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Reviewer A

1. The efficacy of two small size IV needles (20G=0.9mm) & (22G= 0.7 mm) in needle aspiration of a large pneumothorax was tested.

I suspect their question was whether smaller needles are comparable in efficacy to 16G (1.65 mm) and 18G (1.27 mm) needles used in multiple earlier randomized studies. However this is not stated explicitly.

Success rates of 16G needle aspiration ranged from 47.8% to 91.3% in previous studies . For discrete success rates of these randomized needle aspiration comparisons , the authors are advised to refer to Mummadi et al. 2020 [Table 3].

One randomized study reported the efficacy of a somewhat smaller needle aspiration -

Parlak et al reported the use of a 3.9F (1.3mm needle)

Reply: Thank you for your valuable and insightful comments. We changed the manucscript to make it easier to understand and added the references.
Although manual aspiration has already been reported to be useful, the therapeutic effect with a smaller needle, the number of aspiration and the unsuccessful factors are unknown. The primary endopoint of this study was manual aspiration success up to three using a 20- or 22- gauge needle in patients with a large, clinically stable pneumothorax. The secondary goal was to assess the risk factors of manual aspiration failure.

Change in the text.
Line 163-165
The primary endopoint of this study was manual aspiration success up to three using a 20- or 22- gauge needle in patients with a large, clinically stable pneumothorax. The secondary goal was to assess the risk factors of manual aspiration failure.

2. Outdated guidelines (ACCP guidelines based on "expert" opinion and published > 20 yrs. ago were repeatedly cited throughout the manuscript). I think the ACCP guidelines need not be cited as they are no longer relevant.

Reply: We deleted it.

3. Contemporary RCT data about the efficacy of watchful waiting (no intervention at all in large relatively symptomatic PSPs)[13] and usage of self-contained Heimlich valves and narrow bore chest tubes (8F-11F, 2.6 mm- 3.6 mm chest tubes!)[14] were not cited. There is relatively universal agreement that "large bore chest tubes (≥ 14F , > 4.6 mm diameter)" and regular inpatient admission should no longer be used as the primary strategies for treating PSP and maybe other forms of pneumothorax such as iatrogenic[11]. Therefore, the current controversy centers on three competing evidence-based options for ambulatory management of large pneumothoraces (especially primary spontaneous pneumothoraces) : watchful waiting[13,15,16] vs. 16-18G needle aspiration (see above for references) vs. narrow bore chest tubes (8F- 11F)[11,12,14,17,18]. This is not made clear in the manuscript. Instead outdated references and controversies are used for the background. Small-bore chest tubes (8-11F) with self-contained Heimlich valves have been demonstrated to achieve economical outpatient care with relatively safe profile in multiple nonrandomized studies from Korea, Japan, US and the U.K.[19-23]. Given this information and existing evidence, I am unsure if the authors are on a strong footing to recommend that 16G needle aspiration is the only strategy that supports ambulatory strategy (multiple times in the discussion section). As said, narrow bore chest tubes **do support ambulatory strategy and are being widely used across the world**. Ideally, needle aspiration should be compared with narrow bore chest tubes and that is exactly what the RAMPP authors did[14]. There were instances of adverse effects even with narrow bore chest tubes and this certainly supports this current study. However, these adverse effects were not as morbid as we see with large bore chest tubes.

Reply: Thank you for your valuable comments. We added the referecnces and discussion following your advices. Despite many reports, thoracic vent and manual aspiration for pneumothorax have not yet fully penetrated in Japan. Therefore, this study was planned. And please understand that this study was planned from 2013 to 2018, when the literature described by the reviewer is not applicable.

Change in the text:

Line 70-73
Management guidelines for a large pneumothorax in a clinically stable patient remain controversial. Treatment options for these patients include inserting a chest tube, aspiration, thoracic vent, and surgical treatment [3].

Line 79-100

Recently, there has been repoted a careful follow-up for spontaneous pneumothorax [21] and effect on the ambulatory management [22]. A large bore chest tube drainage and regular inpatient admission are becoming less of the primary strategies for treating primary spontaneous pneumothorax (PSP). Therefore, the current controversy centers on three competing evidence-based options for ambulatory management of large pneumothoraces: watchful waiting [20,22,23] vs. 16 gaude (G) needle aspiration [7-10, 12-16] vs. thoracic vent with a 8-11 French tube [21,24-28]. These reports indication are mainly for PSP, but other pneumothorax is well unknown. Standard aspiration needle is mainly used by 16G, and the effect with a smaller needle and the number of aspiration times have not been fully verified. Ambulatory care with a thoracic vent tend to be widespread, but it also concerns about adverse events [22].

