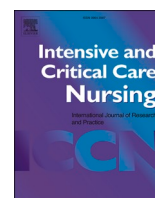




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Research Article

Short and long-term complications due to standard and extended prone position cycles in CoViD-19 patients[☆]

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ABSTRACT

Objective: To investigate short and long-term complications due to standard (≤ 24 hours) and extended (> 24 hours) prone position in COVID-19 patients.

Methods: Retrospective cohort study conducted in an Italian general intensive care unit. We enrolled patients on invasive mechanical ventilation and treated with prone positioning. We recorded short term complications from the data chart and long-term complications from the scheduled follow-up visit, three months after intensive care discharge.

Results: A total of 96 patients were included in the study. Median time for each prone positioning cycle (302 cycles) was equal to 18 (16–32) hours. In 37 (38%) patients at least one cycle of extended pronation was implemented. Patients with at least one pressure sore due to prone position were 38 (40%). Patients with pressure sores showed a statistically significant difference in intensive care length of stay, mechanical ventilation days, numbers of prone position cycles, total time spent in prone position and the use of extended prone position, compared to patients without pressure sores. All lesions were low grade. Cheekbones (18%) and chin (10%) were the most affected sites. Follow-up visit, scheduled three months after intensive care discharge, was possible in 58 patients. All patients were able to have all 12 muscle groups examined using the Medical Research Council scale examination. No patient reported sensory loss or presence of neuropathic pain for upper limbs.

Conclusions: Extended prone position is feasible and might reduce the workload on healthcare workers without significant increase of major prone position related complications.

Implications for clinical practice

- Prone positioning requires a nursing protocol to prevent the occurrence of complications.
- Extended prone positioning is feasible without significant increase of prone position related complications.
- Extended prone positioning could be suggested in a scenario of a pandemic outbreak to reduce nursing workload.
- Prone position avoiding “swimmer position” is safe and could help to reduce long term complications on the upper limbs.

[☆] The present study was performed at the General Intensive Care Unit, Emergency Department and Intensive Care, San Gerardo Hospital – ASST Monza, Via Pergolesi 33 – Monza (MB), Milan-Bicocca University – Italy.

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Introduction

In patients with Adult Respiratory Distress Syndrome (ARDS), prone positioning (PP) decreased 28-day and 90-day mortality (Guérin et al., 2020). Several studies have shown its impact on gas exchange (Gattinoni et al., 2001; Guérin et al., 2018; Taccone et al., 2009). It is crucial to underline that the improvement of the pO_2/FiO_2 mmHg ratio value on its own, does not represent the only parameter to evaluate the benefits of prone position. PP, compared to the supine positioning, markedly reduced the overinflated lung areas while promoting alveolar recruitment (Guérin et al., 2013). These effects may contribute to prevent ventilator-induced lung injury by homogenizing the distribution of stress and strain within the lung and they may represent the mechanisms by which PP reduced mortality independently from its effect on oxygenation. COVID-19 pandemic dramatically increased ICU admission of patients with moderate to severe ARDS, leading to the greatest healthcare crisis of the modern era. The sudden lack of intensive care units (ICU) beds, during the first and the second COVID waves, forced healthcare systems to convert hospital areas to new COVID-19 ICUs (Bambi et al., 2020; Grasselli et al., 2020; Lucchini et al., 2020b). This was accompanied by the recruitment of healthcare workers without previous critical care experience. At a time of uncertain efficacy of the available therapies, PP represented the single intervention with proven efficacy for mortality reduction of COVID-19 related ARDS (Nasa et al., 2021). During the pandemic, in Italy, PP has been adopted in 61% of the COVID-19 ICU population (Langer et al., 2021). Despite PP is a well recognized routine intervention for ARDS patients, with a low incidence of short and long term adverse events, PP sessions may be highly demanding for the whole ICU staff considering the high global workload and limited resources. Prone positioning increases the risk of developing hospital-acquired pressure injury (González-Seguel et al., 2021; Sud et al., 2014). The main preventive strategies to prevent pressure sores development during prone positioning include skin assessment (before, during and after PP), repositioning to offload pressure points on the face and the body, application of dressings, such as hydrocolloids, transparent film and silicone, to decrease facial skin breakdown (National Pressure Injury Advisory Panel, 2019). Many ICUs have updated their protocols for pressure sores prevention in PP patients, reflecting necessary changes related to care for COVID-19 patients (Team et al., 2021b). Johnson et al. (2021) recently reported that having a certified wound and skin care nurse on a multi-professional prone-positioning team could help to reduce odds of pressure injuries developing in patients infected with COVID-19. Development of online learning resources (infographics, learning modules and webinars) and a dedicated checklist for PP procedure (Santos et al., 2021) are recently reported to improve and disseminate knowledge about prevention of PP complications (Team et al., 2021a). Preventive strategies recommended by the guidelines suggest to avoid extended use of prone positioning unless required for the management of the individual's medical condition. (National Pressure Injury Advisory Panel, 2019). However, COVID-19 ARDS management requires prone positioning for extended periods of time (Nasa et al., 2021). A preliminary report of COVID-19 patients proposed the use of prolonged PP (i.e. 36 hours) to improve oxygenation and to reduce nursing workload (Carsetti et al., 2020). The investigators reported that prolonged PP was feasible and safe. The strategy of prolonged pronation cycles may theoretically be of benefit during the low resources of the pandemic by reducing the overall number of daily handling while offering this intervention to the highest number of patients as feasible for a longer time-interval. On the other hand, this intervention may theoretically be associated with a higher risk of pressure sores, facial oedema or peripheral nerve injuries. To our knowledge, these short and long-term consequences of extended pronation cycles have not been systematically investigated to date. Given the growing number of centers adopting this strategy of extended pronation cycles, it would be relevant to collect information on its advantages and shortcomings for a risk–benefit balance. We designed a retrospective cohort

