Author’s response to reviews

Title: Digital versus analogue chest drainage system in patients with primary spontaneous pneumothorax: a randomized controlled trial

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Author’s response to reviews:

Haarlem, March 29, 2020

Dear Editor,

I would like to thank you for the opportunity to submit a revised version of our manuscript “Digital versus analogue chest drainage system in patients with primary spontaneous pneumothorax: a randomized controlled trial”, with submission ID: PULM-D-19-00615.

I hereby mention all comments point-by-point, followed by our response.

1) The figure is a useful flow-chart but this paper is missing a CONSORT diagram. Please provide numbers of patients screened and reasons for non-enrolment. How many were observed, or went direct to surgery?

2) Why was it so difficult to recruit to?
With your approval, we would like to address these two points together. In primary spontaneous pneumothorax, when chest tube placement is indicated, it is usually placed shortly (several hours) after the diagnosis has been made – frequently out of hours. Furthermore, in the five participating hospitals, patients were seen both by doctors working
for the pulmonary division as doctors working in the A&E. The number of doctors who had to be familiar with study procedures was therefore very large. The time it cost to randomize in Research Manager was a barrier during busy shifts. We tried to overcome this barrier by inviting colleagues to call us at any time to randomize for them, but it led to an important lack of inclusions.

Co-authors in the different study sites were urged to provide us with data of missed inclusions, however, we received too little data on missed inclusions for a reliable CONSORT diagram. We have described this in more detail in the revised version of our manuscript:

In PSP, when chest tube placement is indicated, it is usually placed shortly (several hours) after the diagnosis has been made – frequently out of hours. In the five participating hospitals, patients were seen both by doctors working for the pulmonary division as emergency doctors, for whom randomization was often too time-consuming. This led to missed inclusions and a slow inclusion rate. Therefore, the study was terminated before the target sample size was reached. The missed inclusions may have led to a selection bias. (302-307)

3) Why did some patients go directly to surgery? That is not standard practice as per current guidelines.

Patients who were directly referred to surgery were patients with a recurrent pneumothorax (usually ipsilateral). In the revised manuscript, we have explained this in more detail in the section ‘Study Subjects’:

Patients with PSP who were treated with chest tube drainage were asked to participate in the study. Those with recurrent pneumothorax were referred to surgery directly and were therefore not included. (162-163)

4) I note the higher surgery in the digital arm. What was the criteria used to refer patients in the study to surgery? This could introduce bias, if the same criteria were not used in both arms.

As indicated in the flow chart, the surgeon was consulted after more than 72 hours of air leak. This criterium was used in both groups. Whether surgery was actually performed was a clinical decision.

5) Discussion Page 4 Line 200-211: This paragraph is very speculative. For example the sentence "since the digital drainage system appears to have an advantage over analogue systems in uncomplicated PSP" is not true - the primary outcome was negative. Likewise "As soon as the digital device indicates that there is less than 15 ml air flow per minute and 205 the chest X-ray shows no more than a small pneumothorax, the tube can be safely removed." - what is the evidence for this statement? The authors can speculate that digital drainage MAY identify cessation of leak earlier, this was not the focus of this study and is not evidence based at the moment. I would suggest toning down the paragraph.

Thank you for your suggestion, we have rewritten the paragraph:
According to current guidelines, manual aspiration is regarded as first choice therapy in PSP. Based on our subgroup analysis, digital drainage possibly has an advantage over analogue systems in uncomplicated PSP. Digital drainage might be considered a practical alternative for manual aspiration: after insertion of a chest tube, the clinician connects it to a digital device instead of evacuating air manually. As soon as the digital device indicates that there is less than 15 ml air flow per minute and the chest X-ray shows no more than a small pneumothorax, removal of the chest tube appears to be safe. According to our study data, the chance of treatment failure is much lower than the percentages found in trials on manual aspiration (manual aspiration success rates range from 30% to 80% [11], although the definition of success rate varies considerably between the various studies). (272-280)

6) I think that a key point here is that patients NOT requiring surgery MAY benefit from digital drainage, but at present we do not have a good way of predicting who these patients are. There has been another publication which looks at the use of digital airflow measurement in PSP. This would be worth citing: Thorax. 2019 Apr; 74(4): 410-412 (doi: 10.1136/thoraxjnl-2018-212116).

Thank you for this citation, since it was published after we completed our first draft, we have missed this in our literature search. We have cited this article and described the findings in our discussion.

Patients who have a high, non-declining flow rate are likely to have a persistent pleural defect and to benefit from early referral for surgery. Patients with a declining flow rate are likely to benefit from a conservative approach. A recent study by Hallifax et al indeed demonstrated that digital air leak measurements early in the treatment course potentially predicts future treatment failure [24]. (290-294)

7) The authors should be careful to conclude too much from a sub-group analysis. The conclusion section is correct, but the final sentence in the discussion overstates the case and should be removed.

We have rephrased the final sentence: Whether digital drainage has an advantage over manual aspiration, and whether digital drainage has the potential to predict which patients benefit from early referral to surgery, is an important subject for further research. (381-383)

8) Please use "height" rather than "length" in demographics

We have corrected this.

9) Authors state that using digital drainage system has reduced LOS in uncomplicated patients, however analysis excluding surgical patients would not be appropriate. Please delineate the reasons for surgery in all these patients; is it because of persistent air leak detected by digital system or is there any other reason for surgery that could be identified before using digital drainage.

As described in our flow chart, after 72 hours of air leak (as measured by analogue or digital drainage), a surgeon was consulted. In other words, all surgical patients had prolonged air leak. Those who were referred for surgery before digital drainage was used where those with recurrent pneumothorax. (See revised ‘Study Subjects’ section:)
Patients with PSP who were treated with chest tube drainage were asked to participate in the study. Those with recurrent pneumothorax were referred to surgery directly and were therefore not included. (162-163)

10) Discussion on prior studies comparing Digital vs. Analogue drainage system should be mentioned and authors should discuss how these findings are similar or different from the previous studies. 11) It would also be interesting to know, if prior studies also had a similar trend of higher number of surgeries performed in patients with digital drainage for spontaneous pneumothorax.

To our knowledge, these studies have only been performed on surgical patients, not on primary spontaneous pneumothorax. Therefore, we didn’t find it appropriate to discuss these studies in more detail.

We look forward to hearing from you in due time regarding our submission, and to respond to any further questions and comments you may have.

Best regards on behalf of all authors,

Kris Mooren