Thoracic ultrasound in the modern management of pleural disease

Maged Hassan [1], Rachel M. Mercer[2] and Najib M. Rahman[2]

Affiliations: [1]Chest Diseases Dept, Faculty of Medicine, Alexandria University, Alexandria, Egypt. [2]Oxford Pleural Unit, Oxford Respiratory Trials Unit, University of Oxford, Oxford, UK.

Correspondence: Maged Hassan, Chest Diseases Dept, Faculty of Medicine, Khartoum Square, Alexandria, 21521, Egypt. E-mail: magedhmf@gmail.com

@ERSpublications
Widespread use of US as a point-of-care test has revolutionised the management of pleural diseases. A once diagnostic tool for detection of pleural effusion only, the uses of US in pleural diseases have expanded to include therapeutics and prognostication. http://bit.ly/2OQQcHZ

Cite this article as: Hassan M, Mercer RM, Rahman NM. Thoracic ultrasound in the modern management of pleural disease. *Eur Respir Rev* 2020; 29: 190136 [https://doi.org/10.1183/16000617.0136-2019].

ABSTRACT Physician-led thoracic ultrasound (TUS) has substantially changed how respiratory disorders, and in particular pleural diseases, are managed. The use of TUS as a point-of-care test enables the respiratory physician to quickly and accurately diagnose pleural pathology and ensure safe access to the pleural space during thoracentesis or chest drain insertion. Competence in performing TUS is now an obligatory part of respiratory speciality training programmes in different parts of the world. Pleural physicians with higher levels of competence routinely use TUS during the planning and execution of more sophisticated diagnostic and therapeutic interventions, such as core needle pleural biopsies, image-guided drain insertion and medical thoracoscopy. Current research is gauging the potential of TUS in predicting the outcome of different pleural interventions and how it can aid in tailoring the optimum treatment according to different TUS-based parameters.

Introduction

Thoracic ultrasound (TUS) has become an indispensable tool in the arsenal of the chest physician. The 2010 British Thoracic Society (BTS) Pleural Disease Guidelines recommend the use of TUS before pleural procedures as a standard of care [1]. Conventionally, TUS has only been used to assess for the presence of pleural effusion. However, with the widespread availability of TUS machines together with the continuous improvements in image resolution and the ease these machines can be brought to the bedside and inside procedure rooms, the use of TUS in thoracic diseases, and particularly in the pleural discipline, has expanded substantially. Detailed and advanced examination using TUS supports various diagnostic, prognostic and therapeutic purposes. Ultrasound is an excellent point-of-care test that is now undertaken outside Radiology departments by physicians from different medical specialities and has become a standard part of training for chest physicians, acting as a much finer adjunct to the stethoscope and clinical examination in guiding clinical decisions.

This review presents a summary of the different evidence-based uses of TUS in the management of pleural diseases and how its use enhances safety and accuracy of patient management. The review also provides an overview of the roles that TUS can potentially contribute, such as favouring pre-procedure probability of certain aetiologies and outcome prediction of various interventions in pleural medicine. The advantages of using TUS in addition to its pitfalls are summarised in table 1.

This article has supplementary material available from err.ersjournals.com

Provenance: Submitted article, peer reviewed.

Received: 11 Oct 2019 | Accepted after revision: 22 Nov 2019

TABLE 1 Advantages and pitfalls of using ultrasound in pleural diseases

Advantages	Pitfalls
Widely available	Operator dependent
Relatively cheap	Not suitable for examinations in patients with subcutaneous emphysema
Mobile – ideal point-of-care test	Difficult to examine patients with narrow intercostal spaces (*e.g.* fibrothorax)
Lack of ionising radiation (making the test safe to repeat)	Inferior to computed tomography in delineating complex pleural spaces (*e.g.* multi-loculated hydropneumothorax)
Improves safety of pleural procedures	
Allows real-time invasive procedure guidance	
More sensitive than computed tomography for pleural fluid characterisation	

Technical aspects

Transducers (probes) emit ultrasound waves with a given frequency and wavelength. These waves penetrate tissues for variable distances and a portion of these waves are reflected back while the other portion are absorbed into tissues. The traversing ultrasound waves encounter varying degrees of resistance according to the density of a given medium which leads to some attenuation of the amplitude of ultrasound waves. The attenuation potential is lowest for liquids and highest for air. The ultrasound waves returning to the transducer, after being reflected from tissues they encounter, are used to construct a two-dimensional image based on the time the waves take to return to the transducer (determining the distance of the reflecting structure from the surface) and the amplitude of returning waves (determining the brightness or echo-texture of a given structure). The attenuation coefficients for air and bone are very high, meaning that ultrasound waves cannot form an image for bony or air-filled structures [2].

Ultrasound machines come equipped with different probes that have different sizes/footprints and are capable of generating specific ranges of ultrasound frequencies. High-frequency ultrasound waves are only capable of penetrating shallow structures but with very good image resolution. Low frequency waves are useful to image deeper structures but with lower image qualities. Examining the chest wall and parietal pleura can be achieved by a high frequency (usually linear) probe which operates with a frequency range of 7.5–12 MHz, and is capable of penetrating to depths of 2–5 cm. For imaging deeper structures such as a pleural effusion or a lung abnormality, a low frequency probe, which typically has a curvilinear footprint, is more suitable. It generates a frequency range of 2–5 MHz which is capable of penetrating up to a depth of 10–25 cm from the surface of the skin. The latter is the probe most widely used in examining patients with pleural effusion [3].

Image acquisition

In order to access the pleural space, the ultrasound beams need to be directed between the ribs, as bony structures cause complete reflection of ultrasound waves casting shadows and obscuring all deeper tissue. When the ultrasound probe is oriented perpendicular to an intercostal space, two anechoic (black) shadows are created by the bordering ribs and the inside of the chest cavity is only visible from between the ribs (figure 1a). However, by rotating the probe 90° so that its long axis is parallel to the ribs, a complete image of the pleural space is acquired (figure 1b) by carefully accessing the so-called acoustic window between the ribs.

