Adverse Events of Prone Positioning in Mechanically Ventilated Adults With ARDS

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BACKGROUND: Prone positioning is a therapy utilized globally to improve gas exchange, minimize ventilator-induced lung injury, and reduce mortality in ARDS, particularly during the ongoing coronavirus disease 2019 (COVID-19) pandemic. Whereas the respiratory benefits of prone positioning in ARDS have been accepted, the concurrent complications could be undervalued. Therefore, this study aimed to identify the adverse events (AEs) related to prone positioning in ARDS and, secondarily, to collect strategies and recommendations to mitigate these AEs. METHODS: In this scoping review, we searched recommendation documents and original studies published between June 2013 and November 2020 from 6 relevant electronic databases and the websites of intensive care societies. RESULTS: We selected 41 documents from 121 eligible documents, comprising 13 recommendation documents and 28 original studies (involving 1,578 subjects and 994 prone maneuvers). We identified > 40 individual AEs, and the highest-pooled occurrence rates were those of severe desaturation (37.9%), barotrauma (30.5%), pressure sores (29.7%), ventilation-associated pneumonia (28.2%), facial edema (16.7%), arrhythmia (15.4%), hypotension (10.2%), and peripheral nerve injuries (8.1%). The reported mitigation strategies during prone positioning included alternate face rotation (18 [43.9%]), repositioning every 2 h (17 [41.5%]), and the use of pillows under the chest and pelvis (14 [34.1%]). The reported mitigation strategies for performing the prone maneuver comprised one person being at the headboard (23 [56.1%]), the use of a pre-maneuver safety checklist (18 [43.9%]), vital sign monitoring (15 [36.6%]), and ensuring appropriate ventilator settings (12 [29.3%]). CONCLUSIONS: We identified > 40 AEs reported in prone positioning ARDS studies, including additional AEs not yet reported by previous systematic reviews. The pooled AE proportions collected in this review could guide research and clinical practice decisions, and the strategies to mitigate AEs could promote future consensus-based recommendations. *Key words: prone position; mechanical ventilation; ARDS; respiratory failure; adverse events; complications.* [Respir Care 2021;66(12):1898–1911.

Introduction

ARDS has a mortality rate of 20%–48%,[1-3] and survivors commonly experience long-term physical, cognitive, and mental impairments.[4,5] Prone positioning is among the well-known strategies to counteract ARDS[6-8] and is an inexpensive intervention that requires no complex technology, making it feasible worldwide.[9] In particular, early (12–24 h after ARDS diagnosis) and extended prone positioning (> 16 h per d) demonstrated decreased mortality from 41 to 24% in the 2013 Proning Severe ARDS Patients (PROSEVA) trial[10] when compared with supine positioning. Subsequently, prone positioning has been incorporated as a strong recommendation in international practice guidelines of ARDS,[11-14] including the World Health Organization guidelines for the management of the coronavirus disease 2019 (COVID-19).[15]

Although prone positioning is an established therapy worldwide for improving gas exchange, minimizing ventilator-induced lung injury, and reducing mortality in ARDS,[10,16] the literature demonstrates several adverse events (AEs), such as unplanned extubation, removal of invasive devices, transient desaturation, airway obstruction, facial edema, and pressure sores.[10,17-21] Currently, prone positioning has been widely applied even in awake patients supported with noninvasive ventilation or oxygen therapy[22]; however, patients who are mechanically ventilated and sedated are more likely to experience complications related to position changes. Four systematic reviews with meta-analyses involving up to 11 randomized controlled trials published between 2001 and 2013 (including the PROSEVA trial) revealed that a significant increase in new pressure sores, airway obstruction, and unplanned extubation occurred with prone positioning than with supine positioning.[23-26]

Since the publication of the PROSEVA trial, and particularly from the onset of the ongoing pandemic, global recommendations for prone positioning have been given greater emphasis,[11-14] which could lead to an increase in the incidence and intensity of AEs. This is predominantly relevant for inexperienced clinicians in prone positioning processes, who may be compelled to undertake this therapy during the pandemic.[27] To safely prone ventilated patients with ARDS in ICUs, minimizing human resource impacts, appropriate training, simulation, and health system planning must be undertaken.[28] Numerous guidelines recommend safe tips to minimize risk[29-31]; however, to implement prone positioning, clinicians must also recognize and consider the potential AEs. Whereas the respiratory benefits of prone positioning in patients with ARDS are widely accepted, the concurrent complications could be undervalued. Although some reviews on prone positioning have compiled AEs,[21,30,32] there have been no reviews that specifically included studies after the PROSEVA trial. Moreover, there are no reviews that fully collected AEs associated with prone positioning in mechanically ventilated adults with ARDS. Therefore, a scoping review is a recommended first step to systematically map the available literature from this landmark point.[33,34]

Accordingly, the primary objective of this study was to identify AEs related to prone positioning in mechanically ventilated adults with ARDS and, secondarily, to collect strategies and recommendations to mitigate the AEs during prone positioning implementation.

Review of the Literature

Study Design

This scoping review of the AEs of prone positioning was performed according to the Joanna Briggs Institute framework[34,35] and followed the PRISMA extension for Scoping Reviews checklist.[36] The protocol was registered on the International Platform of Registered Systematic Review and Meta-analysis Protocols database (registration number: INPLASY2020120020), which is available at https://doi.org/10.37766/inplasy2020.12.0020. Ethical approval was not required in this study.

