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Point-of-Care Ultrasound for Tuberculosis Management in Sub-Saharan Africa—A Balanced SWOT Analysis

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Abstract

Point-of-care ultrasound (POCUS) is an increasingly accessible skill, allowing for the decentralization of its use to non-specialist healthcare workers to guide routine clinical decision making. The advent of ultrasound-on-a-chip has transformed the technology into a portable mobile health device. Due to its high sensitivity to detect small consolidations, pleural effusions and sub pleural nodules, POCUS has recently been proposed as a sputum-free likely triage tool for tuberculosis (TB). To make an objective assessment of the potential and limitations of POCUS in routine TB management, we present a Strengths, Weaknesses, Opportunities & Threats (SWOT) analysis based on a review of the relevant literature and focusing on Sub-Saharan Africa (SSA). We idenitified numerous strengths and opportunities of POCUS for TB management e.g.; accessible, affordable, easy to use & maintain, expedited diagnosis, extra-pulmonary TB detection, safer pleural/pericardial puncture, use in children/pregnant women/PLHIV, targeted screening of TB contacts, monitoring TB sequelae, and creating AI decision support. Weaknesses and external threats such as operator dependency, lack of visualization of central lung pathology, poor specificity, lack of impact

assessments and data from Sub-Saharan Africa must be taken into consideration to ensure that the potential of the technology can be fully realized in research as in practice.

Point-of-Care Ultrasound for Tuberculosis Management in Sub-Saharan Africa—A Balanced SWOT Analysis

HIGHLIGHTS

- Point-of-care ultrasound (POCUS) is a promising triage tool for TB
- To date there is limited data supporting its use for pulmonary TB
- There is relatively robust data for extrapulmonary TB
- Strengths and opportunities of POCUS for TB management are numerous
- Weaknesses and threats must be considered for full realization of its potential

Introduction

Point-of-care ultrasound (POCUS) is an increasingly accessible skill, allowing for the decentralization of its use to non-specialist healthcare workers to guide routine clinical decision making. The advent of ultrasound-on-a-chip has transformed the technology into a portable, pocket-sized mobile health device, while retaining an acceptable diagnostic performance and the versatility of their costly and cumbersome predecessors.(Rothberg et al. 2021) Owing to its ease-of-use, affordability, and low maintenance and consumable requirements, POCUS has emerged as an attractive skill in resource-limited settings, where out-of-pocket specialist care and inconsistent radiology services erode health equity. (Yadav et al. 2021) Its potential to be integrated into the standard clinical exam analogously to the stethoscope is already well recognized.(Andersen et al. 2019; Abrokwa et al. 2022) There is already moderately strong data to support POCUS of the pericardium, pleural space and abdomen to detect extra-pulmonary tuberculosis (ePTB) in people living with HIV. (Van Hoving et al. 2020; Bobbio et al. 2019; Kahn et al. 2020; Griesel et al. 2019; Schafer et al. 2019). In a recent review on rapid sputum-free diagnostics for active TB, POCUS of the lungs is proposed as a likely triage tool. (Nathavitharana et al. 2022)

However, there is the potential that the introduction of new diagnostic tools can inflate expectations and lead to interpretations beyond competence resulting in incorrect conclusions. To make an objective assessment of the potential and limitations of POCUS in routine TB (ePTB and PTB) management, we present a Strengths, Weaknesses, Opportunities & Threats (SWOT) analysis based on a review of the relevant literature and focusing on Sub-Saharan Africa (SSA).

Strengths

Rapid differential diagnosis of respiratory syndromes

POCUS is established as a reference standard for the point-of-care assessment of many cardiopulmonary conditions. It is widely used by emergency physicians to evaluate patients with dyspnea (Qaseem et al. 2021) and when integrated into routine care, it significantly expedites diagnosis (Laursen et al. 2014). Its potential to differentiate cardiogenic and pulmonic dyspnea is well documented. Lung ultrasound (LUS) is highly effective in detecting lung consolidation in pneumonia (Chavez et al. 2014) and guidelines recommend LUS as an alternative to chest X-ray for pneumonia diagnosis (Ewig et al. 2021). It also has excellent sensitivity (98-100%) for the detection of pleural effusions (Qaseem et al. 2021) and allows clinically useful characterization of its volume and content. The potential of LUS in diagnosing pulmonary TB is increasingly recognized. A recent systematic review (Bigio et al. 2021) showed that the presence of subpleural nodules had the highest sensitivity ranging from 73% to 100%.

