How to cite this article: Véras JB, Martinez BP, Gomes Neto M, Saquetto MB, Conceição CS, Silva CM. Effects of prone position on patients with acute respiratory distress syndrome: a systematic review. J. Physiother. Res. 2019;9(1):129-138. doi: 10.17267/2238-2704rpf.v9i1.2175v9i1.2175

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Literature review

Effects of prone position on patients with acute respiratory distress syndrome: a systematic review

Efeitos da posição prona em pacientes com síndrome do desconforto respiratório agudo: uma revisão sistemática

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RESUMO | INTRODUÇÃO: A síndrome do desconforto respiratório agudo (SDRA) é caracterizada por resposta inflamatória da membrana alvéolo capilar a injúrias pulmonares diretas ou indiretas, cursando com redução de complacência e presença de infiltrados pulmonares. Tal condição provoca alterações na mecânica pulmonar e nas trocas gasosas, gerando hipoxemia. **OBJETIVO:** Revisar sistematicamente ensaios clínicos randomizados que investigaram os efeitos da posição prona e suas repercussões na oxigenação, mecânica respiratória, mortalidade e ocorrência de eventos adversos em pacientes com SDRA. **MATERIAIS E MÉTODOS:** Revisão sistemática da literatura, seguindo as recomendações PRISMA. As buscas foram realizadas nas bibliotecas de dados PubMed, BVS, PEDro e SciELO, por dois revisores independentes. Incluído estudos ensaio clínico randomizado que apresentavam intervenção a terapia de posicionamento em prono, que compararam a ventilação na posição prona com a supina. Os desfechos analisados foram oxigenação, mecânica respiratória, mortalidade e ocorrência de eventos adversos, através de análise descritiva. A qualidade metodológica dos estudos foi avaliada pela escala PEDro. Foram incluídos os ensaios clínicos randomizados **RESULTADOS:** Foram analisados 8 artigos, com média 6 na escala PEDro. Os estudos demonstraram resultados positivos na oxigenação, pouca influência na mecânica respiratória, melhora nas taxas de mortalidade e alta prevalência de efeitos adversos, minimizados com a capacitação da equipe. Destaco a variedade metodológica e dos desfechos como limitação da pesquisa. **CONCLUSÃO:** A posição prona é capaz de promover efeitos benéficos na oxigenação, complacência, mortalidade e queda de eventos adversos em indivíduos com SDRA. Entretanto, destaca-se a necessidade de realização de novos ensaios clínicos sobre o tema, que ofereçam amostras satisfatórias e metodologias semelhantes.

PALAVRAS-CHAVE: Síndrome do Desconforto Respiratório do Adulto. Decúbito ventral. Oxigenação. Mecânica respiratória.

ABSTRACT | INTRODUCTION: The acute respiratory distress syndrome (ARDS) is characterized by an inflammatory response of the alveolar-capillary membrane to direct or indirect pulmonary injuries with a reduction in to complacency and the presence of pulmonary infiltrates. Such condition causes changes in lung mechanics and gas exchange, causing hypoxemia. **OBJECTIVE:** To systematically review randomized clinical trials investigating the effects of the disease and its repercussions on oxygenation, respiratory mechanics, mortality and occurrence of adverse events in patients with ARDS. **MATERIALS AND METHODS:** Systematic review of the literature, following PRISMA recommendations. The searches were performed in the PubMed, BVS, PEDro and SciELO data libraries by two independent reviewers. Included studies randomized clinical trial that presented intervention to positioning therapy in prone, comparing ventilation in prone position with supine. The methodological quality of the studies was evaluated by the PEDro scale. The outcomes analyzed were oxygenation, respiratory mechanics, mortality and occurrence of adverse events, through descriptive analysis. **RESULTS:** Eight articles were analyzed, with an average of 6 on the PEDro scale. Studies have shown positive oxygenation results, low respiratory mechanics influence influence of respiratory mechanics, improved in mortality rates and high of adverse effects minimized with team training. I highlight the methodological variety and outcomes as a limitation of the research. **CONCLUSION:** The prone position is capable of promoting beneficial effects in oxygenation, compliance, mortality and reduction of adverse events in individuals with ARDS. However, it is noteworthy the need to perform new clinical trials on the subject, which offer satisfactory samples and similar methodologies

KEYWORDS: Adult Respiratory Distress Syndrome. Prone Position. Oxygenation. Respiratory mechanics.

