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High-Frequency Jet Ventilation in Infants With Congenital Heart Disease

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BACKGROUND: High-frequency jet ventilation (HFJV) is primarily used in neonates but may also have a role in the treatment of infants with congenital heart disease and severe respiratory failure. We hypothesized that HFJV would result in improved gas exchange in these infants. METHODS: We retrospectively reviewed the records of all pediatric patients with complex congenital heart disease treated HFJV in our pediatric cardiac ICU between 2014 and 2018. Patients in whom HFJV was started while on extracorporeal membrane oxygenation (ECMO) were excluded. We extracted data on demographics, pulmonary mechanics, gas exchange, the subsequent need for ECMO, use of inhaled nitric oxide, and outcomes. RESULTS: We included 27 subjects (median [interquartile range {IQR}] weight 4.4 [3.3–5.4] kg; median [IQR] age 2.5 [0.3–5.4] months), 22 (82%) of whom had cyanotic heart disease. Thirteen subjects (48%) survived and 6 (22%) required ECMO. HFJV was started after a median (IQR) of 8.4 (2.1–26.3) d of conventional mechanical ventilation. The subjects spent a median (IQR) of 1.2 (0.5–2.8) d on HFJV. The median (IQR) pre-HFJV blood gas results ($n = 25$) were pH 7.22 (7.17–7.31), P_{aCO_2} 69 (51–77) mm Hg, and P_{aO_2} 51 (41–76) mm Hg. Median (IQR) initial HFJV settings were peak inspiratory pressure of 45 (36–50) cm H_2O, breathing frequency of 360 (360–380) breaths/min, and inspiratory time of 0.02 (0.02–0.03) s. Compared with conventional mechanical ventilation, at 4–6 h after HFJV initiation, there were significant improvements in the median pH (7.22 vs 7.34; $P = .001$) and P_{aCO_2} (69 vs 50 mm Hg; $P = .001$), respectively, but no difference in median P_{aO_2} (51 vs 53 mm Hg; $P = .97$). CONCLUSIONS: HFJV was associated with a decrease in P_{aCO_2} and an increase in pH in infants with congenital heart disease who remained on HFJV 4 to 6 h after initiation. *Key words: pediatric respiratory failure; high-frequency ventilation; jet ventilation; gas exchange; congenital heart disease; mechanical ventilation; ventilation.* [Respir Care 0;0 (0):1–●. © 0 Daedalus Enterprises]

Introduction

Infants with congenital heart disease often require mechanical ventilation for respiratory failure during the perioperative period. These infants may experience complex cardiopulmonary interactions, especially those infants with single ventricle physiology, intracardiac shunts, pulmonary hypertension, or concomitant lung disease.[1] In particular, infants with intracardiac shunts, pulmonary hypertension, or right heart dysfunction are uniquely sensitive to changes in pulmonary vascular resistance related to lung volumes, oxygenation, and changes in P_{aCO_2}.[2] Although most infants can be supported by conventional mechanical ventilation by using lung-protective settings, infants with complex cases of more severe respiratory failure may require high-frequency ventilation or extracorporeal life support.

High-frequency ventilation can be provided in the form of high-frequency oscillatory ventilation (HFOV), high-frequency percussive ventilation, or high-frequency jet ventilation (HFJV).[3] To date, HFJV has predominantly been used in neonatal ICUs.[4] Case series of HFJV outside of the neonatal ICU have demonstrated increased CO_2 clearance but no improvement in oxygenation.[5,6] Most patients in these case series had severe respiratory failure from viral illnesses, and patients with congenital heart disease were excluded. Small single-center studies of children with congenital heart disease conducted more than 3 decades ago demonstrated that HFJV was associated with improved hemodynamics and adequate gas exchange when using a lower mean airway pressure ($\overline{P}aw$).[7-10] The applicability of these early studies to modern practice is somewhat limited because inhaled nitric oxide is now used to treat pulmonary hypertension, and early extubation has emerged as the

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primary strategy in patients with passive pulmonary blood flow (eg, hemi-Fontan, Glenn, or Fontan circulation). Thus, there is a need to describe the use of HFJV in children with congenital heart disease in the current era. We hypothesized that HFJV would result in improved gas exchange, as measured by a decrease in P_{aCO_2}, in children with congenital heart disease who are unable to be supported with lung-protective conventional mechanical ventilation.

