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# High frequency percussive ventilation and low $FiO_2$

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ABSTRACT

*Background:* High-frequency percussive ventilation (HFPV) is an effective rescue therapy in ventilated patients with acute lung injury. High levels of inspired oxygen ($FiO_2$) are toxic to the lungs. The objective of this study was to review a low $FiO_2$ (0.25)/HFPV protocol as a protective strategy in burn patients receiving mechanical ventilation greater than 10 days.
*Methods:* A single-center, retrospective study in burn patients between December 2002 and May 2005 at the LAC + USC Burn Center. Demographic and physiologic data were recorded from time of admission to extubation, 4 weeks, or death.
*Results:* 32 subjects were included in this study, 1 patient failed the protocol. 23 of 32 (72%) patients were men and mean age was 46 ± 15 years. Average TBSA burn was 30 ± 20 with 9 of 32 (28%) having >40% TBSA involved. Average burn index was 76 ± 21. 22 of 32 (69%) had inhalation injury and 23 of 32 (72%) had significant comorbidities. Average ventilator parameters included ventilator days 24 ± 12, $FiO_2$ 0.28 ± 0.03, $PaO_2$ 107 ± 15 Torr, $PaCO_2$ 42 ± 4 Torr, and $PaO_2/FiO_2$ ratio 395 ± 69. 16 of 32 (50%) patients developed pneumonia and 9 of 32 (28%) died. No patient developed ARDS, barotrauma, or died from respiratory failure. There was no association between inhalation injury and mortality in this group of patients.
*Conclusion:* A low $FiO_2$/HFPV protocol is a safe and effective way to ventilate critically ill burn patients. Reducing the oxidative stress of high inspired oxygen levels may improve outcome.



## 1. Background

Severe burn causes a rapid, intense and systemic inflammatory response [1,2]. Burn patients suffer a number of immunologic and physiologic derangements as a result of dermal and mucosal loss, including multi-system organ failure, acute respiratory distress syndrome (ARDS), and burn wound sepsis [3,4]. Understanding the interplay of epithelial damage and systemic pro-inflammatory cytokines is incomplete; however, it is likely that neutrophil activation and subsequent free radical formation are important causes of host and cellular injury. It is therefore prudent to examine iatrogenic causes of increased inflammatory cytokine and free radical formation, including mechanical ventilation of the burn patient, to limit this potential toxicity.

Mechanical ventilation of the burn patient is a difficult task. The burn intensivist must balance adequate oxygenation and ventilation with hemodynamic stability via high volume resuscitation. Inhalation injury, ARDS, and burn pneumonia further complicate this task.

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Additionally, the intensivist must also avoid causing further harm by their choice of respiratory support.

High-frequency percussive ventilation (HFPV) is a mode of ventilation frequently employed for patients with acute lung injury, specifically ARDS and inhalation injury, since the late 1980s. HFPV is a time-cycled, pressure-limited mode of ventilation that delivers subphysiologic tidal volumes at rates exceeding 500 breaths/min. Tidal volumes are determined by peak inspiratory pressure settings and volume provided by oscillatory function. Gallagher is credited with the first study of HFPV in 1985 [5]. His report showed dramatic improvement in $PaO_2$ levels, slight decrease in $PaCO_2$ levels, and no effect on cardiac output when adult patients with ARDS were switched from mechanical ventilation to HFPV. In patients with ARDS, HFPV has been found to increase oxygenation without increasing peak airway pressures and with minimal effect on hemodynamic parameters [6–11].

In burn patients, HFPV has been reported to decrease both the incidence of barotrauma and pneumonia in inhalation injuries while increasing oxygenation compared to conventional modes of ventilation [12–17]. Some studies also suggest an improved survival [6,13]. The benefits of HFPV have been linked to its percussive effects, including keeping alveoli open and creating a ''pulmonary toilet,'' as well as the protective effect of low peak airway pressure. These effects allow improved functional residual capacity, improved clearance of secretions, and reduced barotraumas.

HFPV also reduces the $FiO_2$ needed to adequately oxygenate critically ill patients. Hyperoxia-induced lung injury (HILI) is a well-known phenomenon in critical care medicine whereby the use of high $FiO_2$ in mechanical ventilation causes a detrimental effect on pneumocytes. Multiple studies have evaluated the effect of supraphysiologic levels of inhaled oxygen on lung cells [18–21].

