Ultrasound in the diagnosis and management of pleural disease

Tzu-Hsiu Tsai, MD,* and Pan-Chyr Yang, MD, PhD*†‡

The authors summarize the current applications of chest ultrasonography in the diagnosis and management of various pleural diseases. Ultrasound has been proved to be valuable for the evaluation of a wide variety of chest diseases, particularly when the pleural cavity is involved. Chest ultrasound can supplement other imaging modalities of the chest and guides a variety of diagnostic and therapeutic procedures. Pleural effusion, pleural thickening, pleural tumors, tumor extension into the pleura and even the chest wall, pleuritis, and pneumothorax can be detected easily and accurately with chest ultrasound. Many ultrasound features and signs of these diseases have been well characterized and widely applied in clinical practice. Under real-time ultrasound guidance the success rates of invasive procedures on pleural diseases increase significantly whereas the risks are greatly reduced. The advantages of low-cost, bedside availability and no radiation exposure have made ultrasound an indispensable diagnostic tool in modern pulmonary medicine.

Keywords
ultrasound, pleural disease, pleural effusion, pleural thickening, pleural tumors

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*Department of Internal Medicine, National Taiwan University Hospital; the †Institute of Biomedical Sciences, Academia Sinica; and the ‡National Health Research Institute, Taipei, Taiwan, ROC.

Correspondence to Pan-Chyr Yang, MD, PhD, Department of Internal Medicine, National Taiwan University Hospital, 7 Chung-Shan South Road, Taipei 100, Taiwan, ROC.

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Abbreviations

UP ultrasound pattern
US ultrasound

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Advances in technology have greatly improved the imaging capabilities of ultrasound (US). US has been proved to be a reliable, efficient, and informative imaging modality for the evaluation of a wide variety of chest diseases [1••,2–4,5••] and is particularly sensitive in imaging the chest wall, pleura, and pleural space because of their superficial locations [6,7,8••,9,10]. Major advantages of US include the absence of radiation, low cost, flexibility and beside availability, and short examination time compared with computed tomography.

Invasive procedures such as aspiration, needle biopsy of the pleura, and closed tube placement for effusion drainage can be performed with more accuracy and safety under US guidance. US is notably helpful for critically ill patients because of its portability and simplicity [11]. The indications and uses of chest US examination for pleural diseases are summarized as follows:

1. To clarify the nature of unknown pleural densities
2. To detect pleural effusion and guide thoracentesis and drainage, especially in minimal or loculated effusions
3. To differentiate subpulmonary effusion from subphrenic fluid accumulation and diaphragm paralysis in radiographically elevated hemidiaphragms
4. To localize pleural tumors or pleural thickening and guide needle biopsy of the pleura
5. To assist the evaluation of patients with pleuritic chest pain
6. To assess the invasion of tumors to the pleura and chest wall, and guide the transthoracic needle biopsy of the tumors
7. To recognize pneumothorax, especially for emergency situations, or when roentgenography equipment is not readily available

Techniques for chest ultrasound examination and normal ultrasound images of the chest

The US equipment suitable for chest US imaging are those equipped with 3.5-, 5-, 7.5-, or 10-MHz linear, convex, and sector transducers. During chest US examination, patients can be scanned in a sitting or supine position. Bedridden patients can be examined by turning them to oblique or decubitus positions. The probe is moved in transverse or longitudinal positions along the intercostal spaces to avoid interference by bony ribs. Normal areas are also scanned for control comparisons. A

higher frequency (5- or 7.5-MHz) transducer provides better resolutions of near structures, such as the chest wall and pleura. Otherwise, a 3.5-MHz transducer is more suitable for visualization of deeper lesions. A linear or convex transducer usually has a broad view of the field and is better than a sector scanner for screening. For lesions with a small US window or a very narrow intercostal space, however, a sector transducer is generally preferred.

Ultrasound images of the chest wall usually show soft-tissue echogenicity with multiple layers of muscle and fascia. When the transducer is oriented perpendicular to the intercostal space, normal ribs may appear as curvilinear echogenic interfaces with prominent acoustic shadow. Just beneath the chest wall, the parietal pleura lining the bony thorax and the visceral pleura covering the lungs are seen as two thin, bright echogenic lines. Normally, the two pleural lines are smooth and less than 2 mm in thickness. Between the parietal and visceral pleural lines is the pleural space, which usually measures only 0.3 to 0.4 mm. The two pleural lines normally glide with each other during respiratory movements in real-time US. This is termed the gliding sign of the pleura (Fig. 1). The gliding sign of the pleura comes from the movement of the pleura during lung excursion.