Submitted 11/12/2018, Accepted 12/20/2018, Published 02/08/2019
J. Physiother. Res., Salvador, 2019 February;9(1):129-138
Doi: 10.17267/2238-2704rpf.v9i1.2175 | ISSN: 2238-2704
Responsible editor: Fernanda Warken Rosa Camelier (Respiratory physiotherapy)

Introduction

Acute respiratory distress syndrome (ARDS) is a pathological condition characterized by an inflammatory response of the alveolar-capillary membrane to direct or indirect pulmonary injuries[1,2]. The syndrome also presents a reduction in pulmonary complacency and the presence of pulmonary infiltrates[2], which causes changes in pulmonary mechanics and gas exchange, leading to hypoxemia[3]. The diagnosis is given when the clinical condition is insult in up to 7 days, bilateral opacities are present in pulmonary images, absence of cardiovascular dysfunction that justifies edema and reduced oxygenation PaO2 / FiO2 ≤ 300 (mild ARDS); PaO2 / FiO2 ≤ 200 (moderate ARDS); PaO2 / FiO2 ≤ 100 (severe ARDS), always measured with final positive expiratory pressure (PEEP) ≥ 5 cmH_2O[4].

The most important treatment for ARDS is pulmonary protection ventilation, with low tidal volume (Vt-6mL / kg) and PEEP (5-10cmH_2O) sufficient for alveolar recruitment. The prone position, in which the patient is positioned in the ventral position, is an important complementary resource in the management of ARDS. In this position, pulmonary parenchyma becomes larger area available by releasing the dependent portion, improving alveolar recruitment and thus gas exchange[5], pulmonary ventilation distribution becomes better[6]. In individuals with severe ARDS, the prono positioning strategy associated with correct levels of PEEP, improves lung volume and reduces lung elastance and resistance[7]. This maneuver can be performed through auxiliary devices (straps and buckles) or automated stretchers[8], with the assistance of the multidisciplinary team.

Despite these benefits, some clinical trials were unable to demonstrate a positive impact on mortality[9], in contrast to a more recent study showing a 50% improvement in the indexes[10]. Prone positioning was commonly used only as rescue therapy when the patient had very severe hypoxemia and other therapies were not able to reverse the condition[8,9,11]. More current studies already propose to institute this decubitus immediately after diagnosis (within the first 12-24 hours), after stabilization of symptoms, and its prolonged maintenance (more than 16 hours)[5,12]. Although it is a low cost and relatively simple maneuver, its use is still scarce in intensive care units (ICUs) due to the risks and their adverse effects, such as edema, scarring, and tube displacement[10].

The contradictory results observed in the literature can be explained by the non-similarity between the patients, the ventilation strategy applied and the different times for the beginning and duration of the prone positioning. Therefore, it is sought to verify if there are benefits in the technique, despite the different methodologies. Therefore, the objective of the present study is to systematically review randomized clinical trials investigating the effects of prone position and its repercussions on oxygenation, respiratory mechanics, mortality and occurrence of adverse events in ARDS patients.

Materials and methods

The present systematic review was elaborated according to the methodological recommendations PRISMA[13] that consists of 27 items and a flow diagram of selection of articles, in four phases. For the extraction of the data of the articles the authors were observed, year of publication, place of publication, type of study, sample size, form of evaluation of the outcome and statistical planning. Articles not found were searched via e-mail contact with the authors. To minimize the risk of bias the data extraction was performed by two reviewers collecting the information from the primary studies independently, and resolving disagreements with a third reviewer or by consensus.

Sources of information and search strategy

We searched the Public Medline (PubMed), Virtual Health Library (VHL), Physiotherapy Evidence Database (PEDro) and Scientific Electronic Library Online (SciELO) data libraries. The research was carried out through combinations, English for inclusion in the study with the following terms: acute respiratory distress syndrome, severe hypoxemia, positioning therapy and prone positioning, through the boolean operators "AND" AND "OR". The detailed search strategy for PubMed is presented in Table 1.

Chart 1. Search strategy in the PubMed.2018 data library

#11 ((((prone position) OR prone positioning) OR prone-positioning)) AND ((((acute respiratory distress syndrome) OR severe hypoxemia) OR ARDS) OR respiratory failure) Filters: Clinical Trial
#10 ((((prone position) OR prone positioning) OR prone-positioning)) AND ((((acute respiratory distress syndrome) OR severe hypoxemia) OR ARDS) OR respiratory failure)
#9 (((acute respiratory distress syndrome) OR severe hypoxemia) OR ARDS) OR respiratory failure
#8 ((prone position) OR prone positioning) OR prone-positioning
#7 respiratory failure
#6 ARDS
#5 severe hypoxemia
#4 acute respiratory distress syndrome
#3 prone-positioning
#2 prone positioning
#1 prone position

The selection of articles was carried out in October 2018 by two independent researchers. No publishing period has been defined. The studies were initially selected by reading the title and abstract. In sequence, a full text reading was made, to guarantee or not the adequacy of the inclusion criteria. A synthesis of each study was carried out, presenting its main information.