At a cellular level, hyperoxia causes intense inflammation by multiple mechanisms including reactive oxygen species (ROS) formation, cytokine upregulation, altered expression of apoptotic and stress response proteins, and destruction of the alveolar-capillary barrier by epithelial and endothelial cell death [22–24]. Considerable evidence also exists that hyperoxia-induced reactive oxygen species alter pulmonary microvasculature by direct damage and reduction of the activity of vasodilator NO in vascular endothelium [23,24]. At a physiologic level, early studies in oxygen toxicity demonstrated decreased vital capacity secondary to atelectasis, tracheobronchitis, and decreased lung compliance [25–27]. The length of initiation phase preceding changes in lung function and histology is believed to vary inversely with concentration of oxygen, although some studies report as little as 14–30 h of 70% inspired oxygen in healthy human subjects may lead to deleterious effects [24,26].

At our institution, we have found that not only is it feasible to provide patients with excellent ventilatory support using HFPV and low $FiO_2$, but that using physiologic or near physiologic levels of inspired oxygen may reduce oxidative stress and inflammation. To date, there are no studies evaluating the use of a low $FiO_2$ and HFPV in burn patients. Our retrospective study is an early attempt to evaluate the beneficial effects of reduced oxygen toxicity on burn patients ventilated for a prolonged period of time.

## 2. Methods

This study was a retrospective study of critically ill burn patients treated with a low $FiO_2$/HFPV mechanical ventilation protocol for greater than 10 days at an urban burn center between 12/2002 and 5/2005. Based on our center's treatment algorithm, it was routine to place all critically ill burn patients requiring mechanical ventilation on our lung protective protocol. Inclusion criteria for this review included age >18 years/old, admission <24 h after-burn, and mechanical ventilation for greater than 10 days. Exclusion criteria included extubation or death before 10 days, as well as extubation with subsequent reintubation during first 10 days of ventilator management. During this time period, approximately 60 patients were admitted receiving mechanical ventilation, all of which were placed on our lung protective protocol. Of this group, 32 patients received longer than 10 days of mechanical ventilation. We chose to exclude patients with less than 10 days of mechanical ventilation in order to capture patients with the most severe lung injury as well as those exposed to longest period of elevated oxygen concentrations. No data was collected on patients excluded from this study.

Patients in this study arrived intubated from an outside hospital or underwent intubation at our center due to suspected inhalation injury or facial edema causing respiratory distress. The initial HFPV settings in this review were: $FiO_2$ of 100%, rate 15 with 500 oscillations/min, PIP 20–25 mmHg, the continuous positive airway pressure (CPAP) at 8 cm $H_2O$, and a positive end-expiratory pressure (PEEP) at 2 cm $H_2O$. In this mode of ventilation, CPAP provides high-frequency baseline pressure as a mean of the peal and nadir of the oscillations during exhalation and PEEP provides static baseline pressure. The $FiO_2$ was initially started at 100% on arrival or on intubation for treatment of carbon monoxide exposure and titrated to goal of 25% as quickly as possible. The CPAP/PEEP ratio was adjusted to maintain $O_2$ saturation above 92%. The PIP was adjusted to keep $PaCO_2 < 60$ or $pH > 7.25$ allowing for permissive hypercarbia. See Fig. 1 for treatment algorithm. There was no specific treatment algorithm for patients that failed the low $FiO_2$ protocol, however, pressure-controlled, volume-limited, synchronized ventilation and airway-pressure release ventilation were options available if the protocol failed. Failure of the low $FiO_2$ protocol was a clinical decision made by the treating clinician and an inability to maintain hemoglobin saturations above 88%.

Regular burn treatment included early excision and grafting after initial hemodynamic and respiratory stabilization, most commonly within 3 days. If patients did not have sufficient soft tissue for grafting at the time of excision, dermal substitutes or local wound care were used until possible. Patients were routinely started on enteric feeds via Dobhoff by day 2–3. The general policy of the LAC + USC burn unit was to not resuscitate patients with burn indices greater than 140. Further, some patients were not resuscitated due to severe comorbidities and previously stated living wills.

