

LASTING LEGACY IN INTENSIVE CARE MEDICINE



In search of the Holy Grail: identifying the best PEEP in ventilated patients

Luciano Gattinoni^{1*}  and John J. Marini²

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Positive end-expiratory pressure (PEEP) has been interwoven with acute respiratory distress syndrome (ARDS) since its first description by Ashbaugh et al. [1]. Thereafter, the potentially competing effects of PEEP on lung volume, gas-exchange, and hemodynamics were quickly recognized, prompting the first proposals for methods to optimize PEEP in the clinical setting. Eight years after the term ARDS was minted, a seminal study by Suter et al. [2] defined “optimal PEEP” as the value associated with best respiratory compliance. That level was associated with the best oxygen delivery and dead space reduction, even though PaO₂ continued to increase at PEEP levels higher than the compliance-defined optimum. This thoughtful approach was based not only on arterial “oxygenation”, but also on hemodynamics and respiratory mechanics. Subsequent research regarding “best PEEP” has resembled the search for the “Holy Grail”, and has developed sequentially along three main lines: oxygenation, lung mechanics, and clinical trials (Fig. 1).

Oxygenation

In the early ‘pre-ventilator-induced lung injury’ era, PEEP was introduced primarily to correct hypoxemia. Unfortunately, the oxygenation target proved difficult to numerically define. The first attempt to set a “best” oxygenation goal was provided by Tenaillon et al. [3], who proposed that best PEEP should reduce the venous admixture to ≤ 15%. This approach encouraged very high PEEP levels (≥ 20 cmH₂O); any resulting hemodynamic impairment was often offset by copious fluid infusion. Perhaps, the strongest rationale for considering hemodynamics in

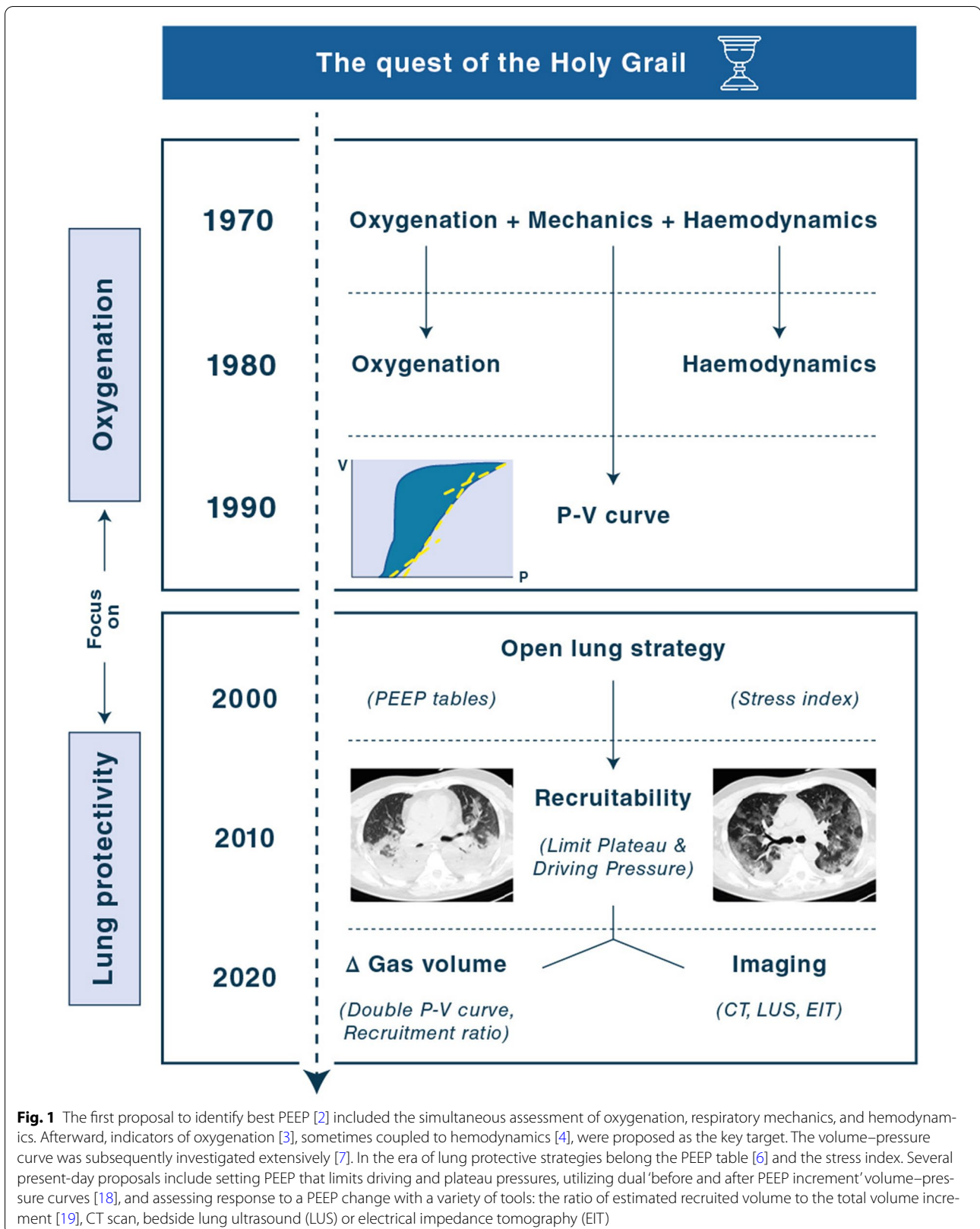
PEEP adjustment was later provided by Dantzker et al. [4], who attributed the beneficial effects of PEEP on oxygenation to the associated decrease of blood flowing through abnormal lung units. Indeed, a strong association was noted between PEEP’s reduction of cardiac output and PaO₂ improvement. This phenomenon, previously observed by Lemaire et al. [5], remains seldom considered at the bedside. Imprecise arterial oxygenation targets continue to be the most widely used indicator of PEEP response in routine practice. Conversely, despite their questionable rationale and safety, convenient and quite specific PEEP tables are extensively used [6].

