Prone positioning improves oxygenation in adult burn patients with severe acute respiratory distress syndrome

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BACKGROUND: Prone positioning (PP) improves oxygenation and may provide a benefit in patients with acute respiratory distress syndrome (ARDS). This approach adds significant challenges to patients in intensive care by limiting access to the endotracheal or tracheostomy tube and vascular access. PP also significantly complicates burn care by making skin protection and wound care more difficult. We hypothesize that PP improves oxygenation and can be performed safely in burn patients with ARDS.

METHODS: PP was implemented in a burn intensive care unit for 18 patients with severe refractory ARDS. The characteristics of these patients were retrospectively reviewed to evaluate the impact of PP on Pao_2:Fio_2 ratio (PFR) during the first 48 hours of therapy. Each patient was considered his or her own control before initiation of PP, and trends in PFR were evaluated with one-way analysis of variance. Secondary measures of complications and mortality were also evaluated.

RESULTS: Mean PFR before PP was 87 (±38) with a mean sequential organ failure assessment score of 11 (±4). PFR improved during 48 hours in 12 of 14 survivors ($p < 0.05$). Mean PFR was 133 (±77) immediately after PP, 165 (±118) at 6 hours, 170 (±115) at 12 hours, 214 (±126) at 24 hours, 236 (±137) at 36 hours, and 210 (±97) at 48 hours. At each measured time interval except the last, PFR significantly improved. There were no unintended extubations. Facial pressure ulcers developed in four patients (22%). Overall, 14 survived 48 hours (78%), 12 survived 28 days (67%), and six survived to hospital discharge (33%).

CONCLUSIONS: PP improves oxygenation in burn patients with severe ARDS and was safely implemented in a burn intensive care unit. Mortality in this population remains high, warranting investigation into additional complementary rescue therapies. (*J Trauma Acute Care Surg*. 2012;72: 1634 1639. Copyright © 2012 by Lippincott Williams & Wilkins)

LEVEL OF EVIDENCE: Therapeutic study, level IV.

KEY WORDS: Burn; prone positioning; ARDS; inhalation injury; hypoxemia.

Of burn patients who require mechanical ventilation, between 40% and 54% progress to meet formal criteria for acute respiratory distress syndrome (ARDS), and these patients have a mortality of between 14% and 42%.[1,2] Severe burns result in massive fluid shifts early with a predisposition to downstream infectious complications resulting in this relatively high prevalence of ARDS. Additionally, severe inhalation injury (II), which may add further insult both in the small airways and the lung parenchyma, significantly contributes to morbidity and independently increases mortality relative to burn patients without II.[3] Consequently, interventions designed to improve oxygenation are of great interest in the burn population, many of whom present with II, who subsequently develop ARDS. In the most severe cases, meeting adequate ventilation and oxygenation goals is particularly challenging for the burn patient who develops ARDS. Hypercatabolism combined with II resulting in reactive airways, small-airway injury, obstruction, and collapse, pulmonary edema from resuscitative fluids, extrapulmonary restriction due to eschar and edema (and scar formation later in the hospital course) are just a few of the challenges that make it difficult for burn providers to extrapolate and apply strict lung-protective ventilation (LPV) strategies.[4] As such, alternative or adjunctive strategies to include high-frequency percussive ventilation (HFPV), airway pressure release ventilation, high-frequency oscillatory ventilation, inhaled nitric oxide,[5–9] a short course of chemical paralysis,[10] and kinetic therapy to include prone positioning (PP)[11] are frequently used.

Although the salient effects of PP on oxygenation have been well documented in patients with ARDS,[12] this therapy has not been well documented in the burn patient population. To our knowledge, this report is the first to describe clinical implementation of PP in burn patients and the acute impact of this therapy on oxygenation. The purpose of our study was to evaluate oxygenation during PP as a rescue maneuver in burn patients with severe ARDS; secondary outcomes were complications encountered and survival. We hypothesize that PP

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This study was conducted under a protocol reviewed and approved by the US Army Medical Research and Materiel Command Institutional Review Board, and in accordance with the approved protocol.

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results in improved oxygenation in burn patients with ARDS. The logistical challenges of this therapy are also discussed along with the complications that we observed as a result of this approach.

METHODS

Clinical Setting

The US Army Institute of Surgical Research Burn Intensive Care Unit (ICU) is a 16-bed unit within a tertiary academic military teaching hospital and Level I trauma center. It serves active-duty military personnel; retired military; family members of active-duty members; and civilians with burns, severe soft-tissue injuries, II, and exfoliating skin conditions.

