ORIGINAL ARTICLE

A Retrospective Analysis of Interventional Flexible Bronchoscopic Procedures in Pediatric Patients

Pediatrik Hastalarda Girişimsel Fleksible Bronkoskopik İşlemlerin Retrospektif Analizi

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ABSTRACT

Aim: Pediatric interventional pulmonology (IP) has significantly advanced in recent years with the integration of minimally invasive techniques such as cryotherapy, balloon dilatation, and endobronchial biopsy. Flexible bronchoscopy, once primarily a diagnostic tool, has now become an essential therapeutic modality in managing complex pediatric airway and pulmonary conditions. This study aimed to retrospectively evaluate interventional procedures performed using flexible bronchoscopy in pediatric patients over a one-year period.

Methods: A retrospective review was conducted on pediatric patients who underwent interventional flexible

Methods: A retrospective review was conducted on pediatric patients who underwent interventional flexible bronchoscopy between June 2024 and June 2025. Data collected included demographic characteristics, indications for bronchoscopy, types of interventional procedures performed and observed complications. All procedures were performed under sedation or general anesthesia by experienced pediatric pulmonologists using age-appropriate bronchoscopes.

Results: A total of 24 patients (13 males) with a median age of 91 months underwent interventional bronchoscopic procedures. The most common indications were subglottic stenosis (16.7%), suspected primary ciliary dyskinesia (16.7%), suspected interstitial lung disease (20.8%), and foreign body aspiration (16.7%). A total of 27 procedures were performed, including balloon dilatation (22.2%), cryobiopsy (37.0%), foreign body removal (14.8%), and cryodevitalization (11.1%). The complication rate was low, with only mild bleeding in two patients and moderate bleeding in one; no cases of pneumothorax were reported.

Conclusion: Pediatric interventional bronchoscopy is a safe and effective method for both diagnosis and therapy in children with complex respiratory conditions. With the availability of thinner instruments and increased expertise, advanced interventional techniques are now more accessible and applicable in pediatric populations. Structured training programs and interdisciplinary collaboration are essential to further develop and standardize pediatric IP practices.

Keywords: balloon dilatation, bronchoscopy, cryotherapy, pediatric, interventional bronchoscopy, flexible bronchoscopy

ÖZ

Amaç: Pediatrik girişimsel pulmonoloji, kriyoterapi, balon dilatasyonu ve endobronşiyal biyopsi gibi minimal invaziv tekniklerin entegrasyonu ile son yıllarda önemli ölçüde ilerleme kaydetmiştir. Başlangıçta yalnızca tanısal amaçlarla kullanılan fleksibl bronkoskopi, artık karmaşık pediatrik hava yolu ve akciğer hastalıklarının tedavisinde vazgeçilmez bir yöntem hâline gelmiştir. Bu çalışmanın amacı, bir yıllık süre içerisinde pediatrik hastalara uygulanan girişimsel fleksibl bronkoskopik işlemleri retrospektif olarak değerlendirmektir.

Yöntem:Haziran 2024 ile Haziran 2025 tarihleri arasında girişimsel fleksibl bronkoskopi uygulanan pediatrik hastalar retrospektif olarak incelendi. Hastalara ait demografik bilgiler, bronkoskopi endikasyonları, uygulanan girişimsel işlem türleri ve gözlenen komplikasyonlar kaydedildi. Tüm işlemler, yaşa uygun bronkoskoplar kullanılarak, deneyimli pediatrik göğüs hastalıkları uzmanları tarafından, sedasyon veya genel anestezi altında gerçekleştirildi. Bulgular: Toplam 24 hasta (13'ü erkek), ortalama 91 ay yaşında idi. En sık bronkoskopi endikasyonları; subglottik stenoz (%16,7), primer siliyer diskinezi şüphesi (%16,7), interstisyel akciğer hastalığı şüphesi (%20,8) ve yabancı cisim aspirasyonu (%16,7) olarak belirlendi. Bu işlemler arasında balon dilatasyonu (%22,2), kriyobiyopsi (%37,0), yabancı cisim çıkarılması (%14,8) ve kriyodevitalizasyon (%11,1) yer aldı. Komplikasyon oranı düşüktü; iki hastada hafif, bir hastada ise orta düzeyde kanama görüldü. Pnömotoraks vakası saptanmadı. Sonuç: Pediatrik fleksibl girişimsel bronkoskopi, karmaşık solunum yolu hastalıklarının tanı ve tedavisinde güvenli ve etkili yöntemlerdir. Daha ince enstrümanlara olan erişim ve artan uzmanlık sayesinde, ileri girişimsel teknikler artık çocuk hastalarda daha yaygın ve uygulanabilir hâle gelmiştir. Bu alanın gelişimi için yapılandırılmış eğitim programları ve disiplinler arası iş birliği büyük önem taşımaktadır.

