Critical Review Form
Therapy

PGY-1

HYPERLINK "http://pmid.us/36693146"Marx T, Joly LM, Parmentier AL, et al. Simple Aspiration versus Drainage for Complete Pneumothorax: A Randomized Noninferiority Trial. Am J Respir Crit Care Med. 2023 Jun 1;207(11):1475-1485.

Objectives: **To determine "whether first-line simple aspiration is noninferior to first-line chest tube drainage to obtain lung expansion during a first episode of complete primary spontaneous pneumothorax." (p. 1476)**

Methods: **This multi-center, randomized controlled trial was conducted at 31 emergency departments (academic and non-academic) in France between June 1, 2009 and March 31, 2015. Patients aged 18-50 years with a first episode of symptomatic, primary, and complete pneumothorax identified on chest radiography were eligible for enrollment. "Complete" pneumothorax was defined as "complete separation of the visceral and parietal pleura from the base to the apex of the pleural space." Exclusion criteria were tension pneumothorax, traumatic or recurrent pneumothorax, presence of pleural effusion, "secondary" pneumothorax with underlying lung disease, pregnancy, lactation, inability to follow up, or inability to give consent.**

Patients were randomized in blocks of 4 or 6 to undergo either simple aspiration using Joly or Monod trocars or chest tube drainage using a 16-French or 20-French large chest tube (at physician preference). In the aspiration group, after 30 minutes of aspiration at -25 cm H_2O a repeat chest radiograph was performed; if this showed lung reexpansion, the aspiration device was removed and the patient was discharged after 24 hours of monitoring in the ED. If the pneumothorax persisted on repeat radiography, an additional 30 minutes of aspiration was performed followed by another repeat radiograph; if pneumothorax persisted at this point, chest tube drainage was performed and the patient was hospitalized.

The primary outcome was pulmonary expansion (absence of residual pneumothorax including apical pneumothorax > 2 cm) 24 hours after the procedure (including up to 2 rounds of aspiration in the aspiration group). Secondary outcomes were pulmonary expansion 7 days after the procedure, recurrent pneumothorax within one year, tolerance of techniques, and adverse events at 24 hours and 7 days. A noninferiority margin for the primary outcome was set at 25% (i.e. simple aspiration was considered noninferior if the upper limit of the 95% CI for the difference between the aspiration and drainage failure did not exceed 25%).

Out of 402 patients recruited during the study period, 200 were assigned to the aspiration group and 202 were assigned to the chest tube drainage group. The mean age was 28 years and 82% were male.

Guide		Comments
I.	**Are the results valid?**	
A.	**Did experimental and control groups begin the study with a similar prognosis?**	
1.	Were patients randomized?	Yes.
2.	Was allocation concealed? In other words, was it possible to subvert the randomization process to ensure that a patient would be "randomized" to a particular group?	Yes. "Patients were assigned randomly to the simple aspiration group or to the chest tube drainage group using a randomization hotline set up to allow investigators at each hospital to do so around the clock 7 days per week by phone call to the server. Block randomization was balanced at each hospital using block sizes of 4 or 6. By varying block sizes, assignment unpredictability was maintained and the number of subjects in each group remained similar. The management and monitoring of randomization were entrusted to a specialized company (ASCOpharm)." (p.1477) This protocol should be sufficient to maintain allocation concealment.
3.	Were patients analyzed in the groups to which they were randomized?	Yes. "Per-protocol followed by intention-to-treat analyses also were conducted."
4.	Were patients in the treatment and control groups similar with respect to known prognostic factors?	Yes. Patients were similar with respect to gender, age, body mass index, pneumothorax side, baseline vitals, symptoms, smoking status, and circumstances of pneumothorax occurrence (rest vs. exertion).
B.	**Did experimental and control groups retain a similar prognosis after the study started?**	
1.	Were patients aware of group allocation?	Yes. "The study was open label, with both patients and physicians aware of the treatment assigned." (p.1477)
2.	Were clinicians aware of group allocation?	Yes. See above.
3.	Were outcome assessors aware of group allocation?	No. "The investigator who included the patient interpreted the chest radiograph at the beside at 24 hours and noted in the case report form if pulmonary reexpansion (primary outcome sought) was obtained. All case reports and radiographic data were then reviewed centrally (blind to the initial assessment) by an expert (study scientific

