# Role and Impact of Flexible Fiberoptic Bronchoscopy in Critically Ill Children: A Prospective Observational Study

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## **ABSTRACT**

**Background:** The most common issue in pediatric and neonatal intensive care units (PICUs and NICUs) is pulmonary diseases. In this group, safe, accurate diagnosis and bedside treatment are essential. Fiberoptic bronchoscopy is being used more often in the treatment of critically sick patients due to its diagnostic and therapeutic benefits as well as its proven safety. **Objective:** This study aimed to determine the diagnostic and therapeutic value of flexible fiberoptic bronchoscope in critical children. **Patients and methods:** A prospective study was conducted on 32 children aged 1 month–12 years who were admitted to the PICU at Abo El Rish Children's Hospital, Cairo University. Clinical data, indications, findings, and outcomes following flexible fiberoptic bronchoscopy (FFB) were analysed.

**Results:** The main indications for FFB were persistent pulmonary infiltrates (54.8%), difficult extubation (19.4%), and stridor or wheeze (19.4%). FFB yielded diagnostic or therapeutic information in 90% of cases; 71% were diagnostic, and 29% were therapeutic. Common findings were airway inflammation (32%) and mucus plugging (29%). Bronchoalveolar lavage (BAL) demonstrated 100% sensitivity compared to blood cultures in detecting infection. Patients under two years showed shorter ventilation duration and lower mortality (p=0.07).

**Conclusion:** Flexible fiberoptic bronchoscopy is a crucial and safe treatment for critically-ill infants and children with various respiratory conditions and considerably aiding in their care.

Keywords: Flexible fiberoptic bronchoscopy, Pulmonary disorders, PICU, NICUs.

### INTRODUCTION

The most common issue in pediatric and neonatal intensive care units (PICUs and NICUs) is pulmonary diseases. In this group, safe, accurate diagnosis and bedside treatment are essential. Fiberoptic bronchoscopy is becoming more and more used in the treatment of critically sick patients due to its diagnostic and therapeutic benefits as well as its proven safety (1).

When diagnosing and treating certain respiratory issues in critically-sick babies and children admitted to the pediatric intensive care unit (PICU), FFB, with or without BAL, is very crucial. These include conditions like difficult intubation, aberrant breathing sounds, chronic recurring atelectasis, examination of anomalies for radiographic findings and/or symptoms of unknown cause, and patients who are difficult to wean (2). FFB is used in the intensive care unit (ICU) for a variety of reasons. The majority are equivalent to a basic bronchoscopy that includes forceps sample, brushing, lavage and exploration. For a variety of therapeutic and diagnostic reasons, it is advised that critical care units permit the prompt and urgent FFB. Timely resolution of respiratory system issues and clinical decision-making are essential in critical care settings (3).

Since its inception in the 1970s, bronchoalveolar lavage (BAL), which is carried out during fiberoptic bronchoscopy, has been widely accepted and is being utilized more often. Cell types and their activation state are identical in both collection methods, according to studies comparing BAL cellular elements to cells taken from open lung biopsies. BAL is a minimally invasive technique that might offer valuable diagnostic information as well as insights into viral, inflammatory, and immunologic processes occurring at

the alveolar level <sup>(4)</sup>. Therefore, this study aimed to evaluate the diagnostic and therapeutic roles of flexible fiberoptic bronchoscopy (FFB) in critically ill paediatric patients and assess its impact on clinical outcomes and ventilation duration.

# PATIENTS AND METHODS

This was a prospective observational study conducted over 12 months in the Paediatric Intensive Care Unit at Abo El Rish Children's Hospital, Cairo University. It included 32 patients, all were Egyptian children (age: 1 month to 12 years old) hospitalized in PICU with persistent pulmonary symptoms.

The primary outcome was diagnostic and therapeutic yield of FFB. Secondary outcomes included duration of ventilation and mortality.

One patient from these 32 patients diagnosed as diffuse pulmonary infiltrates with bilateral pleural effusion developed desaturation while passing the FFB and the procedure was terminated.

**Inclusion criteria:** Persistent or recurrent atelectasis, abnormal breathing sounds, evaluation of abnormalities: for radiographic findings and/or symptoms of unclear etiology, difficult weaning patients, difficult intubation.