Patients who require intubation for airway protection or respiratory failure are managed by a multidisciplinary team consisting of burn surgeons, medical and surgical intensivists, experienced respiratory therapists, occupational therapists, physical therapists, dieticians, and experienced critical care burn nurses. A variety of ventilator modalities are used (i.e., HFPV, airway pressure release ventilation, or LPV); the type of ventilator is specified by the burn attending or intensivist. Rescue therapies are applied at the discretion of the medical and surgical intensivists in patients with refractory hypoxemia.[5–7]

Study Design and Participants

Since November 2004, PP was used as a rescue strategy in patients with refractory ARDS who did not respond to optimal ventilator support. II was diagnosed on admission by fiberoptic bronchoscopy to evaluate the bronchial mucosa. Patients were considered candidates for PP as a salvage maneuver if they met ARDS criteria, were unable to maintain oxygenation, and at the discretion of the attending burn surgeon or intensivist. In general, patients were considered potential candidates for PP if their partial pressure of oxygen (Pao_2) to fraction of inspired oxygen (Fio_2) ratio (PFR) approached less than 150 regardless of ventilator mode or setting. There was not an established protocol for implementation of PP or a set standard rotation back to the supine position. Initially, the prone position was maintained until oxygenation and ventilation allowed ventilator settings to be weaned. If and when the patient demonstrated improvement allowing a decrease in ventilatory settings (typically within 24 hours), the attending surgeon or intensivist determined the suitability of a scheduled rotation on a case-by-case basis. Rotations were subsequently performed at a minimum of once in every 12 hours for wound care or physical examination. All patients were in the prone position for a total of at least 16 hours a day as long as the therapy was prescribed by the attending. A specialty bed (RotoPone, KCI, San Antonio, TX) was used when available in a timely fashion. When the specialty bed was not available, the patient was placed in the prone position on a standard ICU bed. All proning procedures were performed under the direct supervision of an intensivist with prior PP experience. Wound care was performed in an opportunistic fashion depending on the position of the patient. Patient demographic and treatment data were entered into an electronic medical record including arterial blood gas values, ventilator settings, duration of PP, and concurrent critical care therapies. Local institutional review board approval was obtained to retrospectively review all patients managed on the PP through February 2010. Demographic data including age, gender, percentage total body surface area burned (%TBSA), presence of II, concurrent critical care therapies, and rescue interventions during the patients' course of respiratory failure were extracted from the electronic medical record. Specifics of the PP therapy were also recorded including time from burn injury, intubation, and diagnosis of ARDS; days in the prone position; and use of a specialty bed for facilitating PP.

The effects of PP on PFR were also recorded. These values were calculated from arterial blood gases obtained immediately before PP initiation; immediately after PP initiation; and at 6, 12, 24, 36, and 48 hours after PP initiation. Complications related to PP and to the patient's ICU course were identified; and survival at 48 hours, 28 days, to ICU discharge, and to hospital discharge was recorded.

Statistical Methods

A one-way analysis of variance with repeated measures was used to test change in PFR after initiation of PP compared with baseline and compared with the ratio from the preceding time interval with Microsoft Excel 2007 (Microsoft, Redmond, WA). Statistically significant differences were defined as $p < 0.05$. Difference between survivors and nonsurvivors was analyzed using t test in Statistical Package for the Social Sciences version 19 (IBM, New York City, NY).

RESULTS

From November 2004 to February 2010, 1,085 patients were admitted to the US Army Institute of Surgical Research Burn ICU. Of these, 618 (57%) required mechanical ventilation, and 57 (5%) developed ALI/ARDS. Overall, 18 (1.7%) patients with refractory hypoxemia were treated with PP as a rescue maneuver (Fig. 1). Characteristics of the study population are summarized in Table 1. The majority of patients were young with a preponderance of males. Sixteen of 18 patients were thermally burned with a mean TBSA of 37% and 12 (67%) patients were diagnosed with II. There was one patient with isolated II, endotracheally intubated on admission and treated with PP. The other patient was a 21-year-old man who suffered an extensive soft-tissue degloving injury to bilateral lower extremities involving 12% of his TBSA.

Ten patients had a tracheostomy before the time of PP initiation, and sepsis was common, requiring both vasopressor support and use of activated protein C in select cases. Continuous venovenous hemofiltration was initiated in nine (50%) patients for acute kidney injury and volume overload.

