

indications for invasive mechanical ventilation do not progress to ARDS (9) argues against the notion that VILI is an inevitable outcome of mechanical ventilation under all circumstances, including COVID-19. Thus, although VILI has long been a clinical concern, the problem is not initiation of mechanical ventilation *per se* but rather initiation of inappropriate mechanical ventilation strategies, including an overly high tidal volume or distending pressure.

Although we agree with Dr. Kyle-Sidell about the importance of scientific debate, our ultimate concern with the author's letter and statements in other forums is that these and other claims about COVID-19 pathophysiology, such as the predominance of endothelial over epithelial injury, lack supporting evidence and are contradicted by the published physiologic, histopathologic, and radiographic evidence. In a time of high patient volumes and stress, there arises a risk that clinicians will latch onto such claims and abandon the approach to ARDS care that has been developed over many years of well-designed, well-controlled randomized clinical trials, which have yielded impressive improvements in mortality and other clinical outcomes. When faced with new diseases and clinical challenges, we should recognize that novel observations and hypotheses are important for advancing care. We must, however, keep the focus on conducting well-designed studies of these ideas so that we can come out on the other end of the pandemic with a solid sense of what does and does not work. Action based simply on conjecture and unsubstantiated claims will leave us with more uncertainty and may increase the risk of patient harm.

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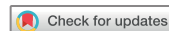
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Medical Thoracoscopy for Pleural Infection: Are We There Yet?

To the Editor:

We read, with keen interest, the randomized clinical trial of intrapleural fibrinolytic therapy versus early medical thoracoscopy (MT) for the treatment of pleural infection, which was published in a recent issue of *AnnalsATS* (1). We congratulate the authors for conducting a randomized study addressing an important clinical question. The authors have concluded that early medical thoracoscopy may have a role in the management of complicated pleural effusion and empyema, leading to a reduced hospital stay.

However, some critical points regarding the reported results need careful consideration and further discussion.

The primary outcome chosen for the trial was the duration of hospital stay. This outcome measure is not ideal for a clinical question concerning the use of medical thoracoscopy. Other parameters, such as radiologic resolution or referral/need for surgery, would have been more meaningful for assessing the benefit of the intervention proposed (2, 3). Even though authors have used the duration of hospital stay as the primary outcome measure, there is no mention of discharge criteria, which should have been objectivized to maintain uniformity. In the inclusion criteria, it is mentioned that patients with not completely drained empyema were enrolled. Authors have not mentioned how long they waited for empyema to drain before enrollment. This time duration is vital because a delay in the intervention may be associated with the failure of the intervention. It is also not clear why the authors chose to put a small-size intercostal tube in all patients before randomization. In patients randomized to the MT arm, the initial tube placement could have

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been avoided because it has, probably, led to the placement of intercostal tube twice in patients undergoing MT (an initial tube of a small size followed by a large tube after MT).

Regarding the performance of the MT, the authors have not mentioned the sedation protocol used for the MT, as it will affect the patient discomfort, procedure duration, ability to complete the procedure, and success achievement in pleural clearance. The proportion of patients undergoing rigid versus semirigid medical thoracoscopy is also not clear. The instrument used may also affect the procedure performance and success (4). The closed forceps used for adhesiolysis are usually large in case of rigid thoracoscope and may be more effective in comparison to thin forceps used with the semirigid instrument. Similarly, the use of a suction irrigation device may also affect the pleural clearance, and it cannot be routinely used for semirigid instruments. In the discussion, the authors have mentioned the utility of obtaining a pleural biopsy during MT to increase the microbiological yield. It is worth mentioning here that the pilot study quoted by the authors used ultrasound-guided pleural biopsies, which are feasible in the intrapleural fibrinolytic arm as well (5). There is no added advantage of MT in obtaining a pleural biopsy to increase the microbiological yield when it can be safely performed under ultrasound guidance.

In view of these issues, we suggest that the trial results should be interpreted with caution while applying in routine clinical practice.

Author disclosures are available with the text of this letter at www.atsjournals.org.



Reply: Medical Thoracoscopy for Pleural Infection: Are We There Yet?

From the Authors:

We thank Dr. Pahuja and colleagues for their interest in our manuscript (1). Length of stay (LOS) has been suggested as a meaningful outcome measure for quality of care (2). LOS following intervention is an indirect measure of clinical improvement in pleural infection. If LOS decreases, then intervention is efficient and effective, as patients with extended LOS often consume substantial hospital resources, increase healthcare costs, and increase the risk of nosocomial infections. In pleural infection, radiological changes can often persist after clinical improvement and should not be the sole criteria for continuation of therapy or would be the only indication of treatment failure. Furthermore, treatment of either intrapleural fibrinolytic therapy or medical thoracoscopy (MT) have been shown to be effective in clinical practice, with only up to 15% requiring any further surgical intervention or referral (3, 4), making a clinical trial design with such primary outcome impractical. It is well recognized that patients with early-stage

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pleural infection who were initially admitted or referred for evaluation will be eventually be discharged home once they have clinical improvement and do not require chest tube or further intervention. Regarding the duration before enrollment, the inclusion criteria clearly mentions that MT could be performed within 48 hours from the time of chest tube placement, or patients would not be considered for enrollment in either arm.

Although historically large-bore chest tubes have been used for drainage of pleural infection, clinical evidence from a large prospective cohort indicated that small-bore chest tubes (≤ 14 F) are as effective and are better tolerated owing to less pain (5). Based on current evidence and extensive experience, our practice is to insert small-bore chest tubes in all patients with an infected pleural space before deciding whether intrapleural fibrinolytic or MT is even needed.

Regarding MT, as mentioned in the METHODS section, thoracoscopy was performed under moderate sedation and local anesthesia, which was consistently done in all centers. The use of either semirigid or rigid thoracoscope, number of ports, and suction irrigator were left to the operator's preference. However, rigid MT was almost exclusively used by all operators with the goal to mechanically remove any adhesions and break down loculations. In any case, the study mentioned by the group (6) confirmed that diagnostic yield and technical success was similar. Furthermore, pleural biopsy can be safely performed using