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Reviewer A

Authors investigated the safety and effectiveness of surgical treatment in patients with pleuro-peritoneal fistula. They reported low incidence of recurrence rate and only one case of reoperation and no mortality.

Small cases of surgical management followed by a difficulty statistical analysis. They compared their series with historical data from Chow et al. This statistical method was not fully explained in the Method of statistical analysis. This uncertainty could not elicit proper conclusions.

Below several errors are shown in the manuscript

- 1) Introduction line 3 (page2)
- The incidence of CAPD related PPF is approximately: No incidence is described.
- 2) Methods line 29 (page2)
- "Continuous variables were analyzed by logistic regression"
- - This is not an appropriate method.
- 3) Tables are not indicated in the context
- 4) Discussion line 18
- "postulated to be due to be due to a" duplicated words
- 5) Discussion line from 23 to 26 (page 4)
- This paragraph is appropriated in the limitation

Comment 1: They compared their series with historical data from Chow et al. This statistical method was not fully explained in the Method of statistical analysis

Reply 1: Thank you for your comment, the manuscript has been modified.

<u>Changes in text</u>: *Page 5, line 22-23. Page 6, line 1-4* "The authors acknowledge that there is a relative scarcity of patients with CAPD associated PPF at each cardiothoracic centre. As such this may complicate the discerning of useful information from providing insight into our clinical practice. Hence, the authors extrapolated data from Chow et al. (1) which described the recurrence rates of CAPD associated PPF by interruption of CAPD for 1-4 months followed by re-initiation alone as well as chest tube pleurodesis (appendix 1). The aforementioned data was used as a baseline for comparison of PPF recurrence and statistical analysis"

Comment 2: - The incidence of CAPD related PPF is approximately: No incidence is

described.

Reply 2: Thank you for your comment, the manuscript has been modified and the incidence has been included with a reference.

Changes in text: *Page 4, line 12-13* "The incidence of CAPD related PPF is approximately 2% (1)"

Comment 3: "Continuous variables were analyzed by logistic regression"

Reply 3: Thank you for your comment. The method statistical analysis has been changed and the manuscript has been modified.

Changes in text: *Page 6, line 5* "Continuous variables were analysed by linear regression"

Comment 4: Tables are not indicated in the context

Reply 4: Thank you for your comment, the manuscript has been modified.

Changes in text: The number of tables have been reduced to slimline the manuscript.

Comment 5: "postulated to be due to be due to a" – duplicated words

Reply 5: Thank you for your comment. The manuscript has been modified.

Changes in text: *Page 10, line 13-15* "The pathophysiology of PPF occurrence in the setting of CAPD is postulated to be due to a previously undiagnosed...."

Comment 6: Discussion line from 23 to 26 (page 4) This paragraph is appropriated in the limitation

Reply6: Thank you for your comment, the paragraph has been deleted and the manuscript has been modified.

Changes in text: The paragraph in question has been moved to the "Limitations" section at page 13, line 13-17

Reviewer B

In the current report the authors describe their experience in 35 patients on continuous ambulatory peritoneal dialysis who developed pleuroperitoneal fistulas treated with VATS pleurodesis and/or repair of diaphragmatic defects They found that mechanical + talc pleurodesis was the most effective form of treatment. Perioperative

- 1. Several grammatical issues require attention. For example:
- a. Page 2 lines 34-36: why is "recurrence" defined twice

complications were rare. Recurrence rate was 22.8%.

- b. Page 4 line 18: to be due to be due to?
- c. Several other minor issues
- 2. Could the authors discuss CAPD in more detail, including selection criteria for this

versus HD (or other types of peritoneal dialysis?), the amount of fluid instilled and length of time it is left in place, etc.

- 3. Why was use of ACEI relevant in this patient population?
- 4. The 8 patients who developed recurrence were from a denominator of how many patients? 31? (35 total but 4 were switched to HD?) That would give a recurrence rate of \sim 26%?
- 5. The stats regarding 8510 patients on RRT, 76% of whom are on peritoneal dialysis, applies to where? Hong Kong?
- 6. At the end of the discussion the authors comment on meticulous hemostasis, which can be challenging and perhaps not applicable after mechanical pleurodesis as the procedure creates a large raw surface bleeding area. In patients with coagulopathy from renal failure. As the authors comment on, what may be more relevant than "meticulous hemostasis" is correction of coagulopathy (ddavp, plts etc).
- 7. Could the authors reference in the results section the tables in which relevant results are presented?
- 8. Is table 6 a logistic regression? If so, this should be stated in the title of the table, the methods described in the methods section (selection of candidate variables (from univariate analysis?), and could the authors include the OR and confidence intervals?
- 9. The data comparing the authors outcomes to a historical report is very interesting. Obviously, the comparison of results from 2 separate single center studies has its flaws. This analysis has to be described in the methods section. And the results should be in the results section.
- 10. In appendix 2 and 3, given the extremely small numbers for all techniques other than mechanical +/- talc pleurodesis, perhaps they can be combined into an "other group" or probably just eliminated. Doing statistical analysis comparing groups with 0 and 1 patients is not really useful or valid. The data regarding the mechanical +/- talc pleurodesis with the historical controls are interesting however.
- 11. Why is the Strobe statement included? Is this for systematic reviews and metaanalyses?