Patient demographics recorded included gender, age, weight, known existing comorbidities, cause of burn, %TBSA burn, calculated APACHE II score, calculated burn index, and evidence of inhalation injury by emergency room reports from

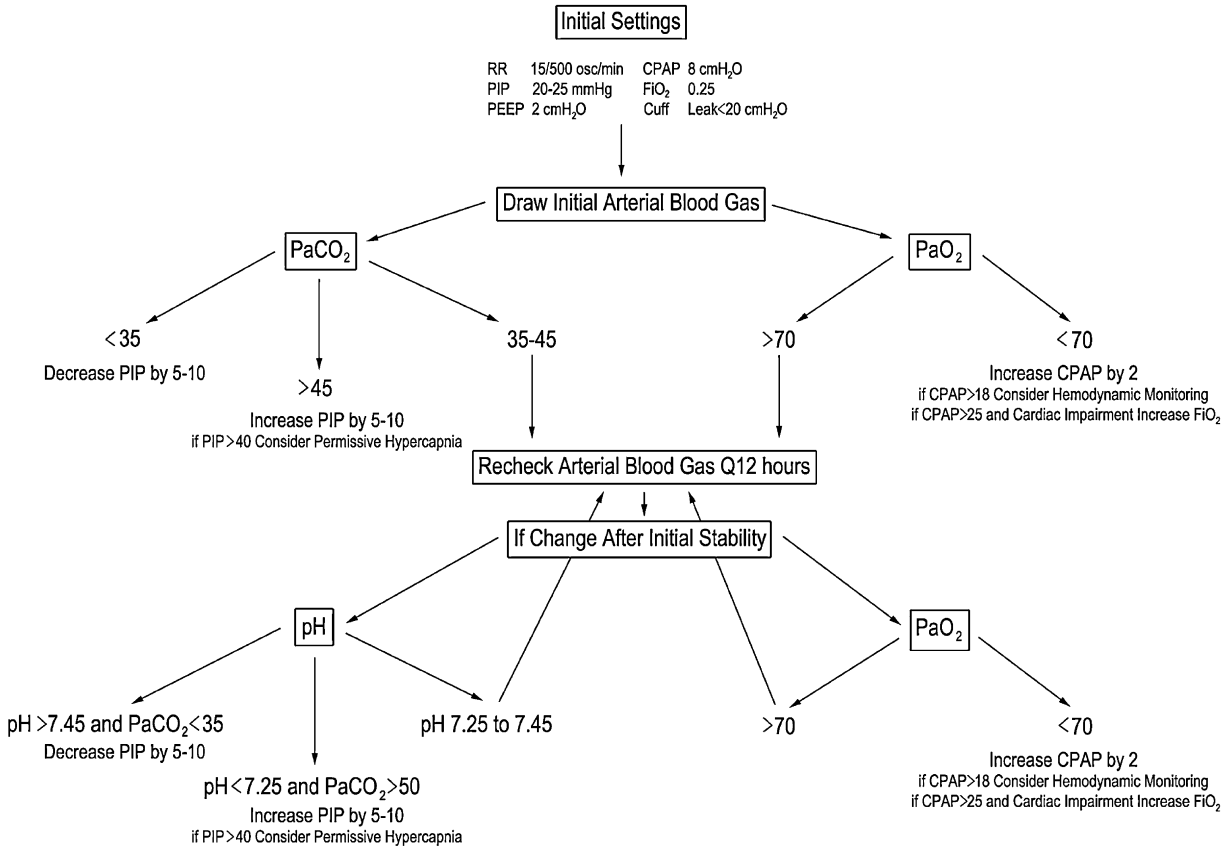


**Fig. 1 – High-frequency percussive ventilator management with low $FiO_2$.**

outside hospital or initial bronchoscopy examination. Inhalation injury was determined by recognized criteria including facial burns, carbonaceous sputum and bronchoscopy findings including severe edema, erythema, and mucosal sloughing.

Each patient was followed until extubation after 10 days, up to 4 weeks ventilated, or death. Data was reviewed four times per day for the first 24 h, then twice daily for the following 2 weeks and then once daily for the remainder of the total 4 weeks. Data reviewed included daily arterial blood gases with associated ventilator settings, calculated *P/F* ratios, vital signs, pertinent labs (CBC and BUN/CR), chest X-rays, and sputum cultures including Actinobacter, Klebsiella and Pseudomonas. By unit protocol, all patients had daily CXRs. Pneumonia was documented if a patient had both positive sputum cultures and consolidation on CXR. ARDS was documented if a patient had both a *P/F* ratio $< 200$ and bilateral pulmonary infiltrates on CXR, without evidence of cardiogenic pulmonary edema as defined by pulmonary capillary wedge pressure (PCWP) $< 18$ mmHg. Barotrauma was diagnosed if a patient had clinical evidence of pneumothorax, pneumomediastinum, or pulmonary interstitial emphysema. Other outcomes recorded included total number of ventilator days, average *P/F* ratios, average $FiO_2$ used, maximum and minimum PIPs, and adverse outcomes including diagnostic criteria of ARDS, failure of low $FiO_2$/HFPV protocol, and cause of death.