Methods

After institutional review board approval, we reviewed the medical records of all subjects admitted to our pediatric cardiac ICU who received HFJV between July 2013 and December 2018. Our pediatric cardiac ICU is a stand-alone unit with dedicated staff treating patients from birth to young adulthood. In our pediatric cardiac ICU, high-frequency ventilation is used as a rescue modality for eligible patients who cannot maintain adequate gas exchange with a conventional ventilator, or those who require unacceptably high peak inspiratory pressure. HFJV is generally our first choice of high-frequency ventilation in infants due to extensive institutional experience, although this varies, depending on the patient's physiology.[5,11] The subjects were identified through a search of electronic medical records. Premature infants with congenital heart disease cared for in the neonatal ICU were excluded. Patients were also excluded if HFJV was started during the course of extracorporeal membrane oxygenation (ECMO). Data were extracted by trained respiratory therapists (AGM, RMG, KEH) and critical care physicians (BLS, DALD) entered into a secure REDCap database. We collected data on subject demographics, the indication for mechanical ventilation, surgical history, pre-HFJV ventilator settings, pre-HFJV arterial blood gas measurements, initial HFJV settings, dynamic compliance, airway resistance, volume of exhaled carbon dioxide ($\dot{V}_{CO_2}$), subsequent need for ECMO, inhaled nitric oxide use, duration of HFJV support, time on mechanical ventilation, and survival. We stopped data collection if the subjects required transition to conventional mechanical ventilation, HFOV, or ECMO.

QUICK LOOK

Current knowledge

Infants with congenital heart disease may require mechanical ventilation for respiratory failure and/or during the perioperative period. These infants are characterized by having complex cardiopulmonary interactions, especially among those infants with single ventricle physiology, intracardiac shunts, pulmonary hypertension, lung disease, or lung injury. In our pediatric cardiac ICU, high-frequency jet ventilation (HFJV) is used as a rescue mode in the settings of inadequate gas exchange, air leak, pulmonary interstitial edema, or an inability to maintain lung-protective ventilation via conventional ventilator.

What this paper contributes to our knowledge

In infants with congenital heart disease and significant respiratory failure, HFJV was associated with an increase in pH and decrease in P_{aCO_2} for the subjects who remained on HFJV after 4–6 h. Mortality was 52%, and nearly half of the survivors required oxygen at discharge. A few subjects required another mode of ventilation or extracorporeal membrane oxygenation within 24 h of initiation of HFJV.

According to our standard practice, all the subjects were monitored continuously with the NM3 monitor (Phillips North America, Andover, Massachusetts) to measure dynamic compliance, airway resistance, tidal volume (V_T), and $\dot{V}_{CO_2}$, and we recorded the most recently documented values before HFJV initiation. Ventilator settings and arterial blood gas results were extracted before HFJV initiation and the first available parameters between 4–6 h, 24 h, and 48 h after HFJV initiation, and after the subjects were transitioned back to conventional mechanical ventilation. All the subjects were managed via a respiratory therapist-driven protocol both during conventional and high-frequency ventilation. No changes were made to the protocol during the study period. The conventional ventilator protocol targeted a V_T of 8–10 mL/kg for postoperative subjects for the first 24 h, then 6–8 mL/kg after 24 h. PEEP was managed via a PEEP/ F_{IO_2} table and the peak inspiratory pressure was maintained at $\leq$ 30 cm H_2O, with a target pH of 7.35–7.45. HFJV was conducted with a Bunnell LifePulse ventilator (Bunnell Incorporated, Salt Lake City, Utah) in

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Dr Rotta discloses relationships with Vapotherm and Breas US. Mr Miller serves as Section Editor for RESPIRATORY CARE. The other authors have disclosed no conflicts of interest.

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Table 1. Demographics, Clinical Characteristics, and Outcomes

Parameter	Result
Subjects, *N*	27
Age, median (IQR) mo	2.5 (0.3 – 5.4)
Weight, median (IQR) kg	4.4 (3.3 – 5.4)
Cyanotic heart disease	22 (81.5)
PIM2, median (IQR)	3.4 (2.1 – 9.1)
Postoperative (within 28 d of cardiac surgery)	14 (51.9)
Reason for mechanical ventilation	
Primary respiratory failure	17 (63.0)
Postoperative (within 28 d of cardiac surgery)	11 (40.7)
Cardiac arrest or other	2 (7.3)
Medical history	
Congenital heart disease	27 (100)
Cardiac surgery	16 (59.3)
Congenital syndrome	4 (14.8)
Chronic lung disease	2 (7.4)
Prematurity	1 (3.7)
Documented infection	
None	15 (55.6)
Bacterial	10 (37.0)
Viral	2 (7.4)
Outcomes	
Survived	13 (48.1)
Inhaled nitric oxide use	18 (66.7)
ECMO at any time	6 (22.2)
ECMO after HFJV	1 (3.7)
Oxygen at discharge	6 (46.2)
Time on mechanical before HFJV, median (IQR) d	8.4 (2.1–26.3)
Time on HFJV, median (IQR) d	1.2 (0.5–2.8)
Total time on mechanical ventilation, median (IQR) d	15.0 (10.8–27.8)