In addition to PP, rescue interventions were aggressively used, including HFPV and inhaled nitric oxide (Table 1). Bilateral chest tubes were placed empirically *in extremis* for 11 patients. Four of the patients had decompressive laparotomies performed at some point before being placed in the PP. Neuromuscular blockers were used in only six patients and continuous sedation in eight patients.

PP was initiated at 12 days after the initial injury (range: 6–30; interquartile range: 1–3) and 3 days after the development of ARDS (range: 0–5). Patients were treated with PP for

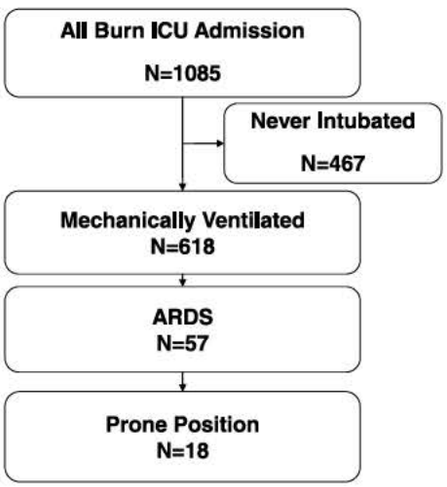

Figure 1. Subject selection flowchart of study population. ARDS, acute respiratory distress syndrome.

3 days (range: 1–6). Burn wound care continued through the PP facilitated by a specialized rotating bed. Of 18 patients treated with PP, 12 (67%) responded with a improved PFR of at least 50% by 48 hours (Fig. 2). Cumulative mean PFR of all 18 patients was 87 (±38) initially, 133 (±77) immediately after PP, 165 (±118) at 6 hours, 170 (±115) at 12 hours, 214 (±126) at 24 hours, 236 (±137) at 36 hours, and 210 (±97) at 48 hours ($p = 0.0005$). PFR progressively improved through the course of therapy relative to baseline and relative to the previous time point with the exception of the interval from 36 hours to 48 hours, where the improvement appeared to plateau (Table 2).

Eight total complications related to PP were noted in six patients. There were also no cases of airway dislodgement. Of the 11 patients with facial burns, two had both facial edema and pressure ulcers, one had only facial edema, and one had only facial pressure ulcers. There were two patients with complications without facial burns; one had a facial pressure ulcer and one had facial edema. In no patients did the facial edema result in significant patient morbidity. ICU complications including venous thromboembolic events and ventilator-associated pneumonia were identified in 6% (n = 1) and 67% (n = 12) of patients, respectively (Table 3).

After PP initiation, 14 (78%) patients survived more than 48 hours (Table 4). Of these, three died from multiple organ failure without recovery of their hypoxemia. Five recovered from their initial hypoxemia (with discontinuation of PP) and subsequently died to multiple organ failure later in their hospital course a median (range) of 17 (6–31) days after initiation of PP. All six who survived showed clinical improvement in their respiratory status and thus able to tolerate varying periods (up to 8 hours a day) in the supine position until PP was discontinued after up to 9 days later. Two patients were discharged from the hospital to home within 90 days. Five of the six patients who survived to discharge were discharged to home; the other patient was discharged to a rehabilitation facility. The patients who survived until discharge of the hospital had higher PFR before PP (114) versus those who did not survive (114 ± 25 vs. 73 ± 34, respectively, $p = 0.02$). They also had a lower sequential organ failure assessment index, survivors versus nonsurvivors (7 ± 1 vs. 12 ± 4, $p = 0.004$). There was no difference in % TBSA survivors versus nonsurvivors (31 ± 29 vs. 40 ± 25, $p = 0.48$); there was no difference with time to diagnosis of ARDS survivors versus nonsurvivors (26 ± 34 vs. 15 ± 25 days, $p = 0.47$). Characteristics of patients who survived to discharge are reported in Table 5.

