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新光醫院急診 CLERK 郭峯華
VS 陳欣伶醫師
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JOURNAL READING

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The use of the pulse oximetric saturation/fraction of inspired oxygen ratio for risk stratification of patients with severe sepsis and septic shock ☆

Ary Serpa Neto MD, MSc[a,b,*], Sérgio O. Cardoso MD[a], David S.Y. Ong MD[c],
Daniel C. Espósito MD[a], Victor GM Pereira MD[a], José A. Manetta MD[a],
Arjen J.C. Slooter MD, PhD[c], Olaf L. Cremer MD, PhD[c]

[a]Department of Critical Care Medicine, ABC Medical School (FMABC), Santo André, Brazil
[b]Department of Critical Care Medicine, Hospital Israelita Albert Einstein (HIAE), São Paulo, Brazil
[c]Department of Intensive Care Medicine, University Medical Center Utrecht, Utrecht, The Netherlands

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Introduction

- Severe sepsis and septic shock are commonly complicated by acute hypoxic respiratory failure

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- Acute hypoxic respiratory failure : low PaO_2 to fraction of inspired oxygen (FIO_2) (P/F) ratio.
- 1994 American European Consensus Conference: P/F ratios ≤300 and≤ 200 are used to define acute lung injury and acute respiratory distress syndrome (ARDS)

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- PaO_2 correlate with pulse oximetric saturation (SpO_2) for saturations in the range of 80% to 100% .
- SpO_2 /FIO_2 (S/F) ratio have recently been determined to assist in the diagnosis of acute lung injury and ARDS

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- The aims of this study : S/F ratio in patients with severe sepsis and septic shock could predict hospital mortality and to compare its prognostic power of P/F ratio.

Methods

- 2-center retrospective cohort study conducted between 2008 and 2009 in a mixed 11-beds ICU in a University Hospital in Brazil and between 2011 and 2012 in a mixed 32-bed ICU in a university hospital in the Netherlands.

Study population

- Patients: older than 18 years, who were admitted to the ICU with severe sepsis or septic shock.

Measurements and data collection

- record demographic data (age, sex, site of origin before ICU arrival), chronic comorbidities (chronic heart failure and chronic pulmonary obstructive disease)
- Data : first available ABG draw, ≤ 8 hours following arrival in the ICU.

- SpO2 accuracy improvement

Statistical analysis

- The S/F ratio is analyzed by tertiles.
- Differences in S/F ratio between survivors and nonsurvivors were analyzed using the Mann-Whitney rank sum test.
- Survival analysis using Cox proportional hazard models.
- Severity of illness assessed by APACHE IV score

- The correlation between S/F ratio and P/F ratio : Pearson correlation coefficient and graphically by a scatter plot.
- ROC curves : assess the degree of discrimination between P/F ratio < 100 and P/F ratio >300.
- The comparison of variables between tertiles of S/F ratio was conducted by analysis of variance.
- cutoff values found by Rice et al .

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Results

- 273 patients met the inclusion criteria during the study period. 13 were excluded due to incomplete follow-up.

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Table 1 Baseline characteristics of the study patients stratified by S/F tertile