Eligibility criteria

The population studied was that of adult patients, from the age of 18, with no upper limit of age, with ARDS. We included randomized clinical trial studies that included an intervention group (patients who underwent prone positioning therapy) vs. control (patients who remained supine and did not undergo prone therapy), comparing data on respiratory mechanics, oxygenation, mortality and occurrence of adverse events. These variables were also confronted between the different articles, as well as the maintenance time of the proposed intervention. Observational studies, those associated with various therapies, and those who the patient was his or her own control were excluded.

Methodological quality

The evaluation of the included studies was performed using the PEDro[14] scale (based on the Delphi[15] list). The objective of this study is to measure the methodological quality of randomized clinical trials through a checklist of 11 items, assigning them a score ranging from 0 to 10 (item 1 is not punctuated). It is also capable of evaluating the presence of key statistical information for a good study quality. Articles with scores below 4 were excluded.

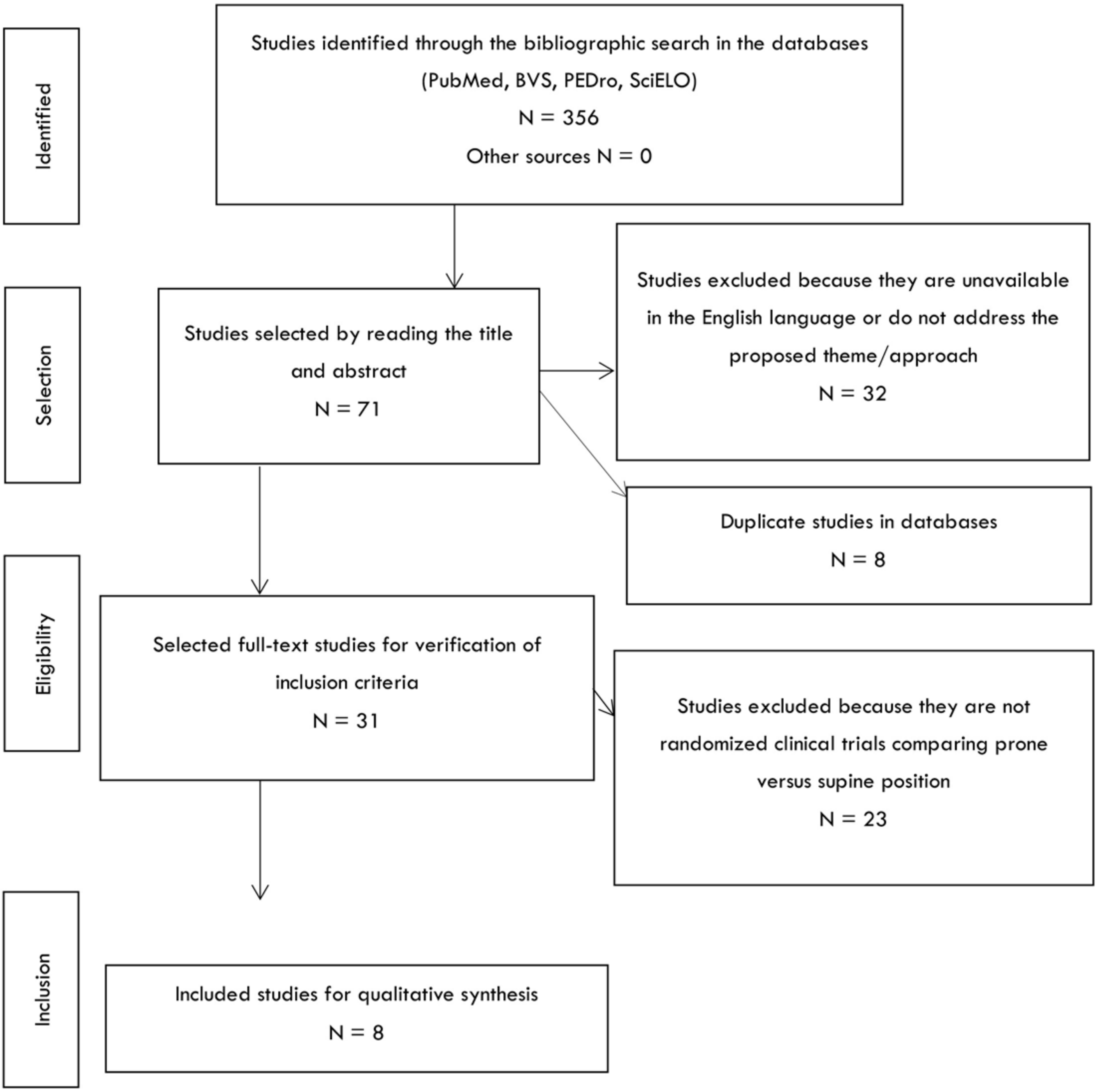
Data analysis

The data analysis was performed in two stages, the first included: evaluation of the abstracts, type of study, years of publication, diagnostic description and evaluation of the outcome. The second stage comprised the complete reading for the extraction of the results of each clinical trial and composition of the outcomes according to the objective of this systematic review. Statistical analysis was done in a descriptive way, the main variables of analysis were the difference between means and standard deviation.

Results

The bibliographic research resulted in 356 articles, of which 285 were excluded due to inadequacy to the theme already found in the title or abstract. A total of 31 studies were analyzed in full text, however, 8 met the inclusion criteria and were selected[16-23]. The flowchart of the identification of references is shown in figure 1.

Figure 1. Search and selection of studies that address the application of the prone position in ARDS, according to the PRISMA-2018 methodology



The 8 articles in question are randomized clinical trials, 7 of which are multicentric[16-20, 22, 23]. All of them compare the prone positioning in maintenance for at least 6[23] up to 20 consecutive hours[18-20], for a minimum of 2[22] up to 90 days[21] with the supine in patients with ARDS. Their samples range from 40[21] to 791[22] individuals, as shown in Table 1.

Chart 2. Characterization of the studies included in the qualitative synthesis regarding the sample and outcomes of individuals with ARDS. 2018