Research Question

The research questions of this scoping review were formulated based on the authors' concern about the type and quantity of AEs associated with prone positioning,

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especially after the publication of the PROSEVA trial,[10] and even more during the ongoing COVID-19 pandemic. We structured the research questions using the population, concept, and context method,[34] searching for AEs related to prone positioning in mechanically ventilated adult subjects with ARDS and strategies or recommendations to mitigate AEs of prone positioning implementation.

Operational Definitions

AEs were defined according to the conceptual framework of the International Classification for Patient Safety[37] as incidents that can be a reportable circumstance, near miss, no-harm incident, or harmful incident involving an unintentional and/or unexpected event or occurrence that may result in injury or death. AEs can be classified as those associated with the prone positioning maneuver and those associated with the management of patients while in the prone position and can be detected during or immediately following the prone maneuver, including oxygen desaturation, loss of intravascular lines, unscheduled extubation, and hemodynamic instability, or as a long-term finding, including peripheral nerve injuries and pressure sores.[30] For the purposes of extraction, AEs were also considered as complications or adverse effects and were classified individually and by domain group according to type or the bodily system affected. Mitigation strategy was defined as any measure, effort, or recommendation to minimize or avoid AEs during the prone positioning maneuver or during the period when the subject was in the prone position.[30]

Search Strategy

Biomedical database searches and hand searching were performed between October 26, 2020, and November 1, 2020, (JJP-C, FG-S) following stages recommended by the Joanna Briggs Institute (for more details of the search strategy, (see the supplementary materials at http://www.rcjournal.com). The main search was carried out in the following biomedical databases: PubMed, CINAHL, Scientific Electronic Library Online Citation Index (Clarivate, London, England), Cochrane Library (free access from the Chilean Ministry of Health), LILACS, and WorldWideScience. The details of the search strategy used for each database are presented in Supplementary Material Table S1 (see the supplementary materials at http://www.rcjournal.com). The hand search was undertaken to acquire recommendation documents in the websites of scientific societies affiliated with the World Federation of Intensive and Critical Care.

Eligibility Criteria

Based on the population, concept, and context method, the following inclusion criteria were established: (1) population: mechanically ventilated subjects who required prone positioning due to ARDS; (2) concept: AE reporting; and (3) context: documents involving subjects in the ICU published from June 1, 2013, to November 1, 2020. The start of the study period was established from the publication date of the PROSEVA trial (included).[10]

We included original studies (randomized, controlled trials; nonrandomized trials; prospective and retrospective observational studies; case reports; and any letter, editorial, or correspondence with original data) and recommendation documents that provided advice to avoid or minimize AEs (including care protocols, guidelines, or any nonoriginal study providing clinical recommendations). The exclusion criteria were documents on awake prone positioning (ie, receiving noninvasive ventilation or high-flow nasal cannula), pediatric or neonatal population, animal or experimental models, unavailable full text, and documents written in languages other than English or Spanish. Documents that did not mention the presence or absence of AEs among subjects who underwent prone positioning were excluded from data extraction. Additionally, reviews were excluded from data extraction but were used to look for nonduplicate citations of pertinent documents.

Document Selection

Two reviewers blinded from each other's judgment (JJP-C, NA) independently screened all documents related to prone positioning in mechanically ventilated adults with ARDS using the title, abstract, and full text according to the eligibility criteria previously described. Any disagreements were resolved by a third reviewer (FG-S). For more details of the document selection, (see the supplementary materials at http://www.rcjournal.com).

Data Extraction and Analysis

The authors (JJP-C, NA, FG-S) collectively developed a standardized data charting form that included relevant variables according to the research questions. The data charting form was iteratively updated as needed, and each author independently abstracted the information from the recommendation documents (JJP-C, NA) and original studies (JJP-C, FG-S), including all supplementary materials (for more details of the data extraction, see the supplementary materials at http://www.rcjournal.com).

We generated summary tables reporting counts and percentages for document characteristics, AE proportions, and a compilation of available mitigation strategies and recommendations to minimize or avoid AEs. To calculate the pooled proportion of AEs according to the subjects in the prone position, we used the proportion of subjects who experienced AE and divided this value by the total number of subjects who received prone positioning (according to the data from the