Its excellent sensitivity to detect even sub-centimeter lesions seems to make LUS a promising triage tool to better identify patients who need further microbiological testing.

Rapid visualization of pericardial effusions

In SSA, an estimated 64 to 70% of pericardial effusions are due to tuberculosis (TB), and up to 85% in people living with HIV (PLHIV).(Isiguzo et al. 2020; Ntsekhe and Mayosi 2013) Confirming the diagnosis of TB pericarditis in resource-limited settings is difficult due to the poor availability of advanced laboratory analysis.(Pankuweit et al. 2005) Thus, the diagnosis is most commonly suspected on a clinical basis.

While complete echocardiography remains firmly in the domain of experts,(Kimambo et al. 2021) the specific skill of identifying pericardial effusion has high diagnostic accuracy in POCUS-trained physicians, with a sensitivity and specificity of 89-91% and 96% respectively.(Chamsi-Pasha, Sengupta, and Zoghbi 2017)

Improving safety of pleural and pericardial interventions

Once pleural or pericardial effusion is detected by POCUS, it can be used to improve the safety and efficacy of thoraco- or pericardiocentesis for diagnostic or therapeutic purposes.(Maggiolini et al. 2016; Peabody and Mandavia 2017) Ultrasound is the only imaging technique that allows real-time visualization of the procedure and characterization of fluid content (loculated, purulent, or haemorrhagic versus non-complicated). In addition, a volume estimation can be made, as well as a basic appreciation of the heart function (e.g., in the case of abundant pericardial fluid).

Accessibility and affordability

POCUS can fill the imaging gap where radiology services are absent as is the case for virtually all basic or advanced healthcare centers in low-income countries (Yadav et al. 2021) or unaffordable, such as in countries without universal health coverage where patients rely on out-of-pocket expenditure for clinical exams. Ultrasound on-a-chip probes are less costly than their piezoelectric predecessors and can be used with different types of smartphones (including some low-end editions) and tablets (Harrington, 2019). (Harrington J. Comparison of pocket ultrasound machines. ACEP *now* 2019. Available from: https://www.acepnow.com/article/whats-the-deal-with-pocket-ultrasound/acep_0719_pg14b/)(Harrington J. Comparison of pocket ultrasound machines. ACEP *now* 2019. Available from: https://www.acepnow.com/article/whats-the-deal-with-pocket-ultrasound/acep_0719_pg14b/) Even the lone consumable of ultrasound gel can be produced locally from a simple mixture of corn or cassava starch and water. (Aziz et al. 2018; Binkowski et al. 2014)

Weaknesses

Operator-dependency

Operator dependency is a well substantiated criticism of POCUS. (Conlon et al. 2021) While acquisition is relatively simple, interpretation suffers from inter-user bias with results varying across experience. This is further compounded by non-standardized nomenclature and acquisition protocols.

Central lung cavities are undetectable

As air reflects ultrasound, aerated lung is an impenetrable barrier to POCUS assessment, limiting the depth of LUS to the pleural line and adjacent pathology. Deeper structures which do not communicate with the pleura such as central consolidations or lung masses remain invisible. For TB, this implies that an isolated central cavity cannot be detected.

Lack of specificity of POCUS signs

Only one study (Montuori et al. 2019) reported on specificity of LUS for the detection of pulmonary TB (PTB) with 67% for the presence of subpleural nodules.

Subpleural nodules are frequently found in lower respiratory tract infections (LRTIs) irrespective of etiology (pulmonary TB, COVID-19, bacterial pneumonia and pneumocystis pneumonia) (Bigio et al. 2021; Giordani et al. 2018). It is possible that more complex diagnostic patterns exist outside the capacity of human visual discernment and thus, specificity could be boosted by auxiliary deep learning tools or through synergy with cumulative imaging findings and complementary clinical and epidemiological signs. A large prospective SSA-based trial has been launched in to evaluate the diagnostic performance of LUS for lower respiratory tract infections including TB (**Tr**iage **U**ltra**s**ound in **T**B-endemic Regions: *TrUST*) (Suttels et al. 2022)

At the moment, however, it should be clear that LUS alone cannot replace microbiological diagnosis, but rather guide further testing for TB.

