Intraoperative Ventilation Strategies to Reduce Pulmonary Complications in Obese Patients - Reply

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Published in:
JAMA

DOI:
10.1001/jama.2019.14400

Published: 01/01/2019

Document Version
Publisher's PDF, also known as Version of record

Citation for pulished version (APA):
Gama de Abreu, M., Schultz, M., & Pelosi, P. (2019). Intraoperative Ventilation Strategies to Reduce Pulmonary Complications in Obese Patients - Reply. *JAMA*, *322*(18), 1828-1829. https://doi.org/10.1001/jama.2019.14400

relations, suggesting various possible motivations. There is nothing to attest to the veracity of the statement.

The letter writers conclude that the records should be released to the study participants "not in the year 2065…but today." In fact, any participant can access records pertaining to their own information by contacting the Jewish Board. The year 2065 pertains only to the public, not the study participants.

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Conflict of Interest Disclosures: None reported.

1. Perlman L. How about the twins who were separated and not studied? Comment on "Three identical strangers and the twinning reaction—clarifying history and lessons for today from Peter Neubauer's twins study." Posted July 19, 2019. https://jamanetwork.com/journals/jama/article-abstract/2737146. Accessed August 10, 2019.

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Intraoperative Ventilation Strategies to Reduce Pulmonary Complications in Obese Patients

To the Editor The Protective Intraoperative Ventilation With Higher Versus Lower Levels of Positive End-Expiratory Pressure in Obese Patients (PROBESE) trial compared intraoperative ventilation strategies using a low level of positive end-expiratory pressure (PEEP) (4 cm H_2O) or a high level of PEEP (12 cm H_2O) plus repeated recruitment maneuvers in obese patients.[1] No difference in the primary outcome, a composite of postoperative pulmonary complications, was found. Several reasons may explain this unexpected result.

First, as in previous trials,[2,3] the main hypothesis was based on the assumption that most patients develop anesthesia-induced atelectasis. However, this assumption could be questioned, especially when preventive measures, such as the use of continuous positive airway pressure during induction, are applied. Second, in patients who developed atelectasis, the proposed pragmatic strategies of recruitment maneuvers and 2 arbitrary levels of PEEP lack pathophysiological support.

Third, the open-lung inspiratory pressures reached were not measured, which makes the protocol difficult to reproduce. Previous studies evaluating individualized PEEP titration in obese patients found consistently higher PEEP levels than the arbitrary PEEP level of 12 cm H_2O.[4,5] However, when lungs are not efficiently recruited, a PEEP level of 12 cm H_2O could be excessive. Importantly, previous studies have shown that individualized PEEP contributes to reduce postoperative pulmonary complications.[3]

Fourth, the use of postoperative interventions, such as noninvasive ventilation, was not mentioned. This could be relevant to the observed lack of prevention for postoperative pulmonary complications because the benefits of an open-lung strategy are immediately lost after extubation in obese patients.[5]

Fifth, the incidence of the composite outcome was less than expected and previously reported.[2,3] Of concern is that most of the complications required the use of chest radiography for diagnosis. However, according to the protocol this was an optional diagnostic test, and it is not known how many patients underwent chest radiography. This may have led to underdiagnosis of the main outcome.

A pragmatic study is appealing because it provides easy-to-implement therapeutic rules. It may, however, oversimplify medical decision-making, failing to appropriately guide interventions in complex patients. We believe that in future studies of open-lung strategies, the following steps need to be taken: first, diagnose the presence of lung collapse and assess the ability to recruit; second, individualize both the recruitment maneuver and the selection level of PEEP; and third, reassess patients to confirm that the desired condition has been reached and is maintained over time. A study testing an intervention whose success depends on reaching a defined physiological condition should ensure that enrolled patients have a measurable response that confirms or rules out that condition.

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Conflict of Interest Disclosures: Dr Ferrando reported receiving nonfinancial support from Getinge and a grant from Air-Liquide. Dr Tusman reported receiving nonfinancial support from Getinge. Dr Suarez-Sipmann reported receiving personal fees and nonfinancial support from Getinge.

1. Bluth T, Serpa Neto A, Schultz MJ, Pelosi P, Gama de Abreu M; Writing Committee for the PROBESE Collaborative Group of the PROtective VEntilation Network (PROVEnet) for the Clinical Trial Network of the European Society of Anaesthesiology. Effect of intraoperative high positive end-expiratory pressure (PEEP) with recruitment maneuvers vs low PEEP on postoperative pulmonary complications in obese patients: a randomized clinical trial. *JAMA*. 2019;321(23):2292-2305. doi:10.1001/jama.2019.7505

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In Reply Dr Ferrando and colleagues raise a number of concerns about the PROBESE trial.[1] General anesthesia induces atelectasis in the vast majority of patients (>90%), especially morbidly obese patients.[2] The recruitment maneuver used in the study does not lack pathophysiological support. Atelectasis is reversible to different extents, depending on the level of pressure at end of inspiration and the time spent at that pressure.[3] These factors were considered when defining the target inspiratory pressure of 40 to 50 cm H_2O and the cumulative time (>9 seconds). Driving pressure increased over time in the low PEEP group, indicating that atelectasis did develop. Importantly, driving pressure was approximately 6 cm H_2O lower in the high PEEP group, supporting the effectiveness of the recruitment maneuver.

