



July 16, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 11700-review.doc).

Title: Positive airway pressure therapy for heart failure

Author: Takao Kato, Shoko Suda, Takatoshi Kasai

Name of Journal: *World Journal of Cardiology*

ESPS Manuscript NO: 11700

The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer

Reponses to the reviewer #00504181

C1: It is important that the chapter on the hemodynamic effects of PAP precedes other chapters, thus explaining the rationale behind using PAP as treatment modality in HF. It would be also interesting to describe the effects of PAP separately for LV and RV dysfunction. This is only briefly attempted in page 9.

R1: We reorder chapters as suggested. We revised some expressions regarding the effects of PAP so that effects of PAP for LV and RV dysfunction can be separately understood.

C2: It would be useful to summarize the clinical trials on PAP in a table.

R2: We agreed with this comment. However, since there are many clinical trials on PAP, it is difficult to summarize them in a table. In addition, the volume of this review will be huge if we add these data as some tables. Therefore, we decided not to add such tables.

C3: Please reduce the number of abbreviations to a minimum, to increase the ease of flow

R3: The number of abbreviations was reduced in the revised manuscript.

C4: Page 11, please delete the sentence 'Finally, intermittent hypoxia and post-apneic reoxygenation cause vascular endothelial damage and possibly atherosclerosis, leading to coronary artery disease and HF due to ischemic cardiomyopathy'. There is no firm evidence to support such a statement.

R4: We eliminated this sentence.

C5: The sentence: 'Since we focused on less-invasive approaches for the care of HF, this review discusses PAP therapy as therapy with any form of non-invasive positive pressure ventilation (NPPV), including continuous positive airway pressure (CPAP), in which PAP is applied without an endotracheal intubation or tracheostomy but through nasal, oro-nasal and face masks.' needs rephrasing to improve clarity.

R5: We revised this sentence.

C6: Please change 'provide relief of cardiac loads' to 'decrease right ventricular afterload'. Similarly, in page 4, change 'cardiac preload' to 'left ventricular preload'.

R6: We revised as suggested.

C7: Please change the phrase '... pressure in entire respiratory cycle' to '.. pressure during the entire

respiratory cycle’.

R7: We revised as suggested.

C8: Page 7, typographical error: ‘efficacy of and’, please delete ‘of and’.

R8: We revised as suggested.

C9: Page 9, please delete cardiac arrest from the list of contraindications for PAP therapy.

R9: We revised as suggested.

C10: Page 13, please change ‘Those’ to ‘These’.

R10: We revised as suggested.

C11: Page 15, typographical error: ‘may also benefits’, should be ‘may also benefit’.

R11: We revised as suggested.

C12: Page 16, typographical error: ‘can suffered’, please change to ‘suffer’.

R12: We revised as suggested.

C13: Page 16, typographical error: ‘who only required’, please change to ‘who only require’.

R13: We revised as suggested.

Reponses to the reviewer #608278

C13: Generally, an excellent reviewer article was often from a well-respected group in the related field. The authors published few OSA papers.

R13: Corresponding author published at least 15 original articles and 4 review articles regarding PAP therapy. Some of them had cited as references. This reviewer miss something or did not search appropriately.

C14: Unfortunately the paper is poorly written, has logic gaps and is confusing and difficult to follow and catch the meaning of whole text and each paragraph.

R14: Considering other reviewers’ positive comments, this comment may be biased. Nevertheless, we revised and reorganized this manuscript extensively.

C15: Acute decompensate heart failure (ADHF) as a key word has been pointed out. However, most information was related to the chronic heart failure (CHF) than to ADHF. The authors can change to HF or CHF. In addition, the authors have mixed to describe the PAP therapies in ADHF and CHF. This reviewer strongly recommend the authors to separate do them.

R15: We changed ADHF to HF in the keywords. In addition, we also changed some “HF” to “chronic HF” in the text, as appropriate.

C16: Make certain that all background information is in the build the rationale for your review. And the author stated that “we also review the indications, recommendations, and evidence supporting the efficacy therapy in patients with HF”. Where are the recommendations? It is essential to summarize the efficacy and safety and limitation for each PAP therapy or/and its model as one or two tables. It will help our readers to flow and understand what the authors said and guide our clinician to treat HF patients with OSA or CSA.

R16: We eliminated “recommendations” from that sentence. We added two tables to summarize equipped functions of each type/mode of PAP and possible indication for each condition.

C17: The section of Types/models of PAP in HF treatment is rather broad like machine instruction and can be condensed. The authors may consider to strengthen and restructure main text in order (separate clearly CHF and ADHF).

R17: We reorganized our manuscript and reordered chapters, as suggested.

Reponses to the reviewer #2446337

C18: The current epidemiology of CV disease (Epidemiology of Cardiovascular Disease in the 21st Century: Updated Numbers and Updated Facts. JCVd 2013;1:1-2) should be mentioned in the intro.

R18: We added this as one of the references in the introduction section.

C19: The following reports should be included: Schaffernocker T, Morrison J. and Khayat RN. Central Sleep Apnea: From Pathophysiology To Clinical Management. JCVd 2014;32-38. Clin Cardiol. 2014 Jan;37(1):57-65.

R19: We added these in the reference list.

C20: A mention to the importance of physical activity and beta adrenergic system in HF (Front Physiol. 2013 Aug 12;4:209) should be provided.

R20: We add this in the reference list.

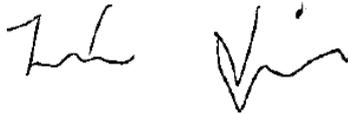
C21: Equally important, the potential functional role of the cardio-adrenal axis (Hypertension. 2014 Feb;63(2):215-6) should be briefly discussed.

R21: This is not relevant topic to our review. Thus, it is difficult to discuss this in our manuscript.

3 References and typesetting were corrected

Thank you again for publishing our manuscript in the *World Journal of Cardiology*.

Sincerely yours,

Handwritten signature of Takatoshi Kasai, consisting of two distinct cursive marks.

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