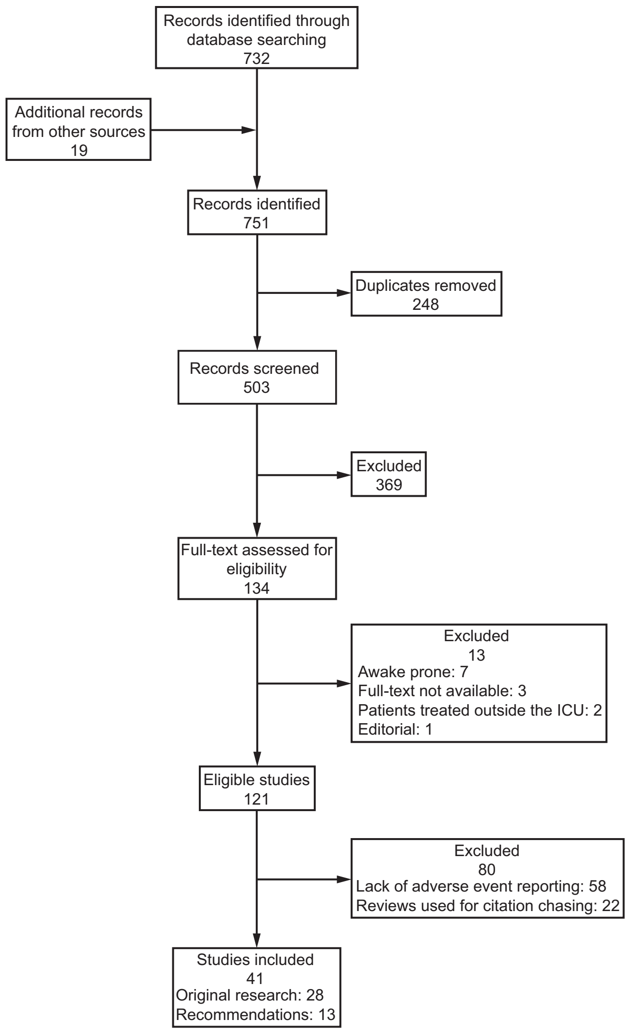

Fig. 1. Flow chart.

original studies). To calculate the pooled proportion of AEs according to the number of prone positioning maneuvers, we used the proportion of the number of AE occurrences during the prone maneuver and divided this value by the total number of positioning change maneuvers performed (according to the data from the original studies). When possible, we presented descriptive data as overall or pooled medians (interquartile range [IQR] or minimum-maximum [min-max]).

Results

Literature Search and Document Characteristics

This scoping review was conducted between August 2020 and March 2021. The literature search identified 732 citations from scientific databases and 19 from the manual searches. After removing duplicates and screening by title and abstract, 134 full texts were reviewed, yielding 121 eligible documents reporting prone positioning in mechanically ventilated subjects with ARDS. Of these documents, 22 (18.2%) were only used to look for relevant citations, and 58 (47.9%) were not selected due to the lack of AE reporting. Finally, 41 documents were selected for this review, including 28 original studies and 13 recommendation documents (Fig. 1). Of these, 39 (95.1%) were written in English and 2 (4.9%) in Spanish. An overview of the document characteristics is presented in Table 1. Remarkably, 19 (46.3%) were published in 2020, and 15 (36.6%) were focused on COVID-19-related ARDS. A summary of the main characteristics of each individual document included in this study is presented in Supplementary Material Table S2 (see the supplementary materials at http://www.rcjournal.com).

Adverse Events Related to Prone Positioning

Nine domain groups of AEs were identified in the original studies (number of studies [percentage]): pressure sores or skin injuries (13 [46.4%]), invasive devices (11 [39.3%]), respiratory system (9 [32.1%]), cardiovascular system (7 [25.0%]), musculoskeletal system (6 [21.4%]), visual system (5 [17.9%]), gastrointestinal system (4 [14.3%]), nervous system (2 [7.1%]), and others (4 [14.3%]). We identified AEs related to the prone position in 25 studies comprising a total of 1,578 subjects who received prone positioning (Table 2), with a pooled median (IQR) age of 57 y (48–60). With the data from 17 studies, the pooled median (IQR) total duration of the prone position was 2 d (0.9–5.0). We also identified AEs related to the prone positioning maneuver in 6 studies comprising 994 prone positioning maneuvers (Table 3). The highest-pooled proportions of AE occurrence were severe desaturation (37.9%), barotrauma (30.5%), pressure sores (29.7%), ventilation-associated pneumonia (28.2%), facial edema (16.7%), and arrhythmia or bradycardia (15.4%). Only 3 studies compared AE occurrence between the supine and prone groups (Supplementary Material Table S3, see the supplementary materials at http://www.rcjournal.com). Among the original studies, 15 (53.6%) reported a total of 14 AE detection methods (Supplementary Material Table S4, see the supplementary materials at http://www.rcjournal.com). In addition, we identified only 4 AEs in the case reports: meralgia paresthetica,[38,39] intraocular pressure increase,[40] optic neuropathy,[41] and lower cranial nerve paralysis.[42]

Mitigation Strategies for Adverse Events Related to Prone Positioning

Combining data from the original studies and recommendation documents, Table 4 presents literature-based matching between AEs related to prone positioning and the identified mitigation strategies. The most frequently reported mitigation strategies for managing subjects in the prone position were as follows: alternate face rotation (18 [43.9%]), repositioning

Table 1. Overview of Included Documents Reporting Adverse Events Related to Prone Positioning in Subjects With ARDS

Characteristics	Original Studies no. = 28, no. (%)	Recommendations no. = 13, no. (%)	Overall no. = 41, no. (%)
Year of publication			
2017–2020*	19 (67.9)	11 (84.6)	30 (73.2)
2013–2016	9 (32.1)	2 (15.4)	11 (26.8)
Region			
Europe†	16 (57.1)	7 (53.8)	23 (56.1)
United States	9 (32.1)	2 (15.4)	11 (26.8)
Asia‡	3 (10.7)	2 (15.4)	5 (12.2)
Brazil	0	2 (15.4)	2 (4.9)
Design			
Retrospective observational study§	15 (53.6)	N/A	15 (36.6)
Case report‖	8 (28.6)	N/A	8 (19.5)
Prospective observational study	4 (14.3)	N/A	4 (9.8)
Randomized controlled trial	1 (3.6)	N/A	1 (2.4)
Clinical practice guideline	N/A	5 (38.5)	5 (12.2)
National guideline	N/A	3 (23.1)	3 (7.3)
Clinical commentary	N/A	2 (15.4)	2 (4.9)
Care protocol	N/A	2 (15.4)	2 (4.9)
Checklist	N/A	1 (7.7)	1 (2.4)
Target population			
Non-COVID-19-related ARDS	17 (60.7)	9 (69.2)	26 (63.4)
COVID-19-related ARDS	11 (39.3)	4 (30.8)	15 (36.6)
Extracorporeal membrane oxygenation¶	2 (7.1)	0	2 (4.9)
Morbid obesity with ARDS¶	1 (3.6)	0	1 (2.4)
Exacerbation of interstitial lung disease¶	1 (3.6)	0	1 (2.4)
Journal or source scope			
Critical care and intensive care medicine	16 (57.1)	7 (53.8)	23 (56.1)
Medicine miscellaneous	2 (7.1)	3 (23.1)	5 (12.2)
Pulmonary and respiratory medicine	3 (10.7)	0	3 (7.3)
Surgery	2 (7.1)	0	2 (4.9)
Anesthesiology	1 (3.6)	1 (7.7)	2 (4.9)
Physical therapy and rehabilitation	1 (3.6)	1 (7.7)	2 (4.9)
Nursing	1 (3.6)	1 (7.7)	2 (4.9)
Nutrition and dietetics	1 (3.6)	0	1 (2.4)
Dermatology	1 (3.6)	0	1 (2.4)