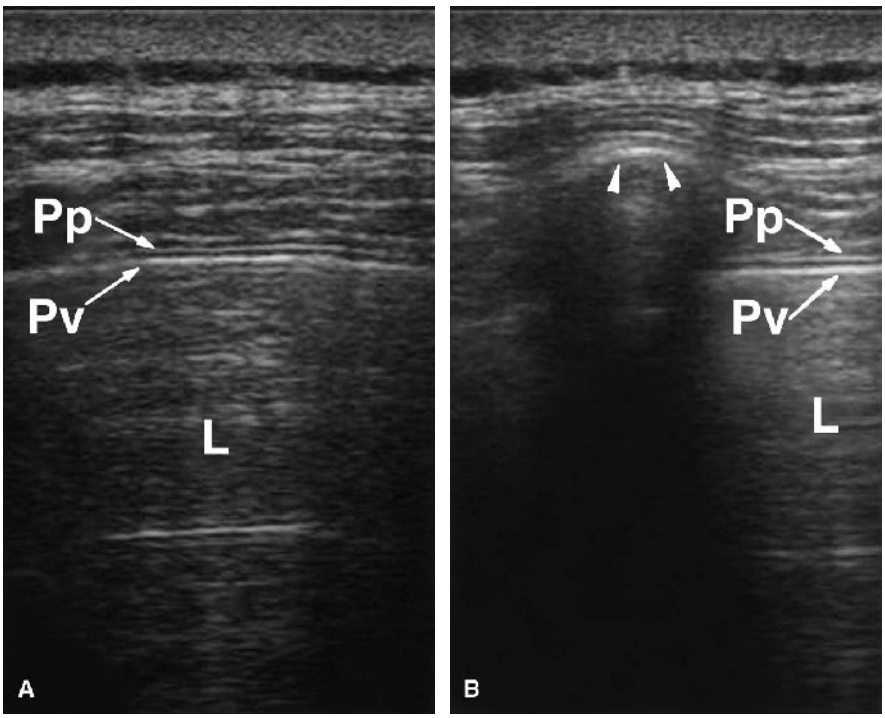
The underlying air-filled lung is a highly reflective interface that may block transmission of US into the lung parenchyma, so US images of the lung parenchyma display a pattern of repeated bright echoes caused by an acoustic reverberation artifact. These echoes are bright but formless, and diminish rapidly in intensity with increasing distance from the transducer. It is not always possible to visualize the two pleural lines and the pleural space between them. Instead, a highly echogenic line representing the pleura and pleuropulmonary surface is seen occasionally with reverberation echo artifacts beneath it. Back-and-forth movements of the echogenic pleural line during respiration (gliding sign) can still be observed in real-time US.

Both of the hemidiaphragms can be visualized just above the liver and spleen, and the respiratory movements of both hemidiaphragms can be observed in real-time US. During inspiration, the reverberation echoes of the lower lung descend progressively with lung excursion and appear like a curtain. The liver and fasted gallbladder can be used as tissue texture references for solid and fluid-containing regions. Hence, the echogenicity of a lesion is compared with that of the liver and is defined as hypoechoic, isoechoic, and hyperechoic accordingly.