**Exclusion criteria:** Absolute contraindication as hemodynamic instability, and relative contraindication as pulmonary hypertension, baseline hypoxia and uncorrected bleeding diathesis.

Pre bronchoscopy testing included chest radiographs, prothrombin time, and complete blood cell count performed prior to the procedure. We collected the following patient' data: Clinical criteria included heart rate, body temperature, blood pressure, pupillary reflexes, conscious level, blood glucose, blood urea

Received: 08/05/2025 Accepted: 12/07/2025 nitrogen, serum potassium, blood gases, white blood cells, prothrombin time, partial thromboplastin time and platelet count in order to calculate Pediatric Risk of mortality III score (PRISM III) in the first 24 hours of each patient <sup>(5)</sup>. Also, we collected sputum and blood culture for 10 patients to compare with BAL.

**Equipment:** Flexible fiberoptic bronchoscopy 2.7 F (pentax). Flexible fiberoptic bronchoscopy 3.4 V (pentax). Disinfectants: glutaraldehyde and disinfectant device (ENDO-TECHNIK).

**Premedication and sedation:** Twenty two patients had the procedure in PICU where they were ventilated and we used extra shots of midazolam in sedation only, but the other ten patients had the procedure in the operating room where they were anesthetized with sevofluorane and intravenous propofol. Lidocaine 2% was applied to the larynx or at the carina in intubated patients.

**Monitoring and support:** Patients were monitored using ECG, pulse oximetry and blood pressure.

Route of insertion: The flexible bronchoscope was introduced via either endotracheal tube (done bedside for 22 patients in ICU using bronchoscopy of 2.7 mm) or laryngeal mask (done for 10 patients in operating room using 3.4 mm device). Two patients had temporary extubation and Laryngeal mask airway (LMA) insertion and then reintubation as one of the patients had suspected foreign body and the other was planned for mucosal bunch biopsy. For the ventilated patients setting of the ventilator were adjusted as follow:

Increasing FIO<sub>2</sub>, decreasing the PEEP and increasing the respiratory rate to compensate for the pathophysiological changes induced by the bronchoscope and reduce the possible hypoxemia.

According to **Lawson** *et al.* <sup>(6)</sup> extremely low tidal volume and high auto-PEEP level may develop unless respiratory rate, endotracheal tube (ETT) size, mode and flow are carefully selected.

Collecting bronchoalveolar lavage (BAL): We collected BAL using normal saline by injecting about two aliquots, each containing 1 ml/kg of the chosen newborn or toddler, while keeping the bronchoscope tip jammed into the chosen location. The fluid was then aspirated right away into a sterile container.

When an infection was suspected, BAL was carried out by wedging the bronchoscope tip in a sub segmental bronchus in the aberrant location seen on physical examination or radiography, or in the right middle lobe or lower lobe in the absence of localizing indications. BAL samples were sent in for fungal smear and culture, aerobic and anaerobic bacterial culture and fungal smear and culture.

Ethical approval: The Ethics Committee of the Cairo Faculty of Medicine authorized this investigation. Parents provided written informed

consents to participate in the investigation. The Helsinki Declaration was followed throughout the course of the investigation.

## Statistical analysis

SPSS version 15.0 was utilized for the collection and analysis of data. The percentage distribution, range and mean  $\pm$  SD were the techniques used. The nonparametric data were shown using the median and IQR. When applicable, the Mann-Whitney U test or the t-student test were used to compare the groups. Numbers and percentages were used to display the qualitative data. When applicable, the  $X^2$ -test or Fischer's exact test was used to compare them. The length of time spent in the intensive care unit following the surgery was evaluated using survival analysis. If the P-value was  $\leq$  0.05, it was deemed significant.

### **RESULTS**

This study included 32 Egyptian critical children from Abo-El Rich Specialized Children Hospital over a period of one year. One patient was excluded from the results of statistics as we terminated the procedure because of marked desaturation of the patient. Most patients were male (61%) and from rural areas (68%), with a median age of 24 months. Clinical parameters were within expected ranges, reflecting a critically-ill but stable cohort suitable for bronchoscopy. Out of 32 patients, there were 20 (61%) males and 12 (39%) female. Their ages have median 24 months, interquartile range (IQR) was 40 and min-max (range) 2-144 months (Table 1).