For the detection of ePTB, the Focused Assessment with Sonography for HIV-associated tuberculosis (FASH-plus) protocol which looks for pericardial effusion, pleural effusion, deep abdominal adenopathies, focal splenic or hepatic lesions and ascites (Heller et al. 2012) has clinically useful specificity, especially when 2 or more concurrent signs are present. (Van Hoving et al. 2020; Kahn et al. 2020; Ndege et al. 2019) A systematic review including 774 patients from Spain, the USA, Argentina and South-Africa found that 21% (95% confidence interval (CI) 10.6 - 33.8) of patients infected with HIV presented with splenic micro-abscesses of which 88.3% (95% CI 72.3 - 97.9) were due to TB.

Opportunities

TB during pregnancy and pediatric TB

To avoid radiation exposure to the fetus, LUS has come forward as an alternative first-line imaging tool in pregnant women with respiratory symptoms (Di Marco et al. 2015) and proved clinically useful during the COVID-19 pandemic. (Kalafat et al. 2020)

Pediatric POCUS is also gaining popularity, partly motivated by its non-invasive advantage over radiation-based imagery. Studies are limited, but indicate that POCUS may hold untapped potential for TB in the pediatric population with a lower yield of microbiological tests. A study supports this hypothesis, showing that ultrasound detected abnormalities more frequently than X-ray, and that these abnormalities were more frequent in cases of PTB.

Further, mediastinal ultrasound visualized lymphadenopathy, and children with confirmed PTB had larger lymph nodes than children with other respiratory diseases.(Heuvelings et al. 2019) Finally, as ePTB is frequently found (30%) in children with confirmed or suspected PTB irrespective of HIV status, diagnosis may be assisted by FASH-plus protocol. These findings suggest that POCUS can support timely diagnosis of childhood TB and could optimize triage of children for TB prevention therapy among those who are household contacts of confirmed PTB patients.

It should be noted that the currently available ultrasound-on-a-chip devices are less suitable for children and mediastinal views (e.g., the head of the probe is too large for a suprasternal notch view). (Fentress et al. 2022)

<u>TB in people living with HIV (PLHIV)</u>

As for pediatric TB, point-of-care diagnostics for TB in PLHIV remain high on the WHO research priority list. (Gebreselassie et al. 2019) The FASH plus protocol is the most commonly used POCUS application in South Africa.(Heller et al. 2012) As explained above, the FASH plus exam evaluates 6 thoracic and abdominal areas in search for extrapulmonary TB (ePTB) signs in PLHIV and showed a good performance in three SSA studies, notably increasing the probability of appropriate TB treatment initiation (Bobbio et al. 2019; Kahn et al. 2020; Van Hoving et al. 2020). Extending the routine clinical exam with a FASH scan can provide valuable clinical arguments to assist frontline healthcare workers in reaching the threshold for initiating TB treatment.

<u>Household contact screening for active TB</u>

As the sensitivity of LUS for the detection of (small) sub-pleural consolidations outweighs that of chest X-ray (Chavez et al. 2014) the role of LUS as a low-cost mobile alternative to

CXR in targeted case-finding for close contacts including children and pregnant women needs to be explored, especially in light of the risk of overdiagnosis.

Follow-up of TB sequelae

The value of LUS for the follow-up and early detection of interstitial lung disease post COVID-19 seems of interest. Albeit small and monocentric datasets, characterization of the sonographic interstitial syndrome seems to correlate well with CT findings such as ground glass opacities or parenchymal bands (Clofent et al. 2021). Where chest X-ray offers a static impression of TB sequelae, lung ultrasound might be a complementary dynamic exam to help identify patients at risk for post-TB fibrosis, pachypleuritis and superinfections. To date, and to our knowledge, there are no POCUS studies published on this population.

Artificial intelligence (AI) guided decision support

As discussed above, ultrasound interpretation suffers from inter-user bias and is ultimately restricted by the human cognitive limits of pattern discrimination. This makes it a good candidate for computer-assisted decision support, where deep learning may help standardize and augment the predictive potential of this tool by guiding more objective interpretations, while tolerating non-standardized acquisition practices. The COVID-19 pandemic has cleared the path to deep-learning applications of LUS (Zhao and Lediju Bell 2022), no studies to date however evaluate the performance of AI-POCUS interpretation for the diagnosis of PTB.

Threats

Lack of SSA data

Digital technology holds potential to replace the missing resources of low-income settings, and SSA is becoming a “new breeding ground for global digital health” (Holst et al. 2020).

Possibly the biggest threat is the sparse evidence of its utility in SSA populations and thus, a lack of performance estimates to guide context-adapted interpretation. Indeed, it is currently unknown how the potentially confounding influence of PTB and its sequelae would influence POCUS performance. For POCUS adoption to be successful in SSA, its implementation should be integrated into local research efforts to cultivate a locally owned evidence base that will foster trust, understanding and a level of caution.