We also examined the differences between survivors and non-survivors as well as differences between inhalation injury and non-inhalation injury patients. The Wilcoxon 2-sample test was used to assess the statistical significance of means for the continuous variables and the 2-sided Fisher's exact test was used for the categorical variables. Mean and standard deviation are reported for continuous variables. A $p$-value $<0.05$ was considered statistically significant.

## 3. Results

The low $FiO_2$/HFPV protocol effectively oxygenated and ventilated 31 of 32 (97%) patients. Of the 32 patients, 72% were male and mean age was $46 \pm 15$ years. Average TBSA burn was $30 \pm 20$ with 10/32 (31%) patients having <20% TBSA, 13/32 (41%) patients having 20–40% TBSA, and 9/32 (28%) patients having >40% TBSA. Average burn index was $76 \pm 21$ and average APACHE II score was $9.1 \pm 6.8$ with 11/32 (34%) having an APACHE II score >10. 22/32 (68%) had inhalation injury. 23/32 (72%) of patients had significant co-morbidities including 2/32 (6%) hypertension, 2/32 (6%) diabetes mellitus, 5/32 (16%) ethanol abuse (7/32) 34% drug abuse, and 9/32 (40%) with preexisting lung disease. Patient demographics are summarized in Table 1.

The average number of ventilator days in this population was $24 \pm 12$. Significant ventilator settings were: average *P/F* ratio $395 \pm 69$ and minimum $197 \pm 87$, average $FiO_2$ $0.28 \pm 0.03$

**Table 1 – Patient demographics.**

| Demographic | | All patients N = 32 |
|---|---|---|
| Age | Mean ± SD | 46 ± 15 |
| Gender | % (n) male | 72% (23) |
| % TBSA | Mean ± SD | 30 ± 20 |
| | % (n) <20% | 31% (10) |
| | % (n) 20–40% | 41% (13) |
| | % (n) >40% | 28% (9) |
| Burn index | Mean ± SD | 76 ± 21 |
| Inhalation injury | % (n) yes | 69% (22) |
| APACHE II | Mean ± SD | 9.1 ± 6.8 |
| | % (n) >10 | 34% (11) |
| Any comorbidities | % (n) | 72% (23) |
| HTN | % (n) | 6% (2) |
| DM | % (n) | 6% (2) |
| EtOH abuse | % (n) | 16% (5) |
| Drug abuse | % (n) | 34% (7) |
| Lung disease | % (n) | 40% (9) |

and maximum 0.61 ± 0.29, maximum PIP 42.5 ± 12.2, average $PaO_2$ 107 ± 15, and average $PaCO_2$ 42 ± 4.2 and maximum 53.3 ± 5.9 (Table 2).

No patient developed ARDS as defined by the American European Consensus Criteria (AECC) of both bilateral pulmonary infiltrates and *P/F* ratio < 200. 13/32 (41%) patients had a single ABG demonstrating *P/F* < 200, but these were not seen on repeat ABG or in conjunction with bilateral pulmonary infiltrates on CXR. A single patient, 1/32 (3%), had a sustained *P/F* < 200 pre-mortality between CPR episodes although he remained adequately oxygenated and ventilated. 1/32 (3%) had low $FiO_2$/HFPV protocol failure in which he was switched to different modes of ventilation, including PRVC and SIMV for greater than 7 days. At the time PRVC was instituted, PIP was 49 and *P/F* was 170. 11/32 (34%) patients were weaned from HFPV and extubated from SIMV or conventional CPAP mode by 4 weeks. One patient underwent tracheostomy placement and was transferred to long-term care facility for rehabilitation (Table 2). No patient suffered respiratory death, barotrauma, or airway hemorrhage. 26/32 (81%) had positive sputum cultures and 16/32 (50%) developed pneumonia. 9/32 (28%) of patients in this study died, 3/32 (9.5%) from multi-system organ failure, 2/32 (6%) from cardiac failure, 1/32 (3%) from renal failure, and 3/32 (9.5%) from other causes (Table 2).

In comparison of the patients who died to patients who survived to at least 4 weeks, patients who died had a greater TBSA involved (44 ± 18 vs. 25 ± 18, $p = 0.016$) and burn index (96 ± 21 vs. 68 ± 15, $p = 0.004$). See Table 2 for results. Patients who died also had a greater APACHE II score (15.2 ± 7.2 vs. 6.7 ± 5.0, $p = 0.005$). There was no significant difference in number with inhalation injury, pneumonia, or co-morbidity. Patients who died did demonstrate a higher maximum PIP (56 ± 10.9 vs. 37.3 ± 8.1, $p = 0.001$).