**Table (1):** Demographic and clinical characteristics of studied patients

Demograghic characteristics	Number	%
Sex	Male 20	61%
	Female 12	39%
Residence	Urban 10	32%
	Rural 22	68%
Age (Month)	Median	Range
	24	2-144
Clinical characteristics	Median	Range
Systolic blood pressure (mmHg)	101.22	80-140
Temperature (°C)	37.25	36.5-38.5
Heart rate (Beat/min)	141	90-170
PH (acid base balance)	7.41	7.35-7.62
Glucose (mg/dl)	150	70-200
Potassium (mmol/L)	3.81	2.5-5.5
Blood urea nitrogen (mg/dL)	23.5	7-66
Creatinine (mg/dL)	0.47	0.3-0.9
Total leucocytic count	13.18	7-31.5
Platelets (mcL)	313.54	80-865
Prothrombin time	13.71	10-18.1
Partial thromboplastin time	31.07	24-45
Prism III score	10	0-18

Out of the 22 patients who were mechanically ventilated, we found the tip of ETT was deep in 5 patients, accounting for 22.7% of ventilated patients. Flexible bronchoscopy was performed mainly via **ETT** (68%), less commonly via LMA (32%). In 22 ventilated patients, 22.7% had deep ETT placement, highlighting bronchoscopy's role in identifying tube malposition (Table 2).

**Table (2):** Route of bronchoscopy

Route of the FFB	Number	%
LMA*	10/32	32%
ETT*	22/32	68%
ETT size		
Mean ±SD	$4.5 \pm 0.7$	
Median	4.5	
Range	3.5 -6.5	

\*LMA: Laryngeal mask airway \*ETT: Endotracheal tube.

The study included 31 patients, 17 of them indicated for FFB due to persistent pulmonary infiltrates where 4 patients of these 17 patients diagnosed as lung collapse, 3 patients as chest infection, 2 patients as Guillain Barre syndrome, 2 patients as heart failure and the rest of patients had the following diagnoses myopathy, encephalitis, bronchopleural fistula, brain atrophy, Werdnig Hoffman syndrome and chest trauma. Persistent pulmonary infiltrates were the leading indication (54.8%), followed by failed

extubation and stridor (≈19% each). This emphasizes FFB's value as a diagnostic tool for unresolved respiratory conditions in PICU (Table 3).

**Table (3):** Indication of FFB in studied patients

	Frequency	Percent
Persistent pulmonary infiltrates	17	54.8 %
Difficult /failed extubation	6	19.4%
Persistent stridor/noisy breathing/wheezing	6	19.4%
Suspecting congenital anomalies	2	6.4%
Total	31	100.0%

Patients included in the study are categorized according to primary diagnosis into three groups' cardiovascular disease, pulmonary disease and neuromuscular disease. Patients with pulmonary disease had higher percentage followed by patients with neuromuscular disease followed by patients with cardiovascular disease. Also infection in pulmonary disease patients had higher frequency than other diagnoses. Pulmonary disease was most common (54.4%), followed by neuromuscular disease (29.6%) and cardiovascular disease (16%). Within pulmonary disease, infection and lung collapse were frequent findings (Table 4).

Table (4): Diagnostic categories of studied patients

Categories	Diagnosis			Bronchoscopic finding							
		Frequency	Foreign body	Mucus plug	Inflammation, infection	Tracheomalachia, bronchomalachia	Hemangioma	Tracheal ulcer	Bronchopleural fistula	Normal bronchoscopy	Percent
Cardiovascular	Heart failure	2			2						6.4%
disease 16%	Postoperative	3				2				1	9.6%
Pulmonary	Infection	7		1	4			1		1	22.4%
disease 54.4%	Stridor	2				1	1				6.4%
	Lung collapse	3	1	2							9.6%
	Interstial lung disease	2			2						6.4%
	Chest trauma	2							2		6.4%
	F.B inhalation	1	1								3.2%
Neuromuscular disease 29.6%	Werdnig Hoffman disease	1		1							3.2%
	Guillain barre syndrome	2		2							6.4%
	Myopathy	1		1							3.2%
	Brain atrophy	1		1							3.2%
	Encephalitis	3		1	1					1	9.6%
	Status epileptics	1			1						3.2%
TOTAL		31									100%

Among the FFB procedures performed in the studied patients, 90.4% had positive finding while 9.6% had normal bronchoscopic finding (Table 5).

