ERNICA Consensus Conference on the Management of Patients with Esophageal Atresia and Tracheoesophageal Fistula:

Follow-up and Framework

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ABSTRACT

INTRODUCTION

Improvements in care of patients with esophageal atresia (EA) and tracheoesophageal fistula (TEF) have shifted the focus from mortality to morbidity and quality-of-life. Long-term follow-up is essential, but evidence is limited and but standardized protocols are scarce. Nineteen representatives of the European Reference Network for Rare Inherited Congenital Anomalies (ERNICA) from 9 European countries conducted a consensus conference on the surgical management of EA/TEF.

METHODS

The conference was prepared by Item generation (including items of surgical relevance from the ESPGHAN-NASPGHAN guidelines on follow-up after EA repair), item prioritization, formulation of a final list containing the domains *Follow-up and Framework*, and literature review. Anonymous voting was conducted via an internet-based system. Consensus was defined as ≥75% of those voting scoring 6-9.

RESULTS

Twenty-five items were generated in the domain *Follow-up* of which 17 (68%) matched with corresponding ESPGHAN-NASPGHAN statements. Complete consensus (100%) was achieved on seven items (28%), such as the necessity of an interdisciplinary follow-up program. Consensus ≥75% was achieved on 18 items (72%), such as potential indications for fundoplication. There was an 82% concordance with the ESPGHAN-NASPGHAN recommendations. Four items were generated in the domain *Framework* and complete consensus was achieved on all these items.

CONCLUSIONS

Participants of the first ERNICA conference reached significant consensus on the follow-up of patients with EA/TEF who undergo primary anastomosis. Fundamental statements regarding centralization, multidisciplinary approach and involvement of

patient organizations were formulated. These consensus statements will provide the cornerstone for uniform treatment protocols and resultant optimized patient care.

INTRODUCTION

Since the first successful primary repair of esophageal atresia in 1941, improvements in operative and perioperative care have led to better outcomes and have shifted the focus from mortality to morbidity and quality-of-life-issues [8, 23, 24, 25, 26, 44, 46, 47, 48]. Esophageal atresia is no more just a neonatal surgical challenge, but rather a lifelong issue for the patient [8, 44, 46, 49]. It appears that respiratory, nutritional, and gastroenterological issues are the most prevalent sequelae – not only in the first years of life, but also in adolescence and adulthood [44, 46] requiring constant long-term follow-up following standardized protocols in specialized centers.

However, precisely formulated guidelines on the follow-up of patients with esophageal atresia are scarce [49, 50].

In 2016, the gastrointestinal working group of the *International Network on Esophageal Atresia* (INoEA) comprising members from *The European Society for Paediatric Gastroenterology Hepatology and Nutrition* (ESPGHAN) and *The North American Society for Pediatric Gastroenterology, Hepatology and Nutrition* (NASPGHAN) published guidelines for the management of gastrointestinal and nutritional complications in children with esophageal atresia with tracheoesophageal fistula [8].

In 2017, the European Reference Network on Rare Inherited and Congenital Anomalies (ERNICA) has been established in response to the European Commission's call for the setup of European Reference Networks for rare diseases [3]. The mission of ERNICA is to promote optimal patient care for rare inherited and congenital digestive track-related disorders from pediatric age to adulthood providing high quality and accessible education, supporting research, improving clinical standards and services and reducing health inequalities in Europe [4, 5, 6, 7, 21].

During recent ERNICA meetings, participants agreed to establish consensus on all relevant aspects of the surgical management of patients with esophageal atresia including *Follow-up* as an urgent objective of ERNICA.

In this first ERNICA consensus conference focusing on the management of patients with esophageal atresia and tracheoesophageal fistula, two priorities were addressed: The recently published results of the first part of the ERNICA consensus conference focused on *Diagnostics, Preoperative, Operative and Postoperative Management* [51]. The second part of the conference mainly dealt with *Follow-up and Framework* from a surgical perspective which will be presented in the following.

