ESPGHAN-NASPGHAN Guidelines for the Evaluation and Treatment of Gastrointestinal and Nutritional Complications in Children with Esophageal Atresia- Tracheoesophageal Fistula

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Abstract

Bckground: Esophageal atresia (EA) is one of the most common congenital digestive anomalies. With improvements in surgical techniques and intensive care treatments, the focus of care of these patients has shifted from mortality to morbidity and quality of life issues. These children face gastrointestinal (GI) problems not only in early childhood but also through adolescence and adulthood. However, there is currently a lack of a systematic approach to the care of these patients. The gastrointestinal working group of International Network on Esophageal Atresia (INoEA) comprised of members from ESPGHAN/NASPGHAN was charged with the task of developing uniform evidence-based guidelines for the management of GI complications in children with EA.

Methods: Forty clinical questions addressing the diagnosis, treatment and prognosis of the common gastrointestinal complications in EA patients were formulated. Questions on the diagnosis, and treatment of GER, management of "cyanotic spells", etiology, investigation and management of dysphagia, feeding difficulties, anastomotic strictures, congenital

esophageal stenosis in EA patients were addressed. The importance of excluding eosinophilic esophagitis and associated GI anomalies in symptomatic EA patients is discussed as is the quality of life of these patients and the importance of a systematic transition of care to adulthood. A systematic literature search was performed from inception to March 2014 using Embase, MEDLINE, the Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Clinical Trials, and PsychInfo databases. The approach of the Grading of Recommendations Assessment, Development and Evaluation was applied to evaluate outcomes. During 2 consensus meetings, all recommendations were discussed and finalized. The group members voted on each recommendation, using the nominal voting technique. Expert opinion was used where no randomized controlled trials were available to support the recommendation.

Keywords: esophageal atresia; guidelines; gastroesophageal reflux; fundoplication; tracheomalacia; Anastomotic stricture; congenital esophageal stenosis; esophageal motility; high resolution manometry; esophageal impedancemetry; aspiration; dysphagia; feeding disorder; transition; esophageal carcinoma; Quality of Life

Introduction

EA is one of the most common digestive malformation occurring in 1 in 2,400 to 4,500 births worldwide.[1] Since the first successful primary repair by Cameron Haight in 1941, postoperative outcomes have changed. With the exception of patients suffering from severe concomitant malformations such as congenital heart disease, improvements in operative and perioperative care issues have shifted the focus from mortality to morbidity and quality of life issues.[2-4] EA is no more just a neonatal surgical problem but a life-long problem.

Other than respiratory problems, nutritional and GI issues are prevalent not only in the first years of life but also in adolescence and adulthood. Gastroesophageal reflux (GER), peptic esophagitis, gastric metaplasia and Barrett esophagus, anastomotic strictures, feeding disorders, dysphagia, esophageal dysmotility are the most frequent GI short and long-term complications encountered in children and adolescents. Concerns in adults include esophageal adenocarcinoma and epidermoid carcinoma which have been recently been reported.[3]

To date, although morbidity is well known and the need for careful multidisciplinary follow up is highlighted, no recommendations on the GI and nutritional management of infants and children with EA are available. There is currently a lack of a systematic approach for the care of these patients not only during childhood but through transition to adulthood. Hence the International Network on Esophageal Atresia (INoEA) was formed in 2013 to help formulate clinical practice guidelines for the care of these patients.

Methods

The project started in February 2014, when under the auspices of INoEA, a working group consisting of selected members including both pediatric gastroenterologists and a pediatric surgeon from ESPGHAN and NASPGHAN was formed to look at formulating evidence-based clinical practice guidelines based on current knowledge for the evaluation and treatment

of GI and nutritional complications in children with EA. Clinical questions relevant for the evaluation and treatment of GI and nutritional complications in children with EA and tracheoesophageal fistula (TEF) were formulated (Table 1).

The questions were formulated by the members of the working group on GI morbidity in children with EA. Members of this working group included both ESPGHAN/NASPGHAN members. After the questions were formulated, the guidelines committee was subdivided into subgroups based on expertise of the individual members and dealt with the questions under each of the sections separately.

Questions were answered using the results of systematic literature searches and based on expert opinion.

Systematic literature searches were performed by a clinical librarian with help from one of the authors (UK) from inception to March 2014. The EMBASE, MEDLINE, Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Clinical Trials and Psychinfo databases were searched. Inclusion criteria were as follows:

1. Systematic reviews, prospective or retrospective controlled studies, prospective or retrospective cohort studies

2. Study population consisting of children aged 0–18 years and adults with EA.

3. The keywords used to identify relevant papers were: esophageal atresia, tracheoesophageal fistula, congenital esophageal stenosis.

Additional strategies for identifying studies included using the keywords mentioned above to search in the reference lists of review articles and the included studies. Furthermore, all of the members of the guidelines committee were asked to search the literature relevant to their assigned topics to possibly uncover further studies that may have been missed by the former

search. After the creation of the initial reference list of review articles and studies, articles published prior to 1980, articles in languages other than English and French, animal studies and case reports with fewer than five patients and abstracts presented only during conference proceedings were excluded.

The approach of the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) was used to identify outcomes [5-10]. The levels and quality of evidence were assessed using the classification system of the Oxford Centre for Evidence-Based Medicine (http://www.cebm.net) (diagnostic and prognostic questions) and the GRADE system (therapeutic questions). Grades of evidence for each statement are based on the grading of the literature. If no therapeutic studies were found, we decided to define the quality of evidence as ''low.'' Using the GRADE system, the quality of evidence was graded as follows[5-10]:

1. **High:** Further research is unlikely to change our confidence in the estimate of effect.

2. **Moderate**: Further research is likely to have impact on our confidence in the estimate of effect and may change the estimate.

3. **Low:** Further research is very likely to have an impact on our confidence in the estimate of effect and likely to change the estimate.

4. **Very low**: Any estimate of effect is very uncertain.

One of the authors (UK) systematically reviewed all the articles selected in the literature review and summarized the important findings in a tabular form. Subsequently a qualified epidemiologist (NH) systematically reviewed and graded, using the GRADE system, the papers chosen in the literature review. Both the summary tables of all the articles and their grading (Supplemental Digital Content 1, Summary Tables, *http://links.lww.com/MPG/A776*) were sent to all the authors before they wrote their relevant sections. (Online-only appendix [Supplemental Digital Content 2, Appendix,

http://links.lww.com/MPG/A777] lists the quality assessment of all included studies.)

Consensus Meeting and Voting

Two consensus meetings were held to achieve consensus on and formulate all of the recommendations: October 2014 and February 2015. Each subgroup presented the recommendations during the consensus meetings, wherein these were then discussed and modified according to the comments of the attendees. The consensus was formally achieved through nominal group technique, a structured quantitative method. The group consisting of members of all the subgroups (UK, HM, LD, RR, CF and FG) anonymously voted on each recommendation. A 9-point scale was used (1- strongly disagree to 9 -fully agree), and votes are reported for each recommendation. It was decided in advance that consensus was reached, if >75% of the working group members voted 6, 7, 8, or 9. The consensus was reached for all of the questions. A decision was made to present 3 algorithms (Figs. 1-3). The final draft of the guidelines was sent to all of the committee members for approval in October 2015, and then critically reviewed by a multidisciplinary panel of members of the INoEA (see acknowledgement).

- **Gastroesophageal reflux (GER)**

1. **Should GER be systematically treated in all EA patients in the neonatal period? (Fig. 1, box 1)**

No study has been published that reports the prevalence of GER in neonates following surgery for EA. However, in EA patients, GER is the most frequent gastrointestinal tract complication with a reported prevalence of 22 to 45% (Table 2), especially in infants and children with isolated EA in whom GER is reported in almost all patients[11].

GER is associated with complications in neonates and infants undergoing surgery for EA. Uncontrolled studies suggest that GER is a major factor for recurrent anastomotic stricture[12-14].

Pulmonary complications associated with GER are persistent atelectasis, aspiration pneumonia, asthma/increased airway reactivity, chronic lung disease with bronchectasis and worsened tracheomalacia[12, 14]. Airway obstruction and/or acute life threatening episodes (ALTE)[*] can result from either proximal GER reaching the larynx or GER in lower esophagus that could be reflexively responsible for respiratory symptoms[15]. Although the panel recognizes that currently no controlled studies have been reported to show benefit of systematic acid suppression in EA patients, due to the high prevalence of GER in this cohort and the potential for GER-associated complications, the panel recommends that GER should be systematically treated with acid suppression in all EA patients starting in the neonatal period. However long-term safety of PPI in this population has not been extensively studied, and concerns on consequences of acid suppression on microbiota and possible higher risk for GI and respiratory infections have recently been highlighted.

Statement 1: It is recommended that GER be treated with acid suppression in all EA patients in the neonatal period.

Expert opinion.

Low level of evidence

VOTES: 8/7/9/9/8/7 Accepted

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[*]During the editorial processing, the term Brief Resolved Unexplained Event (BRUE) has been proposed to replace the term ALTE by the American Academy of Pediatrics (Tieder, J.S., et al., *Brief Resolved Unexplained Events (Formerly Apparent Life-Threatening Events) and Evaluation of Lower-Risk Infants.* Pediatrics, 2016. **137**(5)). A BRUE is defined as an event occurring in an infant younger than 1 year when the observer reports a sudden, brief, and now resolved episode of ≥1 of the following: (1) cyanosis or pallor; (2) absent, decreased, or irregular breathing; (3) marked change in tone (hyper- or hypotonia); and (4) altered level of responsiveness. A BRUE is diagnosed only when there is no explanation for a qualifying event after conducting an appropriate history and physical examination. By using this definition and framework, children with EA-TEF, either < or > 1year of age, who present with a BRUE must be considered at high risk and must not be considered as "unexplained". They should be managed according to the present recommendations.

2. How should GER be managed? (Fig.1, box 2; Fig.2, box 7 & 10)

Most of the complications due to GER in EA are related to acid (peptic esophagitis, Barrett's esophagus, anastomotic stricture). There are no controlled trials on the medical management of GER in patients with EA. Although the quality of literature regarding the use of antireflux medication in children with EA is extremely poor[16], medical management of GER with proton pump inhibitors (PPIs) and H2 receptor antagonists has been reported to be successful by reducing GI and/or respiratory symptoms or by achieving demonstrable weight gain[16]. Due to their superior acid- blocking abilities, PPIs are recommended as the first- line therapy for acid-related gastroesophageal reflux disease (GERD) in children and for this reason are also recommended in the EA population[17]. The benefit/risk ratio of long- term PPI treatment should be balanced in this population, and the need for prolonged use of PPIs should be reassessed regularly (see statement 6).

Statement 2: PPIs should be the first line therapy for GER/GERD.

Expert opinion

Low level of evidence

VOTE: 9/9/9/8/9/9 Accepted

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3. How long GER should be treated? (Fig. 1, box 2 & 4)

No prospective controlled studies have been performed to determine the optimal duration of acid suppression in infants, children, adolescents or adults with EA. GER is very common during infancy but can persist long-term (Table 2). Complications due to GER occur mostly during the first year of life (anastomotic stricture, esophagitis, cyanotic spells, pulmonary problems, failure to thrive), but can also be observed later. A recent study showed that GERD tended to be more prevalent after 1 year of age (43%) compared with before (34%), and significant complications could develop after the 1 year of age even in children who were previously asymptomatic[4]. GERD is one of the factors contributing to failure to thrive

in infancy[18]. The prevalence of peptic esophagitis is high throughout childhood and adulthood (Table 2).

Barrett's esophagus is a long-term complication of EA[11, 19]. GERD also contributes to dysphagia in EA patients[12] and can negatively influence quality of life[18, 20]. Hence persistence of GER should be assessed by regular monitoring (see statement 6).

Statement 3: It is recommended that GER be systematically treated for prevention of peptic complications and anastomotic stricture up to the first year of life or longer, depending on persistence of GERD.

Expert opinion

Low level of evidence

VOTES: 8/7/8/7/9/7 Accepted

4. **What is the role of 24-hour pH- and pH-impedance monitoring in EA patients? (Fig. 1, box 3; Fig. 2, box 8)**

The gold- standard tests for the diagnosis of GERD are currently pH probe testing, pH-impedance testing, and wireless pH testing, all of which measure esophageal reflux burden[17]. 24-hour pH monitoring quantifies the esophageal acid burden, which is highly correlated with peptic esophagitis. pH-impedance (pH-MII) monitoring allows the evaluation of retrograde bolus movements in the esophagus independent of the pH, identifying nonacid reflux in the postprandial period and in patients receiving acid-suppressing therapy[21, 22]. The main use of pH-impedance monitoring is not to diagnose pathologic reflux but rather to try to correlate extra-esophageal symptoms with reflux events. One of the limitations of pH-impedance testing in patients with esophagitis or motility disorders (both of which are commonly found in patients with EA) is that baseline impedances are 75% lower than control patients[23]. Because of these low baselines, the software often fails to detect reflux events, so manual analysis, in addition to automated analysis, is critical to avoid underreporting of reflux. Experience with pH-impedancemetry is increasing in patients with EA showing that reflux

events are equally as likely to be due to nonacid reflux as acid reflux in these patients[22-26].

Since there are currently no medications which are effective in treating non-acid reflux, there

is no practical therapeutic consequence of demonstrating nonacid reflux in EA patients except

consideration for fundoplication.

Statement 4a: pH monitoring is useful in evaluating the severity and symptom association of acid reflux in patients with EA.

Expert opinion

High level evidence

VOTES: 7/9/9/9/8/8 Accepted

Statement 4b: pH-impedance monitoring is useful to evaluate and correlate non-acid reflux with symptoms in selected patients (symptomatic on PPI, on continuous feeding, with extra-digestive symptoms, ALTE, GER symptoms with normal pH-probe and endoscopy).

Expert opinion

Low level of evidence

VOTES: 7/8/9/9/9/7 Accepted

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5. **What is the role of esophagoscopy in EA patients? (Fig. 1, box 3 & 11; Fig. 2, box 5; Fig. 3, box 2)**

In a retrospective study of the results of esophageal biopsies performed during routine

esophagoscopy in children with EA, 80% of patients demonstrated moderate or severe

esophagitis or gastric metapalasia at any time of follow-up[27] . This study however does not

mention whether the patients were on any PPI therapy at time of endoscopy. Multilevel

esophageal biopsies are recommended for screening for peptic and eosinophilic esophagitis.

The number of biopsies should be increased in the presence of macroscopic abnormalities or

for screening for Barrett's esophagus (at least 4 biopsies in each quandrant one cm above

the Z line). Endoscopy is also useful in children post- fundoplication since the recurrence of

GER and peptic esophagitis is possible[11, 28, 29].

Statement 5: Endoscopy with biopsies is mandatory for routine monitoring of GERD in patients with EA.

Expert opinion

High level of evidence

VOTES: 7/9/9/9/9/9 Accepted

6. **How should GER be monitored, and when? (Fig. 1, box 3, 9 & 11; Fig.2, box 8; Fig. 3, box 7 & 10)**

GER remains frequent in EA children after the age of 2 years, even in asymptomatic patients, and can persist lifelong (Table 2). Complications due to GERD can be observed during childhood, adolescence and adulthood and may include late or recurrent anastomotic stenosis, esophagitis, dysphagia, Barrett esophagus, and pulmonary complications (Table 2). Therefore, the panel recommends monitoring acid reflux at time of discontinuation of anti-acid treatment even is asymptomatic children, to confirm the absence of acid reflux, or conversely, the persistence of reflux and the need to continue treatment.