Anahtar kelimeler: balon dilatasyonu, bronkoskopi, çocuk, girişimsel bronkoskopi, fleksibl bronkoskopi, kriyoterapi



INTRODUCTION

Pediatric pulmonology involves the use of bronchoscopyinchildrenforbothdiagnostic and therapeutic purposes. Bronchoscopy has become an indispensable tool in the management of both acute and chronic pulmonary diseases. pediatric Thanks to recent technological advancements, pediatric bronchoscopy has evolved from being merely a diagnostic tool to also enabling therapeutic interventions. These developments have significantly increased pediatric interventional interest in pulmonology (IP) techniques (1, 2). Such techniques are increasingly preferred by pediatric pulmonologists due to their effectiveness treating in respiratory conditions, facilitating diagnosis, and offering minimally invasive optionsespecially when compared to open surgical procedures, as they are associated with shorter hospital stays and a lower risk of complications.

These procedures particularly are utilized in cases such as foreign body aspiration, transbronchial biopsy (TBB) for undiagnosed pulmonary infections, biopsy of endobronchial lesions, and interventions for airway stenosis (2, 3). The development of catheters with a diameter of 1.1 mm, compatible with the working channels of commonly used pediatric flexible bronchoscopes, enabled the performance of numerous minimally invasive procedures. As a result, interventional applications that previously limited in pediatric patients are now being performed more widely and effectively (4).

Interventional pediatric bronchoscopy is currently performed in a limited number of centers worldwide, including in our country. Given its limited availability, these procedures hold significant clinical value in the diagnosis and management of complex respiratory conditions in children. This study aims to evaluate the clinical characteristics of pediatric patients who underwent interventional flexible bronchoscopy and to contribute these experiences to the existing body of literature.

MATERIALS and METHODS

This retrospective study was conducted on children who underwent interventional flexible bronchoscopic procedures between June 2024 and June 2025. Pediatric patients who underwent flexible bronchoscopy for interventional purposes during this period were included in the study.

Patient data were obtained from medical records and included demographic characteristics (age, sex), indications for bronchoscopy, types of interventional procedures performed performed, and any complications observed during or after the procedure. The interventional procedures performed included foreign body removal, TBB, endobronchial biopsy (EBB) biopsy and airway dilatation procedures.

All procedures were performed by experienced pediatric pulmonologists using flexible bronchoscopes (FUJINON EB-530S/530P) appropriate to the age and size of each patient. Bronchoscopies were conducted under sedation or general anesthesia, in accordance with institutional protocols and safety guidelines, using a laryngeal mask airway (LMA).

Cryotherapy (Erbe cryomachine, Tübingen, Germany) has recently emerged as a promising diagnostic and therapeutic tool in pediatric airway endoscopy, enabled by

the development of ultra-thin cryoprobes as small as 1.1 mm. Originally introduced in the 1800s for the treatment of skin tumors, modern cryotherapy utilizes cryogens such as nitrogen, nitrous oxide, or carbon dioxide to achieve temperatures as low as -50 °C. This allows its application in procedures such as EBB, TBB, airway recanalization, and cryodevitalization (5). The cryoprobe was activated using a footswitch. For mucosal biopsies, freezing was applied for an average duration of 3-5 seconds. For cryodevitalization, a freeze-thaw cycle was performed using the cryoprobe, with an average freezing time ranging from 20 to 50 seconds.

Mucosal biopsies are performed during bronchoscopy to obtain tissue samples from the bronchial mucosa, primarily for the evaluation of ciliary structure and function (4, 6). For this purpose, needleless cup forceps (1.8 mm, reusable, OLYMPUS) and cryoextraction using a 1.1 mm cryoprobe (ERBE) were employed. Additionally, needleless cup forceps catheters were used for the removal of foreign bodies.

The electroknifeelectro-knife was used in conjunction with an electrocautery device (Valleylab, Covidien/Medtronic), which is commonly utilized in surgical departments to cut and coagulate tissue using electric current. The electro-knife is equipped with a flexible probe, allowing its integration with flexible bronchoscopes for procedures such as airway incision and coagulation. The electro-knife catheter was used to incise the subglottic web in a patient. In this case, the procedure was performed in cut mode at a power setting of 10 watts.

