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LETTER

Revisiting oxygen dissociation curves and bedside measured arterial saturation in critically ill children

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Dear Editor,

The oxygen dissociation curve (ODC) relates the partial pressure of oxygen in the blood (pO_2) to the hemoglobin oxygen saturation (SO_2) [1, 2]. It is crucial in determining oxygen delivery to the tissues and fundamental to critical care practice [3]. We aimed to revisit this curve in critically ill children using a large physiologic and laboratory dataset.

This study utilizes continuously recorded physiologic data (5,783,484 SpO_2 values) and blood gas tests from patients ≤ 18 years of age (3582 patients with 112,101 tests) who were admitted to the critical care unit at the Hospital for Sick Children, Toronto. Details on data capture, analyses and discussion of the results can be found in the online supplementary material.

Figure 1a–c shows the non-conditional oxygen dissociation distribution. For our patient population, the median ODC is shifted rightward from the classic report [2]. While traditionally viewed as a sigmoid line, examining our large dataset for the relation between blood pO_2 and SO_2 shows a wider distribution. To illustrate this, panels b and c show the distributions of observed SO_2 values at four fixed pO_2 levels and vice versa.

We further explored the relative shifts in the oxygen dissociation curve due to measurable modifiers (pH, pCO_2 and age). Figure 1d shows the mean oxygen saturation of patients with either a low blood pH (< 7.35) or high pH (> 7.45). We included only the subset of samples with normal pCO_2 levels to control for independent effects of pCO_2. Similarly, panels e and f show the effect of varying pCO_2 and age, respectively. Panel g shows the absolute differences between the dissociation curves in d–f for each modifier. Modifying effects of temperature were not tested as all samples are heated/cooled by the blood gas analyzer to 37 °C pre-processing.

We also compared bedside measured SpO_2 values to concurrently measured SaO_2 as extracted from the point of care arterial blood tests [4, 5]. Panel H shows the distribution of SpO_2 and SaO_2 with an overlay of the 25th–75th percentiles of SaO_2 as a function of SpO_2. For any given SpO_2 value, we observe a wide range of SaO_2 values. Moreover, SpO_2 overestimates SaO_2 by an average of ~ 4–5% over a wide range.

An interactive display of the oxygen dissociation distributions can be found at: (http://media.laussenlabs.ca/figures/oxygen-dissociation/).

To summarize, we observed a broader SO_2 distribution associated with any given pO_2, and a rightward shift relative to the original ODC. The modifying effects of pCO_2, pH and age at different pO_2 ranges differed from the classically-described rightward/leftward shift.

Interpretation of the association of SaO_2 and the PaO_2 should take into account the unmeasured confounders and this issue should be disclosed as a limitation.

Hence, the simplified and commonly-used description of a sigmoid curve and a single representative p50 value is insufficient, and a more complete, distribution-based approach is necessary. Moreover, we quantify the bias and variability between bedside SpO_2 and SaO_2. A limitation to any interpretation of hemoglobin–oxygen

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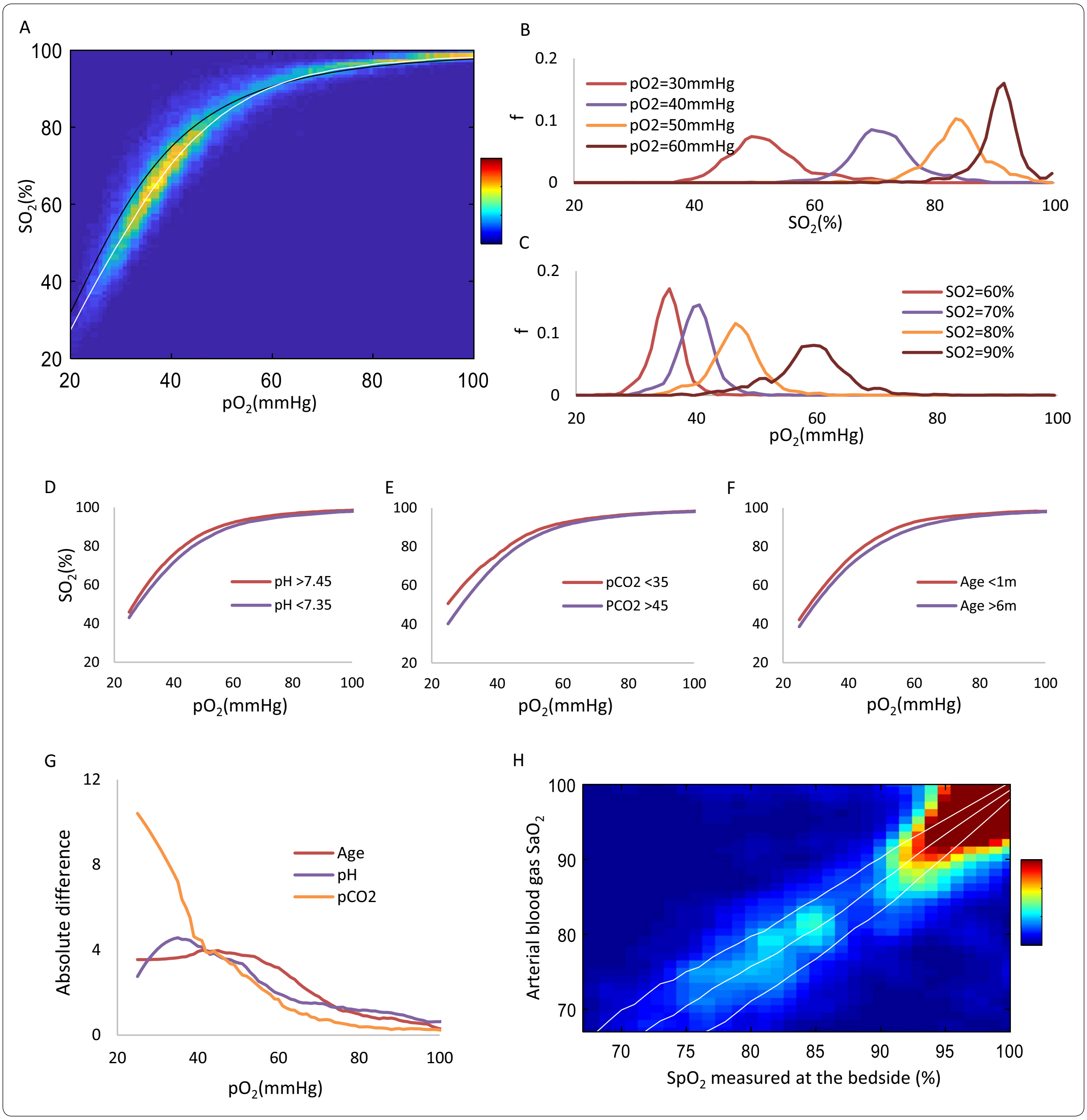
A
SO2(%)
pO2(mmHg)
B
f
pO2=30mmHg
pO2=40mmHg
pO2=50mmHg
pO2=60mmHg
SO2(%)
C
f
SO2=60%
SO2=70%
SO2=80%
SO2=90%
pO2(mmHg)
D
SO2(%)
pH >7.45
pH <7.35
pO2(mmHg)
E
pCO2 <35
PCO2 >45
pO2(mmHg)
F
Age <1m
Age >6m
pO2(mmHg)
G
Absolute difference
Age
pH
pCO2
pO2(mmHg)
H
Arterial blood gas SaO2
SpO2 measured at the bedside (%)

