



ERS statement: interventional bronchoscopy in children

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Interventional bronchoscopy in children: evidence at present, clinical practice and areas for further investigation http://ow.ly/Z7Rv30fuPV6

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ABSTRACT Paediatric airway endoscopy is accepted as a diagnostic and therapeutic procedure, with an expanding number of indications and applications in children. The aim of this European Respiratory Society task force was to produce a statement on interventional bronchoscopy in children, describing the evidence available at present and current clinical practice, and identifying areas deserving further investigation. The multidisciplinary task force panel performed a systematic review of the literature, focusing on whole lung lavage, transbronchial and endobronchial biopsy, transbronchial needle aspiration with endobronchial ultrasound, foreign body extraction, balloon dilation and occlusion, laser-assisted procedures, usage of airway stents, microdebriders, cryotherapy, endoscopic intubation, application of drugs and other liquids, and caregiver perspectives. There is a scarcity of published evidence in this field, and in many cases the task force had to resort to the collective clinical experience of the committee to develop this statement. The highlighted gaps in knowledge underline the need for further research and serve as a call to paediatric bronchoscopists to work together in multicentre collaborations, for the benefit of children with airway disorders.

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Introduction

For decades, interventional bronchoscopy in children was limited to foreign body extraction [1]. In 1978, the first report on diagnostic flexible bronchoscopy in children was published [2]. Subsequently, bronchoscopy has become an increasingly important tool in children with acute and chronic lung diseases. In 2003, a European Respiratory Society (ERS) task force published their results on flexible endoscopy of paediatric airways, concluding that it is a safe procedure provided the child is properly prepared and the procedure is performed by skilled and trained personnel [3]. In parallel with adult bronchoscopy, paediatric airway endoscopy has evolved from a primarily diagnostic procedure to include therapeutic (i.e. interventional) bronchoscopy, facilitated by the development of new and smaller instruments and devices. Today, advanced therapeutic techniques such as laser treatment, balloon dilation and stent placement are used in children in specialised centres, with an expanding number of applications and indications. A recent American Thoracic Society task force has published technical standards on flexible airway endoscopy in children [4]. The aim of this ERS task force was to produce a statement based on a systematic review of the literature on interventional bronchoscopy in children. This statement describes the evidence at present and current clinical practice, and identifies areas for future research, but does not provide recommendations for clinical practice.

Methods

The task force panel consisted of a group of clinicians with internationally recognised expertise in interventional bronchoscopy in children; a member of the early career committee of the ERS; and representatives of the European Lung Foundation (ELF). An ERS methodologist gave feedback on the research strategy and evidence synthesis and overlooked the task force process.

Panel members disclosed potential conflicts of interest according to ERS policies at the start of the task force and prior to the publication of this manuscript. The task force was initiated in September 2015 and held three face-to-face meetings, several telephone conferences and regular exchanges by e-mail. The task force members agreed on the topics that would be the focus of their work, based on clinical importance. It was decided to restrict the focus of this task force to the tracheobronchial tree, excluding the larynx, as this part of the airway is usually dealt with by ear, nose and throat specialists. Each topic of interest was assigned to a subgroup of experts, and each subgroup was led by one colleague.

The subgroups were responsible for performing systematic literature searches using the MEDLINE (accessed *via* PubMed) and Scopus databases. They first looked for systematic literature reviews, then randomised controlled trials (RCTs); if such studies were not available, they searched for observational studies, published between 1996 and 2015 in English, regardless of impact factor. In cases of limited paediatric evidence, position statements from the adult literature were consulted. For the literature searches, the main keywords child* or paediatric or pediatric, and bronchoscopy were used in addition to other relevant specific keywords. The ELF representatives conducted systematic searches of published and grey literature (online parent discussion forums) to identify parent and caregiver concerns and experiences. Records identified through database searching were complemented with additional studies identified by task force members. Duplicates were removed and titles and abstracts screened; the full text was then reviewed in potentially eligible articles.

Selected studies formed the basis of a first draft for each section, which was prepared by the subgroup leaders. The drafts were discussed during subsequent meetings and telephone conferences. Where applicable, the evidence was complemented with descriptions of current practice, based on the experience of the task force members. Thus, this statement describes the evidence at present and current clinical practice, but does not provide recommendations for clinical practice.

An additional final literature search was conducted in December 2016, in order to identify any studies published since the original search.

Advanced drafts were then submitted to the task force chairs who integrated each of the subsections into a uniform manuscript. The final version of this manuscript was reviewed and approved by all task force members prior to submission.

Results

Bronchoalveolar lavage (whole-lung lavage)

Bronchoalveolar lavage (BAL) is the most frequent procedure performed during flexible bronchoscopy, for diagnostic or therapeutic reasons. Technique and indications of diagnostic BAL have been the subject of recent international recommendations [4–6]. Here we focus on whole-lung lavage (WLL) as a therapeutic option.

Overview of the evidence and current practice

Specific search terms were whole lung lavage, interstitial pneumonitis and alveolar proteinosis. 35 articles were selected; there were no meta-analyses or RCTs, but only case series (n=3) and case reports available.

WLL is performed under general anaesthesia and, usually, muscle relaxation, with monitoring including ECG, blood pressure, pulse oximetry and capnography. In children aged ≥8 years, the technique is the same as in adults, using a double-lumen endotracheal tube (ETT) [7]. The smallest double-lumen ETT is 26 French (~8.7 mm). In infants and small children, different techniques have been proposed [8]: WLL through an elongated cuffed ETT [7] or through a balloon catheter [8, 9]; use of two ETTs: a bronchial tube for the lavage and a tracheal tube for ventilation [8, 10, 11]; WLL *via* the channel of a flexible bronchoscope with an external diameter of 2.8, 3.5 or 4.9 mm, according to the age of the patient, which allows direct visualisation and more selective lobar lavages (two techniques have been used, one with the bronchoscope being pushed down alongside a narrow ETT, or with it inserted in a large ETT [12–14]); and in severely ill children, WLL has been performed under extracorporeal membrane oxygenation [15] or liquid ventilation using polyurethane perflubron [16].