Statement 6: All EA patients (including asymptomatic patients) should undergo monitoring of GER (impedance/pHmetry and/or endoscopy) at time of discontinuation of anti-acid treatment and during long-term follow-up.

Expert opinion

High level of evidence

VOTE: 8/9/9/9/9/9 Accepted

7. **How often do EA patients need surveillance endoscopy in childhood and adolescence? (Fig. 1, box 11)**

No studies show benefit of routine upper gastrointestinal endoscopy in the follow-up of EA

patients. However, GER can be asymptomatic and several studies have shown the absence of correlation between symptoms and esophagitis in this population[30, 26, 31-34]. Esophageal mucosal abnormalities can be observed in up to 35% of EA patients at endoscopy despite the absence of symptoms,[33, 34] making the recommendation of endoscopic assessment based solely on symptomatology inappropriate. The goal of surveillance biopsies is to detect early esophagitis (with the opportunity for subsequent intervention) before the development of late complications of strictures, Barrett's esophagus, and cancer.

> **Statement 7: Routine endoscopy in asymptomatic EA patients is recommended. The expert panel recommends 3 endoscopies throughout childhood (1 after stopping PPI therapy, 1 before the age of 10 years, and 1 at transition to adulthood).**

Expert opinion

Low level of evidence

VOTES: 9/7/9/8/7/8 Accepted

8. **What is the role of fundoplication in EA patients with GER? (Fig. 1, box 5; Fig. 2, box 10, Fig. 3, box 8 & 11)**

No controlled trial has been reported regarding the role of surgical management of GER in patients with EA. Cumulative risk of having a fundoplication performed in children with EA ranges from 0 to 45% (Table 2). In long-gap EA, GER is particularly frequent and severe, and leads to a high risk of anastomotic stricture, suggesting that fundoplication should be considered in a large proportion of these children [35-37]. Several studies in non-EA patients report that fundoplication does not consistently reduce the risk of aspiration pneumonia, and respiratory admissions and may, in fact, increase the risk [38-41]. In patients with EA who have poor motility and esophageal clearance, fundoplication may even worsen esophageal stasis by preventing gravity-driven esophageal clearance which may, in turn, worsen respiratory symptoms so the decision to proceed with fundoplication for respiratory symptoms alone, should be made with caution.

In a recent systematic review on the management of GER in EA patients, reasons stated for the need for antireflux surgery included failure of maximum conservative therapy for GER, failure to thrive, acute life threatening event, esophagitis and a recurrent anastomotic stenosis.

Statement 8: Severe esophageal dysmotility predisposes EA patients to post-fundoplication complications. However, EA patients may benefit from fundoplication in:
8a: Recurrent anastomotic strictures, especially in long gap EA

Expert opinion

High evidence

VOTES: 8/9/8/9/8/9 Accepted

8b: Poorly-controlled GERD despite maximal PPI therapy

Expert opinion

High evidence

VOTES: 7/9/7/9/9/7 Accepted

8c: Long term dependency on trans-pyloric feeding

Expert opinion

Very low evidence

VOTES: 7/9/9/9/7/7 Accepted

8d: Cyanotic spells

Expert opinion

Very low evidence

VOTES: 6/7/6/9/7/7 Accepted

9. What evaluations should be performed prior to fundoplication?

The preoperative evaluation should include reflux testing (24-hour pH-metry or pH-MII testing), upper gastrointestinal series and endoscopy[42]. pH-metry is required to confirm and quantify acid reflux; barium contrast study allows the diagnosis of hiatal hernia, associated congenital stenosis, the assessment of the anatomy of the cardiac region, and exclusion ofother intestinal malformations. Endoscopy is required because it allows macroscopic evaluation and biopsies of the esophageal mucosa, for screening for peptic esophagitis and esosinophilic esophagitis or Barrett's esophagus. To date, esophageal manometry, pH metry and pH-impedancemetry have not been shown to be predictive for determining the risk of post-operative dysphagia [43, 44]. No data exist on the predictive value of high- resolution esophageal manometry for the occurrence of post-fundoplication complications in EA patients.

Statement 9: Barium contrast study, endoscopy with biopsies and pH-metry should at least be performed prior to fundoplication.

Expert opinion

High evidence

VOTES: 9/9/9/7/8/9 Accepted

10. What extra-esophageal manifestations of reflux and dysmotility are seen in EA patients? (Fig. 1, box 8 & 13; Fig. 2, box 1; Fig. 3, box 1, 3, 7 & 9)

Extra-esophageal symptoms are common in children, and adults with EA and these symptoms are associated with significant morbidity, especially in childhood [4, 12, 45-50]. 14-40% of patients have pulmonary symptoms which include: cough in 8-75% of patients[18, 47, 48], wheezing in 14-40% [47, 48], dyspnea in 37% [18], bronchitis in 14-74% [18, 46, 47], recurrent infections in 10-53% [50, 51], bronchiectasis in up to 17% [12,], restrictive lung disease in 11-69% [12, 18], obstructive lung disease 38-50% [12, 18], tracheomalacia in 14-29% [12, 33] and pneumonia in 5-50% [46, 47].

The GI causes of pulmonary symptoms are variable and include aspiration due to mucus or food retention in the proximal pouch or distal esophagus, anastomotic stricture, impaired esophageal motility, congenital esophageal stenosis, aspiration during swallowing, GER, recurrent or missed fistulae, eosinophilic esophagitis, and esophageal pooling over a fundoplication. Aspiration of retained food or mucus above or below the anastomosis may occur because of stricture, or dysmotility possibly related to abnormal innervation to the proximal pouch or distal esophagus[52, 53].

Non-gastrointestinal causes also include vocal cord paralysis, laryngeal clefts, vascular rings and aspiration during swallowing[54] . No study has systematically evaluated respiratory symptoms in children to determine the frequency of gastrointestinal etiology for pulmonary symptoms. Additionally, no study has determined the impact of dysmotility, independent of reflux, on respiratory symptoms.

Statement 10: Symptoms of aspiration during swallowing may be identical to GER symptoms in young children.

Expert opinion

Low evidence

VOTE 8/8/8/9/9/9 Accepted

11. **How should clinicians investigate extra-esophageal manifestations in EA patients? (Fig. 2)**

Multidisciplinary care of children with EA is critical and should include gastroenterology, pulmonary and otolaryngology specialists. Upper GI barium imaging is helpful in delineating recurrent or missed fistulae, anastomotic stricture and size of the upper pouch, congenital stenosis and esophageal extrinsic compression by a vascular ring. The diagnostic evaluation of aspiration during swallowing is very important to pursue as 47% of children with EA have direct aspiration or penetration [54]. Diagnostic testing includes modified barium swallow (videofluouroscopic swallow studies) or fibreoptic endoscopic evaluation of swallowing (FEES), both of which assess swallow function [54]. No study compares the sensitivity of these tests in the EA population, although one adult study suggests the techniques are comparable[55]. If aspiration is identified during swallowing, the differential diagnosis must include: (1) developmental delay in swallowing function, (2) neurologic etiology including Chiari malformations, hyper- or hypotonia, (3) laryngeal clefts and/or (4) vocal cord paralysis. Studies of patients with EA suggest that 3-17% have clinically significant vocal cord paralysis and, while the incidence of laryngeal cleft in patients with EA is not known, 27% of patients with laryngeal cleft have EA[56-59] . Therefore, diagnostic evaluation of the larynx and vocal

cord evaluation by an otolaryngologist should be included. A rigid bronchoscopy by a pulmonologist, otolaryngologist or surgeon should also be carried out to rule out a recurrent or missed fistula and to evaluate the degree of tracheomalacia.

GER is commonly implicated in extra-esophageal symptoms since 52-68% of coughs are associated with reflux events, and 25-50% of these are associated with non-acid episodes, particularly in children <1 [22]. In another study, 39% of coughs were associated with reflux, with non-acid reflux correlating to a greater extent than acid reflux [23]. pH impedancemetry may have a role in in the evaluation of extra-esophageal symptoms thought to be secondary to GERD prior to considering fundoplication.

Statement 11a Patients with EA should be evaluated regularly by a multidisciplinary team including pulmonology and otolaryngology, even in the absence of symptoms.

Expert opinion

Low evidence

VOTE 9/9/9/9/9/9 Accepted

Statement 11b Anatomic abnormalities (laryngeal cleft, vocal cord paralysis, missed or recurrent fistulae, anastomotic stricture, congenital stenosis, vascular ring) should be ruled out in EA patients with respiratory symptoms.

Expert opinion

High evidence

VOTE 9/9/9/9/9/9 Accepted

Statement 11c If pH-metry or pH-MII is performed, symptom correlation during reflux testing, rather than total reflux burden is the most important indicator of reflux-associated symptoms.

Expert opinion

Very low evidence

12. How should clinicians treat extra-esophageal manifestations in EA patients? (Fig. 2)

Very little data and no controlled trials exist regarding the management of extra-esophageal symptoms in patients with EA. Hence data available from the literature in children without EA on the treatment of extra-esophageal symptoms need to be extrapolated. In large well-designed randomized controlled trials in both adult and pediatrics, PPIs have failed to improve respiratory symptoms, reduce steroid and bronchodilator medication use, reduce emergency room visits, or improve quality of life in patients with asthma and other chronic lung diseases [60-62]. Furthermore, in randomized controlled studies and case-control studies in adults with chronic lung disease, prolonged acid suppression use has been associated with an increased risk of respiratory infections (pneumonia, upper respiratory tract infections, pharyngitis), which may exacerbate the underlying lung disease [60, 63-65]. These data may not be relevant to children and adults with EA, who are likely at higher risk of reflux related symptoms than patients with other respiratory conditions. Therefore, acid suppression, while helpful for preventing and healing esophagitis, should be used with caution for the sole treatment of extra-esophageal symptoms.

Fundoplication is frequently proposed for the treatment of extra-esophageal symptoms in patients with EA but currently no studies compare fundoplication to alternative therapies for the treatment of extra-esophageal symptoms in EA patients. More

studies are needed to determine the impact of acid suppression, fundoplication and transpyloric feeding on extra-esophageal symptoms.

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Statement 12: Acid suppression should be used with caution in patients with extra-esophageal manifestations of reflux.

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Expert opinion

Low evidence

VOTE 8/7/6/8/7/5 Accepted

13. How should "Cyanotic spells" be investigated and managed in EA patients? (Fig. 2)

The differential diagnosis for cyanotic spells in EA patients includes airway collapse from tracheomalacia, direct oral aspiration, esophageal dysmotility resulting in dysphagia, recurrent TEF, GER related reflux aspiration and events related to associated anomalies such as cardiac events. Anatomic issues such as anastomotic stricture, recurrent or missed fistulae, congenital esophageal stenosis, vascular rings and laryngeal clefts need to be excluded. As no data provides information regarding how frequently ALTE is due to direct oral aspiration or GER related reflux aspiration, no child should undergo fundoplication for ALTE without prior assessment of swallowing function [54]. Evaluation of children with ALTE must include a multidisciplinary team of surgeons, gastroenterologists, pulmonologists and otolaryngologists to ensure that a full differential diagnosis is considered.

The studies of ALTE in EA consist of retrospective case series in which different surgical management approaches were taken with subsequent reviews of the outcomes.[66]

Management includes aortopexy[67], fundoplication, conversion from gastrostomy feeding to transpyloric feeding, tracheostomy placement, and maximization of medical therapy for

reflux disease.

The treatment of direct oral aspiration involves feeding modification. Current literature is focused on the surgical management of ALTE, and no studies focus on the medical management (medications, change in feeding methods etc.) of cyanotic spells or ALTE in this population. No prospective, controlled studies compare diagnostic algorithms or therapeutic outcomes for patients with ALTE.

Statement 13a: The etiology of life-threatening events is multifactorial and merits a multidisciplinary diagnostic evaluation prior to surgical intervention

Expert opinion

Very low

evidence

VOTES: 9/9/9/9/9/9 Accepted

Statement 13b: Anatomic issues (strictures, recurrent or missed fistulae, congenital esophageal stenosis, vascular rings, laryngeal clefts) and aspiration need to be excluded in children with ALTE.

Expert opinion

Low evidence

VOTES: 9/9/9/9/9/9 Accepted

- **Dysphagia and Esophageal Function in EA**

Based on ten series of patients reported over the past three decades, the incidence of dysphagia in infants, children and adolescents with EA after surgical repair ranges between 21-84% [19, 51, 68-72]. Dysphagia is estimated to be more prevalent than reported in the literature, particularly as children may not recognize their symptoms as abnormal and may appear better adapted to their unique situation [72]. Children and adolescents with EA continue to experience dysphagia regardless of the number of years after surgical repair. In a series of 69 patients with EA, 45% had dysphagia at 5 years, 39% at 5-10 years, and 48% at greater than 10 years [51].

In children with EA, the etiology of dysphagia may include inflammatory or anatomic causes such as peptic esophagitis, eosinophilic esophagitis[75], anastomotic stricture[19, 68-70], congenital stenosis[76], peptic stricture, post-fundoplication obstruction, vascular anomalies[77], anastomotic diverticulum [19, 73], mucosal bridge[78, 79] and inlet patch[80]. In the absence of the latter causes, esophageal dysmotility remains the accepted explanation.

Esophageal motility can be assessed by either contrast study, esophageal manometry (either water perfused or high resolution solid state) or videofluoroscopy[74]. The patterns of esophageal dysmotility in a cohort of children with EA were recently described using high resolution manometry and were reported abnormal in all patients, with 3 types of abnormalities observed: pressurization (15%), isolated distal contractions (50%) and aperistalsis (35%)[72]. Consistently, the pattern of esophageal dysmotility was not predictive of the presence or severity of dysphagia. GER-related symptoms are prominant in patients with aperistaltic esophagus[72, 81]. No prospective longitudinal studies of patients with EA document the natural history of esophageal dysmotility and the correlation between symptoms and dysmotility.

The underlying cause of the dysmotility remains unclear and controversial. In EA operated

patients, it has been postulated that dysmotility may be caused either by intrinsic factors related to abnormal development of the esophagus[53, 82, 83] or by operative maneuvers responsible for a partial denervation. Postoperative complications (including leaks, anastomotic stenosis, and subsequent esophageal dilations) could also cause local trauma and inflammation leading to further neuronal and muscular damage. Recently, high-resolution esophageal manometry was found to be severely affected in 2 children with isolated TEF studied prior to surgical repair suggesting that esophageal dysmotility is congenital in nature rather than secondary to surgical intervention[84].

14. When should dysphagia be considered in patients with in EA?

Dysphagia in children with EA can present with simply a complaint of difficulty in swallowing (50%), nausea (27%), epigastric burning (21%), heartburn (14%-50%), postprandial fullness (14%), early satiety (14%), eructation (14%), regurgitation (7%-50%), or epigastric pain (7%) [69]. Choking is reported in 10% of patients at 5 years, 4% at 5-10 years, and 7% at greater than 10 years after surgical repair [51]. Most patients cope with the symptoms and have adapted and consider these symptoms as minor problems [73]. Odynophagia with discomfort or pain with propagation of the food bolus is also reported [74]. Children may have minor or occasional difficulties with swallowing, may eat slowly or drink excessive amounts of liquids with foods, or develop food impaction [68, 72]. Significant changes in eating habits are reported in up to 73% of patients with dysphagia (need to drink, change in diet, last to finish meal) [72].

