The "ARDS CLinIMApp™": A computerized algorithm for assessing patients with ARDS

This app was composed by Bob Demers, and was coded by Javier Morquecho, under the terms of a contract executed by Demers Consulting Services. The app is designed to calculate, accurately, precisely, and in real-time: 1) the gender-adjusted tidal volume; 2) the prevailing P/F Ratio ("P/F"); 3) the prevailing Oxygenation Factor ("OF"); and 4) the shunt level, expressed as a percentage of cardiac output, for a patient whose presumptive diagnosis is acute respiratory distress syndrome (ARDS)

The incidence of ARDS in the U.S. is quite high: "Cross-sectional studies demonstrate that patients with ARDS represent approximately 5% of hospitalized, mechanically ventilated patients" (Esteban A, Ferguson ND, Meade MO, et al. Evolution of mechanical ventilation in response to clinical research. **Am J Respir Crit Care Med**. 2008;177(2):170–177). In 2012, the American-European Consensus Conference (AECC), meeting in Berlin, Germany (The ARDS Definition Task Force. Acute respiratory distress syndrome: the Berlin definition. **JAMA**. Epub May 21, 2012), refined the definition of ARDS such that the severity of the disease is now classified in accordance with the prevailing "P/F Ratio", where that ratio is defined as the numerical value of the arterial oxygen tension (p_aO_2, expressed in torr) divided by the inspired oxygen fraction (F_IO_2, expressed as a decimal between 0.21 and 1.0). Under this classification system: 1) the patient is deemed to be free of ARDS if the P/F Ratio exceeds 300; 2) mild ARDS exists when $300 \geq P/F > 200$; 3) moderate ARDS prevails when $200 \geq P/F > 100$; and 4) severe ARDS is present when $100 \geq P/F$.

Many clinicians have expressed their dissatisfaction with the Berlin definition, owing to the "....sensitivity of the p_aO_2/F_IO_2 ratio criteria to small changes in positive end-expiratory pressure (PEEP)...." (Walkey AJ, Summer R, Vu Ho, Alkana P. Acute respiratory distress sydrome: Epidemiology and management approaches. **Clin Epidemiol** 2012; 4: 159-169 and Villar J, Perez-Mendez L, Lopez J, et al. An early PEEP/F_IO_2 trial identifies different degrees of lung injury in patients with acute respiratory distress syndrome. **Am J Respir Crit Care Med** 2007; 176(8):795–804). A group of researchers in Italy sought to address this problem by recommending that a standardized level of PEEP (5 centimeters of water) be uniformly imposed when the P/F Ratio is measured (Caironi P, Carlesso E, Cressoni M, Chiumello D, et al. Lung recruitability is better estimated according to the Berlin Definition of Acute Respiratory Distress Syndrome at standard 5 cm H_2O rather than higher positive end-expiratory pressure: A retrospective cohort study. **Crit Care Med** 2015; 43: 781-790). Although the recommendation of this group is a valiant attempt to render the process of ARDS diagnosis more consistent than it would otherwise be, their approach suffers from a major flaw. Patients with moderate or severe ARDS usually require a PEEP level considerably in excess of 5 cm H_2O to be managed optimally. Intensive Care Unit (ICU) Teams who were committed to using the method of Caironi et al would be obliged to reduce the prevailing PEEP level to 5 cm H_2O in preparation for measuring the P/F Ratio. Furthermore, the steady-state p_aO_2 would not emerge until at least seven minutes after the readjustment in PEEP (Howe JP III, Alpert JS, Rickman FD, Spackman DG, et al. Return of arterial pO_2 values to baseline after supplemental oxygen in patients with cardiac disease. **Chest** 1975; 67(3): 256-258). Indeed, this seven-minute timeframe is the <u>minimum</u> required for the attainment of steady-state conditions; in certain populations of patients, the lag time has been observed to be as long as twenty-five minutes (Cugell DW. How long should you wait? (editorial). **Chest** 1975; 67(3): 253 and Sherter CB, Jabbour SM, Kovnat DM, Snider GL. Prolonged rate of decay of arterial pO_2 following oxygen breathing in chronic airways obstruction.

Chest 1975; 67(3): 259-261). In view of the fact that the antecedent PEEP level may have far exceeded 5 cm H_2O, a reduction to that lower level would place the patient in jeopardy. Consequently, the recommendations offered by Caironi and colleagues must be viewed as supremely impractical.