Lung mechanics

A widely recognized guide for evaluating lung mechanics, the inspiratory limb of the volume–pressure relationship, was implemented by investigators who proposed setting PEEP 2 cm of water higher than its lower inflection point [7]. This method tacitly assumes that recruitment of viable units is nil at still higher pressures and volumes, and that limited over-distention occurs during tidal ventilation. This misconception motivated research to define and measure recruitment. Unfortunately, the term “recruitment” itself is ambiguous. We and others quantify recruitment through quantitative lung imaging, defining it as the total of gasless tissue regaining aeration. Others assess recruitment as the improved aeration of a predefined lung region [8]. In clinical settings, recruitment has been assumed when tidal compliance increases in response to a PEEP increment [9]. Recruitment estimates measured by improved respiratory mechanics and those quantified by imaging, however, are quite distinct. In fact, better respiratory mechanics result not only from more numerous aerated units, but also from higher compliance of units already open [10]. Other mechanics-based attempts to identify “best PEEP”, an expiratory intervention, have concentrated on the deflation

*Correspondence: gattinoniluciano@gmail.com

¹ Department of Anesthesiology, Medical University of Göttingen, University Medical Center Göttingen, Göttingen, Germany
Full author information is available at the end of the article



limb of the volume–pressure relationship [11]. Accordingly, airway pressures were reduced stepwise from end-inspiration, with ‘best PEEP’ defined as the pressure just above that at which PaO₂ or tidal compliance decreased [12]. This method attributes such changes in respiratory system properties to “de-recruitment” within the lung, ignoring its chest wall enclosure. A sharply different approach, one also based on expiratory mechanics (but of the lung itself), was proposed by Talmor et al. [13]. These authors equated esophageal pressure to pleural pressure and based the elusive “best PEEP” on the level at which the difference between the end-expiratory airway and esophageal pressures turns positive. Apparently, however, doing so offers no clear outcome advantage [14].

Clinical trials

“Best PEEP” has been sought through multiple clinical trials that contrasted outcomes for population cohorts treated with higher vs. lower PEEP or specific approaches to setting it [6]. No single prospective trial, however, has succeeded convincingly, even though impressive meta-analyses favor higher PEEP for specific subgroups [15]. Notably, higher PEEP linked with recruitment maneuvers has been associated with significantly increased mortality [16].

Ideally, a “best PEEP” simultaneously: (1) provides appropriate gas-exchange; (2) keeps the lungs open (prevents phasic airway collapse); (3) avoids alveolar over-distension; and (4) does not compromise hemodynamics. This PEEP ‘grail’ simply does not exist. Any PEEP selected is always a compromise among these objectives—a balance which over time tilts increasingly toward its complications. With only isolated exceptions, the quest for an ‘optimal PEEP’ approach has focused on passive airway pressure and has largely ignored the potentially important influences of disease stage, chest wall stiffness, massive obesity, baby lung capacity, vertical torso angulation, supine/prone body positioning, regional compliance, and need for frequent PEEP reassessment as disease progresses or resolves.

Optimal gas-exchange: PEEP certainly does not require venous admixture to be held < 15%, but it should provide viable gas-exchange (PaO₂ 60/80 mmHg and PaCO₂ < 50/55 mmHg) without excessive dead space generation or potentially toxic levels of FiO₂.

Keeps the lungs open: To maintain all unstable alveoli recruited requires PEEP ≥ 20 cmH₂O. Hence, it may be safer to accept that a fraction of potentially ‘recruitable’ lung always will remain closed.

Alveolar over-distention: Some over-distention is unavoidable when PEEP exceeds 10/15 cmH₂O, a level that causes normal lung units to approach their total capacity.

Hemodynamics: Hemodynamic impairment is, in our opinion, an ever-present side effect whose consequences are largely neglected. PEEP-compromised hemodynamics often are not considered problematic, as they usually respond with apparent ease to fluids and cardioactive drugs. Yet, the resulting histologic consequences of such ‘remedies’ are quite demonstrable in experimental animals [17].

Without question, the judicious application of PEEP has saved many lives. Yet, history has shown that the quest for unique “best PEEP” guidelines is quixotic; rather, best PEEP may simply be that individual-specific, empirical value which provides viable oxygenation (SpO₂ > 90% without excessive FiO₂ (e.g., > 0.7) and acceptable PaCO₂ (< 50/55 mmHg), with minimal need for fluid resuscitation or cardioactive drugs. Starting with a PEEP 10–12 cm H₂O is likely the most prudent approach, staying alert to possible hemodynamic consequences whenever PEEP is increased. Once the level is set, it is wise to periodically question and test its need and adequacy.

Author details

¹ Department of Anesthesiology, Medical University of Göttingen, University Medical Center Göttingen, Göttingen, Germany. ² Pulmonary and Critical Care Medicine, Regions Hospital and University of Minnesota, St. Paul, MN, USA.

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Declarations

Conflicts of interest

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