Statement 14: Dysphagia should be suspected in patients with EA who present with food aversion, food impaction, difficulty in swallowing, odynophagia, choking, cough, pneumonia, alteration in eating habits, vomiting, and malnutrition.

Expert opinion

Low evidence

VOTES: 9/9/9/8/8/9 Accepted

15. **How should dysphagia be investigated in EA patients? (Fig. 2)**

Evaluation of dysphagia should begin with contrast studies that can be helpful in identifying a structural etiology for dysphagia. Esophagography after EA repair should be performed because of the high index of suspicion for the presence of distal congenital esophageal stricture (CES), since the diagnosis and adequate management of CES can often be delayed[76, 85]. Endoscopy with biopsies allows the evaluation of the anastomosis (stricture, diverticulum), the esophageal mucosa (peptic, eosinophilic or infectious esophagitis) and the diagnosis of congenital stenosis, mucosal bridge, inlet patch or extrinsic compression (vascular anomalies, tight fundoplication wrap). In children with EA, dysphagia has very low correlation with mucosal esophageal inflammation[33]. High-resolution esophageal manometry ideally with impedance is also recommended for the investigation of dysphagia in EA patients who have a normal esophagogram and endoscopy with biopsy.

Statement 15: We recommend that all EA patients with dysphagia undergo evaluation with upper GI contrast study and esophagoscopy with biopsies

Expert opinion

Low evidence

VOTES: 8/7/9/9/9/9 Accepted

16. What is the role of esophageal manometry in EA patients with dysphagia? (Fig. 2, box 12)

Esophageal motility testing is useful in patients with EA and dysphagia in whom esophageal stricturing has already been addressed. It is important to classify and categorize the pattern of esophageal dysmotility with esophageal manometry and to correlate the degree of dysmotility with bolus transit (when performed with impedance), However the esophageal dysmotility seen in manometry may not result in changes in medical management because the correlation between dysphagia, motility abnormalities, and bolus transit is imperfect.

> **Statement 16: Esophageal manometry is useful to characterize esophageal motility patterns in EA patients with dysphagia. However, the impact on clinical outcome has yet to be determined.**

Expert opinion

Low evidence

VOTES: 7/8/8/8/9/9 Accepted

17. How should dysphagia be managed in EA patients? (Fig. 2, box 12)

The management of dysphagia must be conducted according to the underlying cause. There is no controlled study on specific treatments of dysphagia in patients with EA. Treatment options may include but not limited to:

- Feeding adaptation

- Treatment of esophagitis (peptic, eosinophilic or infectious) and inlet patch

- Prokinetics

- Treatment of stricture, stenosis, mucosal bridge or anastomotic diverticulum

- Surgical repair of vascular anomaly

- Gastrostomy tube feeding

- Esophageal replacement

- Dilation of fundoplication.

Statement 17: We recommend tailoring management of dysphagia to the underlying mechanisms

Expert opinion

Very low evidence

VOTES: 8/8/9/9/9/9 Accepted

18. How should dysphagia in EA patients post-fundoplication be investigated?

Dysphagia is a frequent complication after fundoplication in the general population but is more frequent in patients operated at birth for EA. In a series of 148 children who underwent fundoplication (87 of whom had EA), dysphagia and/or stenosis occurred in 17.2% of EA patients versus 6.5% of other children [29]. In another study it has been reported to be 31% [42]. In a small series of 14 EA patients who underwent fundoplication, 7 of them developed severe dysphagia requiring feeding gastrostomy[86]. In the series by Levin *et al*., postoperative dysphagia occurred in 45% and 38% of children post partial or total fundoplication respectively [87]. Post-fundoplication dysphagia could be secondary to the combination of reduced esophageal motility and a tight wrap, outflow obstruction at the wrap level or as a result of herniated wrap or paraesophageal hernia. Esophagoscopy with biopsies to exclude

reflux recurrence with esophagitis may also be useful. In young children, post-fundoplication dumping syndrome is a differential diagnosis and must be ruled out because symptoms (feeding difficulties and post prandial discomfort) may be interpreted as dysphagia.

In evaluating dysphagia, contrast studies should be used to assess for anatomic/structural etiology. Post-fundoplication dysphagia should be evaluated by administering contrast orally or via a nasoesophageal tube to assess for flow resistance at the level of the fundoplication wrap. Since dysphagia may be related to etiologies other than the fundoplication, endoscopy with biopsies is necessary for evaluation of the anastomosis (stricture, diverticulum), and the esophageal mucosa (peptic, eosinophilic or infectious esophagitis). Endoscopy may demonstrate the tight wrap (and allow for wrap dilation), though there are no data comparing endoscopic appearance of the wrap to radiological imaging. To assess for the degree to which the fundoplication may contribute to esophageal obstruction, a high-resolution esophageal motility study (combined with impedance) may be used to demonstrate not only fundoplication pressures, but also impaired bolus clearance and elevated intra-bolus pressures. However, there are no prospective studies documenting the effect of results high-resolution manometry on outcomes in EA patients following anti-reflux surgery.

Statement 18: In EA patients with post-fundoplication dysphagia, we recommend a contrast study to rule out mechanical complications, EGD with biopsy and, if inconclusive, high-resolution manometry +/- impedance.

Expert opinion

Very low evidence

VOTES: 9/9/9/8/9/9 Accepted

19. How should dysphagia in EA patients post-fundoplication be managed?

The management of post-fundoplication dysphagia needs to reflect the underlying cause. There are no controlled studies on specific treatments of post-fundoplication dysphagia in patients with EA. Treatment options may include but not limited to:

- Feeding adaptation
- Treatment of esophagitis (peptic, eosinophilic or infectious) and inlet patch
- Prokinetics
- Balloon dilation of the wrap
- Botulinum toxin to the LES
- Gastrostomy tube feeding
- Surgical revision of fundoplication
- Gastrostomy
- Esophageal replacement

Statement 19: We recommend tailoring management of post-fundoplication dysphagia to the underlying mechanism(s).

Expert Opinion

Very low evidence

VOTES: 8/9/8/9/8/7 Accepted

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20. When should we look for associated vascular abnormalities in EA? (Fig. 2, box 6)

In a series of 76 children born with EA/TEF, vascular abnormalities were reported in 18% of children. The most common abnormalities were an aberrant right subclavian artery (ARSA) in 12% (9/76) and right-sided aortic arch in 6% (5/76) [77]. Long gap EA and severe cardiac malformations requiring surgery are both significantly associated with vascular anomalies.

Often asymptomatic from a gastrointestinal perspective, these abnormalities may be the cause of respiratory symptoms (dyspnea, cough, cyanosis) and/or exacerbate gastrointestinal symptoms (dysphagia) when a ring completely or incompletely encircles the trachea and/or the esophagus, resulting in extrinsic compression. Severe complications, such as massive gastrointestinal bleeding secondary to an aberrant right subclavian artery-esophageal fistula related to a stent placement after EA repair due to an ARSA which was not recognized prior to stent placement, have been reported. [88]. A similar phenomenon has been reported after prolonged (>17 days) placement of a nasogastric tube in children without EA[89]. Since an ARSA is not visible during esophageal surgery, and since the diagnostic yield of routinely used techniques (preoperative cardiac ultrasound and esophagram) have low sensitivity and negative predictive value for the diagnosis of ARSA, Computerized Tomographic (CT) angiography or chest Magnetic Resonnance (MR) Imaging should be performed to rule out such malformations prior to placement of a stent or long-term nasogatric tube, or in patients with unexplained respiratory symptoms.

Statement 20: Even though congenital vascular malformations are usually asymptomatic, they may be the underlying etiology for dysphagia, dyspnea, or cyanosis, by causing external compression on the esophagus and/or trachea. We recommend that congenital vascular malformations be excluded in these situations by chest CT or MR angiography.

Expert opinion

Low evidence

VOTES: 9/8/9/9/7/9 Accepted

- **Feeding and Nutrition in EA patients**

The causes of feeding difficulties in children with EA are multifactorial and include oropharyngeal, esophageal and behavioral disorders. No prospective controlled studies describe abnormal feeding behaviours in children with EA. All studies currently rely on recollection of historical details by questionnaire or chart reviews. Koivusalo *et al.*, reported that 94% of 130 EA patients followed up long-term were doing well with oral feeds [90]. In another study, Khan *et al.* found that there was no difference in the achievement of feeding milestones in children with EA compared to controls [91]. In a study of 124 patients by Puntis *et al.*, patients with EA had solid foods introduced at a mean age of 12 months versus 4 months in control group (p=0.003)[92]. Difficulties in feeding can result in added stress in the family unit[93]. The causes of feeding difficulties include aspiration, dysmotility, esophageal outlet obstruction, esophageal inflammation and anastomotic strictures. GER has also been implicated as a cause for feeding difficulties although no data support the fact that patients with EA and GER have worse feeding outcomes than patients without reflux. Fundoplication, which can create a functional esophageal outlet obstruction in the context of dysmotility, can also cause dysphagia and feeding difficulties in children with EA[29]. No studies address the impact of fundoplication on acquisition of feeding milestones or rates of significant food impaction.

Aspiration is an under-recognized cause of feeding difficulty in children with EA. In a case series of patients with laryngeal cleft, many of whom had EA, 18% of patients had feeding difficulties, 4.5% had choking and 4.5% had dysphagia.[58] Smith *et al.* describe a case series in which 61% of all EA patients had coughing during eating, and this, combined with the reports of aspiration during eating, suggests that all of these issues may contribute to

dysfunctional eating patterns [94]. Furthermore, respiratory distress of any nature may predispose patients to feeding difficulties [95, 96]. Finally, patients may develop a fear of eating or texture aversion(s) related to a history of choking on food. Khan *et al*. reported 23% of patients have a history of food impaction which may result in limitation in intake of certain foods, and which result in feeding behaviors which differ from control patients [91].

21. How should abnormal feeding behaviors in EA be prevented and managed?

Neither retrospective nor prospective studies address how to prevent or treat abnormal feeding behaviors in children with EA. In infants before EA repair, case reports of successful sham feeding, when babies are fed small volume feeds which are immediately suctioned from the esophageal pouch, but the studies are limited by their methodologies [97]. Prospective studies documenting the type of feeding difficulties, and the outcomes of standardized interventions in children with EA, are needed.

Statement 21: No data are available on the most efficacious methods of avoiding feeding disorders in children with EA. However, the committee recommends a multidisciplinary approach to prevent and treat feeding difficulties

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Expert opinion

Very low evidence

VOTES: 9/8/8/9/9/9

22. Is there a risk of malnutrition in infants, children and adolescents with EA?

Nutritional outcome studies are limited by a lack of adjustment for comorbidities (cardiac, genetic, neurologic) which may have a large impact on growth. Puntis *et al*. found that while

mean heights and weights (mean height z score -1.78±1.7) and mean weight for height (-1.1±0.9) were lower in children with EA compared with controls (p<0.0001), no correlation was found between feeding scores and growth parameters [92]. A study of 371 patients by Deurloo, *et al*., found that long-term, only 7% of patients were less than the 5th percentile for height and weight. A history of GER and low birth weight were both predictors of reduced growth [14]. A retrospective study of 81 type C EA patients with a mean age of 13.3 years, by Legrand *et al*. reports that 75% had a normal BMI, 16% were obese and 9% were undernourished[18].

Statement 22: Intensive early enteral and oral nutrition intervention and advances in neonatal care and surgery have reduced the risk of long term malnutrition in children with EA; however other associated comorbidities may increase this risk

Expert opinion

Low evidence

VOTES: 9/9/8/9/9/9 Accepted

- **Anastomotic stricture (Fig. 3)**

Anastomotic stricture (AS) has been reported to be the most frequent post-operative complication in EA, occurring in 18-60% of patients [2, 4, 98-101]. Several factors contribute to the development of AS: long gap between the two esophageal pouches and consequent anastomotic tension, post operative anastomotic leak [97,100,] and GER [99, 100, 104]. The presence of a Long Gap (LG) between the two esophageal ends is associated with a higher AS incidence, as reported by several authors[98, 99, 102-107]. Lack of consensus regarding the gap definition, and how and when the gap length between the two esophageal ends should be measured, makes objective comparisons between publications and individual centers difficult. The EA Gross

type A and B, are characterized by an increased risk of stricture [108].

23. What is the definition of a clinically relevant anastomotic stricture in patients with EA? (Fig.3, box 1)

Anastomotic stricture (AS) is defined as a narrowing at the level of the esophageal anastomosis. The severity of esophageal narrowing does not correlate with symptoms. The panel suggests that an AS should be considered clinically relevant only in patients with symptoms, not in asymptomatic patients with relative anastomotic narrowing.

Statement 23: In addition to relative esophageal narrowing at the level of the anastomosis (by contrast and/or endoscopy), significant functional impairment and associated symptoms need to be present for anastamotic strictures to be considered clinically significant.

Expert opinion

No evidence

VOTES:7/8/7/8/9/6 Accepted

24. When should anastomotic strictures in EA be diagnosed?

A variety of symptoms thought to be due to AS have been described in literature. These depend upon the age of the child and the type of food ingested (liquid versus solid). These symptoms are: feeding and swallowing difficulties, regurgitation and vomiting, mucus or food retention in the proximal pouch, cough, drooling, recurrent respiratory infections, foreign body impaction, and poor weight gain. AS should be suspected in presence of any of these symptoms. No studies indicate whether these symptoms alone are sensitive or specific enough to diagnose an anastomotic stricture.

Some groups have proposed aggressive systematic screening for AS and/or routine dilation(s) of the esophagus, even in the absence of symptoms, to prevent symptoms secondary to AS from developing[109-111] . Koivusalo *et al*. compared the effect of routine stricture dilation versus a "wait- and -see approach" and found no differences in the outcomes of the two groups in terms of dysphagia, nutritional status, and respiratory symptoms, suggesting that a "wait- and- see approach" that is less invasive for the patient may be superior to prophylactic dilations. [111]. Others recommend endoscopy or barium swallow 'on-demand' in patients with symptoms suggestive of AS[99-101]. No prospective controlled studies compare the 2 approaches.

Therefore, the panel suggests close follow-up of all EA patients in the first 2 years of life with special attention to symptoms suggestive of AS. Infants fed only with liquids, must be followed during introduction of solid food. Patients with long gap EA and post-operative anastomotic leak (which are risk factors for developing AS) need close follow up to avoid development of a severe/and sometimes complete anastomotic closure with a resultant high risk for aspiration and difficult-to-perform endoscopic dilations.

Statement 24: There is no evidence that routine screening and dilation is superior to evaluation and treatment in symptomatic patients. We recommend that AS be excluded in symptomatic children, and those children who are unable to achieve feeding milestones

Expert opinion

Low evidence

VOTES: 8/7/7/9/8/8 Accepted

25. How should anastomotic stricture be diagnosed in EA? (Fig. 3, box 2)

No studies compare the diagnostic yield of endoscopy versus barium swallow for detection of AS after EA repair. Contrast radiographs allow evaluation of the esophageal morphology

with possible diagnosis of associated congenital esophageal stenosis and planning a patient-specific therapeutic strategy. Endoscopic evaluation offers the opportunity of combined diagnosis and treatment with dilation(s).