Only one lung is washed during each session, using prewarmed normal saline. When using an elongated ETT, lavage is performed using passive gravity. With the other techniques, lavage is performed using a syringe with aliquots of 20–120 mL. The lavage is continued until the effluent is satisfactorily clear. The recovered fluid can be collected via a two-way stopcock into bottles to assess turbidity. Total volume instilled is $\sim 200-300 \text{ mL} \cdot \text{kg}^{-1}$ [9, 10, 12].

WLL is frequently associated with episodes of hypoxaemia and hypercapnia. In one study analysing 64 WLLs [9], oxygen saturation values <70% occurred in the sickest patients and carbion dioxide tension (PCO_2) values increased up to 80 mmHg (10.67 kPa).

WLLs are performed in disease states associated with alveolar filling by abnormal material, with the most frequent being pulmonary alveolar proteinosis [11, 17–25]. In addition, WLLs have been used in children with metabolic disorders such as lysinuric protein intolerance [26, 27], Niemann–Pick disease [28–30] or lipoid pneumonia [31–37].

Conclusions

The role of WLL in children with alveolar filling disorders is well established.

BOX 1

Some members of the task force perform WLL: at institutions with highly experienced bronchoscopy and anaesthesiology teams in children with alveolar filling disorders

Gaps in knowledge/recommendations for future research/training

Studies to work out the best technique for WLL Studies to assess the potential side-effects of WLL on alveolar epithelium

Transbronchial and endobronchial biopsy

Overview of the evidence and current practice

Specific search terms were transbronchial biopsy, endobronchial biopsy, brush biopsy and ciliary biopsy. The search yielded 116 articles, including 20 review papers, 22 prospective and 22 retrospective studies, 30 case–control studies and 22 case series and case reports. Of those, 14 relevant articles were selected.

Transbronchial biopsy (TBB) in children is standard practice to monitor the lung allograft after transplantation, either as a surveillance or clinically indicated procedure. [38, 39]. The technique has been described previously [4, 39]. One study reported that 25% of TBBs performed in lung transplant recipients were undertaken for surveillance, 38% for follow-up of acute rejection and 37% for respiratory symptoms [40]. A treatable grade of acute rejection was found in 24% of the surveillance procedures. Additionally, this study compared findings by whether TBB was performed with adult biopsy forceps or paediatric biopsy forceps. Only 5% of the surveillance TBBs performed with paediatric forceps demonstrated acute rejection compared to 29% of the biopsies performed with adult forceps; the confounder being that the paediatric forceps were used in the younger patients, where the incidence of acute rejection is lower [41]. There was no difference in rates of acute rejection between the different sized forceps when TBB was clinically indicated. Another study of 95 surveillance TBBs in children (aged 4.9–17.3 years at time of transplant) found treatable acute rejection in 4% of asymptomatic children and in 12% of those with symptoms [42]. 11 (12%)

of the procedures recovered an inadequate amount of tissue to grade for rejection. Complications included one pneumothorax, one episode of moderate bleeding and one aspiration event (complication rate 3.2%).

Beside lung transplantation, there is a dearth of data for TBB in paediatric lung disease. One study described the findings of TBB in 38 children ranging in age from 2 weeks to 18 years [40]. Dividing outcomes based on the size of the biopsy forceps, the 1.2-mm paediatric forceps yielded an adequate tissue sample in 14 (88%) of the 16 nontransplant patients compared to adequate sampling in 20 (91%) of the 22 patients biopsied using the 2.0-mm adult forceps. Despite an adequate sample size, the diagnostic yield was 50% for the paediatric forceps and 64% for the adult forceps. In five cases there was a subsequent open lung biopsy or explant, and in three of these cases TBB findings were confirmed without additional diagnostic findings. Pathologic findings included interstitial pneumonitis, bronchiolitis obliterans, lymphoma, eosinophilic pneumonia, sarcoidosis, hypersensitivity pneumonia, asthma, infections and aspiration. The procedure was well tolerated, but the complication rate was higher in the nontransplant (8%) compared to the lung transplant (<2%) group. However, all complications occurred in those children biopsied with the adult forceps and these included pneumothoraces and excessive bleeding. Two of the three pneumothoraces in the nontransplant group occurred in patients with cystic fibrosis.

An earlier study directly compared TBB to video assisted thoracoscopic surgery (VATS) and open lung biopsy (OLB) in immunocompetent children (age 1 month to 18 years) with interstitial lung disease (ILD). In this study, a specific diagnosis could be made 50% of the time with TBB, compared to 60% with VATS and 53% with OLB [43]. The majority of the nondiagnostic procedures were performed in children aged <2 years. The only complication reported in the six children who underwent TBB was minor bleeding.

Beside these studies there are only paediatric case reports or series that contain mostly adult patients [44–50]; no major complications were reported. TBB was not helpful in making a diagnosis of pulmonary cryptococcosis [51]. However, despite the data from two previous studies [40, 43], a recent algorithm proposed by the chILD-European Union Collaboration recommends against TBB, as the consensus opinion was that samples obtained *via* TBB are too small to diagnose most ILDs in children [52].

Endobronchial biopsies in children have been performed for both clinical and research indications in multiple disease states including asthma, cystic fibrosis, chronic cough and recurrent pneumonia [53–55].

Conclusions

The limited data in the literature suggest that TBB, in the hands of experienced bronchoscopists, can provide adequate tissue sampling and has a diagnostic yield of \sim 50%, which compares to a diagnostic yield of 50–80% for OLB or VATS, depending on the underlying diagnosis. Generally, TBB is well tolerated and leads to more rapid postprocedure recovery than either VATS or OLB. The risks associated with TBB may outweigh the benefits in children with hyperinflation, severe hypoxaemia, uncorrectable coagulopathies, cystic fibrosis and children on positive pressure ventilation.