In 2013, we conducted a prospective, two-center study to assess the effectiveness of manual aspiration using a 20 or 22G needle in clinically stable patients with a all type large pneumothorax due to any cause. The primary endopoint was manual aspiration success up to three using a small needle in patients with a large, clinically stable pneumothorax. The secondary goal was to assess the risk factors of manual aspiration failure. This study had some novelties: (1) the indication was independent of the degree of collapse or etiology in clinically stable patients; (2) small needles (20-22G) were used; (3) aspiration was attempted thrice; (4) intrathoracic pressure was measured; (5) serum plasma factor XIII was measured [29, 30]; and (6) the factors of manual aspiration failure was assessed.

Line 163-165

The primary endopoint was manual aspiration success up to three using a 20 or 22G needle in patients with a large, clinically stable pneumothorax. The secondary goal was to assess the risk factors of manual aspiration failure.

Title: Effectiveness and failure factors of manual aspiration using a small needle for large pneumothorax in stable patients

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4. There is an important data point which was not shared in the study. That is – the duration of stay in the ER till the decision to discharge home is made. Given that non emergent patients cannot be observed for a long duration of time (For example, patients cannot be observed for more than 4 hours in Australian

emergency rooms[24,25] [without either discharge or admission], it is usually not feasible in multiple settings to simply observe the patient !. We were not supplied with how long these patients were observed in the ER after needle aspiration and before the chest X ray was performed.

Reply: Thank you for your concern. At our two hospitals, the ER waiting time is very short, about 30 minutes at the longest. And the patient returned home soon after aspiration. If careful observation was desirable for a patient, a patiens was admitted to the hospital. However, no patient was actually hospitalized. We added them.

Change in the text:

Line 148-149

If lung expansion was complete or only small apical pneumothorax was present, the patient was discharged soon.

Line 153-143

If careful observation was desirable for a patient, a patiens was admitted to the hospital.

5. I also have a question about the technique- Was the metallic needle removed before the plastic catheter was fully inserted into the pleural space?

Reply: After advancing to a depth where the catheter can be fully inserted into the pleural space, the metal needle is pulled out.

Change in the text

Line 139-141

After advancing to a depth where the catheter can be fully inserted into the pleural space, the metal needle is pulled out.

6. Except for a smaller needle size used, I am afraid there are no novel findings in the study. However, at the same time, these data support the usage of smaller diameter needles. I would recommend that the authors pursue drastic revision of their background and references. Consideration should be given to shorter forms of communication (Research letter) but an appropriately and thoroughly revised manuscript could make a decent case for a full manuscript version.

Reply: We added referecnces and discussion. Please understand that this study was planned from 2013 to 2018, when the literature described by the reviewer is not applicable. The primary endopoint of this study was manual aspiration success up to three using a 20- or 22- gauge needle in patients with a large, clinically stable pneumothorax. The secondary goal was to assess the risk factors of manual aspiration failure. In this study had other novelties: (1) the indication was independent of the degree of collapse or etiology in clinically stable patients; (2) aspiration was attempted thrice; (3) intrathoracic pressure was measured; and (4) serum plasma factor XIII was measured. There is no paper in your literature that meets these points. Therefore, you cannot tell that this is not novel.

Line 91-100

In 2013, we conducted a prospective, two-center study to assess the effectiveness of manual aspiration using a 20 or 22G needle in clinically stable patients with a all type large pneumothorax due to any cause. The primary endopoint was manual aspiration success up to three using a small needle in patients with a large, clinically stable pneumothorax. The secondary goal was to assess the risk factors of manual aspiration failure. This study had 6 novelties: (1) the indication was independent of the degree of collapse or etiology in clinically stable patients; (2) small needles (20-22G) were used; (3) aspiration was attempted thrice; (4) intrathoracic pressure was measured; (5) serum plasma factor XIII was measured [29, 30]; and (6) the factors of manual aspiration failure was assessed.

