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Driving pressure versus right ventricular echocardiography parameters as a predictive for acute respiratory distress syndrome outcome

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Abstract*---Background:*** Acute respiratory distress syndrome (ARDS) is an inflammatory disease that affects the lung in a heterogeneous manner , so that ,even ideal body weight (IBW) based tidal volume may apply different lung stress and strain according to the available aerated lung areas. Airway driving pressure (DP) is the difference between airway plateau pressure (P plat) and positive endexpiratory pressure (PEEP), it can be used as a bedside surrogate for lung stress in several previous studies. Acute corpulmonale manifested by pulmonary hypertension and right ventricular dysfunction occurs as a consequence for ARDS with a prevalence (25% to 61%) in

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different studies. *Objectives :* This study was designed to show he clinical value of airway driving pressure and right heart echocardiography parameters in predicting ARDS outcome , and to correlate between airway pressures and right ventricle parameters. *Methodology :* fifty ARDS patients were diagnosed by Berlin criteria and monitored for airway pressures including DP and Pplat on day 0, day 3 and day 7. transthoracic echocardiography was used to assess RV parameters on day 0 and day 7 . According the ICU mortality patients are divided into survivors and nonsurvivors . Driving pressure and RV parameters are compared between the 2 groups and Correlated to each other. *Results:* High DP mean ±SD was associated with mortality on day 3 (17.83±3.50 versus 22.0±2.24 cm H_2O, P <0.0001) and on day 7(11.43±2.11 versus 22.95±2.08 cm H_2O, P <0.0001) in survivors versus nonsurvivors respectively. High PASP mean ±SD was associated with mortality on day 0 (33.46 ± 4.24 versus 39.1±5 mm Hg, P < 0.0001) and on day 7(33±4.35 versus 61.1±4.64 mm Hg ,P <0.0001) in survivors versus nonsurvivors respectively , Low TAPSE mean ±SD was associated with mortality on day 7(18.63 ±1.09 versus 12.6±3.8 mm ,P <0.0001) in survivors versus nonsurvivors respectively Increased RV basal diameter mean ±SD was associated with mortality on day 7(2.86±1.1 versus 7.13±1.8 cm, P <0.0001) in survivors versus nonsurvivors respectively. On day 7 PASP was positively correlated with DP(R 0.908, p 0.001), TAPSE was negatively correlated with DP(R -0.713, p 0.001) and RV diameter was positively correlated with DP(R 0.910 , p 0.001). *Conclusion* High PASP is the earliest mortality predictor from day 0 to day 7, high DP predicted mortality on day 3 and day 7 , while right ventricular dilatation , decreased TAPSE and tricuspid regurgitation predicted mortality on day 7 . High Dp correlated with low TAPSE from day 0 up to day 7 ,and with high PASP and RV dilatation on day 7.

***Keywords*---**driving pressure, echocardiography, distress syndrome.

Introduction

Acute respiratory distress syndrome (ARDS) affects the lung in a heterogeneous manner according to the disease severity [i], leaving a highly variable amount of aerated lung areas to be available for the delivered tidal volume [ii,iii], so the IBW based tidal volume apply different lung stress and strain according to the available aerated lung ii. Ventilator induced lung injury (VILI) is more related to the amplitude of cyclic stretch (strain; which corresponds to the ratio of volume change to the resting lung volume) than to the maximal level of sustained stretch (stress; which corresponds to the transpulmonary pressure), as strain causes cyclic open and close causes alveolar wall fracture and so on (VILI) [iv,v,vi].

In ARDS with the heterogeneous lung affection ,though delivering IBW based TV there is still a large variable degree of lung stress and strain limitating the value

of maintaining Pplat below 30 cm H_2O with a larger non-aerated compartment[vii,viii,ix,x].

Airway driving pressure (DP) is equivalent to the rise from PEEP to Pplat. with each inspiration (equivalent to the ratio between the tidal volume and respiratory system compliance). As the preset tidal volume is applied only to the available aerated lung volume corresponding to the driving pressure (Pplat - PEEP) it is presumed to reflect the liability to lung injury iv , also some studies showed the possibility of using airway driving pressure as a possible surrogate for lung stress at bedside[xi] avoiding the use of esophageal manometer and any disconnection from the ventilator that can be technically challenging [xii].
Pulmonary hypertension develops in ARDS patients due to increased pulmonary vascular resistance by numerous factors including hypoxic pulmonary vasoconstriction, vascular endothelial hyperplasia and myo-intimal proliferation, pulmonary vascular thrombosis and destruction, systemic and local release of vasoconstrictive mediators [xiii,xiv,xv,xvi,xvii] , these all are in addition to the cardio-pulmonary interactions induced by mechanical ventilation [xviii].The incidence of pulmonary hypertension and right ventricular dysfunction(acute corpulmonale) in ARDS patients ranges between 25% and 61% [xix,xx] .

Study design
This is a prospective observational study

Study setting
Critical care department, Cairo University

Patients and methodology

Population: This study enrolled 50 mechanically ventilated ARDS patients with ,diagnosed according to Berlin definition criteria[xxi].
Exclusion criteria: left side heart failure (LV EF<50%). Mitral or aortic moderate to severe stenosis or insufficiency .

On admission, demographic data (age, gender ,etc…), history of chronic diseases, severity assessment scores as acute physiology and chronic health evaluation II(APACHE II) score [xxii], sequential organ failure assessment (SOFA) score [xxiii] and simplified acute physiology score(SAPS) score [xxiv]. Complete blood counts , blood chemistries , and arterial blood gases were obtained on admission.
Transthoracic echocardiography (TTE) was performed on day 0 and day 7 to assess left ventricle function (LV EF%) ,basal RV diameter (ref : 2.0-2.8cm)[xxv] ,RV fractional area change(FAC) (ref: 32–60%) ,TAPSE (15-20 mm)[xxv] ,tricuspid valve regurgitation presence and severity by regurgitation jet area (mild if jet area <5cm^2 and severe if jet area > 10cm^2) [xxvi] and venacontracta (severe TR if >7mm[xxvi]), pulmonary artery systolic pressure (PASP) was measured ,pulmonary hypertension was diagnosed if > 37 mm Hg. [xxvii].

Respiratory airway pressures and parameters were measured on day 0 , day3 and day 7 including tidal volume (Vt), respiratory rate (RR) , applied positive end expiratory pressure (PEEP) , peak pressure (P peak) , plateau pressure(P plateau) , static lung compliance (Cstat) (obtained by dividing tidal volume by plateau

pressure), driving pressure (DP) (obtained by subtracting peep from plateau pressure) . All respiratory parameters were obtained during deep sedation and pharmacological paralysis of the ventilated patients to eliminate the spontaneous respiratory efforts and minimize chest wall elastance.

ARDS severity was determined on day 0 , day3 and day 7 according to Berlin criteria[xxi] and Murray scoring system [xxviii] . Berlin criteria graded ARDS into mild , moderate and severe according the ratio between partial arterial oxygen pressure and the fraction of oxygen in the inspired air (PaO_2 /FiO_2). Murray score is calculated using 4 criteria (1- hypoxemia 2- static lung compliance 3- chest radiographic findings 4- PEEP level). Each criterion was scored from 0 to 4 according to its severity. Murray final score is the collective score divided by the number of used components. A final score of zero indicates no lung injury, a score of 1 – 2.5 indicates mild to moderate lung injury, and a score more than 2.5 indicates the presence of ARDS

According to ICU mortality, patients are divided into survivors and nonsurvivors, echocardiographic and ventilator parameters are compared between the 2 groups. Correlations were done between the echocardiographic and ventilator parameters.

Results

The mean(±SD) age of the 50 studied population was 53.36 ±13.77yrs, from them 26 were male (52%). Survivors represented (60%) of the studied population while non survivors nonsurvivors represented (40%).

On admission APACHE II score mean (±SD) was 24 ± 5.09 in the total population, and (21.7± 4.3 versus 27.6 ± 4, P <0.0001) in survivors versus nonsurvivors respectively. SAPS score mean(±SD) was 49.08 ± 10.44 in the total population, and (42.6 ± 7.39 versus 58.8 ± 5.6, P <0.0001) in survivors versus nonsurvivors respectively, while SOFA score mean(±SD) was 7.28 ± 1.45 in the total population,and (6.6±1.2 versus 8.3±1.17, P 0.048) in survivors versus nonsurvivors respectively

As regard ARDS phenotype it was direct (pulmonary) in 37 (74%) and indirect (extrapulmonary) in 13(26%) patients . Duration of mechanical ventilation mean (±SD) in the total population was 11.2±3.03 day (that was about 71% of the whole period of ICU stay) , mechanical ventilation duration was (10.2±2.68 versus 12.8±2.89 day, P 0.002) in survivors and nonsurvivors respectively. Non-survivors group was significantly older than the survivors group as the mean (±SD) age was 62±11.9 versus 47.6±11.8 years old respectively with p value of < 0.0001

ARDS severity

According to *Berlin criteria* PaO_2 /FiO_2 ratio, on day 0 ARDS was mild in 2, moderate in 39 and severe in 9 patients, on day 3 ARDS was mild in 5, moderate in 42 and severe in 3 patients, and on 7^{th} day 18 patients cured from ARDS and 10 patients had mild ARDS and 2 patients had moderate ARDS reaching up to a total of 30 patients survived through our study while the non survivors (20 patients) all were severe on day 7 (P <0.0001).

Murray score mean(±SD) in the studied population was 2.41 ± 0.44 on day 0, 2.24 ± 0.34 on day 3 and 1.77 ± 0.14 on day 7. Murray score mean values changed significantly from day 0 to day 3 (P 0.03), from day 3 to day 7 (P 0.02), and from day 0 to day 7 (p 0.002). High Murray score mean (±SD) was associated with mortality on day 0 (2.3±0.26 versus 2.48±0.36, P 0.045), on day 3 (2.01±0.39 versus 2.56±0.32, P <0.0001) and on day 7 (0.76 ± 0.33 versus 3.27± 0.13, P <0.0001) in survivors versus nonsurvivors respectively.

As regard *Murray score* correlation with respiratory mechanics ,on day 3 it was positively correlated with DP (R 0.657 , p 0.001) and Pplat (R 0.712 , p 0.001) and on day 7 it was positevly correlated with DP(R 0.925 , p 0.001) and P plat (R 0.958 , p 0.001) and negatively correlated with Vt (R -0.915, p 0.0001).

Respiratory mechanics

DP mean (±SD) in the studied population was 22.52±2.64 cm H_2O on day 0, 20.16±4.11 cm H_2O on day 3 and 16.04± 6.06 cm H_2O on day 7. DP mean values changed significantly from day 0 to day 3(P 0.0001), from day 3 to day 7 (P 0.0001), and from day 0 to day 7 (P 0.0001). High DP mean(±SD) was associated with mortality on day 3 (17.83±3.50 versus 23.65±1.87 cm H_2O ,P <0.0001) and on day 7(11.43±2.11 versus 22.95±2.08 cm H_2O ,P <0.0001) in survivors versus nonsurvivors respectively. DP was predictive for mortality on day 3 at a cutoff value 20.5 cm H_2O (P< 0.0001 ,AUC 0.936, sens. 95% and spec. 77%,), and on day 7 at a cutoff value 21 cm H_2O (P < 0.0001 ,AUC 1 , sens. 80% and spec. 100%).

P plat. mean (±SD) in the studied population was 30.22±3.22 cm H_2O on day 0, 27.76±4.97 cm H_2O on day 3 and 23.2±8.18 cm H_2O on day 7 .P plat. mean values changed significantly from day 0 to day 3 (P 0.003), from day 3 to day 7 (P 0.0001), and from day 0 to day 7(P 0.0001). High P plat mean (±SD) was associated with mortality on day 3 (24.96 ±4.39 versus 31.95 ±1.87 cm H_2O , P <0.0001) and on day 7(16.80±2.20 versus 32.8±1.88 cm H_2O, P <0.0001) in survivors versus non survivors respectively. P plat. was predictive for mortality on day 3 at a cutoff value 28.5 cmH_2O (P< 0.0001 , AUC 0.932 , sens. 100% and spec. 90%,), and on day 7 at a cutoff value 25 cm H_2O (P < 0.0001 , AUC 1, sens. 100% and spec. 100%).

Static lung compliance(*Cstat.*)mean (±SD) in the studied population was 25.04±4.52 ml/cm H_2O on day 0, 28.08±7.53 ml/cm H_2O on day 3 and 39.5 ±18.47 ml/cm H_2O on day 7. *C stat.* mean values changed significantly from day 0 to day 3 (P 0.015), from day 3 to day 7 (P 0.0001), and from day 0 to day 7 (P 0.0001). Low *C stat.* mean (±SD) was associated with mortality on day 3 (32.13±7.08 versus 22.0±2.24 ml/ cm H_2O , P <0.0001) and on day 7(52.83 ±10.62 versus 19.50±2.39 ml/cm H_2O , P <0.0001) in survivors versus nonsurvivors respectively. C stat. was predictive for mortality on day 3 at a cutoff value 26 ml/cm H_2O (P< 0.0001 , AUC 0.950 , sens. 80% and spec. 100%), and on day 7 at a cutoff value 32.5 ml /cm H_2O (P < 0.0001 , AUC 1, sens. 100% and spec. 100%).

Tidal volume mean (±SD) in the studied population was 554.6±33.93 ml on day 0, 540.40±37.46 ml on day 3 and 529.20±73.92 ml on day 7, Tidal volume mean value changed from day 0 to day 3(P 0.041), from day 3 to day 7(P 0.182), and from day 0 to day 7(P 0.05) . Low tidal volume mean (±SD) associated with mortality on day 3 (555.0±28.25 versus 518.5±39.50 ml, P <0.0001) and on day 7 (584.66±19.60 versus 446.0+/-36.90 ml, P <0.0001) in survivors versus nonsurvivors respectively. Vt. was predictive for mortality on day 3 at a cutoff value 545 ml (P< 0.001 , AUC 0.788 , sens. 70% and spec. 83%,), and on day 7 at a cutoff value 525 ml (P < 0.0001 , AUC 1, sens. 100% and spec. 99%).

Table (1): respiratory mechanic mean(±SD) on day1,day3 and day7
Vt (ml) , P plat (cm H_2O), Cstat(ml/cm H_2O) ,DP (cm H_2O)

	Day (0)				Day(3)				Day(7)			
	Total population	Survivors	Non survivors	P	Total population	Survivors	Non survivors	P	Total population	Survivors	Non survivors	P
Vt	554.6±33.93	544.33±35.78	570.0±24.49	0.127	540.40±37.46	555.0±28.25	518.5±39.50	<0.0001	529.20±73.92	584.66±19.60	446.0±36.90	<0.0001
Pplat	30.22±3.22	30.3±3.38	30.1±3.04	0.832	27.76±4.97	24.96±4.39	31.95±1.87	<0.0001	23.2±8.18	16.80±2.20	32.8±1.88	<0.0001
Cstat	25.04±4.52	25.06±5.17	25.0±3.46	0.960	28.08±7.53	32.13±7.08	22.0±2.24	<0.0001	39.5±18.47	52.83±10.62	19.50±2.39	<0.0001
DP	22.52±2.64	22.16±2.60	23.05±2.68	0.251	20.16±4.11	17.83±3.50	23.65±1.87	<0.0001	16.04±6.06	11.43+/-2.11	22.95±2.08	<0.0001

Echocardiographic parameters

PASP mean (±SD) in the total population was 35.72±5.33mm Hg on day 0 and 44.18±14.4 mm Hg on day 7 (P 0.0001). High PASP mean (±SD) was associated with mortality on day 0 (33.46 ± 4.24 versus 39.1±5 mm Hg, P < 0.0001) and on day 7(33±4.35 versus 61.1±4.64 mm Hg ,P <0.0001) in survivors versus nonsurvivors respectively. PASP was predictive for mortality on day 0 at a cutoff value 35.5 mm Hg(p P<0.0001,AUC0.820sens90% and spec50%) and on day 7 at a cutoff value 45 mm Hg(p P<0.0001,AUC1,sens100% and spec100%).

TAPSE mean (±SD) in the total population was 18.38±1.17 mm on day 0, 15.8±4.3 mm on day 7 (P 0.0001) . Low TAPSE mean (±SD) was associated with mortality on day 7(18.63 ±1.09 versus 12.6±3.8 mm ,P <0.0001) in survivors

versus nonsurvivors respectively. TAPSE mean was predictive for mortality on day 7 at cutoff value 16 mm with (P<0.0001,AUC1,sens100%. And spec.99%).
RV basal diameter mean (±SD) was 2.83±0.4 cm on day 1 and 4.57±1.4 cm on day 7 (P 0.0001) . Increased RV basal diameter mean (±SD) was associated with mortality on day 7(2.86±1.1 versus 7.13±1.8 cm, P <0.0001) in survivors versus nonsurvivors respectively. RV basal diameter mean was predictive for mortality on day 7 at cutoff value 4.5 cm with (P<0.0001,AUC1,sens100%. and spec.99%).

Tricuspid regurigtation assessment showed TR jet area mean (±SD) was 0.69±0.2 cm^2 on day 1, 4.52±1.5 cm^2 on day 7(P 0.0001). Increased TR jet area mean (±SD) was associated with mortality on day7 (0.77 ± 0.2versus10.15±1.8 cm^2 ,P value<0.0001) in survivors versus nonsurvivors respectively,. TR jet area mean was predictive for mortality on day 7 at cutoff value 5.5 cm^2 with(P<0.0001,AUC1,sens100%. And spec.99%).

TR venacontracta mean (±SD) was 1.44+/-0.71 mm on day 0, 3.44+/-0.9mm on day 7(P 0.0001). Increased TR venacontracta mean (±SD) was associated with mortality on day 7(1.47±0.2 versus 6.65±0.9 mm, P <0.0001) in survivors versus nonsurvivors respectively.TR venaconracta mean was predictive for mortality on day 7 at cutoff value 5.5 mm with (P<0.0001,AUC0.969,sens85%. And spec.10%)
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Table (11) echocardiographic parameters mean(±SD) on day1 and day7

Parameters	Day(0)				Day(7)			
	Total population	Survivors	nonsurvivors	P value	total population	Survivors	nonsurvivors	P value
EF%	59.4±4.47	58.8±4.67	60.3±4.1	0.250	59.98±4.75	59.66±5.51	60.31 ±3.36	0.573
PASP mmHg	35.72±5.33	33.46±-4.24	39.1±5	<0.0001	44.18±14.4	33±4.35	61.1±4.64	<0.0001
TAPSE mm	18.38±1.17	18.4±1.19	18.35±1.18	0.885	15.8±4.3	18.63±1.09	12.6±3.8	<0.0001
RV diameter cm	2.828±0.4	2.83±1.2	2.82±1.5	0.28	4.564±1.4	2.86±1.1	7.13±1.8	<0.0001
TR jet area cm^2	0.698±0.2	0.63±0.15	0.8±0.12	0.13	4.522±1.5	0.77±0.2	10.15±1.8	<0.0001
TV vena contracta mm	1.44±0.71	1.43±0.8	1.45±0.7	0.35	3.44±0.9	1.47±0.2	6.65±0.9	<0.0001

Correlations between RV parameters and respiratory mechanics

On day 7 PASP was positively correlated with DP(R 0.908, p 0.001) and Pplat (R 0.934, p 0.001) and negatively correlated with Vt (R -0.883, p 0.0001) ,while TAPSE was negatively correlated with DP(R -0.713, p 0.001) and Pplat (R -0.751, p 0.001) and positively correlated with Vt(R 0.814, p 0.0001) . Also on day 7 RV diameter was positively correlated with DP(R 0.910 , p 0.001) and Pplat (R 0.937 , p< 0.0001) and negatively correlated with Vt (R -0.908, p< 0.0001) , TR jet area was positively correlated with DP (R 0.906 , p 0.001) and Pplat (R 0.925 , p 0.0001) and negatively correlated with Vt(R -0.852, p 0.0001) ,TR venaconracta was positively correlated with DP(R 0.819 , p 0.001) and Pplat (R 0.844 , p< 0.0001)and negatively correlated with Vt (R -0.759, p< 0.0001).

Discussion

In this study high DP , P plat , and low Vt were significantly associated with mortality on day 3 and day 7 with P<0.0001 for each ,while on day 0 there was no association

Marcelo and Amato et al [xxix] study on 3562 ARDS patients showed that decreases in DP owing to changes in ventilator settings were strongly associated with increased survival(P <0.001) , higher DP predicted lower survival, and that changes in V_T or PEEP were associated with survival only if they led to reductions in DP . *Sandoval G et al.*[xxx] and his colleagues evaluated DP in 56 ARDS patients with H1N1 infection, and showed that DP was the most predictive value for mortality. *Davide Chiumello et al,*[xxxi] in his study on 150 ARDS patients showed that patients with higher airway DP (>15 cm H_2O) had a higher P plat (P <0.001) , higher transpulmonary driving pressure(P <0.001) and higher lung stress (P <0.001) at both low(5cm H_2O) and high(15 cm H_2O) PEEP ,but airway DP was a predictor for mortality only at low PEEP(5cm H_2O) with (P 0.049) while at high PEEP(15cm H_2O) did not predict mortality (P 0.352) ,and this was explained by the study authors that patients after the study underwent different setting of mechanical ventilation and were not managed according to driving pressure to decrease it and that his study has many limitations including that the majority of patients are in the category of mild to moderate ARDS.

Brower RG et al [xxxii], in his study on 861 ARDS patients showed that Pplat is higher significantly in non survivors , the mean plateau pressures were 25+/-6 and 33+/-8 cm of water (P<0.001) in survivors and non survivors respectively . *Jardin F et al* [xviii] in a study on 352 ARDS patients showed an association between high Pplat and mortality. In contrary to our results *Seeley E et al.* [xxxiii] in a study on 149 patients with ALI/ARDS found that Pplat was insignificantly higher and Vt was insignificantly lower in non survival , it can be explained by that in this study the North American–European consensus conference AECC definition[xxxiv] was used for diagnosis of ARDS which is different from ours in which we used Berlin definition criteria AECC defined ALI as respiratory failure of acute onset with a PaO_2/FiO_2 ratio ≤300 mmHg (regardless of the level of positive end expiratory pressure, PEEP), bilateral infiltrates on frontal chest radiograph, and a pulmonary capillary wedge pressure ≤18 mmHg (if measured) or no evidence of left atrial hypertension [8]. ARDS was defined identically except for a lower limiting value of <200 mmHg for PaO_2/FiO_2 [xxxiv] The AECC definition of ALI/ARDS is in common use and simple to apply, but also has serious deficiencies in discrimination. There is often not a good correlation between these broad clinical definitions and diffuse alveolar damage (DAD), which is widely considered to be a major characteristic histological feature of ALI/ARDS[xxxv] [9]. The AECC definitions also do not take into consideration variables such as the mode of ventilation and the level of PEEP, which can significantly influence oxygenation. Additionally with the publication of studies that have shown that routine use of Swan-Ganz catheters can be associated with higher complications, the PCOP component of the definition is not commonly measured[xxxvi,xxxvii]. That places a significant emphasis on chest x-ray interpretation where there is a significant lack of inter-observer reliability. However the AECC definition particularly with the

ARDS component has proven predictability. For instance patients with ARDS per this definition have higher mortality compared to patients without[xxxviii,xxxix]
In contrary to our result *Trushil G. Shah et al* [xl] in his study on 38 ARDS patients showed that there were no difference in driving pressure and plateau pressures between survivors and nonsurvivors , explaining this by that small sample size may have limited the ability to evaluate a difference among these parameters.

In our study the prevalence of pulmonary hypertension (PASP >37mmHg) and RV dysfunction(increased RV basal diameter and low TAPSE) represented 40% of the studied population.

S.A. Ñamendys-Silva, et al [xli] study on 30 ARDS patients showed that prevalence of pulmonary hypertension was 46.6% which is concordant to our study *Beiderlinden et al.* [xlii] in a study on 103 ARDS patients found that the prevalence of pulmonary hypertension was very high 92.2% , explained by that patients had been referred from other hospitals as a result of treatment failure, which suggests that they were in the late stages of ARDS , also ARDS was defined by Murray score greater than 2.5 [xxviii] ,while in our study Berlin definition criteria was used for definition of ARDS . *Sibbald et al.*[xliii] study on 51 ARDS patients showed that the prevalence of pulmonary hypertension was 72.5%; this is explained by that pulmonary hypertension was defined as mPAP >19 mmHg.

Surprisingly *David Osman et al* [xliv] in his study on 145 of ARDS patients found an incidence of RVF only 9.6% , the low incidence of RVF may be related to that it was defined by the concomitant presence of the mean pulmonary artery pressure (mPAP) > 25 mmHg, , the central venous pressure (CVP) higher than pulmonary artery occlusion pressure (PAOP) and the stroke volume index < 30 mL /m^2. *Boissier et al*[xlv] study on 226 ARDS patients showed that right ventricular dysfunction was detected in 22% ,in this study patients were underwent transesophageal echocardiography (TEE) within only the first 3 days after the diagnosis of ARDS, and acute cor pulmonale (ACP) was defined as a dilated right ventricle associated with septal dyskinesia *Lhéritier et al* [xlvi] study on 200 ARDS patients showed that the incidence of right ventricular failure is 22.5%, patients are underwent transthoracic (TTE) and transesophageal echocardiography (TEE) <48 h after admission, and ACP was defined as the conjunction of a dilated RV [end-diastolic RV area/end-diastolic LV area >0.6] and an abnormal septal curvature *Vieillard-Baron et al*[xx] in a study on 75 ARDS found that ACP was found in 25% study population ,in this study ACP was defined as a ratio of right ventricular end-diastolic area to left ventricular end-diastolic area in the long axis >0.6 associated with septal dyskinesia during TEE examination.

We found that high PASP was associated with mortality as early as from day 0 with continuous to day 7($p<0.0001$) . Right ventricular dilatation , low TAPSE and tricuspid regurge predicted mortality only from day 7 ($P<0.0001$).

Bull et al.[xlvii] study on 501 ARDS patients showed that patients with an elevated baseline transpulmonary gradient (PA mean pressure - PA occlusion pressure) had increased 60-day mortality (30 versus 19%; P 0.02). *Squara et al.* [xlviii] in his study on 586 ARDS patients showed that RV dysfunction (high RVSW/LVSW)

can predict mortality early on admission while systolic pulmonary arterial pressure (SPAP) became an independent prognostic parameter from day 2 . *Laghi and colleagues* [xlix] study in 88 ARDS found that RVD(higher RVSWI/LVSWI) was associated with high mortality (P <0.0001). *Steltzer et al* [1] described a significantly depressed right ventricular ejection fraction in nonsurvivors ARDS patients. *Boissier et al*[xlv] enrolled 226 patients with ARDS found that right ventricular dysfunction was a significant and an independent predictor of mortality which is concordant with our results *Mekontso Dessap et al*[li] study on 752 patients with ARDS found that hospital mortality was higher in patients with a severe right ventricular dysfunction and dilatation *Monchi et al.* [lii] reported that right ventricular dysfunction was an independent predictor of mortality in ARDS patients exhibiting an average plateau pressure of 31 cmH_2O.

David Osman et al [xliv] in his study on 145 of ARDS patients pulmonary hypertension defined as high MPAP>25mm Hg and the presence of CVP > PAOP were independently associated with mortality. While RV failure defined as a mean pulmonary artery pressure (MPAP) > 25 mmHg, a central venous pressure (CVP) higher than pulmonary artery occlusion pressure (PAOP) and a stroke volume index < 30 mL/ m^2 was not associated with mortality . It could be postulated that physicians were more tempted to take corrective measures when they detected a low SVI (in addition to elevated mPAP and a CVP > PAOP) than when they detected an elevated mPAP alone or the presence of CVP > PAOP alone.

In contrary to our study results *Cepkova et al* [liii] study on 42 ARDS patients found that on admission no statistically significant difference existed in PASP between survivors and nonsurvivors. *S.A. Ñamendys-Silva, et al* [xli]study on 30 ARDS patients showed that their was no association between pulmonary hypertension and mortality . *Lhéritier et al* [xlvi] study on 200 ARDS showed that right ventricular failure is not a predictor for outcome .This study did not use the Berlin definition of ARDS in the inclusion criteria , but rather the definition of the American European consensus conference. Also echocardiogram was performed once in the first 48 h of admission without follow up. *Vieillard-Baron et al*[xx] in his study on 75 ARDS patients found that acute corpulmonale did not have a negative influence on the patient's outcome , and all echo-Doppler abnormalities were reversible in patients who recovered, and the mortality rate was the same in both groups (32%) which may be explained by the less severe condition in this study (Pplat 25 cm H_2O)

In our study we showed that lower TAPSE was associated with ARDS mortality on day 7 .This is concordant with *Wadia SK et al*[liv], study in which they proved that TAPSE is correlated with ARDS severity with (P 0.004), and was lower among 30-day nonsurvivors compared with survivors (P .002). *Trushil G. Shah et al* [xl] in his study on 38 ARDS patients showed that low TAPSE is associated with mortality(19.12 ± 1.8 Vs 15 ± 1.77) in survivors versus non survivors respectively ,this is in line with our findings that nonsurvivors had an average TAPSE value of <17 mm

In our study Dp and P plat was correlated with TAPSE , PASP and RV dilatation day 7 with . *Mekontso Dessap et al*[li] study on 752 patients with ARDS found that

ARDS was more severe in the severe RV dysfunction group as expressed by the worse respiratory mechanics(higher P plat) and blood gas (hypoxemia and hypercapnia) causing higher pulmonary vascular resistance and RV afterload, *Boissier et al*[xlv] enrolled 226 patients with ARDS ,right ventricular dysfunction was found to be associated with higher driving pressure ,however Pplat did not differ significantly in patients with and without RV , *Jardin F et al* [xviii] in a study on 352 ARDS patients showed an association between high Pplat and mortality and acute core pulmonale ; incidence of mortality rate and cor pulmonale were 80 and 56%, respectively, with plateau pressure > 35 cmHO;; and 30 and 13%, respectively, with plateau pressure < 27 cmH_2O.

Conclusion

We found that high DP and P plat. , and low Vt were associated with mortality on day 3 and day 7 . High PASP was associated with mortality as early as from day 0 continuous to day 7 ,while right ventricular dilatation , decreased TAPSE and tricuspid regurge predicted mortality on day 7. Dp and Pplat were correlated with TAPSE from day 0 upto day 7 ,and were correlated with PASP and RV dilatation on day 7 .Further observational studies with a larger scale are required to confirm these association with underlying pathophysiological mechanisms in the future.

Limitations

A small sample size may have limited the ability of our study. We did not use transesophageal echocardiography or transesophageal manometer to measure transpulmonary driving pressure due to it was not available all over the time in ICU. Pulmonary hemodynamic parameters were measured noninvasively without pulmonary artery cathete

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