BOX 2

All members of the task force perform TBB:

at institutions with bronchoscopy teams experienced in performing TBB and pathologists familiar with reviewing histology from TBB

in children following lung transplantation

Some members of the task force perform TBB:

in children with diffuse lung disease whose clinical state allows for the procedure to be performed safely in children with suspected interstitial lung disease, bronchiolitis obliterans, sarcoidosis, lymphoma and aspiration

Gaps in knowledge/recommendations for future research/training

Studies to assess the efficacy of TBB in children with ILD

Studies to assess the efficacy of TBB in children with nodular lung disease

Studies to assess whether newer techniques, such as transbronchial cryobiopsy or endobronchial ultrasound guided biopsy, are feasible or safe in children and whether they might provide greater diagnostic yield than TBB alone

Transbronchial needle aspiration with endobronchial ultrasound

Overview of the evidence and current practice

Specific search terms were endobronchial ultrasound, EBUS, transbronchial needle aspiration, and TBNA. The search yielded 57 articles, of which 35 were selected.

Transbronchial needle aspiration (TBNA) with or without endobronchial ultrasound (EBUS) is primarily performed in adults for identification of lung cancers [56]. Conventional TBNA allows for sampling of mediastinal and hilar lymph nodes via a flexible bronchoscope, decreasing the need for more invasive techniques. Using a standard lymph node map and endobronchial landmarks, experienced operators blindly sample lymph nodes adjacent to the main airways [57]. Inadvertent puncture of vascular structures is a potential risk, although rarely reported. Conventional TBNA has been used successfully in the diagnosis of isolated intrathoracic tuberculous lymphadenopathy in symptomatic children aged \geqslant 9 months at high risk of tuberculosis [58, 59]. Due to their size, younger children may only be suitable for subcarinal sampling, with a diagnostic yield of \sim 50% [59]. Older children (aged \geqslant 12 years) may be amenable to right paratracheal, bronchial or hilar node sampling, thereby increasing the diagnostic yield to >80% [58].

In contrast, EBUS TBNA allows real-time identification of the puncture site. Two types of EBUS are used in clinical practice. Radial probe EBUS is suitable for localisation and sampling of peripheral lesions such as pulmonary nodules. A 1.2-mm diameter EBUS probe with a 1.7-mm outer plastic guide sheath is passed through the working channel of the bronchoscope. Ideally, under fluoroscopic guidance, the bronchoscope is guided to the lung segment of interest. The EBUS is advanced sequentially into subsegments until the pathological area is identified. The EBUS is withdrawn, leaving the sheath in place, through which the biopsy forceps or brush is then passed and samples taken [60]. Currently, a 4.0-mm bronchoscope is the smallest suitable for radial probe EBUS. Primarily used to identify lung cancer, it has been used to identify other causes of peripheral lung nodules, including mycobacterial infection. A meta-analysis of selected patients in centres of excellence reported a diagnostic yield of 70%; complications are rare, with a pneumothorax rate of 1.5% [60]. In children, EBUS has been used to diagnose vascular malformations affecting the airway [61], but there are no reports of radial probe EBUS for peripheral lung lesions.

Linear (or convex) probe EBUS is performed using a dedicated bronchoscope (6.9-7.4 mm) with a linear array ultrasound transducer built into the tip (puncturescope). A disposable saline-filled balloon can be added to the tip to improve image quality. Lymph nodes of interest are identified by the puncturescope, and a flexible 21-gague or 22-gague needle is passed through the 2-mm instrument channel and then thrust 15-20 times within the lymph node under real-time ultrasound visualisation. Lymph node contents can be aspirated by suction with a syringe [62]. After withdrawal a stylet is inserted through the needle to evacuate residual tissue. For diagnosis of lung cancer, the procedure is repeated a minimum of three times, but additional sampling may be required for microbiological diagnoses. Rapid on-site evaluation of tissue samples can be helpful to improve diagnostic yield, decrease the number of needle passes and reduce the need for additional diagnostic procedures [56]. In adults, linear probe EBUS TBNA is the investigation of choice for mediastinal or hilar lesions to identify lung cancer [63] and sarcoidosis [56], and may be helpful in the diagnosis of lymphoma [56] and mycobacterial infection [64]. It is associated with improved specimen acquisition, improved diagnostic yield, decreased complications or need for more invasive procedures. Diagnostic yield for lung cancer is 89% [63] and for tuberculous lymphadenopathy is 80% [61]. In children, linear probe EBUS TBNA is suitable for investigation of mediastinal or hilar lesions to diagnose leukaemia [65], lymphoma [65], sarcoidosis [66] and tuberculosis [67]. Although a 6.9-mm diameter puncturescope can be passed through a 2.5 larvngeal mask airway (LMA), ventilation is limited and a 4.0 LMA is preferable. EBUS TBNA can be performed under either general anaesthesia or sedation, and is generally well tolerated in children aged ≥9 years [68]. Adequate sampling can be achieved in 95% of cases, although diagnostic yield may only be 47%. The complication rate in children appears to be very low [65-68].

Conclusions

In children, EBUS TBNA can decrease the need for more invasive procedures, although the diameter of the puncturescope may limit its use. Practitioners performing EBUS TBNA should have specific training [69].

BOX 3

Some members of the task force perform EBUS TBNA:

at institutions with highly experienced bronchoscopy and anaesthesiology teams and in conjunction with suitably trained adult bronchoscopists

for mediastinal or hilar lesions to diagnose leukaemia, lymphoma, sarcoidosis and tuberculosis

Gaps in knowledge/recommendations for future research/training

Studies to assess whether EBUS TBNA is safe in children

Studies to assess the efficacy of EBUS TBNA in children with leukaemia/lymphoma

Studies to assess the efficacy of EBUS TBNA in children with granulomatous diseases

Foreign body extraction

Overview of the evidence and current practice

Specific search terms were foreign body aspiration, bronchoscopy, diagnosis, removal and complication. The search yielded 154 articles, including four reviews and 18 prospective studies. Of those, 45 relevant articles were selected.