Data are presented as *n* (%) unless otherwise indicated.
IQR = interquartile range
PIM2 = Pediatric Index of Mortality 2
ECMO=extracorporeal membrane oxygenation
HFJV=high-frequency jet ventilation

tandem with an Avea ventilator (CareFusion, San Diego, California). In accordance with the HFJV protocol, $\overline{P}aw$ was titrated to optimum lung inflation, defined as 8 to 9 ribs of expansion of a bedside chest radiography, and oxygenation, the HFJV rate was adjusted to minimize air-trapping, back-up ventilator frequency was set to 3–5 breaths/min, and the goal pH was 7.35–7.45. Air-trapping was assessed by monitoring the set PEEP and making adjustments when there was a $\geq$ 2 cm H_2O difference between the set and PEEP measured by the HFJV ventilator.

Continuous data are presented as median (interquartile range), and categorical variables are presented as count (%). The paired Wilcoxon signed-rank test was used to compare changes in blood gas values before and after HFJV initiation. Due to potential for survivor bias, we did not evaluate changes in gas exchange or HFJV settings over time. We compared data between survivors and non-survivors by using the Mann-Whitney test for continuous variables and the chi-square test for categorical variables. Statistical significance was set at $P < .05$, and data were analyzed by using SPSS v24 (IBM, Chicago, Illinois).

Results

We identified 41 patients who received HFJV, with 14 having been on ECMO when HFJV was initiated. Therefore, 27 subjects met our inclusion criteria. The median (IQR) age of the included subjects was 2.5 (0.3–5.4) months, and the median (IQR) weight was 4.4 (3.3–5.4) kg. Twenty-two subjects (82%) had cyanotic heart disease, 14 (52%) were within 28 d of cardiac surgery, and 17 (63%) were on mechanical ventilation due to primary respiratory failure. The subjects were on mechanical ventilation for a median (IQR) of 8.4 (2.1–26.3) d before HFJV initiation and spent a median (IQR) of 1.2 (0.5–2.8) d on HFJV. The mortality rate was 52% (14 / 27), and 46% of the survivors (6/13) required oxygen at discharge. Demographic and outcome data are summarized in Table 1.

The pH was significantly higher (7.22 vs 7.34; $P = .001$) and P_{aCO_2} was significantly lower (69 vs 50 mm Hg; $P = .001$) when pre-HFJV measurements were compared with those taken at 4–6 h after HFJV initiation, respectively. Pre-HFJV arterial blood gas measurements, initial HFJV settings, arterial blood gas measurements at 4–6 h after HFJV, and HFJV settings at 4–6 h after initiation of HFJV are reported in Tables 2 and 3. Pre-HFJV ventilator settings were available in 23 of 27 subjects. The median (IQR) conventional mechanical ventilation settings before HFJV initiation were the following: a set breathing frequency of 30 (28–35) breaths/min, set inspiratory pressure of 22 (20–25) cm H_2O, set PEEP of 8 (6–10) cm H_2O, F_{IO_2} of 0.80 (0.53-1.00), $\dot{V}_{CO_2}$ of 31.1 (23.6–51.3) mL/min, compliance of 1.6 (1.2–2.5) mL/cm H_2O, airway resistance of 86.5 (61.3–133.0) cm H_2O/L/s, and V_T of 7.0 (5.2–8.9) mL/kg of actual weight.

