for haemopericardium[4]. Prior to this, intra-abdominal injuries were assessed using peritoneal lavage as well as exploratory laparotomy [5].

In 2009, the RUSH protocol (Rapid Ultrasound in Shock) was first published by Weingart *et al* as a quick bed-side diagnostic tool for evaluating the potential causes of a medical patient with undifferentiated shock [6]. They assessed the heart looking for pericardial tamponade, right ventricular enlargement, and hypodynamic as well as hyperdynamic left ventricular dysfunction. They then assessed the inferior vena cava for volume status, evaluated Morrison's pouch looking at the four quadrants of the abdomen and looking at the thorax for a haemothorax and tension pneumothorax. In the abdomen, they also imaged the aorta for an abdominal aortic aneurysm that may have ruptured [6]. Subsequent review articles sought to simplify the protocol. Seif *et al* simplified the components into: pump (heart), tank (inferior vena cava, thoracic and abdominal compartments) and pipes (large arteries/veins) [7].

While emergency medicine as well as critical care medicine were prompt in employing POCUS, its uptake by internal medicine has been slower. In pulmonology, its applicability is vast, ranging from the early detection and quantification of

pneumothorax, differentiating pulmonary congestion and heart failure from pneumonia, assessing pleural effusions, masses and pleural disease. Its role in procedural guidance is also advantageous, especially in percutaneous guided biopsies, thoracocentesis and catheter placement [8]. This has been shown to enhance diagnostic sensitivity, decrease complication rates and is more cost effective than CT guided biopsies [9].

1.1.2 POCUS in the South African setting

Publications found in the South African literature mostly concentrate on POCUS as used in the emergency setting (FAST in the context of trauma). Smith *et al* [10] undertook a series of cases of blunt and penetrating abdominal trauma wherein FAST was performed and concluded that it had a high specificity (100%) and sensitivity (81.3%) for intraperitoneal bleeding following blunt trauma. Of note, the study was performed in a peripheral hospital in Ngwelezane, Kwa-Zulu Natal, and the ultrasound scans were performed by emergency medicine doctors who had undergone training and ultrasound accreditation [10].

A follow up study from the same centre sub-stratified trauma patients into those who were haemodynamically stable versus unstable and assessed the utility of eFAST once again [11]. Key thoracic findings were that the detection of pneumothorax by ultrasound was comparable to those by radiological (CT scan and/or chest Xray) means (with a specificity of 84.6% and sensitivity of 100%) [11], and they also found that thoracic ultrasound was able to detect pneumothoraces that were too small to be appreciated on chest X-ray [11].

In Hlabisa, Kwa-Zulu Natal, Heller *et al* [12] looked at the utility of POCUS in the diagnosis of HIV associated extrapulmonary tuberculosis and developed a protocol called focused assessment with sonography for HIV-associated TB (FASH). Herein, typical sonographic findings included pericardial effusion, pleural effusion, ascites, focal splenic lesions, focal liver lesions and upper abdominal lymph nodes greater than 1.5cm. The article reported that patient management was influenced as a result in 29 of 62 patients (47%). However no analytic data was offered to assess for impact or clinical significance. The article was also structured as an educational protocol rather than an interventional article.

Another South African study by van Hoving *et al* [13] focused on the modules of emergency ultrasound education in the background of the South African disease spectrum. The study was informed by the training that Emergency Medicine registrars receive (emergency point-of-care ultrasound (EPCUS)) which is imported from industrialised countries (USA, UK and Australia). Van Hoving *et al* sought to resolve whether or not the curriculum was suited to the broader context of the South Africa disease burden [13].

The vast scope of the EPCUS course included aortic ultrasound, eFAST, vascular access and deep venous thrombosis, cardiac, renal (including ureter and bladder), testicular, liver (including gallbladder and cystic ducts), gastrointestinal, first trimester pregnancy/pelvic, musculoskeletal, peripheral nerve blocks, pulmonary, focused assessment with sonography of HIV/tuberculosis (FASH), shock protocols and head and neck ultrasonography [13].

Importantly, this study revealed that the most frequently performed emergency ultrasounds were: pulmonary (26.1% of a total of 1933 scans), followed by musculoskeletal (15.6%), cardiac (11.3%), FASH (9.2%), renal (6.6%) and gastrointestinal (5.7%) [13]. Bias of this study was that it was undertaken in winter, therefore had a higher than usual rate of respiratory complaints. The study population was also skewed by the fact that only patients who presented during working hours were included, therefore the diverse and often complex cases that present at night and on weekends were excluded.

1.1.3 Thoracic sonography explained

In normal thoracic ultrasonography, the skin, muscles and fascial planes are seen as echogenic layers while the parietal and visceral pleura appear as a single highly echogenic line. On inspiration and expiration, the two lines "glide" upon each other giving rise to "lung slide" [14]. The negative predictive value for lung sliding is reported as 99.2–100%, indicating that the presence of sliding effectively rules out a pneumothorax [16]. However, the absence of lung sliding does not necessarily indicate that a pneumothorax is present [16]. The diaphragm is a hyperechoic line which contracts on inspiration and is best visualised through the liver or spleen [14].

The lung is poorly visualised in a normal subject, and instead artefacts created by its aeration can be seen. A-lines are horizontal echogenic parallel lines equidistant to each other from the pleura. They are perpendicular to B-lines, which move synchronously with respiration and are thought to be due to subpleural, interlobular fluid [14].

Major thoracic pathologies that can be appreciated on chest sonography include chest wall masses, pleural pathologies including effusions, pleural thickening and pneumothorax/hydropneumothorax. Within the lung itself, one can also assess for pneumonia, lung abscesses, lung tumours, pulmonary oedema and other interstitial processes, pulmonary embolism and lung cysts. Other pathologies include diaphragmatic abnormalities as well as extrathoracic lymphadenopathy [14].

Chest wall masses can be of variable echogenicity depending on their type [14], for example, a lipoma may be echogenic [17], while an abscess may be hypoechoic [18].
In the assessment of pleural effusions, thoracic ultrasound is more sensitive than expiratory decubitus X-ray in identifying small effusions [14]. The effusion appears as anechoic/hypoechoic and may move with respiration. If large, the compressed, atelectatic lung can be seen as a hyperechoic tongue-like structure [14]. Depending on the nature of the pleural effusion, it may appear as completely anechoic, complex non-septated, complex septated or homogenously echogenic. Transudates universally appear as anechoic homogenous effusions while the other three types are associated with exudates. Malignant effusions are usually anechoic and may be associated with pleural thickening and/or nodularity as well as diaphragmatic thickening and/or nodularity [14]. These pleural features often lend themselves to transthoracic ultrasound guided pleural biopsy. Inflammatory/exudative effusions are

associated with more echogenicity, can have strands/septations [14] or floating debris, referred to as the plankton sign [15].