AUTHOR	SAMPLE	OUTCOMES	MAIN RESULTS
Ayzac *et al.*, 2015[16]	**IG: n = 237** Age: 58±16 years old Man: 166 Woman: 71 **CG: n = 229** Age: 58±16 years old Man: 152 Woman: 77	PAV frequency, MV free days, ICU length of stay, ICU mortality, mortality after 90 days, organic dysfunction, antibiotic therapy.	The IG presented a greater number of cases of VAP and greater cumulative probability, but without statistical significance. PAV was associated with an increase in the mortality rate during ICU stay, longer stay in the unit and more days free of organic failure.
Guérin *et al.*, 2013[17]	**IG: n = 240 (237)** Age: 58±16 years old Man: 166 Woman: 71 **CG: n = 234 (229)** Age: 58±16 years old Man: 152 Woman: 77	Extubation success, MV free days, NIV time, ICU length of stay, mortality after 28 and 90 days, organic dysfunction, arterial gases, respiratory system mechanics, tracheostomy rate.	Rates of use of rescue therapies were higher in GC than in IG. The PaO_2/FiO_2 ratio was higher in IG than in CG on days 3 and 5, while PEEP and FiO_2 were significantly lower. The plateau pressure in the IG was 2 cm of H_2O lower than the CG, on day 3. The $PaCO_2$ and the static compliance of the respiratory system were similar in both groups. Mortality at day 28 was significantly lower in IG than in CG, persisting at day 90. The successful extubation rate was significantly higher in IG. Duration of MV, duration of ICU stay, incidence of pneumothorax, use of NIV after extubation and tracheostomy rate did not differ significantly between the two groups.
Taccone *et al.*, 2009[18]	**IG: n = 168 (134)** **CG: n = 174** (General data) Age: 60±16 years old Man: 244 Woman: 98	MV free days, mortality after ICU discharge, mortality after 28 days and 6 months, organic dysfunction.	20 CG patients were placed in prone as a rescue maneuver. Mortality rates at 28 days and 6 months did not differ significantly between groups, but in the subgroup of severe ARDS, rates were more advantageous. The rates of organic failure, days without ventilator and time in the ICU were similar between the groups.
Fernandez *et al.*, 2008[19]	**IG: n = 22(21)** Age: 53,9±17,9 years old Man: 12 Woman: 9 **CG: n = 20(19)** Age: 55,3±14,6 years old Man: 13 Woman: 6	Oxygenation, length of stay in hospital, mortality in ICU and hospital, mortality after 60 days, organic dysfunction, lung injury severity, hemodynamic, pulmonary mechanics.	The IG had an increase in PaO_2/FiO_2 than the CG, within 6 hrs and reaching statistical significance on the 3rd day. Mortality reduced 15% in the IG compared to CG, with no statistical significance.
Mancebo *et al.*, 2006[20]	**IG: n = 80(76)** Age: 54±17 years old Man: 44 Woman: 32 **CG: n = 62(60)** Age: 54±16 years old Man: 42 Woman: 18	Oxygenation, length of stay in hospital, mortality in ICU and hospital, days under vasopressors.	Five CG patients were crossed into IG and all died. IG patients presented lower FiO_2, higher PaO_2/FiO_2, plateau pressure and PEEP lower than those of the CG. Mortality was slightly lower in the IG, but without statistical significance.