MATERIALS & METHODS

The general methodological approach has been recently published when presenting the first part of the ERNICA consensus conference on *Diagnostics, Preoperative, Operative and Postoperative Management* [51]. The second part which is reported in this manuscript differed from the first part in details. Therefore, the two parts are presented separately.

The conference, which dealt exclusively with the management of patients with esophageal atresia with tracheoesophageal fistula who undergo primary anastomosis, took place in Berlin on the 25th and 26th October 2018. In total, 14 pediatric surgeons, one pediatric gastroenterologist, three representatives of patient support groups acting under the umbrella of the Federation of Esophageal Atresia and Tracheo-Esophageal Fistula Support Groups (EAT) [9], and one non-surgeon pediatric surgery academic took part in all steps of the preparation and the conference itself. All participants were

members of the ERNICA Workstream *Congenital Malformations and Diseases of the Esophagus.*

The preparation and implementation of the conference included the following steps [51]: (1) generation of a list of items; (2) prioritization of the items using the online REDCap electronic data capture tools [10]; (3) discussion of all items during the conference, formulation of statements; (4) anonymous voting via the internet-based system VoxVote [12].

The items of this second part of the conference were attributed to the domains *Follow-up* and *Framework.* For the domain *Follow-up*, the ESPGHAN-NASPGHAN guidelines [8] were reviewed in order to identify matches or similarities in both lists as both focused on patients with esophageal atresia with tracheoesophageal fistula – from a pediatric gastrointestinal and from a pediatric surgical perspective. It has been consciously decided not to adopt the entire list of ESPGHAN-NAPGHAN guidelines including 36 statements. Only items of surgical relevance were finally included.

With regard to literature search, publications with the highest grade of evidence according to the CEBM (Centre for Evidence-Based Medicine) classification were suggested to be preferred [11] as previously reported [51]. Literature was distributed and made available to all participants via a DropBox (Dropbox Inc., San Francisco, California, USA, 2007) link prior to the conference.

In case of available ESPGHAN-NASGPHAN statements, the prevciously presented literature was applied and supplemented with recent literature where appropriate. All participants were aware of the ESPGHAN-NASPGHAN statements. The wordings of

the statements on items were updated during the discussion by the participants of the conference and prepared for voting by the non-surgical academic (SE) who did not vote himself. In the majority of items, the final wording of the statements somehow differed from the wording of the ESPGHAN-NASPGHAN guidelines although both dealt with the same topic **[see supplement]**.

Consensus was defined as ≥75% of those voting scored 6, 7, 8 or 9, excluding those who declared no relevant expertise on that statement [51].

RESULTS AND CONSENSUS STATEMENTS

Item generation and prioritization

The systematic literature search and the discussion of the members of the ERNICA Workstream *Congenital Malformations and Diseases of the Esophagus* during the ERNICA conference in Stockholm on the 18th – 20th April 2018 resulted in a total of 16 items.

After the online prioritization phase, 2 items were excluded. Following the participants´ suggestions, 12 items were added as new items. Consequently, the list included 26 items prior to the conference, for which literature was obtained and circulated.

As a result of the presentations by the domain leaders and discussion during the conference, 6 items were excluded, and 9 items were added as new items as some items were split into several separate questions. Finally, 29 items were confirmed for voting and included 25 items in the domain *Follow-up* **[Table 1]**, and four items in the domain *Framework* **[Table 2]**.

Table 1

Table 2

ESPGHAN-NASPGHAN guidelines

In the domain *Follow-up*, corresponding ESPGHAN-NASPGHAN statements were available for 17 items (68%). Mapping of the ERNICA Consensus conference items to the ESPGHAN-NASPGHAN statements is shown in the **supplementary material**. The participants of this conference divided two of the ESPGHAN-NASPGHAN statements into several items and voted separately: 3 items (item Nº 11, 12, 13) referred to a single ESPGHAN-NASPGHAN statement (statement Nº 28); and 2 items (item Nº 18, 19) also referred to a single ESPGHAN-NASPGHAN statement (statement Nº 7); **[see supplement]**.