**Table (5)**: Bronchoscopic finding in studied patients

Normal Bronchoscopy finding	3	9.6%
Foreign body	2	6.4%
Mucus plug	9	28.8%
Inflammation or infection	10	32%
Tracheomalachia or bronchomalachia	3	9.6%
Laryngeal hemangioma	1	3.2%
Tracheal ulcer	1	3.2%
Bronchopleural fistula	2	6.4%

**Compared to blood culture:** For BAL culture, Sensitivity =5/5=100%, PPV=5/10=50%, Specificity =0/5=0% and No NPV can be calculated. Sputum culture was found to have the least yield among all 3 samples (10%) BAL culture results were similar to blood culture in 50% of sampled patients. In the remaining patients, BAL samples were the only samples that yielded positive results (Table 6).

**Table (6):** BAL, sputum culture and blood culture in 10 studied patients

Patient	Sputum culture	Blood culture	BAL culture
No.1	No growth	Enterobacter	Enterobacter
No.7	Inhibited growth	Acintobacter	Acintobacter
No.8	inhibited growth	Enterobacter&acintobacter	Enterobacter & acintobacter
No.14	Inhibited growth	Inhibited growth	Pseudomonas
No.15	Inhibited growth	No growth	Candida
No.18	Inhibited growth	Enterococci	Enterococci
No.23	Kliebsiella&pseudomonas	no growth	Kliebsiella & pseudomonas
No.24	Inhibited growth	Enterococci	Enterococci
No.25	Inhibited growth	Inhibited growth	Kliebsella pneumonie
No.27	Inhibited growth	No growth	Kliebsiella pneumonie

The only therapeutic indication for FFB in the studied patients was for lavage of mucus plugs in 29 %. Most bronchoscopies were performed for **diagnostic purposes** (71%), while 29% were therapeutic, mainly for mucus plug removal. Although outcomes (discharge vs mortality) did not differ significantly between groups. Therapeutic bronchoscopy demonstrated value in facilitating airway clearance and supporting ventilation. This finding highlights that, beyond its diagnostic yield, FFB also serves an important therapeutic role in the PICU setting, particularly in managing mucus plugging (Table 7).

**Table (7):** 2 groups of studied patients (diagnostic – therapeutic)

	Modalities	Diagnostic	Therapeutic	P value
		Number and %	Number and %	
Sex	Male	14 (45.1%)	5 (16.1%)	0.67
	Female	8 (25.9%)	4 (12.9%)	
Onset of	Acute	11 (35.5%)	4 (12.9%)	0.77
symptoms	Acute on top of pre-existing condition	11 (35.5%)	5 (16.1%)	]
Indication of	Persistent pulmonary infiltrates	8 (25.9%)	9 (29%)	0.58
bronchoscopy	Difficult/failed extubation	6 (19.3%)	0 (0%)	1
	Persistent stridor/noisy breathing/wheezing	6 (19.3%)	0 (0%)	1
	Suspecting congenital anomalies	2 (6.5%)	0 (0%)	1
Outcome after	Discharged	18 (58%)	8 (25.8%)	0.62
bronchoscope	Mortality	4 (13%)	1 (3.2%)	]
Total No		22 (71%)	9 (29%)	

P-value < 0.05 is significant.

Regarding duration of MV, it is found that mean duration of MV before FFB  $15.13 \pm 9.72$  but mean duration post FFB is  $11.40 \pm 7.27$  days, median duration 7 days (Table 8).

**Table (8)**: Duration of MV before and after the FFB

Duration of MV	Mean ± SD	Median	Range
Duration of MV before FFB (days)	$15.13 \pm 9.72$	10	0 - 80
Duration of MV post FFB (days)	$11.40 \pm 7.27$	7	0 - 45

Mortality was higher in patients with older age, higher PRISM scores, tachycardia, and thrombocytopenia. Identifying potential risk factors linked to poor outcomes in this cohort (Table 9).