A pneumothorax can be diagnosed through ultrasound by the absence of lung slide and A-lines; the presence of B-lines and a lung point [14]. A lung point refers to an area of transition between normal and abnormal lung as seen on sonographic M-mode [19]. It represents normal lung moving over the area of abnormal lung during inspiration [19]. The absence of lung slide is also known as the stratosphere sign and is best assessed on M-mode where normal lung sliding causes a course pattern (sandy beach), and its absence causes straight lines (stratosphere sign). The diagnosis of pneumothorax on ultrasound can be limited by emphysema, prior pleurodesis or pleural adhesions, and diaphragmatic paralysis [14].

In the early stages of pneumonia, the consolidated lung appears diffusely echogenic, with tissue-like texture that resembles the liver. Both air and fluid bronchograms are sometimes seen within the consolidation. In the setting of radiologic opacities, ultrasound is also helpful in differentiating pneumonic consolidation versus pleural effusion [14].

Atelectasis is a very common finding in the critically ill patient. It can be evidenced by a change in the cardiac echolocation, absence of dynamic diaphragmatic movement as well as its elevation by at least 2cm and the presence of a small pleural effusion. In complete atelectasis, there is absence of normal lung sliding [19]. The lung pulse is another sign of complete atelectasis where the cardiac pulsation is appreciated through the lung and the pleural lining also tends to pulsate [19].

Lung tumours can be assessed through ultrasonography if they abut the chest wall. A tumour appears as hypoechoic and high resolution ultrasound is superior to CT scan to demonstrate pleural/chest wall invasion [14], which may have implications for tumour staging. If there is associated lung obstructive atelectasis, it can be demonstrated as fluid bronchograms which represent fluid-filled airways that are appreciated on ultrasound as anechoic tubular structures [14]. They can also be caused by dense pneumonic consolidation [14].

Pulmonary oedema and other interstitial lung syndromes are represented chiefly by B-lines (comet tails), which are long vertical pathologic artefacts which obliterate A-lines (normal artefacts). In the setting of acute shortness of breath, they are reliable in differentiating pulmonary oedema from chronic obstructive pulmonary disease (COPD). Acute Respiratory Distress Syndrome (ARDS) tends to demonstrate a more patchy involvement with inhomogenous distribution of B-lines and anterior subpleural consolidation as well as absent lung sliding. Multiple, inhomogenous B-lines may also be seen in patients with diffuse parenchymal lung disease, wherein the areas of B-lines correlate well with CT areas of fibrosis [14].

Pulmonary embolism (PE) may be realised as a peripheral wedge-shaped area of hypoechoic echo pattern associated with a small pleural effusion [14]. According to the

European Society of Cardiology [20], echocardiography has a role in the emergency diagnosis of pulmonary embolism when it is associated with haemodynamic compromise [20]. Signs with the highest positive predictive values for PE include McConnell's sign and the 60-60 sign. McConnell's sign refers to hypokinesia of the free right ventricular wall compared with the right ventricular apex [20]. The 60-60 sign refers to right ventricular outflow tract acceleration time of <60ms occurring simultaneously with pulmonary arterial systolic pressures of <60 mmHg (but >30 mmHg) [21]. In the setting of right ventricular failure, it implies acute elevation in afterload, commonly due to an acute pulmonary embolism [21].

1.1.4 Antecedent South African studies on thoracic POCUS

In terms of local studies making use of POCUS, Koegelenberg *et al* [22] conducted a study in Cape Town where they compared the Abram's needle versus the cutting biopsy needle (Tru-Cut) in the diagnosis of TB pleural disease. The study made use of thoracic POCUS as a means to localise pleural fluid and/or pleural thickening and/or nodules. The outcomes showed that ultrasound guided use of Abram's needle was more likely to contain pleural tissue and that it was superior to the Tru-Cut needle in the diagnosis of pleural TB. The reproducibility of their results in everyday clinical practice may be limited by the added advantage that they had rapid on-site evaluation (ROSE) of cytologic specimens. This could mean that in resource-constrained settings, the high success rates of pleural biopsy may not be easily achieved [22].

Another study by Koegelenberg *et al* [23] looked at the diagnostic yield of ultrasound assisted transthoracic fine-needle aspiration (TTFNA) with ROSE and possible cutting needle biopsy (Tru-Cut) in the same session on patients with anterosuperior mediastinal masses. They had good results with 60% of cases definitively being diagnosed on cytology alone (epithelial malignancies and tuberculosis). The remainder of the cases were inconclusive and hence necessitated cutting needle biopsy. With the added cutting needle biopsies, they were able to make a diagnosis in 93.3% of all cases. The major complication rate was 0% (no pneumothorax or major haemorrhage). The study has the limitation of a small sample size (45 patients) which would seem to diminish the complication rate. However, because safety measures were put in place (bleeding risk ruled out, and at least 1cm tissue interface), it is not surprising that they had such a low complication rate [23].

Koegelenberg *et al* [24] also performed another study where they used thoracic POCUS to evaluate patients with pleural exudates, who had undergone an initial non-diagnostic thoracocentesis. They stratified the types of cases into those with a mass lesion abutting the pleura, those with pleural thickening and those with no/insignificant pleural thickening as seen on ultrasound. Thoracocentesis (repeat) was performed on all cases and, if non-diagnostic, ultrasound-guided closed pleural biopsy was performed. Repeat thoracocentesis was diagnostic of TB in 77.8% of cases, whose yield didn't improve significantly with the addition of closed pleural biopsy. This raises an interesting point that repeat thoracentesis has a role in patients whose initial thoracentesis was non-diagnostic, possibly attributable to the evolution of TB pleuritis. The addition of closed pleural biopsy increased the yield of malignant diagnoses from 31.0% to 89.7%. There was a low complication rate and

the authors therefore concluded that ultrasound guided thoracocentesis and closed pleural biopsy had a high diagnostic yield and was safe [24].

Koegelenberg *et al* [25] performed another study where they sought to outline the causes of malignant pleural effusion in the Western Cape. In this descriptive study, they used data from Tygerberg Hospital's division of Pulmonology as well as data from the Anatomical Pathology department at the same hospital (samples sent to their laboratory through other divisions and centres around the region). The main cause of malignant pleural effusion was lung cancer, represented in 63% of cases (chiefly adenocarcinoma 66%, squamous carcinoma 8%, and unspecified non-small cell lung carcinoma 11%). The second commonest cause was breast carcinoma, causing 11% of all cases of malignant pleural effusion. Mesothelioma accounted for 9.9% of all causes of malignant pleural effusion. They additionally offered palliative chemical pleurodesis to patients with symptomatic effusions and reported great success in terms of symptomatic relief [25].

