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High-frequency percussive ventilation improves oxygenation and ventilation in pediatric patients with acute respiratory failure☆

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ABSTRACT

Purpose: High-frequency percussive ventilation (HFPV) in pediatrics has been described predominantly in burned patients. We aimed to describe its effectiveness and safety in noninhalational pediatric acute respiratory failure (ARF).
Methods: We conducted an observational study in a tertiary care pediatric intensive care unit on 31 patients with ARF failing conventional ventilation transitioned to HFPV. Demographics, ventilator settings, oxygenation index, oxygen saturation index, oxygen saturation as measured by pulse oximetry/fraction of inspired oxygen (FIO_2), and Pao_2/FIO_2 were recorded before and during HFPV.
Results: Initiation of HFPV was associated with improvements in oxygenation index, oxygen saturation index, Pao_2/FIO_2, and oxygen saturation as measured by pulse oximetry/FIO_2 as early as 12 hours ($P < .05$), which continued through 48 hours after transition. Improved oxygenation occurred without an increase in mean airway pressures. Reductions in $Paco_2$ occurred 6 hours after initiation of HFPV and continued through 48 hours ($P < .01$). Improved gas exchange was accompanied by reduced peak-inflating pressures at all time intervals after initiation of HPFV ($P < .01$). Vasopressor scores were similar before and after initiation of HFPV in patients requiring vasoactive support. Twenty-six (83.9%) of 31 patients survived to hospital discharge.
Conclusions: In a heterogeneous population of pediatric ARF failing conventional ventilation, HFPV efficiently improves gas exchange in a lung-protective manner.

1. Introduction

Acute respiratory failure (ARF) is a leading cause of morbidity and mortality in pediatric intensive care units (PICUs), and mechanical ventilation remains the mainstay of therapy. Ventilator-induced lung injury has been a well-documented consequence of mechanical ventilation [1,2], prompting use of lung-protective strategies and the development of alternative nonconventional modes of ventilation [1-5].

High-frequency percussive ventilation (HFPV) is a unique mode that attempts to combine the beneficial effects of conventional and high-frequency ventilation [6]. It stacks successive subtidal volume breaths at a rapid rate superimposed upon conventional cyclic rates, allowing for progressive stepwise inflation of the lung to a set peak pressure, and a passive exhalation to a predetermined lower pressure. Continuous pneumatic compressions also allow for a mobilization of retained airway secretions [7].

High-frequency percussive ventilation was initially described in burned patients with inhalational injury, where it efficiently mobilized retained soot compared with conventional ventilation [8-10]. More recently, HFPV has been described in adult patients without burn injury but with ARF, primarily as a rescue mode for patients unable to meet oxygenation and ventilation goals with conventional ventilation [11-14]. High-frequency percussive ventilation is consistently reported to improve oxygenation at lower pressures than those used for conventional ventilation, despite a lack of reduction of mortality or ventilator days [11,14,15].

In pediatric burned patients [9,10,16-18], retrospective studies have also suggested lower inflation pressures and improved oxygenation. A prospective trial comparing conventional ventilation with HFPV in burned children demonstrated lower inflation pressures and marginally improved oxygenation with HFPV, but showed no significant outcome differences [16]. The single published report of HFPV use in nonburn pediatric ARF was as a salvage mode in an infant with hydrocarbon aspiration [19]. Despite use of this mode of ventilation for more than 3 decades, the use and efficacy of HFPV as

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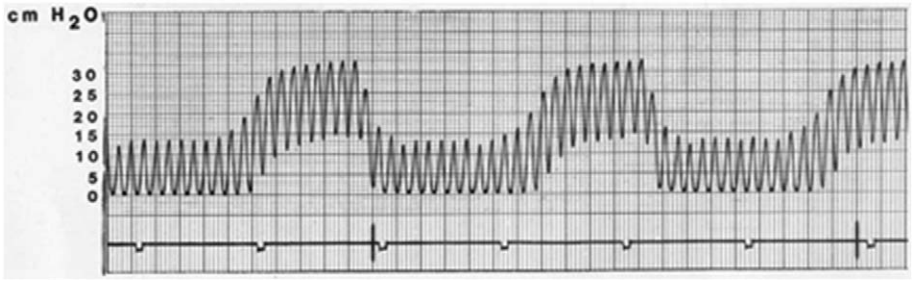


Fig. 1. Time-pressure tracing of the HFPV ventilatory cycle on the VDR-4. The ventilator delivers pneumatically driven, subtidal volume breaths at a set percussive rate (shown as 500 breaths/min) successively to a high pressure (peak inspiratory pressure or, alternatively, the pulsatile flow rate) for a predetermined inspiratory time. Exhalation to a preset low pressure (end-expiratory pressure analogous to positive end-expiratory pressure) is passive and kept there for a preset expiratory time. Reproduced with permission from Percussionaire.

a primary ventilator strategy or rescue mode in nonburn pediatric respiratory failure is unknown.