Voggenreiter *et al.*, 2005[21]	**IG: n = 21** Age: 40±14 years old Man: 18 Woman: 3 **CG: n = 19** Age: 43±10 years old Man: 15 Woman: 4	VAP frequency, oxygenation, time of MV, days with ARDS, mortality, organic dysfunction, severity of lung injury, ventilation/perfusion ratio, static pulmonary compliance.	The duration of ventilatory support did not differ significantly between the two groups. 19 IG and 15 CG patients were breathing spontaneously at the end of the study period. PaO_2/FiO_2 was higher in GI and PEEP was lower. Ventilation/perfusion ratio and static pulmonary compliance did not differ between groups. Prone positioning significantly reduced the number of pneumonias. One IG patient and three CG patients died from multiorgan failure.
Guerin *et al.*, 2004[22]	**IG: n = 385 (378)** Age: 62±15,7 years old Man: 304 Woman: 109 **CG: n = 417 (413)** Age: 62,5±14,7 years old Man: 289 Woman: 89	VAP frequency, oxygenation, time of MV, mortality after 90 days.	Mortality rates did not differ between groups. The time of MV and the successful extubation rate were similar in IG and CG. The EPI rate was significantly lower in the IG. PaO_2/FiO_2 was significantly higher in IG. PEEP, FiO2 and TV were lower than GC in GI. $PaCO_2$ and pH levels did not differ.
Gattinoni *et al.*, 2001[23]	**IG: n = 152** Age: 59±17 years old Man: 100 Woman: 52 **CG: n = 152** Age: 57±16 years old Man: 114 Woman: 38	Oxygenation, mortality during the study, at discharge from the ICU and after 6 months, organic dysfunction.	Mortality rates did not differ significantly between groups. PaO_2/FiO_2 increased in IG. The TV increased in the IG and decreased in the CG. There was no difference in the incidence of organic dysfunction.

Subtitle: IG - intervention group (prone position); CG – control group (supine position); VAP - ventilator-associated pneumonia; ETT - endotracheal tube; TCTT - thoracotomy tube; MV - mechanical ventilation; NIV - non-invasive ventilation; TV - tidal volume

As for methodological quality, the articles were generally well punctuated with an average of 6 points (table 1). Despite the good classification, only 1 article presented blindness of the evaluators[17], while in the others there was no blindness[16,18-23].

Tabela 1. Methodological quality of the studies with individuals with ARDS, according to the PEDro scale, 2018

AUTHOR	1	2	3	4	5	6	7	8	9	10	11	TOTAL
Ayzac *et al.*, 2015[16]	X	X						X	X	X	X	5
Guérin *et al.*, 2013[17]	X	X					X	X	X	X	X	6
Taccone *et al.*, 2009[18]	X	X	X					X	X	X	X	6
Fernandez *et al.*, 2008[19]	X	X		X				X		X	X	5
Mancebo *et al.*, 2006[20]	X	X	X	X				X	X	X	X	7
Voggenreiter *et al.*, 2005[21]	X	X	X	X					X	X	X	6
Guerin *et al.*, 2004[22]	X	X	X	X				X	X	X	X	7
Gattinoni *et al.*, 2001[23]	X	X	X	X				X	X	X	X	7

Subtitle: 1) specification of the inclusion criteria (not punctuated item); 2) random allocation; 3) secrecy in allocation; 4) similarity of the groups at initial or basal phase; 5) blinding of subjects; 6) blinding of the therapist; 7) blinding of the evaluator; 8) measured at least one primary outcome in 85% of subjects allocated; 9) analysis of intention to treat; 10) comparison between groups of at least one primary outcome; 11) report of measures of variability and estimation of the parameters of at least one primary variable.

