References

1. Zhu B, Zhang L. Dexmedetomidine sedation and airway collapsibility: Comment. Anesthesiology 2020; 132:1609
2. Lodenius Å, Maddison KJ, Lawther BK, Scheinin M, Eriksson LI, Eastwood PR, Hillman DR, Fagerlund MJ, Walsh JH: Upper airway collapsibility during dexmedetomidine and propofol sedation in healthy volunteers: A nonblinded randomized crossover study. Anesthesiology 2019; 131:962–73

(Accepted for publication February 25, 2020. Published online first on March 27, 2020.)

Lung-protective Ventilation in Cardiac Surgery: Comment

To the Editor:

We read with great interest the article "Intraoperative Mechanical Ventilation and Postoperative Pulmonary Complications after Cardiac Surgery" by Mathis *et al.*[1] We appreciate the authors' great work. The lung-protection ventilation bundle and its component of driving pressure have a strong correlation with the decrease of postoperative pulmonary complications, but several concerns remain.

First, the definition of postoperative pulmonary complications does reduce the comparability between studies. A recent consensus, cited also by this article, points out that considering the common pathologic pathway, perioperative pulmonary complications should include atelectasis, pneumonia, acute respiratory distress syndrome, and aspiration pneumonia,[2] these indicators are easy to achieve in clinical practice, especially in cardiac surgery with a higher monitoring level. Some of the indicators selected by the authors, including reintubation and prolonged initial postoperative ventilator duration longer than 24 h, might be partially attributed to the patient's circular instability and consciousness disorder, not just the pulmonary complications themselves. Moreover, these endpoints are somewhat like the consensus definition of respiratory failure under mechanical ventilation, a more serious condition requiring respiratory support[2]; it is conceivable that the actual incidence of postoperative pulmonary complications may be underestimated. Different definitions may lead to different results, the inconsistency of endpoint criteria might be solved by further sensitivity analysis.

Second, the cut-off point selection of the lung-protective ventilation bundle and its components is empirical and selective in this article, this may lead to a nonoptimal clinical choice. Moreover, nonsignificant statistical relationship of tidal volume less than 8 ml/kg (according to predicted body weight) and positive end-expiratory pressure (PEEP) greater than or equal to 5 cm H_2O with occurrence of postoperative pulmonary complications may also be attributed to the hasty choice. It might be more appropriate to conduct an exploratory study to analyze the lung-protective ventilation components and the optimal combination in the first step; a previous study showing a PEEP of 5 cm H_2O and median plateau pressure of 16 cm H_2O or less was associated with the lowest risk of postoperative respiratory complications.[3]

Third, according to this article, the probability of postoperative pulmonary complications is higher at both poles of body mass index (BMI) classes (underweight and high-class obesity), and the distribution of pulmonary complications with BMI was unlikely to be linear, but rather binomial, distribution. This may be explained by the accompaniment of malnutrition with being underweight and with severe obesity being prone to atelectasis—both classes are associated with increasing postoperative pulmonary complications.[4,5] Additionally, BMI is associated with increasing intraabdominal pressure and decreasing pulmonary compliance.[5] For example, driving pressure is more difficult to maintain at 16 cm H_2O in severe obesity compared to a normal BMI with the same tidal volume and PEEP. This may lead to a bias in the distribution of protective ventilation across different BMI ranges. Eventually, the interpretation of regression results might be affected by the aforementioned factors. Moreover, in a recent study, airway closure happens with an impressive incidence in patients with obesity, lead to an overestimation of driving transpulmonary pressure.[6] This complicates the interpretation of the findings in patients with obesity. However, in the subgroup analysis, the lung-protective ventilation bundle showed the same protective effect at all BMI levels, alleviating the aforementioned considerations to some extent.

Competing Interests

The authors declare no competing interests.