Pleural effusion

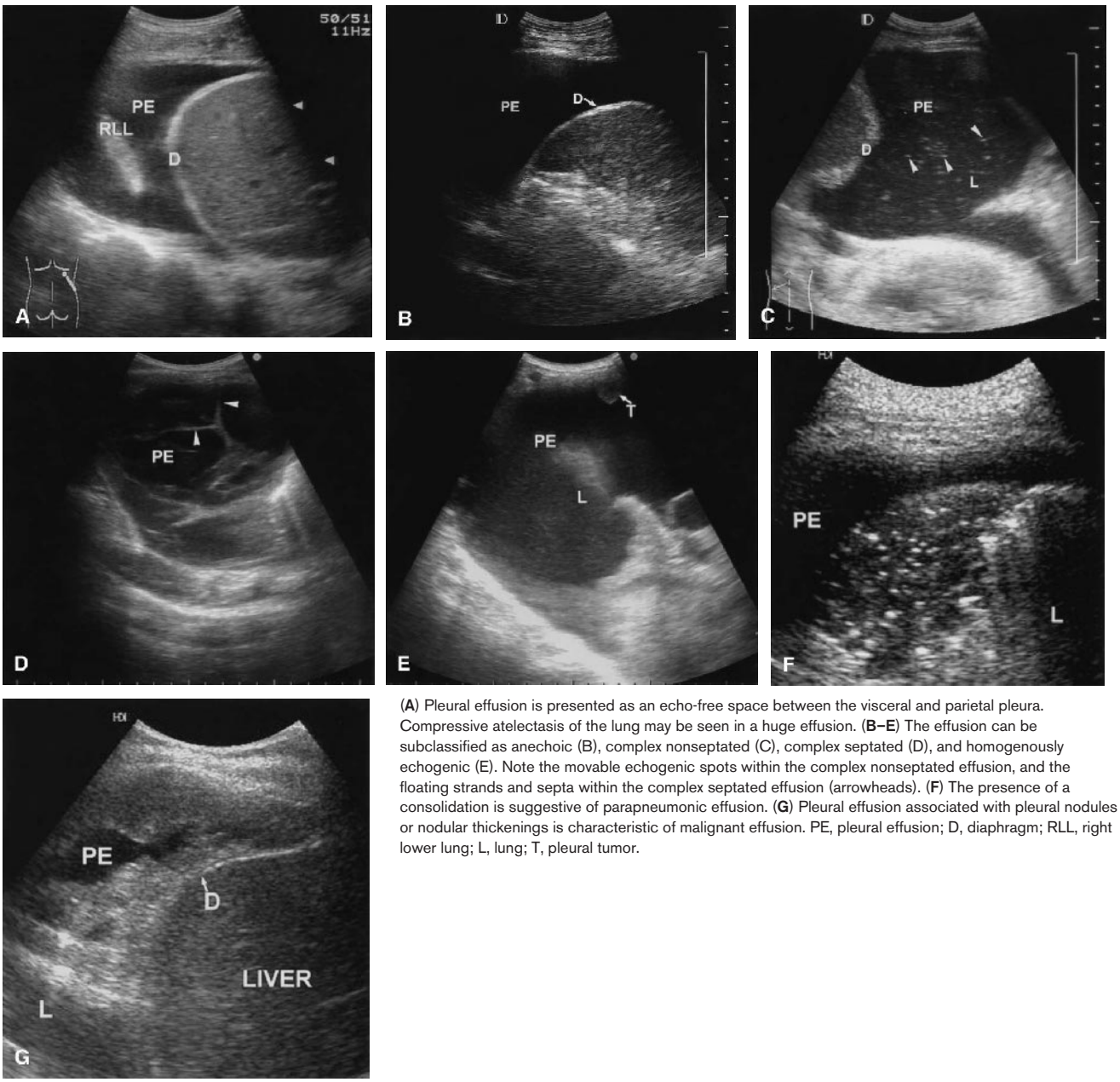
The value of US for diagnosis of pleural effusion is well documented. Even small amounts of pleural effusion can be detected accurately with US examination. The US image of pleural effusion is characterized by an echo-free space between the visceral and parietal pleura. This space may change in shape with respiration (Fig. 2A) [12•,13]. The effusion can be free or encapsulated. The compressive atelectasis of the lungs in a large effusion

Figure 1. Sonographic images of normal pleura and chest wall using a 5- to 10-MHz linear scanner



(**A**) Transverse image through the intercostal space. The chest wall is visualized as multiple layers of echogenicity representing muscles and fascia. The visceral and parietal pleura appear as echogenic bright lines that glide during respiration (gliding sign). Reverberation echo artifacts beneath the pleural lines imply an underlying air-filled lung. (**B**) Longitudinal image across the ribs. Normal ribs are seen as hyperechoic chambered surfaces (arrowheads) with prominent acoustic shadows beneath the ribs. Pp, parietal pleura; Pv, visceral pleura; L, lung.

Figure 2. Sonographic appearance of pleural effusion



(**A**) Pleural effusion is presented as an echo-free space between the visceral and parietal pleura. Compressive atelectasis of the lung may be seen in a huge effusion. (**B–E**) The effusion can be subclassified as anechoic (B), complex nonseptated (C), complex septated (D), and homogenously echogenic (E). Note the movable echogenic spots within the complex nonseptated effusion, and the floating strands and septa within the complex septated effusion (arrowheads). (**F**) The presence of a consolidation is suggestive of parapneumonic effusion. (**G**) Pleural effusion associated with pleural nodules or nodular thickenings is characteristic of malignant effusion. PE, pleural effusion; D, diaphragm; RLL, right lower lung; L, lung; T, pleural tumor.

can be seen as a tonguelike structure within the effusion. US is helpful in determining the nature of pleural opacity, identifying minimal or loculated effusion, and discriminating between subpulmonary and subphrenic effusions. If an abnormal elevation of a hemidiaphragm is noted on the chest radiograph, subpulmonary effusion can be differentiated from subphrenic fluid collection and diaphragm paralysis by defining the position of the diaphragm and by the real-time visualization of diaphragmatic motion [14]. In the presence of hemithorax opacification on chest radiograph, US is also helpful in distinguishing between fluid-filled and solid lesions [15].