N/A = not applicable.
* Includes one study published online in 2020, yet currently publication date is 2021.[64]
† Documents from European countries included France (no. = 7), United Kingdom (no. = 7), Spain (no. = 4), Germany (no. = 2), Italy (no. = 2), and Denmark (no. = 1).
‡ Documents from Asian countries included India (no. = 2), Japan (no. = 1), China (no. = 1), and Saudi Arabia (no. = 1).
§ Includes one secondary analysis[65] and one ancillary study,[66] both originated from PROSEVA trial data.
‖ Includes a research letter with 2 case reports.[38]
¶ Also included in the category: non-SARS-CoV-2–related ARDS.
COVID-19 = coronavirus disease 2019

every 2 h (17 [41.5%]), the use of pillows under the chest and pelvis (14 [34.1%]), one upper limb abducted next to the head (11 [26.8%]), the use of a facial or head padding (11 [26.8%]), the use of protective measures for eyes (11 [26.8%]), placing the subject in a swimming position (10 [24.4%]), placing the subject in the reverse Trendelenburg position (10 [24.4%]), and free abdomen to minimize abdominal pressure (10 [24.4%]) (Table 5). Unexpectedly, no original study or recommendation document reported early mobilization (ie, neuromuscular electrical stimulation or passive mobilization) as a mitigation strategy for prone positioning of mechanically ventilated subjects. The manual prone positioning maneuver was the most common maneuver, reported in 14 (34.1%) documents. The most frequently reported mitigation strategies for performing the prone maneuver were one person being at the head of the subject (23 [56.1%]), the use of a pre-maneuver safety checklist (18 [43.9%]), vital sign monitoring (15 [36.6%]), ensuring appropriate ventilator settings (12 [29.3%]), rotation opposite to the catheter side (10 [24.4%]), pre-oxygenation with 100% O_2 (10 [24.4%]), and interruption of enteral nutrition (10 [24.4%]) (Table 6). The overall median (min-max) number

Table 2. Adverse Events Related to Prone Positioning in Subjects With ARDS

Adverse Event	Studies Contributing Data, no.	Subjects With Adverse Event,† *n*	95% CI
Pressure sores (by body site)‡			
Pressure sores in general	7	195/656 (29.7)	26.2–33.2
Face (ie, chin, cheekbone)	7	113/595 (19.0)	15.8–22.1
Chest	4	40/443 (9.0)	6.4–11.7
Lower limb (ie, foot, heel, knee, trochanter)	4	29/449 (6.5)	4.2–8.7
Ears	2	9/120 (7.5)	2.8–12.2
Back of head	1	6/191 (3.1)	0.7–5.6
Back	1	2/189 (1.1)	0–2.5
Sacrum	1	40/196 (20.4)	14.8–26.1
Pressure sores (by severity grade)			
Grade I	2	17/205 (8.3)	4.5–12.1
Grade II	2	20/205 (9.8)	5.7–13.8
Grade III	2	0/205 (0)	0
Grade IV	2	3/205 (1.5)	0–3.1
Invasive devices			
Removal of venous or arterial lines	7	4/452 (0.9)	0–1.7
Unscheduled extubation	5	32/413 (7.7)	5.2–10.3
Displacement of endotracheal tube	4	9/466 (1.9)	0.7–3.2
Airway obstruction	2	11/272 (4.0)	1.7–6.4
Respiratory system			
Severe desaturation (S_{pO_2} < 85%)	3	162/428 (37.9)	33.3–42.4
Ventilation-associated pneumonia	2	96/340 (28.2)	23.5–33.0
Pneumothorax	2	3/104 (2.9)	0–6.1
Barotrauma	1	11/36 (30.6)	15.5–45.6
Cardiovascular system			
Cardiac arrest	5	19/559 (3.4)	1.9–4.9
Hypotension	3	40/393 (10.2)	7.2–13.2
Arrhythmia or bradycardia	2	42/273 (15.4)	11.1–19.7
Musculoskeletal system			
Peripheral nerve injuries in general	4	15/185 (8.1)	4.2–12.0
Brachial plexus injury	3	4/174 (2.3)	0.1–4.5
Ulnar nerve injury	1	6/83 (7.2)	1.7–12.8
Radial nerve injury	1	3/83 (3.6)	0–7.6
Sciatic nerve injury	1	3/83 (3.6)	0–7.6
Median nerve injury	1	2/83 (2.4)	0–5.7
Back pain	1	1/11 (9.1)	0–26.1
Visual system			
Eye hemorrhage or edema	3	8/226 (3.5)	1.1–5.9
Gastrointestinal system			
Vomit	1	1/66 (1.5)	0–4.5
Hemoptysis	1	6/237 (2.5)	0.5–4.5
Nervous system			
Transient increase in intracranial pressure	2	2/102 (2.0)	0–4.7
Others§			
Facial, periorbital, or tongue edema	3	17/102 (16.7)	9.4–23.9
Bleeding	1	1/66 (1.5)	0–4.5