Traditionally, rigid bronchoscopy has been used for foreign body extraction with very high success rates [3, 4, 70]. It is the primary method of choice for asphyxiating foreign bodies, as it guarantees a secure airway [71–73]. In children with a history of choking, a preceding flexible bronchoscopy reduces the rate of negative rigid bronchoscopies [72, 73]. In recent years, flexible bronchoscopy has increasingly been used for foreign body extraction [74]. There is growing evidence that flexible bronchoscopes can be used as a removal tool (either alone or in combination with a rigid bronchoscope), using biopsy or grasping forceps, or wire baskets, with varying success rates [75–78]. Attempts to extract foreign bodies using a cryoprobe have been reported [79]; however, in children this technique has been associated with a high rate of complications [80]. If a flexible bronchoscope is used for foreign body extraction, immediate availability of a rigid instrument has been repeatedly recommended to guarantee safety of the procedure in case extraction attempts fail or complications occur [74, 75].

Our literature search identified no studies that systematically assessed the rate of complications with foreign body extraction. Mild-to-moderate, as well as severe complications have been reported in varying frequencies [75, 76, 81, 82]. Mortality directly related to the procedure is rare [81]. Complications were found to be more frequent in children with delayed diagnosis and intervention [83].

Conclusions

There is general agreement in published guidelines that bronchoscopy should always be performed in a child with a history of choking, even in the absence of respiratory symptoms, and in a child with suggestive respiratory symptoms and/or suggestive physical and/or radiological findings, even in the absence of a history of choking [72, 84]. In this situation, rigid bronchoscopy is considered the intervention of choice (box 4). In other situations, flexible bronchoscopy is usually considered the primary tool for confirmation or exclusion of foreign body aspiration (FBA). If the foreign body type and location allows, it may be removed with the flexible bronchoscope, after securing the airway with an LMA or ETT and provided immediate availability of a rigid bronchoscope. Otherwise, the procedure is directly converted to rigid bronchoscopy.

BOX 4

All members of the task force perform bronchoscopy in children with a positive history of FBA All members of the task force perform rigid bronchoscopy in children with a positive history of FBA and: asphyxia a radionague forcion body.

a radiopaque foreign body unilaterally diminished breath sounds radiographic abnormalities (e.g. unilateral/focal hyperinflation)

Gaps in knowledge/recommendations for future research/training

Studies to assess the efficacy of different methods for foreign body extraction Studies to assess the rate of complications with foreign body extraction

Balloon dilation and occlusion

Overview of the evidence and current practice

Specific search terms included balloon, ballooning, dilation, dilatation, bronchopleural fistula, haemoptysis and hemoptysis. 30 articles were selected: there were no meta-analyses or RCTs or reviews; only case series and case reports were available.

Since the first description of balloon dilation for tracheal and bronchial stenosis in 1984 [85], balloon dilation has evolved as a treatment for paediatric airway obstruction, especially laryngotracheal stenosis [86]. The procedure is usually performed under general anaesthesia alongside topical anaesthesia with lidocaine to reduce airway irritability. In general, a rigid instrument is preferred, but balloon dilation has been performed *via* LMA with an adult flexible bronchoscope [87] and *via* tracheostomy [88, 89]. Muscle relaxation is not essential, but is preferable to avoid coughing with an inflated balloon in the airway, which might cause dislodgement of the balloon, pneumothorax or

airway rupture [89]. In children, angioplasty balloon catheters are most widely used since they impart a radially directed force against the airway lumen, which is less traumatic to the mucosa than a bougie [86, 90, 91]. Tracheobronchography with small volumes of contrast agent can be performed to assess the location, length and diameter of the stenosis [92]. The procedure begins with a balloon diameter approximating the airway diameter immediately distal to the stenosis. The balloon should be long enough to cover the stenosis and to ensure catheter stability as the balloon is inflated. The small-sized airway balloons can be visualised easily with rigid bronchoscopes during the procedure. The balloon is moved to the airway stenosis and filled with saline solution by an inflation/deflation hand pump connected to a pressure gauge that monitors pressure within the balloon. There is no clear recommendation on optimal time for balloon inflation. Some inflate for 30-60 s, or interrupt if vital signs deteriorate [93]. The procedure can be repeated with the same balloon or a larger one. In case of severe and relapsing stenosis the end-point is best determined under fluoroscopy by the disappearance of the balloon waist during inflation. Carinal stenoses are usually treated by inflating two kissing balloons side by side in both mainstem bronchi to minimise the risk of bronchial rupture [92, 94]. Simultaneous inflation of both balloons allows adequate dilation of the trachea without overdilation of the bronchi. A technique similar to angioplasty based on the use of a standard guidewire under fluoroscopic guidance has also been described [89, 92]. Intravenous corticosteroids are useful to reduce postoperative oedema [95].

Balloon dilation has been used alone or with other techniques such as laser treatment [95–97], stent placement [98–104], mitomycin application [93], injection of intralesional corticosteroids [105] and by anaesthetists during VATS in children [106]. Serial balloon dilation has been used successfully to manage severe complications following slide tracheoplasty in children with congenital tracheal stenosis [97, 104, 105], to treat acquired tracheal [95, 107–109] or bronchial stenosis [110, 111] and to treat stenosis due to granulation tissue after airway stenting [89]. In addition, bronchoplasty by balloon dilation has been used to dilate the airway segment proximal to a foreign body to facilitate extraction [112, 113]. The use of the technique for posterior tracheal splitting [94, 96, 99, 101, 103, 114] is considered hazardous and accepted only as a lifesaving procedure or as a temporary measure until a surgical procedure can be undertaken [115].