TABLE 1. Characteristics of Study Population

Characteristics	Prone Positioning
Age, median ± SEM (range)	35 ± 16 (19 78)
Male	11 (61)
SOFA index, mean ± SEM (range)	11 ± 4 (6 20)
%TBSA, mean ± SEM (range)	37 ± 26 (0 83)
Inhalation injury	12 (67)
Tracheostomy	10 (56)
Decompressive laparotomy	4 (22)
Severe TBI	1 (6)
HFPV at time of PP	15 (83)
Critical care therapies	
Vasopressor support	12 (67)
Activated protein C	8 (44)
CRRT	9 (50)
Paralytics	6 (33)
Continuous sedation	8 (44)
Rescue interventions	
Bilateral tube thoracostomy	11 (61)
iNO	9 (50)
Prone positioning characteristics	
Days from injury to ARDS dx, mean ± SEM (range)	19 ± 28 (0 93)
Days from ARDS dx to PP initiation, mean ± SEM (range)	4 ± 6 (0 22)
Days from injury to PP initiation, mean ± SEM (range)	23 ± 29 (0 105)
Days of PP, mean ± SEM (range)	4 ± 3 (1 9)
Specialty rotating bed	13 (72)

CRRT, continuous renal replacement therapy; iNO, inhaled nitric oxide; SOFA, sequential organ failure assessment; TBI, traumatic brain injury.
Values are n (%) unless otherwise indicated.

DISCUSSION

To date, numerous randomized, controlled trials and meta-analyses have documented the benefits of PP on oxygenation for up to 3 days after implementation.[12–14] However, none of these studies specifically evaluated burn patients which present special challenges. In this retrospective case series, we have demonstrated that in a small population of burn patients with severe refractory ARDS, PP can be a safe and effective salvage maneuver. The majority of our patients (67%) responded to the maneuver with improvement in oxygenation (Fig. 2). PP improves oxygenation by redistributing ventilation toward the dorsal areas that remain well perfused, distributing the tidal volume equally secondary to improved fit of lungs within the chest wall, and relief of heart compression forces on the lungs.[15] Patient responsiveness to PP and the degree of improvement are typically greatest in those with focal airspace

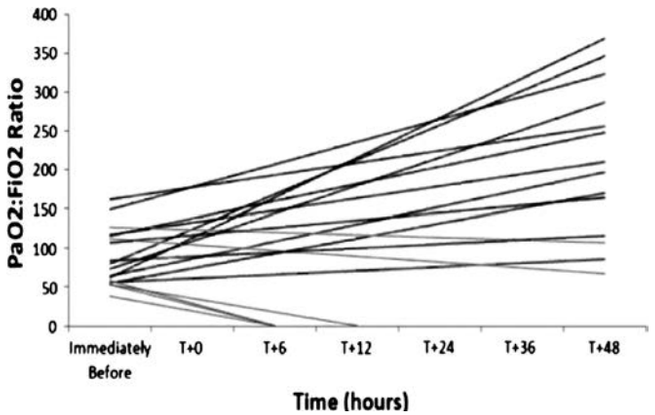

Figure 2. Trend in Pao_2:Fio_2 in all study patients with severe ARDS during 48 hours after initiation of the prone positioning. *Gray* indicates negative slope; *solid black* indicates positive slope.

TABLE 2. Pao_2:Fio_2 Ratio Trends

Time	Pao_2:Fio_2 Ratio (± SD)	$\Delta P:F_{base}$ (%Δ)	$\Delta P:F_{prior}$ (%Δ)
Immediately before PP	87 (±37)		
Immediately after PP	133 (±71)	46 (53%)	46 (53)
6 h	165 (±106)	78 (90%)	32 (24)
12 h	170 (±102)	83 (95%)	5 (3)
24 h	214 (±128)	127 (146%)	44 (26)
36 h	236 (±136)	149 (171%)	22 (10)
48 h	210 (±98)	123 (141%)	26 (11)

SD, standard deviation; $\Delta P:F_{base}$ (%Δ), change in Pao_2:Fio_2 relative to baseline and percent change from baseline; $\Delta P:F_{prior}$ (%Δ), change in Pao_2:Fio_2 relative to previous value and percent change relative to previous value.

TABLE 3. Complications

Complications	n (%)
Airway emergency/dislodgement	0
New pressure ulcer related to proning	4 (22)
Facial edema	4 (22)
Venous thromboembolic complication	
Deep venous thrombosis	1 (6)
Pulmonary embolism	0
Ventilator associated pneumonia	12 (67)

Values are n patients (% of total patients).