In this study, we describe our initial experiences with HFPV in pediatric patients with ARF. We aimed to evaluate the changes in respiratory and hemodynamic function in patients with ARF in whom HFPV was initiated after failure of conventional ventilation. We hypothesized that there would be a significant and sustained improvement in oxygenation and a reduction in peak-inflating pressures after transition from conventional ventilation to HFPV.

2. Methods

2.1. Patient selection and design

We conducted a retrospective observational study in patients receiving HFPV for failure of conventional ventilation at the Children's Hospital of Philadelphia, a 55-bed, tertiary care PICU. All patients were identified from a database of HFPV use. The study was approved by the hospital institutional review board, and the requirement for informed consent was waived. All consecutive patients receiving HFPV between October 1, 2010, and January 31, 2012, were eligible for inclusion, which totaled 40 patients. Patients were excluded if HFPV was initiated for reasons other than failure of conventional ventilation, which removed 9 patients from our consecutive cohort: in 4 patients, HFPV was empirically initiated for smoke inhalation; in another 4 patients, HFPV was used during extracorporeal membrane oxygenation; and in 1 patient, a diagnosis of unrepaired cardiac disease prompted transfer out of our PICU. This left 31 patients available for analysis.

2.2. Conventional ventilation strategy

Determination of failure of conventional ventilation and decision to use alternate modes were left to the discretion of the attending physician. Despite the lack of a formal protocol, our institutional practice for respiratory failure is to initiate conventional ventilation with a minimum of 5 cm H_2O of end-expiratory pressure and 6 to 8 mL/kg of tidal volume and to attempt to wean fraction of inspired oxygen (F_{IO_2}) to 0.60 or less. Inability to wean F_{IO_2} prompts escalation of end-expiratory pressures and subsequent repeat efforts to wean F_{IO_2}, with the goal to maintain peak inspiratory pressures of 32 cm H_2O or less. Persistently elevated peak pressures ($\geq$32 cm H_2O), ongoing hypercarbia ($P_{aCO_2} \geq 80$ or pH < 7.30), or oxygenation difficulties (inability to wean $F_{IO_2} \leq 0.60$ despite increasing end-expiratory pressure) prompt reevaluation of the ventilatory strategy and a change in the mode of ventilation. All patients were ventilated with a decelerating flow waveform on conventional ventilation, justifying our use of peak-inflating pressures as a risk factor for alveolar distension.

2.3. High-frequency percussive ventilation strategy

Our institution uses the VDR-4 (Pecussionaire, Sandpoint, Idaho). Typical HFPV starting settings used were a high-frequency percussive rate of 500 to 600 breaths/min (lower rates for hypercarbia)