Determining the nature of pleural effusion by ultrasound

Although the classification of transudate or exudate is not absolute, the distinction is helpful in suggesting further evaluation and possible diagnosis. The sonographic characteristics of effusion are helpful in differentiating transudates from exudates [12•,13]. According to the internal echogenicity, effusion can be subclassified as anechoic, complex nonseptated, complex septated, and homogenously echogenic. The effusion is defined as anechoic if totally echo-free spaces are present between the visceral and parietal pleura, complex nonseptated if

echogenic materials are inside the anechoic effusions, complex septated if floating fibrin strands or septa are inside the effusions, and homogenously echogenic if homogenously echogenic spaces are present between the visceral and parietal pleura (Fig. 2B–E). In a study of 320 patients [12•], we found that transudates are anechoic, whereas an anechoic effusion can be either a transudate or an exudate. On the other hand, pleural effusion with complex nonseptated, complex septated, and homogenously echogenic patterns are always exudates. Homogenously echogenic effusions are typically seen in hemorrhagic effusion and empyema. These echogenic natures are probably the result of the presence of tissue debris, protein-rich particles, fibrins, or blood in the pleural fluid.

Other associated sonographic findings sometimes may also help to assess the nature of pleural effusion. For example, effusion with adjacent, thickened pleura is usually indicative of an exudate. The presence of a pulmonary consolidation, which is a parenchymal wedge-shaped hypoechoic lesion with air bronchograms, suggests an exudate of infectious origin (Fig. 2F) [16]. Pleural nodules may be seen in patients with malignant pleural effusion (Fig. 2G) [17,18]. It has also been reported that sonographic septation is a useful sign to predict the need for subsequent intrapleural fibrinolytic therapy and surgical intervention in cases of acute thoracic empyema [19].

Estimating the volume of pleural effusion by ultrasound

Several studies have been performed to measure the volume of pleural effusion by means of US [20,21]. We arbitrarily classify the volume of effusion as minimal if the echo-free space is seen within the costophrenic angle; small, if the space is greater than the costophrenic angle but still within a one-probe range; moderate, if the space is greater than a one-probe range but within a two-probe range; and large or massive, if the space is bigger than a two-probe range.

Differentiation of minimal effusion from pleural thickening

Although US is very powerful in the evaluation of pleural effusion, differentiating minimal pleural effusion from pleural thickening may sometimes be difficult. Both lesions can appear as anechoic on grayscale US, and thus "free of echoes" is not a reliable sign for fluid. It has been reported that nearly 20% of echo-free pleural lesions do not yield free fluid, whereas a significant percentage of complex-appearing lesions do [22]. Therefore, predicting whether an echo-free or complex-appearing lesion is amenable to thoracentesis is not always possible with grayscale US.

Marks *et al.* [23] found that if a lesion changed shape with respiratory excursion and if it contained movable strands or echo densities, the lesion contained fluid and could be aspirated. These could be the best criteria to distinguish effusion from solid pleural lesions with grayscale US. However, these criteria still have limitations for detecting loculated and minimal fluid collection. Some pleural lesions do not change shape with respiration or have movable septa or echo densities, but are still amenable to aspiration.

It has been observed that true fluid in cases of loculated or minimal effusion may generate a color flow pattern during respiratory or cardiac cycles, and thus may display a turbulent color signal on color Doppler imaging [24,25•]. This is termed the fluid color sign of pleural effusion. Relatively high sensitivity (89.2%) and specificity (100%) of the fluid color sign in detecting minimal fluid collection have been shown in a study comprising 76 patients [25•]. In brief, an echo-free space between the visceral and parietal pleura that changes shape with respiration or contains movable strands or echo densities on grayscale US, or displays a fluid color sign on color Doppler US, indicates the presence of fluid accumulation and is amenable to thoracentesis.

Pleural thickenings and pleural tumors

Besides pleural effusion, many abnormal findings of the visceral and parietal pleura can be seen in the US images. Pleural thickenings are defined as focal echogenic lesions arising from the visceral or parietal pleura that are greater than 3 mm in width with or without irregular margins. Pleural thickening and adhesion are usually caused by putrid pleuritis, empyema, hemothorax, or iatrogenic pleurodesis. There are various echogenicities of thickened pleura. For instance, in putrid pleuritis resulting in pleural thickening, increasing echogenicity and septation of the pleural lesion may be seen with time as the pleural effusion becomes organized and solid, sometimes resulting in highly echogenic shadows indicative of calcification. It is important to differentiate minimal or loculated pleural effusion from pleural thickening before thoracentesis because both conditions may have similar US pictures [22]. The US features useful to distinguish between minimal pleural effusion and pleural thickening have been described previously [23,24,25•].

In US, pleural tumors are well-defined, hypoechoic or echogenic solid nodular lesions located in the parietal or visceral pleura. Primary neoplasms of the pleura are rare except for benign and malignant mesothelioma. Metastatic pleural tumors or mesothelioma can appear as polypoid pleural nodules or sheetlike pleural thickening combined with pleural effusion (Fig. 3) [17,18,26]. Sometimes, differentiation between pleural fibrosis and pleural tumor is difficult by US. A US-guided core needle biopsy is very helpful for pathologic diagnosis of pleural tumors [26,27].

