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Review of the Oxygenation Index

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Abstract

The oxygenation index (OI) captures the severity of hypoxemic respiratory failure by using two parameters of ventilator settingsbreath as the numerator and a blood oxygenation parameter as the denominator. The two ventilator parameters are Mean Airway Pressure (MAP) in cmH2O and FiO_2 as a percentage. The blood oxygenation parameter is PaO_2 in mmHg.

Oxygenation Index = (FiO2 ×MAP)/PaO2 ×100

OI is built on another commonly used index, the PaO2/FiO2 (P/F) ratio, which accounts for oxygenation and delivered FiO_2, delivery but does not take into account the ventilator pressure required to achieve the PaO2.

WHEN TO USE

Pediatric Acute Respiratory Distress Syndrome (PARDS) definition and severity classification

A consensus conference in 2015 first described a Pediatric ARDS definition.[1,2] It recommends the use of oxygenation index in preference to P/F ratio as the primary metric of lung disease severity for all patients treated with invasive mechanical ventilation. The P/F ratio was recommended for noninvasive ventilation. A closely related Oxygen saturation index (MAP×FiO2×100/SpO2) was recommended when the oxygenation index was unavailable, and the S/F ratio for noninvasive ventilation. The definition of pediatric ARDS was updated in 2023, with minor changes to the cutoff.[3] It again recommended oxygenation index in preference to P/F or S/F ratio as the primary metric of lung disease severity.

Pediatric ARDS was defined as an oxygenation index ≥4 or an oxygen saturation index ≥5 on invasive mechanical ventilation, or a P/F ratio ≤300 or an S/F ratio ≤250 on noninvasive ventilation. Severity classification was to be performed ≥4 hours after initial diagnosis. For invasive mechanical ventilation, mild and moderate categories were defined as oxygenation index <16 or oxygen saturation index <12, and severe ARDS was defined as oxygenation index ≥16 or oxygen saturation index ≥12. For noninvasive ventilation, mild and moderate categories were defined as P/F ratio >100 or S/F ratio >150, while severe ARDS was defined as P/F ratio ≤100 or S/F ratio ≤150. NIV had to be delivered via full-face interface with CPAP/PEEP ≥5.[3]

ECMO candidacy

One of the earliest descriptions of oxygenation index was for selecting candidacy for ECMO in the neonatal population.[4-6] Oxygenation index allows early identification of infants who are highly likely to die when treated with conventional therapy alone, and can be identified well in advance of the terminal event. Early studies on the development of oxygenation index used a threshold of ≥40,[4] or ≥60[5] as a criterion for ECMO candidacy. A large seminal trial on ECMO in neonatal respiratory failure used a threshold of 40 to determine transfer to an ECMO center.[7]

The current literature on ECMO, however, does not support a specific threshold. The Pediatric Acute Lung Injury Consensus Conference (PALICC-2) guidelines recommend (with "very low certainty of evidence") considering ECMO starting at an oxygenation index of 20, with stronger consideration at ≥30.[3] The Extracorporeal Life Support Organization (ELSO) also does not recommend specific OI thresholds. For neonatal ECMO, ELSO guidelines include "sustained elevation of oxygenation index",[8] for pediatric patients, ELSO recommends "ECMO to be considered at 50% mortality risk and indicated in most circumstances at 80% mortality risk".[9] For adult patients, ELSO recommends PaO2/FiO2 of <80 after optimal conventional management as one of the criteria for considering ECMO.[10]

Prognostication

Peak oxygenation index can also be used to predict the risk of mortality from acute respiratory failure. This has

been shown in patients across all age groups, from the neonatal to the adult population.

Neonates: A sustained (>4 hours) oxygenation index of ≥ 40 has been linked to higher mortality in neonatal respiratory failure and is often considered as a threshold for ECMO initiation.[4,7]

Pediatric patients: In children with ARDS, the peak oxygenation index measured at any time point has been shown to be an independent predictor of mortality,[11] however, no clear-cut threshold of oxygenation index has been identified to predict mortality.

Adult Patients: Among the adult population, the oxygenation index has also been shown to be a significant predictor of death and has been shown to be superior to the PF ratio.[12] However, in adult populations, modifications of the oxygenation index with inclusion of plateau inspiratory pressure and age (age-adjusted oxygenation index)

$$\text{aOI} = \frac{Plateau\ pressure \times FiO2 \times 100}{PaO2} + age$$

has been described as a better predictor of mortality. (values <60 had <25% mortality, 80–99 had ~50% mortality, and >120 had ~90% mortality).[13]

PEARLS / PITFALLS

Requires an arterial blood gas: The oxygenation index requires measurement of PaO2. This can be obtained by an arterial stick or from an indwelling arterial line. In many instances, it might be impractical to obtain an arterial blood gas. In the absence of an invasive arterial line, the oxygenation index is less feasible for continuous monitoring.