Balloon dilatation (Leo Medical Co. Ltd) has been an important technique for treating

pediatric airway obstruction-particularly stenosis-since laryngotracheal introduction in 1984. Performed under general anesthesia, often with topical lidocaine, the procedure utilizes ureteral balloon catheter that apply radial force, thereby minimizing mucosal trauma. The balloon size is selected to match the airway just distal to the stenotic segment. In this study, balloon dilatation was attempted using a 6 mm diameter, 20 mm length balloon. The balloon was inflated and deflated in a controlled manner. Initial dilatation began at a pressure of 5 atm, and inflation was continued until resistance was felt on the manometer. The procedure was halted when the patient's oxygen saturation (SpO₂) dropped below 90% (approximately 1 minute). During the second dilatation attempt, the pressure was increased to 8-10 atm. Again, the balloon was inflated until resistance was noted. For safety reasons, the procedure was discontinued when SpO₂ fell below 90% (approximately 1 minute). Following this, some improvement in the degree of stenosis was observed (4,7).

Inclusion and Exclusion Criteria

The inclusion and exclusion criteria for the study were defined as follows:

Inclusion Criteria:

Pediatric patients aged 0–18 years with one or more of the following conditions:

- Diagnosed subglottic stenosis
- Undiagnosed interstitial lung disease
- Persistent atelectasis
- •Foreign body aspiration
- Uncontrolled asthma
- •High clinical suspicion of primary ciliary dyskinesia (PCD)

Exclusion Criteria:

- Presence of pulmonary hypertension (due to increased risk of bleeding during bronchoscopy)
- Known bleeding disorders
- •Refusal to undergo the procedure due to associated risks (e.g., pneumothorax, hemorrhage, arrhythmias, and hemodynamic instability)

The study was approved by the Necmettin Erbakan University Faculty of Medicine ethics committee (Approval No: 2025/5915), and all data were anonymized to ensure patient confidentiality. The study was conducted under the principles of the Declaration of Helsinki.

Statistical Analysis

Statistical analyses were conducted using IBM® SPSS® Statistics Version 25. A p-value of loweress than 0.05 was considered statistically significant. For descriptive statistics, continuous variables that were not normally distributed were expressed as median and interquartile range (Q1–Q3), while categorical variables were presented as frequencies and percentages (%).

RESULTS

1. Patients' Characteristics

Of the total 24 patients, 13 were male. The median age was 91 months (range: 30–156). The most common presenting symptom was frequent lower respiratory tract infections and/or hospitalizations. The demographic characteristics of the patients are presented in Table 1.

Table 1: The demographic characteristics of the patients and the distribution of presenting symptoms.

Age (median)	91(30-156) months
Gender (M/F)	13/11
Initial symptoms	
-Stridor	n=4 (16%)
-Persistent radiological finding	n=7 (30%)
-Frequent lower respiratory tract infections/ hospitalizations	n=12(50%)
-Post-tb complication	n=1(4%)

Tb:tuberculosis

Interventional procedures were performed for the following preliminary diagnoses: four cases of subglottic stenosis, three cases of right middle lobe syndrome, four cases of interstitial lung disease, four cases of suspected primary ciliary dyskinesia, two cases of uncontrolled asthma, three cases of foreign body aspiration removal, one case of respiratory papillomatosis, one case of suspected organizing pneumonia, and one case of post-tuberculosis left main bronchial stenosis.

total of patients underwent interventional bronchoscopic procedures, with 27 procedures performed in total. This is because, during follow-up, two patients diagnosed with subglottic stenosis (SGS) required additional interventions-one patient underwent balloon dilatation twice, and the other required a second balloon dilatation. During the study period, a total of 112 flexible bronchoscopic procedures were performed, 24% of which 24% were interventional. The indications of patients are shown in Table 2.

Table 2: Distribution of Indications for Interventional Bronchoscopy.