Table 1
Characteristics of patient population and HFPV use

Variable[a]	(n = 31)
Age (y)	1.6 (0.6, 6.8)
Weight (kg)	10.0 (7.1, 25.2)
Sex (male), n (%)	15 (48.4)
Race, n (%)	
Asian/Pacific Islander	1 (3.2)
Black/African American	10 (32.2)
Hispanic	3 (9.7)
White	17 (54.8)
PRISM III at 12 h	6.5 (1, 11)
Immunocompromised, n (%)	6 (19.4)
Length of mechanical ventilation before transition to HFPV (d)	1.0 (0.0, 4.0)
Vasopressors, n (%)	18 (58.1)
Vasopressor score[b] before transition to HFPV (n = 18)	5.0 (2.0, 12.0)
Vasopressor score after transition to HFPV (n = 18)	7.5 (5.0, 14.0)
Ancillary therapy used before HFPV[c], n (%)	
Neuromuscular blockade	16 (51.6)
Inhaled nitric oxide	9 (29.0)
HFOV	3 (9.7)
Corticosteroids	5 (16.1)
Prone positioning	2 (6.5)
Exogenous surfactant	1 (3.2)
Severity of oxygenation impairment, n (%)	
PF ratio < 200 (n = 16[d])	15 (93.8)
SF ratio < 264[e] (n = 31)	25 (80.6)
SF ratio < 221[e] (n = 31)	19 (61.3)
Barotrauma, n (%)	
Before transition to HFPV	3 (9.7)
After transition to HFPV	4 (12.1)
Reason for stopping HFPV, n (%)	
Significant improvement in respiratory failure	23 (74.2)
Death or withdrawal of life support	5 (16.1)
Inadequate improvement, dyssynchrony, or poor tolerance	3 (9.7)
Total HFPV days	4.0 (2.3, 6.0)
Total ventilator days	16.0 (10.0, 22.8)
Total PICU length of stay (d)	22.0 (17.0, 34.8)
Mortality, n (%)	5 (16.1)

[a] Continuous data are in the form of median (25th, 75th percentiles), and categorical data are in the form of n (%).

[b] Vasopressor score = dopamine dose ($\mu g\,kg^{-1}\,min^{-1}$) × 1 + dobutamine ($\mu g\,kg^{-1}\,min^{-1}$) × 1 + epinephrine ($\mu g\,kg^{-1}\,min^{-1}$) × 100 + norepinephrine ($\mu g\,kg^{-1}\,min^{-1}$) × 100 + phenylephrine ($\mu g\,kg^{-1}\,min^{-1}$) × 100 + milrinone ($\mu g\,kg^{-1}\,min^{-1}$) × 10. Vasopressor score medians (interquartile range) reflect only the 18 patients ever exposed to these medications.

[c] More than 1 category was possible.

[d] Arterial blood gas data available for 16 patients.

[e] Cutoff values for mild and moderate/severe ARDS using noninvasive, S_{PO_2}-based measures of oxygenation impairment.

superimposed on a convectional rate of 10 to 30 breaths/min, a peak pressure matching that used on the conventional ventilator, an inspiratory/expiratory ratio of 1:1, and an end-expiratory pressure equal to or slightly above the pressure used on conventional (Fig. 1). Adjustments are made on the basis of invasive and noninvasive measurements of oxygenation and ventilation, including pulse oximetry and transcutaneous CO_2 monitoring, with preferential reduction in peak pressures with improving ventilation and reductions in F_{IO_2} until at least 0.60 for improving oxygenation. Pressures are measured at the proximal endotracheal tube; specifically, a pressure manometer connected to the inhalational limb of the circuit adjacent to the proximal endotracheal tube is attached to the VDR-4 and continuously displays measured pressures on the ventilator.

2.4. Data collection

Medical records of patients were reviewed for diagnoses, demographics, the severity of illness Pediatric Risk of Mortality (PRISM) III score at 12 hours of PICU admission, preexisting conditions, indication for mechanical ventilation, length of PICU stay, length of mechanical ventilation, and discharge status. We recorded ventilator settings, vasopressor score, presence of pneumothorax or pneumomediastinum, blood gas measurements, and the use of adjunctive therapies (inhaled nitric oxide, surfactant, methylprednisolone, neuromuscular blockade, and prone positioning) before and after (at 6, 12, 24, and 48 hours) initiation of HFPV.

2.5. Equations

We used a modification of a previously described vasopressor score [20-22]: dopamine dose ($\mu g\ kg^{-1}\ min^{-1}$) × 1 + dobutamine ($\mu g\ kg^{-1}\ min^{-1}$) × 1 + epinephrine ($\mu g\ kg^{-1}\ min^{-1}$) × 100 + norepinephrine ($\mu g\ kg^{-1}\ min^{-1}$) × 100 + phenylephrine ($\mu g\ kg^{-1}\ min^{-1}$) × 100 + milrinone ($\mu g\ kg^{-1}\ min^{-1}$) × 10. Measures of oxygenation recorded in the study were the Pa_{O_2}/F_{IO_2} (PF ratio) and the oxygenation index (OI), calculated as the (mean airway pressure [mPaw] × F_{IO_2} × 100/Pa_{O_2}). In addition, we report the oxygen saturation as measured by pulse oximetry (Sp_{O_2})/F_{IO_2} (SF ratio) and the oxygen saturation index (OSI; [mPaw × F_{IO_2} × 100]/Sp_{O_2}), metrics to describe oxygenation in children with ARF with less readily available arterial access [23-25] that have been associated with mortality [26]. Owing to the nonlinear relationship between Pa_{O_2} and Sp_{O_2} at higher Sp_{O_2} values, patient data were only used when Sp_{O_2} is at least 97%.