* Counting studies that collected data on adverse events, regardless of whether an event occurred.
† Proportion of subjects who experienced the adverse event due to prone positioning divided by the total number of subjects who received prone positioning, from original studies contributing data.
‡ Two other body sites (head and penis) were reported in one study.[67] In this study, it only includes subjects presenting skin injuries; therefore, data of this adverse event were not used for this table.
§ Meralgia paresthetica, intraocular pressure increase, optic neuropathy, and lower cranial nerves paralysis are not presented in this table as they were only informed in case reports.

of staff members involved in the prone positioning maneuver was 5 (3–8) in the original studies and 5 (3–7) in the recommendations, mainly including physicians, nurses, and respiratory therapists. Additionally, the training of staff members involved in the management of subjects placed in the prone position was reported in only 11 (39.3%) original

Table 3. Adverse Events Related to the Positioning Change Maneuver in Subjects With ARDS

Adverse Event	Studies Contributing Data, no.	Maneuvers With Adverse Events[†], no. (%)	95% CI
Invasive devices			
Disconnection of ventilator lines	3	5/920 (0.5)	0.1–1.0
Removal of venous or arterial lines	3	1/250 (0.4)	0–1.2
Removing of nasogastric tube	2	2/441 (0.5)	0–1.1
Unscheduled extubation	2	0/441 (0)	0
Airway obstruction	1	2/74 (2.7)	0–6.4
Respiratory system			
Severe desaturation (S_{pO_2} < 85%)	2	15/441 (3.4)	1.7–5.1
Cardiovascular system			
Hypotension	1	7/74 (9.5)	2.8–16.1
Arrhythmia or bradycardia	1	3/74 (4.1)	0–8.5
Cardiac arrest	1	1/74 (1.4)	0–4.0
Gastrointestinal system			
Vomit	1	5/526 (1.0)	0.1–1.8
Other			
Bleeding[‡]	1	10/74 (13.5)	5.7–21.3

* Counting studies that collected data on adverse events, regardless of whether an event occurred.
† Proportion of the number of occurrences of adverse events during the positioning change maneuver to prone or supine divided by the total positioning change maneuvers performed, from studies contributing data.
‡ Reported in only one study of subjects with extracorporeal membrane oxygenation.

studies and was suggested by 8 (61.5%) recommendation documents.

Discussion

We identified > 40 individual AEs within 9 domains from the original studies, despite almost half of the eligible studies not reporting any AEs. To our knowledge, this is the first scoping review to specifically and comprehensively collect AEs related to prone positioning in mechanically ventilated subjects with ARDS. We identified studies reporting AEs according to the number of subjects placed in the prone position (no. = 25) and the number of prone maneuvers (no. = 6). Moreover, from the original studies and recommendation data, we identified > 30 strategies to mitigate AEs during the prone position and almost 20 strategies to perform the prone positioning maneuver.

Our findings can be contrasted with previous systematic reviews that, as a secondary aim, have also reported the occurrence of AEs in subjects placed in the prone position.[23-26] Considering the AEs reported by systematic reviews, the reported data up to the publication of the PROSEVA trial, and our scoping review, the pooled proportions were similar in terms of pressure sores, ventilator-associated pneumonia, cardiac arrest, pneumothorax, arrhythmia, airway obstruction, unplanned extubation, removal of venous or arterial lines, and endotracheal tube displacement (Supplementary Material Table S5,see the supplementary materials at http://www.rcjournal.com). Remarkably, we identified similar overall values, showing a lower proportion of AEs in our scoping review, except for ventilator-associated pneumonia and arrhythmia, which were slightly higher.

Owing to the wide coverage of scoping reviews, we identified additional AEs from nonrandomized controlled trials and compared the data with preceding randomized controlled trials.[23-26] From single studies, we identified back pain,[43] barotrauma,[44] vomit,[45] hemoptysis,[10] and bleeding[45] as AEs. Additionally, we found relevant AEs reported in at least 2 original studies that were not informed by previous reviews.[23,24] For instance, pressure sores were reported by severity grade in 2 studies,[17,46] highlighting grades I and II (with redness and blisters) as the most prevalent (8.3% and 9.8%, respectively) and showing fewer grades in subjects who received suitable nutritional intake.[46] Severe desaturation was reported in 3.4% of all prone positioning maneuvers[47,48] and in 37.9% of subjects while in the prone position.[10,49,50] In the PROSEVA trial, 65.4% of subjects presented with severe desaturation (pulse oximetry saturation < 8 5%) during prone positioning compared to 71.6% in the supine group.[10] We believe that the proportion of AEs that occurred during the maneuver should be calculated separately from those that occurred while the subjects were in the prone position. Remarkably, acquired peripheral nerve injury associated with the use of prone positioning has been rarely reported and is likely undervalued. However, in 2 recent reports,[51,52] it was surprising that 13.1%–14.5% of subjects with COVID-19 had peripheral nerve injury after prone positioning, including injuries to the brachial plexus, ulnar, radial, sciatic, and median nerves. In our review, only 4 studies reported a pooled