TABLE 4. Outcomes

Outcomes	n (%)
Alive at 48 h after prone positioning	14 (78)
Alive at 28 d from admission	12 (67)
Survival to hospital discharge	6 (33)
18 total patients enrolled	

disease[16] and are proportionally greatest in the first several hours of PP therapy. However, similar to many other so-called "rescue oxygenation therapies," this improvement in systemic oxygenation with PP has not translated into improved patient survival. Although multiple randomized controlled trials have been conducted on PP, these studies have been hampered by numerous factors, which are also true for our study, and are hard to overcome in the clinical setting. These include the enrollment of a mix of patients with mild, moderate, and severe respiratory failure; use of vastly different PP; implementation of PP at greatly different times in the course of the patient's disease; and the concurrent use of a number of other rescue therapies. In several cases, studies were terminated because of slow patient accrual.[17,18] Although the most recent results of the Prone-Supine II Study Group failed to demonstrate a mortality benefit,[19] when these results were included in a meta-analysis of PP randomized controlled trials, a very slight signal in survival benefit appears in patients with ARDS (odds ratio: 0.708; 95% confidence interval: [.503–0.997] $p = 0.048$).[20] These investigators note that this mortality benefit has become apparent as more recent studies on PP contributed results indicating that other advances in critical care in these patients such as LPV and a more uniform approach to proning are likely contributing factors to this newly identified survival benefit. It has also been shown on retrospective analysis of previous prospective studies a 10% survival benefit for the most severe ARDS (PFR $\leq$ 100).[14,21]

Among burn patients, the principal determinants of mortality are age, percentage total body surface area burned, and presence of II.[3] The expected mortality in patients with 30% to 39.9% TBSA burns is 5.4% (or 10.2–17.7% if II is present).[22] Our in-hospital mortality of patients placed on the PP was 67%, suggesting that this population carried an additional mortality related to their high degree of critical illness and multisystem failure. Other studies from our ICU have documented a much lower mortality rate of 19% among patients with mild to moderate respiratory failure.[7] Our future efforts will seek to elucidate the role of PP in permitting the return to safe ventilator settings and, by extension, the impact of PP on ultimate patient outcomes in the burn population. We postulate that unless the ventilator is returned to safe settings after PP or a nonventilatory mode of oxygenation is used, it is unrealistic to expect a mortality benefit from PP alone.

TABLE 5. Characteristics of Patients Who Survived to Hospital Discharge

Age (yr)	Sex	MOI	% TBSA	Facial Burns	II	SOFA	PFR	LOS	To PP	PP	Vent	Concurrent Therapies	Complications	Condition at Discharge
21	M	Flame	12.3	Y	Y	6	73	39	4	9	HFPV	Continuous sedation, trach	VAP	Home on room air
25	M	Blast	83	Y	Y	9	149	377	92	3	HFPV	Vasopressors, APC, CVVH, continuous sedation	Facial edema, VAP	Home on room air
27	M	Flame	26	N	N	7	112	104	32	1	HFPV	Bilateral thoracostomies, iNO, paralytic, trach	VAP	Home with oxygen and physical therapy
33	F	Flame	36	Y	Y	6	107	92	17	8	APRV	Vasopressors, APC, CVVH, iNO, trach	Facial pressure ulcer & edema, VAP	Inpatient rehabilitation with oxygen
36	M	Flash, flame	26.5	Y	Y	7	127	119	32	3	HFPV	APC, Bilateral thoracostomies, iNO, paralytic, trach	Facial pressure ulcer, VAP	Home on room air
37	M	II	0	N	Y	9	116	46	0	9	HFPV	Vasopressors, APC, CVVH, iNO, continuous sedation	VAP	Home on room air

M, male; F, female; MOI, mechanism of injury; flame, flame burn; blast, blast injury; flash, flash burn; II, inhalation injury; SOFA, sequential organ failure assessment score; PFR, Pao_2:Fio_2 ratio before prone; LOS, hospital length of stay; To PP, days from admission to PP; PP, days in prone position; Vent, type of ventilation used during prone; trach, tracheostomy present during prone; APC, Activated protein C; APRV, airway pressure release ventilation.

In a recent report, Diaz et al. advocated the use of PP in patients with life-threatening hypoxemia and in those with a $P_{plat} > 30$ cm to 35 cm H_2O on LPV. They recommended that PP be performed in the context of a protocol or guidelines designed to minimize complications.[5] According to these authors, PP should be performed for at least 20 h/d in those patients whose oxygenation responds favorably within the first day although this therapy may need to be interrupted periodically, as in our study, for nursing care and interventions. If the patient's oxygenation does not improve within the first day of therapy, the patient should be considered a nonresponder; and PP should be discontinued.[5]

PP therapy can be implemented either in isolation or in combination with other rescue therapies in patients with severe ARDS. PP has been shown to be synergistic with positive end expiratory pressure in a recent animal study[23] and high-frequency oscillatory ventilation in several human studies.[24] Strategically timing recruitment maneuvers with PP may also be of some benefit,[25] although more study on the various permutations of this strategy is necessary before an optimal regimen can be recommended.

