Elastic Power

To the Editor:

Recently, mechanical power ventilator-associated lung injury has been identified as an independent risk factor associated with intensive care mortality.[1] Dynamic and static airway pressures, which are the forces of the power concept and other respiratory parameters calculated from these forces (ie, dynamic and static compliances), are the basis of the concepts that have been well-established in intensive care literature for many years.[2] Failure to properly define power components corresponding to dynamic and static airway forces will further increase the current confusion in this regard.[3-6]

In the recently published work of Syed et al[7] in this journal, the elastic component of power is defined as dynamic power on the pressure-time curve. In my opinion, is not correct to define the elastic power component as dynamic power. The force of the driving power component (ie, driving pressure) is the difference between plateau pressure (P_{plat}) and PEEP, which are static airway pressures in the pressure-time curve. Therefore, the compliance calculated using the driving pressure is defined as static compliance. If there is a need for a different definition instead of elastic + PEEP power, I think it would be better to define this field as static power (Fig. 1).

The concept of dynamic power was previously defined by Aşar et al[8] as dynamic mechanical power, and it was proposed with a simple equation that easily calculates dynamic mechanical power at the bedside during volume control ventilation using the ventilator work of breathing (WOB) parameter. In their study, the concept of dynamic power is defined as the sum of resistive power and elastic power defined by Gattinoni et al[9]: MP_{dyn} = ventilator WOB × MVe. Ventilator WOB is the amount of energy consumed for ventilation of 1 L of gas; its unit is expressed in Joule/L and is calculated by the ratio of work in an inspiratory cycle to tidal volume.[10,11] When the contribution of PEEP is added to this and multiplied by the conversion factor, the total dynamic power is calculated: MP_{dyn} = MVe × [(WOB) + (0.098 × PEEP)]. Volume control was compared with the standard power formula in 40 patients with ARDS, and it was shown that the total dynamic power is equal to the total standard power.[8]

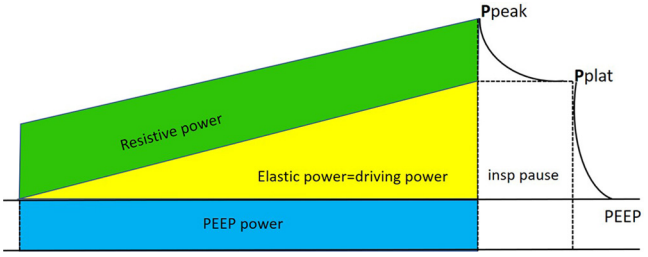

Fig. 1. Pressure-time curve of volume control ventilation. Dynamic mechanical power = resistive power + driving power (green + yellow area). Static power = Driving power + PEEP power (yellow area + blue area). Total power = Static power + resistive power = Dynamic power + PEEP power (green + yellow + blue area). P_{peak} = peak inspiratory pressure; P_{plat} = plateau pressure.

The dynamic mechanical power force (dynamic power) on the pressure-time curve is the peak inspiratory pressure (P_{peak}). Therefore, the compliance calculated using the difference of P_{peak} and PEEP is defined as dynamic compliance. Dynamic power is a concept derived from dynamic respiratory parameters. If the contribution of airway resistance ($P_{peak} - P_{plat}$ = resistive force) is added to the elastic (static) component of power, it can be defined as dynamic power (Fig. 1). Therefore, the concepts of dynamic and static, which are clearly defined by the intensive care scientific community and known to everyone together with the relevant airway forces, are recommended to be used properly and correctly by the authors.

Sinan Aşar
Department of Anesthesiology and Reanimation
Bakırköy Dr. Sadi Konuk Training and Research Hospital
University of Health Sciences
Istanbul, Turkey

Correspondence: Sinan Aşar MD. E-mail: sinan.asaras@gmail.com

The author has disclosed no conflicts of interest.

DOI: 10.4187/respcare.08833

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The authors respond

In Reply:

We appreciate the well-intentioned interest of Dr Aşar and colleagues, who express concern regarding the energy nomenclature that we used in our article. Dr Aşar is correct that there exists considerable variation and, as yet, no broadly accepted definitions in this emerging field directed at the subcomponents of power. However, we respectfully but strongly disagree with several important misconceptions contained within their letter.