The choice of a PEEP level of 12 cm H_2O was based on the literature[4] and aimed at limiting hemodynamic impairment. PEEP always represents a compromise between atelectasis and overdistension: higher levels result in less atelectasis but also more overdistension, whereas lower levels lead to less overdistension and more atelectasis. Ferrando and colleagues claim that individual PEEP titration with postoperative positive airway pressure reduced postoperative pulmonary complications in a recent trial,[5] but that study was not powered for this conclusion. In fact, that study rejected the hypothesis that an individualized high level of PEEP reduces postoperative complications.

In our trial, postoperative noninvasive ventilation was not part of the intervention because the goal was to determine the value of intraoperative PEEP while avoiding confounders. We disagree that the optional use of chest radiography could have resulted in a low incidence of postoperative pulmonary complications being detected. The observed incidence (>20%) is not low and was within the range predicted.[6] Importantly, the use of diagnostic tools in the study did not differ from that in the validation of the scoring tool itself.[6]

In our opinion, pragmatic studies are more than appealing—they are likely the best alternative to address clinically relevant questions conclusively. An intervention that is effective only under totally controlled conditions, or in experts' hands, may be physiologically attractive but will not gain clinical acceptance. The lack of effectiveness of those interventions should not be mistakenly attributed to pragmatism of trials that test them, but rather to incomplete consideration of pathophysiology, overlooking complex interactions, and neglecting the short-lived nature of possible effects. The PROBESE study included several elements of a conclusive study, namely: (1) selection of a population able to benefit from the intervention (individualization); (2) addressing a single, nonbundled intervention (isolation of the intervention); (3) appropriate separation between intervention groups (minimization of overlap); (4) testing under routine clinical conditions in different geographic regions (clinical generalizability); and (5) appropriate statistical power to respond to the original question (comprehensiveness).

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Marcus Schultz, MD, PhD
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on behalf of the Writing Committee for the PROBESE Collaborative Group

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Conflict of Interest Disclosures: Dr Gama de Abreu reported receiving grants from the European Society of Anaesthesiology and Dräger Medical and personal fees from Dräger Medical, GlaxoSmithKline, Ambu, and GE Healthcare. No other disclosures were reported.

1. Bluth T, Serpa Neto A, Schultz MJ, Pelosi P, Gama de Abreu M; Writing Committee for the PROBESE Collaborative Group of the PROtective VEntilation Network (PROVEnet) for the Clinical Trial Network of the European Society of Anaesthesiology. Effect of intraoperative high positive end-expiratory pressure (PEEP) with recruitment maneuvers vs low PEEP on postoperative pulmonary complications in obese patients: a randomized clinical trial. *JAMA*. 2019;321(23):2292-2305. doi:10.1001/jama.2019.7505

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CORRECTION

Incorrect and Omitted Names for Collaborators: In the Original Investigation entitled "Effect of Intraoperative High Positive End-Expiratory Pressure (PEEP) With Recruitment Maneuvers vs Low PEEP on Postoperative Pulmonary Complications in Obese Patients: A Randomized Clinical Trial"[1] published in the June 18, 2019, issue of *JAMA*, some of the names for the collaborators were incorrect or missing. At the end of the article, under "**PROBESE Collaborative Group:** *Steering Committee:*," "Gilda Cinella" should be added and the following names should be corrected: "Markus W. Hollmann, Marc-Joseph Licker, and Gary H. Mills." Under "*PROBESE Investigators:*," the following names should be added: "Ilona Bobek, Sorin J. Brull, Cesare Gregoretti, Göran Hedenstierna, Michael Hiesmayr, Samir Jaber, Archer K. Martin, Gary H. Mills, Jan Paul Mulier, Jon D. Samuels, Jochen Schmitt, and Ary Serpa Neto"; the following names should be corrected: "Cornelius Johannes Busch, Giovanni Camerini, and Jaume C. Canet"; and the following names should be removed: "William Crovetto and Eduardo Scharffenberg." In Supplement 4, under "1.5 PROBESE investigators," the names and affiliations for the following investigators were added or corrected: Brull, Sorin J (Department of Anesthesiology and Perioperative Medicine, College of Medicine, Mayo Clinic Jacksonville, FL, USA); Cinella, Gilda (Department of Anesthesiology and Intensive Care Medicine, University of Foggia, Italy); Machado, Humberto S.* (Serviço de Anestesiologia, Centro Hospitalar do Porto, Porto, Portugal and Instituto Ciências Biomédicas Abel Salazar, Universidade do Porto, Porto, Portugal and Centro de Investigação Clínica em Anestesiologia, Serviço de Anestesiologia, Centro Hospitalar do Porto, Porto, Portugal); Martin, Archer K. (Department of Anesthesiology and Perioperative Medicine, College of Medicine, Mayo Clinic Jacksonville, FL, USA); Nunes, Catarina S. (Universidade Aberta, Departamento de Ciências e Tecnologia, Porto, Portugal and Centro de Investigação Clínica em Anestesiologia, Serviço de Anestesiologia, Centro Hospitalar do Porto, Porto, Portugal); Samuels, Jon D. (Weill Cornell Medicine, Department of Anesthesiology, New York-Presbyterian