Figure 3. Ultrasound (US) images of pleural thickening and pleural tumors

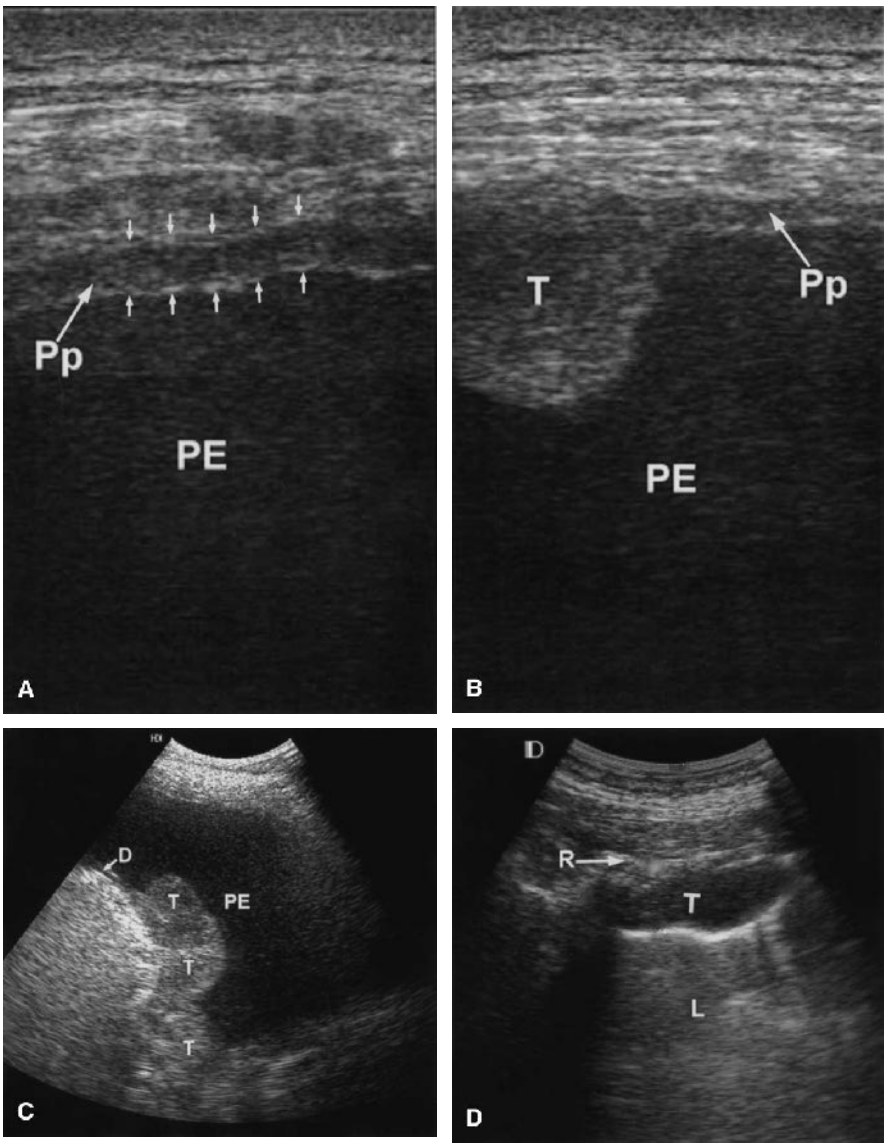


Figure 3. Ultrasound (US) images of pleural thickening and pleural tumors

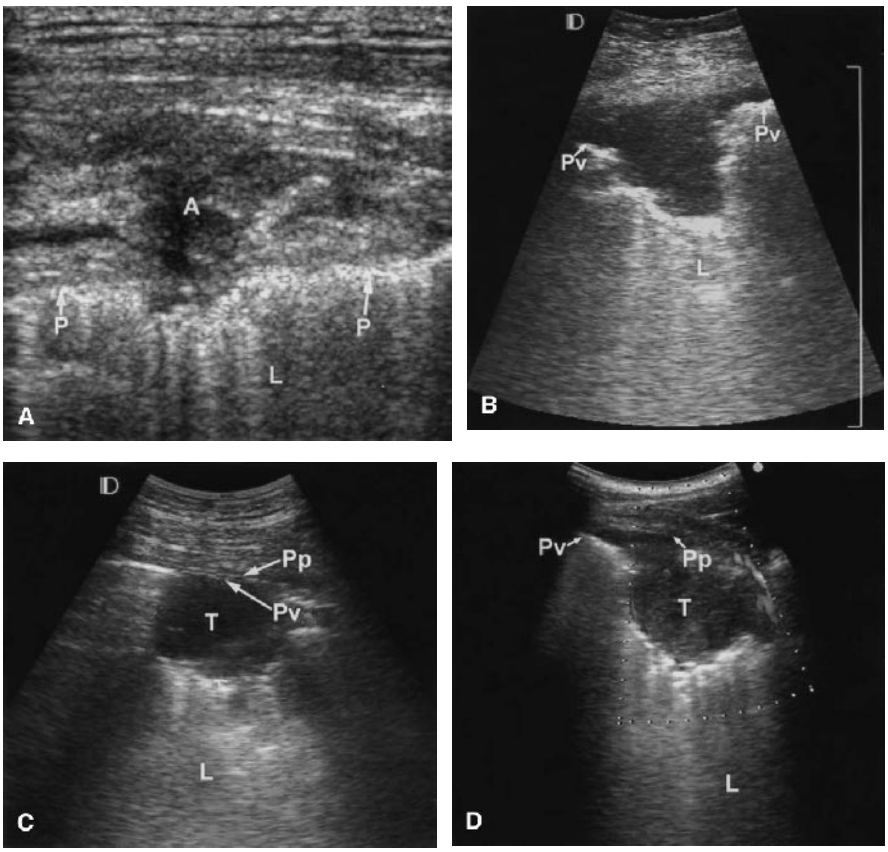
Assessment of pleural and chest wall invasion by lung tumor