First, the term dynamic compliance should not be generally understood to be determined by the difference of peak pressure (which includes the nonelastic, flow resistive element) and PEEP. In fact, the traditional physiologic definition of dynamic compliance is compliance estimated during uninterrupted rhythmic breathing as the slope of the pressure volume loop that links the zero flow points at the extremes of the ongoing tidal cycle.[2] This dynamic compliance differs from (and invariably is less than) the static compliance, which is determined after an occlusion-imposed pause, as in bedside practice. Sustained no-flow conditions allow for stress relaxation and flow redistribution to occur, dropping the recorded value to a plateau pressure that underestimates the zero-flow end-inspiratory pressure that occurs transiently during tidal breathing.

Second, the conceptual basis for the concern regarding inclusion of PEEP in the dynamic power of inflation has been the subject of recent but now resolved debate. When no gas is flowing, PEEP is indeed a static pressure. But PEEP during active inflation is an important component of the applied pressure that must be generated anew with each micro-increment of inflation volume. Therefore, PEEP is a subcomponent of total dynamic energy, joining the pressure related to volume in excess of PEEP (the driving pressure), whose product with volume we term the driving power.

Third, the biologic impact of driving power depends upon the pressure platform (PEEP) from which it begins.[3,4] Along this line, the figure provided by Aşar et al seems to invite confusion rather than clarification. In concept, there can be no "PEEP power" block (as labeled) because PEEP is a static pressure, and power by definition is a dynamic entity. Therefore power, a pressure-flow product, may include a PEEP component during the process of inflation, but "PEEP power" cannot stand alone.

Fourth, what Dr Aşar and colleagues believe everyone knows and accepts is not an accurate assumption. Although he might wish otherwise, the term dynamic mechanical power, as defined in his self-cited paper, is not generally accepted by the academic community engaged in studying these questions and developing this emerging field. Indeed, the publication date of April 2020 hardly allows for the evaluation of its conceptual merit, let alone its adoption for generalized use.

Finally, the paper currently under discussion is not our first to use these specific terms nor to examine the concepts that underpin the components of inflation power.[36]

In the end, although we consider these complaints to be invalid, we do agree that a consistent nomenclature for power components is needed to facilitate communication as research into the emerging energetics of ventilation proceeds. Definitions should be grounded on a firm understanding of the underlying energetics and physiology.

John J Marini
Pulmonary/Critical Care
Regions Hospital
St Paul, Minnesota

David J Dries
Department of Surgery
Regions Hospital
St Paul, Minnesota

Correspondence: John J Marini MD. E-mail: john.j.marini@healthpartners.com.

The authors have disclosed no conflicts of interest.

DOI: 10.4187/respcare.08876

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Neuromuscular Blocking Agents for ARDS: Firm Evidence for ICU Mortality but Not for Long-Term Mortality

To the Editor:

Optimal ventilation and weaning strategies in patients with ARDS should be carefully assessed.[1,2] We read with interest the systematic review by Torbic et al,[3] which sought to evaluate mortality when using neuromuscular blocking agents (NMBAs) in early, moderate-to severe ARDS compared to usual care or placebo. The authors included 6 randomized controlled trials (RCTs), but only 2 of the 6 RCTs had a low risk of bias.[3] We applaud the effort of the authors, but we have some concerns.

First, the fragility index, which is an intuitive measure of the robustness of RCTs, was introduced in critical care medicine and has been utilized in different systematic reviews.[4-6] The fragility index is achieved by using a two-by-two contingency table and *P* value calculated with the Fisher exact test.[4] When we calculated the fragility index of RCTs included in the systematic review by Torbic et al,[3] we found that all of the included studies had a fragility index of zero ($P > .05$). According to this, the RCTs evaluating mortality when using NMBAs in early and moderate-to severe ARDS are very fragile and

the evidence from these studies is very weak.

Second, the authors reported that the use of NMBAs reduced the risk for ICU and 21–28-d mortality but not 90-d mortality. According to these results, we further performed a trial sequential analysis to evaluate whether this meta-analysis had sufficient statistical power to detect or reject the intervention effects.[7] For ICU mortality, the 95% CI adjusted with the trial sequential analysis ranged from 0.41 to 0.8 and indicated that 431 of 433 subjects were enough to reach the required information size. According to this, firm evidence existed in favor of the use of the NMBAs to reduce ICU mortality. For 21–28-d mortality, the trial sequential analysis was not conclusive because the inclusion of 1,485 subjects was far short of the required sample size of 18,618 subjects to ensure conclusive evidence. By evaluating the robustness of RCTs and trial sequential analysis, our analysis supports the reported effects of NMBAs to reduce ICU mortality but not the 21–28-d and 90-d mortality. We believe we would need 18,470 subjects with moderate-to-severe ARDS to be treated with NMBAs to achieve firm evidence on long-term mortality.