Line 346-352

Management of a thoracic vent and narrow bore chest tubes do not always require hospitalization, and have a economical benefit or shorter treatment time [26]. However, there remains a sense of discomfort that foreign matter is indwelling, despite less pain compared to chest tube drainage [7, 15]. The number of aspirationp was reported up to the second time [7], but this time it was performed up to three times. Aspiration up to three times is an effective and safe procedure in patients with large pneumothorax, and aspiration may serve as a life-saving procedure that can be done by a non-specialist.

7. Line 239: Epidemiological data to support the incidence of pneumothorax appears outdated. More contemporary pneumothorax data [2018-2021 data from England[26], France[27], US[28]] are available. Please cite these contemporary sources. Encouraged to use "incidence" rather than "prevalence".

Reply: Thank you for your valuable information. We added them.

Change in the text.

Line 262-263

Pneumothorax is a common disease [36-40]. Despite the incidence of pneumothorax [38-40], several methods for initial treatment exist.

8. Line 305: The authors state that "drainage via chest tube typically requires hospitalization". This is not true especially in the era of self-contained Heimlich valve and narrow bore chest tubes [8-11 French, RAMPP[14] study and in many other studies that pursue narrow bore chest tube as an ambulatory strategy[11]].

Reply: Thank you for your valuable comments. We revised them.

Change in the text:
Line 83-88
A large bore chest tube drainage and regular inpatient admission are becoming less of the primary strategies for treating primary spontaneous pneumothorax (PSP). Therefore, the current controversy centers on three competing evidence-based options for ambulatory management of large pneumothoraces: watchful waiting [20,22,23] vs. 16 gaude (G) needle aspiration [7-10, 12-16] vs. thoracic vent with a 8-11 French tube [21,24-28].

Line 265-269
Although a careful follow-up or effect on the thoracic vent management for spontaneous pneumothorax, there are concerns about adverse events [21, 22]. Thoracic vent had serious adverse events and similar pain compared to the standard care [22]. It is also easy to imagine a sense of discomfort when a patients is inserted a foreign body such as a thoracic vent.

Line 344-350
However, drainage via a larger bore chest tube typically requires hospitalization and may lead to complications, especially in patients with adhesions. Management of a thoracic vent and narrow bore chest tubes do not always require hospitalization, and have a economical benefit or shorter treatment time [26]. However, there remains a sense of discomfort that foreign matter is indwelling, despite less pain compared to chest tube drainage [7, 15]. The number of aspirationp was reported up to the second time [7], but this time it was performed up to three times.

Reviewer B

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Thank you for allowing me to review the manuscript entitled "Effectiveness of manual aspiration using a small needle for pneumothorax in stable patients".

Overall I am impressed by the depth of information and data authors provided. Although not randomized, I wish there is a comparison data from those 62 patients who chose to have a surgery or tube placed. In my opinion it would be valuable to have patient characteristics, complications, length of stay, and pneumothorax characteristics for comparison. However even without it, I feel like this manuscript contains valuable info for future readers. I especially enjoyed data about intrathoracic pressure.

I suggest the following changes:

1. Line 131: change wording from 'apical air' to 'apical pneumothorax'

Reply: Thank you for your point out. I changed.

Changes in the text:
Line 148-149
If lung expansion was complete or only small apical pneumothorax was present, the patient was discharged soon.

2. The process described between lines 134 and 136 is unclear. Authors stated that if the lung expansion was insufficient an additional aspiration was attempted but then also state that if the lung expansion was insufficient patients were discharged. Please re-write and provide clarifications whether more than 1 aspiration was done initially or all subsequent aspirations were done next day.

Reply: Thank your valuable comments. If the lung expansion was insufficient, an additional aspiration was immediately perfomed. So, it's on the same day.

Changes in the text:
Line 148-152
If the lung expansion was insufficient, an additional aspiration was immediately attempted after chest ultrasonography on the same day. A chest X-ray was repeated and patients were discharged, even if the lung expansion was insufficient. If careful observation was desirable for a patient, a patiens was admitted to the hospital. Consecutive aspirations performed on the same day were counted as one.

3. Clarify how many patients with successful outcome had their 2nd and 3rd aspirations done next day during follow up and how many during their initial presentation.

Reply: Thank you for your valuable advices. We revised them.

Change in the text.

Line 55-56
The first aspiration was successful in 57 patients (53.3%), the second in 16 patients (59.2%), and the third in eight patients (80.0%).

Line 224-225
The success rate of the first aspiration was 53.3% (57/107), the second aspiration was 59.2% (16/27), and the third aspiration was 80.0% (8/10). Up to three aspirations, a total of 81 patients (75.7%) were treated successfully by manual aspiration.