Comment 1: a. Page 2 lines 34-36: why is "recurrence" defined twice b. Page 4 line 18: to be due to be due to?

Reply 1: Thank you for your comment, the manuscript has been modified. **Changes in text:** *Page 6, Line 10-16* "PPF recurrence was defined as re-occurrence of ipsilateral pleural effusion after re-initiation of CAPD diagnosed clinically with pleural fluid biochemistry, CT peritoneogram or peritoneal fistulogram. Surgical complications are defined as complications requiring surgical intervention."

Comment 2: Could the authors discuss CAPD in more detail

Reply 2: Thank you for your comment, the manuscript has been modified with a paragraph regarding CAPD in the discussions section.

Changes in text: Page 10, line 1-7 "CAPD is a form of renal replacement therapy performed by protocol set out by the renal team. CAPD is performed by the patient or the carer by instilling dialysate of various dextrose concentrations into the peritoneum through a dialysing catheter. The dialysate is allowed to dwell in the peritoneum for 4-6 hours, where the peritoneum acts as an interface for the exchange of fluid, electrolytes and toxins. After the prescribed time had elapsed, the fluid is then drained out from the catheter and a fresh bag of dialysate is infused. The summation is a continued presence of dialysate in the peritoneum to replicate the function of the kidneys."

Comment 3: Relevance of ACEI

Reply 3: Thank you for your comment, the manuscript has been modified and a paragraph of ACEI induced pleural effusion has been added to the discussions section.

Changes in text: *Page 11, line 3-6* "Published case reports suggested that angiotensin converting enzyme inhibitor (ACEI) induced pleural effusion (9). We postulate that ACEI usage may predispose patients to have recurrence of pleural effusion despite receiving PPF. However, ACEI use was not found to be statistically significant in predicting PPF recurrence in our patient series."

Comment 4: The 8 patients who developed recurrence were from a denominator of how many patients? 31? (35 total but 4 were switched to HD?) That would give a recurrence rate of $\sim 26\%$?

Reply 4: Thank you for your comment, the statistical analysis has been revised accordingly with the exclusion of patients who did not have a trial of CAPD after surgery from the analysis of PPF recurrence.

Changes in text: Multiple changes in the methods, results section and discussion section regarding the data involved. The altered calculations yielded a similar result as previous. Thus it did not alter the direction in which the paper had been discussing VATS in CAPD associated PPF.

Comment 5: RRT statistics

Reply 5: Thank you for your comment, the manuscript has been modified with relevant information added.

Changes in text: *Page 10, line 8-10* "As of 2013, it is estimated that there are 8510 patients requiring renal replacement therapy in Hong Kong, 76.2% of which are receiving peritoneal dialysis (5)"

Comment 6: Hemostasis

Reply 6: Thank you for your comment, the paragraph has been revised and the

manuscript has been modified.

Changes in text: *Page 13, line 9-12:* "As uremic patients may suffer from platelet dysfunction, it should be made aware that proper correction of coagulopathy in uremic patients, such as use of DDAVP prior to surgery is important in reducing the risk of hemorrhagic complications from arising from the surgery."

Comment 7: References of tables:

Reply 7: Thank you for your comment, the manuscript has been modified.

Comment 8: Table 6

Reply 8: Thank you for your comment, combined with the suggestion from Reviewer A, the authors would decrease the number of tables.

Comment 9: comparing historical data

Reply 9: Thank you for your comment, the manuscript has been modified.

Changes in text: Page 5, line 22-23, Page 6, line 1-4"The authors acknowledge that the relatively few accumulative caseloads of CAPD associated PPF at each cardiothoracic centre, may complicate the eluding of useful information to provide insight into our clinical practice. Hence, the authors extrapolated data from Chow et al. (1) which described the recurrence rates of CAPD associated PPF by interruption of CAPD for 1-4 months followed by re-initiation alone as well as chest tube pleurodesis. The aforementioned data is used as a baseline for comparison in terms of PPF recurrence rates against the data collected in this study for statistical analysis with odds ratio."

Comment 10: Combining techniques

Reply 10: Thank you for your comment, the manuscript has been modified

Changes in text: *Page 8, line 7-16* "A variety of operative techniques were employed by the surgical team. Techniques included concomitant mechanical and talc pleurodesis, mechanical pleurodesis alone, talc pleurodesis alone, concomitant mechanical and tetracycline pleurodesis, decortication and direct closure with or without chemical pleurodesis. After reviewing the results, the authors decided to consolidate the operative techniques into concomitant mechanical and talc pleurodesis versus techniques other than concomitant mechanical and talc pleurodesis. This was due to the fact that concomitant mechanical and talc pleurodesis appeared to have the best result in terms of the lowest recurrence rate among surgical techniques at 10%. On the other hand, consolidated results of techniques other than concomitant mechanical and talc pleurodesis yielded a recurrence rate of 33.3%."

Comment 11: STROBE statement

Reply 11: STROBE statement was included as per the editor's request.

Reviewer C

I think this article is comprehensively collected and well analyzed in all data about the VATS for PPF in CAPD patients. However, I suppose the additional figures of the intraoperative photos (especially each operational procedures) would be helpful to image this VATS for PPF.

Reply: Thank you for your comment. Intra-operative photos of suspected diaphragmatic fistula and its closure has been added.