

Rapid Communication

Acute Heart Failure as a Cause of Hypercapnia

Ricoy J¹, Soto-Feijóo R¹, Rodríguez-Núñez N¹,
Toubes ME¹, Rábade C¹, Lama A¹, Riveiro V¹, Casal
A^{1*} and Valdés L^{1,2,3}

¹Department of Pneumology, Clinical-University
Hospital Complex of Santiago, Spain

²Interdisciplinary Research Group in Pneumology,
Santiago Health Research Institute (IDIS), Spain

³University of Santiago de Compostela (Universidad de
Santiago de Compostela), Spain

*Corresponding author: Ana Casal Mouriño,
Department of Pneumology, Clinical-University Hospital
Complex of Santiago, Santiago de Compostela, Spain

Received: October 22, 2022; Accepted: November 18,
2022; Published: November 25, 2022

Abstract

The purpose of this study is to investigate whether hypercapnia in patients with Acute Cardiogenic Pulmonary Edema (ACPE) is secondary to acute Heart Failure (HF) alone or there is underlying Chronic Obstructive Pulmonary Disease (COPD).

We conducted a retrospective study to analyze the characteristics of patients with ACPE hospitalized between 2020 and 2021. Hypercapnia was defined as PaCO₂ >45 mm Hg. The study included patients ≥18 years admitted to an intermediate respiratory care unit.

A total of 156 patients with ACPE were admitted [(mean age: 79±9.8 years; men, 82 (52%); HF, 82 (52.6%); COPD, 43 (27.6%); the two diseases, 27 (17.3%)]. Non-invasive ventilation reduced significantly heart rate, blood pressure, PaCO₂ and the number of patients with HCO₃⁻ <26 mmol/L, and increased significantly SaO₂ and pH. HF patients were prevalently female, significantly older, and exhibited a lower heart rate and PaCO₂ (65±17.2 mm Hg), as compared to patients with COPD (76.8±21.3) or with the two diseases (74.5±23.2).

In ACPE patients, the presence of hypercapnia does not necessary indicate an underlying COPD.

Keywords: Acute cardiogenic pulmonary edema; Acute heart failure; Chronic obstructive; Non-invasive ventilation; Pulmonary disease

Abbreviations

ACPE: Acute Cardiogenic Pulmonary Edema; COPD: Chronic Obstructive Pulmonary Disease; HF, Heart Failure; IRCU: Intermediate Respiratory Care Unit; NIV: Non-Invasive Ventilation

Introduction

Heart Failure (HF) and Chronic Obstructive Pulmonary Disease (COPD) are closely related [1], since they share symptoms and known risk factors, may cause similar functional alterations [2,3] and are frequently concurrent [4].

In patients with HF and COPD who develop respiratory failure, determining whether it is secondary to HF decompensation, COPD exacerbation or to interaction between the two conditions is challenging. In this setting, in the presence of hypercapnic respiratory failure, it is difficult to establish whether it is caused by Acute Cardiogenic Pulmonary Edema (ACPE) alone, or an underlying COPD has contributed to this complication.

The purpose of this study is to elucidate whether hypercapnia in ACPE patients is secondary to acute HF alone or there is an underlying COPD that explains it.

Methods

We conducted a retrospective study to analyze the characteristics of ACPE patients hospitalized between 2020 and 2021. Diagnoses of acute HF, CPE and COPD were established in accordance with *European Society of Cardiology* [5,6] and *Global Initiative for Chronic Obstructive Lung Disease* [7] guidelines, respectively. Hypercapnia

was defined as PaCO₂ >45 mm Hg.

The study population included all adult patients (≥18 years) with a diagnosis of ACPE admitted to an Intermediate Respiratory Care Unit (IRCU) to receive Non-Invasive Ventilation (NIV). Patients younger than 18 years were excluded.

The variables analyzed included 1) demographic (age, gender, smoking, comorbidities); 2) clinical (vital signs on admission and discharge); 3) analytical (pH, pCO₂, pO₂ and HCO₃⁻; on admission and discharge); 4) length of IRCU stay; 5) NIV treatment; and 6) clinical outcome (discharge or exitus). The study was approved by the Ethics Committee of the hospital (2022/016).

Descriptive statistics were used to summarize the characteristics of patients (percentage of qualitative variables and mean ± SD for quantitative variables). Differences in qualitative variables were assessed using Chi-square test, whereas differences in mean values were evaluated using Student's *t*-test for related samples, and ANOVA or (repeated-measures/independent-measures) an analysis of variance for comparison of more than two groups. Statistical significance was established at 5%. All statistical analyses were performed using the IBM SPSS Statistics v20 software package.