Statement 25: Diagnosis of anastomotic stricture can be done by either contrast study and/or endoscopically

Expert opinion

No evidence

VOTES: 9/9/9/9/9/9 Accepted

26. **How should anastomotic strictures be managed? (Fig. 3, box 2)**

Anastomotic dilation is the first line of therapy for AS. The aim of dilation is to obtain an esophageal diameter that allows a normal, age-appropriate capacity for oral feeding, without respiratory or digestive symptoms. General anesthesia with tracheal intubation is recommended for airway protection during the procedure.

A guide wire inserted under endoscopic or X-ray control is helpful to avoid the risk of esophageal perforation by the dilator tip. X-ray evaluation of guide wire passage and correct position in the gastric body should be done in case of difficult wire passage. No controlled studies compare hydrostatic balloon or a semi-rigid dilator for treatment of AS in EA patients. No evidence has been reported of increased effectiveness or safety for one or the other dilator type. The advantage of hydrostatic balloon dilators is the radial force applied on the stricture while avoiding axial forces[112]. The inflating balloon device allows a standard force application. The balloon is filled with water or contrast medium. In the latter

case, fluoroscopic control allows the monitoring of the disappearance of the waist in the balloon caused by the stricture [112]. Persistence of the waist suggests that the procedure was only partially successful [113]. The Savary-Gilliard semi-rigid dilator applies radial force on the stricture but also an axial one with stricture stretching, with may theoretically result in greater esophageal trauma [114]. On the other hand, the experienced operator can apply the correct force with the semi-rigid dilator to obtain the desired dilation. Savary dilators are reusable after sterilization. Careful post-dilation endoscopic evaluation is recommended to check for possible perforation. Dilation must be carried out using the technique with which the operator is most skilled and experienced.

No controlled studies report on the optimal number of dilations and the optimal interval between dilation sessions for treatment of AS after EA repair. Different authors reported on varying intervals between dilations ranging from 7 days [109], 15 days [113], and 21 to 30 days. Others report a dilation session schedule based on the severity of the stricture and symptom relapse or recurrence [108, 115]. No consensus exists regarding the ideal interval between dilation sessions.

Statement 26a: We recommend that dilation be performed in children with EA under general anesthesia and tracheal intubation

Expert opinion

High evidence

VOTES: 9/9/9/9/9/9 Accepted

Statement 26b: We recommend the use of a guide wire to insert the chosen dilator (balloon or semi-rigid) through the stricture under endoscopic or fluoroscopic control.

Expert opinion.

No evidence

VOTES: 7/7/7/7/9/6 Accepted

27. What is the definition of recurrent anastomotic stricture in EA patients? (Fig. 3, box 8 & 10)

No evidence-based definition exists regarding the definition of recurrent AS in EA patients.[116]

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Statement 27: No evidence exists on the definition of recurrent anastomotic stricture in EA patients. Based on expert opinion we believe three or more clinically relevant stricture relapses constitutes recurrent stricture

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Expert opinion

No evidence

VOTES: 7/8/9/9/7/9

28. What adjuvant treatments are available in recurrent strictures in EA patients? (Fig. 3, box 8)

To prevent the recurrence of AS, different adjuvant treatments have been proposed, such as intralesional steroids, mitomycin C, stents, and endoscopic knife. These treatments have been reported in case reports or retrospective small case series, with extremely variable outcomes and definition of recurrence. However currently no controlled studies are reported for any of these treatments for strictures in children with EA.

Corticosteroids. Use of intralesional triamcinolone acetonide injections has been reported, both in adults and children, with inconsistent improvement in AS [10, 116-118]. Potential complications of esophageal injection(s) of steroids include perforation, intramural infection, candida infection, mediastinitis, and pleural effusion, as well as the potential for adrenal suppression from exogenous systemic steroid administration. No side effects have been reported for both local or systemic short-term steroid treatment. Data on systemic steroids in AS are lacking.

Mitomycin C is an antineoplastic antibiotic with anti-fibrotic activities. It has been described to exert inconsistent results at different drug concentrations, when used as a topical agent applied to the AS after the dilation[119]. In a retrospective study of 21 EA patients with recurrent anastomotic stricture, the authors reported similar results in eleven patients that underwent endoscopic dilations plus mitomycin C (0.1 mg/ml), and ten patients that received endoscopic dilations alone [79].

Stents. In a retrospective study, a fully covered metal stent was reported to be effective in 6/23 cases of AS[120]. Another stent type, the "dynamic" custom stent, was reported to be effective in 21/26 patients with AS [121]. Esophageal to aberrant right subclavian artery fistula was reported as a major complication of esophageal stenting in EA patients (see statement 22)[88].

Endoscopic knife. AS section was reported in several patients as an adjuvant effective strategy in resistant and recurrent AS[122].

Statement 28: Potential adjuvant treatments for the management of recurrent strictures in EA patients may include intralesional and/or systemic steroids, topical application of Mitomycin C, stents and an endoscopic knife

Expert opinion

No evidence

VOTES: 8/9/8/9/9/9 Accepted

- **Congenital stenosis in EA**

29. How should congenital stenosis in EA be diagnosed? (Fig. 2, box 6)

Congenital esophageal stenosis (CES) is characterized by an intrinsic circumferential narrowing of the distal esophageal lumen that is present at birth, although it may not necessarily be symptomatic in the neonate. Incidence of CES in patients with EA is high, and has been reported to be present in between 3% and 47% of patients. [76, 123-127] In contrast, the incidence of CES is 1 in 25,000 to 50,000 live births in the general population [127]. In patients with EA, CES may be suspected during the initial surgery [124], or afterwards because of symptoms of dysphagia in patients without AS, or during routine anastomosis evaluation by barium swallow or endoscopy. Diagnosis of CES associated with EA is difficult, and treatment may be delayed. Therefore, in all children operated for EA, a high index of suspicion for associated CES is required, especially in the presence of dysphagia, food impaction, feeding difficulties, failure to thrive, respiratory symptoms, or AS. Esophagogram allows diagnosis of CES in the majority of patients. However, in a retrospective study, more than one radiological examination was required, because the diagnosis of CES was either missed or misinterpreted as transient spasm, dysmotility, or esophageal narrowing due to reflux[76]. Endoscopy confirms

the diagnosis by revealing normal esophageal mucosa and esophageal narrowing distal to the anastomosis.

Three subtypes of CES are known: ectopic tracheobronchial remnants (TBRs) in the esophageal wall, segmental fibromuscolar hypertrophy (FMH) of the muscle and submucosal layers with fibrosis, and a membranous diaphragm [127]. Conventional imaging tools as well as CT scan and magnetic resonance imaging cannot differentiate TBR from FMH [127]. Endoscopic ultrasonography with miniprobes inserted through the operative channel of the standard gastroscope or by the side of a thin endoscope, allows the evaluation of the esophageal wall at level of CES, and can differentiate FMH from TBR subtypes [126, 128-130].

Statement 29: In EA patients we recommend esophagram as the first step in suspected CES, and endoscopy to confirm the diagnosis and exclude other pathology.

Expert opinion.

Low evidence

VOTES: 9/9/9/9/8/9 Accepted

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30. **How should congenital stenosis be managed in EA patients? (Fig. 3, box 6)**

There is no consensus about treatment of CES. Conservative treatment involves endoscopic dilation(s) of CES with balloon or Savary dilator under general anesthesia. Dilation of CES is attempted as a first-step treatment in all patients in many series [76, 123-126]. In a series of 47 patients with CES, Romeo reported that conservative treatment was effective in 96% of cases, for both the tracheobronchial remnants or fibromuscular subtypes of CES [126]. McCann [76] reported that 59% of patients were successfully treated with dilations. Since no technique has been shown to be superior to the other, the choice of dilation technique (bouginage or balloon dilator) depends on personal experience or preference of the operator.

Surgery is reserved for cases where dilations have failed, [76] or in the presence of a diagnosis

of tracheobronchial remnants[76, 125, 127, 128]. However, there is no difference in outcome following dilation of the tracheobronchial remnants or fibromuscular subtypes of CES [126]. Esophageal perforation during dilation may occur in 3.4 to 18% of procedures, especially following treatment of the tracheobronchial remnant subtype [76, 126, 127].

Statement 30: We suggest endoscopic dilation as the first line of treatment in CES.

Expert opinion.

Moderate evidence

VOTES: 9/9/9/7/9/8 Accepted

- **Eosinophilic esophagitis (EoE) in EA**

31. What is the impact of eosinophilic esophagitis on symptoms in EA patients? (Fig. 3, box 8)

There are no case controlled studies on the prevalence of EoE in patients with EA. 48 cases of EoE in EA patients have been reported in literature[25, 75, 131-135]. The largest reported number was in the study by Dhaliwal' *et al.*, which reported a 17% incidence in a retrospective review of biopsies taken from 103 EA patients over a 13-year period., This is greater than the reported incidence of EoE in the general pediatric population, of 1 in 10 000 children, and 8% to 10% in children with suspected GER refractory to antireflux treatment[136]. The higher incidence of EoE in the EA cohort has been ascribed to a possible genetic association, impairment of esophageal mucosal barrier function by acid refluxate and prolonged exposure to acid suppressive medication[75]. The majority of EA patients with EoE had type C EA in these studies. In the study by Dhaliwal *et al* 28% had long gap (LG) EA and EA patients with

LG had an 11.8 times relative risk of developing EoE in this study[75]. As presenting symptoms of EoE are similar to those of GER, misdiagnosis or delayed diagnosis often occurs in EA [75]. Compared to EA patients without EoE, EA patients with EoE had a significantly higher incidence of symptoms of vomiting, dysphagia, or cyanotic spells, and also had a significantly higher incidence of fundoplication and gastrostomy for feeding difficulties [75]. In the study by Dhaliwal *et al.*, 38% had a stricture at the time of diagnosis of EoE, and a significantly greater number of patients with EoE developed late strictures (> 1 year of age) when compared to those without EoE [75]. In this study, EA patients had a 1.9 times relative risk for stricture formation if they had EoE, LG, or both. The relative risk of EA patients with both LG and EoE developing strictures was 4:1[75]. A high prevalence of strictures has been reported in the other studies as well [131-134].

Statement 31: : EoE needs to be excluded in EA patients of all ages with dysphagia, reflux symptoms, coughing, choking or recurrent strictures that are refractory to PPI, before proceeding to anti-reflux surgery,

Expert opinion

Low evidence

VOTES: 9/8/7/9/9/9 Accepted

32. How should EoE be diagnosed and managed in EA patients?

For a proper diagnosis of EoE, it is important to demonstrate hypereosinophilia (>15 eosinophils/High Powered Field) in patients on high-dose acid suppression with PPIs. Multiple esophageal biopsies in keeping with standard guidelines for diagnosis of EoE, need to be taken during esophagoscopy, because EoE is described as a patchy disease process [136]. Moreover, on endoscopy, the typical macroscopic findings of EoE - namely furrows and white exudates - may not be seen in all EA patients [75, 131-133]. There is no evidence that the

treatment and management of EoE in EA patients should be different from other children. Therefore, current recommendations for treatment of EoE in the general population should be followed in EA patients[137, 138]. The only study to look at outcomes post-treatment of EoE in EA patients was by Chan *et al.* They reported that over a median follow up period of 23 months, treatment of EoE resulted in an improvement, not only in histology, with a significant reduction in the intraepithelial eosinophil count, but also in symptoms of dysphagia and reflux, prevalence of strictures, and need for dilations[139].

Statement 32: We recommend multiple esophageal biopsies, both proximal and distal to the anastomosis for the diagnosis of EoE. Management of EA patients with EoE should follow consensus recommendations for treatment of EoE in the general population

Expert opinion

Low evidence

VOTES: 9/8/9/9/9/9 Accepted

- **Associated gastrointestinal conditions in children with EA**

Approximately 50% of EA patients have one or more other gastrointestinal anomalies – mostly commonly part of which the VACTERL association (vertebral, ano-rectal malformations, cardiovascular, renal and limb anomalies) [140]. The incidence of gastrointestinal anomalies, excluding ano-rectal malformations, in association with EA, varies from 3.6% to 7.5% [141].

Hypertrophic pyloric stenosis (HPS). HPS occurs in approximately 1 in 400 live births in the western population [142, 143]. The 7.5% incidence of HPS in EA patients reported by Van Beelan was 30 times higher than the 0.25% incidence of HPS in the normal population [143]. The diagnosis was generally delayed, with a median of 6 days (range, 1–21 days) [144].

Malrotation. The reported incidence of malrotation in EA patients has ranged from 8.6- 12.7% [141]. There is often a delay in diagnosis and there are reports of death due to volvulus[141]. In EA patients, often only the anastomosis is imaged, as a result of which a malrotation can be missed. Upadhyay felt that contrast studies should include the duodenum to note the rotation of the bowel, and at the time gastrostomy is performed, along with searching for other atresias, one should look for malrotation of the small intestine [145].

Heterotopic Gastric Mucosa (HGM). A well-defined area of HGM or "inlet patch", typically located in the proximal esophagus just inferior to the upper esophageal sphincter [146], has been reported in up to 34% of patients with EA [147] versus 0.1% to 10% in adults and up to 21% in children [146]. HGM is typically considered a benign finding, but studies show that gastrointestinal or respiratory complications can occur as a result of acid secretion from HGM [148]. Symptoms described include mild dysphagia, gastrointestinal bleeding, ulceration, fistula formation, strictures, malignancy, cough, wheezing, and asthma [149].

Duodenal Atresia (DA)/Duodenal Stenosis (DS). The association of EA and DA/DS is well recognized, although uncommon [150, 151]. In babies with EA-TEF, the diagnosis of a coexisting duodenal obstructing lesion can usually be made on the basis of a plain radiographic study of the chest and abdomen, while in those with pure EA, the diagnosis may be subtler and may require the use of ultrasound or instillation of contrast material into a gastrostomy [152]. Quite

often, the DA/DS is not appreciated until esophageal continuity is established, or when gastrostomy feedings fail [153].

Heterotopic Pancreas (HP). Heterotopic pancreas (HP) is defined as pancreatic tissue lacking anatomical and vascular continuity with the pancreatic gland, which is most often located along the greater curvature of the prepyloric antrum. A prospective case control study in children with EA reported a significantly higher incidence of gastric HP in 18.7% of EA patients compared with 0.5% in the control group [154]. None developed complications related to HP [154].

Dumping Syndrome. Dumping syndrome can occur after primary anastomosis of EA without anti-reflux surgery [153] . It can manifest as feed refusal, nausea, retching, pallor, lethargy, diaphoresis, and watery diarrhea [155]. Michaud et al have reported the cases of 2 children with EA who presented with dumping syndrome without any known precipitating factors, such as fundoplication or associated microgastria [156]. Previous reports of dumping syndrome in EA had so far been related to fundoplication[29]. Studies have shown that abnormal gastric emptying is frequent in EA patients [74, 157, 158]. Both abnormal gastric emptying and/or damage to the vagus nerve during esophageal anastomosis may lead to dumping symdrome [29, 156].

- **Transition to adulthood**

The first generation of patients successfully operated for EA are reaching their sixth decade of life, highlighting that EA is becoming more and more an adult health issue. Moreover, since the late 1960's, and since, more than 70% (and now more than 90%) of patients survive to adulthood. Therefore, a growing number of EA survivors are adults and focus on the long- term outcomes in these patients is necessary.