Ventilator strategy dependence: MAP is influenced by ventilator mode and settings (e.g., I: E ratio, inspiratory time, PEEP, peak/plateau pressures), so OI can change with ventilator strategy even when gas exchange remains unchanged. The same patient may have a different oxygenation index depending on pressure-control vs. volume-control settings, respiratory rate, etc. MAP on a high-frequency oscillatory ventilator (HFOV) and other settings, such as Airway Pressure Release Ventilation (APRV) (Dräger®) /Bi-Level (Maquet Servo®) ventilation, do not directly correlate with conventional mechanical ventilation settings. Thus, two patients with identical lung disease can have different oxygenation indices depending on the ventilator settings chosen. Suboptimal or excessive ventilator settings can artificially/iatrogenically inflate the oxygenation index (excessive high PEEP or MAP can induce alveolar overdistention leading to V/Q mismatch and decreased PaO2. An elevated numerator [MAP] paired with paradoxically depressed denominator [PaO2] would result in artificially high OI). Due to these limitations, adult ECMO guidelines[10]and ARDS definitions[14] rely on plateau pressure and PEEP rather than MAP.

The relationship between PaO_2 and FiO_2 is not linear: The oxygenation index assumes a linear relationship between PaO_2 and FiO_2. However, because of intrapulmonary shunt, and the complex mathematical relationship between oxyhemoglobin dissociation curve, the changes in FiO2 do not translate proportionally into PaO2, especially at higher FiO2.[15]

Not included in adult ARDS definitions: While multiple studies have shown that the oxygenation index is a predictor of mortality in adult ARDS, it is not included in the ARDS definitions.[14] Adult ARDS trials prioritize plateau pressure and PEEP as they allow clinicians to calculate driving pressure (ΔP= Pplateau−PEEP), which has been strongly related to outcomes.[16]

No single OI cutoff is mandated in modern ECMO guidelines: While prior studies of the oxygenation index showed very specific thresholds, such as 40 or 60 as criteria for ECMO,[4,7] more recent recommendations do not use a specific threshold, even in neonatal populations.[8]

Does not include hypercarbia respiratory failure. The oxygenation index is primarily used to assess the severity of hypoxemia. This only accounts for one element of gas exchange.

Lack of indicators of respiratory mechanics: By relying only on MAP, oxygenation index oversimplifies respiratory mechanics. Variables such as lung compliance, lung stress/strain, driving pressures and mechanical power are related to outcomes including mortality but are not reflected in oxygenation index .[16]

WHY USE

The oxygenation index can be rapidly calculated at the bedside and provides a simple, well-validated marker of the severity of hypoxemic respiratory failure and acute respiratory distress syndrome. It can be used to track the progress of the disease. In pediatric ARDS, the oxygenation index can be used for classification and diagnosis. It can also be used as one of the metrics to assess eligibility for ECMO.

LITERATURE

Some of the earliest references to the oxygenation index were in a 1987 paper on the use of ECMO for neonatal respiratory failure. Ortiz, Cilley, and Bartlett used the oxygenation index as a measure to predict which infants were at risk of dying or developing bronchopulmonary dysplasia.[4]They reported that an oxygenation index of more than 40 correlated with 80–90% mortality at their institution. It was again reported in the neonatal population by Ortega in 1988.[5] In this paper, the authors reviewed all neonates with FiO_2> 0.8 and mean airway pressure> 30 within the first 70 days of life from 1984 to

1986. They calculated the oxygenation index in 37 eligible neonates, with a mortality rate of 43% (16/37). Of the 21 infants who survived, seven developed bronchopulmonary dysplasia. The risk of death and death with bronchopulmonary dysplasia increased with the severity of respiratory failure. Patients with a single oxygenation index of more than 60 had 78% mortality compared to those with all oxygenation index values less than 60, who had 11% mortality. Mean airway pressure and PAO_2 – PaO_2 were less discriminatory than oxygenation index in separating favorable from unfavorable outcomes. The oxygenation index showed early identification of infants who were highly likely to die when treated with conventional therapy alone, and could be identified well in advance of the terminal event. In their study, the median time of death was 10.5 hours from their highest oxygenation index value.

While these are the first reported descriptions of the term Oxygenation Index, the specific formula was first described by Hallman as "ventilatory index".[17] This paper was a randomized controlled trial of surfactant for neonatal respiratory distress syndrome in two institutions in San Diego and Helsinki. The authors described the use of a "ventilatory index," defined as MAP × FiO_2 / PaO_2. In this study, 22 neonates were randomized to receive surfactant, and 23 were in the control group. The authors showed that the ventilatory index was significantly lower during the 48 hours after surfactant use. By the 1990s, the Oxygenation Index was an established index for neonatal respiratory failure. In 1996, a UK collaborative randomized controlled trial on neonatal ECMO was published, which used an oxygenation index of ≥ 40 as a threshold for consideration of ECMO.[7] This trial included 185 infants from 55 UK hospitals. Thirty of 93 neonates randomized to ECMO died (32% mortality) compared to 54 of 92 randomized to conventional management (58% mortality). The authors also stratified respiratory failure by oxygenation index, and those with an oxygenation index greater than 60 had higher mortality. In this cohort (≥60 OI), patients on ECMO had 44% mortality, while patients on conventional management had 67% mortality. The authors concluded that "an oxygenation index of 40 as an entry criterion seems to represent a reasonable marker of disease severity sufficient to warrant ECMO." Oxygenation index in neonatal ECMO was again studied by Bayrakci in 2007 and supported the use of ECMO for an oxygenation index of 33.2, as it was linked to higher mortality and chronic lung disease risk.[18] They found that each unit increase in oxygenation index increased mortality risk by 1%.