**Table (9)**: Comparison between discharged and mortality of the studied patients

	Discharged (n=26)	Mortality (n=5)	P value
Male number and %	16 (61.5%)	3 (60.0%)	1.0
Female number and %	10 (38.5%)	2(40.0%)	
age (months) Median &IQR	21 (41)	78 ( 72)	0.05*
PRISM III Score(mean±SD)	9.12±4.457	13.20±3.271	0.06
Heart rate	139.19±21.698	152.00±10.954	0.07
Temperature	37.20±0.63	37.54±0.68	0.282
Systolic BP	102.42±15.69	95.00±10.00	0.320
Platelets	343.88±183.21	155.80±80.8	0.034*
Duration of MV before the FFB median &IQR	12.5 (28 %)	7 (10 %)	0.51
duration of MV post FFB (days) Median & IQR	7 (45 %)	10(7%)	0.55

<sup>\*</sup>significant.

Overall, FFB was diagnostic or therapeutic in 90% of cases, with mucus plugging and airway inflammation as the most frequent findings. The procedure was well tolerated, with no major complications reported.

# **DISCUSSION**

In our study, which was carried over 1year and included 32 patients and included 20 (61%) males and 12 (39%) females with ratio 1.5: 1 and with age range of 2-144 months, median age 20 and IQR of 40. In studies by **Davidson** *et al.* <sup>(7)</sup>, **Tang and Chen** <sup>(8)</sup> and **Peng** *et al.* <sup>(9)</sup>, the mean age and sex distribution was  $2.4 \pm 0.7$  years with male : female ratio 2.4 : 1 and  $35.7 \pm 48.9$  months with male : female ratio 1.6 : 1 respectively and for **Peng** *et al.* <sup>(9)</sup>, the age range of (2.92 - 42.5) with median age of 9.9 months respectively.

Among the FFB procedures performed in the study period, 87% were for patients on mechanical ventilation. This is similar to other results by **Tang** and Chen <sup>(8)</sup> where the % of mechanically ventilated patients was 71.7 % and 97.5 % in **Davidson** *et al.* <sup>(7)</sup>.

Indication of FFB in the studied patients showed that persistent pulmonary infiltrates as an indication for bronchoscopy accounted for 54.8% followed by failed extubation (19.4%) and persistent stridor or wheezes (19.4%) and this comes with agreement of the literature, which confirm that diagnosis of VAP and treatment of persistent pulmonary infiltrates are the

most common indications for bronchoscopy in the ICU. Pediatric studies have shown that flexible bronchoscopy is beneficial for treating atelectasis and mucus plugging, with a success rate of 40–100% <sup>(2, 10)</sup>.

The study patients were categorized in diagnostic groups according to their primary condition. In this respect, respiratory disorders were the most frequent followed by diagnosis (54.4%) neuromuscular disorders (29.6%)then cardiac disorders. A retrospective study of value of FFB in PICU patients by **Peng** et al. <sup>(9)</sup> demonstrated that the most prevalent conditions were respiratory and cardiovascular. Prematurity and cardiovascular disease considerably (P<0.05) more common in the < 3 y group, whereas neurological and hemato-/oncological diseases were more common in the < 3 y group.

However, in our study there were no hematology or oncology patients. Also, **Davidson** *et al.* <sup>(7)</sup> study had been undertaken in patients requiring ICU because of significant pneumonia (41.5 %) or following cardiac surgery (26.5%), although other diagnoses are also involved. These findings reflect the referral pool for the institution, where oncology patients are not managed in our facility.

We divided the patients according to FFB finding into the following groups: Mucus plug, inflammation or infection, tracheomalachia or bronchomalachia, foreign body inhalation, bronchopleural fistula, laryngeal hemangioma and traumatic tracheal ulcer,

where airway inflammation (32%) and mucus plugging (28%) were the most common findings of the patients. This is relatively close to **Tang and Chen** <sup>(8)</sup> where the result of bronchoscopy findings is: inflammation (55.3%), mucus plugging (19.1%) and foreign body (29.8%). Also, **Peng** et al. <sup>(9)</sup> divided their patients into two groups and found airway malacia, stenosis, esophageal problems and congenital malformation were more common in patients < 3 years, while inflammatory reaction and normal bronchoscopic examination were more common in the older age group  $\geq$  3 years.

FFB can be diagnostic, therapeutic or both. In our study therapeutic interventions were employed in 29 % of patients as a lavage of mucus plugs. A study by **Davidson** et al. (7) in PICUS of UK mentioned that the majority of the FBs were diagnostic (161 of 200). 114 of these were undertaken to exclude underlying airway abnormalities and 47 to aid the diagnosis of pneumonia. Therapeutic procedures including bronchial stenting, directed surfactant instillation and bronchoalveolar toileting were undertaken in 39 cases. However, in our study the only therapeutic indication was lavage of mucus plugs as bronchial stenting and surfactant application are not yet feasible and our patient population didn't include neonates, also our indications for FFB didn't include airway stenosis.