Finally, intensivists are universally aware that alterations in certain other mechanical ventilatory support variables in addition to PEEP (such as inspiratory time fraction, tidal volume, prone positioning, etc.) can elicit appreciable changes in the P/F Ratio. In a monograph that was published in **Chest**, the so-called "Oxygenation Factor" (OF), a novel parameter that specifically quantifies the combined effects of various ventilatory manipulations, is defined (El-Khatib MF, Jamaleddine GW. A new oxygenation index for reflecting intrapulmonary shunting in patients undergoing open-heart surgery. **Chest** 2004; 125: 592-596). The OF is defined as the arithmetic quotient of the familiar P/F Ratio (in the numerator), and the numerical value of mean airway pressure, in centimeters of water (in the denominator). In their discussion, El-Khatib and Jamaleddine also reveal that they find the determination of intrapulmonary shunting to be a valuable assessment tool.

In order to exploit the assortment of monitoring indices that can be useful to ICU Teams that manage ARDS patients, the "ARDS CLinIMApp" has been created. It solicits various keyboard entries from the user (listed in the Appendix) and applies a combination of mathematical algorithms to those inputs. Although the P/F Ratio is defined for F_IO_2 values ranging between 0.21 and 1.0, the app requires that the user key in a value for F_IO_2 that is at least 0.35. This constraint is imposed in order to abolish the effects of diffusion defects and ventilation/perfusion mismatching that would be encountered if the F_IO_2 did not equal or exceed 0.35. In other words, this criterion for F_IO_2 is imposed in order to ensure that the shunt value which the app generates is truly and entirely ascribable to shunting, and to neither V/Q mismatching nor diffusion defects. The methodology by which shunt is determined employs a mathematical model of gas exchange which is described in detail in the "About" section of the Shunt Determination CLinIMApp™. The application ("app") then supplies a list of (digital and graphic) outputs (also enumerated in the Appendix) to the user in real-time. Notice that the app requires that the value for mean airway pressure be at least 1.0 cm H_2O which, in turn, requires that the patient is being ventilated with a positive-pressure ventilator. Hence, the app cannot be applied to spontaneously breathing patients, nor can it be implemented for patients in whom F_IO_2 is less than 0.35. In view of the fact that ARDS patients are uniformly ventilated by means of positive-pressure ventilators and that their F_IO_2 uniformly exceeds 0.35 (because of the severity of their illness), these constraints do not represent a barrier to the applicability of the app.

It is hoped that the ability of the app to dispense a broad range of physiologic indices to the members of the ICU Team will enhance their ability to assess ARDS patients in serial fashion throughout the patients' course of mechanical ventilation.

Appendix: Equations, inputs, algorithms, and outputs incorporated in the ARDS CLinIMApp

Formulas for Predicted Body Weight ("PBW"), in kilograms (retrieved from http://www.ardsnet.org/files/ventilator_protocol_2008-07.pdf on June 9th, 2015)

Males: PBW = 50.0 + ([height in inches - 60] x 2.3)
Females: PBW = 45.5 + ([height in inches - 60] x 2.3)

Formulas for Tidal Volume ("TV"), in mLs (assuming an approximate TV of 6 mL/kg)
Males: TV = (PBW for males) x 6
Females: TV = (PBW for females) x 6

Formula for "P/F ratio": P/F = p_aO_2 in torr / F_IO_2 (in decimal form)
Formula for "Oxygenation Factor" (OF): OF = p_aO_2 in torr / (F_IO_2 • mean P_{aw}), where mean P_{aw} is in cm H_2O

The app solicits the following inputs:

The following text string displays above the input fields: "This app is applicable only to patients whose height is ≥ 60 inches"

Gender (radio button for "male" or "female")

Height in inches

mean airway pressure in cm H_2O

Inputs which are required for the Shunt Determination CLinIMApp™ (arterial pH; F_IO_2 in decimal form [with $0.35 \leq F_IO_2 \leq 1.0$]; barometric pressure, in mm Hg [with a default value of 760]; arterial carbon dioxide tension, in torr; arterial oxygen tension, in torr; hemoglobin concentration, in grams per deciliter; arteriovenous oxygen content difference, in mL O_2 per deciliter of blood [with a default value of 3.50]; and body temperature, in C° [with a default value of 37°]).

The app reads out the following:

"Approximate Tidal Volume, in mLs"
"P/F ratio"
"OF"
"No ARDS" if P/F > 300;
"Mild ARDS" if 300 ≥ P/F > 200;
"Moderately severe ARDS" if 200 ≥ P/F > 100;
"Severe ARDS" if 100 ≥ P/F

The following test string displays: "Ensure that the patient's plateau pressure does not exceed 30 cm H_2O"

In addition, the graphic which displays for the Shunt Determination CLinIMApp displays below the readouts listed above. This graphic is comprised of the discrete and unique points corresponding to p_aO_2 (ordinate) versus percentage shunt (abscissa) for the prevailing F_IO_2 value.