

Early High Frequency Oscillatory Ventilation in Pediatric Acute Respiratory Failure

AHMED M. ABD-ELGAWAD, M.Sc.; KHALED T. ABU-EALA, M.D.; SAHAR A. ABD-ELAZIZ, M.D. and AHMED I. HARKAN, M.D.

The Department of Pediatrics, Faculty of Medicine, Tanta University

Abstract

Background: High frequency oscillatory ventilation (HFOV) has been a staple in the management of children with acute respiratory failure (ARF). HFOV is a mode of mechanical ventilation that recruits diseased lung and improves oxygenation through the use of high mean airway pressures with tidal volumes less than anatomic dead space. Although HFOV is commonly used in children, efficacy data are limited and predate the era of low tidal volume (V_t) conventional mechanical ventilation (CMV).

Aim of the Study: It was to compare the impact of early high frequency oscillatory ventilation (within 24-48 hours of endotracheal intubation) to conventional mechanical ventilation and/or late high frequency oscillatory ventilation in children with acute respiratory failure.

Patients and Methods: The study was carried out on thirty patients with acute respiratory failure (ARF) who attended to the pediatric intensive care unit, Pediatric Department, Tanta University Hospital. All studied children were subjected to detailed history taking, complete physical examination, monitoring of SV, SVI, CO, CI, SVR, SVRI through trans-esophageal doppler monitoring and oxygenation index.

Results: There was significant decrease of O₂Sat of Early HFOV group compared with P-CMV and Late HFOV. there was significant increase of O₂Sat in Early HFOV in 2nd and 3rd days compared with 1st day There was significant decrease of oxygenation index in late HFOV and P-CMV groups compared with Early HFOV group. It is one of most important prognostic factors for detection timing of HFOV according to ROC curve.

Conclusion: As hypoxia worsened, patient percentage with Early HFOV increased Oxygenation index was significant as a predictor and prognostic factor for early HFOV success.

Key Words: HFOV – Trans-esophageal doppler monitoring of CO.

Introduction

HIGH frequency oscillatory ventilation (HFOV) has been a staple in the management of children with acute respiratory failure (ARF). HFOV is a mode of mechanical ventilation that recruits diseased lung and improves oxygenation through the use of high mean airway pressures with tidal volumes less than anatomic dead space. Although HFOV is commonly used in children, efficacy data are limited and predate the era of low tidal volume (V_t) conventional mechanical ventilation (CMV) [1]. Cardiac output (CO) is the volume of blood that is pumped by the heart around the systemic circulation in one minute [2]. The interplay of preload, contractility, heart rate and afterload results in CO control [3].

Continuous mandatory ventilation (CMV) may be insufficient to maintain adequate gas exchange in seriously ill patients and may also cause or aggravate lung injury. HFOV has been used to improve gas exchange in patients who cannot be adequately ventilated by conventional means, while limiting lung injury [4].

Theoretically, HFOV achieves the goals of protective ventilation by optimizing alveolar recruitment through sustained high mean airway pressures, while avoiding lung trauma associated with the swings in pressure associated with conventional methods [5].

Although HFOV is used frequently in ICUs, there are few systematic studies of its hemodynamic (HD) effects 14 years ago. The results of studies using different experimental models have not been consistent. So, it remains unclear as to what, if any, HD consequences should be anticipated when switching from CMV to HFOV [6]. It is known from numerous animal and human studies that

Correspondence to: Dr. Ahmed M. Abd-Elgawad, The Department of Pediatric, Faculty of Medicine, Tanta University

increasing mean airway pressure during CMV adversely affects CO. This reduction in CO could adversely affect oxygen delivery and potentially be harmful. Studies on the effect of HFOV on CO have produced conflicting results. HFOV has been reported not to alter left ventricular output (LVO) in experimental studies and in children [7]. The timing of introduction of HFOV and the claims of its better physiological effects raise the questions on its other effects on HD comparing it to CMV.

Aim of the work:

It was to compare the impact of early high frequency oscillatory ventilation (within 24-48 hours of endotracheal intubation) to conventional mechanical ventilation and/or late high frequency oscillatory ventilation in children with acute respiratory failure.