2.6. Statistical analysis

Continuous data are reported as mean (±SEM) or median (25th, 75th percentiles) for normally and nonnormally distributed variables, respectively. Categorical data are reported as frequencies and percentages. Paired or unpaired parametric and nonparametric comparisons of continuous variables were performed as appropriate. Categorical variables were compared using the Fisher exact test.

Table 2
Gas exchange, ventilator settings, hemodynamics, and other therapies at initiation of, and after transition to, HFPV among patients failing conventional mechanical ventilation (n = 31)

Variable[a]	Conventional ventilation before transition to HFPV (0 h)	HFPV hour 24	P[b]
Ventilator settings			
Peak inspiratory pressure	38.0 (29.5, 41.3)	26.0 (24.0, 33.0)	<.001
End-expiratory pressure	10 (8.5, 12)	10 (8, 12)	.683
Tidal volume (mL/kg)	7.0 (6.2, 7.8)	–	–
Mean airway pressure	18.0 (13.3, 21.5)	17.0 (14.5, 19.3)	.640
Superimposed percussive rate	–	600 (500, 600)	–
Gas exchange			
OI[c] (n = 16)	18.7 (±2.2)	12.0 (±2.2)	.040
PF ratio[c] (n = 16)	131.5 (±17.5)	187.4 (±13.2)	.020
OSI (n = 31)	9.8 (6.8, 14.1)	6.0 (4.8, 9.3)	<.001
SF ratio (n = 31)	182.9 (127.1, 230.9)	250.0 (215.3, 323.5)	<.001
$PaCO_2$[c] (n = 16)	84.1 (±11.7)	57.8 (±10.2)	<.001
$PvCO_2$[d] (n = 15)	61.6 (±7.2)	43.3 (±9.7)	.022
Ancillary therapy			
Neuromuscular blockade	16 (51.6%)	17 (54.8%)	1.0
Inhaled nitric oxide (iNO)	9 (29.0%)	14 (45.2%)	.29
Gas exchange in patients started on iNO during transition to HFPV			
OI[c] (n = 3)	21.6 (21.2, 25.4)	9.8 (6.4, 18)	.250
PF ratio[c] (n = 3)	92.6 (73.7, 108.9)	204.1 (134.3, 220.8)	.250
OSI (n = 5)	19.2 (9.5, 20.4)	9.6 (5, 11.4)	.125
SF ratio (n = 5)	125.0 (95.7, 170.6)	244.9 (192.2, 294.5)	.063
$PaCO_2$[c] (n = 3)	48.7 (45.5, 79.5)	53.7 (42, 57.6)	.500
Gas exchange in patients *not* started on iNO during transition to HFPV			
OI[c] (n = 13)	15.4 (12.5, 26.9)	9.3 (8.2, 11.8)	.063
PF ratio[c] (n = 13)	134.2 (76.4, 187.1)	195.7 (165.3, 209.2)	.077
OSI (n = 26)	8.3 (5.9, 13.8)	5.9 (4.4, 8.6)	.002
SF ratio (n = 26)	186.6 (141.8, 231.9)	250.0 (221.9, 324.8)	<.001
$PaCO_2$[c] (n = 13)	77.7 (67.1, 95.5)	48.0 (41.6, 55.5)	<.001
Vasopressor use	14 (45.2%)	16 (51.6%)	
Vasopressor score[e]	5.0 (2.0, 12.0)	7.5 (5.0, 14.0)	.200
Barotrauma	3 (9.7%)	4 (12.1%)	1.0

PvCO2, partial pressure of carbon dioxide in mixed venous blood.

[a] Continuous data are in the form of mean (±SEM) or median (25th, 75th percentiles), and categorical data are in the form of n (%).

[b] Means are compared using a paired *t* test, and medians are compared using with a Wilcoxon signed rank test for paired data. Categorical variables are compared using a Fisher exact test.

[c] Arterial blood gas data available for 16 patients.