A soft-tissue lesion extending to the surrounding pleura and chest wall is usually characteristic of malignancy. Rarely, inflammatory diseases such as actinomycosis and nocardiosis may spread in this manner (Fig. 4A and B). Evaluation of the extent of tumor invasion to the pleura and chest wall is important and may subsequently influence diagnosis and treatment. CT is usually recommended for determining the extent of pleural and chest wall extension in patients with lung cancer [9,10,28]. However, high-resolution, real-time US, particularly equipment with higher frequency (7.5–10-MHz) scanning probes, have also been found to be valuable in evaluating tumor invasion of the pleura and chest wall [29•,30].

Sugama *et al.* [29•] have defined the US criteria for the extent of tumor invasion. Ultrasound pattern (UP) 1 indicates that the tumor is in contact with the visceral pleura whereas UP2 means the tumor has extended beyond the visceral pleura and is in contact with the parietal pleura. Lastly, UP3 means that the tumor has extended to the chest wall through the visceral and parietal pleura. The visceral pleural lines are intact in UP1, but are invaded or interrupted in UP2 and UP3. Direct visualization of chest wall extension by the tumor is designed as UP3. The movement of the tumor with respiration is unaltered in UP1, disturbed in UP2, and vanished in UP3. Both UP2 and UP3 imply invasion of the tumor beyond the pleura.

High-resolution, real-time US has the advantage of clearer discrimination of the various soft-tissue layers within the chest wall. When a tumor abutted to the chest wall is visualized with US, various layers of the chest wall, including the parietal and visceral pleura, pleural space, and muscle and fascia, can also be examined and

Figure 4. Extension of inflammatory diseases (A, B) or tumors (C, D) to the pleura



(**A**) Ultrasound (US) shows a chest wall abscess in a patient with liver cirrhosis as an ill-defined lesion with soft-tissue echogenicity that extends to the pleura. Puslike material was obtained with transthoracic aspiration under US guidance, which yielded *Aeromonas hydrophila*. (**B**) US shows an irregular and hypoechoic parenchymal lesion with involvement of the pleural cavity. Nocardiosis was proved microbiologically after transthoracic biopsy of the lesion under US guidance. (**C**) US shows a parenchymal tumor with posterior echo enhancement (PEE). Note that both of the visceral and parietal pleural lines are intact, fulfilling the criteria of ultrasound pattern 1 of Sugama *et al.* [29•]. The respiratory movement of the tumor should be preserved in real-time US. (**D**) US shows a peripheral mass that extends beyond the pleura. The visceral pleural line is cut off, and the respiratory movement of the tumor is disturbed in real-time US. Invasion of the pleural cavity by the tumor is evident. A, abscess; P, pleura; L, lung; T, tumor; Pv, visceral pleural; Pp, parietal pleura.

the extent of tumor invasion can be determined (Fig. 4C and D). Disruption of the pleura, extension through the chest wall, and fixation of the tumor during breathing are indicators of pleural and chest wall involvement [30]. The accuracy of US in determining tumor invasion of the pleura and chest wall is better than chest CT. Transthoracic needle aspiration and biopsy of the tumor can be performed for pathologic diagnosis under real-time US guidance [1••,2,3,31].

