Peer Review File
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Reviewer A:

I would appreciate the authors' efforts. I have read the manuscript carefully and made some comments.
This manuscript has been written as a review article concerning cardiac related pleural effusions (PEs).

Comment 1: I recognized the authors gathered enough evidence of PEs based on a comprehensive literature search. However, the description is not summarized well and the text is too long (especially in L246-296 and L377-393). Each searched paper should be introduced by one or two sentences to explain its contents, and I believe that the role of a review is to present the findings that integrate them.

Response 1: We want to thank reviewer A for their comments. We have reviewed L246-296 and L377-393 (new line numbers 248-298 and 382-396) and discussed this will colleagues, and believe the existing description provides an appropriate summary of the key findings of the individual studies that have been referenced which will be compromised by curtailing it further.

Comment 2: When treating pleural effusion due to heart failure, it is important to treat the heart failure itself, and the treatment varies depending on the cause of the heart failure. Reducing pleural effusion is not the treatment goal for heart failure, and it is not always correct to use diuretics, so the description of L126-132 is not completely appropriate. I don't think it is necessary to describe details of treatment for heart failure (delegated to the guidelines for heart failure).

Response 2: We want to thank reviewer A for their comment and suggestions. We have added a sentence to elaborate on your comment (new line numbers 126-136).

Reviewer B:

Comment: Valuable review.
Please check spelling and grammar.

Response: We want to thank reviewer B for their comments. We have gone through the entire manuscript and have corrected spelling and grammar.

Reviewer C:

Comment: This is an excellent review. My only comment relates to English usage. The authors should check that pleural or singular nouns are matched to pleural or singular verbs, and that articles (a, the) are inserted where missing.

Response: We want to thank reviewer C for their comments. We have gone through the entire manuscript and have corrected spelling and grammar.

Reviewer D:

Comment: I congratulate the authors on this well-written review. All three topics are well treated and discussed. I think it will be of use to readers.
In recent years, the possibility of malignancy in transudate fluids has been discussed. Especially in the first group of patients, heart failure, it is not known in which patients with transudate a cytologic examination or pleural biopsy after pleural puncture should be performed. Can the authors give their opinion on this question?

Response: We want to thank Reviewer D for their useful comments. We have added a paragraph to discuss transudative malignant effusions and our opinion on how to approach such a patient (line numbers 155-162).

Reviewer E:
Comment: I appreciate authors' elaborate work of complete review of non-malignant pleural effusion among various group of patients.
There is one thing I would like the authors to add-on. Please mention about ECG characteristics (ubiquitous ST elevation) and unique PEx (friction rub) regarding to post-surgical pleural effusions.

Response: We want to thank Reviewer E for their suggestions. We have added a sentence regarding the above (line numbers 358-360).

Reviewer F:
A very thorough article, the authors are to be commended on their approach and review of available literature. I only have minor comments.
Comment 1: Line 111: Most commonly, patients complain of breathlessness and this may not necessarily correlate with the size of the PE as it is also influenced by concomitant underlying lung and cardiac pathologies.
Consider restructuring this sentence - it is not entirely clear. I would also suggest mentioning the domains of breathlessness in this paragraph.

Response 1: We want to thank Reviewer E for the comment. We have elaborated on the sentence and the domains of breathlessness in HF patients (new line numbers 106-110).

Comment 2: Line 120: However, PEs can be unilateral in the context of CHF and they are often more common on the right side (14).
DO you have a reference to explain the underlying pathology for this phenomenon (I am not aware of a paper that does). If not, suggest mentioning that the pathophysiology behind

right-predominant PEs is unclear.

Response 2: We want to thank Reviewer E for the comment. This phenomenon has been observed in an analysis carried out on a Spanish HF registry. A clear explanation has not been given for the pathophysiology of this phenomenon. We were not able to find any other papers that explained the pathophysiology of this phenomenon (new line numbers 118-119).

Comment 3: Line 122: In certain cases, fluid may collect within the interlobular fissures which simulates a mass that disappear with diuretic treatment and this is known as a "vanishing tumour"(17).
Please restructure this sentence for clarity.

Response 3: We want to thank Reviewer E for the comment. We have restructured this sentence (new line numbers 121-123).

Comment 4: Line 163: The remainder is mislabelled as "exudative" usually by a small difference in the pleural fluid protein and lactate dehydrogenase (LDH) (23).
This sentence does not make sense - suggest you re-phrase eg 'The remainder of effusions are commonly labelled as exudative according to Light's criteria however, due to the nature of their pathogenesis and relatively low protein and LDH values, these could be described as mislabelled.'

Response 4: We want to thank Reviewer E for the comment and suggestion. We have rephrased it as suggested (new line numbers 172-175).

Comment 5: Line 241: First line treatment of PEs secondary to CHF usually needs addressing the underlying disease process with a single agent or a combination of diuretics along with other classes of medication.
Please re-structure this sentence for clarity.

Response 5: We want to thank Reviewer E for the comment. We have rephrased this sentence (new line numbers 242-243).

Comment 6: Line 249: IPCs have shown to be effective in reducing 250 breathlessness, reduce hospitalisation and the number of invasive pleural interventions (mainly therapeutic thoracentesis) when compared to talc pleurodesis in the context of MPE
Citation needed

Response 6: We want to thank Reviewer E for the comment. We have added a reference to this sentence (new line numbers 251-253).

Comment 7: Line 263: Consider mentioning that in this study IPC drainage was not done by healthcare professionals - therefore arguably higher risk of complications especially infection.

Response 7: We want to thank Reviewer E for the comment. We have added a sentence to

explain this. (include line numbers 264-265).

Comment 8: Line 364: various studies have shown the presence of TGF beta and Il-6 in post-cabg effusion PEs. Suggest mentioning these to underline inflammatory nature of effusions following surgical pleural insult.

Response 8: We want to thank Reviewer E for the comment and suggestion. We have added a brief section regarding pro-inflammatory nature of effusions post-CABG (line numbers 367-371).

Comment 9: Line 397: REDUCE 2 is a randomised feasibility study, not an RCT.

Response 9: We want to thank Reviewer E for the comment. We have amended this (new line numbers-400).

Comment 10: Finally, please re-read the article to check for typographical errors. There are some instances of double spacing and missed punctuation.

Response 10: We want to thank reviewer E for their comments. We have gone through the entire manuscript and have corrected spelling, grammar and missed punctuation.