[d] Venous blood gas data available for determination of Pv_{CO_2} (partial pressure of carbon dioxide in mixed venous blood) in the 15 patients without arterial access.

[e] Vasopressor score = dopamine dose ($\mu g\ kg^{-1}\ min^{-1}$) × 1 + dobutamine ($\mu g\ kg^{-1}\ min^{-1}$) × 1 + epinephrine ($\mu g\ kg^{-1}\ min^{-1}$) × 100 + norepinephrine ($\mu g\ kg^{-1}\ min^{-1}$) × 100 + phenylephrine ($\mu g\ kg^{-1}\ min^{-1}$) × 100 + milrinone ($\mu g\ kg^{-1}\ min^{-1}$) × 10. Vasopressor score medians [interquartile range] reflect only the 18 patients ever exposed to these medications.

Comparison of normally distributed variables over time was conducted using a repeat-measure analysis of variance (ANOVA) and post hoc Tukey. Comparisons of nonnormally distributed variables over time were made using a 1-way Friedman rank sum procedure and a paired nonparametric statistic for repeat measures, followed by 2-tailed Wilcoxon matched-pairs test with a Bonferroni correction. All tests compared variables at 6, 12, 24, and 48 hours of HFPV to pretransition (0 hours) values. Significance is defined as $P < .05$ for all analyses after correction for multiple testing. Calculations were performed in SigmaPlot 11.0 (Systat Software Inc, San Jose, Calif).

3. Results

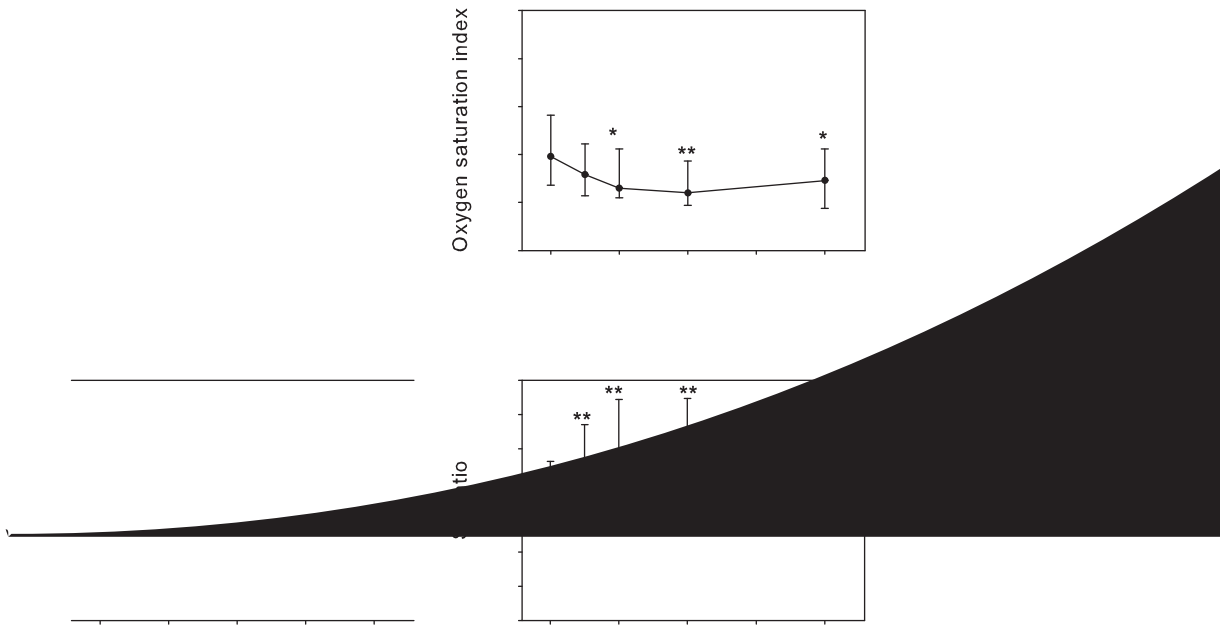
3.1. Patient characteristics and illness severity before initiation of HFPV