study in order to assess safety of extended pronation cycles in COVID-19 ARDS patients, with a specific focus on pressure sores and peripheral nerve injuries assessed at a 3-month follow-up. The secondary aim was to investigate the modifications of the PaO_2/FiO_2 mmHg ratio induced by prone position.

Materials and methods

Study design

This was a retrospective cohort study conducted between February 2020 and January 2021 in the general ICU of San Gerardo University Hospital, Monza, Italy. The ICU consisted of 10 beds before COVID-19 outbreak. During first wave (February-May 2020) ICU beds increased to 21, while in the second wave (October 20-January 21) the beds increased to 19.

Inclusion and exclusion criteria

We enrolled all consecutive patients with a diagnosis of COVID-19 pneumonia, under invasive mechanical ventilation and prone position. Indication for PP was placed in patients with moderate to severe ARDS and PaO_2/FiO_2 ratio < 150 mmHg and $FiO_2 > 0.6$. Every prone position cycle was planned for a minimum of 16 hours according to Guerin et al. (Guérin et al., 2013; Foti et al., 2020; Nasa et al., 2021). However, some patients were maintained prone for more than 24 hours to reduce nursing workload (Rezoagli et al., 2021). We classified as “Standard pronation” every PP cycle lasting ≤ 24 hours, and as “extended pronation” every PP cycle > 24 hours. We registered all complications related to PP applications (i.e. displacement of indwelling catheters, facial oedema, pressure sores, vomiting, unplanned extubation, airway obstruction due to bronchial secretion retention with need of unplanned bronchoscopy and haemodynamic instability) (Lucchini et al., 2020a). The National Pressure Ulcer Advisory Panel (NPUAP) score was used to classify the pressure sores (Edsberg et al., 2016). The Braden Score was used for predicting pressure ulcer risk. We also calculated the PaO_2/FiO_2 ratio, at the following time-points: before pronation (PRE-supine step), one hour after pronation (1 h-PP step), at the end of pronation (END-PP step) and one hour after supination (POST-supine step).

Prone position ICU protocol

Every prone positioning manoeuvre was performed according to our ICU protocol and policy, which is described in detail in [Supplementary material S1](#) (Bein et al., 2015; Bruni et al., 2020; Lucchini et al., 2017; Lucchini et al., 2020a). Prone position protocol includes the need to



Fig. 1. Patient in prone position with transversal rolls.

protect bony prominences with prophylactic dressing prior to prone positioning, lubricate the eyes and tape them closed, ensure that the endotracheal tube be secured with tapes (National Pressure Injury Advisory Panel, 2019). Our ICU policy, from January 2020 avoided implementation of “swimming position”. Fig. 1 showed a patient in prone position. Supplementary material Fig. S2 showed the pillows used in the study period.

Follow-up visit

We followed up COVID-19 patients three months after ICU discharge. In order to detect neuromuscular injuries as long term complications of PP, we extracted Follow-Up reports on the assessment of muscle peripheral strength by the Medical Research Council (MRC) scale and hand-held dynamometry (Council MR, 1976; Hermans et al., 2012; Parry et al., 2015). The MRC Scale for muscle strength is a commonly used scale for assessing muscle strength from Grade 5 (normal) to Grade 0 (no visible contraction). This score was defined as the sum of MRC scores from six muscles in the upper and lower limbs on both sides, so that the score ranged from 60 (normal) to 0 (quadriplegic). Handgrip strength dynamometry has been proposed as a simple and easy diagnostic method for ICU acquired weakness and was performed on both upper limbs (Bragança et al., 2019; Van Aerde et al., 2020).

Ethical issue

Data were collected as part of the “STORM” study (Spallanzani Institute approval number 84/2020; NCT04424992).

Statistical analysis

We performed the D’Agostino-Pearson test to assess the normal distribution of variables. Variables with normal distribution were reported as mean and standard deviation (SD) and comparison between their means was performed using the Student’s *t* test. Variables without a normal distribution were reported as median and interquartile range (IQR) and comparison between two groups was performed using the Mann-Whitney *U* test. Categorical data are reported as frequencies (%) and their difference tested by Chi-Square’s or Fisher’s exact test as appropriate. One-way repeated measures analysis of variance (rmANOVA) were used to evaluate the differences at the different time points (PRE-supine step: before pronation, 1 h – PP step: one hour after pronation, END-PP Step: at the end of pronation, POST-supine step: one hour after resupination) of the PO₂/FiO₂ ratio values and respiratory parameters. A *p* value < 0.05 was considered statistically significant. All data were analysed using the Statistical Social Sciences software, version 22.0, for Macintosh (SPSS Inc., Chicago, IL, USA).