Patients and Methods

This prospective study was carried out upon 30 pediatric patients with ARF (aged from 2-108 months) admitted in PICU, Tanta University Hospital. The duration of research was from December 2016 to December 2017

Patients were divided into 3 groups: Group I (Early HFOV): Fifteen patients were monitored on HFOV. Group II (Late HFOV): Five patients were monitored on HFOV (24hr post-intubation). Group III (P-CMV): Ten patients were monitored on P-CMV. Exclusion criteria: Patient to be extubated within 24 hours. Patients suffering from cardiac arrhythmias. Severe valvular regurgitation (severe aortic and mitral regurgitation) and Complex congenital heart disease.

All the studied patients were subjected to the following: Full history taking, clinical examination, routine investigations (complete blood count, c-reactive protein), scoring systems for patients (PRISM III and SOFA), monitoring of SV, SVI, CO, CI, SVR, SVRI through trans-esophageal doppler monitoring and oxygenation index.

Statistical presentation and analysis of the present study was conducted using the mean, standard deviation, student *t*-test, Chi-square test with $p < 0.05$ means significance, Regression analysis and ROC curve

Results

This prospective study was carried out upon 30 pediatric patients with ARF admitted in PICU, Tanta University Hospital, all patients were cross matched for age and sex.

Table (1) show that regarding demographic and anthropometric data of the Studied Patients. There was no statistically significant difference throughout the study between the studied groups as regard age, sex, height and weight.

Table (1): Demographic and laboratory data of the studied groups.

Table (2): Comparison of Oxygen Saturation (%) between the Studied Groups.

There was statistically significant decrease of O₂Sat of Early HFOV compared with P-CMV and Late HFOV in 1st 2nd and 3rd days.

Comparison inside each group:

- There was statistically significant increase in Early HFOV in 2nd and 3rd days compared with 1st day.
- There was statistically significant increase in Late HFOV in 2nd and 3rd days compared with 1st day.
- There was statistically significant increase in P-CMV in 2nd and 3rd days compared with 1st day.

Table (3): Comparison of Oxygenation Index between the Studied Groups.

There was statistically significant decrease in late HFOV and P-CMV groups compared with Early HFOV group in the 1st, 2nd and 3rd days.

Fig. (1) show that regarding Oxygenation index:

There was statistically significant decrease in late HFOV in 3rd days compared with 1st day.

There was statistically significant decrease in P-CMV in 3rd days compared with 1st and 2nd days.

Table (4): Show that regarding Univariate and Multivariate Analysis for the Parameters Affecting Early high frequency oscillatory ventilation:

Oxygenation index was significant as a predictor for early HFOV success.

Fig. (2): ROC curve for oxygenation index to prognosis cases early high frequency oscillatory ventilation.

Oxygenation index was significant with cut off value >13, sensitivity 73.33, specificity 66.67, PPV 68.7 and NPV 71.4.

Table (1): Comparison of demographic data between the studied groups.

	HFOV (n=20)				P-CMV (n=10)		Test of sig.	P
	Early (n=15)		Late (n=5)		No.	%		
	No.	%	No.	%				
Sex:								
Male	7	46.7	2	40.0	5	50.0	$\chi^2=0.274$	MCP=1.000
Female	8	53.3	3	60.0	5	50.0		
Age (month):								
Min.-Max.	2.50-24.0		2.50-40.0		2.0-108.0		H=0.563	0.755
Mean ± SD	8.83±5.81		15.10± 15.06		21.90±32.64			
Median	8.0		9.0		10.0			
Height (cm):								
Min.-Max.	55.0-90.0		55.0-95.0		50.0-140.0		F=1.355	0.275
Mean ± SD	65.87±9.83		73.0± 18.15		78.50±27.99			
Median	62.0		63.0		72.50			
Weight (Kg):								
Min.-Max.	3.50-15.0		5.0-15.0		3.0-25.0		H=1.998	0.368
Mean ± SD	7.03±3.43		8.80±4.44		10.25±6.45			
Median	6.0		6.0		9.50			

χ^2, p : χ^2 and p values for Chi square test for comparing between the three groups.
 MCP : p-value for Monte Carlo for Chi square test for comparing between the three groups.
 H, p : H and p-values for Kruskal Wallis test.
 F, p : F and p-values for ANOVA test.
 CMV : Conventional mechanical ventilation.
 HFOV : High frequency oscillatory ventilation.
 Data are represented as mean±SD.

Table (2): Comparison of Oxygen Saturation (%) between the Studied Groups.