Consensus

In the domain *Follow-up*, complete agreement, defined as 100% consensus amongst voters, was achieved on 7 items (28%) and general consensus (≥ 75% of those voting having scored 6-9) on 18 items (72%). Eight items (32%) were particularly controversial in that the votes ranged from 1-9; in four (50%) of these consensus was not reached. Detailed results are summarized in **Table 1** and **Table 3**.

Table 1

Table 3

In the domain *Framework*, complete consensus was achieved on all items with no controversial items (n = 4; 100%). Detailed results are summarized in **Table 2** and **Table 3**.

Table 2

Table 3

Abstention

In the domain *Follow-up*, one or more participants declared '*no relevant expertise on this statement*' for 7 (28%) items; for one (4%) item, one participant abstained; for 2 (8%) items, two participants abstained; in 2 items (8%) three participants abstained; in one (4%) items, four participants abstained from voting. There was no abstention from voting in the domain *Framework*.

Controversial Discussion

Several items were discussed controversially as indicated by a wide range from 1-9 **[Table 1, Table 3]**. The controversial discussion included 8 items (32%) in the domain *Follow-up,* of which four items (50%) did not reach consensus. There was no controversial discussion in the domain *Framework*.

Table 1

Table 3

Concordance with ESPGHAN-NASPGHAN guidelines

The majority (n=14; 82.4%) of items that mapped directly to ESPGHAN-NASPGHAN guidelines [8] were voted consensus in, so were in concordance with the ESPGHAN-NASPGHAN recommendations. Concerning the other three items (17.6%), consensus was not reached, so the votes of the participants of the conference were not in line with the ESPGHAN-NASPGHAN recommendations [8], **[Table 1]**:

Table 1

(i) Duration of antacid medication

(ii) Topical application of mitomycin C as a therapeutic option for recurrent strictures

(iii) Administration of intralesional/systemic steroids as a therapeutic option for recurrent strictures

DISCUSSION

The ESPGHAN-NASPGHAN guidelines for the evaluation and treatment of gastrointestinal and nutritional complications in children with esophageal atresia and tracheoesophageal fistula which have been published by Krishnan et al [8] provide a major contribution to the development of generally accepted guidelines for patient care. These guidelines were set up during two consensus meetings using the nominal voting technique. Expert opinion was used where no randomized controlled trials were available to support the recommendations [8]. However, the ESPGHAN-NASPGHAN

guidelines approach the field of *Follow-up* from a rather gastroenterological / non-surgical perspective. The follow-up of this particular group of patients consists undoubtedly of similar contents comparing the medical and the surgical perspective. Nonetheless, the already existing guidelines needed to be evaluated also by pediatric surgeons as being not only responsible for a crucial intervention – the esophageal anastomosis [41] –, but also taking part in subsequent follow-up. Besides the overlap of certain aspects, additional items from a surgical angle needed to be addressed supplementary to the already existing ESPGHAN-NASPGHAN guidelines.

We hereby present for the first time the results of a consensus conference focused on *surgical* aspects of the management of patients with esophageal atresia with tracheoesophageal fistula. In line with the ESPGHAN-NASPGHAN guidelines, this conference was based on two keystones: (i) on expert opinion, and (ii) on evidence from literature.

Participants of this conference achieved general consensus (defined by ≥ 75% of votes scoring higher 6-9) in 72% of items in the domain *Follow-up* and even 100% in the domain *Framework* suggesting predominantly homogeneous approaches in ERNICA institutions. Comparing the results in terms of general consensus in the individual domains including the previously reported domains *Diagnostics (50%), Preoperative (50%), Operative (82.1%)* and *Postoperative Management (70%)* [51], it becomes obvious that consistency of expert opinion reaches highest level in the domains *Operative Management, Follow-up* and *Framework*.