Table 4. Literature-Based Matching Between Adverse Events Related to Prone Positioning and Identified Mitigation Strategies

	Pressure Sores	Peripheral Nerve Injuries*	VAP	Facial Edema	Eye Injuries†	Lower Cranial Nerves Paralysis	Vomit or Hemoptysis	Transient Increase in ICP	Invasive Devices Displacements‡	Airway Obstruction	Barotrauma	Severe Desaturation	Hemodynamic Instability§
Strategies during prone position													
Swimming position‖		✓											
Incomplete prone positioning (135°–180°)		✓		✓									
Reverse Trendelenburg¶	✓		✓	✓	✓	✓	✓	✓				✓	
One upper limb abducted next to the head		✓											
Upper limbs placed alongside the body		✓											
Slide scapula up the back with slight shoulder shrug		✓											
Head placement over the upper edge of the bed	✓				✓				✓				
One lower limb with hip and knee semi-flexed		✓											
Upper limbs placed up straight beside the head		✓											
Keep all joints in a neutral anatomical position		✓											
Avoid neck hyperextension		✓											
Avoid extension of the shoulder		✓											
Avoid arm abduction > 70°		✓											
Avoid depression of the shoulder girdle		✓											
Avoid nonphysiologic limbs movements		✓											
Pillows under chest and pelvis	✓						✓						
Pillow under shinbone minimizing equinus foot		✓											
Alternate face rotation	✓	✓		✓	✓	✓							
Repositioning every 2 h	✓	✓		✓	✓	✓							
Facial or head padding	✓			✓									
Protective measures for eyes					✓								
Free abdomen							✓						
Bony prominences padding	✓												
Hand rolls		✓											
Hourly joint movement and skin marks observation	✓	✓											
Suitable mattress and bed-related characteristics	✓			✓									

(Continued)

Table 4. Continued

	Pressure Sores	Peripheral Nerve Injuries*	VAP	Facial Edema	Eye Injuries†	Lower Cranial Nerves Paralysis	Vomit or Hemoptysis	Transient Increase in ICP	Invasive Devices Displacements‡	Airway Obstruction	Barotrauma	Severe Desaturation	Hemodynamic Instability§
Strategies to perform the prone positioning maneuver													
One person at the head of subject**									✓			✓	
Rotation opposite to the catheter side									✓				
Rotation toward the ventilator side									✓				
Pre-maneuver safety checklist	✓		✓				✓		✓	✓	✓	✓	✓
Vital sign monitoring									✓			✓	✓
Ensuring appropriate ventilator settings											✓	✓	
Pre-oxygenation with 100% O_2												✓	✓
Sedated and paralyzed								✓	✓		✓		
Airway suction prior to procedure			✓							✓			
Interruption of enteral nutrition							✓		✓				
Discontinue nonessential infusions and monitoring									✓				
Arms alongside the body		✓											
Palms facing inward or anteriorly		✓											
Palms under the buttocks		✓											
Avoid nonphysiologic limb movements		✓											

* Peripheral nerve injuries include brachial plexus injury, ulnar nerve injury, radial nerve injury, sciatic nerve injury, median nerve injury, back pain, and meralgia paresthetica.
† Eye injuries include eye hemorrhage or edema, intraocular pressure increase, and optic neuropathy.
‡ Invasive devices removal or displacements include removal of venous or arterial lines, unscheduled extubation, displacement of endotracheal tube, disconnection of ventilator lines, and removal of nasogastric tube.
§ Hemodynamic instability includes cardiac arrest, hypotension, and arrhythmia.
‖ Swimming position definition (also called swim position or swimmer position) varies depending on the reference; mainly it is described as one arm raised (elbow flexed 90° and shoulder abducted 45°–80°) and head rotated toward the raised arm; the other arm is positioned alongside the body with the palms facing inward or upward.
¶ For reverse Trendelenburg position, the following degrees of inclination were reported: 10°, 25°–30°, and 30°.
** One person at the head of subject/bed dedicated to ensure the endotracheal tube, ventilator, and nasogastric tube, directing, coordinating, and supervising the procedure.
VAP = ventilation-associated pneumonia
ICP = intracranial pressure