Zongyang Qu, M.D., Hongye Zhang, M.D., Shuzhen Zhou, M.D. Beijing Hospital, National Center of Gerontology, Beijing, China. qzyqzy007@sina.com

DOI: 10.1097/ALN.0000000000003292

References

1. Mathis MR, Duggal NM, Likosky DS, Haft JW, Douville NJ, Vaughn MT, Maile MD, Blank RS, Colquhoun

DA, Strobel RJ, Janda AM, Zhang M, Kheterpal S, Engoren MC: Intraoperative mechanical ventilation and postoperative pulmonary complications after cardiac surgery. Anesthesiology 2019; 131:1046–62
2. Abbott TEF, Fowler AJ, Pelosi P, Gama de Abreu M, Møller AM, Canet J, Creagh-Brown B, Mythen M, Gin T, Lalu MM, Futier E, Grocott MP, Schultz MJ, Pearse RM; StEP-COMPAC Group: A systematic review and consensus definitions for standardised end-points in perioperative medicine: Pulmonary complications. Br J Anaesth 2018; 120:1066–79
3. Ladha K, Vidal Melo MF, McLean DJ, Wanderer JP, Grabitz SD, Kurth T, Eikermann M: Intraoperative protective mechanical ventilation and risk of postoperative respiratory complications: Hospital based registry study. BMJ 2015; 351:h3646
4. Lawrence VA, Cornell JE, Smetana GW; American College of Physicians: Strategies to reduce postoperative pulmonary complications after noncardiothoracic surgery: Systematic review for the American College of Physicians. Ann Intern Med 2006; 144:596–608
5. Hedenstierna G, Tokics L, Scaramuzzo G, Rothen HU, Edmark L, Öhrvik J: Oxygenation impairment during anesthesia: Influence of age and body weight. Anesthesiology 2019; 131:46–57
6. Grieco DL, Anzellotti GM, Russo A, Bongiovanni F, Costantini B, D'Indinosante M, Varone F, Cavallaro F, Tortorella L, Polidori L, Romanò B, Gallotta V, Dell'Anna AM, Sollazzi L, Scambia G, Conti G, Antonelli M: Airway closure during surgical pneumoperitoneum in obese patients. Anesthesiology 2019; 131:58–73

(Accepted for publication October 4, 2019. Published online first on April 10, 2020.)

Lung-protective Ventilation in Cardiac Surgery: Comment

To the Editor:

The recently published article by Mathis *et al.*[1] showed that the use of an intraoperative lung protective ventilation bundle is associated with a lower rate of postoperative pulmonary complications, but when each strategy of the bundle was individually analyzed, only lower modified driving pressure was coincident with this result. Furthermore, the use of median positive end-expiratory pressure (PEEP) greater than or equal to 5 cm H_2O had an adjusted odds ratio (95% CIs) greater than 1 (1.18, 0.91 to 1.53). What does this mean? Is the use of this level of PEEP hazardous for our patients? It eventually could be. Optimal PEEP during surgery widely vary among patients and its individualization improves postoperative respiratory outcomes.[2] High PEEP could cause hyperdistention of lung units leading to pulmonary complications, but low PEEP could induce collapse of them resulting in the same undesirable effect. Although the study was not designed to, it certainly highlights the fact that PEEP isn't innocuous. Individual PEEP titration is not a standardized practice in the operation room and until we find out how to solve this, we should be prudent when setting PEEP.

Competing Interests

The author declares no competing interests.

Hugo Gil, M.D., San Sebastián University, Puerto Montt, Chile. hugo.gil.m@gmail.com.

DOI: 10.1097/ALN.0000000000003293

References

1. Mathis MR, Duggal NM, Likosky DS, Haft JW, Douville NJ, Vaughn MT, Maile MD, Blank RS, Colquhoun DA, Strobel RJ, Janda AM, Zhang M, Kheterpal S, Engoren MC: Intraoperative mechanical ventilation and postoperative pulmonary complications after cardiac surgery. Anesthesiology 2019; 131:1046–62
2. Pereira SM, Tucci MR, Morais CCA, Simões CM, Tonelotto BFF, Pompeo MS, Kay FU, Pelosi P, Vieira JE, Amato MBP: Individual positive end-expiratory pressure settings optimize intraoperative mechanical ventilation and reduce postoperative atelectasis. Anesthesiology 2018; 129:1070–81

(Accepted for publication October 16, 2019. Published online first on April 10, 2020.)