1.1.5 International use of thoracic POCUS

Sconfienza *et al* [26] did a retrospective comparison of CT versus ultrasound guided biopsies of pleural based and peripheral lung lesions at Istituto di Ricovero e Cura a Carattere Scientifico, in Milan, Italy. They reviewed a total of 273 cases, of which 170 underwent CT guided biopsy and 103 had ultrasound guided biopsy. They did not randomise their two groups but reported similar in characteristics in each. The choice of biopsy strategy was made by the sole radiologist who undertook the biopsies. Their data showed no significant differences in the success rate of tissue retrieval and diagnostic yield but did find statistical significances in the duration of procedure (shorter with ultrasound) and rate of complication (14.7% developed pneumothorax with CT versus 5.8% with ultrasound). The limitation was that their samples were not randomised and therefore allowed for bias in terms of patients' physical characteristics as well as the nature and location of the lesions.

Rahman *et al* [27] conducted a study at the Pleural Diseases Unit, Oxford, UK where they assessed the diagnostic accuracy of respiratory physician-delivered ultrasound and also looked at its safety. The accuracy of pleural sonography was benchmarked against other radiologic modalities, the presence of pleural fluid upon aspiration and, where difficult, radiologists were shown videos of the sonographic images. On this basis, the accuracy of physician delivered ultrasound at diagnosing the presence or absence of pleural fluid was 99.6%. Of the 960 total cases in the study, only 47 were referred for second opinion by a radiologist. Of these, only 4 had discordant findings compared to initial physician findings (i.e. false negatives). In terms of safety, recorded complications only occurred in the ultrasound intervention arm where three out of 558 cases who had thoracocentesis or intercostal drain (ICD) insertion had major complications. Two had intrapleural haemorrhage requiring intervention, while the other developed an intrapleural infection. This study had a large sample size and showed conclusively that physician-delivered ultrasonography is feasible and that ultrasound guided procedures are safe [27].

Hammerschlag *et al* [28] ran a similar study at the Royal Melbourne Hospital in Australia where a series of thoracic ultrasound procedures were analysed to assess diagnostic accuracy for pleural effusion as well as its safety. Cases were seen as

consults for pleural effusions and either had a diagnostic or interventional POCUS or both. They had a database with a total of 357 scans, and a pleural effusion was correctly diagnosed in 98.3% of them. Ultrasound scans were performed variably by registrars in pulmonology (80.7% of total scans) with senior support readily available or by consultant respiratory physicians (19.3%). The major complication rate was 0.9% (2 out of 235 patients).The complications were pneumothoraces that required ICD insertion. There were other minor complications including pain, haemorrhage and pneumothoraces that did not require intervention. The article points out that the complication rate was associated with a registrar doing the procedure, since 28 of the 35 (80%) complications occurred in procedures carried out by them. However, this does not to take into account the fact that the registrars performed the majority of the ultrasound scans. Thus their total complication rate was 28 out of 288 (9.7%) versus 7 out of 69 (10.1%) [28]. All in all, this data showed good diagnostic sensitivity and low complication rates.

There is a paucity of data available on the practice of physician driven thoracic ultrasonography in South Africa. This paper wishes to establish its utility in a specialist setting at Helen Joseph Hospital. Its utility and safety may make it desirable to implement at more centres of secondary and tertiary level care.

1.2 Research Question and Main Objective

To describe the indications, sonographic findings, interventions performed and their outcomes/diagnoses as pertaining to the use of thoracic POCUS at Helen Joseph Hospital.
To identify acute complications (within 24 hours) relating to interventions carried out.

1.3 Hypothesis

Sonographic guidance for interventions has a high diagnostic yield and few complications.

1.4 Specific objectives

1) Describe the demographics of patients undergoing thoracic POCUS, including age, gender, and HIV status
2) Describe the indications for POCUS
3) Describe the interventions performed
4) Describe the intervention outcome in the following categories:
    a) Qualitative POCUS
    b) Thoracocentesis
    c) US guided transthoracic biopsies/fine needle aspirations
    d) Drain insertion under guidance
    e) Other
5) Acute complications, defined as those occurring within 24 hours of ultrasound guided procedures as documented in the POCUS logbook

1.5 Methodology

This is a retrospective descriptive record review of the thoracic POCUS logbook based at Helen Joseph Hospital. The logbook was commenced on 13 October 2017, therefore the data period is from then till 31 July 2019.

1.5.1 Inclusion criteria:

1. Patients >18 years of age
2. Patients who have undergone POCUS by the pulmonology unit at Helen Joseph Hospital. These patients were recorded in the POCUS logbook

1.5.2 Exclusion:

Thoracic ultrasound performed by Radiology
Non thoracic ultrasounds

1.6 Data collection

The following data was collected from the POCUS logbook:

1) Demographics
2) Indication
3) Ultrasound findings
4) Presenting complaint
5) Intervention performed
6) Intervention outcome/diagnosis
7) Acute complications (including, where applicable, death)

Data was captured by the investigator on a data collection sheet (Appendix 1)
These data was then transcribed into electronic format using a specially designed password protected database for analysis.

1.7 Data analysis

Using the aforementioned database, data was analysed using the IBM SSPS® statistical analysis software programme.
Patient demographics, sonographic findings, diagnosis, interventions and complications were summarised using descriptive statistics. Normal distribution was represented by means of standard deviations.
Skewed distributions was represented by medians and interquartile ranges.
A p-value of <0.05 was considered statistically significant.

1.8 Funding

All expenses were covered by the principal investigator.
Costs included the printing of data sheets (200 x R2 → R400)

1.9 Ethics Approval

This research application was submitted to the Wits Human Research Ethics Committee (HREC), M191134. Approval was obtained from the Helen Joseph Hospital head of the division of pulmonology as well as management of Helen Joseph Hospital.

1.10 Intention

This study is being conducted for the purpose of submission for a Master of Medicine degree as well as for publication in a peer reviewed medical journal.

