

# The Kigali modification of the berlin definition: a new epidemiological tool for ARDS?

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We read with great interest the paper by Riviello *et al.* (1) in which they used an “adjustment” of the Berlin definition, the so called “Kigali modification”, to estimate the incidence and outcomes of acute respiratory distress syndrome (ARDS) at a Rwandan referral hospital by the enrollment of every adult patient admitted for hypoxia (saturation less than 90%) throughout a 6-week period. According to the Kigali modification, ARDS was defined without the need of positive end-expiratory pressure, with the presence of bilateral opacities at chest radiograph or lung ultrasound and hypoxia was defined with a cutoff of SpO<sub>2</sub>/FIO<sub>2</sub> less than or equal to 315. The study by Riviello *et al.* (1) interestingly points at a limitation of the Berlin definition, that is the real difficulties in a correct estimation of ARDS incidence in developing countries, taking into accounts differences in resource availability and especially in capacity for positive pressure ventilation and ICU beds.

In keeping with this contention, recent evidence (2) underscores that the global impact of ARDS itself is difficult to estimate due to demographic, economic and health care system differences among developed and developing countries. Moreover, risk factors for ARDS may differ between high and low income countries (3). While the higher percentage of traumatic and infectious disease in resource-poor settings may increase ARDS incidence, the lack of critical care resource may signify that critically ill patients die before the development of ARDS (4). Discrepancies in definition criteria [American Consensus Conference -AECC (5) *vs.* the Berlin Definition (6)] may aggravate objective difficulties in estimating ARDS incidence, especially in the developing world. In a multicenter,

prospective cohort study (7), enrolling 773 patients admitted to 45-ICUs in Brazil over a 2-month period and requiring non invasive or invasive ventilation, ARDS was diagnosed in 31% of the patients according to the Berlin definition. In 4 Argentine ICUs, Estenssoro *et al.* (8) reported an incidence of ARDS of 7.7% of all ICU patients (3,050 adult patients admitted over a 15-month period) according to the AECC criteria. Finally, in a 15-month prospective, observational study, enrolling 7,033 patients in 14 ICUs in Brazil (9), 130 (1.8%) met the Berlin criteria for ARDS. In this context, the Kigali modification of the Berlin definition may help to overcome these difficulties by adapting the ARDS definition to the existing health care system in the developing world. On a conceptual basis, the goal of the Kigali modification was to avoid the underestimation of ARDS incidence in these countries and to obtain an estimate of the actual incidence (and not of the “treated incidence”). The low-availability of positive pressure ventilation and ICU beds led to “eliminate” the need of positive pressure ventilation in the Kigali modification and the scarcity of arterial blood gases and radiographs resulted in the use of SpO<sub>2</sub>/FIO<sub>2</sub> and lung ultrasound, respectively.

Also in the developed world, discrepancies in ARDS occurrence still exist, especially between USA and Europe (2). In a retrospective analysis of patients admitted over a 8-year period [2001–2008] in a US county (Olmsted County, Minnesota, USA), an incidence of ARDS of 33.8/100.000 was reported (10), while in an extensive review of epidemiological studies performed after 2000, the ARDS incidence in Europe ranged from five to eight cases/100,000 (11). The results of the Large Observational Study to Understand the Global

Impact of Severe Acute Respiratory Failure (LUNG SAFE) have been recently published (12). This investigation, which was an international, multicenter, prospective cohort study, was undertaken to assess the ICU epidemiology and outcomes from ARDS (as well as to evaluate clinical recognition of the disease and its management). One of the strengths of this study was that the patients were enrolled from all over the world, in the same period of 4 consecutive winter weeks (February–March 2014 in the Northern hemisphere and June–August 2014 in the Southern hemisphere). The overall incidence of ARDS was 10.4% of ICU admission and 23.4% of all patients requiring mechanical ventilation. Geographic variations were confirmed, with Europe having an incidence of 0.48 cases/ICU bed over 4 weeks; North America, 0.46; South America, 0.31; Asia, 0.27; Africa, 0.32; and Oceania, 0.57 cases/ICU bed per 4 weeks. Taking into account that the Berlin definition was adopted for all cases and the low availability of ICU beds in the developing world, it is conceivable to suppose that ARDS was underestimated in low-income countries. In other words, the results of the LUNG SAFE study strengthens the rationale for the Kigali modification of the Berlin definition.

However, the innovative and challenging investigation by Riviello *et al.* (1) encourages some reflections and stimulates some questions.

When the Berlin definition was elaborated, three criteria were fulfilled: feasibility, reliability and validity (13). Concerning the Kigali modification, feasibility seems to be met since diagnostic tests and/or clinical data (chest radiographs/lung ultrasound and SpO<sub>2</sub>) are routinely used by clinicians in hospital settings in low-income countries. The term reliability indicates observer agreement on case identification but this criterion has still to be assessed with Kigali definition. Similarly, validity has to be proven, and especially the “so called” predictive validity, that is the ability to stratify patients by prognosis or response to therapy. Moreover, though each of the three pieces of the modification has been validated previously, the whole modification has not. All these methodological/technical limitations make the results of the study by Riviello *et al.* difficult to be compared to other studies. Their findings come from a small single center (in one country in sub-Saharan Africa) in one rainy season and indicate an hospital screening, while most previous studies screened intubated ICU patients.

Nevertheless, the clinical need to “adapt” to Berlin definition of ARDS to resource-constrained areas of the world can not be ignored and the Kigali modification may represent a practical response. Thus, its validation should

be encouraged and further studies in other resource-constrained settings should be performed in order to assess reliability and validity of Kigali modification.

The aim of a disease definition has the same clinical importance all over the world, that is to facilitate case recognition and better match treatment options to severity.

A clinical, challenging question arises: is one definition for ARDS enough for developed and developing countries or should different “geographic” definitions for the same disease be used for a proper recognition and a correct estimate of its incidence?

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## Footnote

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