Patient characteristics	All patients (n = 260)	Tertile 1 [b] (n = 86)	Tertile 2 [c] (n = 86)	Tertile 3 [d] (n = 88)	P
	No. (%) of patients [a]				
Age, y (mean ± SD)	62.80 ± 15.03	62.26 ± 12.10	60.06 ± 16.64	66.47 ± 15.00	.061
Female sex	102 (39.2)	30 (34.8)	32 (37.2)	40 (45.4)	.030
Baseline P/F ratio (mean ± SD)	232.99 ±119.8	163.94 ± 110.1	222.52 ± 110.6	299.32 ± 89.46	<.0001
Baseline S/F ratio (mean ± SD)	201.29 ± 72.62	123.81 ± 27.24	199.97 ± 21.71	278.31 ± 50.80	<.0001
SOFA score (mean ± SD)	10.89 ± 6.16	11.34 ± 5.36	11.27 ± 8.31	10.08 ± 4.37	.338
APACHE IV score (mean ± SD)	83.58 ± 29.96	87.05 ± 30.41	84.45 ± 29.69	78.66 ± 29.39	.310
Arterial pH	7.32 ± 0.13	7.31 ± 0.13	7.32 ± 0.16	7.34 ± 0.12	.280
Paco2, mm Hg	42.41 ± 14.42	46.86 ± 16.56	40.63 ± 10.92	39.82 ± 15.00	.002
HCO3, mEq/L	22.05 ± 6.54	23.05 ± 6.29	21.65 ± 6.48	21.45 ± 7.12	.227
Arterial lactate, mmol/L	3.32 ± 3.63	3.44 ± 4.57	3.71 ± 3.89	2.61 ± 2.07	.182
Fio2, %	53.46 ± 20.21	75.99 ± 17.5	48.27 ± 5.66	35.70 ± 5.70	<.0001
Pulse oximetry, %	94.35 ± 8.42	90.90 ± 13.53	95.38 ± 3.49	96.56 ± 2.45	<.0001
Alveolar-arterial gradient, mm Hg	275.49 ± 157.26	407.00 ± 130.31	254.18 ± 108.3	180.94 ± 138.44	<.0001
Chronic comorbidities					
Chronic heart failure	51 (19.6)	9 (10.4)	19 (22.0)	23 (26.1)	.052
COPD	48 (18.4)	17 (19.7)	15 (17.4)	16 (18.1)	.213
Condition					
Septic shock	215 (82.6)	73 (84.8)	67 (77.9)	75 (85.2)	.092
Mortality					
In-ICU	63 (25)	27 (31.3)	17 (19.7)	15 (17)	.352
In-hospital	72 (28)	31 (36)	21 (24.4)	21 (23.8)	.046
Length of stay, median (IQR) (h)					
ICU	174.5 (93.2-353.2)	202.5 (97-445)	182 (72-354)	140 (83-291)	.092
Hospital	432 (240-846)	444 (264-942)	432 (240-768)	408 (204-768)	.825

COPD indicates chronic obstructive pulmonary disease; IQR, interquartile range.
[a] Unless otherwise indicated.
[b] S/F less than 164.
[c] S/F 164 to 236.
[d] S/F more than 236.

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- the mean S/F and P/F ratio was 201.29 (SD, 72.62) and 232.99 (SD, 119.8),
- patients with S/F more than 236 (n =88) constituted the upper tertil (reference group),
- patients with S/F between 164 and 236 (n = 86) and S/F less than 164 (n = 86) made up the middle and lower tertiles.

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- Characteristics of the patients stratified by the severity of disease and according to cutoff values found by Rice et al are shown in.

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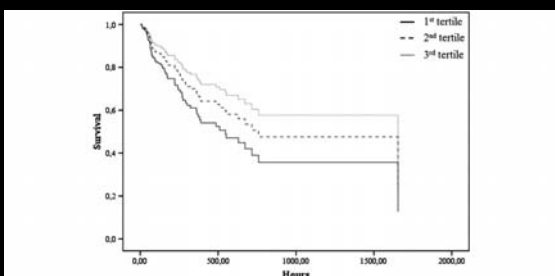### Association between S/F ratio and mortality

Fig. 1 Cox survival curves, adjusted for APACHE IV, are shown for S/F tertiles at ICU admission. First tertile (black line), second tertile (black dotted line), and third tertile (gray line).

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Crude and adjusted hazard ratios (HRs) were calculated relative to the highest tertile of S/F ratio. All HRs are presented with 95% CIs.

- Lower S/F ratio tertile predicted in-hospital mortality.

Table 2 Hazard ratio (95% CIs) for death according to S/F ratio tertiles

S/F ratio	Adjusted HR vs tertile 3 and cutoff >241
Tertiles	
2	1.351 (0.720-2.537)
1	1.871 (1.026-3.413)
Cutoff	
241-192	1.704 (0.769-3.778)
192-154	1.641 (0.659-4.082)
<154	2.054 (1.107-3.813)

Adjusted for APACHE IV.

Stratification by disease severity

- In patients with severe sepsis, the differences in mortality among tertiles of S/F did not reach statistical significance (Figure E1).
- patients with septic shock, those in the lower tertile of S/F ratio had increased mortality compared with those in the reference group (HR, 2.04 [95% CI, 1.05-3.94]; P = .034) (Figure E2).

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Fig. 2 shows adjusted HRs for death, stratified by subgroup of patients.