33. What are the long-term digestive morbidities of EA in adulthood?

Symptoms

In adult EA patients, ongoing GI symptoms are common, whereas respiratory problems are less frequent. Despite the frequency of these GI symptoms, it is striking that most adults born with EA have grown accustomed to living with a degree of dysphagia and reflux symptoms, and often do not consider them problematic enough to seek medical attention. This can result in suboptimal management of GER. Six case series reporting GI symptoms in adult patients older than 18 years have been so far reported[19, 46, 159-161]. Only one compared 101 adult patients operated for EA with their native esophagus born between 1947 to 1985 (mean follow-up 36 years, range 22 to 57 years) with a random selected population of 287 control subjects[19].

a-Dysphagia: Symptoms of dysphagia are extremely frequent and affect 39%[31] to 85%[19] of adults; a significantly higher proportion than in control subjects (2%)[19]. The roles of dysmotility or residual stricture are not yet clear in adults. The benefit of dilation of strictures has not been established in this population.

b-Reflux: The prevalence of symptomatic GER is significantly higher among the patients than among controls (34% vs. 8%), as reported by Sistonen[19]. Taylor *et al*. found that GER symptoms were reported by 63% of subjects, and 25% of these had severe reflux

symptoms, defined as occurring at least 3 days per week.[159]

Statement 33a: Dysphagia and symptoms of GER continue into adulthood in EA patients, and are more frequent in EA survivors than in the general population

Expert opinion

High evidence

VOTES: 9/9/9/9/9/9 Accepted

Esophagitis and Barrett's esophagus

Sistonen *et al*. describe 101 patients with their native esophagus who systematically underwent upper GI endoscopy. GER symptoms and dysphagia were equally common in individuals with normal histology, histologic esophagitis, or epithelial metaplasia[19]. Overall, endoscopic esophagitis was reported in 8 to 58%, histological esophagitis in 24 to 90% and macroscopic Barrett's esophagus in 6 to 31%. Columnar epithelial metaplasia without goblet cells occurred in 0 to 19% of patients, and with goblet cells in 4 to 12%. Based on these findings, the prevalence of Barrett's esophagus is at least 4-fold higher among the adult population with repaired EA compared with general population.

In a multivariate logistic regression analysis, Sistonen *et al*. showed that surgically treated anastomotic stricture during infancy, long gap requiring myotomy to enable primary anastomosis, recurrent TEF, AS in adulthood, and patient age were the most significant predictive factors for the occurrence of epithelial metaplasia with or without goblet cells. Surgical complications, patient age, and impaired esophageal motility were significant predictors of development of epithelial metaplasia.

Statement 33b: The incidence of esophagitis and esophageal gastric and intestinal metaplasia (Barrett's) is increased in adults with EA as compared to the general population.

Expert opinion

High evidence

VOTES: 9/9/9/9/9/9 Accepted

Cancer

To date, eight case reports of esophageal cancer (3 adenocarcinoma[162-164], 5 squamous cell carcinoma[31, 159, 165, 166]) occurring between 20 and 46 years have been reported. One cohort study in Finland revealed that the relative risk of esophageal cancer in adults operated for EA was lower than the calculated 500 fold higher risk when compared with the normal control population[167] . A retrospective review of the EA database from the Royal Children's Hospital in Melbourne (798 patients [309 patients older than 40 years]) was performed to identify cases of esophageal cancer developing in this cohort. At the time of the publication, 4 of 309 patients had developed esophageal squamous cell carcinoma, over the age of 40 years. The cumulative incidence of esophageal squamous cell carcinoma in this age group was 50 times that expected in the general population[166] . No adequately powered study has been published that measures the risk of developing cancer in adults with EA. Mitomycin, usually classified as an alkylating agent, used as an adjuvant therapy in the treatment of recurrent strictures in EA patients, may be an additional long-term risk factor and patients who have been treated with it warrant additional specific surveillance.

Statement 33c: While current studies show no increase incidence of esophageal cancer (adenocarcinoma, squamous cell carcinoma) in adults with EA, esophageal cancer remains a concern

Expert opinion

Low evidence

VOTES: 9/9/9/9/9/9 Accepted

34. Is medical transitioning to adult medico-surgical services necessary?

Studies have shown that most adult patients with EA do not have any follow-up nor any

contact with the hospital beyond childhood[31]. Moreover, they do not seek medical attention for symptoms that have been present since infancy. Only 10% of patients are on appropriate treatment for GER; 34% are symptomatic but do not seek medical attention although they should be treated[19]. Undertreatment leads to the high incidence of unrecognized esophagitis and gastric/intestinal metaplasia. Transitioning is essential to bridge from pediatric to adult care to ensure that comprehensive care is provided throughout the life of all patients with EA. It is essential to plan this transition with the adult health care physician who can be a general practitioner, a surgeon, a gastroenterologist, a pulmonologist, or any informed specialist aware of the specifics of the care of adults operated for EA. No study addresses transition issues in patients with EA.

Statement 34: **We recommend transition of young adults from pediatric care to an adult physician with expertise in EA (general practitioner, surgeon, gastroenterologist, pulmonologist, or any informed specialist aware of the specificities of the care of adults operated for EA).**

Expert opinion

No evidence

Votes: 8/8/8/9/9/9 Accepted

35. **How should surveillance be managed in adult EA patients after transition from childhood? (Fig. 1, box 11)**

The intended effect of surveillance is a comprehensive clinical and endoscopic screening system aiming to start treatment early when indicated, to prevent the development of esophageal malignancy, and to detect early signs of intestinal metaplasia and squamous cell carcinoma. Endoscopic surveillance should be performed: 1-Systematically every 5 to 10 years, 2-If a new esophageal symptom occurs and 3-If regular symptoms (such as dysphagia) worsen. Early evidence of squamous cell carcinoma and adenocarcinoma of the esophagus are generally small, subtle mucosal abnormalities. Therefore, to optimize detection rates, advanced mucosal imaging techniques should be used. Acetic acid staining is a cheap and sensitive technique to accentuate the squamocolumnar junction. Chromoendoscopy with Lugol iodine sprayed onto the mucosal surface improves visualization of subtle squamous dysplasia from the surrounding normal mucosa because the iodine is not taken up by the dysplastic mucosa. Narrow band imaging has also been described detect early squamous cell carcinoma. In cases of endoscopic Barrett's esophagus, 4 quadrants biopsies should be taken every centimeter.

No study reports the benefit of a systematic surveillance in adults with EA.

Statement 35: We recommend regular clinical follow-up in every adult patient with EA, with special reference to presence of dysphagia, GER, respiratory symptoms and anemia with:
1. **Routine endoscopy (with biopsies in 4 quadrants at gastroesophageal junction and anastomotic site) at time of transition into adulthood and every 5 to 10 years**
2. **Additional endoscopy if new or worsening symptoms develop**
3. **In presence of Barrett's as per consensus recommendations**

Expert opinion

No evidence

Votes: 9/9/8/8/7/9 Accepted

- **Quality of life**

36. Is quality of life (QOL) impaired in EA patients?

Children

Three non-controlled studies have evaluated QoL in children and adolescents with EA. Peetsold *et al*. reported global QoL scores to be similar to healthy controls. Children reported their general health perception as being affected by GER symptoms. Older age negatively affects health related-QoL (HRQoL)[20] . Legrand *et al*., using a PedsQL score in 57 type C EA patients with a mean age of 13 years showed a lower score in EA patients when compared to healthy controls, but higher scores in comparison to patients with diabetes and other chronic diseases. Similarly, GER was an independent risk factor for poor QoL[18] . Dingenman *et al*. studied children and adults with complicated EA (delayed anastomosis, stricture requiring >10 dilations, major surgical revision, or esophageal replacement), and the childrens' families. Of note, these patients also had a high incidence (>90%) of associated malformations. The health related QoL was in the normal range in children with delayed anastomosis. The family impact was important, with 30% of parents scoring positive for suspected depression.[168]

Adults

Ure *et al*. reported 50 adults born between 1963-71 (mean age 25y) with EA, without a control group. Those patients with primary anastomosis had unimpaired QOL[169] . Deurloo *et al*. reported 97 patients >16 y (range 16-48 years), with a response rate of 80%. No differences were noted in overall physical and mental health between EA patients and healthy subjects. However, EA patients reported worse general health and less vitality than healthy subjects. 34% of patients perceived their QOL to be impaired due to GI symptoms[170].

Koivusalo *et al*. studied patients born between 1947 and 1956 with isolated EA and very few associated malformations [171]. According to SF-36 and a Visual Analog Scale, the health- related Qol of EA patients was not worse than that of general population. Only the gastrointestinal quality of life index (GIQLI) dimension measuring GER was lower in EA patients.

Statement 36: Although GI and respiratory symptoms and associated comorbidities (esophageal replacement and congenital anomalies) may negatively impact HRQoL, no evidence currently shows that the overall HRQoL is impaired in children and adults with EA compared with the general population. We recommend long-term medical and psychosocial support for these patients and families.

Expert opinion

Moderate evidence

VOTES: 9/9/9/8/7/9 Accepted

SUMMARY OF RECOMMENDATIONS

Number	Statements
1	It is recommended that GER be treated with acid suppression in all EA patients in the neonatal period
2	PPIs should be the first line therapy for GER/GERD
3	It is recommended that GER be systematically treated for prevention of peptic complications and anastomotic stricture up to the first year of life or longer
4a	pH monitoring is useful in evaluating the severity and symptom association of acid reflux in patients with EA
4b	pH-impedance monitoring is useful to evaluate and correlate non-acid reflux with symptoms in selected patients (symptomatic on PPI, on continuous feeding, with
5	Endoscopy with biopsies is mandatory for routine monitoring of GERD in patients with EA
6	All EA patients (including asymptomatics) should undergo monitoring of GER (impedance/pHmetry and/or endoscopy) at time of discontinuation of anti- acid

7	Routine endoscopy in asymptomatic EA patients is recommended. The expert panel recommends 3 endoscopies throughout childhood (1 after stopping PPI therapy, 1
8	Severe esophageal dysmotility predisposes EA patients to post fundoplication complications. However, EA patients may benefit from fundoplication for: 1. Recurrent anastomotic strictures, especially in long gap EA 2. Poorly-controlled GERD despite maximal PPI therapy
9	Barium contrast study, endoscopy with biopsies and pH-metry, at minimum, be performed prior to fundoplication
10	Symptoms of aspiration during swallowing may be identical to GERD symptom in young children
11a	Patients with EA should be evaluated regularly by a multidisciplinary team including pulmonology and otolaryngology, even in the absence of symptoms
11b	Anatomic abnormalities (laryngeal cleft, vocal cord paralysis, missed or recurrent fistulae) should be ruled out in EA patients with respiratory symptoms
11c	If pH-metry or pH-MII is performed, symptom correlation during reflux testing, rather than total reflux burden is the most important indicator of reflux-associated
12	Acid suppression should be used with caution in patients with extra-esophageal manifestations of reflux
13a	The etiology of life-threatening events is multifactorial and merits a multidisciplinary diagnostic evaluation prior to surgical interventions
13b	Anatomic issues (strictures, recurrent or missed fistulae, congenital esophageal stenosis, vascular rings, laryngeal clefts) and aspiration need to be excluded
14	Dysphagia should be suspected in patients with EA who present with food aversion, food impaction, difficulty in swallowing, odynophagia, choking, cough, pneumonia,
15	We recommend that all EA patients with dysphagia undergo evaluations with upper GI contrast study and esophagoscopy with biopsies
16	Esophageal manometry is useful to characterize esophageal motility patterns in EA patients with dysphagia. However, the impact on clinical outcome is yet to be
17	We recommend tailoring management of dysphagia based on the underlying mechanism(s)
18	In EA patients with post-fundoplication dysphagia, we recommend contrast study to rule out mechanical complications, EGD with biopsy and, if inconclusive, high
19	We recommend tailoring management of post-fundoplication dysphagia, based on the underlying mechanism(s)

20	Even though congenital vascular malformations are usually asymptomatic, they may be the underlying etiology for dysphagia, dyspnea, or cyanosis, by causing external compression on the esophagus and/or trachea. We recommend that congenital
21	No data are available on the most efficacious method(s) of avoiding feeding disorders in children with EA. However, the committee recommends a multidisciplinary
22	Intensive early enteral and oral nutrition intervention and advances in neonatal care and surgery have reduced the risk of long-term malnutrition in children with EA,
23	In addition to relative esophageal narrowing at the level of the anastomosis (by contrast and/or endoscopy), the committee believes that significant functional
24	There is no evidence that routine screening and dilation for AS is superior to evaluation and treatment in symptomatic patients. We recommend that AS be
25	Diagnosis of anastomotic stricture can be done with either contrast study and/or
26a	We recommend that dilation be performed in children with EA under general
26b	We recommend the use of a guide wire to insert the chosen dilator (balloon or semi
27	No evidence exists on the definition of *recurrent* anastomotic stricture in EA patients. Based on expert opinion we believe three or more clinically relevant
28	Potential adjuvant treatments for the management of recurrent strictures in EA patients may include: intralesional and/or systemic steroids, topical application of
29	In EA patients we recommend esophagram as the first step in suspected congenital esophageal stenosis and endoscopy to confirm the diagnosis and exclude other
30	We suggest endoscopic dilation as the first line of treatment in CES
31	Eosinophilic esophagitis (EoE) needs to be excluded in EA patients of all ages with dysphagia, reflux symptoms refractory to PPI, coughing, choking or recurrent
32	We recommend multiple esophageal biopsies, both proximal and distal to the anastomosis for the diagnosis of EoE. Management of EA patients with EoE should
33a	Dysphagia and symptoms of GER continue into adulthood in EA patients and are
33b	The incidence of esophagitis and esophageal gastric and intestinal metaplasia
33c	While current studies show no increase incidence of esophageal cancer (adenocarcinoma, squamous cell carcinoma) in adults with EA, esophageal cancer
34	We recommend transition of young adults from pediatric care to an adult physician with expertise in EA (family physician, gastroenterologist, pulmonologist, or any

35	We recommend regular clinical follow-up in every adult patient with EA, with special reference to presence of dysphagia, GER, respiratory symptoms and anemia with: 1. Routine endoscopy (with biopsies in 4 quadrants at gastroesophageal junction
36	Although GI and respiratory symptoms and associated comorbidities (esophageal replacement and congenital anomalies) may negatively impact HRQoL no evidence currently shows that the overall HRQoL is impaired in children and adults with EA

References

1. Shaw-Smith C. Oesophageal atresia, tracheo-oesophageal fistula, and the VACTERL association: review of genetics and epidemiology. J Med Genet 2006;43:545-54.

2. Kovesi T, Rubin S. Long-term complications of congenital esophageal atresia and/or tracheoesophageal fistula. Chest 2004;126:915-25.

3. Rintala RJ, Pakarinen MP. Long-term outcome of esophageal anastomosis. Eur J Pediatr Surg 2013;23:219-25.

4. Castilloux J, Noble AJ, Faure C. Risk factors for short- and long-term morbidity in children with esophageal atresia. J Pediatr 2010;156:755-60.

5. Guyatt GH OA, Vist GE. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ 2008;336:924-6.

6. Guyatt G, Oxman AD, Akl EA, et al. GRADE guidelines: 1. Introduction-GRADE evidence profiles and summary of findings tables. J Clin Epidemiol 2011;64:383-94.

7. Guyatt GH, Oxman AD, Kunz R, et al. GRADE guidelines: 2. Framing the question and deciding on important outcomes. J Clin Epidemiol 2011;64:395-400.