After HFJV initiation, 23 subjects remained on HFJV for at least 4–6 h, 16 remained for >24 h, and 10 remained for >48 h. After 4–6 h of HFJV, 3 subjects transitioned to conventional mechanical ventilation and one was placed on ECMO. Twenty-four hours after HFJV initiation, 8 subjects were transitioned to conventional mechanical ventilation, 2 were transitioned to HFOV, and 1 subject required ECMO. At 48 h after HFJV initiation, 12 subjects transitioned to conventional mechanical ventilation, 2 transitioned to HFOV, 2 died, and 1 required ECMO. Ventilator settings and gas exchange data over time are included in Supplementary Table A (see the supplementary materials at

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Table 2. Pre- and Post-HFJV Arterial Blood Gas Measurements

Arterial Blood Gas Measurement	Before HFJV ($n = 25$)	4–6 h After HFJV ($n = 23$)	P
pH	7.22 (7.17–7.31)	7.34 (7.25–7.43)	.002
P_{aCO_2}, mm Hg	69 (51.0–76.5)	50.0 (41.0–69.0)	.001
P_{aO_2}, mm Hg	51.0 (41.0–76.0)	53.0 (43.0–66.0)	.97
Base excess, mEq/L	–2 (–3.5 to 2.0)	–1.0 (–3.0 to 2.0)	.15
HCO_3^-	28 (25.0–30.0)	27.0 (23.0–30.0)	.10

Data are presented as median (interquartile range).
HFJV=high-frequency jet ventilation

Table 3. Pre- and Post-HFJV Settings

Parameter	Initial HFJV Settings ($n = 27$)	HFJV Settings 4–6 h After Initiation ($n = 22^*$)	P
Measured $\bar{P}$aw, cm H_2O	15 (12–15)	14.1 (11.5–18.2)	.97
Peak inspiratory pressure, cm H_2O	45 (36–50)	41 (35–47)	.36
Breathing frequency, breaths/min	360 (360–380)	360 (300–360)	.008
Inspiratory time, s	0.02 (0.02–0.03)	0.02 (0.02–0.03)	.56
F_{IO_2}	1.00 (0.60–1.00)	0.80 (0.40–1.00)	.28

Data are presented as median (interquartile range).
* Unable to determine HFJV settings in 1 subject.
HFJV = high-frequency jet ventilation
$\bar{P}$aw = mean airway pressure

http://www.rcjournal.com). Subject outcomes over time are summarized in Figure 1.

Seventeen subjects (63%) were transitioned back to conventional mechanical ventilation. The median (IQR) HFJV settings immediately before transition back to conventional ventilation were the following: HFJV inspiratory pressure of 36 (27–46) cm H_2O, $\bar{P}$aw of 14 (11.5–19.5) cm H_2O, and F_{IO_2} of 0.60 (0.40–1.00). After HFJV, the median (IQR) conventional mechanical ventilation settings were a set breathing frequency of 28 (26–31) breaths/min, peak inspiratory pressure of 18 (17–22) cm H_2O, PEEP of 8.5 (6–10) cm H_2O, F_{IO_2} of 0.53 (0.40–1.00), and $\bar{P}$aw of 13 (12.0–15.5) cm H_2O. The median (IQR) measured values were V_T of 8.3 (6.2–8.9) mL/kg, $\dot{V}_{CO_2}$ of 36.3 (24.1–52.0) mL/min, compliance of 2.5 (1.6–3.6) mL/cm H_2O, and airway resistance of 69.0 (64.0–91.0) cm H_2O/L/s. The median (IQR) blood gas measurements after the transition revealed a pH of 7.36 (7.31–7.40), P_{aCO_2} of 54.0 (42.5–62.0) mm Hg, P_{aO_2} of 70 (39.0–107.0) mm Hg, and HCO_3^- of 30.0 (23.5–33.5) mEq/L.

There were no differences between survivors ($n = 13$) and non-survivors ($n = 14$) for age, weight, Pediatric Index of Mortality 2 score, indication for mechanical ventilation, medical history, documented infection, or the presence of cyanotic heart disease. Non-survivors versus survivors were more likely to have received ECMO (43% vs 0%; $P = .01$), but there were no differences in the use of inhaled nitric oxide. Six non-survivors were transitioned to conventional mechanical ventilation and died later in their stay, 3 died while on HFJV, 2 while on HFOV, and 1 while on ECMO, and 2 had withdrawal of life support. There were no differences in pH, P_{aCO_2}, P_{aO_2} HCO_3^-, pre-HFJV ventilator settings, pre-HFJV lung mechanics, or initial HFJV settings between survivors and non-survivors. Data that compared survivors and non-survivors are summarized in Table 4 and Supplementary Table B (see the supplementary materials at http://www.rcjournal.com).

