Predictors of invasive mechanical ventilation use in patients with acute decompensated pulmonary hypertension admitted to the intensive care unit

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To the Editor:

In acute decompensated pulmonary hypertension (ADPH) patients, invasive mechanical ventilation (IMV) use remains challenging, because it has deleterious haemodynamic effects on the right ventricle (RV), which can result in haemodynamic collapse and cardiac arrest [1, 2]. IMV may decrease RV function by reducing RV preload and raising the pulmonary vascular resistance and RV afterload, both decreasing cardiac output. When the compensatory mechanisms are exhausted, ventriculoarterial uncoupling occurs, with drops in cardiac index and pulmonary pressures, as well as increases in central venous pressure, late markers of RV failure and imminent cardiovascular demise [3]. Therefore, unless absolutely required, endotracheal intubation and IMV are strongly advised against [4, 5].

The aim of our study was to identify early predictors of the use IMV in patients with ADPH. Identification of these predictors can minimise complications and supports decision-making about the use of IMV or palliative care.

We conducted a secondary analysis of a larger multicentre retrospective cohort, which included adults with both pulmonary arterial hypertension (PAH) and chronic thromboembolic pulmonary hypertension who were admitted, unplanned, to the intensive care unit (ICU) due to ADPH [6]. ADPH was defined by low cardiac output and/or RV failure [7]. Patients who had previously made the decision to forgo life-sustaining therapies (do-not-resuscitate orders) were excluded. The data for this study were collected from electronic healthcare records spanning the period between January 2014 and December 2019.

To identify predictors for IMV use, we conducted univariate analysis and developed a multivariable logistic regression model. Variables with $p<0.05$ in univariate analysis were included in the multivariable logistic regression model employing the backward conditional method of logistic regression. There were no missing data for any of the variables of interest. Categorical and continuous data are presented as frequencies (percentages) and median (25–75% interquartile range (IQR)). Categorical variables were compared using the Chi-squared test or Fisher's exact test. Continuous variables were compared using the Mann–Whitney test. Odds ratios and 95% confidence intervals were used to measure the association between each variable and renal replacement therapy use. Data analysis was done using Statistical Package for SPSS software (version 23.0; IBM, Armonk, NY, USA).

74 patients with ADPH were included and 11 (14.9%) patients required IMV during the first 48 h of ICU stay. The median (IQR) age was 47 (35–65) years; 75.7% of the patients were female; and 64.9% had group 1 pulmonary hypertension. Baseline and ICU admission data are depicted in table 1. Most common reasons for ADPH were infection (48.6%), hypervolaemia (18.9%) and arrhythmia (8.1%), and in 20.2% of cases no clear cause for ADPH was identified. No cases of acute pulmonary embolism were documented.

Patients in the IMV group were mainly classified as high-risk pulmonary hypertension based on European Respiratory Society/European Society of Cardiology pulmonary hypertension risk assessment (a scoring

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TABLE 1 Patient characteristics before and at admission to the intensive care unit

	All patients	Needed IMV	No IMV	p-value
Patients	74	11	63	
Age (years)	47 (35–56)	37 (31–47)	47 (38–55)	0.61
Female	56 (75.7)	9 (81.8)	47 (74.6)	0.99
PH group				0.99
PAH	48 (64.9)	7 (63.6)	41 (65.1)	
CTEPH	26 (35.1)	4 (36.4)	22 (34.9)	
PH risk assessment				0.03
Low	8 (10.8)	1 (12.5)	7 (11.1)	
Intermediate	44 (59.5)	3 (27.3)	41 (65.1)	
High	22 (29.7)	7 (63.6)	15 (23.8)	
Haemodynamics				
Mean PAP (mmHg)	55 (50–66)	59 (53–65)	55 (49–67)	0.48
PVR (Woods units)	13.0 (8.2–17.0)	12.0 (6.7–13.5)	13.6 (8.4–19.4)	0.86
PAWP (mmHg)	11 (9–15)	14 (11–15)	11 (9–15)	0.14
Right atrial pressure (mmHg)	17 (10–21)	17 (15–19)	16 (10–21)	0.41
Cardiac output ($L \cdot min^{-1}$)	3.7 (2.7–4.3)	3.5 (3.0–3.6)	3.7 (2.7–4.3)	0.40
Charlson index				0.75
0–1	43 (58.1)	7 (63.6)	36 (57.1)	
⩾2	31 (41.9)	4 (36.4)	27 (42.9)	
SOFA	7 (5–8)	9 (8–12)	6 (4–8)	<0.01
Respiratory SOFA	2 (2–2)	2 (2–2)	2 (2–2)	0.19
Non-respiratory SOFA	5 (3–6)	7 (6–10)	4 (3–6)	<0.01
SAPS 3	51 (45–57)	50 (48–52)	51 (41–57)	0.75
P_{aO_2}/F_{IO_2}	144 (89–221)	126 (92–130)	148 (86–219)	0.54
S_{pO_2}/F_{IO_2}	189 (160–310)	180 (168–186)	198 (160–311)	0.45
Respiratory rate	22 (18–25)	22 (21–23)	22 (18–24)	0.47
S_{cvO_2} (%)	61.4 (52.6–68.8)	54.3 (50.5–61.2)	63.2 (53.0–70.3)	0.69
Arterial lactate ($mg \cdot dL^{-1}$)	17 (12–23)	11 (9–20)	18 (13–23)	0.79
BNP ($pg \cdot mL^{-1}$)	647 (331–1058)	650 (417–863)	611 (380–1216)	0.66
Creatinine ($mg \cdot dL^{-1}$)	1.54 (1.02–2.36)	2.00 (1.10–3.93)	1.51 (1.02–2.37)	0.47
Length of hospital stay (days)	8 (4–18)	2 (2–7)	9 (5–14)	<0.01
In-hospital mortality	30 (40.5)	11 (100)	19 (30.1)	<0.01