Results

During the study period, a total of 565 patients were admitted to the IRCU, of whom 156 (27.6%) developed ACPE. Mean age was 79±9.8 years [(male, 82 (52%)]. Previous diagnoses, length of stay, administration of NIV therapy, mortality, vital signs, and arterial blood gas (the two latter on admission and discharge) are

Table 1: Characteristics of patients with acute pulmonary edema.

Characteristics (n = 156)			
Age (mean, years)	79 ± 9.9 (range: 50-94)		
Male [n (%)]	82 (52.6)		
Smokers [n (%)]	74 (47.4)		
Dyslipemia [n (%)]	84 (53.8)		
Arterial hypertension [n (%)]	125 (80.1)		
Ischemic heart disease [n (%)]	20 (12.8)		
Vascular disease [n (%)]	101 (64.7)		
Cardiac arrhythmia [n (%)]	75 (48.1)		
Heart failure [n (%)]	82 (52.6)		
COPD [n (%)]	43 (27.6)		
Heart failure and COPD [n (%)]	27 (17.3)		
DILD [n (%)]	2 (1.3)		
Diabetes mellitus [n (%)]	60 (38.5)		
NIV [n (%)]	155 (99.4)		
ICU stay (days)	6 ± 5.2		
Mortality [n (%)]	15 (9.6)		
Variable	On admission (n = 156)	On discharge (n = 141)	p
Heart rate (bpm)	86 ± 20	76 ± 14	<0.001
Systolic arterial pressure (mm Hg)	143 ± 27	125 ± 19	<0.001
Diastolic arterial pressure (mm Hg)	79 ± 19	68 ± 11	<0.001
Mean arterial pressure.	100 ± 19	87 ± 11	<0.001
SaO ₂ (%)	83 ± 12	93 ± 3	< 0.001
PaO ₂ (mm Hg)	66.2 ± 43	66.5 ± 13.6	0.978
pH	7.28 ± 0.08	7.42 ± 0.06	<0.001
PaCO ₂ (mm Hg)	68 ± 18	49.4 ± 10.6	<0.001
Bicarbonate (mmol/L)	30.8 ± 5.6	31.5 ± 5.2	0.154
Bicarbonate <26 mmol/L [n (%)]	28 (17.9)	24 (15.6)	<0.001

COPD: Chronic Obstructive Pulmonary Disease; **DILD:** Diffuse Interstitial Lung Disease; **ICRU:** Intermediate Respiratory Care Unit; **NIV:** Non-Invasive Ventilation.

Table 2: Differences between patients diagnosed with HF, COPD or both on admission.

Characteristics	HF (n = 55)	COPD (n = 16)	HF + COPD (n = 27)	p
Age (years)	82.6 ± 6.6	73.6 ± 10.3	76.7 ± 11.2	<0.001
Male [n (%)]	20 (36.4)	11 (68.8)	25 (92.6)	<0.001
Smokers [n (%)]	14 (26.5)	15 (93.8)	26 (96.3)	<0.001
Heart rate (bpm)	81 ± 18	101 ± 18	86 ± 20	0.003
Systolic arterial pressure (mm Hg)	147 ± 25	137 ± 26	141 ± 25	0.056
Diastolic arterial pressure (mm Hg)	78 ± 17	80 ± 29	77 ± 19	0.357
Mean arterial pressure.	101 ± 18	99 ± 22	93 ± 15	0.161
SaO ₂ (%)	85 ± 11	78.3 ± 15	85 ± 12	0.159
PaO ₂ (mm Hg)	67.9 ± 39.9	75.4 ± 70	74.9 ± 40	0.732
pH	7.29 ± 0.07	7.24 ± 0.09	7.27 ± 0.08	0.078
PaCO ₂ (mm Hg)	65 ± 17.2	76.8 ± 21.3	74.5 ± 23.2	0.038
Bicarbonate (mmol/L)	30.6 ± 6.2	32.1 ± 5.7	32.9 ± 5.9	0.247
Bicarbonate <26 mmol/L [n (%)]	12 (21.8)	1 (6.2)	2 (7.7)	0.140
NIV [n (%)]	55 (100)	16 (100)	27 (100)	---
Stay (days)	9.7 ± 7.6	10 ± 9	7.8 ± 5	0.485
Mortality [n (%)]	5 (9.3)	1 (6.2)	3 (11)	0.868

COPD: Chronic Obstructive Pulmonary Disease; **HF:** Heart Failure; **NIV:** Non-Invasive Ventilation.

shown in (Table 1). On discharge, non-invasive ventilation reduced significantly heart rate, blood pressure, PaCO₂, the number of patients with HCO₃⁻ <26 mmol/L and increased SaO₂ and pH significantly.

The number of patients with SaO₂ ≤90%, PaO₂ ≤60 mm Hg, pH ≤7.35, PaCO₂ >45 mm Hg and HCO₃⁻ <26 mEq/L on admission was 107 (68.6%), 93 (59.6%), 142 (91%), 149 (95.5%) and 28 (17.9%), respectively. In contrast, 24 patients (15.4%) had a baseline PaO₂ >80 mm Hg.