Modes

The description above details how the image is formed in the brightness (B)-mode which is also termed the greyscale due to the different shades of grey that are imparted to tissues according to their echo-texture. Most of the examination purposes are achieved in this mode, including real-time guidance during procedures. Motion (M)-mode is a useful mode during TUS examination which is used to closely examine (and quantify) the degree of motion of a specific structure or section of the TUS image. A

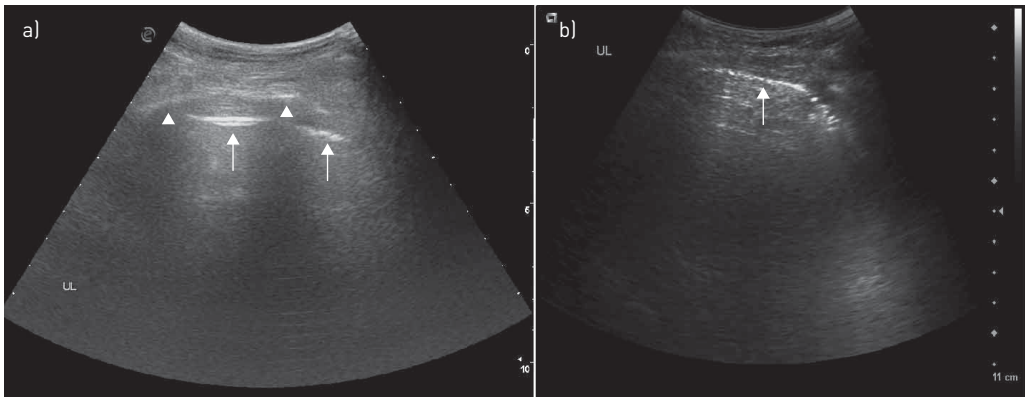

FIGURE 1 a) Thoracic ultrasound using low frequency probe oriented perpendicular to the intercostal space long axis. Note how the ribs (arrowheads) cast deep shadows causing interruption to the pleural line (arrows). b) The same image after orienting the probe to remove the rib shadows. Note the continuous pleural line (arrow).

movable vertical reference line is used to determine the section of interest in the greyscale picture and once M-mode is applied, the image is changed to a strip that shows the movement of structures on this reference line over time. M-mode is a one-dimension image as opposed to the two-dimension image obtained with the B-mode (figure 2a for M-mode examination of diaphragm movement). Doppler scanning can be added to the greyscale image for ease of identification of moving fluids, and particularly blood vessels. This mode applies a colour in the range between red and blue to the vascular structure. The colour is determined according to the speed and the direction of the moving blood towards or away from the transducer (and does not represent arterial or venous blood) (figure 2b).

Anatomy

The most appropriate position to systematically examine the pleural spaces is to sit the patient upright or slightly leaning forward and to examine them from behind. Both sides should be examined even if the abnormality identified by previous imaging was only on one side. Due to the oblique orientation of intercostal spaces at the back, the authors prefer to orient the probe upward and laterally to explore the pleural spaces thoroughly. This starts by identifying the space where the diaphragm and underlying abdominal viscera (the liver and kidney on the right, or the spleen and kidney on the left) are seen. It is the radiological convention to have the probe oriented so that the structures above the diaphragm are on the left side of the image with caudal structures on the right. This is for ease of interpretation of stored images that are reviewed after an examination is finished, and reduces the tendency for error when moving from one side to another. Following the identification of the diaphragm, the probe is moved cranially while maintaining the same angle to inspect the rest of the hemithorax. This is followed by moving the examination laterally to the mid-axillary line and anteriorly and repeating the inspection from the lower most space upwards.

The skin, subcutaneous tissue and intercostal muscles are seen using any probe, although the resolution and the details are much finer with the linear (high frequency) probe [4]. The intercostal vessels can be visualised between the intercostal muscles using Doppler. Except for the first and last 6 cm of their courses, the vessels are usually shielded beneath the lower border of the upper rib in a given space (and hence are not seen by TUS), although variations and tortuosity are occasionally seen, especially in the elderly (figure 2b) [5].

In normal pleura the membranes appear deeper to the intercostal muscles as a single 0.2 mm line (figure 1) that shows in real-time the "sliding" sign; a shimmering movement caused by the gliding of the parietal over the visceral pleura. The underlying lung is not normally visualised as air causes scattering of ultrasound beams, but the presence of pleural fluid (an excellent medium for ultrasound waves' propagation) allows the examination of deeper structures including the collapsed lung. Therefore, it should be noted that the "lung sliding" sign is in fact a sonographic artifact created by the ultrasound waves, and does not represent "normal lung" as opposed to anatomical details that can be delineated during ultrasound examination of other organs, *e.g.* the liver or thyroid gland. However, the normal pattern of artifacts can be used to exclude the presence of pathology such as pneumothorax, peripheral lung consolidation or pulmonary oedema.