Maria Vargas
Giuseppe Servillo
Department of Neurosciences
Reproductive and Odontostomatological Sciences
University of Naples "Federico II"
Naples, Italy

Correspondence: Maria Vargas MD, Department of Neurosciences, Reproductive and Odontostomatological Sciences, University of Naples Federico II, Via Pansini 80100, Naples, Italy. E-mail: vargas.maria82@gmail.com.

The authors have disclosed no conflicts of interest.

DOI: 10.4187/respcare.08926

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Neuromuscular Blocking Agents for ARDS: Incentive for Personalized Medicine

To the Editor:

We thank Drs Vargas and Servillo for their interest in our meta-analysis and the important points they raised regarding the use of neuromuscular blocking agents (NMBAs) in ARDS.[1] Based on the findings from the 6 trials included in our meta-analysis, we reported that early use of NMBAs in moderate-to-severe ARDS improves oxygenation, decreases ventilator-induced lung injury, and decreases 21–28-d mortality.[1] We agree that the current literature does not support a 90-d mortality benefit associated with NMBA use. NMBAs are thought to exert a benefit in ARDS by decreasing nflammatory markers, increasing recruitment, improving ventilation/perfusion matching, and reducing ventilator asynchrony and ventilator-induced lung injury.[2-4] Given the mechanism of action of NMBAs, these benefits may be transient and may only provide a short-term mortality benefit due to the progression of ARDS to a fibrotic phase.[5]

We also agree that there are limitations in concluding that NMBAs provide a short-term mortality benefit, as evidenced by the results of fragility index calculations shared by Drs Vargas and Servillo. The use of the fragility index in critical care, however, has its own limitations due to heterogeneity in critical care trials.[6,7] For example, the I^2 statistics for 21–28-d and 90-d mortality in our meta-analysis were 60% and 54%, respectively.[1] Additionally, trial sequential analysis (TSA) is a complex statistical tool, and application in meta-analyses is not universal. TSA is not routinely employed within the Cochrane Collaboration, with its standardized methods and clinical reviews, and the Cochrane Scientific Committee Expert Panel recommends against the routine use of sequential methods for updated meta-analyses.[8] Although systematic reviews can address the effect of an intervention on different outcomes and subgroups, sequential methods such as TSA cannot accommodate multiple thresholds for different outcomes. Meta-analyses are retrospective and observational by nature; therefore, we are unable to control for the trials that have already been performed and are eligible for the meta-analysis. It is difficult to create a retrospective sequential program that would maintain the prespecified assumptions of a TSA.

In addition to heterogeneity in critical care trials, there are also limitations in study recruitment and trial design. The calculated sample size of almost 19,000 subjects with moderate-to-severe ARDS needed to effectively conclude whether NMBAs impact 21–28-d and 90-d mortality is likely not feasible and is unlikely to ever be completed. We must use existing literature and carefully evaluate for limitations before applying the data to clinical practice. Based on the findings from our meta-analysis and scrutiny of the included trials, we do not believe that NMBA therapy should be applied in all patients with moderate-to-severe ARDS. The use of NMBA therapy is not without risk,[9] and use should be reserved for patients who do not experience improvements in oxygenation and ventilator synchrony despite application of first-line nonpharmacologic interventions.[10] The solution is not larger trials, but more studies evaluating the impact of pharmacologic therapies like NMBAs on ARDS phenotypes and subphenotypes. Application of therapies that specifically target ARDS phenotypes will improve patient outcomes and limit adverse effects associated with these therapies.[11,12]

Heather Torbic
Department of Pharmacy
Cleveland Clinic
Cleveland, Ohio

Sudhir Krishnan
Abhijit Duggal
Department of Critical Care
Respiratory Institute
Cleveland Clinic
Cleveland, Ohio

Correspondence: Heather Torbic PharmD BCPS BCCCP, Department of Pharmacy, Cleveland Clinic, 9500 Euclid Ave, Hb-105, Cleveland, OH 44195. E-mail: torbich@ccf.org

The authors have disclosed no conflicts of interest.

DOI: 10.4187/respcare.08963

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