Author’s response to reviews

Title: Safety and complications of medical thoracoscopy in the management of pleural diseases

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Dear Editor and Reviewers:

Thank you very much for your letter and for the reviewers’ comments concerning our manuscript titled “Safety and complications of medical thoracoscopy in the management of pleural diseases” (PULM-D-18-00024). Those comments are valuable and very helpful for revising and improving our paper, as well as the important guiding significance to our researches. We have studied comments carefully and have made corrections which we hope meet with approval. Major revised portions are marked in red in the paper. We responded, point by point, to the comments as listed below.
Sahajal Dhooria (Reviewer 1)

Major

The study is a single center study which does not offer any novel information on the safety aspect of this procedure. Several previous studies have described the complications associated with the procedure.

Reply: Thank you for your suggestion. We have to admit that there are some limitations in our research. One strengthen of the current research is that a large size of study population is investigated, in which 1926 patients are included. In addition, most of the previous studies summarized complications of pleurodesis, and few clinical trials ever reported complications of MT in the management of pleural diseases, such as adhesiolysis, pleural decortication of empyema and bulla electrocoagulation. The present research is the first time to compare incidence of complications in different thoracoscopic procedures.

Minor

Comment 1: The abstract does not provide the basic details of the study subjects i.e., baseline characteristics.

Reply 1: Thank you for your advice. We have revised the abstract according to the advice.

Comment 2: The method of follow up is not clearly mentioned. How long? How many were lost to follow up?

Reply 2: Thank you for your suggestion. The research studied early complications of MT, which happened in hospital. For patients with lung laceration, bleeding, pulmonary re-expansion oedema and mediastinal emphysema, were regularly seen at ambulatory visits, and chest roentgenograms were obtained 1 month after the procedure and then monthly, for 3 months. Further follow-up was achieved every 3 months for 1 year. About half of the patients were lost to follow-up after 1 year.

Patients with subcutaneous emphysema, prolonged air leak, pain, fever and cutaneous infection in entry site, had outpatient visits when felt uncomfortable.

Comment 3: All figures are superfluous.

Reply 3: Thank you for your advice. The figures could represent the common complications of different therapeutic thoracoscopy groups clearly.
Comment 4: Discussion focus on individual complications and is more like that of a case series rather than an investigative study.

Reply 4: Thank you for your suggestion. The article is an investigative study. We evaluate the safety of medical thoracoscopy in the management of pleural diseases and compare complications in different therapeutic thoracoscopic procedures through a large size of study population. And we elaborated more on the serious complications.

John Corcoran (Reviewer 2)

GENERAL

The manuscript would benefit from the significant input of a proof reader or editor who can improve the use of language throughout. Simply taking the first paragraph of the Background section, "Irish" should be "Ireland"; the following part of the sentence would read better as "…Dr Samuel Gordon reported its use to examine the pleural space of a girl with empyema…"; the final sentence of the paragraph does not really make sense at all although I understand what the authors are trying to say (i.e. that medical thoracoscopy is less invasive and expensive than a traditional surgical approach). Accessing such an editing resource would undoubtedly improve the quality of the manuscript and ensure its messages are conveyed clearly and adequately.

Reply: We are very sorry for our grammatical errors. We have had our manuscript reviewed by someone who is fluent in English and revised the manuscript.

BACKGROUND

Comment 1: Paragraph 2 - do not finish with the phrase "and other procedures"; this is vague and unhelpful. It is sufficient to say "…including pleurodesis, treatment of pleural infection, forceps lung biopsy, and sympathectomy."

Reply 1: Thank you for your advice. We have revised this sentence in the manuscript.

Comment 2: Paragraph 3 - the authors report that there are few trials reporting complication rates from medical thoracoscopy. This slightly contradicts the earlier discussion based on data presented in reference.

Reply 2: Thank you for your suggestion. In the article, it means most clinical trials reported complications of medical thoracoscopy (MT) in patients undergoing diagnostic thoracoscopy or
talc poudrage. However, few clinical trials ever reported complications of MT in the management of pleural diseases, such as adhesiolysis, pleural decortication of empyema and bulla electrocoagulation.