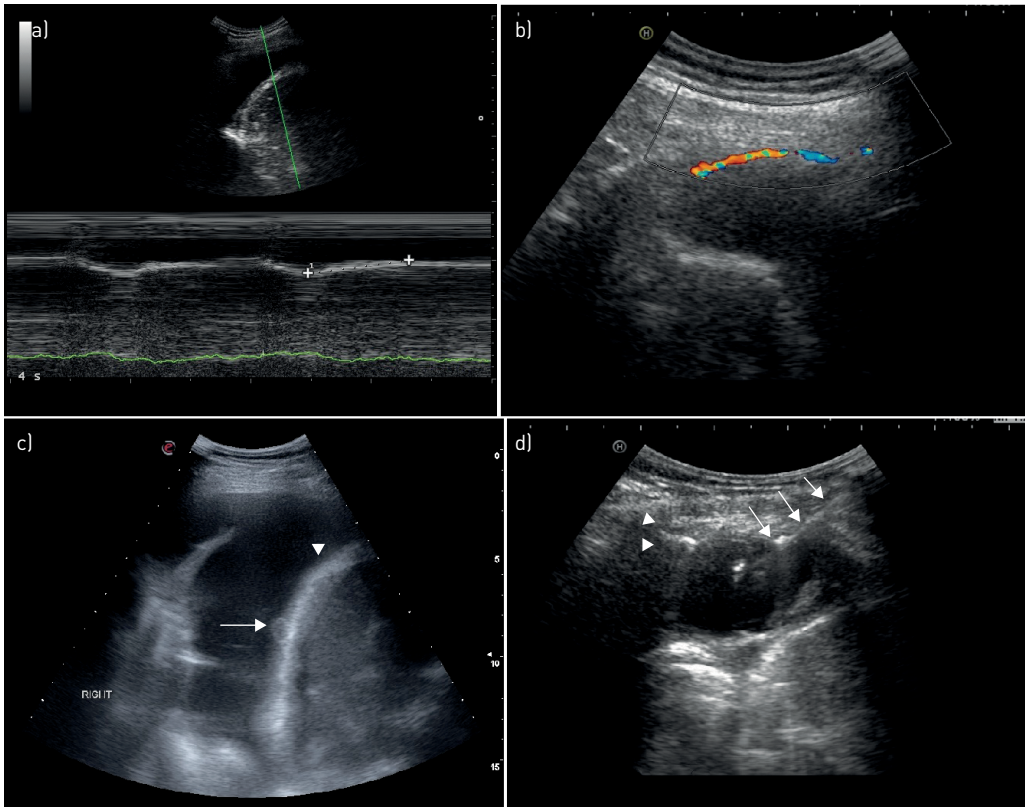

FIGURE 2 a) The upper part of the image is an ultrasound still in B-mode of pleural effusion and hemidiaphragm, with a green line traversing the middle. The lower part of the image corresponds to the M-mode image acquired for the structures traversed by the green line moving over time. Note the wavy white line and the + marks pointing to the degree of diaphragm excursion in one respiratory cycle. b) Doppler examination showing an unshielded intercostal vessel in the deep part of the chest wall. c) Right pleural effusion, collapsed lung and convex thickened hemidiaphragm (arrowhead). Malignancy is confirmed by the presence of a nodule (arrow) on the diaphragm. d) Under real-time ultrasound guidance a core-cutting needle (arrows) is advanced to biopsy the parietal pleural thickening, the extent of which is indicated by two arrowheads.

In the presence of pleural effusion, various characteristics should be evaluated. The size of the effusion should be noted. Semi-quantitative methods measuring the depth of the effusion and its height in rib spaces usually suffice, but various methods exist for more accurate calculations [6]. The echogenicity (brightness) of the effusion should also be noted, as it gives an indication to its aetiology (figure 3a and b). Echogenic effusions are usually due to exudates [7], although concentrated transudates due to diuretic therapy can appear echogenic [8]. Anechoic effusions can be transudative or exudative. Exudative effusions either due to infection or malignancy tend to form fibrous septations (figure 3c), which, if present, have various diagnostic and therapeutic implications. The presence and extent of such septations should also be noted. The parietal and visceral pleurae should be inspected for thickening or nodularity. The latter is highly predictive of pleural malignancy [9].

Inspection of the position of the diaphragm, its configuration and mobility and the presence of any thickening or nodularity of its covering pleura is very useful in cases of suspected pleural malignancy (figure 2c) [10]. The diaphragm should appear convex towards the thorax and should descend towards the abdomen during inspiration, a mechanism which can be impaired with large effusions where paradoxical movement can occur.

Diagnosis

Infection

The ultrasound echo-texture of an effusion can point to its aetiology. Homogeneously echogenic effusions tend to occur with haemorrhagic pleural effusions and empyema [11]. A less known sonographic sign, the "suspended microbubble sign", which describes echogenic shadows floating up the ultrasound screen and represents gas bubbles is occasionally depicted in purulent pleural collections [12, 13].

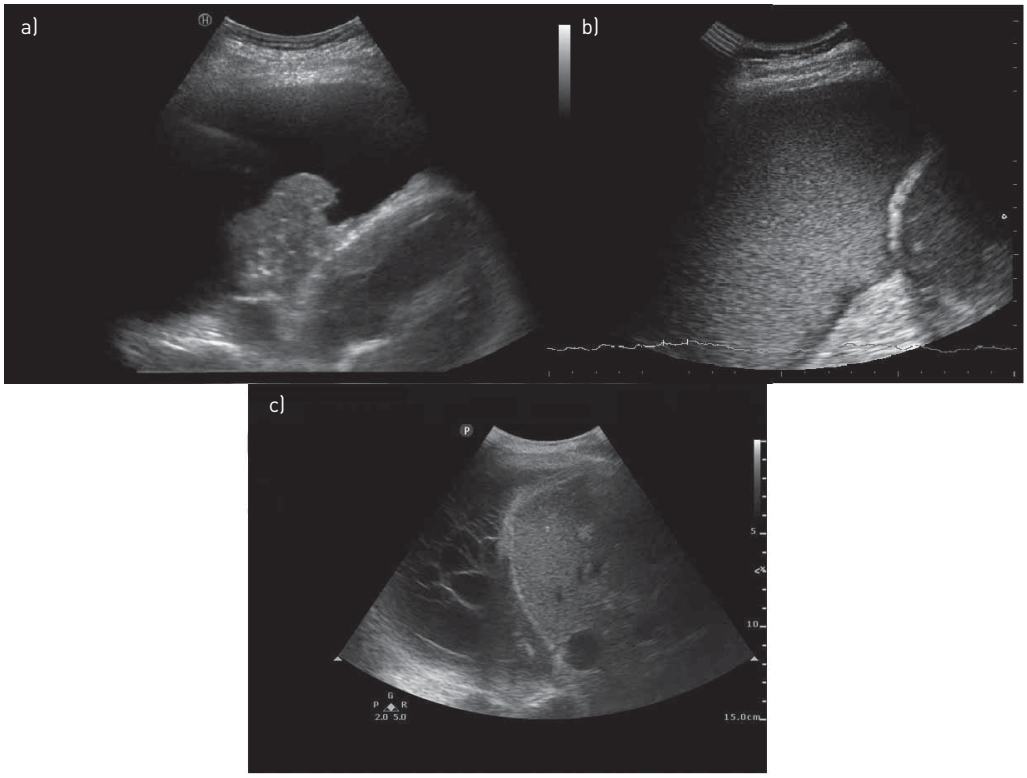

FIGURE 3 a) Non-echogenic pleural effusion and part of the collapsed lung. b) Highly echogenic effusion and underlying diaphragm. c) Complex septated right pleural effusion.