Results

Prone position results during ICU stay

From February 20, 2020 to January 31, 2021, 108 patients were admitted to our ICU with a confirmed diagnosis of COVID-19. A total of 96 patients were included in the study. The median age was 59 years (IQR: 53–66), 22 (23%) were female and the median ICU length of stay was 15 days (7–25). At ICU admission patients presented a median Braden score of 10 (10–11) with a median Body Mass Index of 28 (26–33). Comorbidities included hypertension (52% - *n* = 19), type 2 diabetes mellitus (23%, *n* = 17%) and arteriopathies (10% - *n* = 7). Median pO₂/FiO₂ before the first PP cycle was 116 (82–148), while the median time in hours, from ICU admission to first PP manoeuvre was equal to 8 (4–45) hours. Median time for each PP performed cycle was equal to 18 (16–32) hours. PP was applied for one cycle in 30 (31%) patients, for two cycles in 21 (22%), for three cycles in 16 (17%), while patients who received three or more PP cycles were 29 (30%). In 37

(38%) patients at least one cycle of extended pronation was implemented. The overall time for patients, spent in PP was equal to 48 (31–101) hours. In 13 (13%) subjects PP was adopted while the patient was connected to veno-venous Extracorporeal Membrane Oxygenation. 79 (82%) patients survived and were discharged from ICU.

Pronation-related adverse events

Patients with at least one pressure sore due to PP were 38 (40%). Patients with pressure sores showed a statistically significant difference in ICU length of stay, mechanical ventilation days, numbers of PP cycles, total time spent in PP and the use of extended prone position, compared to patients without pressure ulcers. Chin and cheekbones were the most affected sites, where pressure sores were present in 18% (*n* = 17) and 10% (*n* = 10%) of patients. Regarding the pressure ulcer severity, the most frequent stage of NPUAP score was stage II in 93 out of 105 pressure sores (88%), followed by stage I in 9 pressure sores (8.5%) and stage III in 3 sites (3.5%). No pressure sores with stage IV occurred. The characteristics of the sample, and the difference between patients without and with pressure sore development are presented in Table 1. Incidence of medical device-related pressure injuries in mucosal tissues, because of prone positioning, such as ulcers of the lips were present in 7 patients (7%) caused by endotracheal tubes, but we did not record pressure sores in ala nasi and nostrils due to nasogastric tubes.

Extended PP was implemented in 37 (39%) of enrolled patients. Patients undergoing extended pronation had a median of 34 (30–41) hours versus 16 (15–18) (*p* < 0.0001) of patient receiving standard pronation, a higher total time spent in PP [85(43–136) versus 33 (18–64) hours – *p* < 0.0001] during ICU stay, a higher number of proning cycles [3 (2–4) versus 2 (1–4) – *p* = 0.017]. The prevalence of patients with pressure sore was 51% (*n* = 19) for patient with extended pronation and 32% (*n* = 19) in patient with standard pronation (*p* = 0.032). Difference between patients undergoing standard versus extended pronation are presented in Table 2.

The total pronation manoeuvres investigated were 302. Extended pronation was most commonly used during the second COVID-19 wave. The overall complications related to PP manoeuvre were haemodynamic instability in 29 (10%) manoeuvres, prolonged arterial desaturation involved 57 (19%) of investigated cycles and bronchial secretions retention, with need of unplanned bronchoscopy, occurred in 33 (11%) manoeuvres. No accidental removal of vascular access devices occurred during the study period, while we observed 2 (1%) nasogastric tube and one (0.5%) endotracheal tube displacement, with no necessity to device repositioning (no completely extubation was occurred). No statistically significant differences in these severe complications were detected between standard and extended pronation cycles. Details about all investigated prone position cycles and related complications are reported in Table 3. PO₂/FiO₂ ratio improved during prone position and after resupination compared to baseline (i.e. before prone position) in overall cycles and in extended versus standard pronation groups, as showed in Fig. 2. Table S3 (see Additional file 3) summarizes all mechanical ventilation and oxygenation data.

Three months follow up visit

Follow Up visit, three months after ICU discharge, by anaesthesiologist and ICU nurse was possible in 58 patients. In the remaining 36, the main reasons for the missed visit were: distance from the hospital (patient centralized during COVID and referred to the local hospital) and refusal to visit. No patient reported problems with pressure sores outcomes at the three-month follow-up visit. All patients were able to have all 12 muscle groups examined by MRC examination. Median overall MRC score at Follow Up visit was 60 (59–60). We did not observe significantly difference in MRC score in patients undergoing standard prone position compared to patients with extended pronation [60 (59–60)] versus 60 (58–60) -*p* = 0.395]. For the following tested

Table 1
Descriptive characteristics of enrolled patients. with and without pressure sores.