Table 2 compares the characteristics of patients by diagnosis on admission (HF, COPD, or concurrent HF and COPD). Patients with

HF were significantly older, with a higher prevalence among women and a lower percentage of smokers, and a significantly lower mean HF and PaCO₂ (albeit the latter was >45 mm Hg).

Discussion

The results confirm that i) hypercapnia is very frequent in ACPE patients (95.5%); ii) it is not necessarily secondary to an underlying COPD (absent in 72.4% of cases); and iii) NIV therapy is useful in this setting [5,6,8]. Previous studies uncovered that COPD was not the cause of all cases of acidosis in ACPE patients. In a series of 1069 patients with acidosis (mean PaCO₂ 57±16.5 mm Hg; mean HCO₃⁻

21±4 mmol/L), the percentage of diagnoses of COPD did not reach 20% [9]. In another study, the prevalence of COPD was significantly higher (65%) in patients with hypercapnia and $\text{HCO}_3^- >30$ mEq/L, as compared to patients with $\text{HCO}_3^- <26$ mEq/L (25%) ($p=0.002$) [10]. This may be explained by the different metabolic responses activated to compensate respiratory acidosis depending on whether it is acute (HCO_3^- is increased by 1 mmol/L for each PaCO_2 increase of 10 mm Hg above 40 mm Hg), or chronic (HCO_3^- is increased by 4-5 mmol/L for each PaCO_2 increase of 10 mm Hg above 40 mm Hg) [11]. In a recent study involving 28 ACPE patients treated with NIV, from which COPD patients were excluded, a third of patients exhibited hypercapnia on admission [12]. In our series, in agreement with previous case series reports, a significant proportion of patients showed elevated HCO_3^- , acidosis and hypercapnia unrelated to COPD. This suggests that metabolic response had started some days earlier.

In patients with HF/ACPE without COPD, hypercapnia is related to hypoventilation rather than pulmonary perfusion or diffusion, since it is 20 times higher in CO_2 than in O_2 [13]. Hypoventilation may be mediated by several underlying mechanisms. In HF (both, with preserved or reduced ejection fraction), left-sided filling pressure leads to pulmonary congestion and interstitial edema, resulting in pulmonary hypertension, right heart dysfunction and peripheral congestion [3]. When interstitial edema progresses, alveolar spaces are occupied, resulting in airway obstruction in advanced stages [3], which will cause hypoventilation and hypercapnia [14]. Respiratory muscle fatigue may also induce hypoventilation and hypercapnia [15].

In this study, 24 patients (15.4%) exhibited a $\text{PaO}_2 >80$ mm Hg on ED admission after having received O_2 on the ambulance without O_2 flow control, which would explain the lack of PaO_2 improvement on discharge. In this series, PaCO_2 elevation may be partially explained by this circumstance. However, although it is widely accepted that the administration of O_2 in COPD may cause hypercapnia [16], a consensus document for prehospital management of acute HF [17] does not provide any recommendation about the O_2 administration method. To date, there are no reports of patients with acute decompensated HF who have experienced adverse events such as hypercapnia after an episode of hyperoxia [18,19]. Finally, a recent study revealed a significant association between prehospital hypercapnia in patients with acute HF and NIV administration in the emergency department, ICU admission, and prolonged hospital stays. However, the authors do not mention the deleterious effects of O_2 administration [20].

In summary, in ACPE, the presence of hypercapnia does not necessarily indicate an underlying COPD.

Author Contributions

Jorge Ricoy Gabaldón. Conceived and designed the study. Performed data analysis and interpretation. Reviewed intellectual content. Approved final manuscript.

Roi Soto Feijóo. Performed data analysis and interpretation. Conducted a critical review of intellectual content. Approved final manuscript.

Nuria Rodríguez-Núñez. Statistical analysis. Performed data analysis and interpretation. Conducted a critical review of intellectual content. Approved final manuscript.

M^a Elena Toubes. Performed data analysis and interpretation. Conducted a critical review of intellectual content. Approved final manuscript.

Carlos Rábade Castedo. Performed data analysis and interpretation. . Conducted a critical review of intellectual content. Approved final manuscript.

Adriana Lama López. Performed data analysis and interpretation. . Conducted a critical review of intellectual content. Approved final manuscript.

Vanessa Riveiro Blanco. Performed data analysis and interpretation. Conducted a critical review of intellectual content. Approved final manuscript.

Ana Casal Mourinho. Performed data analysis and interpretation. Conducted a critical review of intellectual content. Approved final manuscript.

Luis Valdés. Conceived and designed the study. Performed data analysis and interpretation. Conducted a critical review of intellectual content. Approved final manuscript.