Data are presented as n, median (interquartile range) or n (%), unless otherwise stated. IMV: invasive mechanical ventilation; PH: pulmonary hypertension; PAH: pulmonary arterial hypertension; CTEPH: chronic thromboembolic PH; PAP: pulmonary arterial pressure; PVR: pulmonary vascular resistance; PAWP: pulmonary artery wedge pressure; SOFA: sequential organ failure assessment; SAPS: Simplified Acute Physiology Score; P_{aO_2}: arterial oxygen tension; F_{IO_2}: inspiratory oxygen fraction; S_{pO_2}: peripheral oxygen saturation; S_{cvO_2}: central venous oxygen saturation; BNP: brain natriuretic peptide.

system that predicts 1-year mortality of patients with pulmonary hypertension) (63.6% *versus* 23.8%, p=0.03) and had a higher sequential organ failure assessment (SOFA) score upon ICU admission (median 9 (IQR 8–12) *versus* 6 (4–8), p<0.01). Hypoxaemia was common during ICU admission, median (IQR) arterial oxygen tension (P_{aO_2})/inspiratory oxygen fraction (F_{IO_2}) was 144 (89–221). Nonrespiratory (NR)-SOFA represents SOFA without the respiratory components and was significantly higher in the IMV group compared to the non-IMV group (median 7 (IQR 6–10) *versus* 4 (3–6), p<0.01).

In our sample, the most common reasons for IMV were worsening hypoxia (54.5%), respiratory distress (18.2%), cardiac arrest (18.2%) and hypercapnia (9.0%). ICU mortality of patients who required IMV was 100%. The IMV group had a shorter hospital stay (2 days) compared to the non-IMV group (9 days); of note, 54.5% of patients in the IMV group had a cardiac arrest following intubation.

All IMV patients in our unit were ventilated with protective ventilation to reduce lung stress (low tidal volumes up to $6\ mL \cdot kg^{-1}$, limitation of plateau pressure <30 cmH_20 and driving pressure <15 cmH_20), normocapnia and prone positioning when indicated (P_{aO_2}/F_{IO_2} ratio <150) [8].

Of note, during the time of this study, high-flow nasal cannula (HFNC) was unavailable and extracorporeal membrane oxygenation (ECMO) was rarely accessible.

NR-SOFA score and pulmonary hypertension risk assessment (independent variables) and IMV (dependent variable) were included in a multivariable logistic regression model. Higher NR-SOFA score was associated with increased IMV use (OR 1.77, 95% CI 1.21–2.57), while pulmonary hypertension risk assessment was not significantly associated with IMV use. The area under the receiver operating characteristic curve of the NR-SOFA score to predict IMV was 0.83 (0.71–0.95, p<0.01), suggesting good discrimination. In a sensitivity analysis, neither pulmonary hypertension group nor subtype of PAH had a significant impact on the use of IMV in our cohort.

The respiratory component of SOFA was similar between IMV group and non-IMV group, which is explained by the fact patients were similarly hypoxic at admission. NR-SOFA was heavily influenced by the cardiovascular component, reflecting more use of inotropes and vasopressors in the IMV group before intubation, and also influenced by acute kidney failure, highly prevalent on ICU admission.

Use of IMV was noted to be associated with poor prognosis and elevated mortality in many cohorts [6, 9, 10, 11]. In-hospital mortality was 100% in the IMV group in our cohort, similar to the 100% mortality of IMV patients described by Campo *et al.* [9]. In the study by Sztrymf *et al.* [12], no patient underwent IMV in the study period, as the authors stipulated that no intubations would be performed due to the poor prognosis associated with IMV. In spite of poor prognosis related to IMV, carefully selected patients with potentially reversible acute RV dysfunction could be considered for IMV [13].

