

PEER-REVIEW REPORT

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Title: Asymptomatic carbon dioxide embolism during transoral vestibular thyroidectomy: A case report and literature review

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Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

General comments: 1. This manuscript describes a single case of presumed carbon dioxide embolus (CDE) associated with carbon dioxide insufflation during endoscopic thyroidectomy. The manuscript has value in that it introduces a new clinical concept to anesthesiologists and surgeons who might be unaware of this possible condition. 2. The incidence of CDE is unknown with this surgical procedure, and the authors miss a great opportunity to inform readers how this might be quantified, and how the risk of CDE affects the risk-to-benefit profile of endoscopic thyroidectomy. I have discussed this further in the Specific Comments to the authors. 3. The Discussion is strikingly similar to an editorial published by Lanier and Warner on CDE in another form of endoscopic surgery. The authors should acknowledge that editorial and its relationship to the current report. 4. The manuscript, particularly the Discussion, is excessively long, and the concepts in the Introduction and Discussion repeat themselves. This needs to be tidied up. 5. The authors tend to “cherry pick” the literature in their discussion. On one hand, they get into the implications of one form of anesthesia versus another, the use of intravascular and positive end-expiratory airway pressure (presumably to increase central venous pressure), which are probably not that important...as I will explain to the Specific Comments. However, they miss an opportunity better describe detection of CDE and differentiate it from similar clinical scenarios. 6. In reality, this manuscript has two portions of original data. The authors place the second part within the Discussion. This needs to be moved out to a separate Methods and Results section. 7. I am a bit surprised that the authors were able to hear both systolic and diastolic murmurs when the patient’s hemodynamics appeared to be unaltered. 8. I think the authors could do a better job of introducing the importance of pressor drugs and applying the concepts of The American Heart Association’s guidelines for advanced cardiac life support if



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there is a catastrophic carbon dioxide embolus. Specific comments: P 1, LM 16, and P 6, LM 13-15: As discussed by Lanier and Warner, gas embolus during endoscopic surgery does not require an identified (or even identifiable) venous injury. P 1, LM 26-27, and P 9, LM 15-17: Given the minimal effects of one anesthetic versus another on blood flow distribution within the body, I seriously doubt that one anesthetic technique versus another is going to affect outcomes during carbon dioxide embolus. To my way of thinking, the predominant factors in dictating outcomes are the volume and rate of gas entered into the circulation, not what anesthetic was present when that occurred. Focusing on anesthetic technique would, in my opinion, lead to a false sense of security. P 2, LM 20: Consider rewording the colloquial “game changer.” P 3, LM 17: Wouldn’t “chest roentgenogram” be preferable to “chest X-ray”? P 3, LM 28: This passage makes it sound like the frenulum is a part of the lower lip. Please reword the passage for clarity, and stick to anatomic terms (eg, superior, inferior, anterior, etc.), not “above,” which will change as the patient’s position changes. P 4, LM 1: Replace “normal saline” with “0.9% saline solution.” P 4, LM 2: Place a comma before “was,” for clarity. P 4, LM 21: The time course of the return of ETCO₂ is interesting. P 5, LM 9-10 and beyond: Inasmuch as most of the concepts within the Discussion are not unique to endoscopic thyroid surgery, I suggest that the authors give consideration to beginning their Discussion with a passage such as this: “Endoscopic surgical techniques, including those that involve insufflation of the tissues with carbon dioxide, are gaining wider acceptance and use worldwide. These advances have introduced the possibility of carbon dioxide embolus (including life-threatening embolus). Such factors introduce challenges in preventing, diagnosing, and treating carbon dioxide embolus, and determining how the risk of embolus affects the risk-to-benefit profile of any new surgical procedure. These issues have recently been reviewed by Lanier and Warner, as related to colorectal surgery. We will discuss some of these same issues as

they apply to endoscopic thyroid surgery.” (The reference mentioned is: (See: Lanier WL, Warner MA. Assessing acceptable risk in new surgical procedures, with special reference to gas emboli in transanal total mesorectal surgery. Dis Colon Rectum. 62:777-780, 2019.) P 6, LM 14: “Veres needles” is an arcane term. Can you use more universally understood terminology? P 6, LM 23-P 7, LM 1: This information appears to be repeated elsewhere in the manuscript. P 7, LM 7 to P 8, LM 14: Here, the authors are describing a separate study. This information should be included in a Methods section (P 7, LM 7 to LM 20) and a Results section (P 7, LM 20 onward). The latter portions of this second segment might even belong in the Discussion regarding discussing the new Methods and Results. P 8, LM 9-10: Please distinguish between the Trendelenburg and left lateral decubitus positions. As such, this word “Trendelenburg” is misplaced. Additionally, please discuss what you hope to achieve by the left lateral decubitus position with the head down. You only mention the head-down portion in your original report. P 8, LM 20-23: I simply find it difficult to believe that this concept has been proven using a sound study design and adequate statistical power. I could be wrong, but I’d still recommend deleting this from the Discussion. P 8, LM 28-P 9, LM 1: The concept of applying positive end-expiratory pressure and expanding intravenous volume, relates to a tired, and largely erroneous, concept that it is possible to increase venous pressure and prevent further embolus. Such a concept ignores the fact that increases in intrathoracic pressure and central venous pressure are somewhat ineffective in altering extrathoracic venous pressures. Further, these concepts ignore the Venturi effect and other mechanisms by which gasses can enter the venous system by methods other than arithmetic changes in central venous pressure. For further discussion, the authors should see both the Lanier and Warner editorial referenced above, as well as this article: Lanier WL, Albrecht RF II, Iaizzo PA: Divergence of intracranial and central venous pressures in lightly anesthetized,

tracheally intubated dogs that move in response to a noxious stimulus. Anesthesiology 84:605-613, 1996. P 9, LM 5: Change “inhaling” to “aspirating.” Figure 2: This figure needs a better legend to describe the two parts and arrows to identify key anatomic features. Otherwise, it is difficult to determine what is going on in the first part of the figure. For the first couple of readings, I thought I was looking a surgeon’s glove, not the patient’s chin and neck. Table1: “Age” should have units of measurement. Expand to “Reduce INSUFFLATION pressure,” “precordial Doppler SONOGRAPHY,” and “Aggressive INTRAVENOUS volume expansion.”