Use of medical thoracoscopy in managing pleural malignancy

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Shareable abstract (@ERSpublications)
1) Medical thoracoscopy is a diagnostic and therapeutic procedure for unexplained pleural effusions. 2) In those patients with a high pre-test probability of mesothelioma, a direct to biopsy approach is advocated. 3) Thoracoscopy is very safe. https://bit.ly/48dgcE3

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Abstract

Local anaesthetic "medical" thoracoscopy is an important tool for the diagnosis and management of a unilateral pleural effusion. It is performed under conscious sedation and has a high diagnostic yield. Clinical experience has demonstrated that thoracoscopy is a safe procedure. This article is an expert review of various aspects of the procedures from two experienced practitioners and we suggest areas for potential future research.

Introduction

Local anaesthetic thoracoscopy (LAT), otherwise known as medical thoracoscopy or pleuroscopy, is used by respiratory physicians as a diagnostic and therapeutic tool in undiagnosed exudative pleural effusions [1–3]. There are multiple reports of the use of this technique in pneumothorax, pleural infection and sympathectomy procedures as well as lung/visceral parietal biopsies; however, this article will only focus on undiagnosed exudative pleural effusions and biopsy of parietal lesions which are the commonest indications for which LAT is performed. The procedure was initially described in 1865 by Sir Francis Richard Cruise and later by Carlo Forlanini in 1882. In 1910, Hans-Christian Jacobaeus precisely described the procedure and associated indications and contraindications. Thoracoscopy enables complete drainage of pleural fluid, direct visualisation and inspection of the pleural surface (both visceral and parietal, lung and diaphragm), biopsy of abnormal areas of parietal pleura and management of further fluid production by talc pleurodesis or inserting an indwelling pleural catheter [4–6].

Who should undergo a medical thoracoscopy?

Pleural space malignancy, either primary or secondary, often manifests as a pleural effusion [7]. Unilateral pleural effusions are usually sampled at first presentation for biochemical, microbiological and cytological analysis. The recent British Thoracic Society (BTS) guidance suggests cytological examination as an appropriate first diagnostic step in suspected malignancy [7], but that depends on the pre-test suspicion of the type of cancer [8, 9]. All cancers can metastasise to the pleural space with breast, lung and lymphoma being the most common. The highest yield from cytological analysis has been reported with breast and ovarian cancers; however, in the age of targeted therapies further sampling may still be required to accurately define appropriate anti-cancer therapy. Biopsies *via* LAT have been proven to be the most useful for molecular analysis in a retrospective case review by Sundaralingam *et al.* [10]. If the pre-test probability of a cancer such as mesothelioma is high, then a direct to LAT approach is advocated as the cytological yield can be as low as 6%, and invasion into the adipose tissue and parietal pleura is needed to complete tumour characterisation [3, 9]. Image-guided biopsy has an important role to play in the diagnosis especially in cases where focal pleural thickening or masses are identified. However, it is worth noting that the commonest imaging modality, computed tomography, can be normal in up to 40% of pleural malignancies [11]. Thus, direct visualisation of the pleura is crucial to enable biopsy of those concerning lesions, the more so as malignancy does not uniformly affect all the pleura as opposed to, for example, pleural tuberculosis. Tuberculosis generally involves the parietal pleura in a uniform blanket like

pattern while malignancy often has focal abnormalities and skip lesions. Sensitivity of thoracoscopic biopsies for malignancy can be as high as 95% [8].

What are the patient selection and anaesthetic considerations?

Contraindications to LAT for undiagnosed pleural effusions are haemodynamic instability, uncorrected coagulopathies, severe hypoxaemia, uncontrollable cough and potentially a severely loculated space that might prevent access to the parietal surface. Figure 1a shows a loculated space, and our opinion is that this is a relative contraindication as experienced LAT practitioners should be able to dissect down to the parietal pleura, potentially with a two-port technique (this is mentioned in the next section). Care should also be taken with patients with morbid obesity due to potentially difficult access to the pleural cavity and complications with sedation. Thoracoscopy is usually performed under conscious sedation using a combination of midazolam or propofol with opiate-based agents, such as fentanyl, for analgesia. There is widespread variability in practice [2, 3, 12, 13].