METHODS

Comment 1: Paragraph 2 - this study covers a substantial period of time (25 years) and the way in which patients are worked up for thoracoscopy, and indeed the way in which thoracoscopy is used, is likely to have evolved substantially over this timeframe. The authors probably need to spend some time outlining how their practice has changed - e.g. did all patients undergo ultrasound examination in 1992, since this seems unlikely? Severe COPD needs to be defined (i.e. spirometry criteria; exercise capacity etc.) What does uncontrollable cough mean - is this an observation immediately prior to or during the procedure? How is the fused pleural space identified (e.g. ultrasonographic absence of lung sliding)? If ultrasound is being used to identify adhesions then appropriate references for how this technique is used should be cited.

Reply 1: Thank you for your advice. There are some changes in the practice during the period of time. For example, at present all patients with pleural effusion underwent ultrasound examination and rigid medical thoracoscopy was widely used. Advanced procedures in medical thoracoscopy were applied increasingly, including adhesiolysis, pleural decortication of empyema and bulla electrocoagulation.


Uncontrollable cough is an observation prior to the thoracoscopy.

Chest US can be very helpful to identify loculations in the pleural cavity and to locate the best entry site for thoracoscopy. (Medford A R. Additional cost benefits of chest physician-operated thoracic ultrasound (TUS) prior to medical thoracoscopy (MT).[J]. Respiratory Medicine, 2010, 104(7):1077-1078.)

Comment 2: Paragraph 5 - there is no mention of the analgo-sedation regimen used by the authors in their centre. This needs to be described in detail - for example, which drugs were used (and range of doses); who was responsible for administration (physician vs. anaesthetist vs. ODP etc.) Pneumothorax induction appears to have been carried out in a subset of these patients, and the technique(s) used needs to be outlined as part of the methodology - e.g. is air allowed to enter the pleural space passively or is an insufflation (positive pressure) method used?

Reply 2: Thank you for your suggestion. Patients were placed in the lateral decubitus position with conscious sedation using diazepam or benzodiazepine. 10 mL of 2% lidocaine (Silver Lake
Shiyao Pharmaceutical Co., Ltd.; Yuncheng, Shanxi Province, China) with 0.5 mg of epinephrine [GrandPharma (China) Co., Ltd.; Wuhan, Hubei Province] was administered to the selected intercostal space for local anesthesia and physician was responsible for administration.

An insufflation (positive pressure) was used to create artificial pneumothorax.

Comment 3: Paragraph 7 - with respect to the use of thoracoscopy in pleural infection, it is not clear to me if and how the authors carried out decortication in a subset of their patient population - this needs to be discussed in more detail, notably the technique(s) used.

Reply 3: Thank you for your advice. Debridement under MT was performed using two ports. The empyema cavity is approached and debrided. If the lung is still covered with fibrotic cortex, then it is stage III empyema and decortication is necessary. Curettage of the chest wall and diaphragm is carried out and decortication is performed using forceps.

RESULTS

When discussing the complications seen with medical thoracoscopy (which is the primary focus of this paper), the authors should divide them into major and minor categories - these can be defined either by the authors themselves, or based on prior publications (e.g. reference #14).

Reply: Thank you for your suggestion. I have divided the complications into major and minor categories.

DISCUSSION

Comment 1: Paragraph 1 - it is not appropriate to describe medical thoracoscopy as minimally invasive, when compared to other pleural interventions carried out by physicians. The authors should outline in this opening paragraph whether medical thoracoscopy is a safe procedure, based on the data they have presented, and where any potential for increased risk might lie (e.g. particular interventions or patient characteristics).

Reply 1: Thank you for your advice. I have revised this paragraph in the article.

Comment 2: Paragraph 2 - this is extremely lengthy and contains a great deal of clinical information and physiological theorising that does not contribute particularly to what I think is striving to be the central message of this manuscript (i.e. the safety profile of medical thoracoscopy). Much of this paragraph can and should be removed from a future revision of the manuscript. The authors also reference the use of a pleural manometer? Is this part of their
standard practice in the context of pneumothorax induction for thoracoscopy? Providing more detail on the techniques used as part of the methods section would resolve this.