Lung-protective Ventilation in Cardiac Surgery: Reply

In Reply:

We thank Qu *et al.* and Dr. Gil for their letters[1,2] and interest in our publication.[3] Both letters examine the components of our lung protective ventilation bundle (tidal volume less than 8 ml/kg ideal body weight, positive end-expiratory pressure [PEEP] greater than or equal to 5 cm H_2O, and modified driving pressure [peak inspiratory pressure − PEEP] less than 16 cm H_2O).

We selected a pragmatic definition that would be amenable to testing *via* future prospective interventional studies. Analogous bundles have shown effectiveness for improving outcomes in other domains such as prevention of ventilator associated pneumonia[4] and central line–associated bloodstream infections.[5] This bundle was defined *a priori* and reflects the multiple simultaneous considerations anesthesiologists make when seeking to reduce postoperative cardiac surgical pulmonary complications. Thresholds were based upon approximately 75% historic compliance rates (Supplemental Digital Content 1A to C, http://links.lww.com/ALN/C26), such that each component remains achievable if tested in an interventional study. Our tidal volume threshold of 8 ml/kg ideal body weight is a commonly accepted goal for protective ventilation[6]; the PEEP threshold of 5 cm H_2O reflects the default setting of on many institutions' ventilators; and the threshold of 16 cm H_2O for driving pressure falls within the range of previously cited thresholds.[7,8] As noted by Qu *et al.*, although our chosen thresholds are consistent with previous literature, an exploratory study investigating combinations of thresholds for lung protective ventilation bundle components may best identify an optimal target. Furthermore, although the interpretability of our study findings benefited from a pragmatic, universal definition of a bundled lung protective ventilation strategy, we agree with Qu *et al.* and Dr. Gil that an individualized approach to lung-protective ventilation—specific to patient and case characteristics—may be the ideal strategy to mitigate postoperative pulmonary complications. While such methods are described in recent studies,[9,10] they may be challenging to implement in a real-world setting across a broad patient population.

Regarding the point that a U-shaped distribution may exist between body mass index and postoperative pulmonary complications, and that lower driving pressures are harder to achieve in obese patients, we agree this issue should be addressed in any study of lung protective ventilation strategies. We categorized body mass index rather than modeling it continuously, such that multivariable models could appropriately adjust for both extremes. While patients with elevated body mass indices are less likely to receive a bundled lung protective ventilation strategy (Supplemental Digital Content 2, http://links.lww.com/ALN/C27), most commonly due to modified driving pressures greater than 16 cm H_2O, we observed no independent association between body mass index and postoperative pulmonary complications (Supplemental Digital Content 3, http://links.lww.com/ALN/C28), and the relationship between bundles and postoperative pulmonary complications were robust when evaluated across prespecified body mass index ranges (Supplemental Digital Content 10, http://links.lww.com/ALN/C35). One potential explanation is that a high airway driving pressure in obese individuals is more likely to reflect to reflect chest wall elastance rather than lung elastance (*i.e.,* higher airway driving pressure without a higher transpulmonary driving pressure).

To Dr. Gil's concern that higher levels of PEEP may be harmful to patients, we agree this may be the case at high levels; however, we disagree that our study provides evidence to support a threshold of 5 cm H_2O as independently protective or harmful. Specifically, our study demonstrated no independent association between PEEP greater than 5 cm H_2O and postoperative pulmonary complications (adjusted odds ratio, 1.18; 95% CI, 0.91 to 1.53; fig. 4).