In our study, 90% of the bronchoscopes carried in critical children showed positive findings. This comes in agreement with **Davidson** et al. (7) as 80% of their flexible bronchoscopies had abnormal findings, and Godfrey et al. (11) as 67% of flexible bronchoscopies had positive findings. Concerning the position of the lower tip of the endotracheal tube, 22.7 % of our patients showed that it was too low despite adequate radiologic appearance. In a similar study by **Davidson** et al. (7), it was found in 14.7 % of the flexible bronchoscopies. A study by Shorr et al. demonstrated that BAL performed using FB was particularly successful in enhancing the targeting of relevant antibiotics. Also **Fagon** et al. (13) found that using FB and BAL resulted in a substantial improvement in mortality rate at 14 days when compared to sampling with endotracheal aspirates

Concerning the nature of lesion in bronchoscopic examination, our younger patients ( $\leq 2$  years) showed a higher occurrence of hemangioma and malacia while older children ( $\geq 2$  years) showed traumatic lesions and inflammatory lesions but the difference was not statistically significant. A similar study by **Peng** *et al.* (9) showed that airway malacia, stenosis, esophageal problems and congenital malformation were more common in patients < 3 years while inflammatory reaction and normal bronchoscopic examination were more common in the older age group  $\geq 3$  years.

In our study patients' age less than 2 years was associated with shorter ventilation days and better

outcome post procedure if compared to those above 2 years, but the P value was only approaching statistical significance (P value=0.07). Also, the group of patients who were weaned early from the ventilator in less than 7 days after the bronchoscopy had also shorter median days of ventilation preprocedure if compared to those who had longer ventilation > 7 days after FFB and were also ventilator dependent for long period before the procedure (P value=0.048). This could be explained by the fact that the older patients had a higher proportion of chronic underlying diseases and their respiratory problems developed secondarily on top during stay and that in younger patients, their chief complaint since admission was respiratory and the procedure could effectively resolved it. This seems to be in contrast with the data by **Payen** et al. (14) as they mentioned that significant risk factors for prolonged invasive mechanical ventilation were age of < 12 months.

Regarding patient outcome of our studied group, the mortality rate accounted for 16% of patients and mean duration of stay 32 days. This compared to total mortality of 30% to the PICU population and mean duration of stay was 7 days in the same period. Higher mortality rate in older may be attributed to the underlying chronic illness. Two out of the deaths in the study had pulmonary BPF. According to the research of **Sarkar** et al. (15), BPF can result in considerable morbidity, protracted hospitalization, and even fatality. Mortality rates range between 18% and 67%. Aspiration pneumonia, followed by acute respiratory distress syndrome or tension pneumothorax, is the leading cause of mortality. Two other deaths were caused by persistent neuromuscular illnesses, and according to a UK research, 27% of all PICU admissions requiring ventilation for more than 28 days following an acute illness had an underlying neuromuscular condition, and 45% of these patients died (16).

Higher PRISM III score has been associated with increased mortality rate. A study by **Tan** *et al.* (17) showed that there was a 15.8 times increased risk of mortality with a PRISM III-24  $\geq$  8. Similarly, in our study group an increased risk of mortality was associated with a higher PRISM score but it was not statistically significant. This finding is not attributable to the procedure itself but it reflects the critical state of patients in PICU that require bronchoscopy due to pulmonary complications of their primary illness or due to mechanical ventilation.

Also, patients with higher mortality rate were also associated with a higher heart rate (152 vs 139) but also was not significant statistically (P-value 0.07).

## **LIMITATIONS**

The main limitations of this study included the small single-center sample size and lack of long-term followup. Nevertheless, it provided prospective evidence supporting FFB as a safe and valuable intervention in critically-ill children.

### **CONCLUSIONS**

Flexible fiberoptic bronchoscopy was a safe and effective diagnostic and therapeutic tool in paediatric intensive care. It contributed significantly to clinical decision-making and may help reduce ventilation duration and complications, particularly in infants with respiratory disorders.

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