In comparison of patients who had inhalation injury to those who did not, the only significant difference was patients with inhalation injury were more likely to have preexisting lung disease (41% vs. 0%, $p = 0.03$). See Table 3 for results. There was no statistically significant difference in TBSA involved, APACHE score, ventilator parameters, pneumonia, protocol failure, or mortality.

## 4. Discussion

Our study describes the outcomes of a low $FiO_2$/HFPV protocol in burn patients requiring prolonged mechanical ventilation. We evaluated the ability to safely oxygenate and ventilate critical burn patients with the lowest $FiO_2$ possible, with the hypothesis that reducing oxygen toxicity would ameliorate further inflammatory stress on patients.

The results demonstrate that burn patients can be successfully ventilated with a low $FiO_2$ on the percussive ventilator. Our study included 32 patients, of which 31 were effectively and safely ventilated. In our total population, mean $PaO_2$ was 107 ± 15, average P/F ratio was 395 ± 16, and average $FiO_2$ used was 0.28 ± 0.03. 11/32 (34%) patients were weaned from HFPV and extubated from SIMV or conventional CPAP mode by 4 weeks. These results document the efficacy and safety of our algorithm.

In a population that can be difficult to ventilate, we found it particularly important that in our study no patients suffered barotrauma, ARDS, or respiratory death as a result of our protocol.

We believe that these results are at least partially due to the percussive effects of HFPV and decreased oxygen toxicity of low $FiO_2$. Of those patients who did die, there were no significant differences between survivors and non-survivors in regards to inhalation injury, pneumonia, or other co-morbidities. Patient who died did have higher PIPs, most likely due to the severity of their lung injury. However, the only factors predictive of death were TBSA involved, burn index, and APACHE II score.

We were surprised by the lack of patients who developed ARDS, a condition that is well known in the burn population especially those with inhalation injury [28,29]. In fact, many authors attribute the increased mortality seen in inhalation injury with the development of ARDS [30,31]. We believe it is due largely to the success of our ventilation strategy, but must acknowledge there could be several other reasons. First, our incidence of ARDS may be low because our patients with respiratory issues were classified as having ARDS only if they had both a $PaO_2/FiO_2$ ratio < 200 and confirmatory X-ray findings. Our numbers might have been more inclusive if either were used as classification for ARDS. Second, HFPV may have used higher PIP to achieve improved $PaO_2/FiO_2$ ratios and may have undetected consequences that were not acknowledged and warrant caution. Third, the ''open-lung'' technique of HFPV may have allowed higher $PaO_2/FiO_2$ ratios in patients that might have had chest X-ray findings consistent with ARDS and the diagnosis may have been limited by strict calculation. However, we feel the ''open-lung'' technique of HFPV is one of the reasons our protocol may have been so successful.

Two modern ventilation techniques for treating acute lung injury are the open lung approach and the low tidal volume approach. The low tidal volume approach involves minimizing the amount of phasic stretch of lung units in inspiration, to prevent ventilator induced lung injury. The open lung approach stents the small airways open at end expiration using PEEP, to reduce shearing injuries caused by re-inflating collapsed lung units. Both techniques were developed on the