In addition, airway ballooning can be performed to obtain endobronchial occlusion in cases of bronchopleural fistula or massive haemoptysis. The technique has been described in only a few case reports, and for bronchopleural fistula consists of placing a guidewire along the endotracheal tube and a balloon angiography catheter with a small volume of contrast agent [94, 116]. Under fluoroscopic guidance the fistula can be detected by inflating the balloon in different sites until the chest tube stops producing bubbles. The balloon should be deflated at intervals for short periods of time to reduce pressure on the bronchial walls, and care must be taken to avoid balloon overdistension. Potential adverse effects include accumulated secretions with a risk of infection, necrosis, stenosis or bronchial wall erosion with potential migration of the balloon [116]. Balloon occlusion has been detailed in only one paediatric case with life-threatening haemoptysis [94]. Due to scarce evidence, the safety and effectiveness of balloon occlusion is still unclear.

Conclusions

In specialised centres, the role of balloon dilation in the paediatric population is expanding for tracheal and bronchial stenoses. Improvement in symptoms and an increased airway diameter are expected end results after balloon dilation, but repeated procedures are usually necessary to effect a long-term improvement.

BOX 5

Some members of the task force perform balloon dilation:

at institutions with highly experienced bronchoscopy and anaesthesiology teams

for complications following slide tracheoplasty, and for acquired tracheal or bronchial stenosis (e.g. due to tracheal or bronchial stents)

Gaps in knowledge/recommendations for future research/training

Studies to assess the efficacy of balloon dilation in acquired tracheal stenosis compared to open surgery Studies to assess the efficacy of balloon dilation in acquired tracheal stenosis compared to a combination of laser-assisted endoscopic surgery and balloon dilation

Studies to assess the optimal balloon diameter and inflation time in relation to the patient's age

Laser-assisted procedures

Overview of the evidence and current practice

Specific search terms included laser, laser surgery, laser therapy and respiratory tract diseases. The search yielded 169 articles, and 40 relevant articles were selected; there were no meta-analyses or RCTs, but only (reviews of) case series and case reports available.

In the 1960s, lasers were introduced to medicine. Since then, their use has rapidly spread to diverse specialties both in adult and paediatric practice. Recent technological development, with miniaturisation of flexible and rigid bronchoscopes and their corresponding accessories, has enabled their use in the airways of small children and infants. Lasers produce a beam of monochromatic, phased and collimated light that can induce tissue vaporisation, coagulation, haemostasis and necrosis. Biological effects depend on the wavelength emitted by the laser source [117]. There are several types of lasers that are currently used in interventional bronchoscopy:

- The carbon dioxide laser is the most frequently used in the larynx, because it is air-transmitted and targeted onto a red light spot with which it is easy to aim under laryngeal suspension [94]. Conversely, when employed in the tracheobronchial tree it becomes more cumbersome because the lesions to be treated are not as easily addressed as the ones in the upper airway [118].
- The Nd:YAG laser is popular in adult practice due to its effectiveness when performing endoluminal
 recanalisation of the trachea or main bronchi in patients with malignant obstructive tumours. Its
 significant in-depth effect, with the potential risk of airway wall perforation, makes it less suitable for
 infants and small children [94].
- KTP (kalium-titanium-phosphate) and diode lasers are transmitted by means of a fibre and when delivered at a low power range (<5 W), the KTP laser can show similar tissue effects as those observed with a carbon dioxide laser. Very thin coated fibres (200−600 µm) can be used with both rigid and flexible paediatric bronchoscopes through the working channel (≥1 mm diameter). Alternatively, the fibre can be taped, with two or three adhesive strips, to the rod lens telescope and handled as a sole device inside the rigid bronchoscope. These types of lasers are the most frequently used when dealing with tracheobronchial lesions in the paediatric setting [117].

Bronchoscopic laser-assisted procedures are performed under general anaesthesia with muscle relaxation to avoid inaccurate targeting due to the child's movement. There is general agreement that specific safety measures must be addressed during the procedure: fractional inspired oxygen must be reduced to <0.25 before firing the laser beam to diminish the risk of airway ignition; smoke should be eliminated from the airway by a suction catheter connected to a side port of the rigid bronchoscope; and any flammable material in the operative field should be removed or protected against ignition [117].

Several tracheobronchial lesions can be managed effectively and safely by means of laser-assisted endoscopic surgery. Acquired web-type tracheal stenosis, without involvement of the cartilage framework, is a well-established indication and is usually treated by performing three or four radial incisions leaving intact mucosal bridges. Balloon dilation is usually performed next, to optimise the outcome. Current practice warns against circumferential resections, or in-depth procedures with cartilage exposure, because of the high risk of severe restenosis [94]. Granulomas, or obstructive granulation tissue, can be photoresected in a safe and haemostatic way by placing the tip of the laser fibre on the protruding surface and vaporising or carbonising the lesion. Excision of suprastomal granulomas prior to tracheostomy tube removal appears to be the most frequent indication in children [119, 120]. In addition, endoscopic laser therapy has been reported in the management of symptomatic tracheal pouches, sealing of recurrent tracheoesophageal fistulas, repair of laryngo-tracheal clefts and splitting complete tracheal rings in congenital tracheal stenosis [96, 121–123].

In contrast to adult practice, laser photoresection of endoluminal airway tumours in children has been reported infrequently and for some entities is not the recommended treatment option. Some authors have reported bronchoscopic resection of inflammatory pseudotumors, endobronchial carcinoids and haemangiomas [124–127]. Respiratory papillomas affecting the tracheobronchial tree can be removed endoscopically with a laser or microdebrider [128].

In primary tuberculosis, endoscopic laser-assisted debulking of enlarged lymph nodes with endobronchial involvement has been reported [117].

Conclusions

Despite the limited information available, indications for laser-assisted endoscopic procedures in the paediatric airway appear to be increasing. There are no well-established criteria for laser intervention in children, and each procedure should be considered on an individual basis.