Pleural aspiration is required to determine the nature of any effusion and, should infection be diagnosed, a small-bore chest tube will be required. As per the BTS guidelines, both procedures should be done with the guidance of TUS to ensure a successful and safe procedure [1]. More recently, it has been demonstrated that obtaining TUS-guided pleural biopsies for microbial cultures on drain insertion for pleural infection improved the microbial yield by 30% in comparison to cultures of pleural fluid alone without imparting any increased risk of complications [14]. This technique can be particularly useful in patients who have received antibiotics prior to sending pleural fluid cultures.

Ultrasound is more sensitive than thoracic computed tomography (CT) in detecting septations in the pleural fluid (figure S1). Extensive septations can complicate the management of pleural infection by impeding thorough drainage (figure 3c), and may be predictors of failed medical treatment and the need for management escalation [15, 16]. In these septated effusions, real-time TUS guidance can be used to direct chest drain placement into the largest locule visualised. Knowing that an effusion is multi-septated is also useful because pleural fluid pH can vary between different locules of fluid which has an important bearing on the management [17].

Malignancy

Mesothelioma is the only major primary pleural malignancy. However, the pleura is more commonly involved by malignancy in the setting of metastatic cancer, with lung and breast being the most common primaries to metastasise to the pleura [18]. TUS can aid in the diagnosis of pleural malignancy and has been demonstrated to have high specificity for malignancy with certain sonographic features. For pleural procedures such as thoracentesis, image-guided pleural biopsies and medical thoracoscopy, which may be needed to obtain cytological or histological confirmation, TUS is required either for procedural planning or execution (see Procedure guidance section).

TUS can delineate pleural thickening and irregularity and can identify biopsy sites in cases of suspected malignancy, even in the absence of a pleural effusion [4]. In cases of malignant pleural effusion (MPE), metastatic pleural nodules >5 mm seen on TUS on the parietal or diaphragmatic pleura is pathognomonic of pleural malignancy (figure 2c) [4]. Other TUS features suggesting malignancy include pleural thickening >1 cm and the presence of hepatic deposits [10]. The combination of the aforementioned sonographic criteria had a sensitivity of 79% and specificity of 100% for diagnosing pleural malignancy [10]. TUS is

particularly helpful in this context, as malignant deposits tend to be most extensive nearer to the diaphragm which is the region most amenable to TUS examination in the presence of pleural fluid [10, 19].

An additional merit for TUS in malignancy is that infiltration of the pleura or chest wall by thoracic malignancy is best delineated by TUS that has a sensitivity of 89%, which is much higher than that of thoracic CT (42%) [20].

A more recent innovation, shear wave elastography, which measures the degree of stiffness of tissue, has been shown to enable differentiation between benign and malignant pleural thickening, where the latter was found to be stiffer, and to facilitate faster propagation of the elastography waves. Using a specific cut-off for the speed of wave propagation, the sensitivity of identifying malignant pleural disease was 83.64% with a specificity of 90.67% [21].

Pneumothorax

Pneumothorax is the abnormal accumulation of air in the pleural space. It seems counter intuitive that ultrasound beams, which are scattered by air, can be used to diagnose pneumothorax. The sonographic features for diagnosing pneumothorax are based on the disappearance of the normal TUS features seen in the presence of normally aerated lung when the pleural layers are opposed. Lack of pleural sliding is one of the signs suggesting the presence of pneumothorax. Applying M-mode can help in the differentiation between present and absent pleural sliding since normal sliding on M-mode exhibits a granular pattern deeper to the pleural line while in the absence of sliding this granular pattern is replaced with multiple parallel hyperechoic lines (the so-called barcode sign). The main caveat with using this sign is that it is not specific to pneumothorax as sliding can be significantly impaired or absent in conditions such as severe emphysema or following pleural infection or pleurodesis [3, 22]. The most specific TUS sign for pneumothorax is the "lung point". This is the point where the sliding lung can be seen together with the non-sliding pleura in the same TUS image and the sliding lung is observed to encroach on the still part and recede again with breathing [22]. In patients with proven pneumothorax, the lung point seen on TUS had a specificity of 100% but with a sensitivity of 66% [23] meaning that the sign is pathognomonic of pneumothorax, but its absence cannot rule out the condition.

TUS is frequently criticised for having considerable limitations in diagnosing pneumothorax [3, 24]. It can be particularly difficult to interpret in large air collections as no lung point is identifiable if the lung is fully collapsed and away from the chest wall [25] and lung sliding can be abolished following pleurodesis or when there is lung bullae. However, there is a wealth of literature supporting the use of TUS as a point-of-care test for patients with suspected pneumothorax in the acute and emergency settings [20]. Two meta-analyses concluded that bedside TUS is more accurate than supine radiography to screen for pneumothorax in trauma patients [26, 27]. Even small pneumothoraces that are not picked up on radiographs are clinically relevant in such patients who are commonly put on positive pressure ventilatory support with its risks of increasing the size of pneumothorax and dictating the need for chest drainage [28]. Following up these patients can be achieved using TUS which can delineate an enlarging pneumothorax if the lung point seen during earlier examination is noticed to move laterally in an intercostal space [29]. It should be noted that the size of pneumothorax (as can be easily seen and quantified on a chest radiograph for the purpose of therapeutic choice) is not measurable using TUS, and complex pneumothoraces where there is tethered lung requires CT imaging for both delineation and intervention and, therefore, the use of TUS to diagnose pneumothorax is better reserved for critical situations where waiting to obtain a radiography may not be safe in the emergency department or intensive care units.