Regular antihypertensive medication, especially angiotensin-converting enzyme inhibitors and angiotensin 2 receptor blockers, should be withheld if propofol is used during LAT due to the risk of significant vasodilatation. Increasingly regional blocks (physician-led or anaesthetist-led) are being used to provide sustained analgesia, supported by observational data from small single-centre case series [14, 15]. Anticoagulation therapy should be withheld according to local protocols; some specific examples are withholding low-molecular weight heparin for 1 day before, direct oral anticoagulants for 2 days (except dabigatran, which might need 4 days dependent on the patient's creatinine clearance), 5 days for warfarin (with a pre-procedure international normalised ratio of <1.5), and clopidogrel for 7 days. This is covered in detail in the BTS clinical statement on pleural procedures [3].

What does the LAT procedure involve?

Pre-procedural steps

Depending on local protocols, patients are nil by mouth or can take clear fluids until the procedure. LAT can be performed in a dedicated interventional suite or a surgical theatre. The patient should be placed in a lateral decubitus position with the effusion side upwards. A point of care ultrasound will determine the point of entry, which should be as close to the mid-axillary line as feasible.

Intra-procedural steps

After sedation under adequate monitoring and infiltration of local anaesthetic, with blunt dissection, a tract can then be created with a small forceps and a 7-millimetre (mm) trocar is passed into the pleura. When the effusion is too small for direct blunt dissection, a Boutin needle (with sharp and blunt ends) can be used to pierce the parietal pleura and induce a pneumothorax with 10–20 spontaneous breaths. This allows suction of fluid (large volumes of fluid can be removed after equalisation of the pleural pressure to the atmospheric pressure without the risk of re-expansion pulmonary oedema), and passage of a zero-degree camera initially for visual inspection of the pleura and then of the biopsy forceps over a fifty-degree camera for targeted biopsies. Talc poudrage with atomisers can be performed post-biopsies and a chest drain, usually large bore

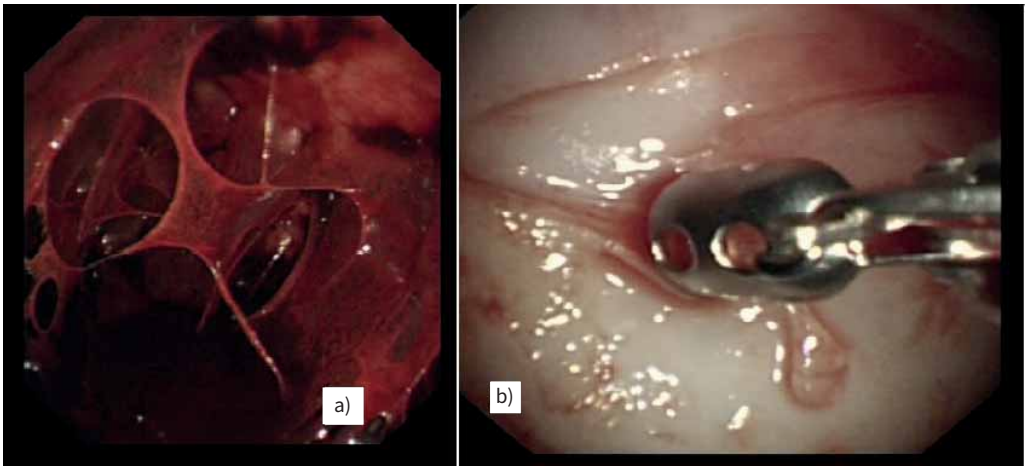

FIGURE 1 a) Loculated pleural space. b) Biopsy of parietal pleura.

(more than 20 French gauge), or increasingly indwelling pleural catheters can be then inserted [3, 6, 16]. Some centres admit patients afterwards, others offer a day case service with same day discharge [17]. This is discussed in more detail later in this article. Figures 1 and 2 show some typical appearances within the pleural space (figure 2a normal appearances, figure 2b malignant nodules on parietal pleura, figure 1a a loculated pleural space and figure 1b biopsy of parietal pleura using a rigid thoracoscope).

