Variable impact of pure Oxygen on Venous Admixture in COVID-19 ARDS

M. Ferrari, A. Santini, C. Mercalli, L. Pugliese, N. Martinetti, F. Dalla Corte, L. Carenzo, G.E. Iapichino, M. Cecconi, A. Protti

Dipartimento di Anestesia e Terapie Intensive – IRCCS Humanitas Research Hospital

BACKGROUND

Hypoxemia in early COVID-19 is caused by pathological venous admixture (Q_s/Q_t) due to two main factors:

i. **True shunt**, i.e. V/Q = 0
ii. **Heterogeneous distribution of ventilation and perfusion**, i.e. V/Q mismatch (V/Q between 0 and 0.8)[1].

In early COVID-19 ARDS, V/Q mismatch has been hypothesized to have a major role over true shunt in determining hypoxemia[2,3]. Increasing the fraction of inspired oxygen (FiO_2) up to 100% should not affect the amount of Q_s/Q_t due to true shunt, but should relieve V/Q mismatch, thus reducing total venous admixture.

METHODS

The study was carried out between March 2020 and March 2022 at our Institution according to local IRB policy. Patients with COVID-19 related ARDS receiving sedation, muscle paralysis and mechanical ventilation within the **first 3 days of ICU stay** were enrolled. After a recruitment maneuver and a 20-minute stabilization period, arterial and central venous blood gases were measured at clinical fraction of inspired oxygen (FiO_2); FiO_2 was then increased to 100% leaving other settings unchanged and blood gas samples were repeated after **20 minutes**. Q_s/Q_t was computed using arterial, pulmonary capillary and central venous oxygen contents as follows:

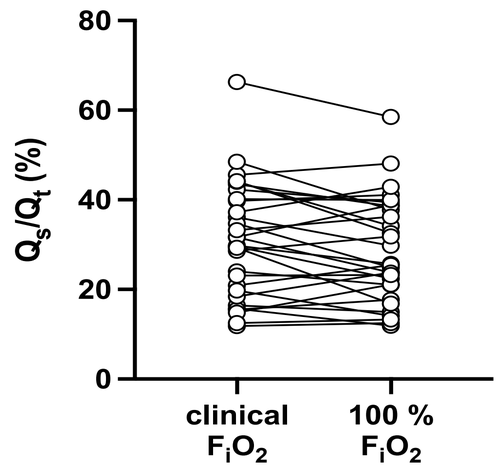
$$Q_s/Q_t = (CcO_2 - CaO_2) / (CcO_2 - CvO_2)$$

RESULTS

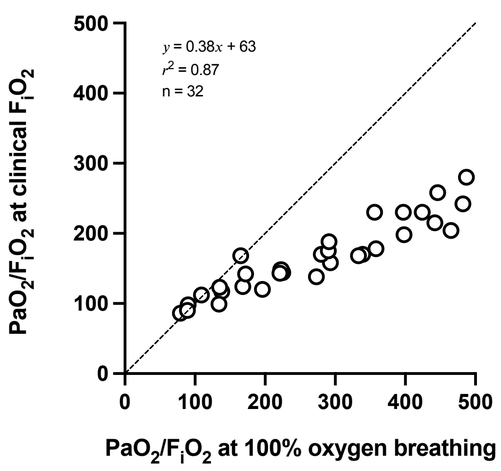
Thirty non-consecutive patients were enrolled. Average tidal volume was 6.2±0.5 ml/kg of ideal body weight and static respiratory system compliance was 46±13 ml/cmH_2O.
Q_s/Q_t values from clinical to 100% FiO_2 in the overall population **decreased** from 31±13 to 29±12 % (p=0.045, paired t-test). In 17 patients Q_s/Q_t decreased by 7±12%, in 13 patients it increased by 3±11%. The ventilatory variables of patients divided into two groups as per Qs/Qt variation are reported in Table 1.
PaO_2/FiO_2 ratio rose from 165±51 to 272±127 mmHg (p<0.0001). Central venous oxygen saturation ($ScvO_2$) also increased from 74±7 to 82±8 % with increasing FiO_2 (p<0.0001).