4. Lines 157 and 164 – correct spelling of pneumothorax and pneumothoraces

Reply: Thank you for your point out. I revised them.

5. Simplify table 1. Please remove aspiration success info from table 1 as this is discussed in the figure 4 and in the body of the manuscript.

Reply: Thank you for your comments. We changed Table 1 and deleted aspiration success info.

6. Line 203 and Figure 4. The success rate of aspiration should be calculated from the aspirations done in any given round. Therefore suggest to change 2nd aspiration success rate to 16/27 (59.2%) and 3rd aspiration success rate to 8/10 (80%). I would leave the info about cumulative success from table 1 out as it does not add any more info to a reader.

Reply: Thank you for your valuable comments. We revised them according to the indications.

Changes in the text:
Line 55-56

The first aspiration was successful in 57 patients (53.3%), the second in 16 patients (59.2%), and the third in eight patients (80.0%).

Line 224-226
The success rate of the first aspiration was 53.3% (57/107), the second aspiration was 59.2% (16/27), and the third aspiration was 80.0% (8/10).

Line 572-576
Figure 4: Follow diagram of the study
Aspiration failure is defined as 2,500 mL of aspirated air, aspiration more than three times, or the requirement of a chest tube or surgery. The success rate of the first aspiration was 53.3% (57/107) of the second aspiration was 59.2% (16/27), and of the third aspiration was 80.0% (8/10). A total of 81 patients (75.7%) were successfully treated with manual aspiration.

7. Conclusion – since the manual aspiration was not compared to chest tube placement in this study please avoid stating whether it can or cannot replace a chest tube placement as initial management. Please simply the conclusion to: a) the safety and effectivity of manual aspiration in initial management of stable asymptomatic patients with non-traumatic etiology b) feasibility of manual aspiration in management of traumatic and iatrogenic pneumothoraces.

Reply: Thank you for your valuable comments. I agree to your advice and revised them according to the indications.

Changes in the text:
Line 65-66 and 375-376
Manual aspiration up to three times using a small needle might be one of a treatment option in clinically stable patients with any large pneumothorax.

Reviewer C

This is a prospective, two-center study to assess the effectiveness of manual aspiration using a 20- or 22- gauge needle in clinically stable patients with a large pneumothorax spontaneous and traumatic.

Some points deserve consideration in order to further improve the paper:

1/ Abstract

The background is unclear and must be modified. Authors explains that the initial management of a large pneumothorax in a clinically stable patient remains controversial, notably regarding the needle size. But the objective of this study was not to determine the minimal size related to success of aspiration. A confusion appears throughout the manuscript concerning the objective of the study :
-Assess the aspiration failure risk factors regarding the needle size? It implies that they compared 2 groups with 20 or 22 gauge with largest needle
-Or assess the aspiration failure risk factors for all types of pneumothorax? In this case, why did the authors not directly compare traumatic and spontaneous pneumothorax?
Authors must precisely explain the objectives and the methods must be adapted to meet them which is not clear in the manuscript currently. Furthermore, I suggest that authors replace “due to any cause” by traumatic and spontaneous pneumothorax.

Reply: Thank you for your valuable comments. Although manual aspiration has already been reported to be useful, it was unknown about the unsuccessful factors, the therapeutic effect with a smaller needle, the pathological conditions other than spontaneous pneumothorax, and the number of aspiration. We revised them.

Changes in the text:
Line 43-48
Manual aspiration as the initial management of a large pneumothorax in a clinically stable patient has been reported to be safe and effective. However, the effect with smaller needles, the number of aspiration, the indication other than spontaneous pneumothorax and failure factors are unknown. We assessed the effectiveness and failure risk factors of manual aspiration up to three using a 20- or 22- gauge needle in patients with a large, clinically stable pneumothorax.

Line 93-102
In 2013, we conducted a prospective, two-center study to assess the effectiveness of manual aspiration using a 20 or 22G needle in clinically stable patients with a all type large pneumothorax due to any cause. The primary endopoint was manual aspiration success up to three using a small needle in patients with a large, clinically stable pneumothorax. The secondary goal was to assess the risk factors of manual aspiration failure. This study had some novelties: (1) the indication was independent of the degree of collapse or etiology in clinically stable patients; (2) small needles (20-22G) were used; (3) aspiration was attempted thrice; (4) intrathoracic pressure was measured; (5) serum plasma factor XIII was measured [29, 30]; and (6) the factors of manual aspiration failure was assessed.