1.11 Timeline

	May '19	Jun '19	Jul '19	Aug '19	Sep '19	Oct '19	Nov '19	Dec '19	Jan '20	Feb '20	Mar '20	Apr '20	May '20	Jun '21
Literature review														
Preparing protocol														
Protocol assessment														
HREC (Ethics)														
Data collection														
Data analysis														
Write up														
Submission														

1.12 Limitations

1. Poor record keeping for retrospective review
2. Missing patient information/documentation
3. Single centre study
4. Operator and training level dependent

1.13 References

[1]. Sofferman RA, Ahuja AT. Ultrasound of the Thyroid and Parathyroid Glands. Springer. 2012. p. 3 – 4. DOI: 10.1007/978-1-4614-0974-8

[2]. Shampo MA, Kyle RA, Dussik KT. Pioneer in Ultrasound. Mayo Clin Proc. 1995 Dec;70(12):1136 DOI: 10.4065/70.12.1136

[3]. Moore CL, Copel JA. Point-of-Care Ultrasonography. N Engl J Med 2011;364:749-57. DOI: 10.1056/NEJMra0909487

[4] Stengel D, Hoenning A, Leisterer J. Point-of-care ultrasonography for diagnosing thoracoabdominal injuries in patients with blunt trauma. Cochrane Database of Systematic Reviews 2017, Issue 5. Art. No.: CD012669. DOI:10.1002/14651858

[5] Richards JR, McGahan JP. STATE OF THE ART: Focused Assessment with Sonography in Trauma. Radiology: Volume 283: Number 1—April 2017. DOI: 10.1148/radiol.2017160107

[6] Weingart DS. EMCrit Blog at *https://emcrit.org/rush-exam/* Accessed on 16/06/2019

[7] Seif D, Perera P, Mailhot T, Riley D, Mandavia D. The RUSH Exam: Rapid Ultrasound in Shock in the Evaluation of the Critically Ill. Emerg Med Clin N Am 2010; 28: 29–56. DOI: 10.1016/j.emc.2009.09.010

[8] Gardecki J, Patel K, Rowshan O. Scan the lung: Point-of-care ultrasound of a pulmonary consolidation with loculated pleural effusion. American Journal of Emergency Medicine 37 (2019) 377.e1–377.e3. DOI: 10.1016/j.ajem.2018.10.054

[9] Laursen CB, Naur TMH, Bodtger U, Colella S, Naqibullah M, Minddal V, et al. Ultrasound-guided Lung Biopsy in the Hands of Respiratory Physicians: Diagnostic Yield and Complications in 215 Consecutive Patients in 3 Centers. J Bronchol Interv Pulmonol. 2016 Jul;23(3):220–8. DOI: 10.1097/LBR.0000000000000297

[10] Smith ZA, Postma N, Wood D. FAST scanning in the developing world emergency department. S Afr Med J 2010; 100: 105-108. PMID: 20459914

[11] Smith ZA, Wood D. Emergency focussed assessment with sonography in trauma (FAST) and haemodynamic stability. Emerg Med J 2014;31:273–277. DOI:10.1136/emermed-2012-202268

[12] Heller T, Wallrauch C, Goblirsch S, Brunetti E. Focused assessment with sonography for HIV-associated tuberculosis (FASH): a short protocol and a pictorial review. Critical Ultrasound Journal 2012, 4:21. DOI: 10.1186/2036-7902-4-21

[13] van Hoving DJ, Lamprecht HH, Stander M, Vallabh K, Fredericks D,Louw P et al. Adequacy of the emergency point-of-care ultrasound core curriculum for the local burden of disease in South Africa. Emerg Med J 2013;30:312–315. DOI: 10.1136/emermed-2012-201358

[14] Koegelenberg CF, von Groote-Bidlingmaier F, Bolliger CT. Transthoracic Ultrasonography for the Respiratory Physician. Respiration 2012;84:337–350 DOI: 10.1159/000339997

[15] Han J, Xiang H, Ridley WE, Ridley LJ. Plankton sign: Pleural effusion. J Med Imaging Radiat Oncol. 2018 Oct;62:35–35. DOI:10.1111/1754-9485.22_12785

[16] Lichtenstein DA, Menu Y. A bedside ultrasound sign ruling out pneumothorax in the critically ill.Lung sliding. Chest. 1995;108:1345–8. DOI:10.1378/chest.108.5.1345

[17] Lipoma | Radiology Reference Article https://radiopaedia.org/articles/lipoma Accessed on 16/06/2019

[18] Abscess Evaluation using Bedside Ultrasonography https://emedicine.medscape.com/article/1379916-overview Accessed on 16/06/2019

[19] Xirouchaki N, Georgopoulos D. The use of lung ultrasound: A brief review for critical care physicians and pneumonologists. PNEUMON Number 2, Vol. 20, April - June 2007

[20] Konstantinides SV, Torbicki A, Agnelli G, Danchin N, Fitzmaurice D, Galie N, et al. 2014 ESC Guidelines on the diagnosis and management of acute pulmonary embolism. Eur Heart J. 2014 Nov 14;35(43):3033–80. DOI:10.1093/eurheartj/ehu283

[21] 60/60 sign (echocardiography) | Radiology Reference Article https://radiopaedia.org/articles/6060-sign-echocardiography. Accessed on 20/06/2019

[22] Koegelenberg CF, Bolliger CT, Theron J, Walzl G, Wright CA, Louw M, et al. Direct comparison of the diagnostic yield of ultrasound-assisted Abrams and Tru-Cut needle biopsies for pleural tuberculosis. Thorax. 2010 Oct 1;65(10):857–62. DOI:10.7196/SAMJ.2018.v108i4.12914

[23] Koegelenberg CF, Diacon AH, Irusen EM, von Groote-Bidlingmaier F, Mowlana A, Wright CA, et al. The Diagnostic Yield and Safety of Ultrasound-Assisted Transthoracic Biopsy of Mediastinal Masses. Respiration. 2011;81(2):134–41. DOI: 10.1159/000322005

[24] Koegelenberg CF, Irusen EM, von Groote-Bidlingmaier F, Bruwer JW, Batubara EMA, Diacon AH. The utility of ultrasound-guided thoracentesis and pleural biopsy in

undiagnosed pleural exudates. Thorax. 2015 Oct;70(10):995–7. DOI: 10.1136/thoraxjnl-2014-206567

[25] Koegelenberg CF, Bennji SM, Boer E, Schubert PT, Shaw JA, Allwood BW, et al. The current aetiology of malignant pleural effusion in the Western Cape Province, South Africa. S Afr Med J 2018;108(4):275-277. DOI:10.7196/SAMJ.2018.v108i4.12914

[26] Sconfienza LM, Mauri G, Grossi F, Truini M, Serafini G, Sardanelli F, et al. Pleural and Peripheral Lung Lesions: Comparison of US- and CT-guided Biopsy. Radiology. 2013 Mar;266(3):930–5. DOI: 10.1148/radiol.12112077

[27] Rahman NM, Singanayagam A, Davies HE, Wrightson JM, Mishra EK, Lee YCG, et al. Diagnostic accuracy, safety and utilisation of respiratory physician-delivered thoracic ultrasound. Thorax. 2010 May 1;65(5):449–53. DOI:10.1136/thx.2009.128496

[28] Hammerschlag G, Denton M, Wallbridge P, Irving L, Hew M, Steinfort D. Accuracy and safety of ward based pleural ultrasound in the Australian healthcare system: Ward-based pleural ultrasound. Respirology. 2017 Apr;22(3):508–12. DOI: 10.1111/resp.12932

Chapter 2: Submissible article

Title:
The Utility of Point of Care Ultrasonography Driven by Clinicians in the Assessment and Investigation of Lung Pathologies.