	All patients n=96 (100%)	Patients without Pressure Sores related to PP n=58 (60%)	Patients with Pressure Sores related to PP n=38 (40%)	p.value
Sex Female n= (%)	22 (23%)	15 (26%)	7 (18%)	0.396
Age (years) - Median (IQR)	59 (53-67)	60 (54-68)	59 (51-66)	0.463
Length of ICU stay (days)	15 (7-25)	15 (6-21)	19.5 (10-28)	0.038
Weight - cm - Median (IQR)	80 (75-95)	80 (75-95)	82.5 (80-95)	0.762
BMI - Median (IQR)	28 (26-33)	28 (26-33)	28 (26-33)	0.784
<24.9 - normal weight	20 (21%)	12 (21%)	8 (21%)	0.961
24.9 -29.9 - overweight	39 (41%)	24 (42%)	15 (40%)	
>30.0 obesity	36 (38%)	21 (37%)	15 (40%)	
Diabetes - yes	17 (23%)	8 (18%)	9 (30%)	0.216
Hypertension - yes	39 (52%)	26 (56%)	13 (43%)	0.22
Arteriopathies- yes	7 (10%)	4 (10%)	3 (12%)	0.79
Alive at ICU discharge - n=(%)	79 (82%)	51 (88%)	28 (74%)	0.074
Median Braden (ICU admission day)	10 (10-11)	10 (10-10)	10 (9-11)	0.899
ARDS classification				
mild	4 (4%)	3 (5%)	1 (3%)	
moderate	53 (55%)	35 (60%)	18 (47%)	0.299
severe	39 (41%)	20 (35%)	19 (50%)	
median PO ₂ /FiO ₂ ratio (first PP manoeuvre)	116 (82-148)	121 (86-150)	98 (69-145)	0.095
Mechanical ventilation days	13 (7-20)	12 (5-18)	15 (10-23)	0.033
Veno-Venous ECMO - yes	13 (13%)	5 (9%)	8 (21%)	0.082
Tracheostomy -yes	21 (22%)	14 (24%)	7 (18%)	0.508
Norepinephrine infusion during PP cycles - yes	57 (60%)	34 (60%)	23 (61%)	0.205
Dopamine infusion during PP cycles	26 (27%)	19 (33%)	7 (18%)	0.631
Median Time from admission to first PP-hours	8 (4-45)	7.5 (4-36)	12 (5-48)	0.324
Median Time for each PP cycle - hours	18 (16-32)	17 (15-32)	21(16-32)	0.053
Median Prone Position cycle per patient	2 (1- 4)	2 (1-4)	3 (2-4)	0.017
1 cycle	30 (31%)	26 (45%)	4 (10%)	0.336
2 cycles	21 (22%)	10 (17%)	11 (29%)	
3 cycles	16 (17%)	6 (10%)	10 (26%)	
> 3 cycles	29 (30%)	16 (28%)	13 (35%)	
Total time in Prone Position - hours	48 (31-101)	38 (20-84)	65 (34-126)	0.005
Extended Prone Position - yes	37 (38%)	18 (31%)	19 (50%)	0.062
PP cycle - Median Highest Time - hours	41 (29-43)	41 (37-42)	41 (40-44)	0.327
Pressure sores at ICU Admission - yes	3 (3%)	0 (0%)	3 (8%)	0.03
Number of body areas with pressure sores at ICU admission	2 (2-2)	0	2 (2-2)	0.074
Pressure sores at ICU discharge - yes	56 (59%)	18 (32%)	38 (100%)	<0.0001
Number of body areas with pressure sores at ICU discharge	2 (1-3)	1 (1-2)	2 (1-3)	0.0721
Pressure sores related to Prone Position				
Median number of body areas with Pressure sores related to PP	1 (1-2)	—	1 (1-2)	—
Forehead	4 (4%)	—	4 (10%)	
Forehead - median NPUAP grade	2 (2-2)	—	2 (2-2)	
Cheekbones	10 (10%)	—	10 (26%)	
Cheekbones - median NPUAP grade	2 (2-2)	—	2 (2-2)	
Chin	17 (18%)	—	17 (44%)	
Chin - median NPUAP grade	2 (2-2)	—	2 (2-2)	
Lips	7 (7%)	—	7 (18%)	
Lips - median NPUAP grade	2 (2-2)	—	2 (2-2)	
Thorax	9 (9%)	—	9 (24%)	1
Thorax - Median NPUAP grade	2 (2-2)	—	2 (1-2)	
Abdomen	1 (1%)	—	1 (3%)	
Abdomen - median NPUAP grade	2	—	2	
Iliac crests	3 (3%)	—	3 (8%)	
Iliac crests - median NPUAP grade	2 (2-2)	—	2 (2-2)	
Tibial plateau	3 (3%)	—	3 (8%)	
Tibial plateau - median NPUAP grade	2 (2-2)	—	2 (2-2)	
Knees	9 (9%)	—	9 (24%)	1
Knees - median NPUAP grade	2 (2-2)	—	2 (2-2)	
Other sites with Pressure sores	4 (4%)	—	4 (11%)	
Other sites - median NPUAP grade	2 (2-2)	—	2 (2-2)	
Pressure sores not related to Prone Position				
Occiput	1 (1%)	—	1	0.214
Occiput - NPUAP grade	2	—	2	
Shoulder blades	14 (15%)	11 (19%)	3 (8%)	0.133
Shoulder blades - median NPUAP grade	2 (2-2)	2 (2-2)	2 (2-2)	
Sacrum	23 (24%)	9 (16%)	14 (37%)	0.017

