ERJ open research
THE BEST IN OPEN ACCESS BASIC, TRANSLATIONAL & CLINICAL RESPIRATORY RESEARCH

Early View

Research letter

Predictors of invasive mechanical ventilation use in patients with acute decompensated pulmonary hypertension admitted to Intensive Care Unit

Marcos V. F. Garcia, Rogerio Souza, Pedro Caruso

Please cite this article as: Garcia MVF, Souza R, Caruso P. Predictors of invasive mechanical ventilation use in patients with acute decompensated pulmonary hypertension admitted to Intensive Care Unit. *ERJ Open Res* 2023; in press (https://doi.org/10.1183/23120541.00598-2022).

Predictors of invasive mechanical ventilation use in patients with acute decompensated pulmonary hypertension admitted to Intensive Care Unit

Marcos VF Garcia, M.D., PhD.[1]

Rogerio Souza, M.D., Ph.D.[1]

Pedro Caruso, M.D., Ph.D.[1,2]

[1] Divisao de Pneumologia, Instituto do Coracao, Hospital das Clínicas HCFMUSP, Faculdade de Medicina da Universidade de Sao Paulo, Sao Paulo, Brazil.

[2]Intensive Care Unit, AC Camargo Cancer Center, São Paulo, Brazil.

Marcos VF Garcia: https://orcid.org/0000-0003-4730-3650

Rogerio Souza: https://orcid.org/0000-0003-2789-9143

Pedro Caruso: https://orcid.org/0000-0002-1051-8458

Corresponding Author:

Marcos Vinicius Fernandes Garcia, M.D., Ph.D.

Pulmonary Division, Heart Institute, Faculty of Medicine, University of São Paulo

Av. Dr. Eneas de Carvalho Aguiar, 44, 8th floor, Respiratory ICU, São Paulo, SP, Brazil. ZIP code: 05403-900 / E-mail: marcos_garcia@usp.br / Phone: +55 11 2661-4198

Authors' contribution

Dr. Garcia made substantial contributions to the conception, design, acquisition, analysis, and interpretation of the work, and drafted the work and approved the version to be published.

Dr. Souza made substantial contributions to the conception of the work, analysis and interpretation of data, revised for critically important intellectual content, and approved the final version to be published.

Dr. Caruso made substantial contributions to the conception, design, analysis, and interpretation of the work, revised it for critically important intellectual content, and approved the version to be published.

Conflict of interest: none

Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Word count: 1195

To the Editor

In acute decompensated PH (ADPH) patients, invasive mechanical ventilation (IMV) use remains challenging because it has deleterious hemodynamic effects on the right ventricle (RV), which can result in hemodynamic 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, ventricle-arterial uncoupling occurs with drop in cardiac index and pulmonary pressures, as well as a rise 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 minimize complications and supports decision-making about the use of IMV or palliative care.

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

To identify predictors for IMV use, we conducted univariate analysis and developed a multivariable logistic regression model. Variables with P value < 0.05 in univariate analysis were included in the multivariable logistic regression model

employing the backward conditional method of logistic regression. There was 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). Categorical variables were compared with the chi-square test or Fisher's exact test. Continuous variables were compared with Mann-Whitney test. Odds ratios and 95% confidence intervals were used to measure the association between each variable and RRT use. Data analysis was done using Statistical Package for the SPSS software (Version 23.0. Armonk, NY: IBM).

Seventy-four patients with ADPH were included and eleven patients (14.9%) required IMV during the first 48h of ICU stay. The median age was 47 years (35-65), 75.7% patients were females and 64.9% had group 1 PH, baseline and ICU admission data are depicted in Table 1. Most common reasons for ADPH were infection (48.6%), hypervolemia (18.9%), 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 on the high-risk PH based on European Respiratory Society/European Society of Cardiology PH risk assessment (a scoring system that predicts one-year mortality of patients with PH) (63.6% vs. 23.8%, respectively, P=0.03) and had a higher sequential organ failure assessment (SOFA) score upon ICU admission [9 (8–12) vs. 6 (4–8), P<0.01, respectively]. Hypoxemia was common during ICU admission, median PaO_2/FiO_2 was 144 (89-221). Non-respiratory SOFA (NR-SOFA) represents SOFA without the respiratory components and was significantly higher in the IMV group compared to no IMV group [7 (6–10) vs. 4 (3–6), P<0.01, respectively].

In our sample, the most common reasons for IMV were worsening hypoxia (54.5%), respiratory distress (18.2%), cardiac arrest (18.2%), hypercapnia (9.0%). ICU mortality of patients who required IMV was 100%. IMV group had a shorter hospital stay (2 days) compared to no IMV group (9 days), of note 54.5% of patients on 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 6ml/kg, limitation of plateau pressure <30 cmH_20 and driving pressure < 15 cmH_20), normocapnia and prone positioning when indicated (PO_2/FiO_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 PH 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 [odds ratio 1.77 (1.21 -2.57; 95% CI)], while PH 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 a good discrimination. In a sensitivity analysis, neither PH 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, similarly to 100% mortality of IMV patients described by Campo et al (9). In the study by Sztrymf et al. no patient underwent IMV in the study period as authors stipulated no intubations would be done due to the poor prognosis associated with IMV(12). In spite of poor prognosis related to IMV, carefully selected patients with potentially reversible acute RV dysfunction could be considered for IMV(13).