**Table 2 – Comparison of demographic and clinical characteristics by survival status.**

| Characteristic | | All patients N = 32 | Died N = 9 | Survived N = 23 | P-value* |
|---|---|---|---|---|---|
| Gender | % (*n*) male | 72% (23) | 78% (7) | 70% (16) | 1.00 |
| Age | Mean ± SD | 46 ± 15 | 52 ± 21 | 44 ± 12 | 0.31 |
| % TBSA | Mean ± SD | 30 ± 20 | 44 ± 18 | 25 ± 18 | 0.016 |
| | % (*n*) <20% | 31% (10) | 0% (0) | 43% (10) | 0.002 |
| | % (*n*) 20–40% | 41% (13) | 33% (3) | 43% (10) | |
| | % (*n*) >40% | 28% (9) | 67% (6) | 13% (3) | |
| Burn index | Mean ± SD | 76 ± 21 | 96 ± 21 | 68 ± 15 | 0.004 |
| Inhalation injury | % (*n*) yes | 69% (22) | 56% (5) | 74% (17) | 0.41 |
| APACHE II | Mean ± SD | 9.1 ± 6.8 | 15.2 ± 7.2 | 6.7 ± 5.0 | 0.005 |
| | % (*n*) >10 | 34% (11) | 78% (7) | 17% (4) | 0.003 |
| Ventilator days | Mean ± SD | 24 ± 12 | 22 ± 8 | 25 ± 14 | 0.87 |
| $PaO_2$ | | | | | |
| Ave | Mean ± SD | 107 ± 15 | 102 ± 14 | 109 ± 15 | 0.10 |
| | % (*n*) >65 | 100% (32) | 100% (9) | 100% (23) | 1.00 |
| $PACO_2$ | | | | | |
| Max | Mean ± SD | 53.3 ± 5.9 | 55.6 ± 6.5 | 52.4 ± 5.6 | 0.22 |
| | % (*n*) >60 | 6% (2) | 11% (1) | 4% (1) | 0.49 |
| Ave | Mean ± SD | 42.0 ± 4.2 | 41.0 ± 3.6 | 42.4 ± 4.5 | 0.41 |
| | % (*n*) >60 | 100% (32) | 100% (9) | 100% (23) | 1.00 |
| $FiO_2$ | | | | | |
| Max | Mean ± SD | 0.61 ± 0.29 | 0.53 ± 0.29 | 0.65 ± 0.30 | 0.22 |
| Ave | Mean ± SD | 0.28 ± 0.03 | 0.30 ± 0.04 | 0.28 ± 0.02 | 0.10 |
| P/F | | | | | |
| Min | Mean ± SD | 197 ± 87 | 148 ± 74 | 216 ± 85 | 0.07 |
| | % (*n*) >200 | 56% (18) | 22% (2) | 70% (16) | 0.022 |
| Ave | Mean ± SD | 395 ± 69 | 361 ± 74 | 409 ± 64 | 0.06 |
| | % (*n*) >200 | 100% (32) | 100% (9) | 100% (23) | 1.00 |
| PIP | | | | | |
| Max | Mean ± SD | 42.5 ± 12.2 | 55.9 ± 10.9 | 37.3 ± 8.1 | 0.001 |
| | % (*n*) <40 | 41% (13) | 0% (0) | 57% (13) | 0.004 |
| | % (*n*) <50 | 75% (24) | 33% (3) | 91% (21) | 0.002 |
| Pneumonia | % (*n*) positive | 50% (16) | 67% (6) | 43% (10) | 0.43 |
| Co-morbidity | % (*n*) yes | 72% (23) | 78% (7) | 70% (16) | 1.00 |
| Ethanol use | % (*n*) yes | 16% (5) | 22% (2) | 13% (3) | 0.60 |
| Drug use | % (*n*) yes | 22% (7) | 33% (3) | 17% (4) | 0.37 |
| COPD | % (*n*) yes | 28% (9) | 11% (1) | 35% (8) | 0.38 |
| Diabetes | % (*n*) yes | 6% (2) | 0% (0) | 9% (2) | 1.00 |
| HFPV failure | % (*n*) yes | 3% (1) | 0% (0) | 4% (1) | 1.00 |
| Cause of death | | | | | |
| MSOF | % (*n*) yes | | 9.5% (3) | | |
| Cardiac failure | % (*n*) yes | | 6% (2) | | |
| Renal failure | % (*n*) yes | | 3% (1) | | |
| Other | % (*n*) yes | | 9.5% (3) | | |

* Two-sided Fisher's exact test for categorical variables; Wilcoxon 2-sample test for continuous variables.

premise that phasic over- or under-inflation of alveoli also causes lung injury and cytokine release. HFPV is an excellent example of a combination of these two techniques by preventing collapse of small alveoli via percussion and using sub-physiologic tidal volumes.

In comparison of ventilation parameters between our patients with and without inhalation injury, there were no statistically significant differences in average $PaO_2$, maximum and average $PaCO_2$, maximum PIP, average and maximum $FiO_2$ used, or minimum and average *P/F* ratio. Additionally, there were no differences in number of days on the ventilator or rate of pneumonia. Most importantly, in our group of patients, those with inhalation injury were not more likely to die than their counterparts. Patients with inhalation injury were more likely to have COPD, although this may be related to mechanism of burn, including oxygen tank explosion. Importantly, we felt that we were able to reduce the potential morbidity of inhalation injury via a successful ventilation protocol.

In comparison to other studies, there was a relatively high rate of pneumonia in our patients. This could suggest that either we under diagnosed ARDS or that our method of ventilation could predispose to ventilation-associated pneumonia. The open-cuff technique used with HFPV can allow secretions and gastric contents to reflux into the lungs more easily, however, for this review we were selecting a population with prolonged ventilation and increased risk of VAP. The fact that mortality was increased in patients with pneumonia may suggest that the burden of respiratory infection is lethal to many patients with otherwise survivable inhalation or soft tissue thermal injuries.