(continued on next page)

Table 1 (continued)

	All patients n=96 (100%)	Patients without Pressure Sores related to PP n=58 (60%)	Patients with Pressure Sores related to PP n=38 (40%)	p.value
Sacrum - median NPUAP grade	2 (2-2)	2 (2-3)	2 (2-2)	0.247
Buttocks	2 (2%)	2 (3%)	—	
Buttocks - median NPUAP grade	2 (1-2)	2 (1-2)	—	

PP: Prone Position. BMI : Body Mass Index. ARDS : adult respiratory distress syndrome. ECMO : extracorporeal membrane oxygenation. NPUAP : National Pressure Ulcer Advisory Panel.

districts: shoulder adductors, elbow flexors and wrist extensor, the MRC score was always ≥ 3 in all patients. Foot dorsiflexors test was equal to zero in one patient (left side) and in two patients was equal to one (right side). We observed one patient with grade zero in MRC score in left foot dorsiflexors test. Hip flexors test was grade two in one patient (right side). Statistically significance was reported in MRC grade distribution, between patients with and without extended pronation only for the right Elbow flexors test ($p = 0.028$). Table 4 summarize results from MRC all 12 muscle groups examined. After physical examination, no patient reported sensory loss or presence of neuropathic pain for upper limbs. The median overall maximum handgrip dynamometry was 33.0 (24–37) kg-force. Finally, we did not observe any difference between standard and extended pronation groups in handgrip dynamometry results [33 (25.0–37) vs. 29 (20–39) kg-force - $p = 0.679$].

Discussion

Prone position for ventilated patients with COVID-19 ARDS was strongly suggested by experts, for a duration of 16–24 hours per session, similar to the indication in non-COVID-19-related ARDS (Nasa et al., 2021). In our study the rate of pressure sores was similar to the results of the studies published before the Covid-era (Lucchini et al., 2018a, 2020a; Sud et al., 2014), but lower if we consider recent studies on PP and COVID-19 patients (Binda et al., 2021; Douglas et al., 2021; Ibarra et al., 2020). Binda and colleagues, in a retrospective study in a single ICU in Italy, involved 63 COVID-19 patients with a total of 219 proning cycles, report an incidence of prone-related pressure ulcers in about 30% of patients (Binda et al., 2021). Ibarra and colleagues, in Spain, published a case-series of patients on invasive mechanical ventilation and PP therapy with 77% of the patients presented pressure sores due to PP (Ibarra et al., 2020). The frequency of pressure sores in the face area, found in our study was lower than those reported in two systematic reviews (Abroug et al., 2008; Sud et al., 2014) and in a narrative review (González-Seguel et al., 2021) in which pressure ulcers occurred in 34%, 43% and 19% of patients, respectively. Important to underline that we didn't detected grade III in the reported pressure sores developed on face area. Low-grade facial pressure sores have less serious consequences, and none of our patients needed special care or treatment. All the pressure sores were managed with dressings, achieving wound healing by secondary intention in all the survivors (Perrillat et al., 2020; Shearer et al., 2021). Once their condition improved and prone positioning was no longer performed, the skin fully recovered in all patients. No patient reported any problems with pressure sore outcomes at the follow-up visit, after ICU discharge.

Comparing the incidence of pressure sores with two studies published by our group (Lucchini et al 2018a, 2020a) in the last 5 years, however, we must note that the global incidence has slightly increased. In our previously study on PP complications, ICU team was composed only by ICU nurses with long experience in nursing and management of ARDS patients. During the COVID-era, human and material health care resources had to be adapted to an unpredictable new “war” scenario in a very short period of time (Bambi et al., 2020; Lucchini et al., 2020b, 2020c). In a few days, the growing demand for COVID-19 patients ICU beds in our region, forced us, during the first wave (February-April 20) to realise 11 new beds in the operating theatre in addition to our 10 bed

ECMO unit. The original ICU staff were divided between the new and the old ICU beds. 33 nurses from the operating theatre were also recruited as new ICU staff. In this context, it is understandable that the complications of this procedure could increase. In order to guarantee a safe PP procedure, at least three experienced operators (critical care nurses and/or Intensivist physicians) were present during each prone position manoeuvre. During second wave only 10 nurses from the operating theatre were recruited. Even for this shortage of nurses, the use of extended prone position became frequent in our ICU, during the second pandemic wave (Rezoagli et al., 2021). In addition to the reduced nurses' experience, the nurse-to-patient ratio changed between the first and second COVID-19 waves. In the first wave there was always, a nurse-to patient ratio equal to 1: 2. In the second wave, the nurse-to-patient ratio of 1:2 was always guaranteed only for ECMO patients. In the other patients, the nurse-to-patient ratio was 1:2.5.

Patients undergoing “extended prone position” in our study, trended to a higher number of proning cycles [3 (2–4) versus 2 (1–4) - $p = 0.017$] and to a longer time spent in prone position during their ICU stay compared to standard PP group [33 (18–64) versus 85 (43–136), $p = 0.0001$]. Oxygenation improvement in our sample seemed to be higher during “extended pronation” than during standard pronation, and after resupination compared to baseline. The risk of developing a higher incidence of pressure sores in the prolonged extended pronation is an issue that should be cautiously monitored in present and future studies (National Pressure Injury Advisory Panel, 2019). In our sample we observed an increased rate of pressure sores (51% extended PP vs. 32% standard PP - $p = 0.0001$), but we did not observe an increase of the others PP complications.

