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OPEN

ΔP-Guided PEEP in the Operating Room—Do We Need More Guidance?

To the Editor

Intraoperative higher positive end-expiratory pressure (PEEP) can prevent atelectasis, which could translate into less postoperative pulmonary complications (PPCs). However, ventilation with higher PEEP can also induce overdistension, which could in part negate these positive effects. A "personalized" PEEP approach may be more appropriate, as the balance between prevention of atelectasis and induction of overdistension probably differs between patients. Since ΔP is a "digital" biomarker for both atelectasis and overdistension, a ΔP-guided PEEP strategy has been proposed before,[1] and recently in your journal, Zhang et al[2] presented the findings of a randomized clinical trial confirming benefit of a ΔP-guided PEEP strategy in patients undergoing open abdominal surgery.

However, it remains uncertain how to titrate "best" PEEP to ΔP—for instance, we can use an incremental PEEP trial, wherein PEEP is gradually increased and set at the level at which ΔP is lowest, or a decremental PEEP trial after a recruitment maneuver, in which PEEP is gradually decreased to find the level at which the ΔP, after an initial decrease, again starts to increase. These 2 approaches may very well result in different levels of "best" PEEP—the first approach favors prevention of atelectasis but may conceal PEEP-induced overdistension and the second approach could result in less prevention of atelectases but takes notion of overdistension caused by PEEP. Advantages of an incremental PEEP trial are that it takes far less time than a decremental PEEP trial, and may also result in less hemodynamic instability induced by the high intrathoracic pressures during a recruitment maneuver.[3,4]

In their study, Zhang et al[2] used the first approach, ie, they used incremental PEEP trials. The "Driving PrESsure DurIng GeNeral AnesThesIa for Open AbdOmiNal Surgery" (DESIGNATION) study is an international multicenter ongoing randomized clinical trial in which a decremental PEEP trial is used to select the best PEEP, after an initial incremental PEEP trial to 20 cm H_2O as a recruitment maneuver.[5] In an interim analysis for study conduct, we compared the ΔP at the recruitment maneuver, ie, at 20 cm H_2O PEEP, and the nadir for PEEP in the successive decremental PEEP trial in a total of 290 patients. While ΔP was 10 (9–12) cm H_2O at the end of the incremental PEEP trial, the nadir ΔP in the decremental PEEP trial was much lower, only 7 (6–8) cm H_2O ($P < .01$).

One interesting finding in the study by Zhang et al[2] was that mechanical power (MP) of ventilation was higher in the ΔP-guided PEEP group. MP can be seen as the amount of energy transferred from the ventilator to the lung, and has been proposed, alongside ΔP, as an additional biomarker to guide ventilation. Given the fact that the MP is calculated from the ΔP, it is surprising to see that while ΔP declines, the MP increases.[6] In fact, the MP is expected to move in the same direction as ΔP. Could the authors provide more insight on how the MP was calculated, and how the other parameters used to calculate the MP differed between the groups?

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Viscoelastic Hemostatic Assays—Training the Next Canary for Hemostatic Resuscitation in Trauma

To the Editor

We read the Pro-Con debate regarding the use of viscoelastic hemostatic assays (VHAs) in trauma resuscitation by Blaine and Dudaryk[1] with great interest. In their article, the authors stressed the importance of early hemostatic resuscitation in trauma patients, whether using a ratio-based or factor concentrate-based strategy. Like a canary in a coal mine, if used in a timely manner and interpreted properly, VHAs can provide several clinically actionable danger signals in trauma-induced coagulopathy. While the authors concisely described the pros and cons of VHAs in severe trauma, we feel it important to provide additional clarifications or alternative views on some points.

First, the authors advocated using contact-activated (intrinsic) VHA clotting time to determine the need for plasma transfusion based on the "rarity of isolated factor VII (FVII) deficiency." However, kaolin-activated reaction time (R-time) on thromboelastography (TEG) is rarely abnormal in severely traumatized patients due to stress-induced factor VIII (FVIII) elevations and far less sensitive than international normalized ratio (INR) to the multifactorial factor deficiency in trauma.[2] Indeed, Chow et al[3] suggested that optimal R-time thresholds for diagnosing an INR over 1.5 and 2.0 were 3.9 and 4.3 minutes, respectively, based on a retrospective analysis of 694 trauma patients. These values are in the lower range of normal (4–8 minutes) for the assay. The same limitation applies to rapid TEG, which uses tissue factor and kaolin as activators. While the use of contact-activated VHAs makes it possible to reduce unnecessary plasma administration, there is also an increased risk of underestimating extrinsic and common pathway factor deficiencies and delaying crucial factor replacement therapy.

Second, the authors seemed to suggest that different VHAs are equally capable of detecting hyperfibrinolysis using device-specific thresholds. On the contrary, VHA's sensitivity for detecting hyperfibrinolysis is highly dependent on the reagents used in the test. For example, sensitivity is lowest with kaolin-activated TEG (23.4% using Lysis30 >8%) but improved with extrinsic pathway rotational thromboelastometry tests, EXTEM and FIBTEM (46.1% and 94.4%), using maximum lysis >15% during liver transplantation.[4] In trauma patients, Raza et al[5] reported the limited overall sensitivity of EXTEM-ML (%) for detecting hyperfibrinolysis. Lysis remained at the median value of 6.6% despite a significant increase in median D-dimer to over 38,000 ng/mL (normal <550 ng/mL). Patients with elevated D-dimer tend to be sicker (eg, high base deficit and hypotension), and thus, clinical judgment remains vital to assess the need for antifibrinolytic therapy.

Finally, the availability and cost of each hemostatic product may influence the local hemostatic resuscitation protocol. At a tertiary trauma center in the United States, thawed plasma is routinely available but is not commonly used in Europe. Factor concentrates are preferred for rapid availability in Europe because they are more reasonably priced than in the United States. The authors cited an example of a VHA-based transfusion algorithm that included 4 grams of fibrinogen concentrate or equivalent amounts of cryoprecipitate. However, optimal thresholds for fibrinogen replacement are not known and variable on VHAs; 20 mm for TEG-FF (functional fibrinogen) and 10 mm for ROTEM-CA5 (clot amplitude at 5 minutes) (note: CA5 parameter is not approved for clinical use in the United States). We speculate that the higher costs of fibrinogen-rich products and additional thawing processes required for cryoprecipitate contribute to the US practice of replacing fibrinogen later (≥3 hours after the admission) in trauma resuscitation.[6]

In the era of the global pandemic, it has become increasingly difficult to staff a centralized laboratory to run comprehensive coagulation testing with a timely turnaround. Automated VHAs that can be performed at the bedside without extensive laboratory training will be increasingly valuable in improving the quality and safety of hemostatic resuscitation in trauma patients. We agree with Blaine and Dudaryk that further modifications and clinical validation studies of VHAs are needed to train the next canary for hemostatic resuscitation in trauma.