8. Balshem H, Helfand M, Schunemann HJ, et al. GRADE guidelines: 3. Rating the quality of evidence. J Clin Epidemiol 2011;64:401-6.

9. Guyatt GH, Oxman AD, Vist G, et al. GRADE guidelines: 4. Rating the quality of evidence--study limitations (risk of bias). J Clin Epidemiol 2011;64:407-15.

10. Hsu J BJ, Terracciano L, Kreis J, Compalati E, Stein AT, Fiocchi A, Schunemann HJ. Application of GRADE: making evidence-based recommendations about diagnostic tests in clinical practice guidelines. Implement Sci 2011;6:1748-5908.

11. Lindahl H, Rintala R. Long-term complications in cases of isolated esophageal atresia treated with esophageal anastomosis. J Pediatr Surg 1995;30:1222-3.

12. Banjar HH, Al-Nassar SI. Gastroesophageal reflux following repair of esophageal atresia and tracheoesophageal fistula. Saudi Med J 2005;26:781-5.

13. McKinnon LJ, Kosloske AM. Prediction and prevention of anastomotic complications of esophageal atresia and tracheoesophageal fistula. J Pediatr Surg 1990;25:778-81.

14. Deurloo JA, Ekkelkamp S, Schoorl M, et al. Esophageal atresia: historical evolution of management and results in 371 patients. Ann Thorac Surg 2002;73:267-72.

15. Cozzi DA, Zani A, Conforti A, et al. Pathogenesis of apparent life-threatening events in infants with esophageal atresia. Pediatr Pulmonol 2006;41:488-93.

16. Shawyer AC, D'Souza J, Pemberton J, et al. The management of postoperative reflux in congenital esophageal atresia-tracheoesophageal fistula: a systematic review. Pediatr Surg Int 2014;30:987-96.

17. Vandenplas Y, Rudolph CD, Di Lorenzo C, et al. Pediatric gastroesophageal reflux clinical practice guidelines: joint recommendations of the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition (NASPGHAN) and the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN). J Pediatr Gastroenterol Nutr 2009;49:498-547.

18. Legrand C, Michaud L, Salleron J, et al. Long-term outcome of children with oesophageal atresia type III. Arch Dis Child 2012;97:808-11.

19.   Sistonen SJ, Koivusalo A, Nieminen U, et al. Esophageal morbidity and function in adults with repaired esophageal atresia with tracheoesophageal fistula: a population-based long-term follow-up. Ann Surg 2010;251:1167-73.

20.   Peetsold MG, Heij HA, Deurloo JA, et al. Health-related quality of life and its determinants in children and adolescents born with oesophageal atresia. Acta Paediatr 2010;99:411-7.

21.   Mousa HM, Rosen R, Woodley FW, et al. Esophageal impedance monitoring for gastroesophageal reflux. J Pediatr Gastroenterol Nutr 2011;52:129-39.

22.   Catalano P, Di Pace MR, Caruso AM, et al. Gastroesophageal reflux in young children treated for esophageal atresia: evaluation with pH-multichannel intraluminal impedance. J Pediatr Gastroenterol Nutr 2011;52:686-90.

23.   Frohlich T, Otto S, Weber P, et al. Combined esophageal multichannel intraluminal impedance and pH monitoring after repair of esophageal atresia. J Pediatr Gastroenterol Nutr 2008;47:443-9.

24.   van Wijk M, Knuppe F, Omari T, et al. Evaluation of gastroesophageal function and mechanisms underlying gastroesophageal reflux in infants and adults born with esophageal atresia. J Pediatr Surg 2013;48:2496-505.

25.   Pedersen RN, Markow S, Kruse-Andersen S, et al. Esophageal atresia: gastroesophageal functional follow-up in 5-15 year old children. J Pediatr Surg 2013;48:2487-95.

26.   Shah R, Varjavandi V, Krishnan U. Predictive factors for complications in children with esophageal atresia and tracheoesophageal fistula. Dis Esophagus 2015;28:216-23.

27.   Schalamon J, Lindahl H, Saarikoski H, et al. Endoscopic follow-up in esophageal atresia-for how long is it necessary? J Pediatr Surg 2003;38:702-4.

28.   Lindahl H, Rintala R, Louhimo I. Failure of the Nissen fundoplication to control gastroesophageal reflux in esophageal atresia patients. J Pediatr Surg 1989;24:985-7.

29.   Holschneider P, Dubbers M, Engelskirchen R, et al. Results of the operative treatment

of gastroesophageal reflux in childhood with particular focus on patients with esophageal atresia. Eur J Pediatr Surg 2007;17:163-75.

30. Koivusalo A, Pakarinen MP, Rintala RJ. The cumulative incidence of significant gastrooesophageal reflux in patients with oesophageal atresia with a distal fistula--a systematic clinical, pH-metric, and endoscopic follow-up study. J Pediatr Surg 2007;42:370-4.

31. Deurloo JA, Ekkelkamp S, Bartelsman JF, et al. Gastroesophageal reflux: prevalence in adults older than 28 years after correction of esophageal atresia. Ann Surg 2003;238:686-9.

32. Krug E, Bergmeijer JH, Dees J, et al. Gastroesophageal reflux and Barrett's esophagus in adults born with esophageal atresia. Am J Gastroenterol 1999;94:2825-8.

33. Castilloux J, Bouron-Dal Soglio D, Faure C. Endoscopic assessment of children with esophageal atresia: Lack of relationship of esophagitis and esophageal metaplasia to symptomatology. Can J Gastroenterol 2010;24:312-6.

34. Sistonen SJ, Pakarinen MP, Rintala RJ. Long-term results of esophageal atresia: Helsinki experience and review of literature. Pediatr Surg Int 2011;27:1141-9.

35. Bergmeijer JH, Tibboel D, Hazebroek FW. Nissen fundoplication in the management of gastroesophageal reflux occurring after repair of esophageal atresia. J Pediatr Surg 2000;35:573-6.

36. Foker JE, Kendall Krosch TC, Catton K, et al. Long-gap esophageal atresia treated by growth induction: the biological potential and early follow-up results. Semin Pediatr Surg 2009;18:23-9.

37. Snyder CL, Ramachandran V, Kennedy AP, et al. Efficacy of partial wrap fundoplication for gastroesophageal reflux after repair of esophageal atresia. J Pediatr Surg 1997;32:1089-91; discussion 1092.

38. Goldin AB, Sawin R, Seidel KD, et al. Do antireflux operations decrease the rate of reflux-related hospitalizations in children? Pediatrics 2006;118:2326-33.

39. Lee SL, Shabatian H, Hsu JW, et al. Hospital admissions for respiratory symptoms and failure to thrive before and after Nissen fundoplication. J Pediatr Surg 2008;43:59-63; discussion 63-5.

40. Srivastava R, Berry JG, Hall M, et al. Reflux related hospital admissions after fundoplication in children with neurological impairment: retrospective cohort study. BMJ 2009;339:b4411.

41. Srivastava R, Downey EC, O'Gorman M, et al. Impact of fundoplication versus gastrojejunal feeding tubes on mortality and in preventing aspiration pneumonia in young children with neurologic impairment who have gastroesophageal reflux disease. Pediatrics 2009;123:338-45.

42. Esposito C, Langer JC, Schaarschmidt K, et al. Laparoscopic antireflux procedures in the management of gastroesophageal reflux following esophageal atresia repair. J Pediatr Gastroenterol Nutr 2005;40:349-51.

43. Cullu F, Gottrand F, Lamblin MD, et al. Prognostic value of esophageal manometry in antireflux surgery in childhood. J Pediatr Gastroenterol Nutr 1994;18:311-5.

44. Loots C, van Herwaarden MY, Benninga MA, et al. Gastroesophageal reflux, esophageal function, gastric emptying, and the relationship to dysphagia before and after antireflux surgery in children. J Pediatr 2013;162:566-573 e2.

45. Lindahl H, Rintala R, Sariola H. Chronic esophagitis and gastric metaplasia are frequent late complications of esophageal atresia. J Pediatr Surg 1993;28:1178-80.

46. Chetcuti P, Myers NA, Phelan PD, et al. Adults who survived repair of congenital oesophageal atresia and tracheo-oesophageal fistula. BMJ 1988;297:344-6.

47. Chetcuti P, Phelan PD. Respiratory morbidity after repair of oesophageal atresia and tracheo-oesophageal fistula. Arch Dis Child 1993;68:167-70.

48. Chetcuti P, Phelan PD, Greenwood R. Lung function abnormalities in repaired oesophageal atresia and tracheo-oesophageal fistula. Thorax 1992;47:1030-4.

49.   Legrand C, Michaud L, Neut D, et al. Long term outcome of children with esophageal

       atresia. J Pediatr Gastroenterol Nutr 2010;50:E133-E134.

50.   Bouguermouh D, Salem A. Esophageal atresia: a critical review of management at a

       single center in Algeria. Dis Esophagus 2015;28:205-10.

51.   Little DC, Rescorla FJ, Grosfeld JL, et al. Long-term analysis of children with

       esophageal atresia and tracheoesophageal fistula. J Pediatr Surg 2003;38:852-6.

52.   Davies MR. Anatomy of the extrinsic motor nerve supply to mobilized segments of

       the oesophagus disrupted by dissection during repair of oesophageal atresia with distal

       fistula. Br J Surg 1996;83:1268-70.

53.   Midrio P, Alaggio R, Strojna A, et al. Reduction of interstitial cells of Cajal in

       esophageal atresia. J Pediatr Gastroenterol Nutr 2010;51:610-7.

54.   Hormann M, Pokieser P, Scharitzer M, et al. Videofluoroscopy of deglutition in

       children after repair of esophageal atresia. Acta Radiol 2002;43:507-10.

55.   Aviv JE. Prospective, randomized outcome study of endoscopy versus modified

       barium swallow in patients with dysphagia. Laryngoscope 2000;110:563-74.

56.   Morini F, Iacobelli BD, Crocoli A, et al. Symptomatic vocal cord paresis/paralysis in

       infants operated on for esophageal atresia and/or tracheo-esophageal fistula. J Pediatr

       2011;158:973-6.

57.   Mortellaro VE, Pettiford JN, St Peter SD, et al. Incidence, diagnosis, and outcomes of

       vocal fold immobility after esophageal atresia (EA) and/or tracheoesophageal fistula

       (TEF) repair. Eur J Pediatr Surg 2011;21:386-8.

58.   Fraga JC, Adil EA, Kacprowicz A, et al. The association between laryngeal cleft and

       tracheoesophageal fistula: myth or reality? Laryngoscope 2015;125:469-74.

59.   Bargy F, Manach Y, Helardot PG, et al. [Risk of recurrent laryngeal nerve palsy in

       surgery of esophageal atresia]. Chir Pediatr 1983;24:130-2.

60.   American Lung Association Asthma Clinical Research C, Mastronarde JG,

       Anthonisen NR, et al. Efficacy of esomeprazole for treatment of poorly controlled

asthma. N Engl J Med 2009;360:1487-99.

61.   Writing Committee for the American Lung Association Asthma Clinical Research C, Holbrook JT, Wise RA, et al. Lansoprazole for children with poorly controlled asthma: a randomized controlled trial. JAMA 2012;307:373-81.

62.   Shaheen NJ, Crockett SD, Bright SD, et al. Randomised clinical trial: high-dose acid suppression for chronic cough - a double-blind, placebo-controlled study. Aliment Pharmacol Ther 2011;33:225-34.

63.   Canani RB, Cirillo P, Roggero P, et al. Therapy with gastric acidity inhibitors increases the risk of acute gastroenteritis and community-acquired pneumonia in children. Pediatrics 2006;117:e817-20.

64.   Laheij RJ, Sturkenboom MC, Hassing RJ, et al. Risk of community-acquired pneumonia and use of gastric acid-suppressive drugs. JAMA 2004;292:1955-60.

65.   Laheij RJ, Van Ijzendoorn MC, Janssen MJ, et al. Gastric acid-suppressive therapy and community-acquired respiratory infections. Aliment Pharmacol Ther 2003;18:847-51.

66.   Nasr A, Ein SH, Gerstle JT. Infants with repaired esophageal atresia and distal tracheoesophageal fistula with severe respiratory distress: is it tracheomalacia, reflux, or both? J Pediatr Surg 2005;40:901-3.

67.   Jennings RW, Hamilton TE, Smithers CJ, et al. Surgical approaches to aortopexy for severe tracheomalacia. J Pediatr Surg 2014;49:66-70; discussion 70-1.

68.   Werlin SL, Dodds WJ, Hogan WJ, et al. Esophageal function in esophageal atresia. Dig Dis Sci 1981;26:796-800.

69.   Montgomery M, Frenckner B, Freyschuss U, et al. Esophageal atresia: Long-term-follow-up of respiratory function, maximal working capacity, and esophageal function. Pediatr Surg Int 1995;10:519-522.

70.   Putnam TC, Lawrence RA, Wood BP, et al. Esophageal function after repair of esophageal atresia. Surg Gynecol Obstet 1984;158:344-8.

71.   Dutta HK, Grover VP, Dwivedi SN, et al. Manometric evaluation of postoperative patients of esophageal atresia and tracheo-esophageal fistula. Eur J Pediatr Surg 2001;11:371-6.

72.   Lemoine C, Aspirot A, Le Henaff G, et al. Characterization of esophageal motility following esophageal atresia repair using high-resolution esophageal manometry. J Pediatr Gastroenterol Nutr 2013;56:609-14.

73.   Tomaselli V, Volpi ML, Dell'Agnola CA, et al. Long-term evaluation of esophageal function in patients treated at birth for esophageal atresia. Pediatr Surg Int 2003;19:40-3.

74.   Montgomery M, Witt H, Kuylenstierna R, et al. Swallowing disorders after esophageal atresia evaluated with videomanometry. J Pediatr Surg 1998;33:1219-23.

75.   Dhaliwal J, Tobias V, Sugo E, et al. Eosinophilic esophagitis in children with esophageal atresia. Dis Esophagus 2014;27:340-7.

76.   McCann F, Michaud L, Aspirot A, et al. Congenital esophageal stenosis associated with esophageal atresia. Dis Esophagus 2015;28:211-5.

77.   Berthet S, Tenisch E, Miron MC, et al. Vascular Anomalies Associated with Esophageal Atresia and Tracheoesophageal Fistula. J Pediatr 2015;166:1140-1144 e2.

78.   Chapuy L, Pomerleau M, Perreault P, et al. Mucosal bridge as a cause of dysphagia after surgery for esophageal atresia. Can J Gastroenterol Hepatol 2014;28:350.

79.   Chapuy L, Pomerleau M, Faure C. Topical mitomycin-C application in recurrent esophageal strictures after surgical repair of esophageal atresia. J Pediatr Gastroenterol Nutr 2014;59:608-11.

80.   Georges A, Coopman S, Rebeuh J, et al. Inlet patch: clinical presentation and outcome in children. J Pediatr Gastroenterol Nutr 2011;52:419-23.

81.   Kawahara H, Kubota A, Hasegawa T, et al. Lack of distal esophageal contractions is a key determinant of gastroesophageal reflux disease after repair of esophageal atresia. J Pediatr Surg 2007;42:2017-21.

82. Zuccarello B, Spada A, Turiaco N, et al. Intramural ganglion structures in esophageal atresia: a morphologic and immunohistochemical study. Int J Pediatr 2009;2009:695837.