Thirty-one patients with ARF who failed conventional mechanical ventilation were treated with HFPV during the 15-month study period (48.4% male), with a median age of 1.6 (0.6, 6.8) years (Table 1). Three patients (9.7%) were managed with high-frequency oscillatory ventilation (HFOV) before initiation of HFPV. Fifteen patients (48%) transitioned from pressure-controlled conventional ventilation, with the remaining 16 patients transitioning from pressure-regulated volume control using a decelerating waveform. The etiology of lung injury in our population (Supplementary Table 1) was predominantly respiratory infection (67.7%). Bacterial and viral pneumonia comprised most of diagnoses (58%). Secondary lung injury from infectious complications occurred in 2 patients, one from *Klebsiella* bacteremia with septic shock and a second from septic emboli from Lemierre disease. Before initiation of HFPV, 6 of 31 patients met the suggested noninvasive oxygenation criteria [24] for mild (SF ratio <264), and 19 of 31 met the suggested criteria for moderate/severe (SF ratio <221) acute respiratory distress syndrome (ARDS). Of the 16 patients with arterial catheters and available Pao_2 data, 15 had a PF ratio less than 200, suggesting more severe lung disease in this subgroup. The median duration of conventional ventilation before transition to HFPV was 1 (0, 4) day. Adjunctive respiratory treatments used before HFPV initiation are detailed in Table 1, with the most common being continuous neuromuscular blockade (51.6%) and inhaled nitric oxide (29.0%).

Median PRISM III score was 6.5 (1, 11), and 6 patients (19.4%) were immunocompromised, reflecting a moderately ill pediatric population. Preexisting comorbid conditions are detailed in Supplementary Table 1. Six patients (19.4%) had underlying chronic lung disease defined by chronic oxygen requirement. One patient had a preexisting tracheostomy without ventilator dependence. No patients had baseline invasive mechanical ventilator support requirements. Four patients (12.9%) had previous organ or stem cell transplantation. Vasopressors were used in 18 (58.1%) patients, with similar vasopressor scores before and after transition to HFPV ($P = .20$ Wilcoxon signed rank test).

3.2. Clinical outcomes

Patients received a median of 4 (2.3, 6) days of HFPV and were ventilated for a median of 16 (10, 22.8) days. The observed frequency of barotrauma as defined by new pneumomediastinum or pneumothorax was not significantly different before and after transition to HFPV ($P = 1.0$, Fisher exact test). Overall mortality was 5 (16.1%) of 31 patients, which represented 5 of the 6 immunocompromised patients. In 3 patients, persistent inadequate oxygenation or patient-ventilator dyssynchrony refractory to neuromuscular blockade led to discontinuation of HFPV (Table 1). One of these patients was transitioned to HFOV, and 2 patients were transitioned to extracorporeal support.



3.3. Respiratory outcomes

Gas exchange was evaluated before and after transition to HFPV. Sixteen of the 31 patients possessed arterial catheters (Table 2), allowing measurement of OI and PF ratios. For all 31 patients, OSI and SF ratios were used to assess response to HFPV. Peak inflating and mean airway pressures were compared for all patients before and after transition to HFPV.

Oxygenation and ventilation both significantly improved after initiation of HFPV. Oxygenation index decreased from a mean of 18.7 (±2.2) to 11.7 (±1.6) at 12 hours of HFPV and remained significantly lower than pre-HFPV levels throughout the 48 hours of measurement. This was paralleled by similar improvements in OSI, PF, and SF ratios (Table 2; Fig. 2). Oxygenation improvement was achieved without an increase in mean airway pressure (Table 2; Figure 3). Significant reduction of $Paco_2$ from a mean of 84.1 (±11.7) to 55.1 (±8.9) mm Hg was achieved by 6 hours after initiation of HFPV and remained significantly lower for 48 hours (Table 2; Fig. 4). Importantly, the peak-inflating pressures required to achieve ventilation were also significantly reduced at 6 hours after HFPV initiation from a median of 38 (29.5, 41.3) to 30 (26, 32) cm H_2O, with sustained reduction through 48 hours (Table 2; Fig. 3).

Improvements in oxygenation and ventilation on HFPV were not associated with a significant increase in the use of neuromuscular blockade or inhaled nitric oxide (Table 2). The 5 patients with initiation of inhaled nitric oxide concurrent with transition to HFPV were analyzed separately and showed substantial but statistically insignificant improvements in all oxygenation parameters (Table 2). The remaining 26 patients had significant improvements in OSI, SF ratio, and $Paco_2$ and insignificant improvements in OI and PF ratio (Table 2). High-frequency percussive ventilation initiation did not result in more air leaks, increased vasopressor requirement, or higher vasopressor scores (Table 2).