BOX 6

Some members of the task force perform laser-assisted endoscopic procedures:

at institutions with highly experienced bronchoscopy and anaesthesiology teams under strict observation of safety measures

for photoresection of granulomas or obstructive granulation tissue

for incision of acquired web-type tracheal stenosis

for the treatment of clefts, tracheal pouches and recurrent tracheo-oesophageal fistulas

Gaps in knowledge/recommendations for future research/training

Studies to assess the most adequate type of laser to be used in the paediatric airway

Studies to assess the optimal laser beam power and way of delivery (continuous, pulsed or ultrapulsed) in relation to specific lesions

Studies to assess the efficacy of laser-assisted endoscopic procedures alone compared to a combination of laser-assisted procedures and balloon dilation

Airway stents

Overview of the evidence and current practice

Specific search terms included airway, bronchus, trachea and stent. 31 relevant articles were selected; there were no meta-analyses or RCTs, but only reviews, case series and case reports available.

Airway stents are routinely placed in adults, mostly for malignant diseases as palliative measures. Stent placement in children must take account for the soft airway structures, the considerable luminal growth that needs to be accommodated by the implants and the usually histologically benign nature of the airway obstruction, in contrast to adults. There are several types of stents currently used in interventional bronchoscopy:

- Silicone stents tend to dislocate [129], and deaths due to airway obstruction caused by dislocated stents have been reported [130]. It has been recommended that these stents should not be used in central airways other than after surgery [131].
- Metal mesh stents (bare or partially covered) tend to cause granulation or wall damage and need to be considered permanent (ingrowth). Thus, they may cause secondary stenosis with airway growth [131].
- Biodegradable stents have theoretical advantages in some circumstances, but they have a tendency to dissolve too early and severe complications (death due to stent fragmentation and aspiration) have been reported [132, 133]. Clearly, biodegradable material would be preferable, as it could avoid the long-term consequences of ingrown metal mesh stents as well as the secretion retention, granulation and displacement issues of removable covered or silicone stents. Currently, there is insufficient experience to draw conclusions regarding the utility of biodegradable stents, and their use is restricted to research protocols. Material improvements and more experience may change this in the future.

A systematic review of earlier case series with mostly metal and some silicone stents, including 121 cases, documented an initial success rate of 92.6% with a mortality of 11.6% [131]. In the same review, a second group of publications focusing on stent-related complications (49 cases) was analysed and showed a 16.3% stent-related mortality; both series taken together amounted to a 12.9% mortality. Subsequently, a number of retrospective case series have been published. Two series with five patients each reported the long-term outcome of stents used in tracheal stenosis after endoscopic dilation, with good functional outcomes, but a high complication rate [103, 134]. Another case series reported on rapamycin-eluting stents after balloon dilation of congenital tracheal stenosis in eight infants, but with only a short follow-up [135]. A retrospective study of 21 severely sick patients in whom stenting was used as the last resort reported clinical improvement in 18 (85%) patients with complications requiring endoscopic treatment or removal of the stent in five (27%) of them; stent related mortality was 4% [136]. Similarly, a recent study on the use of stents in children with severe airway problems due to mucopolysaccharidosis reported considerable and partly severe complications [137]. Another article reported on the use of endotracheal nitinol stents in seven children, again describing a high frequency of complications [138]. A large retrospective case series of 100 patients, in whom 120 metal, 112 silicone and three biodegradable stents were placed, included children with less severe disease than previous series [129]. Although patient selection in this study was different to most other published series, complications were seen in 71-87%, according to stent type. Typical complications include the formation of major granulation tissue requiring laser treatment and/or stent replacement, stent dislocation, ovalisation requiring dilation, airway perforation and infection [129, 131].

Conclusions

In experienced hands, the placement of airway stents is technically feasible, with little directly procedure-related morbidity or mortality. Stent implantation for benign paediatric airway disease can be useful either for temporary luminal stabilisation after airway surgery or for relief of severe airway malacia or stenosis when all other medical and surgical options have failed or are contraindicated. Complications are encountered frequently and their treatment requires considerable expertise, which must be available at centres offering this treatment. Although the usefulness of stents as temporary scaffolding appears to be well established in children post airway surgery [97, 104], available data do not allow a firm conclusion for stent placement in defined clinical circumstances. Metal stents should be avoided in children with benign disease due to the difficulty of removal and complications [139]. If stents are used, comprehensive information must be given to parents/patients about their possible benefits and risks to allow informed consent.

BOX 7

Some members of the task force perform stent placement:

at institutions with highly experienced bronchoscopy and anaesthesiology teams

as a last resort when all other conservative and surgical options have failed to wean off the ventilator over a long period of time or have failed to relieve life-threatening obstructive episodes or are contraindicated

for luminal stabilisation post airway surgery

Gaps in knowledge/recommendations for future research/training

Studies to assess the utility of biodegradable stents

Microdebriders

Overview of the evidence and current practice

Specific search terms included microdebrider and endoscopy. The search yielded five articles; there were no meta-analyses or RCTs, but only reviews and case reports available.

The use of microdebriders has increased in the past decade in adults and children, in a wide spectrum of diseases, from the nasal cavity to the bronchi, but especially recurrent respiratory papillomatosis [140]. There are many microdebriders available with varying diameters, lengths, angles, rotational properties and tip configurations (aggressive cutting or delicate tips). In the distal tip, a vacuum pulls the tissue and the rotating blade amputates it. Due to the lack of haemostatic capability, topical epinephrine or oxymetazoline or, rarely, endoscopic cautery devices are used to control bleeding. Microdebriders have been used for the removal of granulations and thin scar bands in the trachea [141] and in the management of excess suprastromal granulation tissue following tracheostomy [142].

Conclusions

Due to the scarce experience reported, there are no well-established indications for the use of microdebriders in children. This technique should only be performed at institutions with highly experienced bronchoscopy and anaesthesiology teams. None of the task force members uses microdebriders.

Gaps in knowledge/recommendations for future research/training

Studies to assess the utility of microdebriders in children

Cryotherapy

Overview of the evidence and current practice

Specific search terms included cryotherapy and endoscopy. The search yielded 17 articles, of which two were selected; there were no meta-analyses or RCTs or reviews, but only case reports available.

