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Readers’ comments in focus

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Introduction

In the past few months Intensive Care Medicine has received important readers’ comments that address the original articles by Jardin et al. [1], Roupie et al. [2], Villar et al. [3], and the editorial note by Steltzer and Krafitt [4], all published in last year’s September issue. The topics discussed focus on the question of whether mortality rates in acute respiratory distress syndrome (ARDS) have been decreasing, scrutinize the appropriateness of the current definition of the American-European Consensus Conference (AECC) [5] and criticize some methodological issues.

Is there a trend towards decreasing mortality rates in ARDS?

Hughes et al. [6] raise concerns about the widely held opinion that mortality rates in ARDS are decreasing. These authors believe that mortality rates are still around 60%, as found in the study by Roupie et al. [2]. Hughes et al. are correct in that “scientific proof” in the classical sense is lacking, but there are several indications that suggest a trend towards decreasing mortality rates: (a) Single centers comparing two treatment periods observed a decline in mortality rates [1, 7]. (b) The study by Milberg et al. [8] evaluated ARDS mortality rates over an 11-year period in a single center and found a decrease. (c) Schuster [9] plotted mortality rates of 14 clinical studies versus time and found a decrease over the years 1975–1995. (d) A plot of the mortality rates of 51 major clinical ARDS studies covering the time period from 1967 to today displays a trend towards lower mortality [10]. (e) In their randomized controlled trial of 1994 comparing two treatment strategies for ARDS, Morris et al. [11] reported that in both treatment arms mortality rates were significantly lower than those assessed in the historic extracorporeal membrane oxygenation trial of 1979 that had had a similar study design [12]. (f) Numerous uncontrolled trials have been published which found mortality rates markedly lower than those of historical controls [13, 14, 15, 16, 17]. (g) Several expert opinions expressed in editorials reflect a positive judgement on decreased mortality rates [18, 19, 20]. (h) Very recently Luhr et al. [21] published the first large multicenter trial, in which a survival rate of as high as 59% was observed.

In my opinion, we must learn to live happily with the above cited assembled “evidence.” I doubt that, at least in the near future, “clear evidence” for an improvement in mortality rates as demanded by Hughes et al. [6] will become available.

Do we need a new ARDS definition?

The communication between Artigas [22] and Villar and Kacmarek [23] puts into focus the problem of the appropriateness of the current ARDS definition of the AECC [5]. Why does the AECC definition raise so much discussion? The definition offers a set of criteria, but does not provide sufficient details of their clinical measurement. This prevents the clinician from establishing a clear diagnosis and the researcher from recruiting a homogeneous ARDS series. This problem refers
to the determination of the “acute onset” of the disease, measurement of $\text{PaO}_2/\text{FiO}_2$, interpretation of the chest radiography, assessment of clinical signs of left-heart failure, and measurement of pulmonary capillary wedge pressure. The common ground in the positions of Villar and Kacmarek [23] and Artigas [22] is their demand for a more precise definition of ARDS. While Villar’s and Kacmarek’s [23] intention is to add a specific level of positive end-expiratory pressure to the AECC criteria of ARDS to recruit a homogeneous patient population for future studies, Artigas [22] would maintain the current AECC definition but give detailed information on the method for assessing the individual criteria. Both proposals are tempting and will surely be a major topic of a future AECC.

Mortality assessed at various time points

Another problem addressed by Hughes et al. [6] is that Villar et al. [3] failed to specify “mortality” in their original contribution. In today’s published medical literature, mortality is assessed at various time points, for example, after 28, 30, and 120 days or as ICU mortality and hospital mortality. As the following example shows, mortality rates may differ widely at different time points. In their study on 153 ARDS patients Sloane et al. [24] found a 28-day mortality of 44%, a 5-week mortality of 51%, and a mortality of 54% at hospital discharge. This demonstrates how essential it is to specify the time point at which mortality is assessed.

A word about scores and indices

When applying scores or indices to patients, it is vital to follow exactly the guidelines developed by the original authors. Any modification in the original formulas used for calculation leads to irrelevant data that cannot be used for comparisons.

Jardin [26] detected that Villar et al. [3] in their original article did not use the original formula for calculating the respiratory severity index (RSI). When Jardin et al. [25] originally published the index in 1982, they specified the following formula for its calculation:

1. $\text{RSI} = \text{OI} + 0.014 \times \text{PEEP}$
2. $\text{OI} = \left(\text{PaO}_2 - \text{PaO}_2^\prime\right)/\left(\text{FiO}_2 - \text{FiO}_2^\prime\right)$
3. $\text{PaO}_2 = \left(\text{P}_{B-47}\right) \times \text{FiO}_2 - \text{PaCO}_2$
4. $\text{FiO}_2 = \left(\text{P}_{B-47}\right) \times \text{FiO}_2$

where OI is oxygenation index, PEEP is positive end-expiratory pressure (in cmH$_2$O), $\text{PaO}_2$ is partial pressure of oxygen in the alveolar gas, $\text{P}_{B}$ is barometric pressure, $\text{PaO}_2$ is partial pressure of arterial oxygen, $\text{PaCO}_2$ is partial pressure of arterial carbon dioxide, $\text{FiO}_2$ is partial pressure of inspired oxygen. Villar et al. [3] replaced $\text{PaO}_2$ by $\text{PaO}_2$ in the original formula. This modification led to falsely high RSI values in all patients. In conclusion, I would recommend recalculating the data and publishing them as an “erratum” in this journal.

Readers’ watchful eyes

Each manuscript submitted for publication in this journal is reviewed by expert medical personnel before acceptance. Reviewers from all around the world devote their time and expertise to making sure that the contents of Intensive Care Medicine are as accurate, balanced, and up-to-date as possible. However, these reviewers, as with all humans, are not infallible, and we should excuse their failure to detect that the formula for calculating the RSI in the contribution by Villar et al. [3] contained a mistake, that there were errors in the organ dysfunction and/or infection scores in the paper by Roupie et al. [2], for not having corrected Villar’s et al. [3] erroneous assumption that the data of the European Collaborative ARDS Study did not undergo the peer review process, and for not criticizing the lack of specification that “mortality” was “ICU mortality” [3]. We are grateful to the journal’s attentive readers and explicitly encourage them to keep their watchful eyes on its articles in the future and to contribute “Letters to the Editor.”

References