Reply 2: Thank you for your suggestion. The patient was died when artificial pneumothorax was being established, but the cause of death is not definitely confirmed. Therefore, it is necessary to analyze the potential causes of death.

During the creation of pneumothorax, we usually feel pleural pressure until 800-1000 ml air has been insufflated. The use of a pleural manometer was cited from an article. (Faurschou P, Viskum K. Artificial pneumothorax by the Veress cannula: efficacy and safety[J]. Respiratory Medicine, 1997, 91(7):402.)

Comment 3: Paragraph 3 - again, lung laceration appears to occur in the context of pneumothorax induction; the failure to describe how this is carried out in the methods section compromises the interpretation of subsequent results. How would the authors detect air leak from the laceration during the procedure if it was occurring in the context of an already partially collapsed lung and open pleural space? How much pleural fluid is "sufficient" to allow trocar insertion? How is the trocar introduced? Again, the methods section needs to be expanded to discuss the technique by which thoracoscopy is carried out in more detail.

Reply 3: Thank you for your advice. In our article, lung laceration happened in patients in whom artificial pneumothorax was not established. Establishment of artificial pneumothorax a few hours or one day before MT can prevent lung laceration. In the context of an already partially collapsed lung and open pleural space, lung laceration was usually detected by excessive bleeding.

In our article, the amount of pleural effusion is undefined. When there is a small amount of pleural effusion without extensive adhesions in the pleural cavity, it is safe to introduce the trocar. If extensive adhesions exist in pleural cavity, location with chest US or CT before MT is necessary.

The trocar was inserted perpendicular to the chest wall with a rotating motion. In order to prevent damage to the intercostal vessels and nerves, it is safer to locate the tip over the border of the inferior rib at the chosen port of entry.

Comment 4: Paragraph 4 - again, I do not think there is much value to be added by discussing the details of individual cases. REPE is a rare complication, as shown in the authors' series, and instead this part of the discussion should focus (briefly) on the postulated risk factors for the development of this complication and its subsequent management.
Reply 4: Thank you for your suggestion. I have revised this part according to the advice.

Comment 5: Paragraph 5 - the authors highlight the risk of severe pain developing during pleurodesis; again, the missing detail on how analgo-sedation is managed during procedures would allow this observation to be considered appropriately.

Reply 5: Thank you for your advice. When severe pain was developed during pleurodesis, conscious sedation using diazepam or benzodiazepine was managed.

Comment 6: Paragraph 6 - did the authors carry out bulla electrocoagulation (presumably for recurrent pneumothorax) without concurrent pleurodesis? This therapeutic strategy needs to be justified if so, given the published evidence base (including that from VATS or surgical procedures) demonstrating that it is pleurodesis that is the key intervention when looking to reduce the risk of future recurrence.

Reply 6: Thank you for your suggestion. Bulla electrocoagulation was performed without concurrent pleurodesis in 6 patients with prolonged air leak.


Comment 7: Paragraph 7 - if discussing the place of NSAIDs in the context of pleurodesis, the authors should cite https://www.ncbi.nlm.nih.gov/pubmed/26720026 as a high-quality RCT relating to this area of practice. The recommended use of physical cooling needs to be supported by an appropriate reference. The risk of port site infection is greatest in those with pleural infection - presumably these patients would already be on antibiotics? There is no evidence I know of to support the use of prophylactic antibiotic therapy post-thoracoscopy otherwise.

The use of physical cooling was mainly depended on our clinical experience.

Although routine prophylactic antibiotics are not necessary, they are advised to be used in neutropenic patients. (Francisco Rodríguez-Panadero, Beatriz Romero Romero. Complications of Thoracoscopy[J]. 2014, 56(3):796-8.) And the use of a one-off dose of intravenous broad spectrum antibiotic at the time of the procedure may also lead to a reduction of infections following thoracoscopy. (Brims F J, Arif M, Chauhan A J. Outcomes and complications following medical thoracoscopy[J]. Clinical Respiratory Journal, 2012, 6(3):144-149.)