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Incidence, prevalence and prognostic implications of right-sided heart failure in acute respiratory distress syndrome: A prospective observational study

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ABSTRACT

Objective: Acute respiratory distress syndrome is a heterogeneous disease which involves both the alveoli and pulmonary vessels. Acute cor pulmonale was initially considered as a marker of severity but its impact on outcome is still controversial.

Materials and Methods: This was a prospective observational study conducted over a period of nine months in ICU of a tertiary care center in India. Out of 2028 patient admitted in ICU 64 patients with ARDS (Berlins definition) underwent transthoracic echocardiography within 3 days of admission after diagnosis.

Result: Acute cor pulmonale (ACP) was detected in 23 (36%) patients. Patients with ACP have greater the severity of disease and higher APACHE score as compared to those without ACP. PCO_2 and P/F ratio appears to be the independent risk factor in patients for ACP in ARDS. Patients with ACP in ARDS had a higher incidence of shock and mortality (43.5%).

Conclusion: ACP is quite common in ARDS. Due to its effect on the outcome, it appears to be a major factor in deciding ventilatory strategy in patients with ARDS. Right ventricle protective approach of ventilation keeps lung and heart connected.

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1. Introduction

Acute respiratory distress syndrome (ARDS) is heterogeneous and challenging disease with various pathophysiologic mechanisms responsible for different degrees of severity. Substantial progress has been made in the understanding of the pathogenesis of the disease and different treatment strategies have been proposed accordingly.

ARDS was considered mainly as a disease of alveoli, so “opening the lung” and targeting the arterial oxygen saturation and restricted fluid therapy are considered the

mainstay of management. The ventilatory management and protocols for ARDS has been regularly modified with the enhancement of our knowledge of the physiopathology of ARDS, the mortality of ARDS still remains significant.^{1,2} Even though the most hypoxemic patient has the greatest mortality,^{1,3} but still the severity of hypoxemia per se does not reliably predict the outcome.⁴ A possible reason for this could be an under-recognized involvement of the pulmonary vasculature and the right side of the heart in ARDS.

Zapol and Snider first described that ARDS which affects both the alveoli and the pulmonary circulation.⁵ The pulmonary vessels are high capacitance and low resistance system and the right ventricle provides blood

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flow at low pressure to pulmonary vasculature.⁶ Right ventricle(RV) is thin-walled and works against low-pressure pulmonary circulation. ARDS causes inflammation, edema, vasoconstriction, micro-thrombi, and vascular remodeling of the pulmonary vasculature.⁷ Other factors which increase RV after-load are ARDS induced reduction in lung compliance which increases pleural pressures, trans-pulmonary pressures, mechanical ventilation and positive end-expiratory pressure (PEEP) induced an increase in intrathoracic pressures.⁸ This elevated RV after load further increases right ventricle stroke-work index which progresses to RV dysfunction and cor pulmonale.⁹

The incidence of ACP has reduced with the implementation of lung protective ventilation which was around 60% in the 1990s to 20% - 25%.¹⁰ Mortality of ARDS remains high so the hemodynamic management in ARDS especially on the protection of RV appears to be the way to reduce mortality. So the primary objective of the prospective study was to determine the incidence, prevalence, prognostic implication and the outcome of patients with cor pulmonale in ARDS.

2. Materials and Methods

This was a prospective observational study conducted in tertiary care hospital intensive care unit (ICU) with 40 bedded capacity. After taking approval by the ethical and the research committee of our institute, informed and written consent was taken from the patients relative. Between June 2016 and January 2017 all patients (> 10 years of age), who develop ARDS as defined by Berlins definition³ and who underwent trans thoracic echocardiography(TTE) within 3 days of ICU admission were included in this study. Exclusion criteria were chronic pulmonary diseases, chronic cor pulmonale, cardiogenic pulmonary edema and age<10 yrs. Cardiogenic pulmonary edema was ruled by doing an echocardiographic assessment and finding low LV filling pressures. The lung protective strategy of mechanical ventilation using low tidal volume was used keeping plateau pressure target ≤ 30 cm H₂O.

