Vagus nerve stimulation in postoperative thoracic surgery: the obstacle is the path

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Comment on: Carvalho EA, Terra RM, Pinheiro Campos AC, *et al.* Vagal electrostimulation in postoperative thoracic surgery reduces the systemic inflammatory response and cardiopulmonary complications: an experimental study in pigs. Ann Transl Med 2023;11:347.

Keywords: Vagus nerve stimulation (VNS); postoperative inflammation; thoracic surgery

Submitted Oct 09, 2023. Accepted for publication Oct 19, 2023. Published online Oct 30, 2023.
doi: 10.21037/atm-23-1889
View this article at: https://dx.doi.org/10.21037/atm-23-1889

In the realm of surgical innovation, the quest to minimize complications and improve patient outcomes is an ongoing and challenging journey. The evolution from conventional thoracotomy (CT) to minimally invasive techniques, including robotic surgery (RS), has propelled the field of cardiothoracic surgery forward, but novel approaches beyond surgical techniques hold the potential to further revolutionize clinical practice. Notably, systemic inflammation, measured with C-reactive protein (CRP) and interleukin (IL)-6, has been shown to be crucial in the pathogenesis of postoperative complications (1).

Vagus nerve stimulation (VNS), an innovative therapeutic technique involving electrical stimulation of the vagus nerve, has captured the medical community's attention due to its ability to modulate various human body functions. The vagus nerve, a critical component of the parasympathetic nervous system, plays a pivotal role in regulating cardiac, pulmonary, and gastrointestinal functions, and even inflammation (2). By harnessing the power of VNS, we unlock a promising avenue for addressing a spectrum of conditions, including—but limited to—epilepsy, depression, and inflammatory disorders. As the landscape of VNS research continues to unfold, it holds the potential to revolutionize the way we approach and manage a variety of medical conditions.

The recent study by Carvalho *et al.* (3) sheds light on VNS in the context of postoperative inflammatory responses following thoracic surgery. This preclinical study explores the use of VNS to reduce the systemic inflammatory response syndrome (SIRS) and clinical complications associated with CT and RS in a pig model which is comparable to human physiology, histology, and immune response (4).

Their results indicate that VNS led to a more stable heart rate during the postoperative period and reduced cardiac complications, making it a potential non-pharmacological tool for mitigating the inflammatory response and complications, particularly in aggressive surgical procedures. While applauding the authors' dedication to advancing surgical outcomes, several key points deserve further discussion and clarification.

The application of VNS in the reduction of proinflammatory cytokines like IL-6 levels after thoracic surgery is attractive. However, human studies have already established the potential of autonomic neuromodulation, including VNS, in reducing IL-6 levels post-cardiac surgery (5). Therefore, it is of utmost clinical significance to explore the effect of VNS on clinical outcomes beyond surrogate inflammatory biomarkers and physiological responses. Clinical endpoints, such as the incidence of postoperative atrial fibrillation, infection rates, recovery duration, and mortality rates are essential for assessing the translational potential of this approach in

clinical practice.

Furthermore, the invasive nature of mediastinal VNS, involving electrode implantation, raises concerns about its impact on surgery duration and potential complications, such as vascular and neurological injuries (6). These considerations may outweigh the perceived benefits of VNS in the postoperative period. Exploring less invasive alternatives, like transcutaneous auricular VNS, which has yet to prove equivalent to cervical or mediastinal VNS, might hold promise. Moreover, the authors found that the pigs that have undergone CT benefited the most from the VNS. As CT has been to a significant extent replaced by minimally invasive approaches, the applicability of mediastinal VNS in routine thoracic surgery becomes less feasible and practical, warranting the exploration of alternative methods, including but not limited to noninvasive VNS.

Last, although this study's findings demonstrated a reduction in the postoperative inflammatory response, it's worth noting that the study did not delve into the underlying mechanisms responsible for this anti-inflammatory effect. Overall, prior work has described the action of VNS via the anti-inflammatory pathway at the spleen, further mechanistic studies within the specific context of postoperative thoracic surgery are essential. Specific aspects of postoperative complications such as postoperative atrial fibrillation have been recently elucidated, and these could serve as the basis for future work on this condition (6).

In conclusion, the investigation into VNS as a means to mitigate postoperative inflammatory responses in thoracic surgery is a commendable endeavor. However, a comprehensive approach that incorporates existing knowledge, delves into mechanistic insights, prioritizes clinical outcomes, and elucidates the feasibility of VNS in practical surgical settings will enhance the impact and relevance of this research. Addressing these key points will undoubtedly bolster the advancement of surgical techniques and, most importantly, enhance the well-being of patients undergoing thoracic surgery.

Acknowledgments

Funding: None.

Footnote

Provenance and Peer Review: This article was commissioned by the editorial office, *Annals of Translational Medicine*. The article did not undergo external peer review.

Conflicts of Interest: The author has completed the ICMJE uniform disclosure form (available at https://atm.amegroups.com/article/view/10.21037/atm-23-1889/coif). The author has no conflicts of interest to declare.

Ethical Statement: The author is accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Cite this article as: Zafeiropoulos S. Vagus nerve stimulation in postoperative thoracic surgery: the obstacle is the path. Ann Transl Med 2023;11(12):406. doi: 10.21037/atm-23-1889