Table 5. Mitigation Strategies to Manage Subjects While in the Prone Position

Strategies	Original Studies no. = 28, no. (%)	Recommendations no. = 13, no. (%)	Overall no. = 41, no. (%)
Prone whole-body position			
Swimming position*	3 (10.7)	7 (53.8)	10 (24.4)
Reverse Trendelenburg†	6 (21.4)	4 (30.8)	10 (24.4)
Complete prone positioning (180°)	7 (25.0)	1 (7.7)	8 (19.5)
Incomplete prone positioning (135°–180°)	1 (3.6)	1 (7.7)	2 (4.9)
Limbs and head position			
One upper limb abducted next to the head	3 (10.7)	8 (61.5)	11 (26.8)
Upper limbs placed alongside the body	8 (28.6)	0	8 (19.5)
Avoid neck hyperextension	2 (7.1)	3 (23.1)	5 (12.2)
Slide scapula up the back with slight shoulder shrug	1 (3.6)	3 (23.1)	4 (9.8)
Avoid extension of the shoulder	1 (3.6)	3 (23.1)	4 (9.8)
Head placement over the upper edge of the bed	3 (10.7)	1 (7.7)	4 (9.8)
Arm abduction of 80°	1 (3.6)	2 (15.4)	3 (7.3)
Avoid arm abduction > 70°	0	2 (15.4)	2 (4.9)
Avoid depression of the shoulder girdle	0	2 (15.4)	2 (4.9)
One lower limb with hip and knee semi-flexed	1 (3.6)	1 (7.7)	2 (4.9)
Upper limbs placed up straight beside the head	1 (3.6)	0	1 (2.4)
Keep all joints in a neutral anatomical position	0	1 (7.7)	1 (2.4)
Avoid nonphysiologic limbs movements	1 (3.6)	0	1 (2.4)
Pillows use			
Pillows under chest and pelvis	7 (25.0)	7 (53.8)	14 (34.1)
Pillow under shinbone minimizing equine position	4 (14.3)	3 (23.1)	7 (17.1)
A triangular pillow under the anterior iliac crests	1 (3.6)‡	0	1 (2.4)
Care measures			
Alternate face rotation	11 (39.3)	7 (53.8)	18 (43.9)
Repositioning every 2 h	11 (39.3)	6 (46.2)	17 (41.5)
Facial or head padding§	6 (21.4)	5 (38.5)	11 (26.8)
Protective measures for eyes	4 (14.3)	7 (53.8)	11 (26.8)
Free abdomen	5 (17.9)	5 (38.5)	10 (24.4)
Bony prominences padding	4 (14.3)	4 (30.8)	8 (19.5)
Hand rolls	0	3 (23.1)	3 (7.3)
Repositioning every 1 h	1 (3.6)	1 (7.7)	2 (4.9)
Hourly joint movement and skin marks observation	1 (3.6)	1 (7.7)	2 (4.9)
Bed-related characteristics			
Alternating-pressure mattress	3 (10.7)	1 (7.7)	4 (9.8)
Prone positioner‖	0	3 (23.1)	3 (7.3)
Suitable mattress	1 (3.6)	1 (7.7)	2 (4.9)

* Swimming position definition (also called swim position or swimmer position) varies depending on the reference; mainly it is described as one arm raised (elbow flexed 90° and shoulder abducted within 45°–80°) and head rotated toward the raised arm; the other arm is positioned alongside the body with the palms facing inward or upward.
† For reverse Trendelenburg position, the following degrees of inclination were reported: 10°, 25°–30°, and 30°.
‡ Reported in only one study of subjects with extracorporeal membrane oxygenation.[62]
§ Includes half a crescent jelly, sponge donuts, C-letter–shaped pad, facial padding if the subject has a tracheostomy, and bite block (for macroglosia).
‖ Includes Vollman Prone Positioner (Hill-Rom), RotoProne bed, and the continuous lateral rotation therapy.

proportion of any peripheral nerve injury (8.1%),[43,49,52,53] which could indicate an underestimation in other studies.

We found relevant mitigation strategies for AEs related to body position in subjects placed in the prone position. The swimming position was reported in 7 (53.8%) recommendations but was performed in only 3 (10.7%) original studies, whereas the complete prone positioning (180°) was mentioned in only one recommendation but was performed in 7 (25.0%) studies. Although the PROSEVA trial used complete prone positioning with arms placed alongside the body, we also observed a trend in the recommendation of the swimming position; however, there is heterogeneity in its description, with the majority of documents describing it as placing the face toward the abducted and flexed arm,[29,30,54] whereas others describing it as placing the face toward the straight arm.[55] Currently, there is no completely safe and suitable positioning of the body that will ensure the minimization of nerve injury in every patient, but some

Table 6. Mitigation Strategies to Perform the Prone Positioning Maneuver

Strategies	Original Studies no. = 28, no. (%)	Recommendations no. = 13, no. (%)	Overall no. = 41, no. (%)
Practical execution maneuver			
Manual prone positioning maneuver	12 (42.9)	2 (15.4)	14 (34.1)
Cornish Pastry technique (envelope maneuver)*	1 (3.6)	6 (46.2)	7 (17.1)
Tortoise Turning and Positioning System Prone†	1 (3.6)	0	1 (2.4)
Safety strategies			
One person at the head of subject‡	16 (57.1)	7 (53.8)	23 (56.1)
Pre-maneuver safety checklist	10 (35.7)	8 (61.5)	18 (43.9)
Vital sign monitoring	12 (42.9)	3 (23.1)	15 (36.6)
Rotation opposite to the catheter side	8 (28.6)	2 (15.4)	10 (24.4)
Interruption of enteral nutrition	2 (7.1)	8 (61.5)	10 (24.4)
Discontinue nonessential infusions and monitoring	2 (7.1)	5 (38.5)	7 (17.1)
Rotation toward the ventilator side	1 (3.6)	5 (38.5)	6 (14.6)
Respiratory strategies			
Ensuring appropriate ventilator settings	9 (32.1)	3 (23.1)	12 (29.3)
Pre-oxygenation with 100% O_2	4 (14.3)	6 (46.2)	10 (24.4)
Sedated but paralyzed when necessary	4 (14.3)	5 (38.5)	9 (22.0)
Sedated and paralyzed	2 (7.1)	1 (7.7)	3 (7.3)
Airway suction prior to procedure	3 (10.7)	5 (38.5)	8 (19.5)
Limbs positioning			
Arms along the body	2 (7.1)	4 (30.8)	6 (14.6)
Palms facing inward or anteriorly	1 (3.6)	3 (23.1)	4 (9.8)
Palms under their buttocks	1 (3.6)	1 (7.7)	2 (4.9)
Avoid nonphysiologic limbs movements	1 (3.6)	0	1 (2.4)
Participating health staff members			
Physician§	6 (21.4)	7 (53.8)	13 (31.7)
Nurse	4 (14.3)	7 (53.8)	11 (26.8)
Respiratory therapist	3 (10.7)	5 (38.5)	8 (19.5)
Physiotherapist	1 (3.6)	4 (30.8)	5 (12.2)
Anesthetist	1 (3.6)	3 (23.1)	4 (9.8)
Occupational therapist	1 (3.6)	0	1 (2.4)
Medical student	1 (3.6)	0	1 (2.4)