Authors:
SD Molepo [1]
SA van Blydenstein [2], AK Graham [3]

Affiliations:
1. Department of Internal Medicine, Helen Joseph Hospital, Johannesburg, South Africa, University of the Witwatersrand
2. Division of Pulmonology, Department of Internal Medicine, Chris Hani Baragwanath Academic Hospital, Johannesburg, South Africa, University of the Witwatersrand.
3. Division of Pulmonology, Department of Internal Medicine, Helen Joseph Hospital, Johannesburg, South Africa, University of the Witwatersrand

Conflict of Interest: Nil

Keywords: Point of care ultrasound, HIV, tuberculosis, adenocarcinoma, South Africa

Corresponding Author:
Dr Samuel Ditau Molepo,
Department of Internal Medicine, Helen Joseph Hospital, 1 Perth Road, Auckland Park, University of the Witwatersrand, Johannesburg
Email: sam.molepo@gmail.com
Telephone: +27764677663
Total word count: 2549
Total abstract word count: 226

2.1 Background

Point of care ultrasonography is an increasingly valuable adjunct in making a rapid clinical assessment with the option of real time intervention. POCUS has been adopted readily by non-radiologists over the past decade, including emergency and critical care physicians, but the uptake amongst physicians and pulmonologists has been slower. Little is known about its use as a point-of-care tool in the hands of respiratory physicians. The above question is especially important when practicing in areas where TB prevalence is high, and with limited access to interventional radiology.

Rahman et al [1] conducted a study at the Pleural Diseases Unit, Oxford, looking at the utility of physician driven lung ultrasonography. They undertook 960 ultrasound (US) scans over a period of three years, wherein 25.6% were qualitative (imaging only) and 58.1% were interventional. Of the interventional ultrasounds, 25.4% were thoracocenteses and 32.7% were intercostal drain (ICD) insertions. The reported major complication rate was three out of 558 (0.5%); two cases of intrapleural bleeding requiring intervention, and one case of pleural infection. There were no deaths.

Meena and Bartter [2] performed a retrospective review of percutaneous fine needle aspirations (PFNA) done by two pulmonologists under ultrasound guidance, of which the diagnostic yield was 81%. Of 109 cases that underwent PFNA, 90 were diagnostic. Squamous cell carcinoma (SCC) of the lung was the most common histopathological diagnosis (32% of cases), followed by adenocarcinoma (21%). The total complication rate was 15% (nine had pneumothorax and seven had haemoptysis). Only one patient had a complication severe enough to require hospital admission. There were no deaths.

These applications make POCUS a very attractive modality with which to immediately investigate patients especially given that it offers real time sensitive and specific results and permits interventional procedures to be carried out with low risk of complication. The lack of ionising radiation also makes it appealing to the field of paediatrics where children may be more susceptible to the long term effects of radiation [5]. It's also valuable in patients who need frequent re-assessment [3] and in pregnancy. Apart from the upfront cost of a new ultrasound machine, the running costs are more affordable than other alternatives to this modality. This is of particular value in resource-constrained settings where other imaging modalities are limited or unavailable.

2.2 Methodology and Study population

This was a retrospective descriptive record review of the thoracic POCUS logbook based at Helen Joseph Hospital. Permission was obtained from the Helen Joseph Hospital Research Committee as well as from the Helen Joseph Hospital head of the Division of Pulmonology. Ethics clearance (M191134) was also obtained prior to the examination of this data.

Data collected was from 13 October 2017 till 31 July 2019. The data analysed included age, sex, indication for thoracic POCUS, ultrasound findings, intervention

performed, results thereof, and acute complications arising from interventions performed.

Patients included were those who had undergone thoracic POCUS by the pulmonology division at Helen Joseph Hospital and were recorded in the POCUS logbook. They were all in-patients for which the pulmonology division was consulted by general medical and surgical units. Patients had initial work-up including chest x-rays but required further assistance with diagnosis or tissue acquisition. The POCUS assessments and interventions were performed variably by internal medicine registrars rotating in pulmonology, pulmonology fellows as well as consultant pulmonologists, each with variable expertise and training in the procedure. Biopsies were only performed by consultants and fellows in training. Samples collected were requested by the same pulmonology team mentioned above, with no standardisation of biochemical or microbiological tests. 2D ultrasound scanning with colour Doppler was employed using a *Mindray M7 Premium* in the pulmonology procedure room. Both real-time and non-real-time guidance for biopsies and aspirates were performed.

All patients were least 18 years of age and excluded ultrasound studies done by the department of radiology.

2.3 Data analysis

All logged POCUS entries were digitised on Microsoft Excel® and a study number assigned to individual patients. Demographic data and variables relating to the POCUS assessment were analysed. Normal distribution is represented by means. Skewed distributions are represented by medians and interquartile ranges. The Wilcoxon-Mann-Whitney rank sum test was used to compare median age in males and females.

2.4 Results

There was total of 141 patients that were consulted for thoracic POCUS during the study period. The study population ranged broadly in age, with a bimodal distribution. The first peak had an age ranging from 30-39 years, and the second 60-69 years. The median age was 51 years for both males and females.

Table 1. The demographics of patients undergoing thoracic POCUS

Variable	**Total N= 141 (100.0%)**
Age at presentation/years	
Median Age (Interquartile range)	51 (37-64)
<30	12 (8.5%)
30-39	29 (20.6%)
40-49	25 (17.7%)
50-59	22 (15.6%)
60-69	32 (22.7%)
≥70	21 (14.9%)

Most of the consults that underwent thoracic POCUS were for therapeutic purposes as opposed to qualitative (80.1% vs 19.9%). The term therapeutic is used in this sense to refer to procedure-related ultrasonography, which included interventions such as thoracocentesis, ultrasound guided biopsies and intercostal drain insertion. Qualitative ultrasounds were those in which the consultation was to qualitatively assess and describe the thorax and provide feedback (imaging only). This was performed when chest x-ray revealed an abnormality but a distinction was needed to be made between mass versus fluid versus consolidation.

Of the ultrasound guided interventions, thoracocentesis was the most frequently performed (43.3%), followed by ultrasound guided percutaneous biopsies (22%) and indwelling pleural catheter insertion (7.1%).