4. Discussion

The major finding of this study is the significant improvement in gas exchange with HFPV at lower peak-inflating pressures in pediatric patients with ARF caused by heterogeneous primary and secondary lung insults. Importantly, oxygenation improved without an increase in mean airway pressures. Lower peak pressure was achieved and sustained during the 48 hours after initiation of HFPV.

Although this mode of ventilation has been used in clinical practice for several decades, its reported use in pediatrics has been limited to patients with smoke inhalational injury [9,10,16-18]. Carman et al [16] studied 64 pediatric burned patients randomized to HFPV or conventional ventilation managed with a low-tidal volume strategy. High-frequency percussive ventilation improved oxygenation at lower peak-inflating pressures when compared with conventional. No significant differences were noted in other outcome measures, including sepsis, pneumonia, ARDS incidence, or mortality.

High-frequency percussive ventilation has been described in the adult population in scenarios ranging from polytrauma with ARDS to inhalational injuries. A recent prospective trial in adult burned patients randomized 62 patients to HFPV or conventional ventilation at admission [15]. The HFPV group demonstrated significantly improved oxygenation with lower peak-inflating pressures during the first 48 hours after initiation with no significant change in hemodynamics or clinically evident barotrauma. There were no differences in ventilator-free days or mortality. Cioffi et al [8] reported a series of 54 burned patients with inhalation injury placed on “prophylactic” HFPV within 1 hour of admission to the hospital, compared results in this population with historical controls, and found that the HFPV group had a significantly lower incidence of pneumonia and improved mortality.

Part of the reluctance to apply this mode to traditional ARDS may be due to the inability to accurately record delivered tidal volumes on HFPV, a shortcoming shared by other modes of high-frequency ventilation, including high-frequency oscillation and high-frequency jet ventilation [27]. This raises the concern that dangerously high-tidal volumes may be delivered unmonitored, risking volutrauma and worse outcomes in this population. Despite this, HFPV has been studied as salvage therapy for adult ARF and ARDS refractory to other modes of ventilation [11-14,28,29]. In a prospective trial of 100 adults with ARF, patients were randomized to conventional mechanical ventilation or HFPV and treated to predefined respiratory parameters. Each group met predefined gas exchange end points; however, the subset of patients with ARDS treated with HFPV maintained significantly lower airway pressures when compared with the ARDS group managed with conventional ventilation. There were no reported differences between the 2 groups in mortality or hospital length of stay [30].

Limitations of this study are inherent to the single-center, retrospective nature of this report. Approaches to conventional ventilation and ventilator escalation were subject to the clinician's discretion before transition to HFPV. Respiratory adjuncts were used in differing order and for varied durations before initiation of HFPV. Strengths of this study include the heterogeneity of disease processes in this data set that accurately represents the pediatric patient population with ARF and the magnitude and consistency of the