O ₂ Sat	1 st day	2 nd day	3 rd day	F	p
HFOV early:					
Min.- Max.	70.0-73.0	68.0-80.0	67.0-87.0	4.983*	0.014*
Mean ± SD	71.93±1.28	74.20±4.71	76.33±8.18		
Median	72.0	75.0	80.0		
Sig. bet. periods.	$p_3=0.048*, p_4=0.041*, p_5=0.044*$				
HFOV late:					
Min.- Max.	55.0-70.0	77.0-95.0	83.0-95.0	43.240*	<0.001 *
Mean ± SD	63.80±6.06	86.80±7.63	90.20±4.76		
Median	63.0	85.0	92.0		
Sig. bet. periods.	$p_3=0.002*, p_4=0.002*, p_5=0.226$				
P-CMV:					
Min. - Max.	50.0-70.0	93.0-100.0	93.0-100.0	282.148*	<0.001 *
Mean ± SD	63.90±6.77	96.10±2.08	96.30±2.0		
Median	66.50	96.0	96.50		
Sig. bet. periods.	$p_3<0.001*, p_4<0.001*, p_5=0.619$				
F2	11.309*	68.163	32.170		
p2	<0.001*	<0.001*	<0.001*		

F1, p1 : F and p-values for ANOVA with repeated measures test for comparing between different periods.
 F2, p2 : F and p-values for ANOVA test for comparing between the three groups.
 p3 : p-value for 1st day and 2nd day.
 p4 : p-value for 1st day and 3rd day.
 p5 : p-value for 2nd day and 3rd day.
 *5 : Statistically significant at p≤0.05.
 CMV : Conventional mechanical ventilation.
 HFOV : High frequency oscillatory ventilation.

Table (3): Comparison of oxygenation index between the studied groups.

Oxygenation index	1st day	2nd day	3rd day	Fr χ^2	p ₁
<i>HFOV early:</i>					
Min.– Max.	13.0–17.0	8.0–18.0	5.0–20.0		
Mean \pm SD	14.67 \pm 1.45	13.07 \pm 3.84	12.60 \pm 5.89	0.414	0.813
Median	14.0	12.0	10.0		
<i>HFOV late:</i>					
Min.– Max.	11.0–14.0	6.0–11.0	5.0–9.0		
Mean \pm SD	11.80 \pm 1.30	8.60 \pm 1.82	7.16 \pm 2.01	9.579*	0.008*
Median	11.0	9.0	8.0		
Sig. bet. periods.	$p_3=0.082, p_4=0.003^*, p_5=0.206$				
<i>P-CMV:</i>					
Min. – Max.	10.0–16.10	8.0–15.60	5.0–11.0		
Mean \pm SD	12.75 \pm 1.94	11.52 \pm 2.37	6.90 \pm 1.97	16.200*	<0.001*
Median	12.30	11.50	7.0		
Sig. bet. periods.	$p_3=0.044^*, p_4<0.001^*, p_5=0.044^*$				
H	10.095*	6.256	7.257		
p ₂	0.006*	0.044*	0.027*		

Fr χ^2, p_1 : Chi square and *p*-value for Friedman test for comparing between different periods in each group
H, p₂ : H and *p*-values for Kruskal Wallis test
p³ : *p*-value for 1st day and 2nd day
p⁴ : *p*-value for 2nd day and 3rd day
p⁵ : *p*-value for 1st day and 3rd day
* : Statistically significant at *p*≤0.05
P-CMV : Conventional mechanical ventilation
HFOV : High frequency oscillatory ventilation

Table (4): Univariate and multivariate analysis for the parameters affecting early high frequency oscillatory ventilation.

	Univariate		#Multivariate	
	<i>p</i>	OR (95% C. I)	<i>p</i>	OR (95% C. I)
Sex (Female)	1.000	1.000 (0.238–4.198)		
Age (month)	0.214	0.951 (0.877–1.030)		
Height	0.148	0.964 (0.916–1.013)		
Weight	0.140	0.868 (0.719–1.047)		
Hb	0.396	0.835 (0.550–1.266)		
WBCs (x10 ³)	0.293	0.923 (0.795–1.072)		
PLTs (x10 ³)	0.871	1.001 (0.992–1.010)		
CRP	0.681	0.991 (0.948–1.035)		
MABP (mmHg)	0.833	1.006 (0.952–1.063)		
Oxygenation index	0.007*	2.306 (1.527–4.229)	0.010*	2.300 (1.216–4.349) @
O ₂ Sat	0.993	–		
CO	0.122	0.186 (0.022–1.567)		
CI	0.826	0.902 (0.359–2.265)		
SV	0.124	0.183 (0.021–1.590)		
SVI	0.162	0.861 (0.699–1.062)		
SVR	0.268	1.000 (1.0–1.0)		
SVRI	0.512	1.000 (1.0–1.0)		
TI	0.999	–		

OR: Odd's ratio. C.I: Confidence interval. # : All variables with *p*<0.05 was included in the multivariate.
@ : Adjust Odd's ratio by age and sex. * : Statistically significant at *p*≤ 0.05.