Table 2. Pocus interventions performed, stratified by sex and HIV status

Intervention	Overall N=141	Females N=62	Males N=79	HIV Positive N=45	HIV Negative N=70
Qualitative POCUS	28 (19.85%)	16 (25.8%)	12 (15.2%)	11 (24.4%)	12 (17.14%)
Therapeutic POCUS					
Thoracocentesis	61 (43.3%)	26 (41.9%)	35 (44.3%)	26 (57.8%)	26 (37.1%)
Abscess aspiration	2 (1.4%)	1 (1.6%)	1 (1.3%)	1 (2.2%)	1 (1.4%)
Other ultrasound Guided Procedures	50 (35.5%)	19 (30.6%)	31 (39.2%)	7 (15.6%)	31 (44.3%)
Guided ICD	4 (7.8%)	3 (15.0%)	1 (3.2%)	1 (14.3%)	0 (0.0%)
Guided IPC	10 (20.0%)	5 (25.0%)	5 (16.1%)	0 (0.0%)	6 (18.75%)
Guided lung biopsy	26 (51.0%)	5 (25.0%)	21 (67.7%)	3 (42.9%)	20 (62.5%)
Guided lung FNA	4 (7.8%)	2 (10.0%)	2 (6.5%)	2 (28.6%)	0 (0.0%)
Guided pleural biopsy	5 (9.8%)	3 (15.0%)	2 (6.5%)	0 (0.0%)	5 (15.6%)
Guided pleurodesis	1 (2.0%)	1 (5.0%)	0 (0.0%)	1 (14.3%)	0 (0.0%)

ICD = intercostal drain insertion, IPC = indwelling pleural catheter insertion, FNA = fine needle aspiration.

Of the 141 patients consulted, 28 were for qualitative POCUS and 28% of them were requested for differentiating an opacity on chest xray as to whether it was a pleural effusion or consolidation (or both). Where an effusion was found and aspirated, the consult was deemed as interventional and not qualitative. Where the effusion was small or complex, and no thoracocentesis was done, the consult was deemed qualitative. In one case, an ICD was placed by clinicians and a concern was raised that the ICD may have been in the spleen. POCUS assessment could not assist in this regard and an abdominal CT scan was advised. Unfortunately, the POCUS logbook did not indicate the findings of this CT scan. In one case, lung consolidation was found but with an associated subpulmonic effusion. In one case, the patient was known to have an empyema from a previous aspiration and an intercostal drain inserted; POCUS was requested to assess whether or not there was residual fluid, which found residual empyema.

Table 3.1. Outcomes for qualitative POCUS (N=28)

Outcomes	N	(%)
Atelectasis	**3**	**10.71**
Infectious	**5**	**17.85**
Empyema	*1*	*20.00*
Consolidated lung	*4*	*80.00*
Other Pleural effusions	**10**	**35.71**
Loculated pleural effusion	*3*	*30.00*
Simple, large pleural effusion	*2*	*20.00*
Simple, small pleural effusion	*3*	*30.00*
Pseudotumour post ICD	*1*	*10.00*
Subpulmonic effusion	*1*	*10.00*
Other specific findings	**4**	**14.28**
Possible ICD in spleen → inconclusive	*1*	*25.00*
IPC amenability → complex space	*1*	*25.00*
IPC amenability → minimal fluid	*1*	*25.00*
Lung mass, not amenable to biopsy	*1*	*25.00*
No abnormality detected	**2**	**7.14**
No mass visualised	*1*	*50.00*
No pleural fluid	*1*	*50.00*
Other	**4**	**14.29**
Pericardial effusion	*2*	*50.00*
Pneumothorax	*2*	*50.00*

ICD = intercostal drain, IPC = indwelling pleural catheter insertion.

Of the consults where thoracocentesis was performed, the majority of results (34.4%) were exudative samples that could not otherwise be specified. That is, only biochemistry was requested on those samples, showing exudative effusions with no specific aetiology determined. Three of the pleural effusions were definitively confirmed to be caused by *Mycobacterium tuberculosis as* demonstrated by culture. The second largest proportion of cases (29.5%) was for fluid sent for microscopy, culture and sensitivity as well as cytological evaluation for malignancy. These cases all had negative results and were not evaluated further on those samples. Of note, only one of 61 cases (1.64%) was an unsuccessful attempt at thoracocentesis. In one case, fluid was aspirated but the sample could not be traced. In one case, a consult was received for thoracocentesis, but only minimal fluid was aspirated, therefore not sent for laboratory evaluation.

In four cases (6.56%), cytology was positive for malignancy. Of the two cases with adenocarcinoma one was of endometrial origin and the other could not be determined in terms of origin.

Table 3.2. Diagnoses for thoracocentesis (N=61)

Outcomes	N	(%)
Infectious	**8**	**13.11**
Empyema	*2*	*25.00*
Klebsiella pneumoniae	*1*	*12.50*
Salmonella enterica	*1*	*12.50*
Staphylococcus aureus	*1*	*12.50*
Tuberculosis	*3*	*37.5*

Malignancy	**4**	**6.56**
Non-Hodgkin's lymphoma	*1*	*25.00*
Metastatic adenocarcinoma	*2*	*50.00*
Squamous cell carcinoma of the lung	*1*	*25.00*
Exudative pleural effusion	**21**	**34.43**
Other pleural effusions	**2**	**3.28**
Transudative pleural effusion	*1*	*50.00*
Minimal fluid	*1*	*50.00*
Non diagnostic	**6**	**9.84**
Cytology non-representative	*1*	*16.67*
Failed tap	*1*	*16.67*
Untraceable specimen	*1*	*16.67*
Specimen leaked	*3*	*50.00*
Negative culture/cytology	**18**	**29.51**
Therapeutic thoracocentesis	**2**	**3.28**

A total of 31 POCUS guided biopsies were performed, of which 26 were percutaneous lung biopsies involving juxta-pleural masses. A total of three biopsies were non-representative, two of which were attempts at pleural sampling (both showed non-pleural tissue). A total of five pleural biopsies were performed, of which three had a positive result (representative samples). One of the pleural biopsy specimens showed non-necrotising granulomatous inflammation, the differential to which includes tuberculosis, sarcoidosis, granulomatosis with polyangiitis and rheumatoid arthritis [11]. Of the 31 biopsies, 77.4% were malignancies while 6.0% were of infectious aetiology. Adenocarcinomas were the most common histological subtypes (41.67%) detected through percutaneous core biopsies. One of the samples could not be traced to a result. All biopsies were core biopsies obtained using a large bore needle (14G).

Table 3.3. Diagnoses for POCUS guided transthoracic/pleural biopsies and other procedures (N=50)

Outcomes	N	(%)
Infectious/inflammatory	**3**	**6.00**
Non-necrotising granulomatous pleuritis	*1*	*33.33*
Parenchymal TB (cavity)	*1*	*33.33*
TB pleuritis	*1*	*33.33*
Malignancy	**24**	**48.00**
Adenocarcinoma	*10*	*41.67*
Squamous cell carcinoma of the lung	*3*	*12.5*
Small cell carcinoma of the lung	*2*	*8.33*
Neuroendocrine carcinoma	*2*	*8.33*
Non-Hodgkin's Lymphoma	*2*	*8.33*
Hodgkin's Lymphoma	*1*	*4.17*
Other	*4*	*16.67*
Non diagnostic procedure	**7**	**14.00**
Insufficient cellular material	*1*	*12.50*
No traceable result	*1*	*12.50*
Non-representative biopsy	*3*	*37.50*
Necrotic tissue	*1*	*12.50*

Reactive lymph node	*1*	*12.50*
Negative cytology	**1**	**2.00**
Therapeutic procedures	**15**	**30.00**
Intra-pleural bleomycin	*1*	*6.67*
ICD inserted	*4*	*26.67*
IPC inserted	*10*	*66.67*

ICD = intercostal drain, IPC = indwelling pleural catheter insertion.