Diagnosis/Indication	n=24, Frequency (%)
SGS	4 (16.7%)
MLS	3 (12.5%)
ILD/ Suspected organizing pneumonia/ Suspected GLILD	5 (20.8%)
Suspected PCD	4 (16.7%)
Uncontrolled Asthma	2 (8.3%)
Foreign body aspiration	4 (16.7%)
Respiratory papillomatosis	1 (4.2%)
Post-tb stenosis	1 (4.2%)

SGS: Subglottic stenosis, MLS: Middle lobe syndrome, ILD: Interstitial lung disease, GLILD: Granulomatous-lymphocytic interstitial lung disease, PCD: Primary ciliary dyskinesia, Post-tb: Post tuberculosis

2. Indications and Interventional Procedures

All patients with SGS had been previously diagnosed. Interventional bronchoscopic procedures were performed to dilate the stenotic area. The SGS in these patients had developed as a complication following endotracheal intubation. One case was associated with postoperative congenital heart disease, another with respiratory failure secondary to Guillain–Barré

syndrome, one due to bronchopulmonary dysplasia, and one following severe pneumonia.

In one patient, no intervention could be performed due to fibrosis in the subglottic area. One patient underwent balloon dilatation only (Figures 1, 2); this patient required two additional balloon dilatations during follow-up bronchoscopies performed one month apart.

In another patient, a complete subglottic web was incised using an electrocautery knife at the 11, 1, and 6 o'clock positions in a Mercedes-Benz pattern. This was followed by two rounds of balloon dilatation (each lasting approximately one minute, until hypoxia developed), and cryodevitalization was applied twice—20 seconds of freezing followed by 20 seconds of thawing—across the entire web area to prevent restenosis (Figures 3–5).

In another case, two crescent-shaped subglottic webs were identified. The webs were disrupted using forceps (Figure 6), followed by balloon dilatation and cryodevitalization using the same protocol. On follow-up bronchoscopy performed one





Figure 1-2: Patient 1 with subglottic stenosis, (left) before dilatation, (right) after dilatation





Figure 3-4: Patient 2 with subglottic stenosis, (left) before dilatation, (right) after dilatation



Figure-5: Freezing moment in a patient who underwent cryo-devitalization

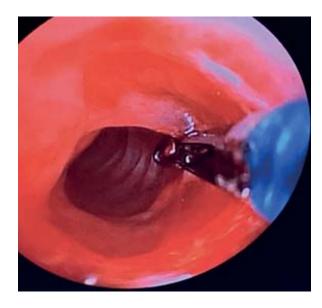


Figure-6: Disruption of web continuity with forceps in subglottic stenosis

month later, neither of these two patients required additional balloon dilatation procedures.

In all three patients with a preliminary diagnosis of right middle lobe syndrome, macroscopic bronchoscopic evaluation revealed a 70-80% narrowing at the entrance of the right middle lobe. Balloon catheter dilatation was performed twice, each lasting one minute. Following the dilatation, dornase alfa was administered to the atelectatic region, and oxygen insufflation was applied. Post-procedure, all patients received respiratory physiotherapy training. On follow-up chest radiographs at one month, resolution of the atelectatic area was observed in two patients (Figure 7), while one patient required surgical intervention.

In patients scheduled for pathological sampling due to a preliminary diagnosis of interstitial lung disease, the biopsy site was determined based on the patient's computed tomography (CT) findings. At least three tissue samples were obtained using a cryoprobe and forceps passed through the working channel of a flexible bronchoscope. Prior to biopsy, the selected area was evaluated using fluoroscopy to assess its proximity to the pleura, and a bronchial blocker was employed to ensure bleeding control (Figures 8–10).

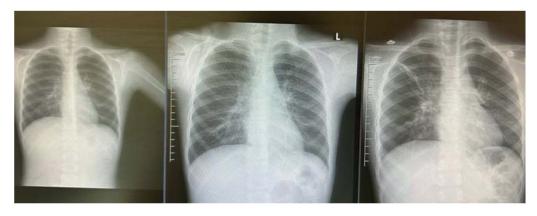


Figure-7: Patient diagnosed with right middle lobe syndrome, right (before the procedure), middle 1 month after the procedure, left (2 months after the procedure)



Figure-8: Determining the biopsy site under fluoroscopic quidance



Figure-10: 2 biopsy specimens obtained by transbronchial cryobiopsy



Figure-9: Use of endobronchial blockers during transbronchial biopsy

In three patients with suspected foreign body aspiration, flexible bronchoscopy and forceps were used for removal, while in one patient, rigid bronchoscopy with forceps was performed. The foreign bodies were located in the right main bronchus in two patients and in the left main bronchus in the remaining two. Three of the foreign bodies were organic in nature, while one was composed of inorganic material.