The high mortality observed in the IMV group was explained by peri-intubation cardiac arrest, but probably reflects that sicker patients tend to receive IMV. NR-SOFA offers an appropriate refinement for the prediction of IMV, since it reflects how sick those patients were, apart from the hypoxaemia, which was common in this population, and should not be taken as an isolated indication for IMV. Oxygen induces pulmonary vasodilation in PAH patients and it can improve RV cardiac output. Therefore, the ideal method of oxygenation is the one that causes the least negative impact in the pulmonary circulation.

There is scarce literature on the alternatives to IMV in this high-risk population. HFNC was associated with improved oxygenation in ADPH in a preliminary study [14]. Physiological effects of HFNC in ADPH are promising, but its role remains unclear and we need further investigation in this area.

We were unable to assess the impact of noninvasive ventilation (NIV) due to a lack of consistent data on NIV in patient charts. It is worth noting that NIV was generally avoided in ADPH patients in our units.

ECMO may be considered for patients with refractory ADPH due to severe hypoxaemic respiratory failure in whom conventional support is not resulting in improvement, as a bridge to lung transplantation or a bridge to recovery. If possible, ECMO should preferably be used in awake and spontaneously breathing patients, who are non-intubated, to reduce risks related to general anaesthesia vasodilation and prevent the negative consequences of positive pressure [15].

NR-SOFA was associated with a higher use IMV in ADPH, independent of hypoxaemia and the baseline severity of pulmonary hypertension. In ADPH, IMV should be carefully considered, and alternative modes of oxygenation such as HFNC and ECMO should be considered.

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References

1 Lahm T, McCaslin CA, Wozniak TC, *et al.* Medical and surgical treatment of acute right ventricular failure. *J Am Coll Cardiol* 2010; 56: 1435–1446.
2 Wanner PM, Filipovic M. The right ventricle – you may forget it, but it will not forget you. *J Clin Med* 2020; 9: 432.
3 Esquinas AM, Petroianni A. Pulmonary hypertension in critically ill patients with mechanical ventilation: still a greatest challenge for intensivists. *J Crit Care* 2014; 29: 166.
4 Aryal S, King CS. Critical care of patients with pulmonary arterial hypertension. *Curr Opin Pulm Med* 2020; 26: 414–421.
5 Humbert M, Kovacs G, Hoeper MM, *et al.* 2022 ESC/ERS guidelines for the diagnosis and treatment of pulmonary hypertension. *Eur Heart J* 2022; 43: 3618–3731.
6 Garcia MVF, Souza R, Costa ELV, *et al.* Outcomes and prognostic factors of decompensated pulmonary hypertension in the intensive care unit. *Respir Med* 2021; 190: 106685.
7 Hoeper MM, Granton J. Intensive care unit management of patients with severe pulmonary hypertension and right heart failure. *Am J Respir Crit Care Med* 2011; 184: 1114–1124.
8 Vieillard-Baron A, Schmitt JM, Augarde R, *et al.* Acute cor pulmonale in acute respiratory distress syndrome submitted to protective ventilation: incidence, clinical implications, and prognosis. *Crit Care Med* 2001; 29: 1551–1555.
9 Campo A, Mathai SC, Le Pavec J, *et al.* Outcomes of hospitalisation for right heart failure in pulmonary arterial hypertension. *Eur Respir J* 2011; 38: 359–367.
10 Naranjo M, Mercurio V, Hassan H, *et al.* Causes and outcomes of ICU hospitalisations in patients with pulmonary arterial hypertension. *ERJ Open Res* 2022; 8: 00002-2022.
11 Rush B, Biagioni BJ, Berger L, *et al.* Mechanical ventilation outcomes in patients with pulmonary hypertension in the United States: a national retrospective cohort analysis. *J Intensive Care Med* 2017; 32: 588–592.
12 Sztrymf B, Souza R, Bertoletti L, *et al.* Prognostic factors of acute heart failure in patients with pulmonary arterial hypertension. *Eur Respir J* 2010; 35: 1286–1293.
13 Price LC, Dimopoulos K, Marino P, *et al.* The CRASH report: emergency management dilemmas facing acute physicians in patients with pulmonary arterial hypertension. *Thorax* 2017; 72: 1035–1045.
14 Gupta B, Kerai S, Kakkar K, *et al.* Role of high-flow nasal oxygen therapy in cases with pulmonary hypertension in an intensive care unit setting. *Indian J Crit Care Med* 2019; 23: 458–461.
15 Hoeper MM, Benza RL, Corris P, *et al.* Intensive care, right ventricular support and lung transplantation in patients with pulmonary hypertension. *Eur Respir J* 2019; 53: 1801906.