

Supplemental file 1: ESPGHAN-NASPGHAN guideline recommendations regarding GERD management in EA patients

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Guideline recommendations based on the GRADE scoring system (2):

The GRADE scoring system is used for the classification of level of evidence, with:

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 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 uncertain.

Recommendations regarding acid suppressive therapy

- It is recommended that GER be treated with acid suppression in all EA patients in the neonatal period.
 - Expert opinion.
 - Low level of evidence.
- PPIs should be the first-line therapy for GER/GERD.
 - Expert opinion
 - Low level of evidence
- 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
- Acid suppression should be used with caution in patients with extra-esophageal manifestations of reflux.
 - Expert opinion

- Low level of evidence

Recommendations regarding GERD evaluation

- pH monitoring is useful in evaluating the severity and symptom association of acid reflux in patients with EA.
 - Expert opinion
 - High level of evidence
- 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
- All EA patients (including asymptomatic patients) should undergo monitoring of GER (impedance/pH-metry and/or endoscopy) at time of discontinuation of anti-acid treatment and during long-term follow-up.
 - Expert opinion
 - High level of evidence
- 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 level of evidence
- Endoscopy with biopsies is mandatory for routine monitoring of GERD in patients with EA.
 - Expert opinion
 - High level of evidence
- 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

Fundoplication recommendations

- Severe esophageal dysmotility predisposes EA patients to post-fundoplication complications. However, EA patients may benefit from fundoplication in: Recurrent anastomotic strictures, especially in long-gap EA; poorly controlled GERD despite maximal PPI therapy; long-term dependency on trans-pyloric feeding; cyanotic spells.
 - Expert opinion
 - High level of evidence

- Barium-contrast study, endoscopy with biopsies and pH-metry should at least be performed before fundoplication.
 - Expert opinion
 - High level of evidence

- The etiology of life-threatening events is multifactorial and merits a multidisciplinary diagnostic evaluation before surgical intervention.
 - Expert opinion
 - Very low level of evidence

- 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 with impedance.
 - Expert opinion
 - Very low level of evidence

- 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 level of evidence

Other recommendations on GERD management

- Patients with EA should be evaluated regularly by a multidisciplinary team including pulmonology and otolaryngology, even in the absence of symptoms.
 - Expert opinion
 - Low level of evidence

- Symptoms of aspiration during swallowing may be identical to GER symptoms in young children.
 - Expert opinion
 - Low level of evidence

- 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 level of evidence

Reference:

1. Krishnan U, Mousa H, Dall'Oglio L, Homaira N, Rosen R, Faure C, et al. ESPGHAN-NASPGHAN Guidelines for the Evaluation and Treatment of Gastrointestinal and Nutritional Complications in Children With Esophageal Atresia-Tracheoesophageal Fistula. *J Pediatr Gastroenterol Nutr.* 2016;63(5):550-70.
2. Guyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ.* 2008;336(7650):924-6.

Supplemental file 2: questionnaire regarding GERD management in EA patients

1. What type of institution do you work at?
 - a. Secondary hospital
 - b. Tertiary hospital
 - c. Academic hospital
 - d. Other

2. In which country do you practice?

3. What is your speciality?
 - a. Pediatric surgeon with special interest in Esophageal Atresia (EA)
 - b. Pediatric gastroenterologist with special interest in Esophageal Atresia (EA)
 - c. Pediatric surgeon
 - d. Pediatric gastroenterologist
 - e. Other

4. Are you a member of the ESPGHAN EA Working Group?
 - a. Yes
 - b. No

5. Are you a member of the International Network on Esophageal Atresia (INoEA)?
 - a. Yes
 - b. No

6. Are you aware of the ESPGHAN / NASPGHAN guideline for the management and follow up of gastrointestinal and nutritional complications in children with EA?
 - a. Yes

b. No

7. Do you have a local / national guideline for the management and follow up of EA?

a. Yes

b. No

8. On average, how many patients undergo surgical repair EA in your hospital each year?

9. On average, how many EA patients (new and follow up) do you see each year?

10. Is a multidisciplinary team involved in the care for EA patients in your hospital?

a. Yes

b. No

11. If "Yes" to the previous question, which specialties are part of the multidisciplinary team?

(multiple answers possible)

a. Pediatric surgeon

b. Pediatric gastroenterologist

c. Pediatric Pulmonologist

d. Pediatric ENT specialist

e. Clinical geneticist

f. Dietician

g. Speech therapist

h. Physiotherapist

i. Psychologist

j. Social worker

k. Clinic nurse coordinator

1. Other

12. Is there a standard follow-up schedule for EA patients in your hospital?

a. Yes

b. No

13. Who primarily manages the long term follow up of children born with EA after surgery?

a. Pediatric surgeon

b. Pediatric gastroenterologist

c. The multidisciplinary EA Team

d. Other

14. How do you manage gastroesophageal reflux disease (GERD) after EA repair, do you routinely prescribe acid suppressive therapy to all EA patients for the prevention of peptic complications and / or anastomotic strictures?

a. Yes

b. No

15. If "Yes" to the previous question, for how long?

16. How do you diagnose GERD in EA patients? (Multiple answers possible)

a. Based on clinical symptoms

b. PPI trial

c. 24 hour pH-measurement

d. 24 hour pH-impedance measurement

e. Gastroduodenoscopy with biopsies

f. Gastroduodenoscopy without biopsies

g. Other

17. Do you have facilities to perform esophageal high resolution manometry /or esophageal high resolution impedance manometry in your hospital?