TTE examinations were performed by the cardiologist or the intensivist highly trained in critical care echocardiography using the “Philips Clearvue 350” machine. Briefly, the following echocardiographic views were examined: four-chamber long-axis view to assess the end-diastolic right ventricle/left ventricle (RV/LV) area ratio and LV ejection fraction; para-sternal short-axis view of the LV to evaluate the motion of the interventricular septum during end systole. ACP was identified by a combination of RV enlargement with septal dyskinesia. RV dilatation will be defined by an RV end-diastolic area (RVEDA)/left ventricular end-diastolic area (LVEDA) with both measured at the end diastole 0.6.¹¹

2.1. Statistical analysis

The data were collected and entered in MS Excel 2010. Statistical analysis was performed using SPSS software version 22. The one-sample Kolmogorov-Smirnov test was employed to determine whether the data sets differed from a normal distribution. Descriptive statistics were calculated for variables like age, sex, etc. Mean \pm SD for continuous variables and frequency (%) for quantitative variables were calculated. Normally distributed data were analyzed using the unpaired t-test for continuous variables and categorical variables were analyzed using the chi-square test.

If $p < .05$, then the hypothesis is said to be statistically significant.

3. Result

Out of 2028 patients who were admitted in ICU over 8 months period 64 patients were included in the study with a mean age of 40 with 29 males and 35 females. 23(36%) of patients with ARDS had cor pulmonale. The group with or without cor pulmonale were not significantly different in various demographic parameters like age, sex or cause of ARDS as shown in Table 1.

The patients who had cor pulmonale had more severe disease with higher APACHE 2 score, more acidosis, higher PaCO₂ and lower PaO₂/FiO₂ ratio as compared to patients without cor pulmonale which was statistically significant as shown in Table 2. Mortality was higher in cor pulmonale group(43.5%) as compared to non Cor pulmonale group (14.6%) though not statistically significant.

4. Discussion

ARDS is a challenging disease which is a major cause of morbidity and mortality in ICUs throughout the world.

Suter et al defined the best ventilatory strategy in ARDS as the one which allows the best oxygen delivery.¹² He showed that while increasing the PEEP from 0 to 7 cm H₂O the compliance increased in parallel with oxygen transport and dead space decreased, whereas further increasing PEEP from 7 cm H₂O to 13 cm H₂O, compliance decreased in parallel with a decrease in oxygen transport and an increase in dead space. From here the concept of heart-lung interaction and its impact of ventilatory settings on it were introduced. Unfortunately, most of the guidelines focus on lung even though the mortality remains unchanged.¹³ A new area to decrease mortality appears to be focusing on ARDS induced pulmonary vascular injury, its effects on the right ventricle, and finally its effect on hemodynamics.

In the past, the Pulmonary artery catheter was used to diagnose ACP but now with the development of non-invasive critical care echocardiography, echocardiography now appears as the “gold standard” to diagnose ACP.¹⁴

Transesophageal echocardiography(TEE) is considered to be a more effective approach but both the approaches,

Table 1: General profile of patients

	Without cor pulmonale	With cor pulmonale	P value
No. of patients n(%)	41(64%)	23(36%)	
Age groups(Yrs)			
10-20	5(12.2%)	1(4.3%)	
21-30	14(34%)	5(21.7%)	
31-40	7(17.1%)	6(26.1%)	
41-50	6(14.6%)	7(30.4%)	.477
51-60	2(4.9%)	2(8.7%)	
61-70	5(12.2%)	28(7%)	
>70	2(4.9%)	1(4.3%)	
Male sex n(%)	18(43.9%)	11(47.8%)	.798
Cause of ARDS			
Pneumonia	4(9.8%)	7(30.4%)	
Sepsis	11(26.8%)	7(30.4%)	
Scrub typhus	23(56.1%)	5(21.7%)	
Dengue fever	1(2.4%)	2(8.7%)	.20
Trauma	2(4.9%)	1(4.3%)	
Aspiration		1(4.3%)	
Malaria			
Apache 2			
Mean±SD	15.83±2.9	18.61±4.26	.003
Severity of ARDS			
Mild	6(14.63%)	2(8.69%)	
Moderate	24(58.53%)	7(30.43%)	.027
severe	11(26.8%)	14(60.86%)	
PH Mean±SD	7.33±.10	7.25±.16	.021
P/F ratio Mean±SD	138.5±50.05	98.7±46	.003
PCO ₂	39.8 ±3.8	45 ±5.32	<.02
PEEP Mean±SD	9.87±1.33	10.73±1.57	.038
NIV Support n(%)	4(9.75%)	1(4.34%)	
Mechanical ventilation n(%)	37(91.25%)	22(95.66%)	

Table 2: Outcome of patients

	Without cor pulmonale	With cor pulmonale	p-value
Shock	12(29.3%)	16(69.6%)	.003
Proning	2(4.9%)	2(8.7%)	.614
Mechanical ventilation days (mean)	4.65	5.81	.284
Icu stay days(mean)	5.90	7.43	.165
Outcome			
Improved	31(75.6%)	10(43.5%)	
LAMA*	4(9.8%)	3(13%)	.024
Expired	6(14.6%)	10(43.5%)	

*left against medical advise

transesophageal and transthoracic, can be used for diagnosis.¹⁰ In some studies cardiac MRI is considered as the gold standard for diagnosing ACP but it is practically difficult in critically ill patients.¹⁵ In our study we used transthoracic echocardiography as a modality to diagnose ACP. The cor pulmonale was detected in 36% out of 64 ARDS ventilated with lung protective ventilation, which was slightly higher than other studies which reported the incidence of 20-25%.¹⁶

The ventilatory strategies have an indirect effect on pulmonary circulation by their effect on oxygenation and

ventilation. Higher the carbon dioxide levels more are the pulmonary vasoconstriction and so more right ventricle load.¹⁷ PaO₂/FiO₂ ratio and PaCO₂ appears to be an independent factor for ACP in our study which is similar to other studies.¹⁶ So the ventilatory support should focus on the improvement of oxygenation and at least to some extent control hypercapnia to decrease the right ventricular load. Circulatory failure is common in ARDS. A European survey performed during the era of protective mechanical ventilation, such circulatory failure is either related to the septic shock for half of the patients or for the other half

to another cause, which could be right ventricular (RV) failure-related ARDS, also named acute cor pulmonale.¹ In our study higher incidence of shock was seen in ACP patients which were 69.6% patients as compared to non-ACP patients. Similarly Boissier et al.¹⁶ also showed that in 226 ARDS patients, ACP was associated with a higher incidence of shock. In another study by Lhéritier G et al done on 200 patients with ARDS, 64% of patients with ACP required norepinephrine infusion as compared to 49% of patients without ACP.¹⁰ Pulmonary embolism which is also a reason for cor pulmonale was not present in both the group in our study.

Cor pulmonale was associated with higher mortality which was 43.5% in our study. The study by Boissier et al.¹⁶ also showed that ACP was independently associated with Mortality and the result were similar in an observational study by Todd M et al.¹⁸ These the finding differs from a landmark study by Lheritier et al.¹⁰ as they applied airway pressure limitation measures to correct cor pulmonale, so it did not affect mortality. Increased mortality may be attributed to more incidence of shock in cor pulmonale group and the oxygenation compromise in our study. Prone positioning which is considered as a rescue ventilatory strategy for refractory hypoxemia was more frequently done in the patients with cor pulmonale in our study.¹⁹

5. Limitation

The facility of TEE is not available in our institute, so we rallied on TTE. We did only a single TTE while serial TEE is required for the management of patients. The number of patients included in the study were only 64 which were also less.

6. Conclusion

RV function should be identified early for the ventilatory management of ARDS as it has an impact on mortality. The echocardiography of the ventilated patients should be done bedside and various measures to reduce RV afterload should be taken. Lungs and RV are interconnected and what is good for the lung is good for RV and vice versa should always be taken into account. The French Society of Intensive Care Medicine has recognized the need for monitoring the right ventricle in patients with ARDS. Further studies are required to consider it as a standard of care. The valuable information is provided by echocardiography for hemodynamic monitoring for optimizing ventilatory strategies in ARDS.

7. Source of Funding

None.

8. Conflict of Interest

The authors declare no conflict of interest.

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