Pleuritic chest pain and pleuritis

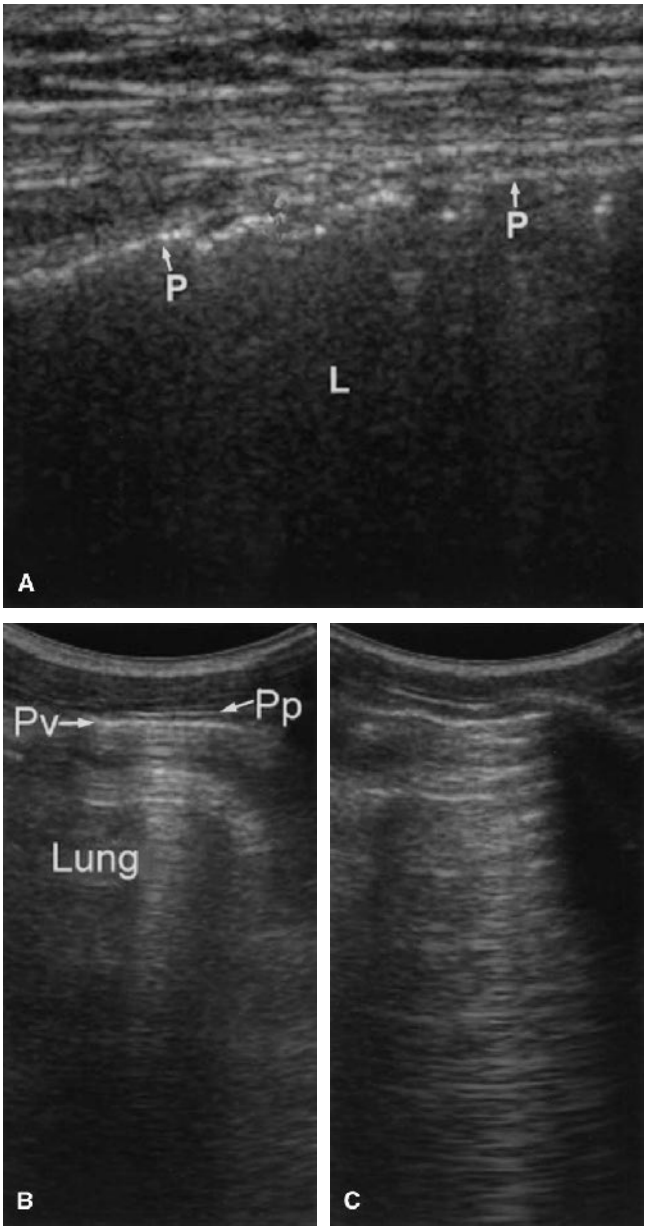
Pleuritis is usually diagnosed clinically with the presentation of sharp chest pain magnified by breathing. Pleural effusion and consolidations may be suggestive findings on the chest radiographs. However, the chest radiographs may be normal because the inflamed pleura and small amounts of pleural effusion are not visible on chest radiographs. Gehmacher *et al.* [32] reported that abnormal US findings could be observed in 91% of the total 47 patients with clinical diagnosis of pleuritis and normal chest radiographs. The abnormal US features included interrupted pleural line in 42 (89%), irregularly formed and less demarcated subpleural hypoechoic consolidations in 30 (64%), localized pleural effusion in 35 (74%), and increased blood flow in 11 (23%) by color Doppler (Fig. 5A). Of course, the more apparent changes that can be found on chest radiographs may also be seen on US.

Pneumothorax and hydropneumothorax

The majority of pneumothoraces are diagnosed by chest radiographs or CT, although US also may be helpful. Because of its simplicity and portability, US could be especially useful for emergency or clinical situations in which no roentgenographic equipment is readily available. In pneumothorax, loss of the gliding sign of pleura with respiration can be verified [33]. The reverberation comet-tail artifacts may be enhanced markedly in small pneumothorax (Fig. 5B and C), but the artifacts are occasionally absent in extensive pneumothorax [7]. US could be an accurate tool for diagnosis of clinically suspected pneumothorax. Targhetta *et al.* [33] reported the successful detection of the absence of gliding sign in 24 patients with radiographically confirmed pneumothorax. Although the extent of lung collapse and breadth of the pneumothorax could not be evaluated, it was possible to determine the areas of partial pneumothorax.

The gliding sign of the pleura in real-time US comes from the movement of the pleura during respiratory excursion. Diaphragmatic paralysis or pleural adhesion may result in impaired lung excursion and, consequently, the

Figure 5. Ultrasound findings in patients with pleuritic chest pain and partial pneumothorax



(**A**) Ultrasound (US) findings in a patient with pleuritic chest pain. The grayscale US reveals irregularity and interruption of the pleura. (**B, C**) Sonographic features in a patient with partial pneumothorax. Real-time US of the healthy side of the chest (**B**) shows normal gliding of the visceral and parietal pleura with respiration. On the other side with partial pneumothorax (**C**), the gliding sign of the pleura is absent in real-time US. Markedly enhanced comet-tail reverberation artifacts are seen compared with the US image of the healthy side. P, pleura; L, lung; Pv, visceral pleura; Pp, parietal pleura.

absence of gliding sign may be misinterpreted as pneumothorax. However, paralysis of the diaphragm can be diagnosed easily by the disappearance of diaphragmatic kinetics in real-time US, whereas pleural thickening can be identified directly in patients with pleural adhesion. It would be better to compare the US findings suggestive of pneumothorax with those of the healthy side of the chest. In patients with hydropneumothorax, US can recognize the pneumothorax more easily by identifying the air–fluid boundary [34], which can move with respiration. The gliding sign above the air–fluid level is absent.