One third of items in the domain *Follow-up* were discussed controversially, out of which half did not reach consensus:

According to the ESPGHAN-NASPGHAN guidelines, it is recommended that gastroesophageal reflux should be systematically treated for prevention of peptic complications and anastomotic stricture up to the first year of life or longer, depending on persistence of gastroesophageal reflux disease [8]; **[see supplement]**. Stenström et al investigated the incidence of stricture formation, comparing outcomes of 3- and 12-month antacid prophylactic regimens [34]. They demonstrated in their study including 63 patients with esophageal atresia that the development of anastomotic stricture in the first year after esophageal reconstruction was not reduced by prolonged antacid prophylaxis (12 versus 3 months), but initial balloon dilation procedures were performed later in infants who were treated longer [34]. In contrast, another study by Donoso et al aimed to assess the efficacy of postoperative antacid prophylaxis in reducing the incidence of anastomotic strictures in 128 patients with esophageal atresia [33]. They concluded that prophylactic antacid treatment does not appear to reduce the rate of anastomotic strictures at all [33].

Participants of the conference discussed these details intensively and did not reach consensus on the item “duration of administration of antacid medication” as they felt a lack of evidence from the current literature [8].

There was also controversial discussion on the item “topical application of mitomycin C as an option in patients with recurrent strictures”. Mitomycin C is an antineoplastic and antifibroblastic agent which has been described to exert inconsistent results at different drug concentrations, when used as a topical agent applied to the anastomotic stricture after dilatation [42]. According to the ESPGHAN-NASPGHAN guidelines, mitomycin C has been recommended as potential adjuvant treatment for the management of recurrent strictures in esophageal atresia patients among other options [8] **[see supplement]**. Recently, treatment with mitomycin C has been reported to significantly reduce stricture recurrence after endoscopic dilatation

[37, 38]. In contrast, Chapuy et al postulated that there is no benefit in the resolution of the stricture when adding mitomycin C treatment compared with repeated esophageal dilations alone [35]. Madadi et al also failed to exhibit a beneficial effect of mitomycin C [36]. Given the fact that there is limited data to prove the beneficial effect of mitomycin C treatment, it should be carefully considered whether the advantages of this therapy outweigh the necessity of life-long endoscopic follow-ups. Therefore, participants of the conference agreed that further randomized controlled studies are mandatory and did not reach consensus on this item.

During the conference, participants agreed on the routine use of pH-studies for monitoring patients with esophageal atresia according to a specific schedule and at time of discontinuation of antacid therapy. However, due to a lack of evidence in the current literature and controversial opinions among the participants, no consensus could be achieved on the frequency of pH studies until transition.

For the same reasons, no consensus could be reached on the routine use of contrast study of the upper gastrointestinal tract for monitoring patients with esophageal atresia according a specific schedule. As in the previous presented item, participants of the conference hold very divergent opinions and approaches on these aspects indicating certain heterogeneity of applied protocols in ERNICA centers.

In the vast majority of votes (82.4%), results of this ERNICA consensus conference were consistent with the ESPGHAN-NASPGHAN guidelines [8] except in three (17.6%) votes: The items “administration of antacid medication for 12 months” and “topical application of mitomycin C” have already been discussed above.

The third item with divergent results is on the “administration of intralesional / systemic steroids as a therapeutic option in patients with recurrent strictures”. The use of intralesional steroids has been reported with inconsistent improvement of anastomotic

strictures [38, 39, 40]. Potential complications such as perforation, infection, pleural effusion, or adrenal suppression are well known [8]. No side effects have been reported for both local and systemic short-term steroid treatment [8]. Based on a recently published case series by Ten Kate et al [52], a multicenter, single-blind randomized controlled trial (*STEPS-EA trial;* approval number MEC-2018-1586/NL65364.078.18) involving ERNICA centers is currently being conducted on the use of intralesional steroid injections to prevent refractory strictures in patients with esophageal atresia. After extensive discussion, participants of the conference did not reach consensus on this item.

The domain *Framework* focuses on centralization, multidisciplinary treatment and participation of patient organizations in the management of patients with esophageal atresia. Particular attention should be paid to the fact that complete consensus (defined as 100% consensus) was achieved on all items in this domain. The uniformity of opinions regarding these aspects is also reflected by the lack of abstention from voting on these items.

