A recent multicenter, randomized, controlled trial has concluded that the use of low tidal volumes (VT) for ventilation during surgery improves postoperative outcomes. The report is based on the context of a general acceptance that survival is increased when lower tidal volumes are used in patients with acutely diseased lungs, such as acute respiratory distress syndrome (ARDS) or asthma, who require mechanical ventilation in intensive care units (ICUs). Although extensive laboratory and clinical data confirm that higher VT worsens lung inflammation and lowers survival when lung injury is established, recent data suggest an analogous phenomenon during general anesthesia; in this study, using higher VT to ventilate patients whose lungs are normal seems to cause lung injury. Because choosing lower VT incurs no financial cost and is within the skill set of all anesthesia providers, many think that low VT should be the standard for ventilating all patients during surgery. As approximately 250 million people undergo general anesthesia each year throughout the world, broad acceptance of this approach would cause a massive change in worldwide practice. In addition, because the frequency of morbidity or mortality after general anesthesia is generally low, risk–benefit analysis is complex. This perspective examines the evidence to support a widespread shift in standard care and proposes approaches for going forward.

Lung Protection—Knowledge Transfer from Intensive Care

The idea of lung-protective ventilation originated in critical care medicine with the recognition that high inflation pressure or VT caused lung damage (and possibly decreased survival) in mechanically ventilated patients with neonatal lung disease, chronic obstructive pulmonary disease, asthma, or ARDS. Among these conditions, ARDS became a particular focus because it is associated with substantial mortality, healthcare costs, and long-term disability in survivors; and patients with ARDS commonly require mechanical ventilation.

Although classic barotrauma from excessive ventilator pressures can cause air leaks (e.g., pneumothorax) that are usually obvious at the bedside, the consequences of ventilator-associated lung injury are insidious. This type of injury has several elements (e.g., barotrauma, volutrauma, and biotrauma), and laboratory studies over 4 decades clearly demonstrate that higher VT causes greater lung injury. In addition, the histologic appearances of such injury are indistinguishable from the changes observed in ARDS. Categorical confirmation of much of this research came in 2000 with a landmark randomized trial demonstrating that lower VT improves survival in ventilated patients with ARDS. This knowledge has resulted in adoption of lower VT as a standard of care in patients with ARDS.
Although lower $V_T$ is widely recognized as a key element in protective ventilation, laboratory studies have identified a second component: maintenance of lung volume. This is usually accomplished by a “recruitment maneuver” and maintained with ventilator pressure applied throughout expiration (termed positive end-expiratory pressure [PEEP]). Maintenance of lung volume lessens the amount of atelectatic lung, thereby lessening intrapulmonary shunt and more evenly distributing inhaled $V_T$.12 Despite compelling rationale and consistent laboratory data, the role of recruitment maneuvers or PEEP remains uncertain in patients with ARDS.

**Background—Protective Ventilation in Healthy Lungs**

Patients undergoing general anesthesia—up to 250 million per annum by recent estimates6—constitute a far larger population of mechanically ventilated patients than those with ARDS, but protective ventilation is not universally practiced during anesthesia. If the gains associated with protective ventilation in the ICU could be translated to the operating room, then substantial numbers of patients might benefit. Indeed, a recent prominent randomized trial of 400 patients reported that the use of lower $V_T$ during anesthesia resulted in a better postoperative outcome;1 this study followed several uncontrolled studies as well as two smaller clinical trials that yielded mixed results.13,14 However, in weighing translation from critical care to the operating room, it is important to understand that the populations are very different: patients in the operating room usually have normal lungs whereas patients with ARDS—by definition—do not.

A randomized study of 56 patients undergoing open abdominal surgery compared “standard” ventilator management ($V_T$ 9 ml/kg ideal body weight; PEEP 0 cm H2O) versus protective management ($V_T$ 7 ml/kg ideal body weight, together with recruitment maneuvers and PEEP).13 Thus, “lung protection” consisted of only a slight reduction in $V_T$ but considerable attention to lung recruitment, and this resulted in superior intermediate outcomes (e.g., atelectasis, oxygenation, and lung infection) with some effects lasting up to 5 days.

A larger (101 patients) double-blind study focused primarily on the impact of $V_T$;14 the difference in $V_T$ between the groups was large, with the control patients receiving 12 ml/kg predicted body weight compared with 6 ml/kg predicted body weight in the “protective” group. In addition, maintenance of lung volume was minimal—and equal—in each group (only PEEP, 5 cm H2O, no recruitment maneuvers). This protective strategy did not provide benefit; moreover, lower $V_T$ was associated with lower arterial oxygen tension ($P_{O_2}$) immediately after surgery, and more atelectasis by day 5.

The composite message from these two randomized, controlled trials13,14 might be that during anesthesia, protective ventilation is beneficial when both lower $V_T$ and a recruitment strategy are included, but not when lower $V_T$ is used alone. This conclusion would be consistent with findings initially reported 50 yr ago,15 where low $V_T$ during general anesthesia without a volume recruitment strategy resulted in progressive atelectasis that impaired lung compliance and oxygenation.