a. Yes

b. No

18. What type of manometry system does your hospital have?

a. Manoscan

b. MMS

c. Both

d. I don't know

19. If you have a MMS manometry system, which of these manometry/impedance manometry catheters do you use?

a. 36 Pressure sensors, 12 Impedance sensors: K103659-E-1236-DK62559-E-10107-D

b. 20 channels water perfused

c. 25 Pressure sensors, 12 Impedance sensors: K102559-E-1245-DK82559-E-1738-DK62559-E-1022-D

d. I don't know

20. Are you familiar with the swallow gateway web based platform for analysis of HRIM tracing using pressure flow metrics?

a. Yes

b. No

21. Which EA patients would you consider referring to the pediatric surgeon for fundoplication?

(Multiple answers possible)

- a. All Long Gap EA patients
- b. EA patients with recurrent strictures
- c. EA patients with poorly controlled GERD with *persistent symptoms* on maximal PPI therapy
- d. EA patients with poorly controlled GERD with *reflux esophagitis* on maximal PPI therapy
- e. EA patients with cyanotic spells/acute life threatening episodes (ALTE)/brief unexplained respiratory episodes (BRUE)
- f. EA patients dependent on trans-pyloric feeds
- g. EA patients dependent on long term PPI therapy
- h. EA patients with feeding difficulties and failure to thrive
- i. EA patients with chronic cough

22. What investigations do you normally do before a fundoplication is performed in a EA patient?

(Multiple answers possible)

- a. Barium contrast study
- b. Endoscopy with biopsies
- c. pH measurement
- d. pH-impedance measurement
- e. Esophageal manometry
- f. No investigation needs to be done in symptomatic EA patient with GERD
- g. I leave the decision to test pre-operatively to the surgeon
- h. Other (please specify)

23. Who looks after EA patient post fundoplication in your hospital?

- a. Pediatric surgeon
- b. Pediatric gastroenterologist
- c. Both

d. The multidisciplinary EA Team

24. How many funduplications have been done in EA patients in your hospital in the last year?

25. How many funduplications have been performed on normal children with GERD without EA in your centre in the last year?

26. Are you interested in being part of an international prospective multicentre study evaluating fundoplication outcomes in children with EA?

27. If "Yes" to the previous question, will you be able to do:

- a. Only validated symptom and quality of life questionnaire at baseline and on follow up.
- b. High resolution esophageal manometry/High resolution impedance manometry of esophagus and a validated symptom and quality of life questionnaire at baseline and on follow up.

Supplemental file 3: countries represented by respondents

Country	Number of respondents	Percent
Australia	6	15,0
Portugal	4	10,0
Chile	1	2,5
Finland	1	2,5
France	3	7,5
Canada	4	10,0
England	1	2,5
Sweden	2	5,0
Israel	3	7,5
Belarus	1	2,5
Italy	1	2,5
India	1	2,5
China	1	2,5
New Zealand	1	2,5
Turkey	2	5,0
Sri Lanka	1	2,5
United States of America	2	5,0
Belgium	1	2,5
Lithuania	1	2,5
The Netherlands	1	2,5
Unknown*	2	5,0
Total	40	100,0

* A total of 40 clinicians from 23 different hospitals (n=13 did not mention where they work; 4 hospitals had 2 respondents) in at least 19 different countries (n=2 respondents did not mention the country they work in).

Supplemental file 4: subgroup analyses regarding differences in GERD management

Management of GERD did not significantly differ between gastroenterologists and surgeons, nor between general gastroenterologists or surgeons with and those without a declared special interest in managing EA patients.

		gastroenterologists (n=17)	surgeons (n=20)	P value*
Difference in the use of diagnostic tools for the diagnosis of GERD (p)	EGD or pH(-MII) only	4	9	ns (0.131)
	EGD or pH(-MII) only AND contrast esophagram	0	2	
	EGD AND pH(-MII)	13	10	
Difference in indications considered for fundoplication (p)	None of the recommended indications	0	1	ns (0.445)
	1 of the recommended indications	1	0	
	2 of the recommended indications	1	0	
	3 of the recommended indications	3	7	
	4 of the recommended indications	6	9	
	all 5 recommended indications	6	3	
Difference in preoperative workup prior to fundoplication (p)	1/3 recommended tests performed	1	2	ns (0.448)
	2/3 recommended tests performed	5	7	
	All 3 recommended tests performed	11	11	

GERD = gastroesophageal reflux disease.

*Chi square test for trend was used to compare outcomes per specific treatment strategy; A p value of <0.05 was considered statistically significant.

		General clinicians (n=17)	Expert clinicians (n=20)	P value*
Difference in the use of diagnostic tools for the diagnosis of GERD (p)	EGD or pH(-MII) only	8	5	ns (p=0.115)
	EGD or pH(-MII) only AND contrast esophagram	1	0	
	EGD AND pH(-MII)	8	15	
Difference in indications considered for fundoplication (p)	0 of the recommended indications	1	0	ns (p=0.861)
	1 of the recommended indications	0	1	
	2 of the recommended indications	1	0	
	3 of the recommended indications	4	6	
	4 of the recommended indications	5	10	
	all 5 recommended indications	6	3	
Difference in preoperative workup prior to fundoplication (p)	1/3 recommended tests performed	1	2	ns (p=0.992)
	2/3 recommended tests performed	6	6	
	All 3 recommended tests performed	10	12	

GERD = gastroesophageal reflux disease.

*Chi square test for trend was used to compare outcomes per specific treatment strategy; A p value of <0.05 was considered statistically significant.