Over the last two decades, important contributions were made at national, European, and international levels to foster collaboration in rare diseases research [4]. The European legislation calls for multidisciplinary centers treating children with rare diseases and proposes clear and demanding quality criteria [18]. Centralization in surgical patient care is a topic that is increasingly becoming important due to the growing number of reports that the level of care has improved and the number of complications, including mortality, have decreased with an elevation in the number of treated patients per surgeon and center [5, 13, 18, 19]. Pediatric surgery is a specialty of rare cases and low numbers [13]. It is therefore all the more important to pool

expertise and corresponding infrastructure in a specialized center. Thus, participants of this conference strongly believe that the implementation of a minimum average caseload of new patients with esophageal atresia per year per center is mandatory to define the requirements of a “specialized” center.

Until today, the optimal way to concentrate pediatric surgical experience in each European country remains unclear and depends on multiple national features, such as size and distribution of the population, geographical distances, local surgical expertise, organization of the health care system, and political agendas [16, 17, 18, 22]: The architype for centralization in the United Kingdom, for example, is the management of biliary atresia being exclusively managed in three centers [15]. All the Nordic countries (Finland, Norway, Sweden, and Denmark) have a relatively small population making it necessary to concentrate advanced pediatric surgical care to one or a few specialized centers to ensure adequate caseload and high-quality care [16, 19]. In France, the results strongly suggest that centralization, specialization, and connections between specialized and routine pediatric surgical departments can greatly improve management of and outcomes in children [18].
It could be demonstrated that efforts towards further centralization of pediatric surgery have already resulted in reduced morbidity and mortality [15, 18, 22]. These endeavors should be urgently pursued implementing the mission of ERNICA.

As defined in the European Commission Delegated Decision [29], European Reference Networks have to demonstrate that they are patient-centered and empower patients [4]. Patients and patient organizations play a critical role in rare disease European Reference Networks due to their expertise [4, 28, 30, 31]. Patients or their representatives become increasingly involved in addressing ethical issues,

transparency in quality of care, safety standards, and contributing to research [4, 27, 32]. The involvement of representatives of patient support groups in this consensus conference allowed a unique perspective to all discussed aspects of patient care and management and emphasizes the benefits of collaboration as already proved in the past [27, 53].

CONCLUSION

Participants of this ERNICA conference reached significant consensus on the follow-up of patients with esophageal atresia and tracheoesophageal fistula who undergo primary anastomosis. Fundamental statements regarding centralization, multidisciplinary approach and involvement of patient organizations were formulated. These consensus statements will provide the cornerstone for uniform treatment protocols and resultant optimized patient care.

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Table 1 Consensus statements on the follow-up of patients with esophageal atresia and tracheoesophageal fistula

