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**To:** Editor, World Journal of Clinical Cases

**Re:** Manuscript ID: **72089**

**“Paradoxical carbon dioxide embolism during laparoscopic hepatectomy without intracardiac shunt: A case report”**

Dear Editor,

This letter is intended for the revision of the manuscript according to your request. First of all, we would like to appreciate editorial suggestions and assessors' comments. We corrected the manuscript according to the assessors' comments.

We included a cover letter responding to assessor and detailing all changes and corrections we've done. Again, we would like to appreciate your suggestions and assessors' comments. I believe that this revised manuscript is highly likely to achieve the priority for publication in World Journal of Clinical Cases. I am looking forward to your early and favorable response.

Sincerely,

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## **Responses to Assessors' Comments**

We appreciate your excellent advice. We have added content based on your comments.

### **• Reviewer #1:**

It would be also interesting to discuss other risk factors for CO<sub>2</sub> embolism; if there are any situations where you recommend to do TEE pre-insertion; and the importance of dedicated and well trained teams in this type of complex surgery.

### **Answer)**

1) For “discuss other risk factors for CO<sub>2</sub> embolism”, we added common risk factors for CO<sub>2</sub> embolism that may occur during laparoscopic surgery with references.

#### **Details are as follows (Page 9, line 3):**

CO<sub>2</sub> embolism is mainly caused by incorrect insertion of a Veress needle, and surgical sites with many venous channels or the generation of pressure gradients for gas entry into circulation also increase the risk of CO<sub>2</sub> embolism during laparoscopic surgery [7]. Particularly, the risk may increase in patients with primary biliary cirrhosis by upregulated angiogenesis or with unanticipated anatomical variations such as patent paraumbilical veins [8,9].

#### **Referenced by:**

7. de Jong KIF, de Leeuw PW. Venous carbon dioxide embolism during laparoscopic cholecystectomy a literature review. Eur J Intern Med 2019;60:9–12 [PMID: 30352722 DOI: 10.1016/j.ejim.2018.10.008]

8. Cadis AS, Velasquez CD, Brauer M, Hoak B. Intraoperative management of a carbon dioxide embolus in the setting of laparoscopic cholecystectomy for a patient with primary biliary cirrhosis: A case report. Int J Surg Case Rep. 2014;5:833–5 [PMID: 25462045 DOI: 10.1016/j.ijscr.2014.09.002]

9. Mattei P, Tyler DC. Carbon dioxide embolism during laparoscopic cholecystectomy due to a patent paraumbilical vein. J Pediatr Surg 2007;42:570–2 [PMID: 17336203 DOI: 10.1016/j.jpedsurg.2006.10.051]

2) For “any situations where we recommend doing TEE pre-insertion”, we think it would be good to do TEE pre-insertion when the possibility of fatal CO<sub>2</sub> embolism is high, though we could not find a direct reference.

**Details are as follows (Page 12, line2):**

Therefore, if CO<sub>2</sub> embolism is suspected or if it is necessary to differentiate it from other causes, we recommend quick identification using TEE. Kim et al. described that although most venous air embolism is asymptomatic, caution is needed because fatal air embolism can occur in patients with cardiopulmonary disease or intracardiac shunt [22]. Therefore, pre-insertion of TEE may be helpful for these patients.

**Referenced by:**

22. Kim CS, Kim JY, Kwon JY, Choi SH, Na S, An J, Kim KJ. Venous air embolism during total laparoscopic hysterectomy: comparison to total abdominal hysterectomy. *Anesthesiology* 2009;111:50-54 [PMID: 19512874 DOI: 10.1097/ALN.0b013e3181a05ac7]

3) For “the importance of dedicated and well-trained teams in this type of complex surgery”, we totally agree with your opinion. We have revised our manuscript to reflect your views.

**Details are as follows (Page 12, Line 18):**

Although the Trendelenburg position is helpful, the position was not changed to ensure optimal viewing of the surgical field during laparoscopic repair in this case. Therefore, communication with the surgeon is essential for such a complex surgery, and a dedicated and well-trained team is important.

● **Reviewer #2:**

The agitated saline test may be helpful in differentiating the intracardiac or extracardiac causes resulting in the paradoxical embolism. The emergence of the left side gas bubbles after over 5 heart-beats indicates the existence of the abnormal communication of pulmonary arterioles and venous.

**Answer)**

Thank you for your valuable feedback. Our manuscript has been revised as follows:

**Details are as follows (Page 10, Line 28):**

The existence of communication of pulmonary arterioles and venous cannot be completely excluded in this patient. For confirmation, the agitated saline test may be helpful. If the left side gas bubble appears after 3 to 8 heartbeats, the existence of the abnormal communication of pulmonary arterioles and venous may be suspected [20]. However, considering the improvement of symptoms after repairing damaged blood vessels, we presumed that the overflow of a large amount of venous gas bubbles entering the damaged blood vessel was the main mechanism.

**Referenced by:**

20. Saboo SS, Chamarthy M, Bhalla S, Park H, Sutphin P, Kay F, Battaile J, Kalva SP. Pulmonary arteriovenous malformations: diagnosis. *Cardiovasc Diagn Ther* 2018;8:325–37 [PMID: 30057879 DOI: 10.21037/cdt.2018.06.01]