Cryotherapy is performed by using a freezing instrument during bronchoscopy. The cryogen is liquid carbon dioxide. An ice ball is generated by inserting the freezing probe into the lesion, then the crystallised lesion is removed from the airway. This procedure is repeated several times to remove the lesion. To stop bleeding, argon plasma coagulation is used. In children, cryotherapy has been used in

association with argon plasma coagulation for removing a low-grade bronchial mucoepidermoid carcinoma [143] and an inflammatory myofibroblastic tumour [144].

Conclusions

Due to the scarce experience reported, there are no established indications for cryotherapy in children. None of the task force members uses cryotherapy.

Gaps in knowledge/recommendations for future research/training

Studies to assess the utility of cryotherapy in children

Endoscopic intubation

Overview of the evidence and current practice

Specific search terms included endoscopic intubation. The search yielded 11 articles of different types; there was no meta-analysis available.

Flexible bronchoscopic intubation represents the most frequent primary indication for interventional bronchoscopy in paediatric intensive care patients [145, 146], particularly for critically ill [147] and syndromic [148] patients. In children nasal intubation tends to be easier than oral intubation, because the angle around the base of the tongue is less sharp than in adults. Moreover, it is preferred to oral intubation when full access to the oral cavity is required for surgery or when the mouth opening is limited. Oral flexible intubation can be performed via a modified oropharyngeal Guedel airway (cut through its entire dorsal length to facilitate the removal of the flexible bronchoscope) or via LMA [149]. Nasal intubation can be achieved either through an appropriately modified ventilation mask (Frey type) or mask adapter with port opening, or without an aiding device. The ETT is mounted on a flexible bronchoscope (with an external diameter $\geqslant 1$ mm smaller than the ETT diameter) and secured near the proximal end. The patient's head is maintained in neutral position. The lubricated bronchoscope is introduced via a nostril or the mouth and advanced into the larynx after topical lidocaine administration. Once in the trachea the ETT is advanced over the bronchoscope [4]. To avoid getting hung up at the arytenoids, a 90° counterclockwise rotation of the ETT has been recommended [150].

Conclusions

The role of flexible bronchoscopy in the intubation of children with difficult airways is well established. This technique is usually available in every paediatric intensive care unit and operating room and it is usually a skill of every paediatric anaesthesiologist. All members of the task force perform flexible bronchoscopic intubation in children with difficult airways.

Gaps in knowledge/recommendations for future research/training

Every paediatric bronchoscopist should be trained in endoscopic intubation of children of all ages

Application of drugs and other liquids

Several bronchoscopic techniques for local drug application have been developed. They are mostly applied in adults; for children, there are only occasional reports or small case series available.

Tracheo-oesophageal fistula repair

Overview of the evidence and current practice

Specific search terms included tracheoesophageal fistula. The search yielded 26 articles of different types; there was no meta-analysis available.

Tracheo-oesophageal fistula (TOF) repair has been performed *via* bronchoscopy as an alternative to open surgery. Different techniques have been described to achieve endoscopic TOF closure, such as injection of a sealant, de-epithelialisation of the fistula, or a combination of both [151–154]. These techniques have a low risk and are associated with less morbidity, but a lower success rate, with very high refistulation rates [153]. Endoscopic closure is preferred in recurrent TOF after unsuccessful attempts with open surgery and isolated TOF without oesophageal atresia [155, 156].

Conclusions

Due to the scarce experience reported, the most appropriate technique for endoscopic closure of a TOF is unclear. With relatively low success rates, only recurrent TOF or a second, so far unnoticed, fistula (*i.e.* in the already operated child) appears to be an indication for endoscopic closure. Some members of the task force perform endoscopic TOF repair.

Gaps in knowledge/recommendations for future research/training

Studies to assess the efficacy of endoscopic TOF repair

Bronchopleural fistula treatment

Overview of the evidence and current practice

Specific search terms included bronchopleural fistula. The search yielded six articles; there was no meta-analysis available.

In the paediatric literature, aetiologies for bronchopleural fistula (BPF) have included mainly empyema/ necrotising pneumonia, but also FBA and iatrogenic causes. Flexible bronchoscopy has been used to confirm and/or treat persistent BPF [157, 158]. When a BPF is not clearly visible on bronchoscopy, selective bronchography at the suspected site may be utilised [159]. Alternatively, selective instillation of methylene blue into segmental bronchi with its subsequent appearance in the chest drainage may help confirm and localise BPF [160]. The technique of endobronchial occlusion using a balloon is described earlier.

Conclusions

In clinical practice, depending on the individual situation and given the difficulty and the limited experience with the procedure, other options (e.g. wait and see, surgery, application of a sealant via the drain or intrabronchial valves) are usually preferred over interventional bronchoscopy. None of the task force members performs endoscopic bronchopleural fistula treatment.

Gaps in knowledge/recommendations for future research/training

Studies to assess the utility of endoscopic bronchopleural fistula treatment

Atelectasis treatment

Overview of the evidence and current practice

Specific search terms included atelectasis. The search yielded 33 articles; there was no meta-analysis available.

Atelectasis usually resolves spontaneously. Persistent and recurrent atelectasis are important indications for diagnostic flexible bronchoscopy [3, 4]. Depending on the endoscopic findings, further targeted actions may be undertaken, such as suctioning, foreign body extraction, sampling of various materials and other more specific procedures. An attempt to re-inflate the atelectatic lung parenchyma with repeated saline lavages is considered standard practice [4]. In refractory atelectasis, bronchoscopic applications of various drugs have been tried. Surfactant administration was reported to improve ventilation by re-aeration of atelectatic regions and help wean children from mechanical ventilation [161]. Similarly, bronchoscopically administered recombinant human DNase has been used in cystic fibrosis patients [162], non-cystic fibrosis patients [163], and premature neonates [164], with variable success.