To Qu *et al.*'s point that consensus definitions of postoperative pulmonary complications exist—acknowledged by our study[11,12]—we agree that such definitions are useful for improving comparisons across studies. We carefully selected a composite pulmonary complication comprised from consensus definitions, but strategically omitted several components (atelectasis, aspiration, pleural effusion, bronchospasm, and pneumothorax) due to either limitations in our observational data quality or lack of an underlying mechanism amenable to treatment *via* lung-protective ventilation. Heterogeneous definitions may lead to varied outcome incidences and associations. We emphasize these incidences (table 2) and explore associations *via* sensitivity analyses (Supplemental Digital Content 6, http://links.lww.com/ALN/C31). We observed that a lung-protective ventilation bundle remained protective against each pulmonary complication outcome component except for prolonged ventilation. As Qu *et al.* suggest, the lack of independent association between a lung-protective ventilation bundle and prolonged ventilation may have existed, as other mechanisms (*e.g.,* neurologic and hemodynamic derangements precluding safe early extubation) may better explain this finding.

We thank Qu *et al.* and Dr. Gil for their comments regarding our study. Although the optimal target for intraoperative lung protective ventilation in the cardiac surgical patient is yet to be fully elucidated, our study supports the importance of further studies of intraoperative ventilator management.

Research Support

All work and partial funding attributed to the Department of Anesthesiology, University of Michigan Medical School (Ann Arbor, Michigan). The project was supported in part by the National Heart, Lung, and Blood Institute (grant no. 1K01HL141701-02; Bethesda, Maryland) and the National Institute of General Medicine Sciences (grant no. 5T32GM103730-05; Bethesda, Maryland). Dr. Likosky received support (R01-HS-022535) from the Agency for Healthcare Research and Quality. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health or Agency for Healthcare Research and Quality.

Competing Interests

Dr. Kheterpal declares financial relationships with entities outside the scope of this project, including support from Merck (Kenilworth, New Jersey; utilization patterns and outcomes of sugammadex administration); Apple (Cupertino, California; health trajectories as observed via wearable technologies); and Blue Cross Blue Shield Michigan (Detroit, Michigan; anesthesiology quality improvement). The other authors declare no competing interests beyond those described in the funding statement.

Michael R. Mathis, M.D., Donald S. Likosky, Ph.D., Jonathan W. Haft, M.D., Michael D. Maile, M.D., M.S., Randal S. Blank, M.D., Ph.D., Douglas A. Colquhoun, M.B., Ch.B., M.Sc., M.P.H., Allison M. Janda, M.D., Sachin Kheterpal, M.D., M.B.A., Milo C. Engoren, M.D. University of Michigan Medical School, Ann Arbor, Michigan. mathism@med.umich.edu