Nº	Statement	ESPGHAN-NASPGHAN Statement available [8]	Consensus	%	Votes	Median [range]
1	There should be a structured schedule for life-long follow-up	**-**	**+**	100	18/18	9 [8-9]
2	There should be an interdisciplinary follow-up program including surgery, gastroenterology, pulmonary, nutrition counselling, otolaryngology and others, with one specialist leading	**+**	**+**	100	18/18	9 [8-9]
3	Antacid medication should be routinely administered to all patients after correction of EA	**+**	**+**	88.9	16/18	9 [2-9]
4	Proton pump inhibitors should be used for antacid prophylaxis in EA patients	**+**	**+**	100	16/16	8 [6-9]
5	Antacid medication should be routinely administered for 12 months after correction of EA, although it is noted that the evidence base is limited	**+**	**-**	66.7	12/18	7 [1-9]
6	Antacid therapy should be tapered at the end of prophylaxis	**-**	**+**	94.4	17/18	9 [4-9]
7	Anastomotic stricture should be diagnosed by either contrast study and/or endoscopy	**+**	**+**	94.4	17/18	8.5 [3-9]
8	Anastomotic stricture should be managed by balloon or semi-rigid dilatation	**+**	**+**	100	15/15	9 [6-9]
9	The definition of recurrent anastomotic stricture is 3 anastomotic stricture relapses requiring dilatation	**+**	**+**	94.4	17/18	9 [4-9]
10	The maximum number of esophageal dilatations for recurrent anastomotic strictures until a fundoplication should be considered is 5	**-**	**+**	83.3	15/18	8 [1-9]
11	Topical application of mitomycin C should be recommended as an option in patients with recurrent strictures	**+**	**-**	26.7	4/15	3 [1-9]
12	Intralesional/systemic steroids should be recommended as an option in patients with recurrent strictures	**+**	**-**	46.2	6/13	5 [3-9]
13	Customized stents /indwelling balloons should be recommended as an option in patients with recurrent strictures	**+**	**+**	100	14/14	8 [6-9]
14	24-hour-pH- or pH-impedance monitoring should be routinely used for monitoring children and adolescents with EA according a specific schedule	**+**	**+**	93.8	15/16	9 [5-9]
15	24-hour-pH- or pH-impedance monitoring should be routinely performed at time of discontinuation of antacid therapy	**+**	**+**	83.3	15/18	8.5 [2-9]
16	At least two additional pH studies should be routinely performed until transition	**-**	**-**	55.6	10/18	6 [1-9]
17	Endoscopies of the upper gastrointestinal tract should be routinely used for monitoring children and adolescents with EA according a specific schedule	**+**	**+**	94.4	17/18	9 [2-9]
18	Endoscopies of the upper gastrointestinal tract should be routinely performed at 1 year	**+**	**+**	83.3	15/18	9 [2-9]
19	At least two additional endoscopies of the upper gastrointestinal tract should be routinely performed until transition	**+**	**+**	100	18/18	9 [6-9]
20	Lung function tests should be routinely used for monitoring children and adolescents with EA according a specific schedule	**-**	**+**	77.8	14/18	8 [1-9]
21	Contrast study of the upper gastrointestinal tract should be routinely used for monitoring children and adolescents with EA according a specific schedule	**-**	**-**	27.8	5/18	3.5 [1-9]
22	Bronchoscopy should be routinely used for monitoring children and adolescents with EA according a specific schedule	**-**	**-**	11.8	2/17	2 [1-7]
23	The following are potential indications for fundoplication: (i) recurrent anastomotic strictures, (ii) poorly controlled GERD despite maximal PPI therapy, (iii) long-term dependency on trans-pyloric feeding, (iv) cyanotic spells	**+**	**+**	94.4	17/18	8.5 [1-9]

24	Adult EA patients need surveillance as per ESPGHAN guidelines: (i) 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, (ii) additional endoscopy if new or worsening symptoms develop, (iii) in presence of Barrett as per consensus recommendations	**+**	**+**	100	18/18	9 [6-9]
25	Quality of life assessment using a validated instrument should be offered during follow-up in children	**-**	**+**	94.4	17/18	9 [1-9]

Table 2

Consensus Statements on framework conditions in the management of patients with esophageal atresia with tracheoesophageal fistula

Nº	Statement	Consensus	%	Votes	Median [range]
1	When EA is suspected, referral to antenatal multidisciplinary counselling in a specialized center should be made	**+**	100	18/18	9 [8-9]
2	There should be a minimum average caseload of 5 new EA per year to meet the requirement of a specialized center	**+**	100	18/18	9 [6-9]
3	EA patients should be operated on and treated in specialized centers with a multidisciplinary team with follow-up including transition	**+**	100	18/18	9 [6-9]
4	Parents of EA patients should be recommended to be involved in parent and patient support groups as early as possible	**+**	100	18/18	9 [6-9]

Table 3

Summary of the voting results of the first ERNICA consensus conference on the management of patients with esophageal atresia and tracheoesophageal fistula; Part I was published elsewhere [51]

Part of the Consensus Conference	Domain	Complete Consensus, 100% Consensus	General Consensus, ≥ 75% Consensus*	No Consensus, < 75% Consensus	Controversial Discussion, [range 1-9]	Total Number of Items per Domain	Total Number of Items per Part
I	Diagnostics	3 (50%)	3 (50%)	3 (50%)	3 (50%)	6	52
	Preoperative Management	3 (37.5%)	4 (50%)	4 (50%)	1 (12.5%)	8	
	Operative Management	9 (32.1%)	23 (82.1%)	5 (17.9%)	7 (25%)	28	
	Postoperative Management	5 (50%)	7 (70%)	3 (30%)	2 (20%)	10	
II	Follow-up	7 (28%)	19 (76%)	6 (24%)	8 (32%)	25	29
	Framework	4 (100%)	4 (100%)	0 (0%)	0 (0%)	4	
							81