		committee member) with a standardized grid. If the investigating physician and the expert disagreed, a second expert was consulted." (p. 1477) Therefore the outcome was initially assessed by a clinician aware of group allocation, with subsequent interpretation by a blinded clinician. However, it seems likely that said blinded interpreter would be able to distinguish a trocar from a thoracostomy tube on the radiograph.
4.	Was follow-up complete?	Yes. The authors make no mention of any patients being lost to follow-up.
II.	**What are the results ?**	
1.	How large was the treatment effect?	● The failure rate at 24 hours was higher in the aspiration group than in the chest tube group in both the per-protocol analysis (risk difference 11.3; 95% CI 2.6% to 20%) and the intention to treat analysis (RD 9.7%; 95% CI 1.1% to 18.3%). o Neither of the two confidence intervals includes the fixed absolute margin of 0.45 (45%). o For the ITT analysis, this corresponds to a RR of 1.49 (95% CI 1.04 to 2.15). ● The failure rate at 7 days was similar in both groups in the per protocol (RD 0.004; 95% CI -0.073 to 0.081) and intention to treat analyses (R D 0.005; 95% CI -0.070 to 0.080). ● Pneumothorax recurred within 1 year in 20% of the aspiration-treated cases and 27% of the chest tube cases (frequency difference, -7%; 95% CI, -16% to 2%). ● Tolerance (pain scores) were lower in the aspiration group than the chest tube group (mean difference -1.4; 95% CI -1.89 to -0.91). ● Minor complications occurred slightly less frequently in the aspiration group while major complication rate were similar in the two groups. ● Mean hospital length of stay was similar in the two groups in the intention to treat analysis (mean difference -0.81 days, 95% CI -2.26 to – 0.64).

2.	How precise was the estimate of the treatment effect?	See above.
III.	**How can I apply the results to patient care?**	
1.	Were the study patients similar to my patient?	Yes. Although this study was conducted in France, which differs in ethnic and racial makeup from the US, it seems unlikely that these differences would affect outcomes in the case of spontaneous pneumothorax.
2.	Were all clinically important outcomes considered?	Yes. The authors considered short and long-term treatment failure, hospital length of stay, tolerance of procedure, and complication rates.
3.	Are the likely treatment benefits worth the potential harm and costs?	Uncertain. While the authors conclude that their findings "support the adoption of simple aspiration as the initial treatment for complete primary spontaneous pneumothorax…" they concede that aspiration alone is associated with higher failure rates. While aspiration was associated with shorter hospital length of stay, in the intention to treat analysis this difference was quite modest (a mean difference of 0.81 days). Aspiration may therefore be considered when managing spontaneous pneumothorax, and shared decision making with the patient regarding the risks of failure and shorter length of stay is of vital importance.

Limitations:

1. **This study was, understandably, unblinded, and is at some risk of performance bias on the part of the clinicians.**

2. **The exact mechanism of determining the primary outcome was somewhat ambiguous, and seems to rely primarily on radiographic determinations made by the unblinded clinicians caring for the patient.**

3. **The method for determining the appropriate non-inferiority margin was overly complicated and difficult to comprehend. The ultimate decision to use a margin of 0.45 feels arbitrary and includes the possibility of a significant difference in failure rates between the groups.**

Bottom Line:

This multicenter, open-label, randomized controlled trial from France found that simple aspiration of spontaneous pneumothorax was associated with significantly higher failure rates (relative risk 1.49; 95% CI 1.04 to 2.15), with a modest reduction in hospital length of stay (mean difference -0.81 days, 95% CI -2.26 to – 0.64). These findings along do not dictate the most appropriate course of action, and shared decision making with the patient's preferences in mind will be important when considering these treatment options in practice.