A criticism of our study is that our patients also had a relatively high rate of mortality for a group with an average

**Table 3 – Comparison of demographic and clinical characteristics between inhalation and non-inhalation injured patients.**

| Characteristic | | All patients $N = 32$ | Inhalation injured ($N = 22$) | Non-inhalation injured ($N = 10$) | $P$-value* |
|---|---|---|---|---|---|
| Gender | % (*n*) male | 72% (23) | 68% (15) | 80% (8) | 0.68 |
| Age | Mean ± SD | 46 ± 15 | 44 ± 12 | 51 ± 20 | 0.52 |
| % TBSA | Mean ± SD | 30 ± 20 | 29 ± 21 | 33 ± 18 | 0.64 |
| | % (*n*) <20% | 31% (10) | 36% (8) | 20% (2) | 0.32 |
| | % (*n*) 20–40% | 41% (13) | 32% (7) | 60% (6) | |
| | % (*n*) >40% | 28% (9) | 32% (7) | 20% (2) | |
| Burn index | Mean ± SD | 76 ± 21 | 73 ± 19 | 84 ± 24 | 0.18 |
| APACHE II | Mean ± SD | 9.1 ± 6.8 | 8.9 ± 6.0 | 9.7 ± 8.6 | 0.95 |
| | % (*n*) >10 | 34% (11) | 32% (7) | 40% (4) | 0.70 |
| Ventilator days | Mean ± SD | 24 ± 12 | 24 ± 14 | 24 ± 7 | 0.49 |
| Hospital days | Mean ± SD | 39 ± 29 | 38 ± 34 | 40 ± 15 | 0.17 |
| $PaO_2$ | | | | | |
| Ave | Mean ± SD | 107 ± 15 | 107 ± 15 | 107 ± 14 | 1.00 |
| | % (*n*) >65 | 100% (32) | 100% (22) | 100% (10) | 1.00 |
| $PaCO_2$ | | | | | |
| Max | Mean ± SD | 53.3 ± 5.9 | 53.3 ± 5.5 | 53.3 ± 7.2 | 0.63 |
| | % (*n*) >60 | 6% (2) | 5% (1) | 10% (1) | 0.53 |
| Ave | Mean ± SD | 42.0 ± 4.2 | 42.1 ± 4.5 | 41.7 ± 3.8 | 0.87 |
| | % (*n*) >60 | 100% (32) | 100% (22) | 100% (10) | 1.00 |
| $FiO_2$ | | | | | |
| Max | Mean ± SD | 0.61 ± 0.29 | 0.66 ± 0.30 | 0.52 ± 0.27 | 0.21 |
| Ave | Mean ± SD | 0.28 ± 0.03 | 0.28 ± 0.03 | 0.28 ± 0.03 | 0.54 |
| P/F | | | | | |
| Min | Mean ± SD | 197 ± 87 | 183 ± 84 | 229 ± 88 | 0.16 |
| | % (*n*) >200 | 56% (18) | 50% (11) | 70% (7) | 0.45 |
| Ave | Mean ± SD | 395 ± 69 | 394 ± 71 | 398 ± 68 | 0.98 |
| | % (*n*) >200 | 100% (32) | 100% (22) | 100% (10) | 1.00 |
| PIP | | | | | |
| Max | Mean ± SD | 42.5 ± 12.2 | 41.3 ± 12.4 | 45.2 ± 12.4 | 0.44 |
| | % (*n*) <40 | 41% (13) | 45% (10) | 30% (3) | 0.47 |
| | % (*n*) <50 | 75% (24) | 77% (17) | 70% (7) | 0.68 |
| Pneumonia | % (*n*) positive | 50% (16) | 45% (10) | 60% (6) | 0.70 |
| Co-morbidity | % (*n*) yes | 72% (23) | 82% (18) | 50% (5) | 0.10 |
| Ethanol use | % (*n*) yes | 16% (5) | 18% (4) | 10% (1) | 1.00 |
| Drug use | % (*n*) yes | 22% (7) | 27% (6) | 10% (1) | 0.39 |
| COPD | % (*n*) yes | 28% (9) | 41% (9) | 0% (0) | 0.03 |
| Diabetes | % (*n*) yes | 6% (2) | 5% (1) | 10% (1) | 0.53 |
| HFPV failure | % (*n*) yes | 3% (1) | 5% (1) | 0% (0) | 1.00 |
| Mortality | | | | | |
| MSOF | % (*n*) yes | 9.5% (3) | 6% (2) | 3% (1) | 1.00 |
| Cardiac failure | % (*n*) yes | 6% (2) | 3% (1) | 3% (1) | 0.53 |
| Renal failure | % (*n*) yes | 3% (1) | 3% (1) | 0% (0) | 1.00 |
| Other | % (*n*) yes | 9.5% (3) | 3% (1) | 6% (2) | 0.22 |