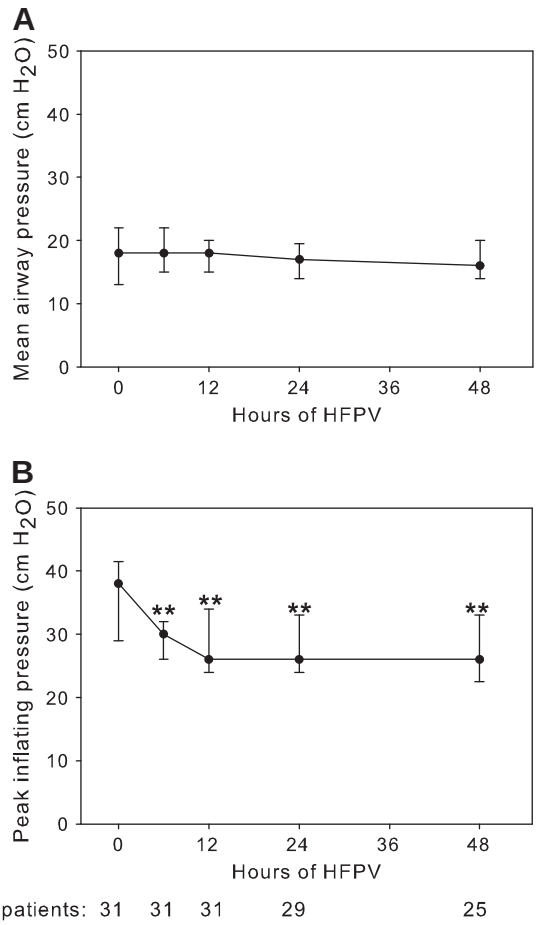


Fig. 3. Changes in mean airway pressure (A) and peak-inflating pressure (B) after 48 hours of HFPV in patients failing conventional mechanical ventilation (n = 31). The first measurement represents values of these variables just before initiation of HFPV (0 hours). Measurements are taken at 6, 12, 24, and 48 hours after HFPV initiation. Values are expressed as median (25th, 75th percentiles), and comparison of these variables over time was made using a 1-way Friedman rank sum procedure and a paired nonparametric statistic, followed by 2-tailed Wilcoxon matched-pairs test with a Bonferroni correction. All tests compared variables at 6, 12, 24, and 48 hours of HFPV to pretransition (0 hours) values. $^{**}P < .01$ after correction for multiple testing. The number of patients still on HFPV at each time point is given below.

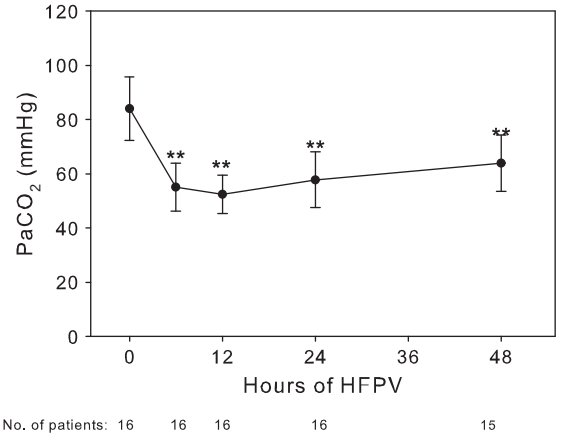


Fig. 4. Changes in $Paco_2$ after 48 hours of HFPV in patients failing conventional mechanical ventilation (n = 16 patients with arterial blood gas data available). The first measurement represents $Paco_2$ just before initiation of HFPV (0 hours). Measurements are taken at 6, 12, 24, and 48 hours after HFPV initiation. Values are expressed as mean (±SEM), and comparison over time was conducted using a repeated-measure ANOVA and a post hoc Tukey honestly significant difference (HSD). All tests compared variables at 6, 12, 24, and 48 hours of HFPV to pretransition (0 hours) values. $^{**}P < .01$ after correction for multiple testing. The number of patients still on HFPV at each time point is given below.

response to HFPV. Patients had significant oxygenation defects before transition, and despite lack of a standardized ventilator escalation protocol, transition to HFPV occurred fairly early in patients' course while on escalating conventional ventilation settings. It is possible that these patients would have had improved gas exchange with reduced peak airway pressures had they remained on conventional ventilation. However, at the time of transition to HFPV, all were failing to meet oxygenation and ventilation goals with lung-protective settings on conventional ventilation, and it was this failure that prompted a transition to HFPV. The retrospective, noncontrolled nature of the study precludes firm conclusions regarding the benefits of HFPV leading to improved gas exchange at lower peak-inflating pressures but does support a future prospective investigation of HFPV vs other modes of nonconventional ventilation for pediatric ARF failing conventional. Finally, the use of noninvasive measures of oxygenation, such as SF ratio and OSI, allowed us to extract meaningful data from nearly twice the number of patients than reliance on arterial blood gas data alone would have allowed. This requirement for invasive arterial sampling has limited recruitment in several pediatric studies of ARF [23,31], and our study represents an example of reliable noninvasive markers based on pulse oximetry, thereby facilitating pediatric ARF research.

5. Conclusions

Use of HFPV results in a consistent and sustained improvement in oxygenation and ventilation at reduced peak-inflating pressure in pediatric ARF, achieving goals consistent with lung-protective ventilation. Oxygenation improved without increased mean airway pressure. Further prospective studies are needed to define the population that can be maximally benefited by HFPV, to identify the optimal time for initiation, and to better elucidate secondary benefits that may be gained by airway clearance.

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.jcrc.2013.11.009.

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