Discussion

In this study of infants with congenital heart disease and respiratory failure for whom conventional mechanical ventilation failed, we found that HFJV was associated with an increase in pH and decrease in P_{aCO_2} for the subjects who remained on HFJV after 4 - 6 h. Mortality was 52%, and nearly half of the survivors required oxygen at discharge. Only 3 subjects required another high-frequency mode of ventilation or ECMO within 24 h of HFJV initiation. The non-survivors were more likely to require ECMO, although our study was underpowered to detect other differences between the 2 groups.

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The mortality rate in our study was higher than that in previous studies of HFJV in infants with severe respiratory failure, likely because our cohort included infants at higher risk and with complex congenital heart disease who had been excluded in previous reports.[5,6] In addition, HFJV was started later in the course of mechanical ventilation than in our previous study,[5] although it is unclear whether this could have influenced the outcomes. Only 2 subjects in our study had documented viral infection, which contrasted to much higher rates (63% to 100%) reported in recent studies of HFJV.[5,6] The primary indication for mechanical ventilation in those studies was respiratory failure, but this represented just over half of our patient cohort. Infants with respiratory failure from viral illness are expected to have an overall lower risk of mortality.[12] The higher mortality in our study likely reflects the proportion of subjects with very complex cardiac physiology who would be expected to have an higher risk of mortality than a cohort composed predominantly of subjects with bronchiolitis.[13] Thus, this high mortality rate may be related to sequalae of cardiac surgery, complex cardiopulmonary physiology, and/or inoperable and/or nonsurvivable cardiac lesions, and not necessarily failure of HFJV as a respiratory support modality. We did not record the cause of death in our subjects because we were primarily interested in the effect of HFJV on gas exchange; our sample size was too small to make inferences about the effect of HFJV on patient-oriented outcomes, for example, mortality.

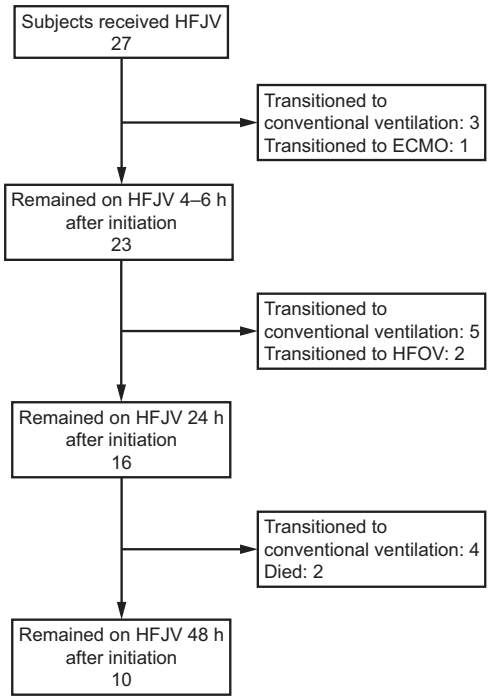

Fig. 1. Flow chart.

Early studies in infants with congenital heart disease published in the 1980s and 1990s demonstrated salutary effects of HFJV on hemodynamics, while achieving comparable gas exchange with a lower $\overline{P}aw$ relative to conventional ventilation.[7-10] A single study of HFJV as a rescue mode demonstrated success in subjects who met pulmonary criteria for ECMO.[7] However, that study predated the use

Table 4. Comparison of Survivors and Non-Survivors

Parameter	Survivors ($n = 13$)	Non-Survivors ($n = 14$)	P
Age, mo	2.6 (0.2 – 5.8)	2.6 (0.3 – 5.5)	.87
Weight, kg	4.4 (3.1 – 5.6)	4.4 (3.3 – 5.4)	.83
Time on mechanical ventilation before HFJV, d	7.8 (1.3 – 14.5)	14.2 (3.6 – 33.1)	.59
ECMO at any time, *n* (%)	0 (0)	6 (42.9)	.01
Medical and surgical history, *n* (%)			
Cardiac surgery	9 (69.2)	5 (35.7)	.08
Cyanotic heart disease	12 (92.3)	10 (71.4)	.16
Within 28 d of surgery	5 (38)	7 (50)	.18
Pre-HFJV arterial blood gas			
pH	7.28 (7.18 – 7.32)	7.20 (7.17 – 7.24)	.27
P_{aCO_2}, mm Hg	64.0 (52.5 – 79.0)	70.0 (50.0 – 76.5)	.81
P_{aO_2}, mm Hg	50.0 (40.0 – 72.5)	56.5 (42 – 81.3)	.47
Post-HFJV arterial blood gas			
pH	7.36 (7.24 – 7.46)	7.33 (7.28 – 7.42)*	.55
P_{aCO_2}, mm Hg	52.0 (40.8 – 69.3)	46 (40.3 – 57.8)*	.51
P_{aO_2}, mm Hg	48.0 (38.0 – 63.3)	60.0 (44.5 – 72.0)*	.21