Oxygenation

In the study by Guérin et al.[17,] oxygenation was better in the prone group than in the supine group in the first days of intervention, with PaO2 / FiO2 179 ± 100 and 157 ± 68 (p <0.01), respectively, and with loss of significance at day 7 (173 ± 62 versus 170 ± 80). Fernandez et al.[19] showed that prone ventilated patients had an apparent increase in PaO2 / FiO2 within 6 hours (202 ± 78 versus 165 ± 70 mmHg in the supine group, with p = 0.16), and this increase reached significance statistic on day 3 (234 ± 85 versus 159 ± 78, p = 0.009). Mancebo et al.20 observed greater proportions of PaO2 / FiO2 (p = 0.002) on the 2nd day in the intervention group (GI - prone position) than in the control group (GC - supine position) - 218 ± 85 and 171 ± 85, respectively. On the 20th day, the control group presented the highest PaO2 / FiO2 - 225 ± 93, against 197 ± 79 (p = 0.43). In the study by Voggenreiter et al.[21] the PaO2 / FiO2 index increased slightly, in the prone group compared to the supine group in the first 4 days (p = 0.03), varying from 71.8 ± 75.5 versus 27.7 ± 78.9 with a variation of 44.1 ± 3.4 but lost significance on the 10th day - 80.7 ± 77.3 versus 66.5 ± 89.1 (p = 0.31). Guérin et al.[22], on the 7th day, observed PaO2 / FiO2 values of 206 ± 78 in GC and 228 ± 91 in GI (p <0.001). Gattinoni et al.[23] showed a variation of 44.6 ± 68.2 in the supine group and 63.0 ± 66.8 in the prono group (p = 0.02), in PaO2 / FiO2.

Respiratory mechanics

In Guérin et al.[17] the static compliance of the respiratory system did not differ between groups, with values of 31 ± 17 ml.cmH_2O^{-1} in the GI and 35 ± 16 ml.cmH_2O^{-1} in the GC, on day 7 and plateau pressure 22 ± 4 cmH2O versus 24 ± 5, respectively (p <0.01). Mancebo et al.20 observed that prone ventilated patients had lower plateau pressure levels (28 ± 7 cmH2O) than supine ventilators (31 ± 6 cmH2O), with p = 0.01. Voggenreiter et al.[21] found an improvement in GI compliance (5.2 ± 12.8 ml.cmH_2O^{-1}) higher than GC (2.4 ± 15.4 ml.cmH_2O^{-1}) (p = 0.24) on the 4th day. However, this was reversed on the 10th day, with the CG showing a greater positive variation in compliance (22.3 ± 29.4 versus 2.8 ± 18.1).

Mortality

In the study by Ayzac et al.[16], of the 466 individuals analyzed, 93 developed ventilator-associated pneumonia (VAP) and 31 died during the ICU stay. The mortality rate among those who did not develop VAP was 25.5% (p = 0.28). In Guérin et al.[17], mortality at day 28 was lower in the prone group than in the supine group: 16.0% versus 32.8% ($p < 0.001$). The significant difference in mortality persisted on day 90 (23.6% versus 41%). Taccone et al.[18] observed that ICU mortality was different in the intervention and control groups, at 28 days and 6 months - approximately 47% and 52%, respectively - although there was no difference between the groups. Fernandez et al.[19] found that there was a 15% reduction in mortality in the prone group compared to supine (38% versus 53%), however, it did not reach statistical significance due to the small sample. Mancebo et al.[20] demonstrated that the ICU mortality was 58% in patients ventilated in dorsal decubitus and 43% in patients ventilated in a statistically insignificant prone ($p = 0.12$) the difference in mortality for the group that underwent therapy with position. In Voggenreiter et al.[21], 5% for IG and 16% for CG ($p = 0.27$) were observed. Guerin et al. (2004)[22] confirmed that on day 28, 31.5% of patients in the supine group and 32.4% of the prone group died ($p = 0.85$). At 90 days, the mortality rate was 42.2% in the supine group and 43.3% in the prone group ($p = 0.83$). In Gattinoni et al.[23], it was observed that the mortality rate did not differ between the prone group and the supine group at the end of the 10-day study (21.1% versus 25%) and at the ICU discharge (50.7 % vs. 48%).

Adverse events

The number of complications due to the prone position was high[16-23]. Among the most common adverse events are: accidental extubation or tube displacement[17-23], edema[20,21], eschar[20-20], PAV[16,19]. Table 3 shows the general characterization of the articles included for analysis.