Endobronchial biopsies were obtained from patients with suspected uncontrolled asthma and PCD for diagnostic evaluation.

In the patient with a preliminary diagnosis of respiratory papillomatosis, widespread lesions were observed in the mid-to-lower trachea and carina. An endobronchial cryobiopsy was initially performed to obtain tissue for human papillomavirus (HPV) genotyping. After the administration of three doses of the HPV vaccine, persistent lesions were treated with cryodevitalization.

The interventional flexible bronchoscopic procedures performed on the patients are presented in Table 2. In three patients, combined interventional procedures were applied, including electrocautery, balloon dilatation, and cryodevitalization.

The short-term outcomes of this study were favorable; among the procedures performed, biopsy material was insufficient in two patients, resulting in an overall success rate of 90%.

3. Complications

The interventional procedures were generally well tolerated. Mild bleeding requiring the administration of epinephrine was observed following TBB biopsy. No cases of pneumothorax or moderate-tosevere bleeding were reported.

During episodes of hypoxia, the procedure was temporarily paused, and the team waited until SpO₂ and end-tidal CO₂ levels returned to normal. Bronchospasm observed during the recovery period after the procedure, rather than during bronchoscopy itself. Patients who experienced desaturation were treated with supplemental oxygen, and all of them received inhaled salbutamol. None of the patients required non-invasive ventilation support, and no cases of refractory bronchospasm encountered. were The complications observed following

interventional procedures are presented in Table 3.

Table 3: Classification of undertaken intervention procedures

Procedure	n=27	Frequency (%)
Balloon dilatation	6	22.2%
Electrocautery knife	1	3.7%
Endobronchial forceps biopsy	2	7.4%
Endobronchial cryobiopsy	6	22.2%
Transbronchial forceps biopsy	1	3.7%
Transbronchial cryobiopsy	4	14.8%
Cryodevitalization	3	11.1%
Foreign body removal with forceps	4	14.8%

Table 4: Categorization of complications

Complication	n=24	Frequency (%)
Mild bleeding	2	8.3%
Moderate bleeding	1	4.2%
Pneumothorax	0	0.0%
Bronchospasm	4	16,6%

DISCUSSION

Pediatric IP has emerged as an effective diagnostic and therapeutic approach various respiratory conditions children. Although its development has been slower than in adults-mainly due to smaller working channels in pediatric bronchoscopes—the introduction of 1.1 mm cryoprobes has enabled a wider range of minimally invasive procedures. These techniques are increasingly preferred for their safety and low complication rates compared to surgery (7, 8). The 2017 European Respiratory Society (ERS) statement emphasized the limited data

available and recommended that such procedures be performed in experienced centers (9). In our study, we found that interventional pediatric bronchoscopic procedures were safe and well tolerated.

The field of pediatric IP is rapidly expanding beyond traditional procedures such as foreign body removal. Modern advancements include now airway dilatation, cryotherapy, laser ablation, balloon bronchoplasty, and endobronchial stenting-offering minimally invasive yet highly effective options for managing complex pediatric airway conditions. These procedures significantly reduce recovery time and lower the risks associated with conventional surgery. Emerging technologies such as endobronchial ultrasound (EBUS), 3D imaging, virtual bronchoscopy, robotics, and navigation systems are further enhancing procedural precision and safety, marking transformative era in the care of pediatric respiratory disorders (10-12). study, advanced interventional methods such as balloon dilatation, biopsy, and cryodevitalization were performed.

Most pediatric bronchoscopic interventions are relatively recent developments, and comprehensive data on their precise indications and contraindications remain limited. Whenever possible, these procedures should be performed under deep sedation, with an anesthesiologist present. Each intervention must be carefully assessed in terms of its risk-benefit ratio, the availability of alternative approaches, and overall procedural safety. Performing such procedures without adequate training or proper equipment may lead serious complications. Therefore, potential risks should be anticipated, and a clear management plan must be established beforehand. The interventional pulmonologist should be proficient in rigid bronchoscopy, and the procedure suite must be fully equipped with essential tools, including a complete set of rigid bronchoscopes, bronchial blockers, hemostatic agents (such as cold saline, tranexamic acid, and epinephrine), and an intercostal drainage kit (13, 14).