LAT is usually performed with only one port, but two ports can sometimes be used by experienced practitioners for better views and biopsies of the parietal pleura or for bleeding control. Of note, "dry" thoracoscopy, the practice of LAT in a patient without an effusion, can also be performed; it requires experience in thoracic ultrasound assessment of the pleural surfaces for lung sliding, careful dissection up to the pleural surfaces with curved forceps and then induction of a pneumothorax [18].

Post-procedural steps

Depending on local protocols, the patient will be either admitted to a ward for observation, with the chest drain connected to an underwater seal and might be connected to low volume thoracic suction to enhance pleural apposition, or will be discharged (usually with the placement of an indwelling pleural catheter) with appropriate community nursing follow-up for drainage. The BTS pleural procedure statement suggests observations every 30 min for 1 h after the procedure followed by observations every 4 h.

What are the potential complications of LAT?

LAT is overall a very safe procedure. Common complications include pain at the entry site, ooze from the biopsy areas, localised surgical emphysema and skin infection. More serious complications are air leaks due to lung injury, inadvertent organ puncture, intercostal artery bleeding and empyema. There are no prospective studies looking at complications of thoracoscopy and the most recent meta-analysis did not consider peri-procedural hypotension, respiratory issues, pain, dislodged drains, inadequate sampling, post-procedure fever that resolved in <72 h, additional chest tube use and minor bleeding as complications. Out of a total of 90 studies selected, 47 reported complications with significant variation on the type of thoracoscope (semi-rigid or rigid) used. 41 studies with a total of 2963 patients were included in this meta-analysis. The pooled complication rate was then 0.040 (95% CI 0.029–0.052), and an estimated mortality of <0.54%, which was mostly previously related to the use of ungraded talc [9]. Management of the major complications, such as intercostal bleeding and air leaks, includes resuscitative measures, insertion of large bore drains, direct pressure onto bleeding points and liaison with cardiothoracic services [3].

How does LAT compare with surgical video-assisted thoracoscopy? How can the diagnostic yield of LAT be increased? What are the procedures that can be combined with LAT?

LAT is usually carried out under conscious sedation, and through one port only, using either semi-rigid or rigid thoracoscopes. Surgical video-assisted thoracoscopy (VATS) involves general anaesthesia and single lung ventilation with single lumen intubation. Two or three ports are used (camera, biopsy and retraction instruments) [19]. There are no direct comparative studies between LAT and VATS. Complication rates and diagnostic yields are comparable. However, VATS is perhaps better at draining loculated effusions and

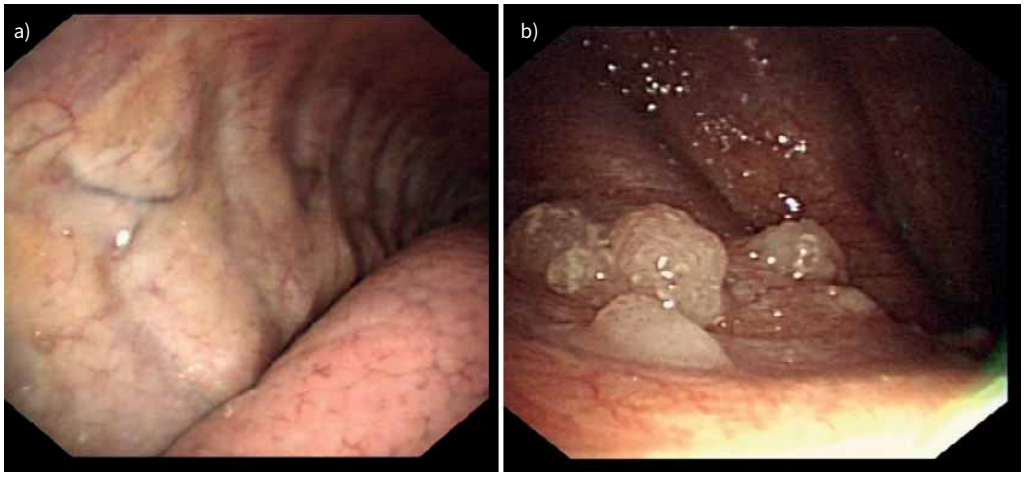

FIGURE 2 a) Normal parietal pleura with lung down. b) Malignant nodules on parietal pleura.

division of dense fibrous bands and conversion to open thoracotomy can be performed if required. Thoracoscopy can also be performed in an endoscopy suite with appropriately trained staff but VATS can only be performed in a surgical operating theatre. Ultimately, the choice between VATS and LAT comes down to resource availability, expertise at performing the procedures and patient choice.