If safe ventilator settings cannot be reinstated with PP complemented by other rescue interventions, a nonventilatory strategy for respiratory support (i.e., extracorporeal life support [ECLS]or extracorporeal CO_2 removal) should be considered. Such an approach is the only way of truly resting injured lungs, thereby eliminating all possibility of volutrauma, barotraumas, and biotrauma so long as the ventilator is returned to lung protective settings after initiation of extracorporeal support. A recently published animal model for respiratory dialysis showed the ability to use a venovenous extracorporeal CO_2 removal system to effectively reduce the minute ventilation and maintain normocarbia during a 72-hour time frame in a healthy mechanically ventilated swine.[26] Furthermore, the recently published Conventional ventilation or ECMO for Severe Adult Respiratory failure trial has demonstrated a survival benefit to referring patients with severe ARDS to a center capable of offering the full complement of advanced respiratory failure therapies including ECLS.[27] In light of these results and other advances in this rapidly progressing field,[28] we are incorporating ECLS as a treatment option for patients in our ICU with severe respiratory failure to complement PP and other rescue measures.

This study has several limitations related to its retrospective nature and small sample size. Most significantly, the diverse cohort of patients, diagnoses, concurrent therapies, and modes of ventilation limited this study. Ideally, a comparison with a matched cohort would have been helpful. However, given our implementation of this strategy as a salvage maneuver, we were not able to identify an adequately matched cohort, historical, or otherwise. A carefully designed prospective study may be the only way to identify a truly matched cohort. Furthermore, our retrospective analysis limited our ability to assess the resultant changes in ventilator settings after the improvement in oxygenation. Because of the retrospective nature and inconsistencies in documentation, the daily duration of PP therapy was not reliably quantifiable along with reasons for interruption in PP. Finally, our outcomes data were limited to the hospitalization and did not include long-term outcomes.

These limitations notwithstanding, this report documents that a PP can be safely implemented in a burn ICU. We advocate the use of provider training in this technique and the use of a specialized PP bed or apparatus to enhance the safety of this approach. When not using the specialized bed, extra padding may be necessary particularly around the face and other at risk areas. For most patients, neuromuscular blockade and continuous sedation are not absolutely necessary, likely due to the degree of metabolic encephalopathy present in the setting of severe ARDS. For those patients who are more aware, we recommend heavy sedation and paralysis as necessary. Tracheostomy placement is also not an absolute necessity for PP as most of patients were unable to tolerate the procedure at the

time of salvage. Having a person assigned to airway during each turning maneuver has assisted in preventing endotracheal tube or tracheostomy dislodgement and proven effective in our population. For physicians caring for these patients, improvements in oxygenation should result in an aggressive attempt to return the ventilator to lung protective settings. If the patient's oxygenation does not improve in the first day of therapy, the patient should be considered a nonresponder, and PP should be attempted only with caution. If PP and other rescue modalities do not permit the elimination of volutrauma, barotrauma, and biotrauma, alternative modes of oxygenation and ventilation such as ECLS should be considered.

CONCLUSIONS

PP can be safely used in burn patients with severe ARDS. The logistical challenges of implementing this PP can be overcome with a group of experienced providers committed to this therapy and can be facilitated by the use of a specialized bed designed specifically for implementing PP therapy. It improves oxygenation for at least 48 hours without significant morbidity and should be added to the routine toolset in managing burn patients with ARDS. Although PP improved oxygenation in 12 of 18 patients, mortality remained high which compels us to continue pursuing additional or alternative strategies for managing these critically ill patients.

AUTHORSHIP

K.K.C. conceived of this study, which A.I.B., C.E.W., J.K.A., L.C.C., E.M.R., L.H.B., and K.K.C. designed. D.F.H. and J.W.C. acquired the data. All authors participated in data analysis. D.F.H. and J.W.C. drafted the manuscript, which the remaining authors critically revised. K.K.C. gave final approval of the manuscript.

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DISCLOSURE

The authors declare no conflict of interest.

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