Procedure guidance

Planning

The risk of iatrogenic complications or a "dry tap" following blind thoracentesis has long been acknowledged [30]. In 2008, a safety alert was raised in the UK calling for a change of practice to guard against the avoidable complications of blind pleural procedures [3]. The BTS guidelines strongly recommend using TUS before procedures involving pleural effusion [1]. Previously, TUS "guidance" for pleural procedures was accomplished by sending the patient for TUS assessment at the Radiology department where the safe point of entry was marked and then the patient was transported back to the ward or room where the procedure was to be performed. This so-called "X marks the spot" method was found to be associated with an unacceptable risk of iatrogenic pneumothorax [31] due to the inevitable changes in the patient's position and the relationship between the effusion position and the skin mark from when the TUS was performed until the actual execution of the procedure. Thus, it is necessary to minimise any repositioning or time lapse between the TUS examination and the procedure to ensure success of the intervention and maintain patient's safety [3]. A large nationwide study from the USA

found that TUS guidance for pleural aspiration resulted in a reduction in the incidence of iatrogenic pneumothorax by 19% in comparison to procedures carried out blindly (OR 0.81, 95% CI 0.74–0.90) [32].

With the widespread availability of competence in TUS by chest physicians, sending a patient with an effusion to the radiologist for a TUS scan has become uncommon. However, to minimise any potential harm to patients, cases with small fluid collections that require real-time TUS guidance during the procedure should be referred to an individual with appropriate experience of conducting such techniques; either an experienced pleural physician or interventional radiologist.

The usual position of the patient for TUS scanning is the sitting position, which is also suitable for thoracentesis that is typically carried out in one of the intercostal spaces at, or very close to, the mid-axillary line. With loculated effusions, this position may need to be altered. Patient positioning during TUS examination is shifted to the lateral decubitis posture for procedures that are carried out in this position. This includes pleural biopsies either *via* medical thoracoscopy or TUS-guided tru-cut needle and indwelling pleural catheter insertion [3, 33].

Conventionally, before a pleural procedure, prior imaging in the form of a chest radiograph or CT scan will have been performed. A comprehensive TUS mapping of the identified effusion (or any other lesion) is attempted as described above. The point of intervention should preferably be in the mid-axillary line, or at least >6 cm from the spine, to stay away from the unguarded intercostal bundle [34]. Once a spot is identified for intervention, the authors prefer to screen for a vulnerable intercostal artery using Doppler scanning (figure 2b) and to avoid, where possible, any point where the artery is in the middle of the space since its laceration can potentially lead to serious bleeding [35].

During planning for medical thoracoscopy, TUS should be performed while the patient is on the table as it ensures safe entry to the pleural cavity without injury to the underlying lung [36, 37]. Centres with advanced capabilities in medical thoracoscopy perform pneumothorax induction prior to procedures where there is little or no pleural effusion. In this situation it is very important to ensure that the lung is not tethered to the chest wall which means that if air is allowed into the pleural space, the lung will collapse and a space will be created to enable performing the procedure [33, 37]. TUS is useful in predicting lung tethering by observing lung sliding [38]. In cases where there is no lung sliding, patients can be triaged to TUS-guided core-cutting pleural biopsy while on the table in order to avoid futile and complication ridden attempts to conduct medical thoracoscopy. In a review from a dedicated pleural unit, 5.2% of 252 attempted medical thoracoscopy procedures over a 4-year period were converted to TUS-guided pleural biopsy due to lack of safe TUS features to proceed [39]. Of these converted procedures, 85% provided sufficient tissue for diagnosis using a TUS cutting needle technique, avoiding a further procedure [39].

Real-time guidance

TUS-guided pleural biopsies are now carried out by chest physicians in several centres around the world which means that fewer procedures are carried out by radiologists and under CT guidance [3, 33]. TUS involvement during a procedure can be described as assistance (the freehand approach) or guidance (the real-time approach). Real-time TUS guidance, where the needle is introduced into tissues and biopsies are taken under full ultrasound vision (figure 2d) is more time consuming and requires more training and experience.

In the setting of high tuberculosis prevalence (where lesions diffusely affect the pleura), the yield from TUS-assisted biopsies approach 90% with a very low rate of complications [40]. For suspected pleural malignancy, TUS-guided (but not TUS-assisted) pleural biopsies had a diagnostic yield similar to CT-guided biopsies and a better safety profile [39, 41, 42]. The improved safety with TUS guidance compared to CT is related to the real-time capability of the former which allows for compensation of respiratory movements while advancing the needle under vision, ensuring that the pleural surface or thickening is tangentially biopsied [43]. Other advantages include lower cost, shorter procedure times and no exposure to ionising radiation.

As previously mentioned, sliding seen on TUS permits medical thoracoscopy to proceed safely in patients who require pleural biopsy without having pleural effusion. Moreover, TUS can be used to guide the needle used to induce pneumothorax, to visualise pneumothorax induction in real-time and to confirm the formation of pneumothorax before introducing the trocar [44].

Post-procedure complications

The authors routinely perform TUS examination following any pleural intervention to screen for any complications that may occur early in their course which facilitates appropriate and timely management. Post-intervention bleeding can be noted either on Doppler scanning [45] or occasionally as spreading echogenic material from the puncture site [46]. Early recognition expedites management and minimises

the potential for harm to the patient [34]. In addition, TUS is useful as a tool to detect the formation and enlarging of a pneumothorax following interventions in the thorax [25].

Prognostication

Symptomatic benefit

Pleural fluid accumulation leads to breathlessness and in many, but not all, cases its drainage improves breathing. The growing effusion causes compression of the underlying lung together with an increase in the size of the affected hemithorax which manifests as bulging of the chest wall (due to loss of the pulling forces of the lung) and flattening or even inversion of the ipsilateral diaphragmatic cupola (figure 4) [47]. Animal studies have shown that the functional residual capacity of the lung shrinks by only one-third of the volume of the accumulated fluid [48] and that the rest of the volume of the effusion is accommodated by the downward displacement of the diaphragm [49]. The abnormal shape of the diaphragm puts it in a disadvantageous point in its length-tension curve which impairs its capacity to generate trans-diaphragmatic pressure in a way similar to that seen in patients with hyperinflation due to emphysema [50]. This mechanical disadvantage causes dissociation between the neural drive to the diaphragm and the actual tension generated which is responsible for the sensation of significant breathlessness [47].