The commonest interventional complication was minor bleeding, occurring in 12% of 50 procedures. Minor bleeding has been defined as bleeding easily stopped by external compression and/or not causing haemodynamic instability nor requiring blood transfusion. There was no record of complications in 40% of cases.

Table 4. Acute complications occurring within 24 hours of ultrasound-guided procedures

Complications	All N=50	*Guided ICD N=4*	*Guided IPC N=10*	*Guided lung biopsy N=26*	*Guided lung FNA N=4*	*Guided Pleural biopsy N=5*	*Guided pleurodesis N=1*
Minor bleeding	6 (12.0%)	-	-	5 (19.2%)	1 (25%)	-	-
Nil	22 (44.0%)	2 (50%)	5 (50.0%)	11 (42.3%)	1 (25%)	2 (40%)	1 (100%)
Not reported	20 (40.0%)	2 (50%)	4 (36.4%)	9 (34.6%)	2 (50%)	3 (60%)	-
Pain	2 (4.0%)	-	1 (9.0%)	1 (3.9%)	-	-	-

ICD = intercostal drain insertion, IPC = indwelling pleural catheter insertion, FNA = fine needle aspiration.

2.5 Discussion

The study population had a bimodal age distribution representing a younger HIV positive cohort of patients as well as an older cohort with traditional risk factors for malignancies.

The largest proportion of patients who underwent thoracocentesis had an exudative pleural effusion, which could not be specified further (no microbial culture or nucleic acid testing was positive). As a consequence, only three cases had a definitive diagnosis of TB pleuritis (all diagnosed by culture, GeneXpert® negative) made on thoracocentesis, which is unusual considering the incidence of TB in our population.

The World Health Organisation places South Africa in the top 30 countries in terms of TB burden of disease [6]. In 2018, South Africa had a TB incidence rate of 520 per 100 000 persons, with an HIV coinfection rate of 59% [6]. Koegelenberg *et al*, from the Western Cape province found that pleural TB was still the commonest cause of exudative pleural effusions in their study [7]. Although diagnosed by pleural biopsy using an Abram's needle under POCUS guidance, they found TB in 66 out of 89 (74.2%) cases of exudative pleural effusions.

There are several factors that could explain our low number of TB cases by thoracocentesis. During the time within which data was recorded, Helen Joseph Hospital's National Health Laboratory Service (NHLS) had not been performing *Mycobacterium tuberculosis* polymerase chain reaction (PCR) test by GeneXpert® yet. And so, if one wanted such a test, one would have had to request it separately through the TB clinic. This speaks to a need for improved linkage of care. The other noticeable trend is that biochemistry was often sent alone without conventional culture and phenotypic sensitivity as well as DNA amplification techniques. Such a predicament would be improved by reflex testing of exudative pleural samples. There are numerous differential diagnoses for exudative pleural effusions including autoimmune diseases, uraemia, pulmonary embolism, pancreatitis and asbestos-related pleural disease etc. which may have accounted for some of the cases that did not have a definitive diagnosis. The other limitation in making the diagnosis of TB pleurisy by nucleic acid testing is that the Xpert MTB/RIF® only has a sensitivity of 28.3% in a high TB prevalence setting [8].

The diagnostic challenge wherein exudative pleural effusions do not yield a diagnosis is not unique to our setting. Solari et al [9] did a study in Peru, where they looked at certain clinical prediction rules that could aid in the diagnosis of TB. They found that the adenosine deaminase activity (ADA) test yielded the best sensitivity and specificity (86% and 87% respectively) in comparison to set gold standards (TB PCR, culture and histology) [9]. Its utility is best demonstrated in a patient with a high pretest probability of tuberculosis such as the presence of constitutional symptoms (night sweats, fever, and weight loss) [9]. ADA is a purine-degrading enzyme found in lymphocytes [10], as a result it can be raised in other conditions leading to a lymphocytosis such as lymphoma, rheumatoid effusion, mesothelioma, lung cancer and parapneumonic effusion [8]. It would, however, be very useful if TB GeneXpert® testing was negative in a patient who had other features leading to a high suspicion for TB [10]. Its yield is also improved when used in settings of a high TB burden, with a lymphocyte rich exudative fluid as well as a high ADA cut off value (≥40IU/L) [10]. In this setting, it has a positive predictive value of 98%, and serves as a good basis to initiate TB pharmacotherapy [10]. Conversely, in a low TB prevalence setting, it has a high negative predictive value and can be used as a rule out tool [8]. Additionally, ADA has two isoenzymes (ADA-1 and 2), where ADA-2 is more specific for TB [8].

This study had three biopsies with non-representative tissue results; two out of three, were from pleural biopsy attempts. This is too small a sample to make any meaningful conclusions, but could allow a further area of research into the yield of POCUS guided pleural biopsies, particularly regarding the utility and accessibility of ROSE.

The overall yield for diagnostic interventions (excluding thoracocentesis) was 81.1%, 30 of 37 ultrasound guided investigations returned a definitive result. Diagnostic yield for thoracocentesis was less favourable at 23.7% (only 14 of 59 cases returned with a definitive result).

Adenocarcinoma was the commonest malignant histological subtype found at percutaneous biopsy. Primary lung adenocarcinomas tend to present more

peripherally while squamous cell carcinomas (SCC) more centrally [11]. This is in contrast to the predominant diagnosis of SCC that was found by Meena and Bartter [2], whose studies were also peripheral samples of malignancies (percutaneous FNA).

Although not demonstrated in our study, there is an association between malignancy and HIV positivity. Kirk *et al* [12] conducted a literature review where they found that HIV was associated with up to 3.6-fold increased risk of lung cancer, when adjusted for other risk factors such as smoking. Akhtar *et al* [13] described two possible mechanisms by which this may happen. There is suppression of p53, a tumour suppressor gene, by the gene transactivator of transcription (Tat), itself involved in HIV replication [13]. Another mechanism is by upregulation of HIV Tat-interacting protein (TIP30), which is noted in the pathogenesis of metastatic lung cancer [13].