2/ Introduction

The authors states that this study has 5 novelties. Authors must explain this before the objective of the study and better specify how these proposed factors are relevant to the study. The introduction must be more organized to explain the interest of carrying out this study and what is the objective. Finally, the authors do not explain at all the recommendations of management for a traumatic pneumothorax. However, it is a real problem to justify their method with the absence of recommendation to perform aspiration for these patients.

Reply: Thank you for your valuable comments. We changed the introduction.

Change in the text:
Line 71-100
The initial management of pneumothorax is decided based on the patient's clinical stability, pneumothorax size, and risks of recurrent pneumothorax [1, 2]. Management guidelines for a large pneumothorax in a clinically stable patient remain controversial. Treatment options for these patients include inserting a chest tube, aspiration, thoracic vent, and surgical treatment [3]. The British Thoracic Society (BTS) pleural disease guidelines 2010 recommend needle aspiration [1]. Simple aspiration is as effective and more feasible than chest tube insertion [1-17]. One of the background is the placement of a chest tube includes the risks of severe pain, intercostal vessel bleeding, intercostal nerve injury, and injury to the lung, kidney, liver, and heart [18-20]. These risks are increased in patients with intrathoracic adhesions, a history of pneumothorax, and severe emphysema, depending on the physician or assistant's inexperience. Recently, there has been repoted a careful follow-up for spontaneous pneumothorax [21] and effect on the ambulatory management [22]. A large bore chest tube drainage and regular inpatient admission are becoming less of the primary strategies for treating primary spontaneous pneumothorax (PSP). Therefore, the current controversy centers on three competing evidence-based options for ambulatory management of large pneumothoraces: watchful waiting [20,22,23] vs. 16 gaude (G) needle aspiration [7-10, 12-16] vs. thoracic vent with a 8-11 French tube [21,24-28]. These reports indication are mainly for PSP, but other pneumothorax is well unknown. Standard aspiration needle is mainly used by 16G, and the effect with a smaller needle and the number of aspiration times have not been fully verified. Ambulatory care with a thoracic vent tend to be widespread, but it also concerns about adverse events [22].

In 2013, we conducted a prospective, two-center study to assess the effectiveness of manual aspiration using a 20 or 22G needle in clinically stable patients with a all type large pneumothorax due to any cause. The primary endopoint was manual aspiration success up to three using a small needle in patients with a large, clinically stable pneumothorax. The secondary goal was to assess the risk factors of manual aspiration failure. This study had some novelties: (1) the indication was independent of the degree of collapse or etiology in clinically stable patients; (2) small needles (20-22G)

were used; (3) aspiration was attempted thrice; (4) intrathoracic pressure was measured; (5) serum plasma factor XIII was measured [29, 30]; and (6) the factors of manual aspiration failure was assessed.

3/ Methods
The study design and patients should be better defined.
-First episode or recurrence is not specified. However, management also depends on the first episode or recurrence status of the pneumothorax.

Reply: Thank you for your valuable comments.
Changes in the text:
Line 127-128
Patients were indicatied regardless of whther the first or the recurrence.

- It is not clear how the size of the pneumothorax was determined. Indeed, the authors mixed the recommendations of the ACCP and BTS. Only one should be chosen.

Reply: The size of pneumothorax was basically followed the ACCP guidleline. When the decision was difficult due to intrathoracic adhesions, the size was determined as the presence of a visible rim of >2 cm between the lung margin and chest wall at the level of the hilum following the BTS guideline. In addition, the size was also evaluated at the same time by the BTS guidline, the Light index, and the Japan Society for Pneumothorax and Cystic Lung Diseases classifications on chest X-rays because there are some diffirecnces depending on the report.

Changes in the text
Line 114-118
A large pneumothorax was basically defined as ≥3 cm from the apex to the cupola following the ACCP guideline. When the decision was difficult due to intrathoracic adhesions, the size was determined as the presence of a visible rim of >2 cm between the lung margin and chest wall at the level of the hilum following the BTS guideline.

-Patients with chest tube drainage were not included in the study. Why and in which case chest tube drainage was performed? The authors could specify if the characteristics of these patients were different.