In response to the growing number of interventional bronchoscopy procedures reported in the literature, the ERS released its first consensus statement on the topic in 2017. As expected, due to the predominance of pediatric case reports and small series, only a few interventions such as endobronchial and transbronchial biopsies, foreign body removal, balloon dilatation, cryotherapy, and laser-based techniques-were considered established standards of care (5, 9, 15). Since then, an increasing number of studies have reported the successful removal of foreign bodies using flexible bronchoscopy, the effective diagnosis of interstitial lung disease via transbronchial cryobiopsy, and the successful treatment of SGS through bronchoscopic techniques. The success rates of the study are consistent with those reported in the literature (15-17).

Bronchoscopy may lead to complications such as excessive coughing, patient movement (bucking), mucosal bleeding and edema, laryngospasm, bronchospasm, unexpected or prolonged apnea with hypoxemia and subsequent bradycardia, and pneumothorax. Post-procedure fever is common, typically appearing 4–9 hours after bronchoscopy. Routine antibiotic use is not recommended and should be guided by endoscopic findings, such as in cases of

bacterial bronchitis. Other possible postinterventional issues include increased oxygen requirements, persistent coughing, and pneumothorax. Although the risk of life-threatening complications is very low, it varies depending on the patient's individual risk profile, the complexity of the procedure, and the experience and proficiency of the bronchoscopist and their team (18). Our study showed that pediatric flexible bronchoscopic procedures are safe and well tolerated with a low risk of complications.

ERS Statement's response to the call for collaboration among pediatric bronchoscopists, the field has significant progress, driven by joint efforts between pediatric pulmonologists, adult interventional pulmonologists, and pediatric otolaryngologists. These interdisciplinary partnerships have begun to address many previously identified knowledge and training gaps. Consequently, a growing number of pediatric pulmonologists are integrating advanced bronchoscopy procedures into their clinical practice and actively seeking opportunities for structured-if not yet formal—training (2, 13).

formal guidelines advanced for pediatric bronchoscopy are still under development, there is a growing demand pediatric pulmonologists among structured training programs. Currently, procedural training advanced largely relies on informal mentorship from adult interventional pulmonologists and pediatric otolaryngologists, as well as short adult-focused courses. Recently, handson programs specifically designed for pediatric specialists have emerged to help bridge this gap. However, comprehensive training-either through enhanced pediatric

pulmonology fellowships or dedicated interventional bronchoscopy fellowshipswill be necessary to build true expertise. Short courses will continue to play a key role in maintaining procedural skills, especially given the variability in case volume across centers. A structured curriculum incorporating simulation, as used in adult programs, could be adapted to pediatric training for improved skill development and competency assessment. With enthusiasm for pediatric advanced bronchoscopy at an all-time high, the field must continue to grow thoughtfully and safely (3, 4). Prior to performing these procedures, I attended several official international on advanced pediatric interventional bronchoscopy and subsequently implemented the techniques in our center through international collaboration. While we await the development of formal training programs in pediatric IP, I urge leading centers and administrative bodies to be more proactive in fostering international collaborations and in supporting guest observer or trainee rotations in wellequipped, experienced centers (13).

The limited number of paediatricpediatric appropriate indications with patients compared to the adult pulmonology group, along with challenges in securing technical devices and support needed to establish a paediatricpediatric IP centrecenter, makes it difficult to gain experience in this field. Additional limitations include limited access equipment, regulatory challenges, and the lack of multidisciplinary teams. One of the limitations of the study is that some patients required repeated procedures over specific time intervals, and in conditions such as PCD, definitive success rates are difficult to

determine due to the prolonged duration needed for immunological and electron microscopy evaluations. Long-term follow-up of these patients is necessary to accurately assess treatment outcomes.

CONCLUSION

The development of pediatric flexible bronchoscopy has traditionally been limited bythelackofappropriatelysizedinstruments. Although equipment constraints are no longer the primary barrier to the field's expansion, the careful implementation of emerging techniques remains essential and should be guided by collaboration with experienced practitioners. These efforts ultimately aim to provide the safest, most minimally invasive, and effective diagnostic and therapeutic options, thereby improving care and outcomes for pediatric patients. Such initiatives are especially critical to ensuring that, in countries like TurkiyeTürkiye, all children have equitable access to less invasive healthcare interventions, just as children do elsewhere.

Highlights

1-Minimally invasive bronchoscopic procedures hold a critical position, as they have the potential to replace more invasive modalities.

2-Flexible interventional bronchoscopy seems a safe and well-tolerated modality in pediatric patients.

3-Technological advancements have significantly expanded its therapeutic capabilities.

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