***** including items with complete consensus

SUPPLEMENT – Reference to the ESPGHAN-NASPGHAN guidelines

Follow-up of patients with esophageal atresia and tracheoesophageal fistula

ERNICA Consensus Statement Nº	ESPGHAN-NASPGHAN Statement	ESPGHAN-NASPGHAN Statement Nº
2	Patients with esophageal atresia should be evaluated regularly by a multidisciplinary team including pulmonology and otolaryngology, even in the absence of symptoms.	**11a**
3	It is recommended that gastroesophageal reflux be treated with acid suppression in all esophageal atresia patients in the neonatal period.	**1**
4	Proton pump inhibitors should be the first-line therapy for gastroesophageal reflux/gastroesophageal reflux disease.	**2**
5	It is recommended that gastroesophageal reflux should be systematically treated for prevention of peptic complications and anastomotic stricture up to the first year of life or longer, depending on persistence of gastroesophageal reflux disease.	**3**
7	Diagnosis of anastomotic stricture can be done by either contrast study and/or endoscopically.	**25**
8	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.	**26b**
9	No evidence exists on the definition of recurrent anastomotic stricture in esophageal atresia patients. Based on expert opinion we believe 3 or more clinically relevant stricture relapses constitutes recurrent stricture.	**27**

11	Potential adjuvant treatments for the management of recurrent strictures in esophageal atresia patients may include intralesional and/or systemic steroids, topical application of **mitomycin C**, stents and an endoscopic knife.	**28**
12	Potential adjuvant treatments for the management of recurrent strictures in esophageal atresia patients may include intralesional and/or **systemic steroids**, topical application of mitomycin C, stents and an endoscopic knife.	**28**
13	Potential adjuvant treatments for the management of recurrent strictures in esophageal atresia patients may include intralesional and/or systemic steroids, topical application of mitomycin C, **stents** and an endoscopic knife.	**28**
14	a: pH monitoring is useful in evaluating the severity and symptom association of acid reflux in patients with esophageal atresia. b: pH-impedance monitoring is useful to evaluate and correlate non-acid reflux with symptoms in selected patients (symptomatic on proton pump inhibitors, on continuous feeding, with extra-digestive symptoms, acute life-threatening episodes, gastroesophageal reflux symptoms with normal pH-probe and endoscopy).	**4**
15	All esophageal atresia patients (including asymptomatic patients) should undergo monitoring of gastroesophageal reflux (impedance/pH-metry and/or endoscopy) at time of discontinuation of anti-acid treatment and during long-term follow-up.	**6**
17	Endoscopy with biopsies is mandatory for routine monitoring of gastroesophageal reflux disease in patients with esophageal atresia.	**5**
18	Routine endoscopy in asymptomatic esophageal atresia patients is recommended. The expert panel recommends 3 endoscopies throughout childhood (**1 after stopping proton pump inhibitor therapy**, 1 before the age of 10 years, and 1 at transition to adulthood).	**7**

19	Routine endoscopy in asymptomatic esophageal atresia patients is recommended. The expert panel recommends 3 endoscopies throughout childhood (1 after stopping proton pump inhibitor therapy, **1 before the age of 10 years, and 1 at transition to adulthood**).	**7**
23	Severe esophageal dysmotility predisposes esophageal atresia patients to post-fundoplication complications. However, esophageal atresia patients may benefit from fundoplication in: a: Recurrent anastomotic strictures, especially in long-gap esophageal atresia. b: Poorly controlled gastroesophageal reflux disease despite maximal proton pump inhibitor therapy. c: Long-term dependency on trans-pyloric feeding. d: Cyanotic spells.	**8**
24	We recommend regular clinical follow-up in every adult patient with esophageal atresia, with special reference to presence of dysphagia, gastroesophageal reflux, 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 as per consensus recommendations.	**35**