Reply:

Chest tube drainage was peformed when a paitent want to do chest tube drainage (Line 118-126) and when manual aspiration was unsuccessful (Line 149-151 and 159-160). Could you please read them?

-Page 6 line 118, the authors must remove “Chest ultrasonography was performed to confirm pneumothorax” because it was confirmed previously by a chest radiography.

Reply:
Thank you for the comment. We’re sorry for the misunderstanding. Chest ultrasonography was performed to confirm intrathoracic adhesions. We changed them to make it easier to understand.

Changes in the text:
Line 134-135
Chest ultrasonography was performed to confirm intrathoracic adhesions and the distance from the skin to the pleural space at the puncture site [13, 14]

-Why a chest radiography was performed after each aspiration and not a chest ultrasonography?

Reply: It was to evaluate the extension of the lung and pleural effusion because ultrasound may be insufficient for evaluation.

- Using JSPCLD classifications, the pneumothoraxes were divided into three categories: but only the part of severe pneumothorax was presented in the table 1.

Reply: Thank you for the comment. JSPPCLD classification’s mild pneumothorax does not correspond with large pneumothorax under ACCP and BTS guidelines. In other words, no patient was included according to the JSPPCLD’s mild. So, Table 1 was listed modetate and severe.

-The primary endpoint and secondary endpoints were not well defined.

Reply: Thank you for your valuable comment. We added them.

Changes in the text:
Line 43-48

Manual aspiration as the initial management of a large pneumothorax in a clinically stable patient has been reported to be safe and effective. However, the effect with smaller needles, the number of aspiration, the indication other than spontaneous pneumothorax and failure factors are unknown. We assessed the effectiveness and failure risk factors of manual aspiration up to three using a 20- or 22- gauge needle in patients with a large, clinically stable pneumothorax.

Line 93-102
In 2013, we conducted a prospective, two-center study to assess the effectiveness of manual aspiration using a 20 or 22G needle in clinically stable patients with a all type large pneumothorax due to any cause. The primary endopoint was manual aspiration success up to three using a small needle in patients with a large, clinically stable pneumothorax. The secondary goal was to assess the risk factors of manual aspiration failure. This study had some novelties: (1) the indication was independent of the degree of collapse or etiology in clinically stable patients; (2) small needles (20-22G) were used; (3) aspiration was attempted thrice; (4) intrathoracic pressure was measured; (5) serum plasma factor XIII was measured [29, 30]; and (6) the factors of manual aspiration failure was assessed.

-Is the measure of the intrathoracic measure consensual and if so, the authors must cite the references.

Reply: Thank you for your valuable comment. We added them.

Changes in the text:
Line 304-309
Tension pneumothorax is known that intrathoracic cavity presseure tend to be positive and affects hemodynamics [50, 51]. Although tension pneumothorax was excluded from this study, we assumed that persistent air leaks cases were higher intrathoracic pressure. There may be a causal relationship between the degree of collapse and intrathoracic pressure, but at least in this study there was no statistical result as a failure factor.
[50] Zwischenberger JB, Bowers RM, Pickens GJ. Tension pneumothorax during extracorporeal membrane oxygenation. Ann Thorac Surg 1989;47:868-71.
[51] Chinet AE. Chest-lung statics: a realistic analog for student laboratory. Am J Physiol 1989; 257: S9-10. doi: 10.1152/advances.1989.257.6.S9.

4/ Results
Figure 1 is not clear to understand the management in case of success or failure at each aspiration.

Reply:
Thank you for your comment. I simplified Figure 1.

Change in the text.
Please see new Figure 1.

A table comparing the characteristics of traumatic and spontaneous pneumothorax would be interesting.
The table 1 could be divided into 2 tables.

Reply:
This study included 4 types pneumothorax; spontaneous primary, spontaneous secondary, traumatic, and inatrogenic. So, I think it is unnatural to divide it into two types, spontaneous and traumatic. How about classifying them into 4 types?

Changes in the text:
Please see New Table 1.

5/ Discussion
-page 10 line 240, the methods for initial treatment vary according to the recommandations and not by region. Therefore, it is essential that the authors apply only one recommendation and not mix several recommendations. On the other hand, they could compare them as secondary objectives but this must be explained in the methods.

Reply: Thank you for your valuable comments. We changed the confusing expression.

Change in the text:
Line 245
Despite the prevalence of pneumothorax, several methods for initial treatment exist.