Visualisation of malignant areas allows direct biopsies and thus sensitivity of thoracoscopy can be very high (above 95%) [9]. High pre-test probabilities for malignancy at LAT are associated with pleural masses, nodules, thickening, and irregularity on contemporaneous radiological imaging with reported sensitivities of 36–51% and specificity between 88% and 100% [8, 9]. In those instances, a negative result (one showing no malignancy) is likely to be a false negative. Barring an onwards referral for a VATS biopsy or the use of alternative techniques such as image-guided biopsies, some centres use rapid onsite evaluation (ROSE), although there are limitations with application of ROSE to mesothelioma [20]. The implications of a true negative biopsy for malignancy, often labelled as nonspecific pleuritis (NSP), are subject to much debate. The latest retrospective case series in the literature summarised the outcomes of 175 patients with NSP from various international centres. 6% of patients developed a malignancy after a median time of 12 months, expert opinion suggests that patients with NSP should be followed up for at least 24 months and undergo with regular imaging [21]. An ongoing observational trial is in progress looking at the evolution of NSP in patients previously exposed to asbestos, which should provide robust prospective data [22]. Confocal laser endomicroscopy is another exciting new development which can highlight malignant areas and thus offer up targets for biopsy, but its use is not widespread [20, 23]. The use of semi-rigid thoracoscopes appears not to confer a diagnostic disadvantage despite smaller samples [24, 25].

At the time of LAT, talc pleurodesis (poudrage with graded talc) can be performed. 4 g of graded talc can be insufflated *via* the initial 7 mm port using a hand-held pump to ensure a uniform coating over the visceral and parietal surfaces to enable pleurodesis. Low-level thoracic suction can also be applied to any drains inserted into the pleural space after poudrage to bring the visceral and parietal surfaces together to potentially increase the chance of pleurodesis success. The poudrage can thus be done through a large bore chest drain or through an indwelling pleural catheter. However, the evidence is that poudrage was not more successful than talc slurry at 90 days [26]. Thus, performing a LAT for fluid control only in cases of confirmed malignant effusions is probably not worthwhile, but would ultimately depend on resource availability and patient choice. Sometimes, further biopsies for molecular tumour characterisation are required. Some centres have been placing indwelling pleural catheters as part of day case thoracoscopy services [17]. A 4–5 cm tract is made from the 7 mm port distally towards the front of the patient and the indwelling pleural catheter tubing placed within that tract so that the cuff is midway and the distal end of the catheter can simply be threaded into the port. A more in-depth discussion of this is provided by Turner *et al.* [17]. The indwelling catheters can stay in place until pleurodesis has been achieved, either *via* talc instillation or aggressive drainage; these techniques are beyond the scope of this article.

What are the future directions for medical thoracoscopy?

While the choice between talc slurry and poudrage is less of an unknown, despite the limitations of the data, other aspects of thoracoscopy need further study. The true incidence of complications is unknown and there is a prospective study currently ongoing which will hopefully answer this question [27]. While day case thoracoscopy with pleural catheter insertion was adopted very quickly during the coronavirus disease 2019 pandemic, the true cost-effectiveness remains unknown. A trial is currently underway in the UK (The Randomised Thoracoscopic Talc Poudrage and Indwelling Pleural Catheters *versus* Thoracoscopic Talc Poudrage only in Malignant Pleural Effusion trial (TACTIC)) [28], which aims to provide answers to this, as well as the overall effectiveness over more conservative LAT practices (admission with chest drain and poudrage).

Key points

- Medical thoracoscopy is a diagnostic and therapeutic procedure for unexplained pleural effusions.
- In those patients with a pleural effusion and high pre-test probability of mesothelioma, a direct to biopsy approach *via* medical thoracoscopy is advocated.
- Thoracoscopy is very safe.

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