In terms of complications of POCUS guided interventions, the most significant limiting factor was the large proportion of patients (40%) with no recorded complications. This is possibly due to the recording of an incident only when it occurs, as opposed to when procedures remain incident free. There were no acute complications in 44% of cases, while 12% experienced minor bleeding. No major complications were reported. Major complications would be those which required interventional management such as pneumothorax needing ICD placement or therapeutic decompression, bleeding requiring a blood transfusion or surgical intervention.

In another physician driven study, Rahman et al [1] had a major complication rate of 0,5% (3 of 558 cases), all from POCUS guided interventions. Two of their cases were due to intrapleural bleeding necessitating intervention and the other, a subsequent pleural infection.

2.6 Limitations

Due to the inherent limitations of a retrospective audit, this study relied upon existing records, which were limited by inconsistent record keeping, scanty documentation and missing patient information. In addition, the POCUS logbook was not standardised in terms of patient details, investigations leading up to POCUS assessment, rank of clinician performing the POCUS and his/her skills set, battery of tests submitted for a specific sample.

2.7 Conclusion

Our data shows a diagnostic yield of 80.5% for POCUS guided biopsies and other interventions although with less impressive yields with regards to thoracocentesis. This may be due to the skewed nature of cases with more complex cases being referred for pulmonology consultation. POCUS guided interventions were safe, with no major complications reported and a minor complication rate of 12%. It seems reasonable to implement lung POCUS in internal medicine in the South African setting with the view to improve diagnostic yield, decrease length of stay (allows rapid bed side testing) and maximise procedural safety.

2.8 References

[1]. Rahman NM, Singanayagam A, Davies HE, Wrightson JM, Mishra EK, Lee YCG, et al. Diagnostic accuracy, safety and utilisation of respiratory physician-delivered thoracic ultrasound. Thorax. 2010 May 1;65(5):449–53. DOI:10.1136/thx.2009.128496

[2]. Meena N, Bartter T. Ultrasound-guided Percutaneous Needle Aspiration by Pulmonologists: A Study of Factors With Impact on Procedural Yield and Complications. J Bronchol Interv Pulmonol. 2015 Sep 4 DOI:10.1097/LBR.0000000000000175

[3] Cho Y-J, Song K-H, Lee Y, Yoon JH, Park JY, Jung J, et al. Lung ultrasound for early diagnosis and severity assessment of pneumonia in patients with coronavirus disease 2019. Korean J Intern Med. 2020 Jul 1;35(4):771–81. DOI:10.3904/kjim.2020.180

[4] Pare J, Camelo I, Mayo K, Leo M, Dugas J, Nelson K, et al. Point-of-care Lung Ultrasound Is More Sensitive than Chest Radiograph for Evaluation of COVID-19. West J Emerg Med. 2020 Jun 19;21(4). DOI:10.5811/westjem.2020.5.47743

[5] Miller DL, Abo A, Abramowicz JS, Bigelow TA, Dalecki D, Dickman E, et al. Diagnostic Ultrasound Safety Review for Point-of-Care Ultrasound Practitioners. J Ultrasound Med. 2020 Jun;39(6):1069–84. DOI:10.1002/jum.15202

[6] WHO | Global tuberculosis report 2019 https://www.who.int/tb/publications/global_report/en/ Accessed on 05/08/2020

[7] Koegelenberg CF, Bolliger CT, Theron J, Walzl G, Wright CA, Louw M, et al. Direct comparison of the diagnostic yield of ultrasound-assisted Abrams and Tru-Cut needle biopsies for pleural tuberculosis. Thorax. 2010 Oct 1;65(10):857–62. DOI:10.7196/SAMJ.2018.v108i4.12914

[8] Vorster MJ, Allwood BW, Diacon AH, Koegelenberg CFN. Tuberculous pleural effusions: advances and controversies. Journal of Thoracic Disease. 2015;7(6):11.

[9] Solari L, Soto A, Van der Stuyft P. Performance of clinical prediction rules for diagnosis of pleural tuberculosis in a high-incidence setting. Trop Med Int Health. 2017 Oct;22(10):1283–92. DOI:10.1111/tmi.12932

[10] Shaw JA, Irusen EM, Diacon AH, Koegelenberg CF. Pleural tuberculosis: A concise clinical review. Clin Respir J. 2018 May;12(5):1779–86. DOI:10.1111/crj.12900

[11] Kumar P, Clark M. Clinical Medicine. 6th Edition. Elsevier. 2005. p. 948

[12] Kirk GD, Merlo C, O'Driscoll P, Mehta SH, Galai N, Vlahov D, et al. HIV Infection Is Associated with an Increased Risk for Lung Cancer, Independent of Smoking. Clin Infect Dis. 2007 Jul 1;45(1):103–10. DOI:10.1086/518606

[13] Akhtar N, Bansal JG. Risk factors of Lung Cancer in nonsmoker. Curr Probl Cancer. 2017 Sep;41(5):328–39. DOI:10.1016/j.currproblcancer.2017.07.002

DATA SHEET

Study Reference No.: _____
Patient Hospital No.: _____
Age: _____

Sex: M☐ F☐

HIV Status: Negative☐ Positive☐ Unknown☐

Indication(s) for POCUS[1]: Diagnostic ☐ Therapeutic ☐

Guided intervention ☐ Other: _____

POCUS Intervention:

Diagnostic ☐, Result:_____ Complication(s):_____

Thoracocentesis ☐, Result:_____ Complication(s):_____

Guided biopsy ☐, Result:_____ Complication(s):_____

Guided ICD[2] ☐, Result:_____ Complication(s):_____

Legend:
* Pack years as defined by number of years of smoking divided by number of packs of cigarettes smoked (or number of cigarettes divided by 20).
** Exposures that are risk factors for effusive/neoplastic lung diseases such as asbestos
[1]POCUS = Point of care ultrasound
[2]ICD = intercostal drain

UNIVERSITY OF THE WITWATERSRAND JOHANNESBURG

R14/49 Dr Samuel Molepo et al

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M191134

NAME: (Principal Investigator)	Dr Samuel Molepo et al
DEPARTMENT:	Internal Medicine Helen Joseph Hospital Division of Pulmonology
PROJECT TITLE:	The Utility of Point of Care Ultrasonography Driven by Clinicians in the Assessment and Investigation of Lung Pathologies
DATE CONSIDERED:	29/11/2019
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Dr Alex Van Blydenstein
APPROVED BY:	Dr CB Penny, Chairperson, HREC (Medical)
DATE OF APPROVAL:	29/11/2019

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary on the Third Floor, Faculty of Health Sciences, Phillip Tobias Building, 29 Princess of Wales Terrace, Parktown, 2193, University of the Witwatersrand. I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to resubmit the application to the Committee. **I agree to submit a yearly progress report**. The date for annual re-certification will be one year after the date of convened meeting where the study was initially reviewed. In this case, the study was initially reviewed in **November** and will therefore be due in the month of **November** each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).

Principal Investigator Signature

Date 31/11/2019

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES