technique is performed very early. Transcranial Doppler ultrasound, which can be repeated as often as needed, may be an option capable of securing earlier detection.[1,2,10]

References

1. Rommel O, Niedeggen A, Tegenthoff M, Kiwitt P, Bötel U, Malin J. Artery injury following severe head or cervical spine trauma. Cerebrovasc Dis. 1999;9:202–9.
2. Srinivasan J, Newell DW, Sturzenegger M, Mayberg MR, Winn HR. Transcranial Doppler in the evaluation of internal carotid artery dissection. Stroke. 1996;27:1226–30.
3. Wang GM, Xue H, Guo ZJ, Yu JL. Cerebral infarct secondary to traumatic internal carotid artery dissection. World J Clin Cases. 2020;8:4773–849.
4. Kowalski RG, Haarbauer-Krupa JK, Bell JM, Corrigan JD, Hammond FM, Torbey MT, et al. Acute ischemic stroke after moderate to severe traumatic brain injury: incidence and impact on outcome. Stroke. 2017;48:1802–9.
5. Aries MJ, De Jong BM, Uyttenboogaart M, Regtien JG, van der Naalt J. Traumatic cervical artery dissection in head injury: the value of follow-up brain imaging. Clin Neurol Neurosurg. 2010;112:691–4.
6. Paiva WS, Morais BA, de Andrade AF, Teixeira MJ. Mild traumatic brain injury associated with internal carotid artery dissection and pseudoaneurysm. J Emerg Trauma Shock. 2018;11:151.
7. Esnault P, Cardinale M, Boret H, D'Aranda E, Montcriol A, Bordes J, et al. Blunt cerebrovascular injuries in severe traumatic brain injury: incidence, risk factors, and evolution. J Neurosurg. 2017;127:16–22.
8. Miller PR, Fabian TC, Croce MA, Cagiannos C, Williams JS, Vang M, et al. Prospective screening for blunt cerebrovascular injuries: analysis of diagnostic modalities and outcomes. Ann Surg. 2002;236:386–93.
9. Robba C, Taccone FS. How I use Transcranial Doppler. Crit Care. 2019;23:420.
10. Bouzat P, Francony G, Brun J, Lavagne P, Picard J, Broux C, et al. Detecting traumatic internal carotid artery dissection using transcranial Doppler in head-injured patients. Intensive Care Med. 2010;36:1514–20.

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Validation of the P/FPE index in a cohort of patients with ARDS due to SARS-CoV-2

Validación del índice P/FPe en una cohorte de enfermos con SDRA secundario a SARS-CoV-2

Based on the limitations that the partial pressure arterial oxygen (PaO_2)-fraction of inspired oxygen (FiO_2) ratio shows in the classification of severity in patients with acute respiratory distress syndrome (ARDS),[1] recently, Martos-Benítez et al.[2] assessed the severity of ARDS using the FiO_2-adjusted PaO_2 and positive end-expiratory pressure (PEEP): PaO2/(FiO_2 x PEEP) or P/FPE ratio.[3] Due to the differences between ''traditional'' ARDS and ARDS due to COVID-19 (C-ARDS) like the underlying cause, mechanism of pulmonary lesion, clinical presentation, and therapeutic management,[4] we believe that the hypothesis that the utility of the P/FPE ratio to predict mortality in C-ARDS is not the same for patients with ''traditional'' ARDS.

A cohort of 507 patients with C-ARDS treated at Hospital Universitario Marqués de Valdecilla, Santander, Spain, and another cohort of 217 patients with ''traditional'' ARDS previously published by Martos-Benítez et al.[2] were studied using the inclusion and exclusion criteria described by them. In both cases, the registries used had been accepted by the local Research Ethics Committee of each center. In the Spanish series, informed consent from the patients/legal representatives (written or over the phone) was required. In the Cuban series consent was not required due to the retroactive nature of the data collected. The severity of ARDS was evaluated within the first 24 h after starting invasive mechanical ventilation with the patient while in the supine position. All individuals were categorized as having mild, moderate or severe ARDS according to the Berlin definition.[5] Based on the P/FPE ratio, patients were categorized into mild ($40 <$ P/FPE ratio ≤ 60), moderate ($20 <$ P/FPE ratio ≤ 40) or severe ARDS (P/FPE ratio ≤ 20).

Descriptive statistics and a multivariate logistics regression analysis to explore the impact of ventilatory configurations and respiratory indices on in-hospital mortality were used. The area under the operator receiving characteristics curve (AUC) was used to assess the performance of respiratory indices. A multivariate logistics regression analysis was used to explore the impact of respiratory indices with the following primary endpoint: 28-day mortality rate. To inter-

DOI of refers to article: https://doi.org/110.1016/j.medin.2023.03.008

Table 1 Main clinical-demographic variables, severity indices, ventilatory and evolutionary parameters of the cohort of patients analyzed, C-ARDS.

	C-ARDS, N = 506
Variable	
Age, years	65 (56–72)
Sex, man	352 (69.6%)
Obesity	88 (17.3%)
AHT	235 (46.4%)
DM	101 (19.9%)
Length of stay prior to ICU admission	0 (0–2)
Reason for admission: respiratory failure	500 (98.8%)
Severity indices	
SOFA score	5 (4–6)
PaO_2/FiO_2 ratio	110 (90–134)
P/FPE ratio	9 (7–12)
Main ventilatory parameters within the first 24 h after starting MV	
TV/kg	6.1 (5.9–6.4)
PEEP	11 (10–12)
Respiratory rate	18 (16–18)
Peak pressure	29 (26–31)
Plateau pressure	22 (20–25)
Driving pressure	11 (9–14)
Evolutionary variables	
Use of vasoactive drugs	286 (56.5%)
Use of the PRONE position	268 (52.9%)
Duration of MV, days	10 (7–18)
ICU stay, days	13 (9–23)
28-day mortality rate	74 (14.6%)
In-hospital mortality	109 (22.2%)

AHT, arterial hypertension; DM, diabetes mellitus; MV, mechanical ventilation; SOFA, Sepsis related Organ Failure Assessment; TV, tidal volume.

pret the results the following covariables were included: the characteristics that showing significant differences in the bivariate analysis would not show any muticollinearity issues (assessed with a Variance Inflation Factor (VIF) < 3). The models analyzed are expressed as odds ratio (OR) with its 95% confidence interval (95%CI).

The characteristics of the 506 patients from the cohort of patients with C-ARDS are shown on Table 1. The median of the PaO_2/FiO_2 ratio in the C-ARDS cohort was 110 mmHg (p25–75: 90–134 mmHg) vs 187 mmHg (p25–75: 117–221 mmHg) in the ''traditional'' ARDS cohort. The median of the P/FPE ratio was 9.5 (p25–75: 7.2–12.16) in the C-ARDS group vs 21.6 (p25–75: 10.2–33.2) in the traditional'' ARDS cohort. Same as it happened in the cohort of patients with ''traditional'' ARDS described by Martos-Benítez et al.[2] in patients with C-ARDS, the P/FPE ratio was reclassified in most patients into a different category of severity compared to the Berlin classification (Table 2). In the logistics regression multivariate analysis, the P/FPE ratio was not associated with in-hospital mortality in the C-ARDS cohort (odds ratio [OR], 0.97; 95%CI, 0.93–1.01; $P = .187$), but it was indeed associated with a lower mortality rate in the cohort of patients with ''traditional'' ARDS (OR, 0.93; 95%CI, 0.89–0.97; $P = .001$). Same as it happened with ''traditional'' ARDS, conduction pressure (OR, 1.09; IC95%:1.00–1.20; $P = .046$) and the SOFA value (OR, 1.75; 95%CI, 1.26–2.43; $P < .01$) kept a significant correlation with mortality. In the C-ARDS cohort, the P/FPE ratio in term of AROC was 0.54 (95%CI, 0.49–0.58) vs 0.52 (95%CI, 0.47–0.56) of the PaO_2/FiO_2 ratio. In the ''traditional'' ARDS cohort, the P/FPE ratio in term of AROC was 0.72 (95%CI, 0.65–0.78) vs 0.63 (95%CI, 0.54–0.69) of the PaO_2/FiO_2 ratio.

These results prove that the P/FPE ratio behaves different when it comes to predicting mortality between patients with ''traditional'' ARDS and those with C-ARDS. Also, the clinical-epidemiological characteristics of both groups, and the reasons for this difference can be explained by the severity of hypoxemia (wrongfully called ''happy hypoxemia''), and the heterogeneity of pulmonary damage in patients with C-ARDS compared to patients with ''traditional'' ARDS due to the microthrombotic component of COVID-19, and the predominant change of the hypoxic pulmonary vasoconstriction reflex.[6] This heterogeneity could lead to lower values of the P/FPE ratio in patients with C-ARDS.[7]

The addition of the PEEP value to the PaO_2/FiO_2 ratio seems appealing because it takes into account the compliance of the respiratory system, as well as pulmonary recruitment.[8] Therefore, it can be useful to identify patients with ARDS who may benefit from individual therapies.[9,10] However, in patients with C-ARDS, both the PaO_2/FiO_2 and the P/FPE ratios do not perform well when it comes to predicting the in-hospital mortality rate. We should double down to identify better predictors in this group of patients.

Table 2 Classification of the cohort of patients studied based on their severity according to the Berlin classification and the P/FPE ratio within the first 24 h after starting MV.

Patients with C-ARDS				
	Patients with ARDS based on the Berlin criteria on mechanical ventilation day 1, N = 506			
	Mild ARDS, N = 44 (9%)	Moderate ARDS, N = 327 (65%)	Severe ARDS, N = 135 (26%)	
Severity based on the P/FPE ratio	**Mild, N = 5 (1%)**	2 (4%)	1 (< 1%)	2 (1%)
	Moderate, N = 13 (3%)	4 (9%)	8 (2%)	1 (< 1%)
	Severe, N = 488 (96%)	38 (86%)	318 (97%)	132 (98%)

Funding

None reported.

Conflicts of interest

None whatsoever.

References

1. González-Castro A, Cuenca Fito E, Gonzalez C. Acute respiratory distress syndrome: a definition on the line. Med Intensiva (Engl Ed). 2023;3, http://dx.doi.org/10.1016/j.medine.2023.01.001. S2173-5727(23)00001-00002.
2. Martos-Benítez FD, Estévez-Muguercia R, Orama-Requejo V, Del Toro-Simoni T. Prognostic value of the novel P/FPE index to classify ARDS severity: a cohort study. Med Intensiva (Engl Ed). 2022;4, http://dx.doi.org/10.1016/j.medine.2022.06.023. S2173-5727(22)00309-5.
3. Villar J, Pérez-Méndez L, Basaldúa S, Blanco J, Aguilar G, Toral D, et al. A risk tertiles model for predicting mortality in patients with acute respiratory distress syndrome: age, plateau pressure, and P(aO(2))/F(IO(2)) at ARDS onset can predict mortality. Respir Care. 2011;56:1774–9, http://dx.doi.org/10.4187/respcare.01113.
4. Gattinoni L, Coppola S, Cressoni M, Busana M, Rossi S, Chiumello D. COVID-19 does not lead to a ''typical'' acute respiratory distress syndrome. Am J Respir Crit Care Med. 2020;201:1299–300, http://dx.doi.org/10.1164/rccm.202003-0817LE.
5. Ranieri VM, Rubenfeld GD, Thompson BT, Ferguson ND, Caldwell E, Fan E, et al. ARDS Definition Task Force. Acute respiratory distress syndrome: the Berlin Definition. JAMA. 2012;307:2526–33, http://dx.doi.org/10.1001/jama.2012.5669.
6. Gupta S, Hayek SS, Wang W, Chan L, Mathews KS, Melamed ML, et al. STOP-COVID Investigators. Factors associated with death in critically ill patients with coronavirus disease 2019 in the US. JAMA Intern Med. 2020;180:1436–47, http://dx.doi.org/10.1001/jamainternmed.2020.3596.
7. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020;395:497–506, http://dx.doi.org/10.1016/S0140-6736(20)30183-5.
8. Wu C, Chen X, Cai Y, Xia J, Zhou X, Xu S, et al. Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China. JAMA Intern Med. 2020;180:934–43, http://dx.doi.org/10.1001/jamainternmed.2020.0994.
9. Palanidurai S, Phua J, Chan YH, Mukhopadhyay A. P/FP ratio: incorporation of PEEP into the PaO2/FiO2 ratio for prognostication and classification of acute respiratory distress syndrome. Ann Intensive Care. 2021;11:124, http://dx.doi.org/10.1186/s13613-021-00908-3.
10. Chiumello D, Cressoni M, Carlesso E, Caspani ML, Marino A, Gallazzi E, et al. Bedside selection of positive end-expiratory pressure in mild, moderate, and severe acute respiratory distress syndrome. Crit Care Med. 2014;42:252–64, http://dx.doi.org/10.1097/CCM.0b013e3182a6384f.

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