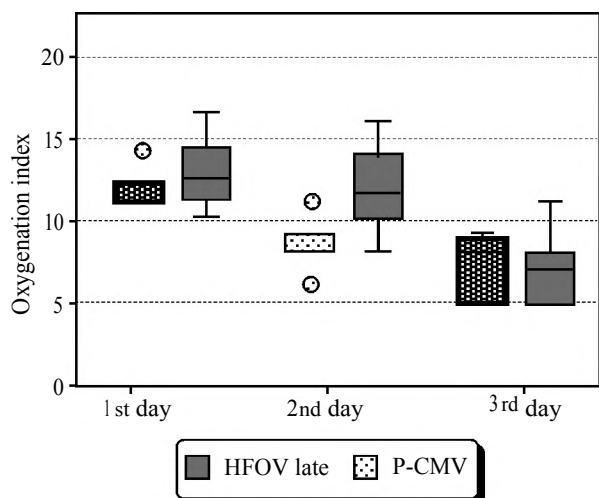


Fig. (1): Comparison of oxygenation index between studied groups.

Discussion

For over 20 years, high frequency oscillatory ventilation has been a staple in the management of children with acute respiratory failure. HFOV is a mode of mechanical ventilation that recruits diseased lung and improves oxygenation through the use of high mean airway pressures with tidal volumes less than anatomic dead space. Although HFOV is commonly used in children, efficacy data are limited and predate the era of low tidal volume conventional mechanical ventilation [8].

A commonly accepted strategy for initiation of HFOV is to maximize airway recruitment by placing a patient on an oscillatory ventilator at a MAP higher than P-CMV. In this "high-volume" strategy, the patient is ventilated at a higher MAP, but with less PIP and less VT variation [9].

The negative impact on CO made by P-CMV is secondary to decreased venous return, compression of the pulmonary vascular bed, and a shift of the interventricular septum. This negative impact could be worsened by HFOV because higher MAP is used. Because patients who are candidates for HFOV often have hemodynamic compromise, they may not tolerate a significant alteration in their CO [10].

The objective of this study was to compare the effects of early HFOV versus late HFOV and P-CMV on some HD parameters in critically ill children admitted to Tanta PICU. It was carried out on 30 children, 15 males, 15 females, from 2 to 108 months. Patients were divided into three groups: Group I (Early HFOV), Group II (Late HFOV) and Group III (P-CMV): Each group was hemodynamically monitored for three consecutive

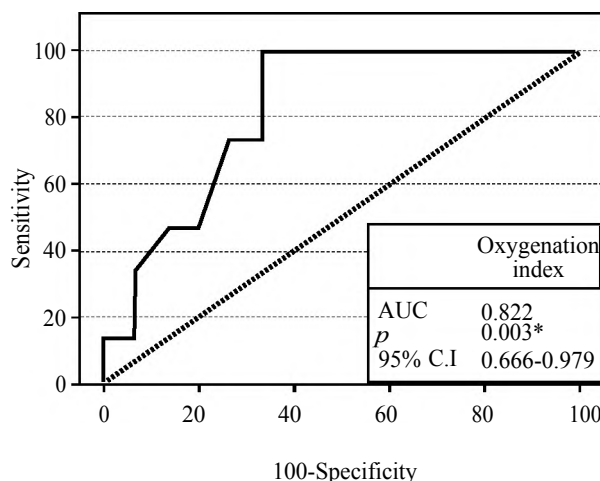


Fig. (2): ROC curve for oxygenation index to prognosis cases early high frequency oscillatory ventilation

days. This study was conducted between December 2016 to December 2017.

The present study showed that regarding age, weight and sex there was no significant difference in age and sex in early HFOV compared with late HFOV/P-CMV. The present study showed that regarding PRISM there was no significant difference between studied groups during study period. The non-significant difference found in age, weight, sex and PRISM III score demonstrates the non-bias choice of the study cases.