Chart 3. Caracterização dos estudos incluídos na síntese qualitativa quanto às características da intervenção, indivíduos com SDRA. 2018

AUTHOR	RANDOMIZATION	POSITIONING TIME	ADVERSE EVENTS
Ayzac *et al.*, 2015[16]	IG: n = 237 CG: n = 229	At least 16 consecutive hours 28 days	VAP: IG - 52; CG - 41
Guérin *et al.*, 2013[17]	IG: n = 240 (237) CG: n = 234 (229)	At least 16 hours/day 28 days	Accidental extubation: IG - 31; CG - 25 Selective intubation: IG - 6; CG - 5 ETT obstruction: IG - 11; CG - 5 Hemoptysis: IG - 6; CG - 12 Cardiac arrest: IG - 16; CG - 31 SpO2 < 85 or PaO2 < 55 mmHg: IG - 155; CG - 164 Heart rate < 30 bpm/min: IG - 26; CG - 27 Systolic blood pressure: IG - 35; CG - 48
Taccone *et al.*, 2009[18]	IG: n = 168 (134) CG: n = 174	At least 20 hours/day 28 days or until improvement	Need for increased sedation: IG - 80.4%; CG - 53.3% Airway obstruction: IG - 50.6%; CG - 33.9% Transient desaturation: IG - 63.7%; CG - 50.6% Vomiting: IG - 29.1%; CG - 12.6% Cardiovascular complication: IG - 72%; CG - 54.6% Loss of venous access: IG - 16.1%; CG - 4% Displacement of ETT: IG - 10.7%; CG - 4.6% Displacement of TCTT: IG - 4.2%; CG - 1.7%
Fernandez *et al.*, 2008[19]	IG: n = 22(21) CG: n = 20(19)	At least 20 hours/day 7 days or until improvement or death	Pneumothorax: IG - 0; CG - 1 Accidental extubation: IG - 1; CG - 1 VAP: IG - 3; CG - 1
Mancebo *et al.*, 2006[20]	IG: n = 80(76) CG: n = 62(60)	20 hours/day 10 days average	Edema: IG - 14 Conjunctival hemorrhage: IG - 2 Pressure ulcers: IG - 2 Vascular catheter malfunction: IG - 1 Catheter Displacement: IG - 3 Cardiac arrest: IG - 1 TET and drain torsion: IG - 2 Accidental extubation: IG - 1

Chart 3. Caracterização dos estudos incluídos na síntese qualitativa quanto às características da intervenção, indivíduos com SDRA. 2018

AUTHOR	RANDOMIZATION	POSITIONING TIME	ADVERSE EVENTS
Voggenreiter *et al.*, 2005[21]	IG: n = 21 CG: n = 19	At least 8, up to 23 hours/day Maximum of 90 days	Pressure ulcers: IG - 19; CG - 12 Edema (head and neck): IG - 6; CG - 11 Displacement of ETT: IG - 1; CC - 1 Transient decrease of PaO_2: GI - 1; CG - Bradi or tachycardia: IG - 8; CG - 3 Enteral feeding delay: IG - 1; CG - 1
Guerin *et al.*, 2004[22]	IG: n = 385 (378) CG: n = 417 (413)	At least 8 hours/day 2 to 6 days	Accidental extubation: IG - 44; CG - 47 Selective intubation: IG - 6; CG - 0 TET obstruction: IG - 34; CG - 12 Hemoptysis: IG - 45; CG - 34 SpO_2 < 85%: IG - 236; CG - 207 Cardiac arrest: IG - 87; CG - 88 Heart rate < 30 bpm/min: IG - 81; CG - 72 Pressure ulcers: IG - 208; CG - 157 Atelectasis: IG - 28; CG - 28 Intracranial hypertension: IG - 9; CG - 3 Pneumothorax: IG - 22; CG - 28
Gattinoni *et al.*, 2001[23]	IG: n = 152 CG: n = 152	At least 6 hours/day 10 days	Pressure ulcers: IG - 2.7%; CG - 1.9% Displacement of ETT: IG - 7.9%; CG - 9.9% Loss of venous access: IG - 5.3%; CG - 9.2% Displacement of TCTT: IG - 3.9%; CG - 0.7%

Subtitle: IG - intervention group (prone position); CG – control group (supine position); VAP - ventilator-associated pneumonia; ETT - endotracheal tube; TCTT - thoracotomy tube; MV - mechanical ventilation; NIV - non-invasive ventilation; TV - tidal volume.