(See figure on previous page.)

Fig. 1 **a** The oxygen dissociation distribution (ODD). Two-dimensional distribution relating pO_2 and SO_2 derived from 112,101 blood gas tests, bin size 1 mmHg by 1%. Probability density presented using a gray colormap with higher probabilities presented using a white color. The continuous white overlaid line is the median population SO_2 for any given pO_2 value, representing the traditional portrayal of the oxygen dissociation curve for our patient population. White intermittent line shows the classic Severinghaus equation. **b** Four representative distributions of measured SO_2 levels on the blood gas tests for four different pO_2 levels (30, 40, 50, 60 mmHg, greyscale coded). Each represents the distribution as derived by passing a vertical line on the ODD presented in **a** at the four different pO_2 values. **c** Four representative distributions of measured pO_2 levels on the blood gas tests for four different SO_2 levels (60, 70, 80, 90%, greyscale coded). Each represents the distribution as derived by passing a horizontal line on the ODD presented in **a** at the four different SO_2 values. **d** Effects of pH on the oxygen dissociation distribution. Average dissociation curves relating SO_2 to pO_2 for 14,159 samples with a pH < 7.35 and a normal pCO_2 (35–45 mmHg) and 5277 samples with a pH > 7.45 and a normal pCO_2 (35–45 mmHg). **e** Effects of pCO_2 on the oxygen dissociation distribution. Average dissociation curves relating SO_2 to pO_2 for 4298 samples with a $pCO_2 < 35$ mmHg and a normal pH (7.35–7.45) and 25,967 samples with $pCO_2 > 45$ mmHg and a normal pH (7.35–7.45). **f** Effects of age on the oxygen dissociation distribution. Average dissociation curves relating SO_2 to pO_2 for 23,757 samples with patient's age at the time of sampling less than 1 month, and 56,161 samples with patient's age at the time of sampling more than 6 months. **g** Absolute differences between the mean oxygen dissociation curves. Absolute differences between the mean oxygen dissociation curves for each modifier's condition (high or low) as depicted in **d**–**f**, for each modifier (age, pH and pCO_2). **h** Comparing bedside measured SPO_2 values to concurrent SaO_2 derived from point of care preformed arterial blood gas. Two-dimensional distribution of bedside recorded SpO_2 and concurrent point of care measured SaO2 with an overlay of the 25th, 50th and 75th percentiles of SaO_2 as a function of any given bedside SPO_2. Distribution smoothed using a 2-D Gaussian smoothing kernel with standard deviation of 1, presented as a grayscale with a saturation of the scale at 0.003 to allow appreciation of the smaller number of low SpO_2 values

dissociation lies in the need to account for unmeasured confounders. Still, the fundamental interpretation for blood gas analysis so elegantly described many years ago remains valid. The era of big data analysis provides new insights into the broad distributions and conditional probabilities affecting oxygen dissociation. We believe that these observations are relevant to the fragile population of critically-ill patients in whom adequacy of oxygen delivery drives decisions.

Electronic supplementary material

The online version of this article (https://doi.org/10.1007/s00134-019-05792-x) contains supplementary material, which is available to authorized users.

Abbreviations

ODC: Oxygen dissociation curve; SpO_2: Peripheral oxygen saturation derived from the pulse oximeter; SO_2: Blood hemoglobin oxygen saturation; pO_2: Partial pressure of oxygen in the blood; pCO_2: Partial pressure of carbon dioxide in the blood.

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Compliance with ethical standards

Conflicts of interest

Peter Laussen—lead developer T3 software platform, and unpaid medical consultant Etiometry LLC, Boston, Massachusetts. None of the other authors have any conflict of interest.

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