For older children, Trachsel et al. from Canada assessed oxygenation index as a predictor of outcome in acute hypoxemic respiratory failure in 2005.[11] The authors prospectively assessed 131 patients with acute hypoxemic respiratory failure, with an overall mortality of 27%. They reported that the peak oxygenation index measured at any time point and PRISM score within the first 12 hours of mechanical ventilation were independent predictors of mortality. However, no clear-cut threshold of oxygenation index was identified to predict mortality. The oxygenation index showed a direct correlation with outcomes in a time-independent manner.

A consensus conference in 2015 developed a pediatric ARDS definition that uses oxygenation index in preference to the P/F ratio as the primary metric of lung disease severity for all patients treated with invasive mechanical ventilation.[1] P/F ratio was recommended for noninvasive ventilation. Oxygen saturation index was recommended when the oxygenation index was unavailable, and the S/F ratio was recommended for noninvasive ventilation. Cutoffs for oxygenation index for ECMO candidates were not provided. Pediatric ARDS was classified as mild, moderate, or severe based on oxygenation index and oxygen saturation index cutoffs. This definition was updated in 2023 with minor changes to the cutoffs, but OI was again recommended in preference to P/F or S/F ratio as the primary metric of lung disease severity.[3] The 2023 PARDS consensus conference defines as oxygenation index ≥4 or oxygen saturation index ≥5 on invasive mechanical ventilation, or P/F ratio ≤300 or S/F ratio ≤250 on noninvasive ventilation. Severity classification was to be performed at least 4 hours after the initial diagnosis. For invasive mechanical ventilation, mild and moderate categories were defined as oxygenation index <16 or oxygen saturation index <12, and severe ARDS was defined as oxygenation index ≥16 or oxygen saturation index ≥12. For noninvasive ventilation, mild and moderate categories were defined as P/F ratio >100 or S/F ratio >150, while severe ARDS was defined as P/F ratio ≤100 or S/F ratio ≤150. NIV had to be delivered via full-face interface with CPAP/PEEP ≥5. Again, the No oxygenation index threshold for ECMO was provided, stating that "no evidence supports strict criteria for selection of patients who will benefit from ECMO in pediatric ARDS." A schematic summary suggested increasing support with oxygenation index from 4 to 40, with ECMO considered around 20 and strongly considered above 30.[3]

The oxygenation index has also been validated in adult patients with acute respiratory failure. Seeley et al. (2008) assessed predictors of mortality in ARDS among 149 patients, with a 41% mortality rate.[12] They found that the oxygenation index was a significant predictor of death with an adjusted odds ratio of 1.84 (CI 1.13 to 2.99) per standard deviation increase, and was superior to the P/F ratio, which was not statistically significant predictor of death on adjusted analysis (aOR1.29 [C.I 0.82 – 2.02] per standard deviation decrease). This analysis was a secondary analysis of ongoing ARDS trials conducted from 2002 to 2003. Oxygenation index was described as the best bedside surrogate for intrapulmonary shunt, one of the primary pathological derangements of ARDS. In 2016, Balzer from Berlin, Germany, assessed 442 patients

with ARDS and found that the oxygenation index was the most accurate parameter for mortality prediction.[19] An oxygenation index of more than 15 on day three after ARDS criteria were met was associated with higher mortality, longer ICU length of stay, and longer duration of mechanical ventilation. However, MAP is not routinely reported in adult ARDS literature, and modification of OI have been described. Dechert and Bartlett analyzed the association between oxygenation index in the first 4 days of ARDS and 28-day mortality across three ARDSNet databases (ALVEOLI, ARMA, FACTT) in 2014.[13] Since mean airway pressure was not available, they used plateau inspiratory pressure. The area under the curve for oxygenation index on day one for 28-day mortality was 0.61. Because age was a significant predictor of mortality in adults, they created an adjusted oxygenation index (age + oxygenation index), which increased the area under the curve to 0.74. For adjusted oxygenation index, values <60 had <25% mortality, 80–99 had ~50% mortality, and >120 had ~90% mortality. The area under the curve for the adjusted oxygenation index was higher than that for other predictors, such as the P/F ratio. In 2016, Go et al. evaluated the estimated oxygenation index (map, calculated as PIP+PEEP/2) and the change in the first 7 days among patients enrolled in the three large randomized controlled trials. They found that the 7-day change in oxygenation index correlated closely with the trial's ultimate outcome. They recommended that the seven-day oxygenation index change can be used as an intermediate outcome to select therapies for further testing in a large randomized controlled trial. However, they also noted that the seven-day oxygenation index change had limited utility in predicting mortality at the patient level.[20]

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