High mortality observed in the IMV group was explained by peri-intubation cardiac arrest but likely reflects that sicker patients tend to receive IMV. Non-respiratory SOFA offers an appropriate refinement for the prediction of IMV since it reflects how sick those patients were apart from the hypoxemia, 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 the causes less negative impact in the pulmonary circulation.

There is scarce literature on the alternatives for 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 non-invasive 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 hypoxemic respiratory failure in whom conventional support is not resulting in

improvement, as a bridge to lung transplantation or bridge to recovery. If possible, ECMO should preferably be used in awake and spontaneously breathing patients, non-intubated, to reduce risks related to general anesthesia vasodilation and prevent the negative consequences of positive pressure (15).

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

TABLE 1: Patients characteristics before and at ICU admission

Variables	All patients (N=74)	Needed IMV (n=11)	No IMV (n=63)	*P*
Age (years)	47 (35–56)	37 (31–47)	47 (38–55)	0.61
Female, n (%)	56 (75.7)	9 (81.8)	47 (74.6)	0.99
PH group, n (%)				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, n (%)				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)	
Hemodynamics				
Mean PAP (mmHg)	55 (50–66)	59 (53–65)	55 (49–67)	0.48
PVR (Woods)	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/min)	3.7 (2.7–4.3)	3.5 (3.0–3.6)	3.7 (2.7–4.3)	0.40
Charlson index, n (%)				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
PaO_2/FiO_2	144 (89-221)	126 (92-130)	148 (86-219)	0.54
SpO_2/FiO_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
$ScvO_2$ (%)	61.4 (52.6–68.8)	54.3 (50.5–61.2)	63.2 (53.0–70.3)	0.69
Arterial lactate (mg/dL)	17 (12–23)	11 (9–20)	18 (13–23)	0.79
BNP (pg/mL)	647 (331–1058)	650 (417–863)	611 (380–1216)	0.66
Creatinine (mg/dL)	1.54 (1.02–2.36)	2.00 (1.10–3.93)	1.51 (1.02–2.37)	0.47
Length of stay hospital (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

Categorical and continuous data are presented as frequencies (percentages) and median (25-75% interquartile range). PH: pulmonary hypertension; PAH: pulmonary arterial hypertension; CTEPH: chronic thromboembolic pulmonary hypertension; PAP: pulmonary artery pressure; PVR: pulmonary vascular resistance; PAWP: pulmonary artery wedge pressure; SOFA: sequential organ failure assessment; SAPS 3: simplified acute physiology score; PaO_2/FiO_2: pressure of arterial oxygen to fractional inspired oxygen concentration ratio; SpO_2/FiO_2: oxygen saturation to fractional inspired oxygen concentration ratio; $ScvO_2$%: central venous oxygen saturation; BNP: brain natriuretic peptide.

References

1. Lahm T, McCaslin CA, Wozniak TC, Ghumman W, Fadl YY, Obeidat OS, et al. Medical and surgical treatment of acute right ventricular failure. J Am Coll Cardiol. 2010;56(18):1435-46.
2. Wanner PM, Filipovic M. The Right Ventricle-You May Forget it, but It Will Not Forget You. J Clin Med. 2020;9(2).
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(1):166.
4. Aryal S, King CS. Critical care of patients with pulmonary arterial hypertension. Curr Opin Pulm Med. 2020;26(5):414-21.
5. Humbert M, Kovacs G, Hoeper MM, Badagliacca R, Berger RMF, Brida M, et al. 2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension. Eur Heart J. 2022.
6. Garcia MVF, Souza R, Costa ELV, Fernandes CJCS, Jardim CVP, Caruso P. 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(10):1114-24.
8. Vieillard-Baron A, Schmitt JM, Augarde R, Fellahi JL, Prin S, Page B, et al. Acute cor pulmonale in acute respiratory distress syndrome submitted to protective ventilation: incidence, clinical implications, and prognosis. Crit Care Med. 2001;29(8):1551-5.
9. Campo A, Mathai SC, Le Pavec J, Zaiman AL, Hummers LK, Boyce D, et al. Outcomes of hospitalisation for right heart failure in pulmonary arterial hypertension. Eur Respir J. 2011;38(2):359-67.
10. Naranjo M, Mercurio V, Hassan H, Alturaif N, Cuomo A, Attanasio U, et al. Causes and outcomes of ICU hospitalisations in patients with pulmonary arterial hypertension. ERJ Open Res. 2022;8(2).
11. Rush B, Biagioni BJ, Berger L, McDermid R. Mechanical Ventilation Outcomes in Patients With Pulmonary Hypertension in the United States: A National Retrospective Cohort Analysis. J Intensive Care Med. 2017;32(10):588-92.
12. Sztrymf B, Souza R, Bertoletti L, Jaïs X, Sitbon O, Price LC, et al. Prognostic factors of acute heart failure in patients with pulmonary arterial hypertension. Eur Respir J. 2010;35(6):1286-93.
13. Price LC, Dimopoulos K, Marino P, Alonso-Gonzalez R, McCabe C, Kemnpy A, et al. The CRASH report: emergency management dilemmas facing acute physicians in patients with pulmonary arterial hypertension. Thorax. 2017;72(11):1035-45.
14. Gupta B, Kerai S, Kakkar K, Gupta L. 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(10):458-61.
15. Hoeper MM, Benza RL, Corris P, de Perrot M, Fadel E, Keogh AM, et al. Intensive care, right ventricular support and lung transplantation in patients with pulmonary hypertension. Eur Respir J. 2019;53(1).