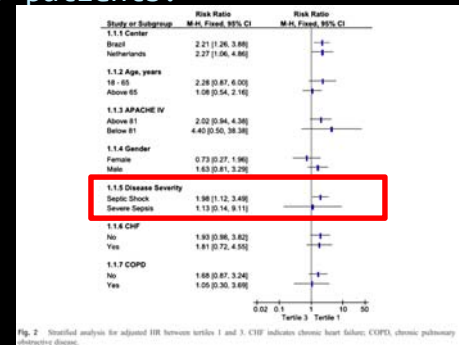| Study or Subgroup	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
1.1.1 Center		
Brazil	2.21 [1.26, 3.88]	
Netherlands	2.27 [1.06, 4.86]	
1.1.2 Age, years		
18 - 65	2.28 [0.87, 6.00]	
Above 65	1.08 [0.54, 2.16]	
1.1.3 APACHE IV		
Above 81	2.02 [0.94, 4.36]	
Below 81	4.40 [0.50, 38.38]	
1.1.4 Gender		
Female	0.73 [0.27, 1.96]	
Male	1.63 [0.81, 3.29]	
1.1.5 Disease Severity		
Septic Shock	1.98 [1.12, 3.48]	
Severe Sepsis	1.13 [0.14, 9.11]	
1.1.6 CHF		
No	1.93 [0.98, 3.82]	
Yes	1.81 [0.72, 4.55]	
1.1.7 COPD		
No	1.68 [0.87, 3.24]	
Yes	1.05 [0.30, 3.69]	

Fig. 2 Stratified analysis for adjusted HR between tertiles 1 and 3. CHF indicates chronic heart failure; COPD, chronic pulmonary obstructive disease.

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- According to S/F cutoffs found by Rice et al , patients in the lower tertile (< 235) showed increased mortality compared with those in the reference group (HR, 5.016 [95% CI, 1.50-16.67]; P = .009).

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Correlation between S/F and P/F ratio

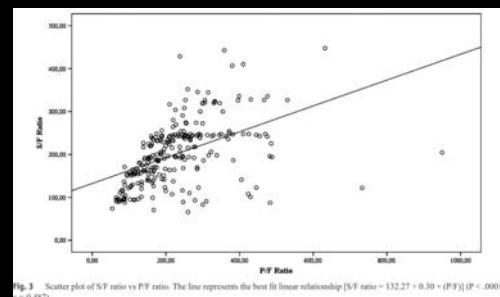- A scatter plot of concurrent S/F and P/F measurements at ICU admission.

Fig. 3   Scatter plot of S/F ratio vs P/F ratio. The line represents the best fit linear relationship [S/F ratio = 132.27 + 0.30 × (P/F)] (P < .0001; r = 0.487).

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- S/F ratio = 132.27 + 0.30 × (P/F) [95% CI, S/F = (115.22 −149.31) + (0.235 – 0.367) × P/F] (P < .0001; r = 0.48)
- excellent ability to discriminate between patients with or without severe hypoxemia (P/F ratio b 100; area under the curve, 0.926) and
- excellent ability to discriminate : with or without hypoxemia (P/F ratio N 300; area under the curve, 0.743).

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linear regression equation

- S/F ratio154-241
- P/F ratio 100-300

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Discussion

- increases in the HR of death with decreasing S/F ratio tertiles appeared to be independent of severity of illness.
- first study on the use of the S/F ratio as independent predictor of mortality in adult septic shock patients.

- significant correlation between S/F and P/F ratios at ICU admission.
- represent the first study of the relationship between SpO_2 and PaO_2 in critically ill patients with sepsis.

- Limitations of SpO_2 monitoring : patient's race, oximeter location, and low cardiac output states or methemoglobinemia .
- The " gold standard " for arterial oxygenation determination : PaO_2 , influenced by patients' agitation, position, and endotracheal suctioning .

- decrease inappropriate use of blood in ICU patients and to increase the use of invasive techniques.

- The advantages of the S/F ratio in the diagnosis
- Many organ failure scores use P/F ratios
- Using S/F ratio as a surrogate measure of hypoxemia.

- Pandharipande et al : total Sequential Organ Failure Assessment (SOFA) scores calculated with S/F ratio are highly correlated with the total SOFA scores calculated with the P/F ratio.
- Leteurtre et al : S/F ratio could be used instead of P/F for calculating Pediatric Index of Mortality 2.

limitation

- retrospective cohort study

- undocumented confounders.
- directly affect the P/F ratio

Conclusions

- low S/F ratio upon ICU admission is associated with an increased risk of mortality in patients presenting with septic shock.