The present study showed that regarding HR there was no significant difference between studied groups during study period. This was in accordance with Mehta S et al., [11] who found no significant differences in HR in HFOV (early and late) and CVM groups over the initial 72 hours of treatment. Similarly, Guttormsen et al., [12] who found no changes in HR noted during transition from CMV to HFOV.

The present study showed that regarding MABP there was no significant difference between studied groups during study period. This was in accordance with Levin D L et al., [13]. who found that there was no significant difference between patients undergoing early and late HFOV versus those submitted to CMV within the first 72 hours of treatment regarding MABP.

The present study showed that Hb, WBCs, PLTs and CRP there was no significant difference between studied groups during study period. The non-significant difference proved in Hb, WBCs, PLTs and CRP demonstrates the non-bias choice of the cases.

The present study showed that regarding $O_2\text{Sat}$ There was significant decrease of $O_2\text{Sat}$ of Early HFOV compared with P-CMV and Late HFOV in 1st, 2nd and 3rd days. Also, there was significant increase in Early HFOV in 2nd and 3rd days compared with 1st day. Likewise, there was significant increase in Late HFOV in 2nd and 3rd days compared with 1st day. Similarly, there was significant increase in P-CMV in 2nd and 3rd days compared with 1st day.

This was in accordance with, Pinzon et al., [14] who conducted a study to show the effects of Late HFOV in children with ARDS after failure of CMV. They found that after 48 hours of HFOV, a significant increase in $O_2\text{Sat}$ was achieved. Equally, Moniza et al., [15] found that with Late HFOV, immediate and significant increase was achieved in the $O_2\text{Sat} / F_iO_2$ ratio that was sustained until 24 hours of HFOV after transition from CMV.

The present study showed that regarding F_iO_2 There was significant decrease in Early HFOV in 3rd day compared with 1st day. This was in accordance with Mohamed et al., [16] who found that after 3hrs. From starting HFOV, patients showed a significant decrease of F_iO_2 . Too, the HIFO trial [17] found that in the first 24 hours after randomization, infants on HFOV required lower F_iO_2 when compared with infants on CMV. Likewise, Pinzon et al., [14] found that After 48 hours of HFOV, F_iO_2 decrease. Moreover, Andersen et al., [12] found that within 4h after transition from CMV to late HFOV, there was a significant reduction in F_iO_2 .

The present study showed that regarding SV There was significant increase in P-CMV in 2nd day compared with 1st day.

The present study showed that regarding SVI There was significant increase in P-CMV in 2nd and 3rd days compared with 1st day. This was in contrast With David et al., [18]. who conducted a study to show cardiovascular changes in patients with acute ARDS during transition from P-CMV to late HFOV, using transesophageal echocardiography and invasive hemodynamic monitoring. They reported that during HFOV there were decreased SVI.

The present study showed that regarding CO there was no significant difference between studied groups. However, there was significant increase in cardiac output in the 2nd, 3rd days compared with 1st day in late HFOV group. This was in accordance with Gutierrez et al., [13] who found that there was no evidence of decrease CO after transition from CMV to late HFOV. They explained

that by that they used enough pressure to obtain adequate oxygenation but reduced pressures when lung compliance and oxygenation were improved. Additionally, Kinsella et al., [19] showed that there were no deleterious cardiovascular effects were observed with Late HFOV or IMV. In addition, Vincent et al., [20] observed that there were no hemodynamic effects on cardiac post-operative patients ventilated with low MAP Late HFOV compared with CMV. Likewise, Derdak et al., [11] found no significant differences in CO in late HFOV and CVM groups over the initial 72 hours of treatment. Moreover, Pinzon et al., [14] who found that although CO was not measured in their study, the observed hemodynamic performance suggests that there was no additional blood flow impairment in their patients, as MABP remained stable and HR decreased. However, this was in contrast also with Mehta et al., [21] who showed that Late HFOV can lead to increased filling pressures and significant decrease in CO.

The present study showed that regarding CI there was no significant difference between studied groups. Which may be explained by the small number of the studied cases (Pilot study). This was in accordance with Gutierrez et al., [13] who found that CI did not change significantly in the group as a whole after transition from CMV to late HFOV.

The present study showed that regarding SVR There was no significant difference between the studied groups. This was in contrast with Goodman et al., [22] who found that SVR and MABP were reduced immediately after late HFOV was initiated after failure of CMV.

