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EDITORIAL

The definition of ARDS revisited: 20 years later

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More than 20 years ago we set out to create a definition for the acute respiratory distress syndrome (ARDS) in order to standardize clinical and research communication regarding ARDS. Ashbaugh and Petty had described most of the important clinical features of ARDS in 1967, which included hypoxemia, bilateral pulmonary infiltrates, decreased lung compliance, and microscopic evidence of diffuse alveolar damage, but they did not offer specific criteria of the type that could readily be used to define the disorder for clinical, epidemiology, and research purposes [1]. Under the auspices of the American Thoracic Society and the European Society of Intensive Care Medicine we co-chaired the American European Consensus Conference (AECC) on ARDS; this committee met formally in Miami on 15 May 1992 and concluded its work on 26 October 1992 in Barcelona. Membership on the committee included scientists from around the world [2–4]. The AECC recommended that patients be defined as having acute lung injury (ALI) if, in the context of a risk factor for ARDS, they had recent onset of hypoxemia (P/F $\leq$ 300 mmHg regardless of use of PEEP) and a chest radiograph consistent with bilateral pulmonary edema. Those with a P/F ratio $\leq$200 mmHg were defined as ARDS. In both cases, patients were excluded if they had evidence of left atrial hypertension or a pulmonary artery wedge pressure of >18 mmHg that explained the pulmonary edema.

The AECC recognized that much remained to be done in this area and it was hoped that their work and future conferences would spur the development of an integrated international strategy for defining, quantifying, and studying ALI and ARDS. Indeed research was spurred given that the AECC publications have been cited more than 7300 times and additional conferences have been conducted, e.g., the second AECC held in several cities in the USA and Europe from May 1993 until September 1996 [5] and the Berlin Conference held in Berlin in 2011. The second AECC did not change the definition whereas the Berlin conference resulted in recommendations that amended the AECC definition (Fig. 1).

The stated goals of the Berlin committee were to address perceived deficiencies in the definition of ARDS including: lack of explicit criteria for defining "acute," sensitivity of PaO_2/FiO_2 to different ventilator settings, poor reliability of the chest radiograph criterion, and difficulties distinguishing hydrostatic edema on frontal chest radiograph. The conceptual pathophysiologic model of ARDS was confirmed by the Berlin group [6] but correlations between pathologic findings and the clinical definition remain less than ideal [7].

The Berlin group clarified the AECC definition by defining "acute" to mean present for no more than 1 week. The addition of chest computed tomography as a tool for diagnosing pulmonary edema is a logical addition to the chest radiograph, though there are no validation studies that would indicate how such a tool is actually used for this purpose. The allowance for use of Swan–Ganz catheter measurements to exclude hydrostatic edema has been removed because this tool is less often used and because cardiac failure or volume overload can co-exist with ARDS. However, when the situation becomes confusing such as when there is no risk factor present, an echocardiogram is suggested. It is not clear how an echocardiogram is not similarly confounded in the situation where cardiac and non-cardiac pulmonary edema co-exist. Perhaps the greatest improvement in the definition comes from modification of the naming conventions. The concept of ALI being inclusive of the more severe ARDS has always been a bit confusing and was the subject of much debate at the AECC meetings. The change to mild, moderate, and severe ARDS for the same PaO_2/FiO_2 range of

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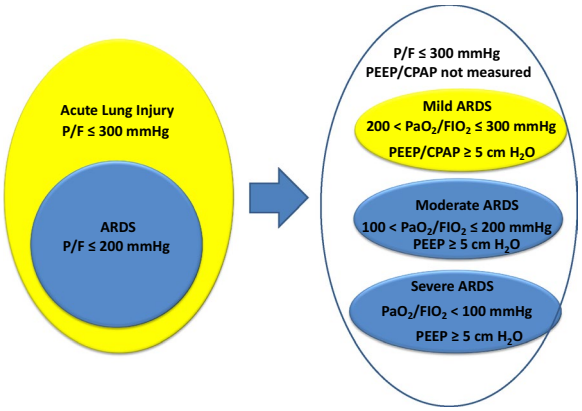

Fig. 1 Illustration of changes in ARDS definition moving from the AECC definition to the Berlin definition. For purposes of this figure all patients must have acute changes in chest radiograph consistent with pulmonary edema

0–300 mmHg greatly simplifies reporting. Unfortunately, the cutoffs for these categories were made by consensus rather than being data-driven, albeit ultimately the more severe category the worse the mortality.

One modification that is less clearly useful is the requirement for 5 cmH_2O of PEEP. The fact that PEEP can improve P/F ratio seems irrelevant. If the lung is injured such that it meets the criteria of either definition, the fact that oxygenation can be made better with a clinical intervention does not negate the presence of injury. It seems similar to saying one does not have congestive heart failure if the condition responds to a small dose of diuretic. Indeed, the Berlin report indicates that approximately 12 % of the 4188 patients in the databases used for validation of the definition did not have PEEP measured. One can only imagine how many people around the world with ARDS never have PEEP measured because they died before intubation or they were never mechanically ventilated perhaps foregoing end-of-life interventions. For clinical, research, or epidemiological purposes, do those patients NOT have ARDS? The Berlin group reports that the Berlin definition has better predictive validity for mortality than the AECC definition did, AUROC of 0.577 (95 % CI 0.561–0.593) vs. 0.536 (95 % CI 0.520–0.553). The AUROC difference of 0.041 was found to be statistically significant but it is hard to know that there is clinical meaning in such a small difference. The Berlin group considered new criteria but jettisoned these other requirements such as measurement of dead space or respiratory system compliance in the name of simplicity. The point was made that detailed evaluation of these measures for validity did not pan out such that a needlessly complex definition of ARDS was avoided. It seems that the PEEP requirement should have gone the same route.

For all of the improvements brought by the new ARDS definition, problems remain. Most frustrating is the lack of a biomarker (clinical laboratory test) that can be used to make the diagnosis. Even groups of biomarkers combining clinically available measures with the latest research-generated biomarkers, though promising, have not been compelling enough to be moved into clinical practice [8, 9]. We still cannot readily measure permeability which is often considered the hallmark of ARDS. The role of hydrostatic pressure remains a major confounder and is not readily clarified by the use of echocardiograms or CT scans. Perhaps tools that hold potential for diagnosing increased lung water and/or permeability may take hold clinically [10–12]. Particularly important would be development of tools/criteria that may even be able to reliably predict development of ARDS [13].

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Compliance with ethical standards

Conflicts of interest
On behalf of all authors, the corresponding author states that there is no conflict of interest.

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