83. Nakazato Y, Landing BH, Wells TR. Abnormal Auerbach plexus in the esophagus and stomach of patients with esophageal atresia and tracheoesophageal fistula. J Pediatr Surg 1986;21:831-7.

84. Lemoine C, Aspirot A, Morris M, et al. Esophageal dysmotility is present before surgery in isolated tracheoesophageal fistula. J Pediatr Gastroenterol Nutr 2015;60:642-4.

85. Yoo HJ, Kim WS, Cheon JE, et al. Congenital esophageal stenosis associated with esophageal atresia/tracheoesophageal fistula: clinical and radiologic features. Pediatr Radiol 2010;40:1353-9.

86. Curci MR, Dibbins AW. Problems associated with a Nissen fundoplication following tracheoesophageal fistula and esophageal atresia repair. Arch Surg 1988;123:618-20.

87. Levin DN, Diamond IR, Langer JC. Complete vs partial fundoplication in children with esophageal atresia. J Pediatr Surg 2011;46:854-8.

88. Lo A, Baird R, De Angelis P, et al. Arterioesophageal fistula after stenting for esophageal atresia. J Pediatr Gastroenterol Nutr 2013;56:e30-1.

89. Millar A, Rostom A, Rasuli P, et al. Upper gastrointestinal bleeding secondary to an aberrant right subclavian artery-esophageal fistula: a case report and review of the literature. Can J Gastroenterol 2007;21:389-92.

90. Koivusalo AI, Pakarinen MP, Rintala RJ. Modern outcomes of oesophageal atresia: single centre experience over the last twenty years. J Pediatr Surg 2013;48:297-303.

91. Khan KM, Krosch TC, Eickhoff JC, et al. Achievement of feeding milestones after primary repair of long-gap esophageal atresia. Early Hum Dev 2009;85:387-92.

92. Puntis JW, Ritson DG, Holden CE, et al. Growth and feeding problems after repair of oesophageal atresia. Arch Dis Child 1990;65:84-8.

93. Faugli A, Emblem R, Veenstra M, et al. Does esophageal atresia influence the mother-infant interaction? J Pediatr Surg 2008;43:1796-801.

94. Smith IJ, Beck J. Mechanical feeding difficulties after primary repair of oesophageal atresia. Acta Paediatr Scand 1985;74:237-9.

95. Khoshoo V, Edell D. Previously healthy infants may have increased risk of aspiration during respiratory syncytial viral bronchiolitis. Pediatrics 1999;104:1389-90.

96. Khoshoo V, Ross G, Kelly B, et al. Benefits of thickened feeds in previously healthy infants with respiratory syncytial viral bronchiolitis. Pediatr Pulmonol 2001;31:301-2.

97. Golonka NR, Hayashi AH. Early "sham" feeding of neonates promotes oral feeding after delayed primary repair of major congenital esophageal anomalies. Am J Surg 2008;195:659-62; discussion 662.

98. Chittmittrapap S, Spitz L, Kiely EM, et al. Anastomotic stricture following repair of esophageal atresia. J Pediatr Surg 1990;25:508-11.

99. Michaud L, Guimber D, Sfeir R, et al. Anastomotic stricture following the surgical repair of esophageal atresia: Frequency, risk factors, and the efficacy of esophageal dilatation. [French]. Arch de Pediatr 2001;8:268-274.

100. Spitz L. Esophageal atresia. Lessons I have learned in a 40-year experience. J Pediatr Surg 2006;41:1635-40.

101. Serhal L, Gottrand F, Sfeir R, et al. Anastomotic stricture after surgical repair of esophageal atresia: frequency, risk factors, and efficacy of esophageal bougie dilatations. J Pediatr Surg 2010;45:1459-62.

102. Brown AK, Tam PK. Measurement of gap length in esophageal atresia: a simple predictor of outcome. J Am Coll Surg 1996;182:41-5.

103. Sillen U, Hagberg S, Rubenson A, et al. Management of esophageal atresia: review of 16 years' experience. J Pediatr Surg 1988;23:805-9.

104. Peyvasteh M, Askarpour S, Shoushtari MHS. A study of esophageal strictures after surgical repair of esophageal atresia. Pak J Med Sci 2006;22:269-272.

105.   Upadhyaya VD, Gangopadhyaya AN, Gupta DK, et al. Prognosis of congenital tracheoesophageal fistula with esophageal atresia on the basis of gap length. Pediatr Surg Int 2007;23:767-71.

106.   Lilja HE, Wester T. Outcome in neonates with esophageal atresia treated over the last 20 years. Pediatr Surg Int 2008;24:531-6.

107.   Chang EY, Chang HK, Han SJ, et al. Clinical characteristics and treatment of esophageal atresia: a single institutional experience. J Korean Surg Soc 2012;83:43-9.

108.   Parolini F, Leva E, Morandi A, et al. Anastomotic strictures and endoscopic dilatations following esophageal atresia repair. Pediatr Surg Int 2013;29:601-5.

109.   Said M, Mekki M, Golli M, et al. Balloon dilatation of anastomotic strictures secondary to surgical repair of oesophageal atresia. Br J Radiol 2003;76:26-31.

110.   Hagander L, Muszynska C, Arnbjornsson E, et al. Prophylactic treatment with proton pump inhibitors in children operated on for oesophageal atresia. Eur J Pediatr Surg 2012;22:139-42.

111.   Koivusalo A, Pakarinen MP, Rintala RJ. Anastomotic dilatation after repair of esophageal atresia with distal fistula. Comparison of results after routine versus selective dilatation. Dis Esophagus 2009;22:190-4.

112.   Tam PK, Sprigg A, Cudmore RE, et al. Endoscopy-guided balloon dilatation of esophageal strictures and anastomotic strictures after esophageal replacement in children. J Pediatr Surg 1991;26:1101-3.

113.   Antoniou D, Soutis M, Christopoulos-Geroulanos G. Anastomotic strictures following esophageal atresia repair: a 20-year experience with endoscopic balloon dilatation. J Pediatr Gastroenterol Nutr 2010;51:464-7.

114.   Yeming W, Somme S, Chenren S, et al. Balloon catheter dilatation in children with congenital and acquired esophageal anomalies. J Pediatr Surg 2002;37:398-402.

115.   Michaud L, Gottrand F. Anastomotic strictures: conservative treatment. J Pediatr Gastroenterol Nutr 2011;52 Suppl 1:S18-9.

116. Levesque D, Baird R, Laberge JM. Refractory strictures post-esophageal atresia repair: what are the alternatives? Dis Esophagus 2013;26:382-7.

117. Gandhi RP, Cooper A, Barlow BA. Successful management of esophageal strictures without resection or replacement. J Pediatr Surg 1989;24:745-9; discussion 749-50.

118. Zamiara P, Thomas KE, Connolly BL, et al. Long-term burden of care and radiation exposure in survivors of esophageal atresia. J Pediatr Surg 2015;50:1686-90.

119. Berger M, Ure B, Lacher M. Mitomycin C in the therapy of recurrent esophageal strictures: hype or hope? Eur J Pediatr Surg 2012;22:109-16.

120. Manfredi MA, Anjum MW, Jennings R, et al. Externally removable tracheal stents to treat recalcitrant esophageal anastomotic strictures in pediatric patients with long gap esophageal atresia. Gastrointest Endosc 2011;1):AB117.

121. Caldaro T, Torroni F, De Angelis P, et al. Dynamic esophageal stents. Dis Esophagus 2013;26:388-91.

122. Tan Y, Zhang J, Zhou J, et al. Endoscopic Incision for the Treatment of Refractory Esophageal Anastomotic Strictures in Children. J Pediatr Gastroenterol Nutr 2015;61:319-22.

123. Vasudevan SA, Kerendi F, Lee H, et al. Management of congenital esophageal stenosis. J Pediatr Surg 2002;37:1024-6.

124. Newman B, Bender TM. Esophageal atresia/tracheoesophageal fistula and associated congenital esophageal stenosis. Pediatr Radiol 1997;27:530-4.

125. Ibrahim AH, Al Malki TA, Hamza AF, et al. Congenital esophageal stenosis associated with esophageal atresia: new concepts. Pediatr Surg Int 2007;23:533-7.

126. Romeo E, Foschia F, de Angelis P, et al. Endoscopic management of congenital esophageal stenosis. J Pediatr Surg 2011;46:838-41.

127. Michaud L, Coutenier F, Podevin G, et al. Characteristics and management of congenital esophageal stenosis: findings from a multicenter study. Orphanet J Rare Dis 2013;8:186.

128. Takamizawa S, Tsugawa C, Mouri N, et al. Congenital esophageal stenosis: Therapeutic strategy based on etiology. J Pediatr Surg 2002;37:197-201.

129. Usui N, Kamata S, Kawahara H, et al. Usefulness of endoscopic ultrasonography in the diagnosis of congenital esophageal stenosis. J Pediatr Surg 2002;37:1744-6.

130. Kouchi K, Yoshida H, Matsunaga T, et al. Endosonographic evaluation in two children with esophageal stenosis. J Pediatr Surg 2002;37:934-6.

131. Batres LA, Liacouras C, Schnaufer L, et al. Eosinophilic esophagitis associated with anastomotic strictures after esophageal atresia repair. J Pediatr Gastroenterol Nutr 2002;35:224-6.

132. Oliveira C, Zamakhshary M, Marcon P, et al. Eosinophilic esophagitis and intermediate esophagitis after tracheoesophageal fistula repair: a case series. J Pediatr Surg 2008;43:810-4.

133. Yamada Y, Nishi A, Kato M, et al. Esophagitis with eosinophil infiltration associated with congenital esophageal atresia and stenosis. Int Arch Allergy Immunol 2013;161 Suppl 2:159-63.

134. Kassabian S, Baez-Socorro V, Sferra T, et al. Eosinophilic esophagitis in patients with esophageal atresia and chronic dysphagia. World J Gastroenterol 2014;20:18038-43.

135. Gorter RR, Heij HA, van der Voorn JP, et al. Eosinophilic esophagitis after esophageal atresia: is there an association? Case presentation and literature review. J Pediatr Surg 2012;47:e9-13.

136. Liacouras CA, Furuta GT, Hirano I, et al. Eosinophilic esophagitis: updated consensus recommendations for children and adults. J Allergy Clin Immunol 2011;128:3-20 e6; quiz 21-2.

137. Dellon ES, Gonsalves N, Hirano I, et al. ACG clinical guideline: Evidenced based approach to the diagnosis and management of esophageal eosinophilia and eosinophilic esophagitis (EoE). Am J Gastroenterol 2013;108:679-92; quiz 693.

138. Papadopoulou A, Koletzko S, Heuschkel R, et al. Management guidelines of eosinophilic esophagitis in childhood. J Pediatr Gastroenterol Nutr 2014;58:107-18.

139. Chan LJ, Tan L, Dhaliwal J, et al. Treatment outcomes for eosinophilic esophagitis in children with esophageal atresia. Dis Esophagus 2015.

140. Pedersen RN, Calzolari E, Husby S, et al. Oesophageal atresia: prevalence, prenatal diagnosis and associated anomalies in 23 European regions. Arch Dis Child 2012;97:227-32.

141. Raffensperger J. Gastrointestinal-tract defects associated with esophageal atresia and tracheo-esophageal fistula. Arch Surg 1970;101:241-4.

142. Pandya S, Heiss K. Pyloric stenosis in pediatric surgery: an evidence-based review. Surg Clin North Am 2012;92:527-39, vii-viii.

143. Krogh C, Gortz S, Wohlfahrt J, et al. Pre- and perinatal risk factors for pyloric stenosis and their influence on the male predominance. Am J Epidemiol 2012;176:24-31.

144. van Beelen NW, Mous DS, Brosens E, et al. Increased incidence of hypertrophic pyloric stenosis in esophageal atresia patients. Eur J Pediatr Surg 2014;24:20-4.

145. Upadhyay V, Hea CM, Matthews RD. Oesophageal atresia: a handshake with malrotation. Eur J Pediatr Surg 2001;11:368-70.

146. Powell RW, Luck SR. Cervical esophageal obstruction by ectopic gastric mucosa. J Pediatr Surg 1988;23:632-4.

147. Emery JL, Haddadin AJ. Gastric-type epithelium in the upper esophageal pouch in children with tracheoesophageal fistula. J Pediatr Surg 1971;6:449-53.

148. Galan AR, Katzka DA, Castell DO. Acid secretion from an esophageal inlet patch demonstrated by ambulatory pH monitoring. Gastroenterology 1998;115:1574-6.

149. Tran S, Misra S, Bittner JGt, et al. Heterotopic gastric mucosa of the upper esophagus following repair of esophageal atresia with tracheoesophageal fistula. J Pediatr Surg 2011;46:e37-9.

150. Young DG, Wilkinson AW. Abnormalities associated with neonatal duodenal obstruction. Surgery 1968;63:832-6.

151. Fonkalsrud EW, DeLorimier AA, Hays DM. Congenital atresia and stenosis of the duodenum. A review compiled from the members of the Surgical Section of the American Academy of Pediatrics. Pediatrics 1969;43:79-83.

152. Ein SH, Palder SB, Filler RM. Babies with esophageal and duodenal atresia: a 30-year review of a multifaceted problem. J Pediatr Surg 2006;41:530-2.

153. Spitz L, Ali M, Brereton RJ. Combined esophageal and duodenal atresia: experience of 18 patients. J Pediatr Surg 1981;16:4-7.

154. Moreau B, Levesque D, Faure C. Association of ectopic pancreas (EP) and esophageal atresia/tracheo-esophageal fistula (EA-TEF) in children. Gastroenterology 2009;1):A504-A505.

155. Bufler P, Ehringhaus C, Koletzko S. Dumping syndrome: a common problem following Nissen fundoplication in young children. Pediatr Surg Int 2001;17:351-5.

156. Michaud L, Sfeir R, Couttenier F, et al. Dumping syndrome after esophageal atresia repair without antireflux surgery. J Pediatr Surg 2010;45:e13-e15.

157. Yagi M, Homma S, Iwafuchi M, et al. Electrogastrography after operative repair of esophageal atresia. Pediatr Surg Int 1997;12:340-3.

158. Cheng W, Spitz L, Milla P. Surface electrogastrography in children with esophageal atresia. Pediatr Surg Int 1997;12:552-5.

159.	Taylor AC, Breen KJ, Auldist A, et al. Gastroesophageal reflux and related pathology in adults who were born with esophageal atresia: a long-term follow-up study. Clin Gastroenterol Hepatol 2007;5:702-6.

160.	Gatzinsky V, Jonsson L, Johansson C, et al. Dysphagia in adults operated on for esophageal atresia - Use of a symptom score to evaluate correlated factors. Eur J Pediatr Surg 2011;21:94-98.

161.	Huyn-Trudeau V, Maynard S, Terzic T, et al. Dysphagia among adult patients who underwent surgery for esophageal atresia at birth Can J Gastroenterol Hepatol 2015;29:91-94.

162.	Adzick NS, Fisher JH, Winter HS, et al. Esophageal adenocarcinoma 20 years after esophageal atresia repair. J Pediatr Surg 1989;24:741-4.

163.	Alfaro L, Bermas H, Fenoglio M, et al. Are patients who have had a tracheoesophageal fistula repair during infancy at risk for esophageal adenocarcinoma during adulthood? J Pediatr Surg 2005;40:719-20.