Data are presented as median (interquartile range) unless otherwise noted.
*$n = 10$
HFJV = high-frequency jet ventilation
ECMO = extracorporeal membrane oxygenation

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of inhaled nitric oxide, and hyperventilation was used as a treatment for pulmonary hypertension.[7] In our study, HFJV was used largely as a rescue modality in the subjects with respiratory acidosis and not for compromised hemodynamics. A previous study from the same institution used HFJV in subjects after a Fontan operation[8]; however, current postoperative management of patients with passive pulmonary blood flow centers on early extubation and avoidance of positive-pressure ventilation. Furthermore, it may not be possible for current HFJV ventilators to support the larger subjects (mean 13.9 kg) managed in that study.[8]

Our study shows that HFJV was associated with improved P_{aCO_2} in infants with congenital heart disease for whom conventional mechanical ventilation failed. A small minority of the subjects required transition to HFOV or ECMO, in contrast with our results from our pediatric ICU, where 43% of subjects required other support modalities.[5] This could have been related to selection bias, reluctance in using other high-frequency modalities, or rapid resolution of the underlying disease process that required HFJV. Only 10 subjects required HFJV for >48 h, which suggests that the underlying cause may have resolved rapidly in many of the subjects. This may reflect unique characteristics of infants with congenital heart disease compared with more protracted resolution of primary lung disease seen in our pediatric ICU cohort.[5]

Future studies of HFJV should prospectively evaluate the effect of HFJV on hemodynamic parameters, lung volumes by using electric impedance tomography, lung ultrasound, and near-infrared spectroscopy, in addition to gas exchange. In particular, investigations of strategies to select PEEP or $\overline{P}aw$ to guide clinicians in setting these parameters are needed because the effect of PEEP and $\overline{P}aw$ may be amplified in infants with complex congenital heart disease. Also, further research should focus on identifying thresholds of peak inspiratory pressure, plateau pressure, and driving pressure for when to initiate high-frequency ventilation. Multi-center studies or a large HFJV registry is needed to increase the generalizability of future studies of HFJV. Studies of HFJV, including ours, are limited by sample size and are potentially biased by individual center clinical practice and experience.[3-6,14,15] Given the rarity of HFJV use outside of the neonatal ICU, a multi-center database of subjects who received HFJV in the pediatric ICU and pediatric cardiac ICU is warranted. This would allow increased sample sizes and comparisons of outcomes between centers while identifying risk factors for HFJV failure. This proposed collaboration could include all ventilator modes currently used for rescue in pediatric subjects and would allow more robust statistical treatments that would better inform the field.[3] Such a registry could be modeled after the HFOV database used by the Pediatric Acute and Critical Care Medicine Asian Network, which has recently provided us with valuable insight into the use of HFOV in pediatric ARDS.[16]

Limitations

Our study had several limitations. First, due to the retrospective nature of our data collection, we were limited to information that was available in the medical record. Second, although we were able to make descriptive observations on the effect of initiating HFJV, our relatively small sample size precluded us from performing more-sophisticated comparisons or a multivariable analysis. Third, adverse events, such as development of a pneumothorax or the effect of HFJV on hemodynamics, were not consistently recorded and, therefore, not analyzed. Fourth, we were unable to calculate driving pressure for this cohort because the plateau pressure was not consistently documented for all the subjects. Fifth, we could not assess the effect of HFJV on oxygenation because our cohort had a high percentage of subjects with single ventricle physiology in whom the calculation of a P_{aO_2}/F_{IO_2} or oxygenation index would be misleading due to right-to-left shunting or complete intracardiac mixing. Sixth, given the small sample size and our center's extensive experience in the use of HFJV, our results may not be generalizable to other centers where this modality is not commonly used.

Conclusions

In a cohort of infants with congenital heart disease for whom conventional mechanical ventilation failed, HFJV was associated with decreased P_{aCO_2} 4–6 h after initiation. Few subjects required other high-frequency modalities, and hospital mortality was 52%.

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