**Protective Ventilation for Abdominal Surgery—Recent Results**

The most recent study examined 400 patients undergoing abdominal surgery who were considered to be at higher risk for postoperative pulmonary complications and incorporated both elements (lower $V_T$ and volume recruitment) into the study design.1 These patients were randomized to a control ventilation strategy (i.e., standard $V_T$ without PEEP) or a protective strategy (i.e., low $V_T$, recruitment maneuvers every 30 min, and PEEP), and the composite primary outcome (major pulmonary or extrapulmonary events) was measured on day 7 after surgery. The results were striking; the primary outcome was reduced by over 60% (control 55 of 200, protective 21 of 200), and the control group had higher rates of noninvasive ventilation and sepsis and had a longer length of hospital stay.

There are reasons for caution in implementing the conclusions of this article. First, the title and conclusions of the article suggest that low $V_T$ is beneficial.1 However, the protective intervention applied low $V_T$, PEEP, and recruitment maneuvers, and assuming the results are valid, it is not possible to be certain which elements (or combinations thereof) are responsible for the outcome differences. Second, the effect size seems unrealistically high. In any outcome with a multifactorial etiology (especially when measuring a composite outcome), the effect size from a single intervention will necessarily be modest,16 suggesting that imbalances in the group characteristics (notwithstanding randomization) may magnify (or account for) the observed effect. Such imbalance is not surprising in a moderate-sized study,17 and additional indicators suggest that the two groups were not balanced at baseline. For example, the rate of anastomotic leak is significantly different between groups (44 of 200 control, 24 of 200 protective; $P = 0.009$); but, anastomotic leak is not pathogenically linked with ventilator strategy, and it can therefore be considered a “tracer” to detect between-group imbalances.18 Because the causes of the imbalance are unknown, the imbalance cannot be corrected by multivariate adjustment.

**Differences between ICU and Operating Room**

Important differences between the ICU and the operating room may impact ventilator management. In the operating room, the patients’ lungs are usually normal, compliant, and readily oxygenated. In addition, important surgical events are often predictable (or controllable), and a single specialist physician (or other anesthesia provider) is present to manage all aspects of care. In many anesthesia practices, intraoperative PEEP is seldom used. Finally, optional therapies can be discussed with the patient beforehand. In the ICU, most of these circumstances differ considerably; thus “cultural” and context differences may need to be considered when translating practices from the ICU to the operating room.
perioperative cardiac complications, largely based on two embraced elements of evidence-based practice and patient safety initially a single, although promising, study. For example, proponents of evidence-based practice based on such findings is understandable, especially because baseline risk is exceedingly low (as indicated in fig. 1). In addition, the large population size (thought to be 250 million people per year) results in a large absolute number of patients being harmed, in spite of a low risk of harm. In the high-risk population of smaller size (right), there is more opportunity for the benefit of the treatment to be actualized. As such, a greater percentage of patients will benefit, and due to the small population size (an estimate of 3.2 million cases of acute respiratory distress syndrome [ARDS] worldwide per year), a smaller absolute number will be harmed. This effect forms the basis for the suggestion that an intervention that will be applied to a large, low-risk population requires extensive study before implementation, because the potential for harm, in terms of absolute patient number, is high.

Lessons from Previous Perioperative Interventions

The large treatment effect observed by Futier et al. has already led several outlets to champion an immediate adoption of this ventilation strategy for most surgical patients. Such enthusiasm is not surprising, for at least two reasons. First, protective ventilation with low VT and lung recruitment is a simple inexpensive intervention that seems to cause major reductions in postoperative morbidity without important adverse effects. The desire to immediately change clinical practice based on such findings is understandable, especially when perioperative medicine lacks much in the way of interventions proven to prevent important morbidity and mortality. Nonetheless, several examples in the literature should warn us against rapidly changing clinical practice based on a single, although promising, study. For example, proponents of evidence-based practice and patient safety initially embraced β-blockade as a simple intervention to prevent perioperative cardiac complications, largely based on two small randomized trials. Nonetheless, subsequent larger trials found instead that this seemingly safe intervention could also increase patients’ risks of postoperative stroke and mortality. Similarly, two initial randomized trials identified supplemental perioperative oxygen as a simple and physiologically sensible intervention for preventing surgical-site infections, yet these benefits were not replicated by a subsequent large randomized trial. These two examples demonstrate the importance of replicating the results of a single promising study in different populations.

Second, the previously observed benefits of protective ventilation in critically ill patients with ARDS may have led to insufficient skepticism of studies showing such benefits in surgical patients with healthy lungs. Indeed, it is highly unlikely that the overall risk–benefit profile of protective ventilation is similar in the two populations. Patients with ARDS by definition already have lung injury, yet the overall risk of postoperative pulmonary complications after elective surgery may be as low as 1.5%. Thus, the relative magnitude of any adverse effects from protective ventilation will be much larger in surgical patients versus critically ill patients (fig. 1). When the overall level of patient risk is low, the harmful effects of a therapy tend to dominate.
Going Forward
In summary, we believe that the balance of rationale, evidence, and experience suggests that the ideal approach to intraoperative ventilation is certainly an important question, but that the answer remains unknown. The experience from the ICU, coupled with extensive laboratory data and provocative clinical studies, has set the scene for large-scale trials in the field. In addition, the design—and reporting—of such studies should carefully detail the interventions used in terms of $V_T$ and lung recruitment. Fortunately, large-scale perioperative clinical consortia exist that have the capacity to execute such studies. Finally, for anesthesia providers who decide that the current level of evidence is sufficient to change practice, we suggest that they consider carefully the interventions detailed by Futier et al. (i.e., management of both $V_T$ by predicted body weight and lung recruitment) and perhaps restrict the specific intervention to comparable patient populations.1

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Competing Interests
The authors declare no competing interests.

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