DOI: 10.1097/ALN.0000000000003294

References

1. Qu Z, Zhang H, Zhou S: Lung-protective ventilation in cardiac surgery: Comment. Anesthesiology 2020; 132:1610–11
2. Gil H: Lung-protective ventilation in cardiac surgery: Comment. Anesthesiology 2020; 132:1611
3. Mathis MR, Duggal NM, Likosky DS, Haft JW, Douville NJ, Vaughn MT, Maile MD, Blank RS, Colquhoun DA, Strobel RJ, Janda AM, Zhang M, Kheterpal S, Engoren MC: Intraoperative mechanical ventilation and postoperative pulmonary complications after cardiac surgery. Anesthesiology 2019; 131:1046–62
4. He S, Chen B, Li W, Yan J, Chen L, Wang X, Xiao Y: Ventilator-associated pneumonia after cardiac surgery: A meta-analysis and systematic review. J Thoras Cardiovasc Surg 2014; 148:3148–55
5. Costello JM, Morrow DF, Graham DA, Potter-Bynoe G, Sandora TJ, Laussen PC: Systematic intervention to reduce central line-associated bloodstream infection rates in a pediatric cardiac intensive care unit. Pediatrics 2008; 121:915–23
6. Serpa Neto A, Hemmes SN, Barbas CS, Beiderlinden M, Biehl M, Binnekade JM, Canet J, Fernandez-Bustamante A, Futier E, Gajic O, Hedenstierna G, Hollmann MW, Jaber S, Kozian A, Licker M, Lin WQ, Maslow AD, Memtsoudis SG, Reis Miranda D, Moine P, Ng T, Paparella D, Putensen C, Ranieri M, Scavonetto F, Schilling T, Schmid W, Selmo G, Severgnini P, Sprung J, Sundar S, Talmor D, Treschan T, Unzueta C, Weingarten TN, Wolthuis EK, Wrigge H, Gama de Abreu M, Pelosi P, Schultz MJ; PROVE Network Investigators: Protective *versus* conventional ventilation for surgery: A systematic review and individual patient data meta-analysis. Anesthesiology 2015; 123:66–78
7. Neto AS, Hemmes SN, Barbas CS, Beiderlinden M, Fernandez-Bustamante A, Futier E, Gajic O, El-Tahan MR, Ghamdi AA, Günay E, Jaber S, Kokulu S, Kozian A, Licker M, Lin WQ, Maslow AD, Memtsoudis SG, Reis Miranda D, Moine P, Ng T, Paparella D, Ranieri VM, Scavonetto F, Schilling T, Selmo G, Severgnini P, Sprung J, Sundar S, Talmor D, Treschan T, Unzueta C, Weingarten TN, Wolthuis EK, Wrigge H, Amato MB, Costa EL, de Abreu MG, Pelosi P, Schultz MJ; PROVE Network Investigators: Association between driving pressure and development of postoperative pulmonary complications in patients undergoing mechanical ventilation for general anaesthesia: A meta-analysis of individual patient data. Lancet Respir Med 2016; 4:272–80
8. Ladha K, Vidal Melo MF, McLean DJ, Wanderer JP, Grabitz SD, Kurth T, Eikermann M: Intraoperative protective mechanical ventilation and risk of postoperative respiratory complications: Hospital based registry study. BMJ 2015; 351:h3646
9. Pereira SM, Tucci MR, Morais CCA, Simões CM, Tonelotto BFF, Pompeo MS, Kay FU, Pelosi P, Vieira JE, Amato MBP: Individual positive end-expiratory pressure settings optimize intraoperative mechanical ventilation and reduce postoperative atelectasis. Anesthesiology 2018; 129:1070–81
10. Fumagalli J, Berra L, Zhang C, Pirrone M, Santiago RRS, Gomes S, Magni F, Dos Santos GAB, Bennett D, Torsani V, Fisher D, Morais C, Amato MBP, Kacmarek RM: Transpulmonary pressure describes lung morphology during decremental positive end-expiratory pressure trials in obesity. Crit Care Med 2017; 45:1374–81
11. Abbott TEF, Fowler AJ, Pelosi P, Gama de Abreu M, Møller AM, Canet J, Creagh-Brown B, Mythen M, Gin T, Lalu MM, Futier E, Grocott MP, Schultz MJ, Pearse RM; StEP-COMPAC Group: A systematic review and consensus definitions for standardised end-points in perioperative medicine: Pulmonary complications. Br J Anaesth 2018; 120:1066–79
12. Jammer I, Wickboldt N, Sander M, Smith A, Schultz MJ, Pelosi P, Leva B, Rhodes A, Hoeft A, Walder B, Chew MS, Pearse RM; European Society of Anaesthesiology (ESA) and the European Society of Intensive Care Medicine (ESICM); European Society of Anaesthesiology; European Society of Intensive Care Medicine: Standards for definitions and use of outcome measures for clinical effectiveness research in perioperative medicine: European Perioperative Clinical Outcome (EPCO) definitions: A statement from the ESA-ESICM joint taskforce on perioperative outcome measures. Eur J Anaesthesiol 2015; 32:88–105

(Accepted for publication February 28, 2020. Published online first on April 10, 2020.)