Diaphragm dysfunction can be observed sonographically as the paradoxical movement of the hemidiaphragm towards the thorax with inspiration [3]. It has been shown that patients whose effusion causes flattening, diaphragm inversion (figure 4) or paradoxical movement experience considerable symptomatic improvement following effusion drainage [51]. This means that TUS can be useful in complex patients who suffer from pleural effusion besides other pathologies that can contribute to breathlessness (such as lung masses or pulmonary embolism), as identifying distorted diaphragm shape and movement on TUS means that the effusion is contributing to breathlessness and that draining the effusion is likely to improve symptoms [3]. However, it should be noted that the opposite is not proven to be true, *i.e.* even if the diaphragm is not flat/inverted, thoracentesis may result in symptom improvement. Additionally, if thoracentesis is performed, the aim should be to drain until the diaphragm reverts to its normal shape instead of targeting a pre-specified volume.

Non-expandable lung

In patients with large symptomatic MPE, the ability to predict the likelihood of lung re-expansion following complete drainage is beneficial to tailor the most suitable therapeutic option for managing such effusions. The lung that does not re-inflate following pleural fluid drainage is termed non-expandable lung (NEL). In the presence of NEL, long-term management of symptomatic MPE should be in the form of indwelling pleural catheter insertion and not pleurodesis which is not achievable if the two layers of the pleura cannot be brought into apposition. For a long time, the only method available to diagnose NEL was to perform pleural manometry which entails serial pleural pressure measurements during effusion drainage [52], or to conduct a large volume thoracentesis and a post-procedure chest radiograph. Manometry is a tedious procedure that is seldom carried out outside research and in a number of interested centres. A group of investigators studied the potential use of TUS to predict the presence of NEL [53]. They looked at the degree of movement and deformation of the collapsed lung secondary to heart beats during breath-hold. Lung movement was measured in the M-mode (figure S2) while lung strain was measured using the speckle tracking function of echocardiography [53]. The group found that NEL showed less movement and deformation in comparison to lungs that eventually expanded following drainage. Moreover, in the same study, the sensitivities of both methods to predict NEL exceeded that of pleural manometry [53]. Another group found that the degree of displacement of the collapsed lung measured in M-mode could predict incomplete lung re-expansion following medical thoracoscopy [54].

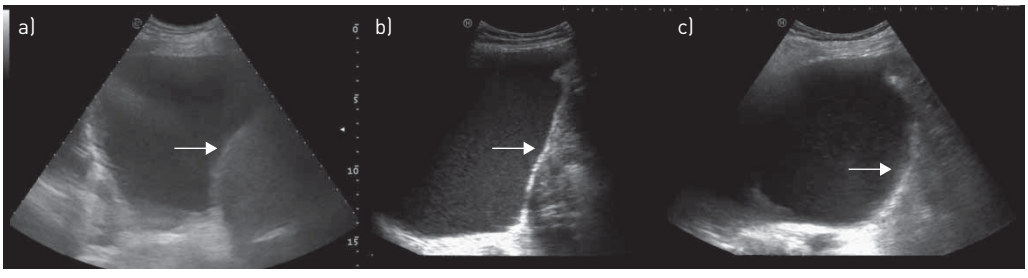

FIGURE 4 Three images showing the effect of the weight of pleural effusion on the configuration of the corresponding hemidiaphragm that changes from a) its normal convex shape, b) to be flattened and c) with larger effusions becoming inverted.

This is a promising technique that can become a simple and noninvasive tool in predicting whether the lung would re-expand following intervention. The information gained from the technique that can be easily performed by chest physicians could inform the discussion between the clinician and the patient regarding the management plan and the possible therapeutic options.

Pleurodesis success

Pleurodesis is the application of an injurious substance into the pleura with the aim of causing symphysis of the two layers and obliteration of the potential space between them. This is most commonly carried out in MPE or in recurrent pneumothorax [55]. Given that sliding is a TUS sign caused by gliding of the pleural membranes, pleurodesis intuitively is expected to abolish this sign. This was tested in patients with pneumothorax who underwent surgical pleurodesis either by pleurectomy or pleural abrasion. The investigators found that 3 weeks after surgery, pleural sliding as assessed by TUS was abolished in all chest regions in patients who underwent pleurectomy and in most of the chest regions in those who had pleural abrasion [56]. In an animal study, the lack of pleural sliding on TUS was strongly correlated with macroscopic and microscopic pleural symphysis in pigs with artificial pneumothorax exposed to talc pleurodesis [57]. In a recent case series of patients with MPE who underwent talc slurry pleurodesis, a TUS pleural adherence score obtained 24 h post-pleurodesis could predict effusion recurrence [58]. The SIMPLE randomised trial is currently enrolling to further assess the role of TUS in outcome prediction of pleurodesis and whether its use can expedite the decision for chest tube removal and discharge in patients with MPE by studying the pattern of pleural sliding before and after pleurodesis [59].

Another sonographic feature that has been recently studied as an outcome predictor for talc pleurodesis success in patients with MPE is the echo-texture of the pleural effusion. The presence of echogenic swirling, a finding that is commonly seen in MPE [60], was associated with lower incidence of pleurodesis success when compared to effusions that lack this feature [61].

Conclusions and future directions

The introduction and widespread use of TUS as a point-of-care test has revolutionised the management of pleural diseases. A once diagnostic tool for detection of pleural effusion only, the uses of TUS in pleural diseases have expanded to include various diagnostic and therapeutic indications enhancing the accuracy of diagnosis and refining treatment decisions. Further work is ongoing to explore the potential use of TUS for prognostication in different pleural diseases. Newer techniques are emerging such as elastography and contrast-enhanced TUS and current research is looking at its role in differentiating benign from malignant pleural disease and whether it can be used to direct biopsy sites in cases of suspected thoracic malignancy.

Author contributions: M. Hassan conceived the report and prepared the first draft. All authors contributed in data collection. R.M. Mercer and N.M. Rahman critically reviewed the draft and bibliography. All authors reviewed and agreed to the final manuscript.

Conflict of interest: None declared.