Conclusions

Due to the scarce experience reported, and with the vast majority of atelectases resolving spontaneously, the most appropriate endoscopic treatment of persistent atelectasis is unknown. All members of the task force perform endoscopic treatment of atelectasis, with various agents such as acetylcysteine, saline, sodium bicarbonate and recombinant human DNase.

Gaps in knowledge/recommendations for future research/training

Studies to assess the efficacy of endoscopic treatment of persistent atelectasis with various agents

Plastic bronchitis treatment

Overview of the evidence and current practice

Specific search terms included plastic bronchitis. The search yielded 14 articles; there was no meta-analysis available.

Management of plastic bronchitis is difficult, and aggressive measures to remove casts combined with intensive medical care are often necessary. In refractory cases bronchoscopic drug application has been tried. It appears that endoscopic administration of tissue plasminogen activator (tPA) is a safe and effective option [165]. Airway clearance with inhaled tPA may be effective in both patients with inflammatory disease and patients undergoing surgery for congenital heart disease [165, 166]. In addition, intrabronchial DNase [167] and nebulised hypertonic saline have been reported to be beneficial [168].

Conclusions

Due to the scarce experience reported, the most appropriate (endoscopic) treatment of plastic bronchitis is not known. All members of the task force perform endoscopic treatment of plastic bronchitis with various agents, including tPA.

Gaps in knowledge/recommendations for future research/training

Studies to assess the efficacy of endoscopic treatment of plastic bronchitis with various agents

Haemoptysis control

Overview of the evidence and current practice

Specific search terms included haemoptysis and hemoptysis. The search yielded 13 articles; there was no meta-analysis available.

Haemoptysis is a relatively uncommon indication for diagnostic bronchoscopy in children. Flexible bronchoscopy is generally contraindicated for investigation or treatment of massive haemoptysis [3]. Effective intervention in patients with excessive bleeding into the airways may include endoscopic evaluation with the rigid bronchoscope and possibly local application of vasoconstrictors. Therapeutic lavages with epinephrine (1:10 000 or 1:20 000 solution) or cold saline at 4°C have been suggested [169].

Conclusions

In clinical practice, flexible or rigid bronchoscopy with or without application of cold saline or adrenaline are used to control haemoptysis depending on the individual situation. Some members of the task force perform therapeutic lavages with epinephrine or cold saline.

Gaps in knowledge/recommendations for future research/training

Studies to assess the role of endoscopic evaluation and therapeutic lavages in the multidisciplinary management of patients with massive haemoptysis

Caregiver perspectives

Specific search terms included bronchoscope, bronchoscopy, communication, concerns, experience, foreign body aspiration, foreign object removal, interventional bronchoscopy, parent, patient and perspective.

Caregiver experiences relate to two uses of bronchoscopy: exploratory use and foreign body removal. Key themes are understanding, reassurance, discomfort and sedation. Postbronchoscopy caregiver reflections are generally positive, due to infrequent adverse side-effects and the outcome of knowing more about their child's condition or successful treatment.

Exploratory bronchoscopy

Caregivers are often anxious about the procedure, which increases with lack of information and reassurance from healthcare professionals before and after the procedure. Information about noninvasive alternatives is desirable, with interventional bronchoscopy prescribed only when there are no noninvasive alternatives [115]. Caregivers recognise the value of bronchoscopy to gain information about a respiratory condition, but have concerns about the sedation of young children [170]. Anxiety could be relieved to a large extent with information and reassurance on the purpose of the procedure; sedation/anaesthesia and

side-effects, e.g. disorientation; discomfort, e.g. sore throat, coughing; duration of the procedure and side-effects; and caregiver accompaniment, e.g. staying with the child until sedated [115, 170].

Foreign body removal

Caregivers and primary care professionals should be able to recognise the potential signs of FBA, especially in nonemergency situations, *e.g.* when a caregiver visits the local doctor with a child with acute-onset breathing difficulties [171–173]. Recognising FBA as a potential cause of breathing difficulties and performing a bronchoscopy within 24 h of symptom onset reduces the risk of complications [83, 174]. As a preventative strategy, primary care professionals are ideally placed to educate parents about FBA from birth and during early childhood [173].

Caregiver education and awareness is essential in reducing the incidence of FBA in preschool children [171, 172, 174]. Caregivers and healthcare professionals have called for the general public, and especially parents of young children, to be made aware of the risks of giving children foods that are too small for them to chew and swallow safely, or toys with small detachable parts, and how to identify the signs of FBA [171, 174–176]. If caregivers are aware of the risks, and supervise the handling of foreign objects by children, any ingestion, insertion or inhalation can be reported and responded to promptly, thus reducing the risk of damage or even death [175]. Caregiver information is essential from the age at which children start eating solid foods, with nuts and crunchy foods such as carrots of particular concern [174, 177]. Information is also vital at the point of discharge following a FBA incident to prevent reoccurrence [176, 177].

Conclusion

The advent of suitably sized paediatric bronchoscopes with a working channel provides the well-trained bronchoscopist the ability to offer appropriately selected children interventional bronchoscopic procedures. However, the number of children requiring interventional bronchoscopic procedures is small constraining the training experience for paediatric bronchoscopists. Yet, for an individual child an interventional bronchoscopic procedure may significantly limit morbidity from either the underlying disease process or from a more invasive procedure.

Adult bronchoscopists possess greater experience and training in the field, but are not familiar with the unpredictable nature of the paediatric airway. Novel approaches in the training of paediatric bronchoscopists in collaboration with adult bronchoscopists needs to be considered, as does the establishment of paediatric centres of excellence in interventional bronchoscopy to assure that individual practitioners maintain their skills.

The scarcity of published studies in this field in general underlines the need for further research, but meaningful advancement in the field will require multicentre collaboration. The highlighted gaps in knowledge throughout the manuscript serve as a call to paediatric bronchoscopists to work and learn together for the benefit of children with airway disorders.

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