Lack of trials showing an impact

All studies conducted to date are retrospective and prospective cohort studies. We need randomized controlled trials (RCT) to show the impact and safety of the use of POCUS on patients' management. For ePTB, a two-center RCT is underway in Tanzania to evaluate whether ultrasound in combination with other tests can increase the proportion of correctly treated patients. (Ndege et al. 2020)

Poor standardization of skills

POCUS is now rapidly being adopted by non-radiologist clinicians. Many studies therefore compare the skills of the clinician with that of the radiologist and often show encouraging outcomes (Strøm et al. 2020). These results, however, do not guarantee safe POCUS practices. In 2020, the Emergency Care Research Institute (ECRI – United States) identified POCUS as the second most important technology hazard in healthcare (Conlon et al. 2021). Over-enthusiastic or unframed use of POCUS remains an important pitfall. Availability of training and standardized skill evaluation are essential quality control measures to develop safe practice. This is especially true for SSA where gaining oversight is even more challenging due to a paucity of expertise and data collection constraints. To develop a context-adapted training program, it is important to promote an SSA ultrasonography community through which standardization can be strengthened by crowdsourced professional development and large-scale case-exchange networks. Accessible continuous training and high-standard local expertise are essential for safe POCUS adoption.

Data accessibility, ownership and privacy

Most POCUS devices can be configured to store images for DICOM or PACS. Some devices however pass via a proprietary cloud service that may raise questions about data privacy, sovereignty, and ownership. In SSA, many health workers communicate via diverse social media applications such as WhatsApp*(inc)*. (Meyer et al. 2021) There is currently no framework in SSA for the safe sharing of medical images through these channels. Moreover, most other imaging is still stored in analogue format, such as printed x-rays which are given to the patient and thus not readily accessible or catalogued for long-term monitoring.

Unstable internet connection

In order to upload POCUS images from an ultrasound-on-a-chip device, a relatively robust and reliable internet connection is required. This is often unavailable especially in remote areas and it is important that POCUS applications provide access to extended or totally offline modes. They should also require a minimal update to guarantee longevity in circumstances with poor connection. Many conventional machines allow offline image transfer from the original device to external storage with a flash drive.

Especially for novice sonographers who are less sure or technically capable of capturing the most convincing still image, short ultrasound videos are often the most interesting and relevant to store or share but consume 1 to 2 MB per recorded second. At an average cost of 0.5 to 35 USD per GB when working with mobile data in SSA (World Wide Web Foundation, 2022) (A4AI (World Wide Web Foundation) - Mobile Broadband Pricing data for 2020 available from:https://a4ai.org/extra/baskets/A4AI/2020/mobile_broadband_pricing_usd)(A4AI (World Wide Web Foundation) - Mobile Broadband Pricing data for 2020 available from:https://a4ai.org/extra/baskets/A4AI/2020/mobile_broadband_pricing_usd), this can rapidly become too expensive for local healthcare workers.

Sustainability of material and suitability for the tropics

POCUS devices have not been specifically designed for tropical weather conditions such as high humidity or extreme heat. Probes using ultrasound-on-chip technology have a tendency to overheat. This requires the user to interrupt the exam while the probe cools down. To our knowledge, there are no data on sustainability and longevity of POCUS devices in the tropics. Successful adoption of POCUS will require robust devices adapted to SSA working conditions.

Nosocomial fomite-borne transmission

Ultrasound probes can play a role in nosocomial cross-contamination of infectious disease through fomite transmission. Hospital hygiene is already challenging in SSA and requires massive coordination of consumables, training, and monitoring. (Ssekitoleko et al. 2020) Integrating hygiene awareness into POCUS training could be an opportunity to contribute to this critical issue.

Conclusion

Overall, this SWOT analysis highlights key factors for the successful integration of POCUS into routine TB care (figure 1). POCUS is a valid candidate for technology frog-leaping in SSA and is reaching a tipping point in transforming the routine clinical exam of frontline healthcare workers. Strengths and opportunities are numerous. However careful attention must be given to its various weaknesses and external threats to ensure that the potential of the technology can be fully realized

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Figure 1: Schematic overview of Strengths, Weaknesses, Opportunities and Threats for POCUS integration in routine TB care in SSA.

Declaration of interests

☒ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

☐The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: