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# **Driving pressure is not predictive of ARDS outcome in chest trauma patients under mechanical ventilation**

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# ABSTRACT

## **Background:**

The relationship between the driving pressure of the respiratory system (DPrs) under mechanical ventilation and worse outcome has never been studied specifically in chest trauma patients. The objective of the present study was to assess in cases of chest trauma the relationship between DPrs and severity of acute respiratory distress syndrome (ARDS) or death and length of stay.

## **Methods:**

A retrospective analysis of severe trauma patients (ISS > 15) with chest injuries admitted to the Trauma Centre from January 2010 to December 2018 was performed. Patients who received mechanical ventilation were included in our analysis. Mechanical ventilation parameters and DPrs were recorded during the stay in the intensive care unit. Association of DPrs with mortality and outcomes was specifically studied at the onset of ARDS (DPrs-ARDS) by receiver operator characteristic curve analysis, Kaplan-Meier curves, and multivariate analysis.

## **Results:**

Among the 266 chest trauma patients studied, 194 (73%) developed ARDS. DPrs was significantly higher in the ARDS group versus in the no ARDS group (11.6 +/- 2.4 cm H<sub>2</sub>O vs. 10.9 +/- 1.9 cm H<sub>2</sub>O,  $p = 0.04$ ). Among the patients with ARDS, no difference according to the duration of mechanical ventilation was found between the high DPrs group (DPrs-ARDS > 14 cm H<sub>2</sub>O) and the low DPrs group (DPrs-ARDS < 14 cm H<sub>2</sub>O), ( $p = 0.75$ ). DPrs-ARDS was not independently associated with the duration of mechanical ventilation (hazard ratio [HR], 1.006; 95% CI, 0.95–1.07;  $p = 0.8$ ) or mortality (HR, 1.07; 95% CI, 0.9–1.28;  $p = 0.45$ ). High mechanical power ( $\geq 12$  J/min) was associated with a lower time for weaning of mechanical ventilation in Kaplan-Meier curves but not in multivariate analysis (HR, 0.98; 95% CI, 0.94–1.02;  $p = 0.22$ ).

## **Conclusion:**

A high DPrs-ARDS was not significantly associated with an increase in mechanical ventilation duration or mortality risk in ARDS patients with chest trauma in contrast with medical patients.

# Background

Traumatic chest injuries are responsible for significant morbidity and are the cause of trauma-related death in 20%–25% of cases [1]. Following a trauma, patients affected by thoracic injuries are at risk of significant worsening of respiratory function, leading to mechanical ventilation need and acute respiratory distress syndrome (ARDS) in the most severe cases [2]. Causes of ARDS include direct injuries to the lungs and/or secondary mechanisms induced by the trauma setting (e.g., fat embolism, systemic inflammatory response, and abdominal compartment syndrome). These physiopathological phenomena and the influence of harmful factors explain why many cases of ARDS occur more than 48 hours after admission [3]. In addition to these respiratory impairments related to trauma, lung injuries may also be aggravated by deleterious effects of mechanical ventilation, such as barotrauma or biotrauma [4,5]. To prevent or minimise these expected complications, called ventilator-induced lung injury (VILI), current guidelines for lung-protective ventilation in patients with ARDS suggest the use of a low tidal volume (VT), higher levels of total positive end-expiratory pressure (PEEP) and limitation of the inspiratory plateau pressure of the respiratory system (PPLAT) under 30 cm H<sub>2</sub>O [6,7]. Based on the same rational design, most experts strongly recommend this therapeutic approach in trauma patients [8]. However, this extrapolation of the medical setting is based on populations affected by ARDS from multiple origins. Post-traumatic ARDS represented only 8% to 13% of these cohorts [3]. Specific studies focusing on populations of trauma patients are lacking.

The driving pressure of the respiratory system (DPrs) is defined as the difference between PPLAT and PEEP [9]. Many studies demonstrated that high DPrs in ARDS patients was associated with worst outcome [9,10]. DPrs is a marker of alveolar collapse as well as lung strain and correlates well with lung stress [11]. High DPrs is therefore the reflection of a baby lung ventilation and would be incriminated into the phenomena of VILI. However, those findings remain to be confirmed in trauma patients.

The main goal of the present study was to assess in a population of severe trauma patients with chest injuries the relationship between DPrs observed at the onset of ARDS (DPrs-ARDS) and outcomes.

# Methods

## Study design

The charts of severe trauma patients (Injury Severity Score [ISS] > 15) admitted to Lapeyronie University Hospital (Level I Regional Trauma Centre, Montpellier, France; Occitrauma network) over a 9-year period (January 2010 to December 2018) were reviewed retrospectively. We obtained approval from the local scientific and ethics committee of Montpellier University Hospital, Comité d'Organisation et de Gestion de l'Anesthésie Réanimation (COGAR), who stated that informed consent from the patient or next of kin was not required. As a matter of fact, our databank has been validated by the COGAR and appears

on nominative list of our institution. Patients and relatives have been informed that their data during and after their ICU stay could be used for analysis and medical publication. Thereby, in this retrospective analysis, no supplemental ethics Committee approval was necessary.

### **Inclusion criteria**

Consecutive trauma patients with chest trauma (Abbreviated Injury Scale [AIS]  $\geq 1$ ) who required invasive mechanical ventilation for a minimum of 48 hours were included in the present study [12]. Intubation was performed following standard care: respiratory failure, coma with GCS  $< 8$ , haemodynamic instability, need for urgent surgery. Exclusion criteria were as follows: minors, immediate death, admission from another hospital, absence of initial computed tomography (CT) scan and incomplete medical records.

### **Respiratory management of patients**

All patients included in the study were ventilated in our unit using a lung-protective mechanical ventilation protocol as defined in the literature: low tidal volume between 6 and 8 ml/kg of predicted body weight and limited PPLAT [13]. Ventilatory parameters were set to avoid intrinsic PEEP. There was no standardised protocol for setting PEEP. Different methods were used with the evolution of medical literature. We therefore used Fio<sub>2</sub>/Peep tables, pressure/volume curves, titration of PEEP until achievement of maximal Plateau pressure. All the PEEP setting were guided by clinical responses and haemodynamic tolerance. Recruitment manoeuvres were performed at the discretion of the clinician. Thoracic drainage was performed, if necessary, with surgical dissection by an anterior approach for pneumothoraces (14 Fr) and axillary approach for haemothoraces (24 or 28 Fr). In specific settings such as severe bronchopleural fistulae, unilateral lung injuries, or refractory hypoxaemia, an alternative to conventional mechanical ventilation may be used; for example, separated lung ventilation in the prone position, high-frequency percussive ventilation, or veno-venous extracorporeal membrane oxygenation in extreme cases.

### **Data collection**

The following data were extracted from the medical records: age, sex, mechanism, characteristics of injuries, mortality, duration of mechanical ventilation, length of stay in the intensive care unit (ICU) and hospital length of stay. In addition, ISS and AIS scores were obtained for each body region as well as the Simplified Acute Physiology Score (SAPS) II. Prone position, pH, partial pressure of carbon dioxide in arterial blood (PaCO<sub>2</sub>), PaO<sub>2</sub>/FIO<sub>2</sub>, lactate, haemoglobin, base deficit, respiratory rate, VT, PEEP, PPLAT, respiratory system compliance (C<sub>rs</sub>), DPrs and PaO<sub>2</sub>/FIO<sub>2</sub> were recorded using daily ventilatory monitoring. PPLAT was systematically assessed using an inspiratory pause, whereas PEEP was systematically assessed using an expiratory pause to reflect total PEEP. Mechanical power (MP) was also computed as the product of DPrs in Newtons (cm H<sub>2</sub>O x 0.098), tidal volume and respiratory rate. It was expressed as J/min and was included in the analysis [14]. For the no ARDS group respiratory parameters were collected the day of admission following initial stabilisation. For the ARDS group, these parameters were collected on the onset day of ARDS.

In addition, specific data on chest trauma were collected based on the CT scan on admission (size of pulmonary contusions, pneumothoraces, haemothoraces, rib fractures, flail chest and atelectasis) allowing the Thoracic Trauma Severity (TTS) score on admission to be determined on a scale ranging from 0 to 25 points [15,16].

### **Study definitions**

ARDS was defined using the Berlin criteria consensus definition [17]. ARDS severity was classified using the Berlin criteria. The ARDS diagnoses were retrospectively reviewed by two physicians (SR and MA). We collected PaO<sub>2</sub>/FiO<sub>2</sub> ratio twice a day for all the patients. When patients met the Berlin criteria, they were included in the ARDS group. When the ratio became superior to 300, the patient was no longer categorised in ARDS. Patients were thus categorised into two groups according to the occurrence (ARDS group) or the absence of ARDS (no ARDS group). Timing was also considered: early ARDS (onset in the first 48 h after admission) and late ARDS (onset 48 h after admission). Ventilatory parameters were collected daily for all patients including DPrs. In the subgroup of ARDS patients, DPrs-ARDS was the DPrs value that was observed the day of ARDS diagnosis. For no-ARDS patients, DPrs of reference was the driving pressure at admission after initial resuscitation and stabilisation. The duration of mechanical ventilation, length of stay in the ICU and hospital length of stay for the ARDS group were extracted from medical records.

### **Statistical analysis**

The study population was first divided into two groups according to the occurrence of ARDS (ARDS and no ARDS groups) and compared. Quantitative variables were expressed as the mean (standard deviation [SD]) or median (interquartile range, 25%– 75%) and compared using the Student t test or Wilcoxon-M

Whitney test as appropriate. Qualitative variables were expressed as number (%) and compared using the Chi-squared test or Fisher test as appropriate. A descriptive analysis of the ARDS group focused on respiratory parameters was thus performed. Box plots were used to expose these data. In the case of missing data, the number of missing values is clearly stated for each variable. An a priori threshold for DPrs was defined based on previous results in the field (> 14 cm H<sub>2</sub>O) [9,18]. Similarly, the threshold for MP was defined a priori as  $\geq$  12 J/min [14].

A ROC curve was drawn to analyse the capacity of DPrs-ARDS to predict severity of ARDS in the ARDS subgroup. The area under the ROC curve (AUC) was expressed with the 95% confidence interval (CI). A survival analysis for weaning from mechanical ventilation was performed. Weaning from mechanical ventilation is censored by death before extubation. To draw Kaplan-Meier curves, the ARDS subgroup was divided according to the value of DPrs

or MP. The thresholds defined a priori for DPrs and MP ( $> 14$  cm H<sub>2</sub>O and  $\geq 12$  J/min, respectively) were conserved in this part of the analysis. The log-rank test was used to compare these curves. False-positive and false-negative rates were determined.

Finally, the relationship between DPrs or MP and different outcomes (duration of mechanical ventilation, occurrence of death, length of stay in the hospital and in the ICU) were assessed using a multivariate Cox regression analysis. In this analysis, the occurrence of ventilator-associated pneumonia was particularly considered as a confounding factor with the duration of mechanical ventilation. The statistical analysis was performed by CD and KB from the Clinical Research and Epidemiology Unit of Montpellier University Hospital using SAS statistical software (version 9.4; SAS Institute; Cary, NC). Statistical significance was set at a bilateral alpha risk  $< 0.05$ .

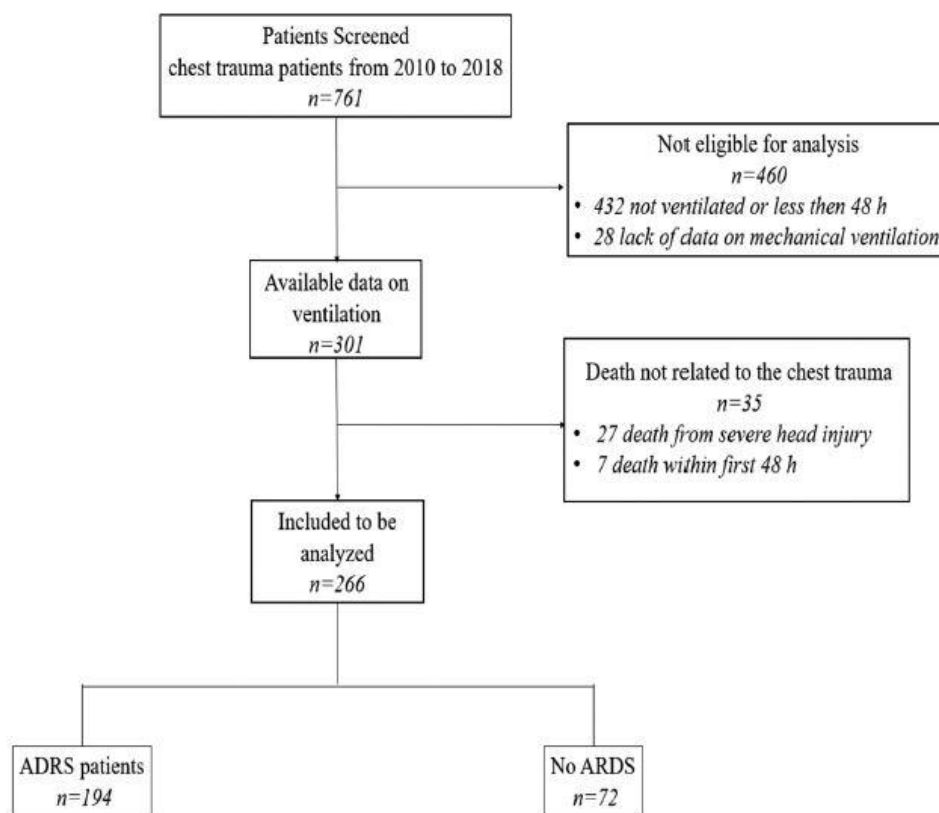


Fig. 1. Flowchart of the study.

## Results

Among the 1669 patients admitted with chest trauma to our trauma ICU during the study period, 761 (46%) met the inclusion criteria. Of these, 460 (60%) were not eligible for

analysis due to duration of mechanical ventilation less than 48 h in 432 cases and a lack of data in 28 cases. Finally, 301 patients were included in the study. Of these, 35 patients (11%) were excluded from our analysis due to early death. The 266 remaining patients were thus included in our analysis. The flowchart of the study is presented in Fig. 1. Among the study population, 204 patients were male (77%), the mean age was 43.0 ( +/-19.3) years, and the mean ISS was 32 ( +/-10). One hundred and fifty patients (56%) were classified as AIS  $\geq$  3 thoracic trauma, 84 (31%) were AIS  $\geq$  3 abdominal trauma and 135 (51%) were AIS  $\geq$  3 traumatic brain injury. The mean TTS score was 9.5 ( +/- 4.9). The mortality rate was 6%; 15 patients died during the hospital stay. The mean PaO<sub>2</sub>/FiO<sub>2</sub> ratio on admission was 317 (+/- 173) mmHg. A total of 194 patients (73%) experienced ARDS in the first week after admission; 52% early ARDS and 48% late ARDS (Appendix A). The median duration of mechanical ventilation was 12.13 (18.50) days. The main demographic characteristics of the patients are presented in Table 1.

Sixty-four (33%) patients experienced mild ARDS, 100 (51.6%) moderate ARDS and 30 (15.5%) severe ARDS. DPrs was significantly higher in the ARDS group than in the no ARDS group; 11.8 (+/-2.9) cm H<sub>2</sub>O vs. 12 (+/- 2.1) cm H<sub>2</sub>O (p = 0.04). P<sub>PLAT</sub> and MP showed the same behaviour; 18 ( +/-3) cm H<sub>2</sub>O vs. 16 ( +/- 2) cm H<sub>2</sub>O, (p < 0.001) and 11.5 (+/-3.6) J/min vs. 9.6 (+/-3.0) J/min (p < 0.001), respectively. The characteristics of the ventilatory parameters and outcomes of the patients are presented in Table 2. The AUC of the ROC curve for DPrs- ARDS in predicting the severity of ARDS was 0.59 (95% CI, 0.48–0.71; p = 0.06) for moderate and severe ARDS (Appendix B) and 0.60 (95% CI, 0.58–0.61; p = 0.04) for severe ARDS. A DPrs-ARDS value > 14 cm H<sub>2</sub>O had a sensitivity of 20.8% (95% CI, 13.8%–27.7 %), a specificity of 88.9% (95% CI, 81.1%–96.6%), a predictive positive value of 79.4 (95% CI, 65.8%–93 %) and a negative predictive value of 35.2 (95% CI, 27.8%– 42.6 %) for predicting severe ARDS. In the survival analysis using the a priori DPrs-ARDS threshold > 14 cm H<sub>2</sub>O, the duration of mechanical ventilation in ARDS patients did not differ between the high and the low driving pressure groups: HR = 0.82 (95% CI, 0.57-1.2), p = 0.3 (Fig. 2). This was also observed for ICU length of stay (p = 0.78) and hospital length of stay (p = 0.75). Kaplan-Meier curves using MP are presented in (Fig. 3). In the multivariate analysis, DPrs-ARDS was not found to be independently associated with the duration of mechanical ventilation (hazard ratio [HR], 1.01; 95% CI, 0.95–1.07; p = 0.8) or mortality (HR, 1.07; 95% CI, 0.9–1.28; p = 0.45) (Table 3). When considering DPrs-ARDS in two groups ( $\leq$  14 cm H<sub>2</sub>O and > 14 cm H<sub>2</sub>O) no association was found for mortality or duration of mechanical ventilation (Table 3). Similarly, in the multivariate analysis, no other respiratory parameters, such as P<sub>PLAT</sub> (HR, 0.98; 95% CI, 0.93–1.02; p = 0.33), Crs (HR, 0.98; 95% CI 0.98–1.00; p = 0.12) and MP (HR, 0.98; 95% CI, 0.94–1.02; p = 0.22), were found to be independently associated with duration of mechanical ventilation or mortality (Appendix C).



**Table 1**  
Baseline characteristics.

Variable		Total population n = 266	ARDS		p
			No n = 72	Yes n = 194	
Sex, n (%)	Men	204 (76.7)	50 (69.4)	154 (79.4)	0.09
Age (years)		43.6 ( $\pm$ 19.3)	34.9 ( $\pm$ 16.6)	46.8 ( $\pm$ 19.3)	< 0.01
BMI (kg/m <sup>2</sup> )		25.0 ( $\pm$ 4.6)	23.7 ( $\pm$ 4.9)	25.5 ( $\pm$ 4.4)	< 0.01
SAPS II		39.9 ( $\pm$ 15.6)	35.4 ( $\pm$ 12.1)	41.5 ( $\pm$ 16.4)	0.01
ISS		31.7 ( $\pm$ 9.9)	31.4 ( $\pm$ 9.4)	31.8 ( $\pm$ 10.2)	0.81
TTS		9.5 ( $\pm$ 4.9)	5.7 ( $\pm$ 3.3)	10.9 ( $\pm$ 4.6)	< 0.01
Thoracic trauma, n (%)					0.03
	Mild (AIS 1 or 2)	116 (43.6)	41 (56.9)	75 (38.7)	
	Moderate (AIS 3 or 4)	133 (50.0)	28 (38.9)	105 (54.1)	
	Severe (AIS 5 or 6)	17 (6.4)	3 (4.2)	14 (7.2)	
Pneumothoraces, n (%)					0.05
	No	129 (48.5)	34 (47.2)	95 (48.9)	
	Mild (AIS 1 or 2)	58 (21.8)	23 (31.9)	35 (18.0)	
	Moderate (AIS 3 or 4)	30 (11.3)	7 (9.7)	23 (11.9)	
	Severe (AIS 5 or 6)	49 (18.4)	8 (11.1)	41 (21.1)	
Haemothoraces, n (%)					0.09
	No	177 (66.5)	56 (77.8)	121 (62.4)	
	Mild (AIS 1 or 2)	28 (10.5)	5 (6.9)	23 (11.9)	
	Moderate (AIS 3 or 4)	36 (13.5)	8 (11.1)	28 (14.4)	
	Severe (AIS 5 or 6)	25 (9.4)	3 (4.2)	22 (11.3)	
Traumatic brain injury, n (%)					0.70
	No	106 (39.8)	28 (38.9)	78 (40.2)	
	Mild (AIS 1 or 2)	25 (9.4)	9 (12.5)	16 (8.3)	
	Moderate (AIS 3 or 4)	112 (42.1)	28 (38.9)	84 (43.3)	
	Severe (AIS 5 or 6)	23 (8.7)	7 (9.7)	16 (8.3)	
Abdominal trauma, n (%)					0.30
	No	130 (48.9)	31 (43.1)	99 (51.0)	
	Mild (AIS 1 or 2)	52 (19.6)	12 (16.7)	40 (20.6)	
	Moderate (AIS 3 or 4)	68 (25.6)	24 (33.3)	44 (22.7)	
	Severe (AIS 5 or 6)	16 (6.0)	5 (6.9)	11 (5.7)	
Haemoperitoneum, n (%)					0.08
	No	186 (69.9)	43 (59.7)	143 (73.7)	
	Mild (AIS 1 or 2)	37 (13.9)	16 (22.2)	21 (10.8)	
	Moderate (AIS 3 or 4)	24 (9.0)	8 (11.1)	16 (8.3)	
	Severe (AIS 5 or 6)	19 (7.1)	5 (6.9)	14 (7.2)	
pH at entry		7.3 ( $\pm$ 0.1)	7.4 ( $\pm$ 0.1)	7.3 ( $\pm$ 0.1)	0.01
Base deficit at entry		5.7 ( $\pm$ 3.6)	5.6 ( $\pm$ 3.9)	5.8 ( $\pm$ 3.5)	0.43
Lactates at entry		3.6 ( $\pm$ 2.6)	3.6 ( $\pm$ 2.4)	3.6 ( $\pm$ 2.7)	0.94
Haemoglobin at entry		11.5 ( $\pm$ 2.6)	11.3 ( $\pm$ 2.8)	11.6 ( $\pm$ 2.6)	0.47

Data are expressed as mean  $\pm$  SD, or as number of patients (percentage) as appropriate.  
BMI, body mass index; SAPS II, Simplified Acute Physiology Score 2; ISS, Injury Severity Score; TTS, Thoracic Trauma Severity score; AIS, Abbreviated Injury Score.

## Discussion

This is the first study to assess the association of  $\Delta$ Prs with outcomes in a specific population of chest trauma patients. The main finding is that the  $\Delta$ Prs value at the onset of ARDS was not associated with the duration of mechanical ventilation, mortality risk or ICU length of stay either in survival analysis or multivariate analysis. Our analysis demonstrates therefore that  $\Delta$ Prs is an unreliable predictor of outcomes in this specific population. Nowadays, DPrs, usually called the driving pressure, is used universally in clinical practice to reflect lung strain and correlates well with the mechanical stress generated by VT on the ventilated lung [11].

$\Delta P_{rs}$  also means respiratory system compliance for a given VT. Thus, a high  $\Delta P_{rs}$  may indicate impairment of respiratory system compliance by a decrease in the functional size of the lung. This phenomenon, called baby lung within context of ARDS, is partly related to alveolar collapse. Many studies have demonstrated that  $\Delta P_{rs}$  is associated with mortality in patients with ARDS [9,10,18]. However, these previous studies focused on ARDS in medical settings. The morbid association between  $\Delta P_{rs}$  and mortality may nevertheless be altered in different clinical situations. Thus, De Jong et al. [18] have reported that in obese patients with ARDS,  $\Delta P_{rs}$  was not associated with mortality. Similarly, our data suggest the absence of a relationship between  $\Delta P_{rs}$  and outcomes in the case of patients with ARDS related to trauma. One of the main physiopathological explanations for this difference observed between the medical and trauma contexts could be significant modifications of chest wall compliance related to traumatic injuries. Traumatic parietal dehiscence increases chest wall compliance, which may lead to an increase in  $\Delta P_{rs}$  [19]. Thus,  $\Delta P_{rs}$  reflects both chest wall and lung compliance and it may be directly modified by strong variation in chest wall compliance in cases of severe chest trauma.  $\Delta P_{rs} = \Delta P_{cw} + \Delta P_{l}$ ,  $\Delta P_{cw}$  being the chest wall driving pressure and  $\Delta P_{l}$  being the transpulmonary driving pressure.  $\Delta P_{l}$  would offer a better reflection of actual lung compliance and alveolar collapse [20]. Similarly, to obese patients, in chest trauma patients, much of the pressure provided by the ventilator will be used to distend the chest wall rather than the lung. Hence, there may not be an increase in transpulmonary pressure with accompanying lung overdistension. The only way to monitor the  $\Delta P_{l}$  of real interest from bench to bedside is to measure oesophageal pressure, which is an estimation of pleural pressure and allows to determine  $\Delta P_{cw}$  [21]. Thus, physicians may quickly differentiate a high  $\Delta P_{rs}$  due to an increase in  $\Delta P_{cw}$ , without a real lung injury, or inversely a high  $\Delta P_{rs}$  with a normal  $\Delta P_{cw}$ , a sign of lung pathology.

ARDS related to chest trauma represents a low percentage of case of ARDS and has its own specific properties. Its incidence is estimated to be between 10% and 30% of critically ill trauma patients, mainly depending on the severity of the trauma in injured patients. Trauma-related ARDS is known to be twice less likely to lead to death than medical ARDS [22]. Our cohort presents similar results with a low mortality rate in the ARDS group (7%). Traumatic ARDS is characterised by a typical immunological profile different from ARDS in a medical setting. The early phase following trauma is thus characterised by an important and uncontrolled inflammatory response in the lung tissues. The importance of this inflammatory response depends on the intensity of the initial trauma but also on the genetic profile of the patient. A previous work by Xiao et al. [23] in a severe trauma population showed the early leukocyte genomic response was simultaneously associated with increased expression of genes involved in the systemic inflammatory, innate immune, and compensatory anti-inflammatory responses, as well as in the suppression of genes involved in adaptive immunity. All these modifications induce a massive release of damage-associated molecular pattern molecules from injured tissues [24]. Massive release of epithelial biomarkers such as sRAGE, for example, is responsible for dysfunction of the capillary-alveolar barrier, increase in inflammation, and oxidative stress favouring fibrosis in cases of ARDS [25,26]. These

specific characteristics explain the specificities of ARDS after chest trauma, its lower lethality rate, and maybe the absence of association between  $\Delta$ Prs and outcomes in the trauma context.

The present study has some limitations. First, its design was monocentric with a retrospective analysis, which limits extrapolation of the results. However, the data were collected prospectively with the ICU software, and the management of patients with ARDS was standardised according to international recommendations. Only a few data are missing regarding the driving pressure (28 of 329; 8%) in trauma patients under mechanical ventilation. Second, no threshold analysis was performed according to the  $\Delta$ Prs. Patients who died from traumatic brain injury or from haemorrhagic shock in first 48 h after admission were excluded from our study. Consequently, only 15 non-survivors are present in our final analysis. This may lead to a lack of power and threshold analysis is impossible. However, previous work also used a threshold of 14 cm H<sub>2</sub>O for DPrs [9,18]. Third, patients in our cohort were severely injured with a mean ISS of 32, and about 25% of the cohort also had abdominal injuries. Increase in abdominal pressure may also be involved in the change in chest wall compliance and create an analysis bias. It is therefore impossible to exclusively attribute our results only to chest injuries. However, multiple traumas are a frequent situation, which makes our study close to real life. Fourth, only 36 patients (14%) had  $\Delta$ Prs > 14 cmH<sub>2</sub>O; this induces a lack of statistical power and does not allow to definitively exclude a significant association. However, this is a large cohort with 761 patients initially screened, making it one of the largest study about this subject. Fifth, the presence of an airway closure might distort the actual value of DPrs in providing a wrong PEEP value [27]; unfortunately, phenomenon of airway closure could not be assessed due to our retrospective design.

## Conclusion

The results of the present study demonstrate that driving pressure in a specific population of chest trauma patients was a poor predictor for ARDS severity and had no correlation with worse outcomes. Changes in chest compliance due to traumatic injuries could explain this unexpected observation. Therefore, our results suggest that the use of transpulmonary pressure would be relevant in chest trauma patients to directly monitor injured lungs and guide an optimal mechanical ventilation strategy. Further studies will be necessary to prove the positive impact of transpulmonary pressure on chest trauma management.

### **Ethics approval and consent to participate**

We obtained approval from the local scientific and ethics committee of Montpellier University Hospital, Comité d'Organisation et de Gestion de l'Anesthésie Réanimation (COGAR), who stated that informed consent from the patient or next of kin was not required.

### **Consent for publication**

Informed consent from the patient or next of kin was not required.

### **Availability of data and materials**

All data are extracted from medical record.

### **Competing interests**

The authors declare no competing interests. Funding Support was provided solely from institutional and departmental resources. Authors' contributions S.R., M.A, and K.B collected clinical data for this study; S.R., M.A, and K.B collected pharmaceutical and blood requirements. J.C, S.R, A. DJ, C.D prepared the draft of the study and conducted the statistical analysis. S.R. and M.A. wrote the article, which was revised by S.J, T.L, A.DJ and X.C.

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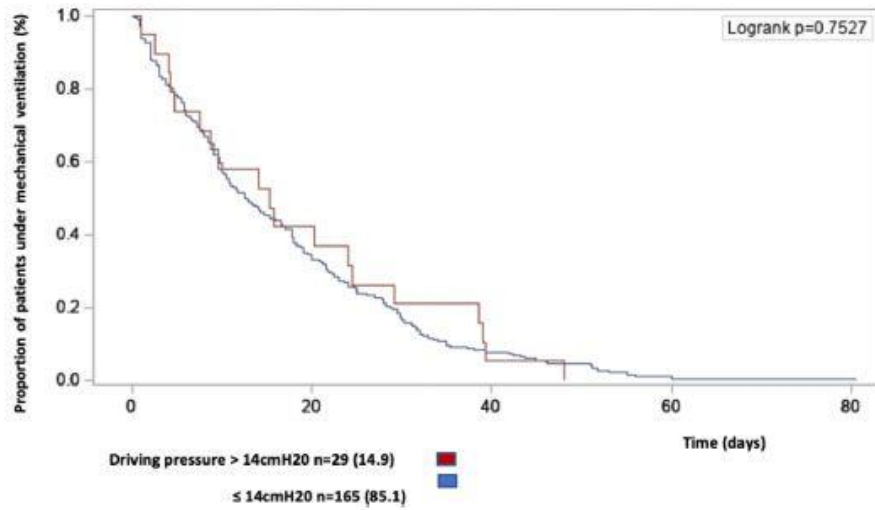


Fig. 2. Kaplan-Meier curves for time to weaning from mechanical ventilation according to driving pressure.

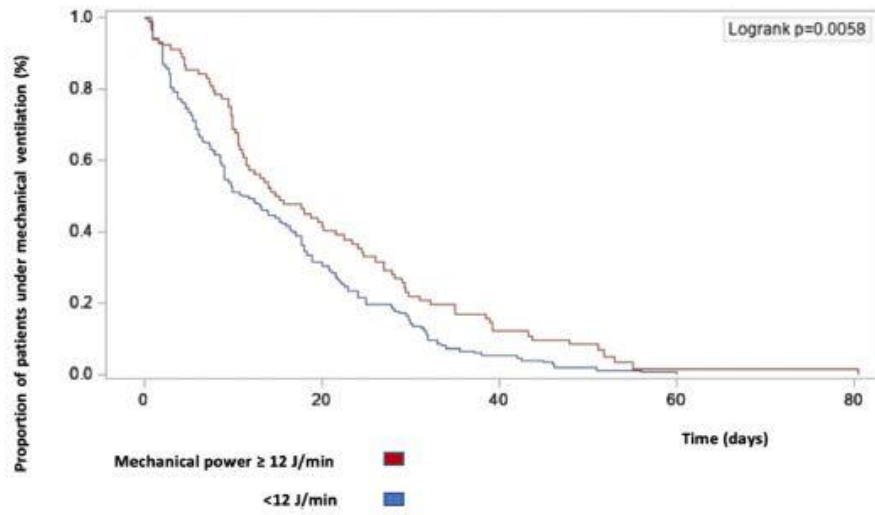


Fig. 3. Kaplan-Meier curves for time to weaning from mechanical ventilation according to mechanical power level.

**Table 2**  
Respiratory characteristics and outcome.

Variable		Total population	ARDS		p
		n = 266	No n = 72	Yes n = 194	
PAO <sub>2</sub> /FiO <sub>2</sub> at entry		317.0 (± 173.3)	494.5 (± 166.9)	251.1 (± 121.9)	< 0.01
Worst PaO <sub>2</sub> /FiO <sub>2</sub>		232.5 (± 120.7)	397.1 (± 75.9)	171.4 (± 63.3)	< 0.01
ARDS severity, n (%)					
	Mild	64 (24.1)		64 (33.0)	
	Moderate	100 (37.6)		100 (51.6)	
	Severe	30 (11.3)		30 (15.5)	
Early ARDS, n (%)					
	< 48 h	101 (37.9)		101 (52.1)	
	≥ 48 h	93 (34.9)		93 (47.9)	
Day of occurrence of ARDS		2.2 (± 2.4)		2.2 (± 2.4)	
Driving pressure (ΔPrs; cm H <sub>2</sub> O)		11.6 (± 2.7)	10.9 (± 2.0)	11.8 (± 2.9)	0.04
Driving pressure, n (%)					0.27
	≤ 14 cm H <sub>2</sub> O	230 (86.5)	65 (90.3)	165 (85.1)	
	> 14 cm H <sub>2</sub> O	36 (13.5)	7 (9.7)	29 (14.9)	
Mean Driving pressure over the first 5 days (cm H <sub>2</sub> O)		11.5 (± 2.2)	10.9 (± 1.8)	11.7 (± 2.3)	0.02
Plateau pressure (P <sub>PLAT</sub> ; cm H <sub>2</sub> O)		17.3 (± 3.1)	16.2 (± 2.3)	17.6 (± 3.3)	< 0.01
Static compliance (C <sub>rs</sub> ; cm H <sub>2</sub> O)		47.5 (± 11.5)	47.7 (± 8.4)	47.5 (± 12.4)	0.53
Mechanical power (MP; cm H <sub>2</sub> O)		11.0 (± 3.5)	9.6 (± 2.9)	11.5 (± 3.6)	< 0.01
VAP, n (%)					< 0.01
	No	110 (41.4)	47 (65.3)	63 (32.5)	
	Yes	156 (58.7)	25 (34.7)	131 (67.5)	
Death n (%)					0.08
	No	251 (94.3)	71 (98.6)	180 (92.8)	
	Yes	15 (5.6)	1 (1.4)	14 (7.2)	
Length Duration of mechanical ventilation (median) (days)		12.13 (18.50)	8.63 (14.88)	13.63 (19.75)	< 0.01
28 days free of ventilation		13.1 (± 9.9)	16.8 (± 9.4)	11.7 (± 9.83)	< 0.01
Length of stay in ICU (days)		26.3 (± 20.4)	20.7 (± 18.0)	28.4 (± 20.9)	< 0.01
Length of hospital stay (days)		36.2 (± 28.6)	30.5 (± 19.1)	38.4 (± 31.2)	0.03

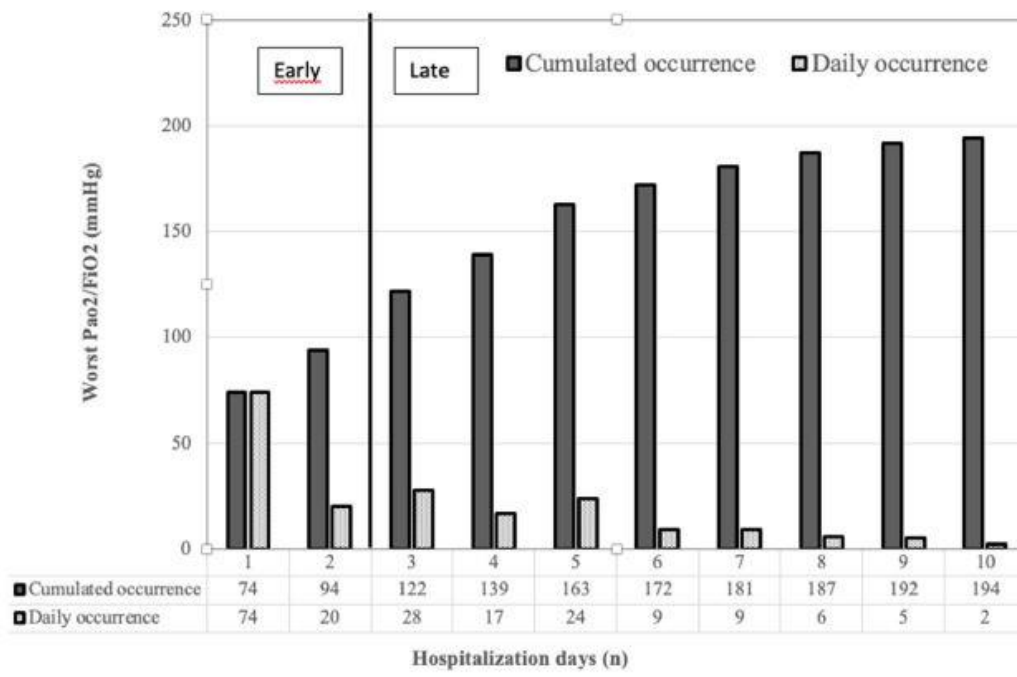
Data are expressed as mean ± SD, or as number of patients (percentage) as appropriate, or median (IQR) for length duration of mechanical ventilation. VAP ventilator-acquired pneumonia.

**Table 3**  
Multivariate Cox regression analysis results on duration of ventilation (ΔPrs as a continuous variable) and ΔPrs<sub>ARDS</sub> according to the group (superior or inferior to 14 cm H<sub>2</sub>O) outcome.

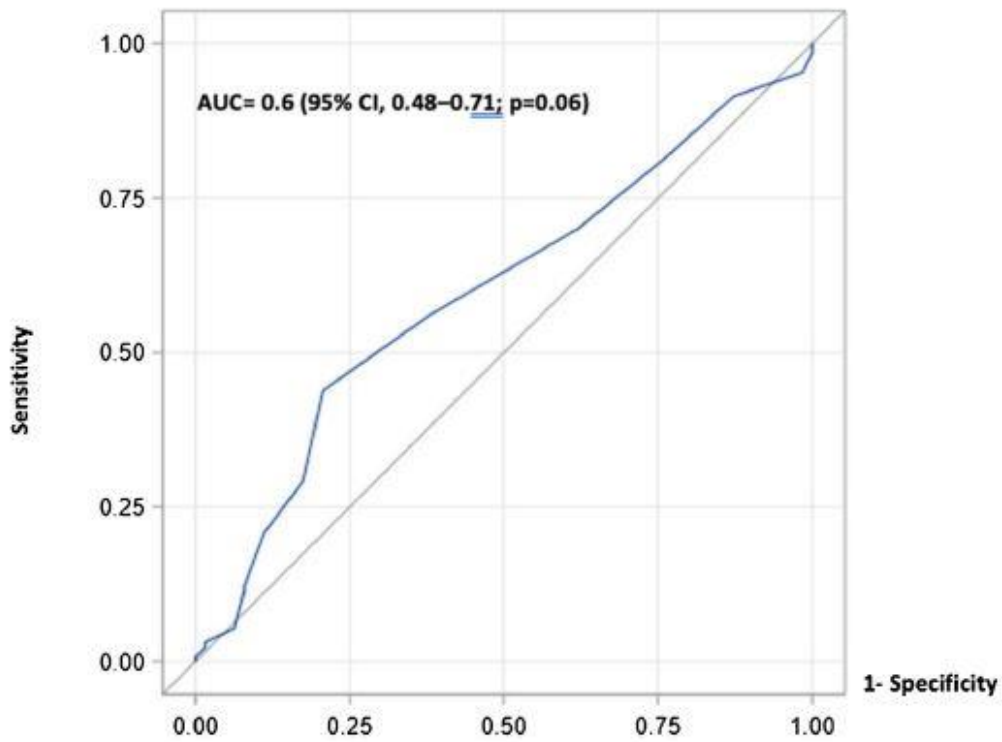
Variable	Modality	Hazard ratio	95% confidence interval	p
<b>Duration of ventilation</b>				
Age (years)	+1 year	0.99	0.99-1.00	< 0.04
SAPS II	+ 1 point	0.97	0.96-0.99	< 0.0001
ISS	+ 1 point	0.99	0.97-1.01	0.25
Chest injury				
Reference	AIS < 2			
	≥ 2 AIS ≤ 4	0.95	0.7-1.29	0.75
	AIS > 4	0.51	0.26-0.97	0.04
Head injury				
Reference	No injury			
	AIS < 2	0.91	0.56-1.48	0.7
	≥ 2 AIS ≤ 4	0.84	0.6-1.18	0.31
	AIS > 4	0.45	0.25-0.81	0.007
ΔPrs <sub>ARDS</sub>	+ 1 cm H <sub>2</sub> O	1.01	0.95-1.08	0.84
<b>Group outcome<sup>a</sup></b>				
Mortality	ΔPrs <sub>ARDS</sub> > 14 cm H <sub>2</sub> O	1.42	0.44-4.54	0.56
Ventilation duration	ΔPrs <sub>ARDS</sub> > 14 cm H <sub>2</sub> O	0.9	0.61-1.33	0.59

<sup>a</sup> Cox model for mortality was adjusted on SAPS II and arterial pH. Cox model for ventilation duration was adjusted on age, SAPS II, ISS, AIS thorax, AIS skull, haemopentoneum, driving pressure in trauma ICU and ventilator-associated pneumonia.

**Appendix A. Occurrence of ARDS over 10 days**



**Appendix B. Roc curve for predicting moderate and severe ARDS using driving pressure**



**Appendix C. Multivariate Cox regression analysis results using plateau pressure or compliance or mechanical power as a predictive variable instead of driving pressure**

Variable <sup>a</sup>	Modality	Hazard ratio	95% confidence interval	p
Plateau pressure	+1 cm H <sub>2</sub> O	0.98	0.93–1.02	0.33
Plateau pressure	<25 cm H <sub>2</sub> O	0.84	0.36–1.92	0.67
Compliance	+1 ml/cm H <sub>2</sub> O	0.99	0.98–1.00	0.12
Compliance	>31 ml/cm H <sub>2</sub> O	1.16	0.67–2.01	0.6
Mechanical power	+1 J/min	0.98	0.94–1.02	0.22
Mechanical power	<12 J/min	0.92	0.68–1.23	0.57

Cox models for each variable were adjusted on age, SAPS II, ISS, AIS thorax, AIS skull, haemoperitoneum, driving pressure in trauma ICU and ventilator-associated pneumonia.

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