* The Cornish Pastry technique (also called envelope maneuver) is described as a prone positioning maneuver that uses double sheets cocooning the subject inside (one below and one above).
† The Tortoise Turning and Positioning System prone (Mölnlycke Health Care, Gothenburg, Sweden) consists of 2 low-pressure air-filled pads and 2 fluidized positioners to support and off-load the subject.[49]
‡ One person at the head of subject/bed dedicated to ensure the endotracheal tube, ventilator, and nasogastric tube, directing, coordinating, and supervising the procedure.
§ Physician: including senior physicians and critical care specialists.

authors promote an understanding of the principles of a safe position and encourage the maintenance of a high clinical suspicion of potential brachial plexus injury during the prone position, especially for unconscious and paralyzed patients.[54] To reduce the risk and impact of brachial plexus injury, some guidelines recommend the swimming position, avoiding excessive rotation, neck extension, shoulder extension or subluxation, arm abduction beyond 70° with elbow extension, and external rotation of the shoulder beyond 60°.[54] Regarding the application of thoraco-pelvic supports (pillows under the chest and pelvis), 7 (25.0%) studies and 7 (53.8%) recommendations reported minimizing the intra-abdominal pressure. Controversially, Chiumello et al[56] demonstrated that these supports decrease chest wall compliance, increase pleural pressure, and slightly deteriorate hemodynamics without any advantage in gas exchange, along with a higher likelihood of pressure sores. Regardless of the main position of the entire body, the reverse Trendelenburg[57] position has been reported as a recommended strategy to mitigate face pressure sores, ventilator-associated pneumonia, facial edema, eye injuries, lower cranial nerve paralysis, vomiting, transient increase in intracranial pressure, and severe desaturation (Table 4) and is even better if combined with alternating face rotation and repositioning every 2 h. Despite the well-known safety and benefits of passive mobilization and neuromuscular electrical stimulation in sedated subjects,[58-61] no study has reported early mobilization as a mitigation strategy, which is likely vital to minimize nerve injuries and ICU-acquired weakness after prone positioning.

AEs related to prone maneuvers can be mitigated by following at least 20 strategies identified in our scoping review, including using a pre-maneuver safety checklist, monitoring vital signs, ensuring appropriate ventilator settings, and having a leader (physician or respiratory therapist) at the head of the subject, which have also been previously reported.[30] The number of staff members is also important, as it influences the occurrence of AEs during the maneuver.[30] The median number identified was 5 staff members, but this number depends on each team's experience level and the subject type. For those with extracorporeal membrane oxygenation or morbid obesity requiring prone positioning, the number of members reported ranged from 4–8[47,62] and 5–6,[45] respectively.

Although preceding meta-analyses support the significant reduction in overall mortality of subjects with ARDS treated with prone positioning,[23-26] the risk of AEs should be carefully considered during the decision-making process, especially in ICUs with less experience.[23,27] Whereas most AEs can be severe but immediately corrected, others may be less prevalent but may require long-term care. In this scoping review, several mitigation strategies related to maintaining safe body positions were collected, emphasizing the prevention of AEs originating from incorrect body and limb positions that could be maintained over time. Future clinical trials should incorporate the screening of long-term AEs, which we believe are still underestimated, as well as peripheral nerve and eye injuries, which could be determinants of the quality of life of survivors. In addition, future studies should report the presence and absence of AEs in both the prone and supine groups to minimize design-related bias.

This review is not exempted from limitations. The findings of this scoping review cannot be generalized beyond subjects with ARDS treated in the ICU with prone positioning. Due to the emerging need to obtain recent information on prone positioning, we did not include documents published before 2013. However, we captured useful data on AEs that became available after the landmark PROSEVA trial. We did not identify new randomized or controlled clinical trials reporting AEs related to prone positioning between 2013 and 2020, limiting the comparison of AE occurrence between the prone and supine groups. Due to the observational nature of the original studies included, the causality of AE occurrence likewise cannot be confirmed. Moreover, additional confounding and mediator factors could explain an AE,[63] and the prone position itself could be a mediator of the greater severity experienced by a patient presenting with an event. Finally, no cause-effect analysis had been performed between the mitigation strategies and the occurrence of AEs, nor did we explore the relationships between the length of prone positioning sessions and AEs. However, the findings of our review could serve as precursors for future studies.

Conclusions

Several AEs related to prone positioning in mechanically ventilated subjects with ARDS were identified, involving additional AEs not yet reported by previous systematic reviews. The pooled AE proportions reported in this scoping review might guide research and clinical practice decisions, especially for ICU teams with little to no experience in the management of patients who need prone positioning. The strategies for mitigating AEs that have been collected in this scoping review could promote future consensus-based recommendations.

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