164.	Pultrum BB, Bijleveld CM, de Langen ZJ, et al. Development of an adenocarcinoma of the esophagus 22 years after primary repair of a congenital atresia. J Pediatr Surg 2005;40:e1-4.

165.	Deurloo JA, van Lanschot JJ, Drillenburg P, et al. Esophageal squamous cell carcinoma 38 years after primary repair of esophageal atresia. J Pediatr Surg 2001;36:629-30.

166.	Jayasekera CS, Desmond PV, Holmes JA, et al. Cluster of 4 cases of esophageal squamous cell cancer developing in adults with surgically corrected esophageal atresia--time for screening to start. J Pediatr Surg 2012;47:646-51.

167.	Sistonen SJ, Koivusalo A, Lindahl H, et al. Cancer after repair of esophageal atresia: population-based long-term follow-up. J Pediatr Surg 2008;43:602-5.

168. Dingemann C, Meyer A, Kircher G, et al. Long-term health-related quality of life after complex and/or complicated esophageal atresia in adults and children registered in a German patient support group. J Pediatr Surg 2014;49:631-8.

169. Ure BM, Slany E, Eypasch EP, et al. Quality of life more than 20 years after repair of esophageal atresia. J Pediatr Surg 1998;33:511-5.

170. Deurloo JA, Ekkelkamp S, Hartman EE, et al. Quality of life in adult survivors of correction of esophageal atresia. Arch Surg 2005;140:976-80.

171. Koivusalo A, Pakarinen MP, Turunen P, et al. Health-related quality of life in adult patients with esophageal atresia--a questionnaire study. J Pediatr Surg 2005;40:307-

Table 1: Overview of clinical questions

1. **GER in esophageal atresia (EA) patients**

   a. Should GER be systematically treated in all EA patients in the neonatal period?

   b. How should GER be managed?

   c. How long should GER be treated?

2. **Role of reflux testing in EA patients**

   a. What is the role of 24 hour pH and pH-impedance monitoring in EA patients?

   b. What is the role of esophagoscopy in EA patients?

   c. How should GER be monitored, and when?

   d. How often do EA patients need surveillance endoscopy in childhood and adolescence?

3. **Fundoplication**

   a. What is the role of fundoplication in EA patients with GER?

   b. What evaluations should be performed prior to fundoplication?

4. **Extraesophageal manifestations of GER and Dysmotility**

   a. What extra esophageal manifestations of reflux and dysmotility are seen in EA patients?

   b. How should clinicians investigate extraesophageal

manifestations in EA patients?

    c. How should clinicians treat extraesophageal

manifestations in EA patients?

5. How to investigate and manage "Dying/cyanotic spells" in EA

patients?

6. Dysphagia and Esophageal Function

    a. When should dysphagia be considered in patients with in

EA?

    b. How to investigate dysphagia in EA patients?

    c. What is the role of esophageal manometry

in EA patients with dysphagia?

    d. How should dysphagia be managed in EA patients?

    e. How should dysphagia in EA patients

post-fundoplication be investigated?

    f. How should dysphagia in EA patients

post-fundoplication be managed?

7. When should we look for associated vascular abnormalities in

EA?

8. Feeding and Nutrition

    a. How should abnormal feeding behaviors in

EA be prevented and managed?

  b. Is there a risk for malnutrition in infants, children and adolescents with

EA?

9. **Anastomotic Stricture**

   a. What is the definition of a clinically relevant anastomotic stricture in

   patients with EA?

   b. When should anastomotic strictures in EA be diagnosed?

   c. How should anastomotic stricture be diagnosed in EA?

   d. How anastomotic strictures be managed?

   e. What is the definition of recurrent anastomotic stricture in EA patients?

   f. What adjuvant treatments are available in recurrent strictures in EA

   patients?

10. **How to diagnose and manage congenital stricture in EA?**

11. **Eosinophilic esophagitis and other gastrointestinal anomalies**

   a. What is the impact of eosinophilic esophagitis on symptoms in EA

   patients?

   b. How should eosinophilic esophagitis be diagnosed and managed in EA

   patients?

12. **What are the other gastrointestinal conditions (apart from anal stenosis/ano-rectal malformations) that can be associated with EA?**

13. **Transition to adulthood and Quality of Life**

   a. What are the long term digestive morbidities of EA in adulthood?

b. Is medical transitioning to adult medico-surgical services necessary?

c. How should surveillance be managed in adult EA patients after transition from childhood?

d. Is QOL impaired in EA patients?

Table 2: Prevalence of GER, esophagitis and fundoplication in EA patients

Authors	Number	Age at evaluation	Prevalence of GER	Diagnosis of GER	Prevalence of esophagitis	Prevalence of antireflux surgery
Curci [1]	36	NA	NA	NA	NA	45%
Montgomery [2]	110	NA	30%	Barium study	NA	8%
Engum [3]	227	1 month-22 years	58%	NA	NA	44%
Chetcuti [4]	125	>18 years	46% (11% >one	Clinical signs (heartburn)	NA	NA
Somppi [5]	42	3-30 years (mean: 12.6)	22%	pH-metry	6%	8%
Krug [6]	39	18-26 years	33%	Clinical score	23%	NA
Bergmeijer [7]	125	NA	NA	NA	NA	23%
Yanchar [8]	90 excluding type A	NA	46%	NA	NA	33%

Authors	Number	Age at evaluation	Prevalence of GER	Diagnosis of GER	Prevalence of esophagitis	Prevalence of antireflux surgery
Deurloo [9]	371	1-54 years	40%	pH-metry	NA	23%
Deurloo [10]	40	28-45 years	52%	Heartburn Retrosternal pain	9% (90% histo)	2.5%
Koivusalo [11]	50	2.5-95 months	20%	pH-metry	26%	24%
Konkin [12]	144	Post operative period	31%	NA	NA	12%
Taylor [13]	132	20-48 years	63%	Symptoms	58% (histo)	11%
Koivusalo [14]	61 type C	1-10 years (median 5 years)	46%	Fundoplication Or pH-metry Or endoscopy	NA	30%

Authors	Number	Age at evaluation	Prevalence of GER	Diagnosis of GER	Prevalence of esophagitis	Prevalence of antireflux surgery
Castilloux [15]	134	0.3-16 years (mean: 5)	<1yr 34% >1yr 43%	Severe GER: moderate to severe esophagitis on biopsy and/or intestinal metaplasia on esophageal biopsies and/or need	NA	NA
Castilloux [16]	45	0.5-18 years	20%	Regurgitation Pyrosis	31% (histo)	44%
Sistonen [17]	101	21-56 years (mean: 36)	34%	Clinical symptoms	8% (25 % histo)	10%
Catalano [18]	22	3–40 months (median: 15)	45.5% (acidic)	Impedance-pHmetry	NA	0%

Authors	Number	Age at evaluation	Prevalence of GER	Diagnosis of GER	Prevalence of esophagitis	Prevalence of antireflux surgery
Legrand [19]	81 type C	9.5-18.5 years	35%	Heartburn/regurgitation and/or pH-metry, endoscopy	NA	39%
Pedersen [20]	59	5-15 years	56%	Clinical symptoms pH-metry	49% (44% histo)	NA
Shah [21]	110	6+/-3.5 years	39%	Symptoms+/- pH-impedancemetry+/- endoscopy	40% histo	17%
Bouguermouh	45	3 months-10 years	49%	NA	NA	18%

NA : not available

1. Curci MR, Dibbins AW. Problems associated with a Nissen fundoplication following tracheoesophageal fistula and esophageal atresia repair. Arch Surg 1988;123:618-20.

2. Montgomery M, Frenckner B. Esophageal atresia: mortality and complications related to gastroesophageal reflux. Eur J Pediatr Surg 1993;3:335-8.

3. Engum SA, Grosfeld JL, West KW, et al. Analysis of morbidity and mortality in 227 cases of esophageal atresia and/or tracheoesophageal fistula over two decades. Arch Surg 1995;130:502-8; discussion 508-9.

4. Chetcuti P, Myers NA, Phelan PD, et al. Adults who survived repair of congenital oesophageal atresia and tracheo-oesophageal fistula. BMJ 1988;297:344-6.

5. Somppi E, Tammela O, Ruuska T, et al. Outcome of patients operated on for esophageal atresia: 30 years' experience. J Pediatr Surg 1998;33:1341-6.

6. Krug E, Bergmeijer JH, Dees J, et al. Gastroesophageal reflux and Barrett's esophagus in adults born with esophageal atresia. Am J Gastroenterol 1999;94:2825-8.

7. Bergmeijer JH, Tibboel D, Hazebroek FW. Nissen fundoplication in the management of gastroesophageal reflux occurring after repair of esophageal atresia. J Pediatr Surg 2000;35:573-6.

8. Yanchar NL, Gordon R, Cooper M, et al. Significance of the clinical course and early upper gastrointestinal studies in predicting complications associated with repair of esophageal atresia. J Pediatr Surg 2001;36:815-22.

9. Deurloo JA, Ekkelkamp S, Schoorl M, et al. Esophageal atresia: historical evolution of management and results in 371 patients. Ann Thorac Surg 2002;73:267-72.

10.   Deurloo JA, Ekkelkamp S, Bartelsman JF, et al. Gastroesophageal reflux: prevalence in adults older than 28 years after correction of esophageal atresia. Ann Surg 2003;238:686-9.

11.   Koivusalo A, Pakarinen M, Rintala RJ, et al. Does postoperative pH monitoring predict complicated gastroesophageal reflux in patients with esophageal atresia? Pediatr Surg Int 2004;20:670-4.

12.   Konkin DE, O'Hali W A, Webber EM, et al. Outcomes in esophageal atresia and tracheoesophageal fistula. J Pediatr Surg 2003;38:1726-9.

13.   Taylor AC, Breen KJ, Auldist A, et al. Gastroesophageal reflux and related pathology in adults who were born with esophageal atresia: a long-term follow-up study. Clin Gastroenterol Hepatol 2007;5:702-6.

14.   Koivusalo A, Pakarinen MP, Rintala RJ. The cumulative incidence of significant gastrooesophageal reflux in patients with oesophageal atresia with a distal fistula--a systematic clinical, pH-metric, and endoscopic follow-up study. J Pediatr Surg 2007;42:370-4.

15.   Castilloux J, Noble AJ, Faure C. Risk factors for short- and long-term morbidity in children with esophageal atresia. J Pediatr 2010;156:755-60.

16.   Castilloux J, Bouron-Dal Soglio D, Faure C. Endoscopic assessment of children with esophageal atresia: Lack of relationship of esophagitis and esophageal metaplasia to symptomatology. Can J Gastroenterol 2010;24:312-6.

17.   Sistonen SJ, Pakarinen MP, Rintala RJ. Long-term results of esophageal atresia: Helsinki experience and review of literature. Pediatr Surg Int 2011;27:1141-9.

18. Catalano P, Di Pace MR, Caruso AM, et al. Gastroesophageal reflux in young children treated for esophageal atresia: evaluation with pH-multichannel intraluminal impedance. J Pediatr Gastroenterol Nutr 2011;52:686-90.

19. Legrand C, Michaud L, Salleron J, et al. Long-term outcome of children with oesophageal atresia type III. Arch Dis Child 2012;97:808-11.

20. Pedersen RN, Markow S, Kruse-Andersen S, et al. Esophageal atresia: gastroesophageal functional follow-up in 5-15 year old children. J Pediatr Surg 2013;48:2487-95.

21. Shah R, Varjavandi V, Krishnan U. Predictive factors for complications in children with esophageal atresia and tracheoesophageal fistula. Dis Esophagus 2015;28:216-23.

22. Bouguermouh D, Salem A. Esophageal atresia: a critical review of management at a single center in Algeria. Dis Esophagus 2015;28:205-10.

Table 3: **Studies conducted in adults > 18 years with esophageal atresia**

Author	Number of	Age (years)	Dysphagia (%)	Reflux symptoms	Patients who underwent	Endoscopic Esophagitis	Histological Esophagitis	Endoscopic Barrett's	Gastric Metaplasia	Intestinal Metaplasia	Cancer (N)
Chetcutti	125	18-39	53	46	NA	NA	NA	NA	NA	NA	NA
Krug	39	18-26	77	33	34	26	24	6	0	6	0
Deurloo	38	28-45	39	49	23	9	90	9	4	4	1 (squamous
Taylor	132	20-48	52	63	62	58*	NA	26	15	11	1 (squamous
Sistonen 2010[5]	101 (vs 287	22-57	85	34	101	8	25**	11	15	6	0
Hyunh-Trudeau	41	18-44	73	29	32	19	25	31	19	12	0

NA: not available

*Mild esophagitis, 8%; moderate esophagitis 40%; severe esophagitis 10%

** Esophagitis mild in 22 patients, and moderate in 3 patients.

1.   Chetcuti P, Myers NA, Phelan PD, et al. Adults who survived repair of congenital oesophageal atresia and tracheo-oesophageal fistula. BMJ   1988;297:344-6.

2.   Krug E, Bergmeijer JH, Dees J, et al. Gastroesophageal reflux and Barrett's esophagus in adults born with esophageal atresia. Am J Gastroenterol   1999;94:2825-8.

3.   Deurloo JA, Ekkelkamp S, Bartelsman JF, et al. Gastroesophageal reflux: prevalence in adults older than 28 years after correction of esophageal   atresia. Ann Surg 2003;238:686-9.

4.   Taylor AC, Breen KJ, Auldist A, et al. Gastroesophageal reflux and related pathology in adults who were born with esophageal atresia: a long-   term follow-up study. Clin Gastroenterol Hepatol 2007;5:702-6.

5.   Sistonen SJ, Koivusalo A, Nieminen U, et al. Esophageal morbidity and function in adults with repaired esophageal atresia with tracheoesophageal   fistula: a population-based long-term follow-up. Ann Surg 2010;251:1167-73.

6.   Huyn-Trudeau V, Maynard S, Terzic T, et al. Dysphagia among adult patients who underwent surgery for esophageal atresia at birth Can J   Gastroenterol Hepatol 2015;29:91-94.

Symptomatic patient with EA — 1

Esophagram +/- Swallow study — 2

Abnormal? — 3

Refer to Statements and treat accordingly — 4

EGD +/- bronchoscopy +/- laryngoscopy — 5

Stricture? Stenosis? Tracheomalacia? Fistula? Vascular compression? Vocal cord paralysis? Laryngeal cleft? — 6

Peptic

Eosinophilic

Infectious

Refer to statements & Treat accordingly — 8

Esophagitis? — 7

pH-MII probe (symptoms correlation) — 9

Consider:
PPIs
2. Prokinetics
3. Feeding modifications
Transpyloric feeding
Fundoplication
Periodical reassessement — 11

Reflux? — 10

Consider:
Esophageal high resolution manometry & Esophageal dysmotility
Gastric dysmotility
Behavioral feeding disorders
Functional disorders — 12

Symptomatic
Anastomotic Stricture
1

Esophagogram
Esophagoscopy
& Dilation
Biopsies above & below
anastomosis*
2

Symptoms?
3

Monitor
4

Repeat dilation
within 2-4 weeks.
Treat Reflux.
Rebiopsy if
inflammation*
5

Symptoms?
7

Monitor
6

Repeat dilation within
2-4 weeks.
+/- adjuvant therapy.
Consider
fundoplication**
8

Symptoms?
9

Monitor

Consider repeat
dilations.
Consider
fundoplication
Surgery
10