References

1 Havelock T, Teoh R, Laws D, *et al.* Pleural procedures and thoracic ultrasound: British Thoracic Society pleural disease guideline 2010. *Thorax* 2010; 65: i61–i76.
2 Alerhand S, Graumann O, Nelson BP. Physics and basic principles. *In:* Laursen CB, Rahman NM, Volpicelli G, eds. Thoracic Ultrasound (ERS Monograph). Sheffield, European Respiratory Society, 2018; pp. 1–13.
3 Corcoran JP, Tazi-Mezalek R, Maldonado F, *et al.* State of the art thoracic ultrasound: intervention and therapeutics. *Thorax* 2017; 72: 840–849.
4 Hassan M, Rahman NM. Chest wall and parietal pleura. *In:* Laursen CB, Rahman NM, Volpicelli G, eds. Thoracic Ultrasound (ERS Monograph). Sheffield, European Respiratory Society, 2018; pp. 31–42.
5 Helm EJ, Rahman NM, Talakoub O, *et al.* Course and variation of the intercostal artery by CT scan. *Chest* 2013; 143: 634–639.
6 Hassan M, Rizk R, Essam H, *et al.* Validation of equations for pleural effusion volume estimation by ultrasonography. *J Ultrasound* 2017; 20: 267–271.
7 Yang PC, Luh KT, Chang DB, *et al.* Value of sonography in determining the nature of pleural effusion: analysis of 320 cases. *AJR Am J Roentgenol* 1992; 159: 29–33.
8 Asciak R, Hassan M, Mercer RM, *et al.* Prospective analysis of the predictive value of sonographic pleural fluid echogenicity for the diagnosis of exudative effusion. *Respiration* 2019; 97: 451–456.
9 Rahman NM, Gleeson FV. Lung, pleura and chest wall. *In:* Allan PL, Baxter GM, Weston MJ, eds. 3rd Edn. Clinical Ultrasound. London, Elsevier, 2011; pp. 1005–1021.
10 Qureshi NR, Rahman NM, Gleeson FV. Thoracic ultrasound in the diagnosis of malignant pleural effusion. *Thorax* 2009; 64: 139–143.
11 Davies HE, Davies RJO, Davies CWH. Management of pleural infection in adults: British Thoracic Society pleural disease guideline 2010. *Thorax* 2010; 65: ii41–ii53.
12 Hassan M, Asciak R, Rizk R, *et al.* Lung abscess or empyema? Taking a closer look. *Thorax* 2018; 73: 887–889.
13 Lin FC, Chou CW, Chang SC. Usefulness of the suspended microbubble sign in differentiating empyemic and nonempyemic hydropneumothorax. *J Ultrasound Med* 2001; 20: 1341–1345.