Table 1	Delta Q_s/Q_t < 0 (n=17)	Delta Q_s/Q_t ≥ 0 (n=13)	P value
Tidal volume (ml/kg IBW)	6.3 ±0.1	6.1 ±0.1	0.12
Respiratory rate (bpm)	20.8 ±0.9	17.8 ±0.8	0.03
Minute ventilation (L/m)	8.5 ±2.1	7.2 ±1.4	0.06
PEEP (cmH_2O)	10.6 ±0.4	10.8 ±0.9	0.85
P_{aw} plateau (cmH_2O)	21.6 ±0.9	19.9 ±1.3	0.26
Driving pressure (cmH_2O)	10.3 ±0.2	8.8 ±0.6	0.24
Resp sys compl (ml/cmH_2O)	43.7 ±3.4	47.8 ±3.7	0.42
C-reactive protein (mg/L)	12.8 ±8.7	9.7 ±8.2	0.31
D-dimer (ng/mL)	573.0 ±307.4	1485.9 ±2412.3	0.14

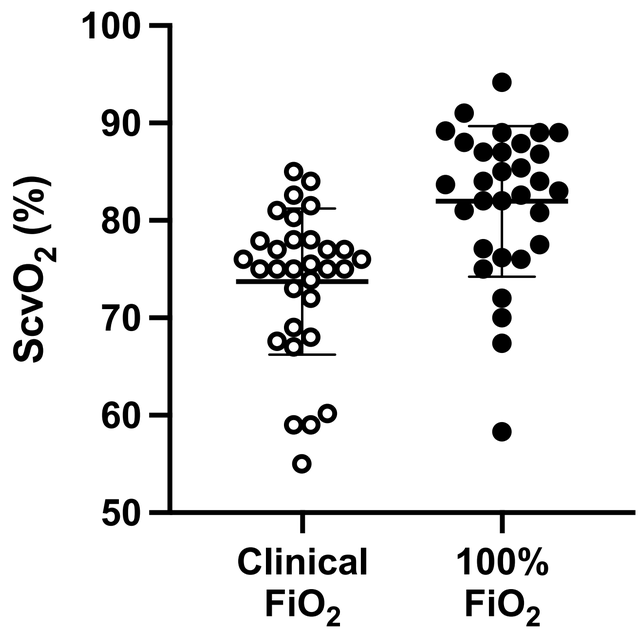
Venous admixture at clinical and 100% F_iO_2



PaO_2/F_iO_2 at clinical and 100% F_iO_2



$ScVO_2$ at clinical and 100% F_iO_2



CONCLUSIONS

When FiO_2 was increased to 100% in intubated patients with early COVID-19 pneumonia, the total pulmonary venous admixture fraction was reduced by a very small amount (2%) overall. In almost half of the patients, venous admixture increased, suggesting a negligible effect of V/Q mismatch. In patients in whom venous admixture did decrease, the reduction was quite low (7%). Our results suggest that V/Q mismatch plays only a marginal role in severe COVID-19 hypoxemia.

REFERENCES

1. RILEY RL, COURNAND A. Ideal alveolar air and the analysis of ventilation-perfusion relationships in the lungs. J Appl Physiol. 1949;1:825-847.
2. Santamarina MG, Boisier D, Contreras R, Baque M, Volpacchio M, Beddings I. COVID-19: A hypothesis regarding the ventilation-perfusion mismatch. *Critical Care*. 2020;24(1). doi:10.1186/s13054-020-03125-9
3. Gattinoni L, Coppola S, Cressoni M, Busana M, Rossi S, Chiumello D. COVID-19 does not lead to a "typical" acute respiratory distress syndrome. *American Journal of Respiratory and Critical Care Medicine*. 2020;201(10):1299-1300. doi:10.1164/rccm.202003-0817LE