Line 71-92
The initial management of pneumothorax is decided based on the patient's clinical stability, pneumothorax size, and risks of recurrent pneumothorax [1, 2]. Management guidelines for a large pneumothorax in a clinically stable patient remain controversial. Treatment options for these patients include inserting a chest tube, aspiration, thoracic vent, and surgical treatment [3]. The British Thoracic Society (BTS) pleural disease guidelines 2010 recommend needle aspiration [1]. Simple aspiration is as effective and more feasible than chest tube insertion [1-17]. One of the background is the

placement of a chest tube includes the risks of severe pain, intercostal vessel bleeding, intercostal nerve injury, and injury to the lung, kidney, liver, and heart [18-20]. These risks are increased in patients with intrathoracic adhesions, a history of pneumothorax, and severe emphysema, depending on the physician or assistant's inexperience. Recently, there has been repoted a careful follow-up for spontaneous pneumothorax [21] and effect on the ambulatory management [22]. A large bore chest tube drainage and regular inpatient admission are becoming less of the primary strategies for treating primary spontaneous pneumothorax (PSP). Therefore, the current controversy centers on three competing evidence-based options for ambulatory management of large pneumothoraces: watchful waiting [20,22,23] vs. 16 gaude (G) needle aspiration [7-10, 12-16] vs. thoracic vent with a 8-11 French tube [21,24-28]. These reports indication are mainly for PSP, but other pneumothorax is well unknown. Standard aspiration needle is mainly used by 16G, and the effect with a smaller needle and the number of aspiration times have not been fully verified. Ambulatory care with a thoracic vent tend to be widespread, but it also concerns about adverse events [22].

Line 262-269
Pneumothorax is a common disease [36-40]. Despite the incidence of pneumothorax [38-40], several methods for initial treatment exist. Placement of a chest tube is common in the nations following the ACCP guidelines, while aspiration is recommended by the BTS. Although a careful follow-up or effect on the thoracic vent management for spontaneous pneumothorax, there are concerns about adverse events [21, 22]. Thoracic vent had serious adverse events and similar pain compared to the standard care [22]. It is also easy to imagine a sense of discomfort when a patients is inserted a foreign body such as a thoracic vent.

-Page 12, the role of plasma factor XIII is interesting but could be further developed.

Reply: Thank you for the comment. We added in detail.

Change in the text:
Additionally, plasma factor XIII has been reported to be a fistula-healing factor and intraoperative bleeding [29, 30, 45, 46]. In lung disease, there are some reports related to therapeutic effect of pneumothorax and prolonged air leak after pulmonary lobectomy [47, 48]. However, effect of plasma factor XIII is controversial [49]. At least, plasma factor XIII was not found to be associated with the success of manual aspiration in this study, although it cannot be ruled out that it is associated with the development of pneumothorax.

[45] Lassila R. Clinical use of factor XIII concentrates. Semin Thromb Hemost

2016;42:440-4.

[46] Watanabe N, Yokoyama Y, Ebata T, et al. Clinical influence of preoperative factor XIII activity in patients undergoing pancreatoduodenectomy. HPB 2017;19:972-7.

[47] Murata A, Kouno A, Yamamoto K, et al. The treatment of refractoy pneumothorax in diffuse panbronchiolitis by intravenous administration of coagulation factor XIII concentrate. J Nippon Med Sch 2006;73:89-92.

[48] Inoue H, Nishiyama N, Mizuguchi S, et al. Clinical value of exogenous factor XIII for prolonged air leak following pulmonary lobectomy: a case control study. BMC Surg 2014; 14:109. doi:10.1186/1471-2482-14-109.

[49] Takeda Y, Mise Y, Ishizuka N, Harada S, et al. Effect of early administration of coagulation factor XIII on fistula after pancreatic surgery: the FIPS randomized controlled trial. Langenbecks Arch Surg 2018;403:933-40.

-The authors cannot say that aspiration may be a more preferred option for iatrogenic and traumatic pneumothorax because they did not compare aspiration with chest tube drainage or surgery.

Reply: It's certainly not comparable to chest tube drainage, but at least we think that manual aspiration might be one of option for all pneumothorax.

Change in the text
Line 375-378
Manual aspiration up to three times using a small needle might be one of a treatment option in clinically stable patients with any large pneumothorax. Aspiration failure was correlated with an inter-pleural distance >20 mm at the level of the hilum, spontaneous secondary pneumothorax, and ≤24 h from onset to presentation.