14 Psallidas I, Kanellakis N, Bhatnagar R, *et al.* S24 A phase I feasibility study in establishing the role of ultrasound-guided pleural biopsies in pleural infection (the audio study). *Thorax* 2017; 72: A17–A18.
15 Chen KY, Liaw YS, Wang HC, *et al.* Sonographic septation: a useful prognostic indicator of acute thoracic empyema. *J Ultrasound Med* 2000; 19: 837–843.
16 Shankar S, Gulati M, Kang M, *et al.* Image-guided percutaneous drainage of thoracic empyema: can sonography predict the outcome? *Eur Radiol* 2000; 10: 495–499.
17 Maskell NA, Gleeson FV, Darby M, *et al.* Diagnostically significant variations in pleural fluid pH in loculated parapneumonic effusions. *Chest* 2004; 126: 2022–2024.
18 Roberts ME, Neville E, Berrisford RG, *et al.* Management of a malignant pleural effusion: British Thoracic Society pleural disease guideline 2010. *Thorax* 2010; 65: ii32–ii40.
19 Ferrari G, Helbo Skaarup S, Panero F, *et al.* The diaphragm. *In:* Laursen CB, Rahman NM, Volpicelli G, eds. Thoracic Ultrasound (ERS Monograph). Sheffield, European Respiratory Society, 2018; pp. 129–147.
20 Bandi V, Lunn W, Ernst A, *et al.* Ultrasound *vs* CT in detecting chest wall invasion by tumor. *Chest* 2008; 133: 881–886.
21 Jiang B, Li X, Yin Y, *et al.* Ultrasound elastography: a novel tool for the differential diagnosis of pleural effusion. *Eur Respir J* 2019; 54: 1802018.
22 Oveland NP. Pneumothorax. *In:* Laursen CB, Rahman NM, Volpicelli G, eds. Thoracic Ultrasound (ERS Monograph). Sheffield, European Respiratory Society, 2018; pp. 43–63.
23 Lichtenstein D, Mezière G, Biderman P, *et al.* The "lung point": an ultrasound sign specific to pneumothorax. *Intensive Care Med* 2000; 26: 1434–1440.
24 Tschopp J-M, Bintcliffe O, Astoul P, *et al.* ERS task force statement: diagnosis and treatment of primary spontaneous pneumothorax. *Eur Respir J* 2015; 46: 321–335.
25 Hallifax RJ, Talwar A, Wrightson JM, *et al.* State-of-the-art: radiological investigation of pleural disease. *Respir Med* 2017; 124: 88–99.
26 Ding W, Shen Y, Yang J, *et al.* Diagnosis of pneumothorax by radiography and ultrasonography: a meta-analysis. *Chest* 2011; 140: 859–866.
27 Alrajhi K, Woo MY, Vaillancourt C. Test characteristics of ultrasonography for the detection of pneumothorax: a systematic review and meta-analysis. *Chest* 2012; 141: 703–708.
28 Ball CG, Hameed SM, Evans D, *et al.* Occult pneumothorax in the mechanically ventilated trauma patient. *Can J Surg* 2003; 46: 373–379.
29 Volpicelli G. Sonographic diagnosis of pneumothorax. *Intensive Care Med* 2011; 37: 224–232.
30 Duncan DR, Morgenthaler TI, Ryu JH, *et al.* Reducing iatrogenic risk in thoracentesis: establishing best practice *via* experiential training in a zero-risk environment. *Chest* 2009; 135: 1315–1320.
31 Barnes TW, Morgenthaler TI, Olson EJ, *et al.* Sonographically guided thoracentesis and rate of pneumothorax. *J Clin Ultrasound* 2005; 33: 442–446.
32 Mercaldi CJ, Lanes SF. Ultrasound guidance decreases complications and improves the cost of care among patients undergoing thoracentesis and paracentesis. *Chest* 2013; 143: 532–538.
33 Bhatnagar R, Corcoran JP, Maldonado F, *et al.* Advanced medical interventions in pleural disease. *Eur Respir Rev* 2016; 25: 199–213.
34 Psallidas I, Helm EJ, Maskell NA, *et al.* Iatrogenic injury to the intercostal artery: aetiology, diagnosis and therapeutic intervention. *Thorax* 2015; 70: 802–804.
35 Kanai M, Sekiguchi H. Avoiding vessel laceration in thoracentesis. *Chest* 2015; 147: e5–e7.
36 Hersh CP, Feller-Kopman D, Wahidi M, *et al.* Ultrasound guidance for medical thoracoscopy: a novel approach. *Respiration* 2003; 70: 299–301.
37 Marchetti G, Valsecchi A, Indellicati D, *et al.* Ultrasound-guided medical thoracoscopy in the absence of pleural effusion. *Chest* 2015; 147: 1008–1012.
38 Cassanelli N, Caroli G, Dolci G, *et al.* Accuracy of transthoracic ultrasound for the detection of pleural adhesions. *Eur J Cardiothorac Surg* 2012; 42: 813–818.
39 Hallifax RJ, Corcoran JP, Ahmed A, *et al.* Physician-based ultrasound-guided biopsy for diagnosing pleural disease. *Chest* 2014; 146: 1001–1006.
40 Koegelenberg CFN, Irusen EM, von Groote-Bidlingmaier F, *et al.* The utility of ultrasound-guided thoracentesis and pleural biopsy in undiagnosed pleural exudates. *Thorax* 2015; 70: 995–997.
41 Koegelenberg CFN, Bolliger CT, Theron J, *et al.* Direct comparison of the diagnostic yield of ultrasound-assisted Abrams and Tru-Cut needle biopsies for pleural tuberculosis. *Thorax* 2010; 65: 857–862.
42 Chang DB, Yang PC, Luh KT, *et al.* Ultrasound-guided pleural biopsy with Tru-Cut needle. *Chest* 1991; 100: 1328–1333.
43 Asciak R, Rahman NM. Malignant pleural effusion. *Clin Chest Med* 2018; 39: 181–193.
44 Corcoran JP, Psallidas I, Hallifax RJ, *et al.* Ultrasound-guided pneumothorax induction prior to local anaesthetic thoracoscopy. *Thorax* 2015; 70: 906–908.
45 Corcoran JP, Psallidas I, Ross CL, *et al.* Always worth another look? Thoracic ultrasonography before, during, and after pleural intervention. *Ann Am Thorac Soc* 2016; 13: 118–121.
46 Hassan M, Rana M, Rahman NM. A patient with effusion undergoing pleural biopsy. *Chest* 2018; 154: e37–e39.
47 Thomas R, Jenkins S, Eastwood PR, *et al.* Physiology of breathlessness associated with pleural effusions. *Curr Opin Pulm Med* 2015; 21: 338–345.
48 Dechman G, Mishima M, Bates JH. Assessment of acute pleural effusion in dogs by computed tomography. *J Appl Physiol* 1994; 76: 1993–1998.
49 Sousa AS, Moll RJ, Pontes CF, *et al.* Mechanical and morphometrical changes in progressive bilateral pneumothorax and pleural effusion in normal rats. *Eur Respir J* 1995; 8: 99–104.
50 Donaldson AV, Maddocks M, Martolini D, *et al.* Muscle function in COPD: a complex interplay. *Int J Chron Obstruct Pulmon Dis* 2012; 7: 523–535.
51 Wang L-M, Cherng J-M, Wang J-S. Improved lung function after thoracocentesis in patients with paradoxical movement of a hemidiaphragm secondary to a large pleural effusion. *Respirology* 2007; 12: 719–723.
52 Huggins JT, Maldonado F, Chopra A, *et al.* Unexpandable lung from pleural disease. *Respirology* 2018; 23: 160–167.

53 Salamonsen MR, Lo AKC, Ng ACT, *et al.* Novel use of pleural ultrasound can identify malignant entrapped lung prior to effusion drainage. *Chest* 2014; 146: 1286–1293.
54 Leemans J, Dooms C, Ninane V, *et al.* Success rate of medical thoracoscopy and talc pleurodesis in malignant pleurisy: a single-centre experience. *Respirology* 2018; 23: 613–617.
55 Mercer RM, Hassan M, Rahman NM. The role of pleurodesis in respiratory diseases. *Expert Rev Respir Med* 2018; 12: 1–12.
56 Leo F, Dellamonica J, Venissac N, *et al.* Can chest ultrasonography assess pleurodesis after VATS for spontaneous pneumothorax? *Eur J Cardiothorac Surg* 2005; 28: 47–49.
57 Tazi-Mezalek R, Frankel D, Fortin M, *et al.* Chest ultrasonography to assess the kinetics and efficacy of talc pleurodesis in a model of pneumothorax: an experimental animal study. *ERJ Open Res* 2018; 4: 00158–02017.
58 Corcoran JP, Hallifax RJ, Mercer RM, *et al.* Thoracic ultrasound as an early predictor of pleurodesis success in malignant pleural effusion. *Chest* 2018; 154: 1115–1120.
59 Psallidas I, Piotrowska HEG, Yousuf A, *et al.* Efficacy of sonographic and biological pleurodesis indicators of malignant pleural effusion (SIMPLE): protocol of a randomised controlled trial. *BMJ Open Respir Res* 2017; 4: e000225.
60 Chian C-F, Su W-L, Soh L-H, *et al.* Echogenic swirling pattern as a predictor of malignant pleural effusions in patients with malignancies. *Chest* 2004; 126: 129–134.
61 Hassan M, Asciak R, Mercer RM, *et al.* Echogenic swirling seen on ultrasound and outcome of pleurodesis in malignant pleural effusion. *Arch Bronconeumol* 2019; 55: 659–666.