In previously published meta-analyses and narrative reviews (Abroug et al., 2008; González-Seguel et al., 2021; Sud et al., 2014;) the total percentage of airway related complications described for prone position were present in a range between 20 and 40% of investigated cycles. We did not observe any unplanned extubation. In all patients, our ICU policy provided that the artificial airway was secured with a 5 cm canvas tape placed upon a thin hydrocolloid (Lucchini et al., 2018b). Before every pronation, the tape was replaced in order to guarantee better stability (National Pressure Injury Advisory Panel, 2019). Moreover, before pronation, the tube was displaced on the side of the mouth not leaning on the pillow (for example when the head was rotated on the right side, the tube was fixed on the right, and vice versa). Our protocol included the use of thin hydrocolloid as protective skin coverings, under devices and over bony prominences (forehead, cheeks, chin, iliac crest, ribs and patella and tibial plateau) (Lucchini et al., 2020a; Peko et al., 2020). The regular use of hydrocolloids, may be a beneficial factor in decreasing skin breakdown in PP (National Pressure Injury Advisory Panel, 2019). The current evidence suggests that positioning devices to offload pressure points on the face and body are a useful addition within an overall PU prevention strategy (Binda et al., 2021; Peko et al., 2020; Rodríguez-Huerta et al., 2021).

Finally, no long term adverse events due to PP have been observed during the follow-up visit. Nerve injuries are uncommon following prone positioning (Goettler et al., 2002), but brachial plexus injuries have been recently reported (Brugliera et al., 2021; Douglas et al., 2021; Miller et al., 2021). Brachial plexus injuries could occur in PP patients when shoulders are positioned in abduction with external rotation and

Table 2
Descriptive characteristics of patients undergone standard versus extended pronation.

	Patients without extended prone position n=59 (61%)	Patients with extended prone position n=37 (39%)	p. value
Sex Female - n= (%)	15 (26%)	7 (20%)	0.461
Age (years) - Median (IQR)	60.0 (53.0-68.0)	58.0 (55.0-66.0)	0.851
Length of ICU stay (days)	15.0 (7.0-20.0)	20.0 (11.0-28.0)	0.039
Weight cm - Median (IQR)	85.0 (75.0-96.0)	80.0 (80.0-90.0)	0.256
BMI - Median (IQR)	27.7 (26-32.7)	27.75 (25.7 - 32.9)	0.161
Alive, n= (%)	48 (81%)	31 (84%)	0.762
Median PO ₂ /FiO ₂ ratio (first Prone Position manoeuvre)	120 (86-150)	111 (71 -145)	0.328
Mechanical ventilation days	13 (6-18)	15 (10-24)	0.096
Veno-Venous ECMO - yes	6 (10%)	7 (19%)	0.223
Tracheostomy - yes	12 (20%)	9 (24%)	0.646
Median Time from admission to first prone position - hours	8 (4-60)	6 (4-41)	0.281
Median Time for each prone position cycle - hours	16 (15–18)	34.0 (30-41)	0.0001
Median Prone Position cycle per patient	2 (1-4)	3 (2-4)	0.017
Total time in Prone Position - hours	33 (18-64)	85 (43-136)	0.0001
Highest Cycle Time in extended prone position- hours		41 (39-43)	0.327
Median Braden score (ICU admission day)	10 (9 -10)	10 (10 -11)	
Pressure sores due to prone position	19 (32%)	19 (51%)	0.032
Number of body areas with Pressure sores related to PP	1 (1-1)	2 (1-3)	0.042
Forehead	1 (2%)	3 (8%)	0.126
Forehead - median NPUAP grade	2 (2-2)	2 (2-2)	1.000
Cheekbones	6 (10%)	4 (10%)	0.920
Cheekbones - median NPUAP grade	2 (2-2)	2 (2-2)	0.662
Chin	8 (14%) (2-2)	9 (24%) (2 (2-2)	0.179 0.481

Table 2 (continued)

	Patients without extended prone position n=59 (61%)	Patients with extended prone position n=37 (39%)	p. value
<i>Chin - median NPUAP grade</i>			
Lips	3 (5%)	4 (11%)	0.294
Lips - median NPUAP grade	2 (2-2)	2 (2-3)	0.629
Thorax	3 (5%)	6 (16%)	0.069
Thorax - Median NPUAP grade	2 (1-2)	2 (2-2)	0.517
Abdomen	0 (0%)	1 (3%)	0.204
Abdomen - median NPUAP grade	—	2	—
Iliac crests	2 (3%)	1 (3%)	0.851
Iliac crests - median NPUAP grade	2 (2-2)	2 (2-2)	1.000
Tibial plateau	0 (0%)	3 (9%)	0.026
Tibial plateau - median NPUAP grade	—	2 (2-2)	—
Knees	1 (2%)	6 (16%)	0.069
Knees - median NPUAP grade	1 (1-2)	2 (2-2)	0.117
Other sites with Pressure sores	1 (1%)	3 (8%)	0.126
Other sites - median NPUAP grade	2 (2-2)	2 (2-2)	0.988
Pressure sores not related to Prone Position			
Occiput	0 (0%)	1 (3%)	0.204
Occiput - NPUAP grade	—	2	—
Shoulder blades	11 (19%)	3 (8%)	0.155
Shoulder blades - median NPUAP grade	2 (2-2)	2 (2-2)	0.458
Sacrum	16 (27%)	7 (19%)	0.360
Sacrum - median NPUAP grade	2 (2-3)	2 (2-2)	0.671
Buttocks	1 (2%)	1 (3%)	0.737
Buttocks - median NPUAP grade	2	1	0.987