The present study showed that regarding SVRI there was there was no significant difference between the studied groups. This was in accordance with Gutierrez et al., [13] who found no significant changes in SVRI after transition from CMV to late HFOV. This may be explained by that SVRI decreased as a compensation of increase of CO in HFOV in the 3rd day compared with 1st day. There was non-significant decrease in MAP and AP as time pass. However, the non-significant decrease may be explained by the small number of the studied cases. (Pilot study).

The present study showed that There was significant decrease in PIP in the 2nd and 3rd days compared with 1st day. There was significant decrease in RR in the 2nd day compared with 1st day.

The present study showed that regarding Oxygenation Index There was significant decrease in late HFOV and P-CMV groups compared with

Early HFOV group in the 1st, 2nd and 3rd days. There was significant decrease in late HFOV in 3rd days compared with 1st and 2nd days. It is one of most important prognostic factors for detection timing of HFOV according to ROC curve for oxygenation index to prognosis cases early HFOV.

The present study showed that regarding regression analysis Oxygenation index was significant as a predictor for early HFOV success.

The present study showed that regarding ROC curve; oxygenation index was significant as a prognostic test with early HFOV with cut off value >13, sensitivity 73.33, specificity 66.67, PPV 68.7 and NPV 71.4.

This was in accordance with Ritacca FV, [23] who found OI was associated with mortality independently of other disease markers and could be important for selecting ARDS patients that could benefit from HFOV.

Conclusion:

As hypoxia worsened, patient percentage with Early HFOV increased. Oxygenation index was significant as a predictor and prognostic factor for early HFOV success.

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Conflicts of interest:

No conflicts of interest declared.

Authors' Contributions:

All authors had equal role in design, work, statistical analysis and manuscript writing. All authors have approved the final article work.

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التهوية التذبذبية عالية التردد المبكرة في حالات الفشل التنفسي الحاد في الأطفال

تعتبر التهوية التذبذبية عالية التردد عنصراً أساسياً في إدارة الأطفال الذين يعانون من فشل الجهاز التنفسي الحاد. وهو وسيلة من التهوية الميكانيكية التي تجند الرئة المريضة وتحسن الأكسجين من خلال استخدام ضغط الهواء المتوسط.

الهدف من الدراسة: الهدف من هذا مقارنة نتائج الاستخدام المبكر للتهوية التذبذبية عالية التردد في غضون ٢٤ ساعة للمرضى الذين يعانون من متلازمة الضائقة التنفسية الحادة لأولئك الذين يتلقون التهوية التقليدية الميكانيكية أو التهوية التذبذبية عالية التردد في وقت متأخر

طرق البحث: أجريت الدراسة على ثلاثون طفلاً من ذوي الحالات الحرجة الموضوعين على جهاز التهوية التذبذبية عالية التردد وجهاز التهوية الإلزامية المستمرة المتحكم بها بالضغط بوحدة العناية المركزة بقسم طب الأطفال بجامعة طنطا. تم إخضاع المرضى الذين أشتملت عليهم الدراسة إلى تسجيل التاريخ المرضي، الفحص الكليني الشامل، متابعة عدد دقات القلب، مستوى تشبع الدم بالأكسجين و ضغط الدم بصورة منتظمة. متابعة وظائف القلب عن طريق دوبلر المرئ مثل أنتاج القلب، مؤشر نقص الأكسجين.

النتائج: تسبب وضع الأطفال على جهاز التهوية التذبذبية عالية التردد المتأخر وجهاز التهوية الإلزامية المتحكم بها بالضغط في تقليل مؤشر نقص التنفس على الأطفال الذين تم وضعهم على جهاز التهوية التذبذبية عالية التردد المبكر.

الاستنتاج: يعد مؤشر الأكسجين أحد أهم العوامل النذيرية لتحديد توقيت استخدام التهوية التذبذبية عالية التردد وفقاً بمنحنى ROC يعتبر مؤشر نقص الأكسجين كمتنبئ لاستخدام جهاز التهوية التذبذبية عالية التردد المبكر.

التوصيات: نحن نوصي باستخدام مؤشر نقص الأكسجين كمتنبئ للحالات التي يتم وضعها على التهوية التذبذبية عالية التردد المبكر. ويمكن تطبيق التهوية التذبذبية عالية التردد المبكرة في الأطفال الذين يعانون من الضائقة التنفسية الحادة، وبترافق معها التحسينات الأولية في الأكسجين والتهوية الكافية ولكن من دون أي فائدة في نسبة الوفيات.