* Two-sided Fisher's exact test for categorical variables; Wilcoxon 2-sample test for continuous variables.

burn index less than 100. The prognostic burn index (PBI) is calculated based on the patient's age added to the TBSA. A burn index of 90–100 is now generally associated with a 50–70% mortality, which has improved steadily over decades with changing burn treatment. The burn index in this series may have been low because patients with massive soft tissue burns, or high TBSA, died before 10 days. However, we believe it is important to recall that based on the traditional ''rule of nines'' to calculate TBSA involved, and therefore calculate PBI, inhalation burns are not included. The adult lungs have nearly 300–500 million alveoli and 750 square feet (70 square kilometers) of surface area and this exclusion from TBSA and PBI in inhalation injuries is a gross underestimation of total disease burden. This may also explain the increased mortality rate in our study, which specifically selected these patients. Due to the lethal nature of burn injuries, we felt our ventilation protocol was appropriately aggressive in patients with a relatively low TBSA.

Furthermore, although patients who died had a mean burn index less than 100, many patients presented with significant comorbidities or extremes of age that significantly increased their risk of death. Comorbidity was very high in our patient population compared to other similar studies. Our patient population comes from socioeconomically deprived area as well multiple long-term care facilities, nursing homes, and jail population. We felt this especially increased our numbers of patients with comorbidities compared to average centers. However, despite these comorbidities, we felt that our protocol offered the same advantages to all patients, and did not affect survival negatively.

One of the most important attributes of HFPV is the ability to keep small airways open for a larger portion of the

respiratory cycle, allowing use of lower $FiO_2$. In our patients, using the low $FiO_2$/HFPV protocol the average $FiO_2$ used was $0.28 \pm 0.03$ and maximum was $0.61 \pm 0.29$. We believe the use of the HFPV was paramount to our ability to achieve these protective fractions of inspired oxygen. Multiple studies elucidate the danger of high levels of inspired oxygen and its ability to exacerbate oxidative stress including the increased production of free radicals. In 2009, Bin-Jaliah evaluated the effect of hyperoxia on the ultrastructural pathology of ratalveolar epithelium. Post-exposure to hyperoxia, the production of free radicals increased, alveolar cells showed degeneration with swollen mitochondria, and glutathione peroxidase and lactate dehydrogenase levels showed decreased glycolysis [31]. In a recent article in the pediatric literature, preterm infant resuscitation with low $FiO_2$ levels caused less oxidative stress, inflammation, and chronic lung disease such as bronchodysplasia [32]. In another recent study, significantly altered levels of serum IL-4, IL-6, IL-7, IL-10, and IL-13 were detected within the first 7 days of after admission in burn patients with concomitant inhalation injury who did not survive when compared with similar patients who did [33]. Furthermore, alterations in these cytokines were associated with increased incidence of ARDS, number of days under ventilation, increased PIP, and a lower $PaO_2/FiO_2$ ratio. Therefore, minimizing oxygen toxicity may be paramount to reducing oxidative stress.

Our study is a retrospective case review and cannot provide the strength of data that is attained by a randomized controlled trial. Additionally, we excluded patients ventilated for less than ten days in the hope of assessing those with most severe lung injury exposed to the longest period of elevated oxygen, although we could have excluded a particular population of patients with the gravest of lung injury that therefore died before ten days. This clearly would have changed our data.

Our study is, however, an excellent example of the safety and efficacy of ventilating critically ill burn patients with a low fraction of inspired oxygen via HFPV. Furthermore, low $FiO_2$ may prevent further lung damage in patients with inhalation injury and reduce their incidence of respiratory injury associated complications. Further studies are warranted to elucidate the potential benefit of a low $FiO_2$/HFPV protocol. Mechanical ventilation is a prime example of an ICU intervention that may actually exacerbate acute lung injury if not employed with a protective strategy in mind.

## Conflict of interest

None.

## Contributions

Margaret Starnes-Roubaud is the first author and the primary author of this paper. Elizabeth Bales is credited with data collection and assistance with writing. Alex Williams-Resnick was involved with data collection and Philip Lumb assisted with study design. Linda Chan is credited with statistical analysis. Joe Escudero provided technical information and support regarding the percussive ventilator. Warren Garner is corresponding author and ICU director.

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