Conflict of Interest

Authors declare no conflict of interest.

References

- Rabe KF, Hurst JR, Suissa S. Cardiovascular disease and COPD: dangerous liaisons?. *Eur Respir Rev.* 2018; 27: 180057.
- Roversi S, Fabbri LM, Sin DD, Hawkins NM, Agusti A. Chronic obstructive pulmonary disease and cardiac diseases. An urgent need for integrated care. *Am J Respir Crit Care Med.* 2016; 194: 1319-36.
- Magnussen H, Canepa M, Zambito PE, Brusasco V, Meinertz T, Rosenkranz S. What can we learn from pulmonary function testing in heart failure?. *Eur J Heart Fail.* 2017; 19: 1222-9.
- Hawkins NM, Petrie MC, Jhund PS, Chalmers GW, Dunn FG, McMurray JJ. Heart failure and chronic obstructive pulmonary disease: diagnostic pitfalls and epidemiology. *Eur J Heart Fail.* 2009; 11: 130-9.
- Masip J, Peacock WF, Price S, Culler L, Martin-Sanchez FJ, Seferovic P, et al. Indications and practical approach to non-invasive ventilation in acute heart failure. *Eur Heart J.* 2018; 39: 17-25.
- McDonagh TA, Metra M, Adamo M, Gardner RS, Baumbach A, Böhm M, et al. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. *Eur Heart J.* 2021; 42: 3599-726.
- Singh D, Agusti A, Anzueto A, Barnes PJ, Bourbeau J, Celli BR, et al. Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Lung Disease: the GOLD science committee report 2019. *Eur Respir J.* 2019; 53: 1900164.
- Gray A, Goodacre S, Newby DE, Masson M, Sampson F, Nicholl J. Noninvasive ventilation in acute cardiogenic pulmonary edema. *N Engl J Med.* 2008; 359: 142-51.
- Gray AJ, Goodacre S, Newby DE, Masson MA, Sampson F, et al. A multicentre randomised controlled trial of the use of continuous positive airway pressure and non-invasive positive pressure ventilation in the early treatment of patients presenting to the emergency department with severe acute cardiogenic pulmonary oedema: the 3CPO trial. *Health Technol Assess.* 2009; 13: 1-106.

10. Aliberti S, Brambilla AM, Cosentini R. Noninvasive ventilation or continuous positive airway pressure in pulmonary edema patients with respiratory acidosis? Look at the bicarbonates. *Intensive Care Med.* 2011; 37: 2050-1.
11. Berend K, de Vries APJ, Gans ROB. Physiological approach to assessment of acid-base disturbances. *N Engl J Med.* 2014; 371: 434-45.
12. Valipour A, Cozzarini W, Burghuber OC. Non-invasive pressure support ventilation in patients with respiratory failure due to severe acute cardiogenic pulmonary edema. *Respiration.* 2004; 71: 144-51.
13. Wagner PD. The physiological basis of pulmonary gas exchange: implications for clinical interpretation of arterial blood gases. *Eur Respir J.* 2015; 42: 227-43.
14. Sforza A, Guarino M, Cimmino CS, Izzo A, Cristiano G, Mancusi C, et al. Continuous positive airway pressure therapy in the management of hypercapnic cardiogenic pulmonary edema. *Monaldi Arch Chest Dis.* 2021; 91: 1725.
15. Konishi M, Akiyama E, Suzuki H, Iwahashi N, Maejima N, Tsukahara K, et al. Hypercapnia in patients with acute heart failure. *ESC Heart Fail.* 2015; 2: 12-19.
16. Jacono FJ. Control of ventilation in COPD and lung injury. *Respir Physiol Neurobiol.* 2013; 189: 371-6.
17. Mebazaa A, Yilmaz MB, Levy P, Ponikowski P, Peacock WF, Laribi S, et al. Recommendations on pre-hospital and early hospital management of acute heart failure: a consensus paper from the Heart Failure Association of the European Society of Cardiology, the European Society of Emergency Medicine and the Society of Academic Emergency Medicine – short versión. *Eur Heart J.* 2015; 36: 1958-66.
18. Cornet AD, Kooter AJ, Peters MJL, Smulders YM. Supplemental oxygen therapy in medical emergencies: More harm tahn benefit? *Arch Intern Med.* 2012; 172: 289-90.
19. Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JGF, Coats AJS, et al. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. *Eur Heart J.* 2016; 37: 2129-2200.
20. Fabre M, Fehlmann CA, Gartner B, Zimmermann-Ivoll CG, Rey F, Sarasin F, et al. Prehospital arterial hipercapnia in acute heart failure is associated with admission to acute care units and emergency room length of stay: a retrospective cohort study. *BMC Emerg Med.* 2021; 21: 14.