ECMO: extracorporeal membrane oxygenation, NPUAP : National Pressure Ulcer Advisory Panel.

posteriorly displaced and this position causes compression and stretching of the brachial plexus, usually affecting the upper nerve roots (Bozentka, 1998). Recently Miller et al. (2021), in a study involving 256 COVID-19 patients with PP, reported that in 12 (5%) patients the ulnar nerve was injured, and in 11 patients, an injury was presents at the cords of the brachial plexus. 30 (10%) patients reported neuropathic pain, and all patients presented with motor weakness. Brugliera et al, (2021) reported 7 (5%) cases of brachial plexopathy out of 135 patients who had undergone in PP, in an Italian ICU. Douglas et al. (2021) reported brachial plexus palsies in five (8.2%) of 61 patients treated with extended pronation. In all these studies, the ICU teams used a standard protocol for PP, with implementation of the “swimming position”, always combined with alternating arm reposition, performed between 2 or 4 h. Generally, authors that reported the “swimming position” adoption, are unable to extract exactly data on the frequency of arm cycling while patients were proned. The “swimming position” involves raising one arm on the same side to which the head is facing while placing the other arm by the patient’s side. The shoulder should be abducted to 80 degrees and the elbow flexed 90 degrees on the raised arm. This is, however, a

Table 3
Description of prone positioning cycles and complications

		All cycles n=302 (100%)	Standard pronation n=227 (75%)	Extended pronation n=75 (25%)	p.Value
COVID-19 Wave	first	144 (48%)	143 (63%)	1 (2%)	<0.0001
	second	158 (52%)	84 (37%)	74 (98%)	
Veno-Venous ECMO (yes)		36 (16%)	30 (16%)	6 (14%)	0.734
Norepinefrine infusion – (yes)		120 (48%)	91 (51%)	29 (39%)	0.077
Norepinephrine dosage (mcg/Kg/min)		0.06 (0.04-0.07)	0.06 (0.04-0.08)	0.04 (0.03-0.07)	0.007
Dopamine infusion – (yes)		53 (23%)	42 (26%)	11 (16%)	0.088
Dopamine dosage (mcg/Kg/min)		4.1 (2.35 - 5.19)	4.1 (2.3-5.26)	3.07 (2.42-5.00)	0.080
Medical device displacement	Endotracheal tube n= (%)	1 (0.5%)	1 (0.5%)	0 (0%)	0.565
	Nasogastric Tube n= (%)	2 (1%)	2 (1%)	0 (0%)	0.455
	Vascular catheters n=(%)	0 (0%)	0 (0%)	0 (0%)	—
Hemodynamic instability - n=(%)		29 (10%)	22 (10%)	7 (9%)	0.927
Prolonged Arterial Desaturation - n=(%)		57 (19%)	45 (20%)	12 (16%)	0.463
Bronchial secretions retention - n=(%)		33 (11%)	26 (12%)	7 (9%)	0.610
Vomit – n=(%)		0 (100%)	0 (0%)	0 (0%)	—

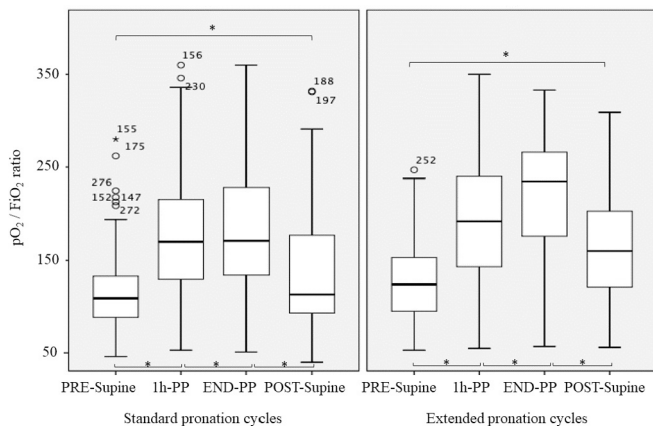


Fig. 2. pO₂/FiO₂ ratio in the investigated time steps: before pronation (PRE-supine step), one hour after pronation (1h-PP step), at the end of pronation (END-PP step) and one hour after supination (POST-supine step).

potential stretch position for the ulnar nerve at the elbow (Bozentka, 1998). Before the study period, the prone position protocol in our unit involved the use of the “swimming position”. In this position, our protocol before December 2019, required that only the left arm was raised (Lucchini et al., 2018a, 2020a). In an internal audit (December 2019) we reported two cases of brachial plexus injury detected at the scheduled follow-up visit. For this reason, in order to investigate the possible rule of “swimming position” in those adverse events developments, we decided, starting from January 2020, avoid it during PP. Shortly after

Table 4
MRC Test results in patients undergoing three months follow-up visit.