Ultrasound-guided invasive interventions

Besides the imaging of various pleural diseases, another important use of chest US in pleural disease is that US can guide many invasive or interventional procedures, including diagnostic thoracentesis, closed tube drainage for pleural effusion, and needle biopsy of the pleura [1••,2,3,35,36]. US guidance increases the success rates while decreasing the complications of these procedures. Compared with other imaging modalities, the advantage of the US-guided procedures is that the convenience and portability of US can easily provide complementary help for these procedures. Moreover, the lesions can be accurately visualized, located, and marked with US before the procedure is done, especially when the lesion is small. The lesion can even be monitored with dynamic images of real-time US during these procedures.

The main contraindication to these procedures is hemorrhagic diathesis. Mild coagulation abnormalities, however, are acceptable for simple thoracentesis. Other contraindications include uncooperative patients who are unable to control breathing or cough on demand, especially when the lesion is small. The site of aspiration or biopsy should exclude the presence of local cutaneous lesions such as pyoderma or herpes zoster infection. Although the risk of complications decreases with US guidance, these procedures should still be performed with caution in patients with borderline respiratory failure.

Thoracentesis and closed tube drainage for effusion

For pleural effusion of unknown etiology, it is usually necessary to obtain the fluid for biochemical, cytologic, or microbiologic examinations. US is superior to chest radiographs in identifying the fluid and choosing the optimal site for diagnostic thoracentesis. The largest and most accessible area of fluid accumulation can be identified, and the depth for the needle to penetrate can be measured by chest US. With real-time US, direct visualization of the effusion during thoracentesis is applicable. All these US-guided measures help to improve the success rate of thoracentesis and avoid complications, such as pneumothorax. It is especially helpful when the effusion is minimal or loculated, when tedious radiographic study is not possible, or when safe thoracentesis is mandatory in a critically ill patient. The success rate of US-guided thoracentesis can be as high as 97% [3]. By differentiating minimal or loculated effusion from pleural thickening using the US criteria described earlier, US helps to predict the presence of fluid in an echo-free space and to decide whether it is amenable for thoracentesis [23,24,25•].

There are several clinical situations in which closed tube drainage for effusion is needed. These include huge effusion compromising the respiratory condition, complicated parapneumonic effusion and empyema, hemothorax, and malignant effusion preparing for pleurodesis. Complications related to these drainage procedures, such as laceration of the lung, diaphragm, liver, and spleen, could be disastrous. Malposition of the tube can result in failure of the drainage, particularly in loculated effusion. As with diagnostic thoracentesis, it is clear that US can decrease the risk of malposition and various complications by identifying the suitable site for the procedures. In cases of acute thoracic empyema, sonographic septation of the effusion is a useful sign to predict the need for subsequent intrapleural fibrinolytic therapy or for surgical intervention in addition to drainage [19].

Needle biopsy of the pleura

Conventional closed pleural biopsy with the Cope or Abram needle must be performed in the presence of pleural effusion or pneumothorax. Chest US has some advantages in guiding pleural biopsy of focal pleural lesions. Hence, one advantage of US-guided pleural biopsy is in cases when the pleural involvement of various diseases may be focal. Because focal pleural thickening or pleural tumors can be identified clearly with US, the pleural biopsy can aim at the focal area with sonographic abnormalities. The chances of obtaining pleural tissues with significant pathologic findings will thus increase. Another advantage is that, with real-time US, the advance of the needle can be monitored, and overpenetration of the needle to the underlying lung parenchyma can be prevented. This is particularly true for patients with minimal pleural effusion or even without pleural effusion [27].

Conclusion

Chest US is well documented as a valuable tool for pleural diseases. US helps to clarify the cause of pleural opacities, estimate the volume of pleural effusion, identify minimal or loculated pleural effusion, and differentiate between minimal pleural effusion and pleural thickening. US characteristics of effusion provide helpful information regarding the nature of the effusion. Variable pleural diseases, such as pleuritis, pleural fibrosis, pleural tumors, and pneumothorax, display different diagnostic US features. The extension of tumors to the pleura and chest wall can be assessed with US. Safe thoracentesis and drainage of effusion can be carried out under US guidance with a high success rate. Needle biopsy of the pleura can pinpoint the area with significant US abnormalities, thus increasing the diagnostic yield. With continuous monitoring of real-time US, overpenetration of the biopsy needle to the lung parenchyma can be avoided in patients with minimal effusion.

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