Discussion

ARDS is a subject of great dedication in the ICUs, in the investigation of the effects of prone position and its repercussions, we observed that this therapy increases oxygenation and respiratory mechanics with occurrence of adverse events and no response in mortality in patients with ARDS. Although there is extensive knowledge about the pathophysiology of the syndrome, the mechanisms that provide improvement in the condition through the prone position are not yet consensual and well defined in the literature. One possible explanation is the methodological variety of the published studies[5,12].

Of the 8 articles selected, 6[17, 19-23] demonstrated positive effects on oxygenation of patients positioned prone versus supine. This is because with the prone position there is more even distribution of ventilation, providing recruitment of dorsal regions. This is explained by the alveolar decompression and re-expansion of the dorsal segments, areas of more involvement by atelectasis and edema in the supine position. There is also heart displacement ventrally, providing greater volume available for ventilation and maintenance of blood flow, which makes the lung well perfused and ventilated - reducing the shunt[6, 24]. However, in some cases, these values lost a difference[17,21] or inveteram[20], which in a way suggests that it is not necessary several days under the intervention.

According to Koulouras et al.[6], the total mechanics of the respiratory system are not altered by prone positioning, which contradicts the results of Guinin et al.,[17] Mancebo et al.[20] and Voggenreiter et al.[21], who observed values positive in the static compliance and plateau pressure between the IG and the GC. What may occur is an improvement in mechanics after return to the supine position, suggesting positive structural effects arising from the prone position. It is believed that in patients with systemic ARDS, there is an increase in pulmonary complacency with pronation6. Setten, Plotnikow and Accoce[5] affirm that when there is alveolar recruitment the pulmonary elastance decreases according to the degree of recruitment. If this decrease is equivalent to increased elastance of the chest wall (caused by prone positioning), the elastance of the respiratory system is maintained unchanged. In contrast, if the decrease is higher, there will be a decrease in the elastance of the respiratory system and, thus, an increase in compliance.

Regarding the mortality rates, all studies analyzed showed reduction with prone ventilation. However, only one[17] reached statistical significance, which confirms the claims that older researches were not able to demonstrate real benefits over death rates[12, 6, 5]. This fact can be justified by some limitations such as: small sample size, beginning delayed positioning, low duration and absence of pulmonary protection ventilation. These benefits are said to be more important in the severe classification of ARDS (according to the Berlin Definitions)[4,25]. Additionally, Ayzac et al.[16] reported a higher mortality with the occurrence of VAP, an important complication in individuals with ARDS.

The occurrence of adverse events is a factor to be considered, since they were present in all articles analyzed[16-23]. However, this should not be the focus, because the literature already shows that the occurrence of complications is minimal when the positioning process is performed by a skilled and experienced team[12].

In contrast, data found in the literature vary due to non-compliance with standardized protocols and heterogeneity of patients included[12], which may be justified by the evolution of ARDS concepts and therapeutics for its control[2]. In this scenario of changes, the pulmonary protection strategy is highlighted, which was applied in six of the studies analyzed[16-21].

The present study has important strengths, such as the performance of a sensitive and systematic bibliographic research - with well defined eligibility criteria by two independent researchers. With adequate methodological analysis of the included studies, as well as a good score of these, being important for health professionals, since it allows to solve controversies in studies, being able to estimate the effect of the treatment with better understanding, besides generalizing the data and increasing the external validity of studies, in this way provides an effective approach for patients and safe for intensive care.

As weaknesses, we highlight the methodological and outcome variety of articles analyzed, the impossibility of access to the translation of two articles (in Chinese) and the small number of databases consulted.

Conclusion

The present systematic review suggests that the prone position is capable of promoting increases in oxygenation and in the compliance of the pulmonary system of patients with ARDS. It may also be able to reduce mortality rates in the severe ARDS subgroup, in addition to presenting low occurrence of adverse effects. However, it is necessary to carry out new clinical trials on the subject, which offer satisfactory samples and similar methodologies, as well as the alignment of the protocols of the techniques of positioning therapy applied in ARDS.

Contributions of authors

Véras JACB contributed to the data collection of these articles. Martinez BP contributed to the study design and writing of the article. Gomes Neto M contributed to the analysis of the data of the articles. Saquetto MB contributed in the final essay of the article. Conceição CS contributed to the analysis of the articles and the final essay. Silva CMS contributed in the study design and writing of the article.

Conflicts of interest

No financial, legal or political conflict involving third parties (government, business and private foundations, etc.) was declared for any aspect of the work submitted (including but not limited to grants and funding, advisory board, study design, manuscript preparation , statistical analysis, etc.).

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