Muscle	Side	MRC Scale					
		Grade 0	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Shoulder adductors	Left	0 (0%)	0 (0%)	0 (0%)	1 (2%)	12 (21%)	45 (78%)
	Right	0 (0%)	0 (0%)	0 (0%)	2 (3%)	8 (14%)	48 (83%)
Elbow flexors	Left	0 (0%)	0 (0%)	0 (0%)	0 (0%)	8 (14%)	50 (86%)
	Right	0 (0%)	0 (0%)	0 (0%)	1 (2%)	6 (10%)	51 (88%)
Wrist extensor	Left	0 (0%)	0 (0%)	0 (0%)	0 (0%)	7 (12%)	51 (88%)
	Right	0 (0%)	0 (0%)	0 (0%)	1 (2%)	6 (10%)	51 (88%)
Hip flexors	Left	0 (0%)	0 (0%)	0 (0%)	0 (0%)	9 (16%)	49 (84%)
	Right	0 (0%)	0 (0%)	1 (2%)	0 (0%)	8 (14%)	49 (84%)
Knee extensors	Left	0 (0%)	0 (0%)	0 (0%)	0 (0%)	9 (16%)	49 (84%)
	Right	0 (0%)	0 (0%)	0 (0%)	0 (0%)	8 (14%)	50 (86%)
Foot dorsiflexors	Left	1 (2%)	0 (0%)	0 (0%)	1 (2%)	9 (16%)	47 (81%)
	Right	0 (0%)	2 (3%)	0 (0%)	1 (2%)	8 (14%)	47 (81%)

Grade 5: Normal, Grade 4: Movement against gravity and resistance, Grade 3: Movement against gravity over (almost) the full range, Grade 2: Movement of the limb but not against gravity, Grade 1: Visible contraction without movement of the limb (not existent for hip flexion), Grade 0: No visible contraction.

this decision, the COVID-era began in Italy and in our ICU (Giani et al., 2020; Lucchini et al., 2020b). All enrolled patients in our study were pronated by keeping the limbs along the body and avoiding programmed repositioning. The upper limbs were positioned trying to avoid shoulders abduction and external rotation or posteriorly displacing and to avoid elbow flexion positions. For the lower limbs, we maintained a slight flexion of the knees, trying to avoid the extra rotation of the feet.

MRC scale carried out during the three-month visit after discharge from the ICU showed the absence of complications related to the upper limbs in the investigated patients. Our results are encouraging, albeit not definitive. Future multicentric studies on the role of “swimming position” and frequency of arm cycling, on peripheral nerve injuries development could provide increased insights and help to design new guideline for prone position. The consequences of upper limb peripheral nerve injuries are potentially life changing and devastating for ICU survivors.

Limitations

Several limitations should be considered in the interpretation and generalization of these findings. First, one limitation may be considered the single-centre, retrospective design. Second, data on complications were recorded in a pandemic period characterized by a reduction in the usual nurse-patient ratio, and an increased workload with a potential for underestimation of pressure sores detection. However, this is the first study which primarily investigated and reported the most expected complications from prolonged pronation cycles. Third, follow-up visit was possible only in 58 patients and we cannot exclude the presence of complications in patients missed to follow-up.

Conclusions

This retrospective study has shown that, even during a pandemic surge, coupled with limited resources, prone position could be applied with an acceptable increase in complications rate. Extended prone positioning is feasible although with a slight increase in the incidence of low severity pressure sores respect to standard prone position and no major serious complications have been reported. Extended prone positioning could be currently suggested in a scenario of a pandemic outbreak. Prone position protocol should include the need to protect bony prominences with prophylactic dressing, lubricate the eyes and tape them closed and endotracheal tube securing only with tapes, repositioning to offload pressure points on the face and the body and use of positioning devices. Prone position avoiding “swimmer position” is safe and could help to reduce long term complications on the upper limbs. Preventive measures of potential complications of prone positioning, including airway obstruction, pressure injuries, and brachial plexopathies, should be implemented in intensive care settings whenever possible, even during a pandemic period. Monitoring of prone position long term complications should be part of the follow-up programs for ICU survivors. Future research in prevention of short and long term complication should address at least the following four issues: 1) impact of “swimmer position” on upper limb peripheral nerve injuries on a large population, 2) role of different positioning devices (viscoelastic versus polystyrene balls or polyurethane, 3) identification of the best prophylactic dressing (hydrocolloids, transparent film, and silicone) to decrease facial skin breakdown, 4) impact on gas exchange and mortality of extended pronation cycles.

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Author contributions

AL, VR, MV, RR, RF and GF conception and design of the study, manuscript writing and final approval. NB, MV, GC, YM, BZ, DC, GV : data collection. AL, MV, NB GC, YM.: statistical analysis. All authors have read and approved the final manuscript.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.iccn.2021.103158>.

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