


ESPGHAN

 European Society for Paediatric
 Gastroenterology, Hepatology and Nutrition

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 www.espghan.org

Working Group - Report for Gastroenterology Committee Strategy Day

Working Group Title: Esophageal atresia

 (date of completion **7 August.2019**; **Gottrand**)

Working Group Members and Mandates

Name	Date of entry	1 st Term	2 nd Term	Positions held within WG (e.g. Secretary treasurer etc.)	Dates held of these positions
Gottrand frederic	2013	2018		chair	2018
Krishnan Usha	2013	2018		Secretary	2018
Dall'Oglio Luigi	2013	2018		Co-chair	2018
BORRELLI OSVALDO CABRA WILLIAM CONTINI ANNA ESCARCIA HADAASHA HOMAN MELEK NAMEDAR NOUVILI ORTIZ PALMER PANAYOTOU PARDO SALEH SILBERMINTZ SOSA SPOLIDORO TAMBUCCI Renato TRAN LEA VAN WIJK MICHIEL VILA MIRAENET ZANGEN ZERZERI BRINI A.PAPADOPOULOU	2018				
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VAN BIERVLIET Stéphanie					
VAN LENNEP Marinde					
VEEREMAN Gigi VILA MIRANET Victor					
VILA Victor Yvan Vandenplas ZAARI JABIRI Youssef					
ZANGEN Tsili ZERZERI BRINI Inès					

Summary of Activities in 2019

A. WG meetings (date and any main points/activities)

(one table per meeting – please just copy and paste the tables as often as needed)

Meeting	WG annual meeting
Location	Glasgow
Date	05 June
Main Points / Activities	<p>1 News from « EA World » INoEA : Rome meeting, ESPGHAN monothematic conference on the esophagus, ERNICA, terms of reference (Frederic Gottrand)</p> <p>The 5th INoEA international conference on EA will be organized in Rome from 24 to 28th June in Rome</p> <p>An ESPGHAN monothematic conference on the esophagus is organized in Lille 3 and 4th of October. Registration opened until July 21th, fees 100 euros including one hotel nights and gatherings. http://www.espghan.org/index.php?id=569&eventId=164</p> <p>Terms of reference have been modified following suggestion of the GIC, confirming we are a working group, and introducing simplification, and the need of writing an annual report and a annual plan. All these changes were discussed and approved (voting) by the members. The final version was sent to GIC at the end of the meeting.</p> <p>2 Update on the network on EoE in EA (Frederic Gottrand and Usha Krishnan)</p> <p>The Eosinophilc esophagitis in Esophageal atresia patients in a ESPGHAN network from 2017, aiming to create a database (retrospective and prospective) of the cases of EA patients presenting with EoE. @CRF has been created by Usha university BUT due to the General Data Protection Regulation (GDPR) adopted by the EU in 2016 and enforced in May 2018 it is impossible to send data (even anonymized) from EU patients to Australia. Agreement is pending between Sydney and Lille to have the datbase hosted in France. Ethical clearance obtained in France. Following step is to sign agreement between Lille and every investigator (if you have cases of EoE associated with EA you can write an email to Frederic Frederic.gottrand@chru-lille.fr or Usha please complete usha for being added to the list. Each center will have to submit the study to its competent authorities (ethics), data protection office, and approval must be obtained before starting the study. Hope to be able to start before the end of 2019</p> <p>2 Comparison of balloon and bougies (Renato Tambucci, Rome)</p> <p>Anastomotic stricture (AS) is the most common complication following operative EA repair. The cornerstone of treatment is dilation whose primary aim is to achieve symptom relief, permit maintenance of oral nutrition, and reduce the risk of pulmonary aspiration. This is obtained through application of expansible forces against a luminal stenosis. Two</p>



categories of dilators are used in GI endoscopy: fixed-diameter push-type dilators (bougie dilators) and radial expanding balloon dilators.

Bougie dilators exert radial forces and also cause a shearing effect that exerts longitudinal forces as they are advanced through a stenosis. Balloon dilators only exert radial forces when expanded within a stenosis which is delivered simultaneously over the entire length of the stenosed segment rather than progressively from its proximal to its distal extent. Overall, no clear advantage of either balloon or bougie dilation has been demonstrated. Since, there are no controlled trials comparing efficacy and safety of hydrostatic balloon with bougie dilator for treatment of AS in EA patients, current guidelines suggest that the choice between balloon dilation and bougie is based only on operator experience and comfort with the equipment.

The present research is a multi-center, non-randomized, observational, prospective study on dilations of AS in EA. All the procedures performed on the patients are standard of care and the study does not involve any additional hospital visits for the subjects or parents/guardians.

Primary endpoints of the study are to compare:

- the efficacy of balloon vs bougie dilations in terms of number of anastomotic dilatation sessions per patient needed to achieve AS resolution
- the safety of balloon with bougie dilations in terms of frequency of adverse events after dilation (early and late complications)

Secondary endpoints are:

- Establish a multi-center database and organize an international registry focused on AS in EA children.
- Provide a descriptive epidemiological analysis of AS in EA

Inclusion criteria

- Diagnosis of congenital EA undergoing surgical repair
- Legally acceptable representative (parents or caregivers) capable of understanding the informed consent document and providing consent on the participant's behalf

Exclusion criteria

- Referred EA patients with insufficient medical history information

Sample size: 75 patients per group (balloon and bougie).

Participants of this study will receive standard follow-up care according to the ESPGHAN and NASPGHAN EA Guidelines. Children undergoing surgical repair of congenital EA, both born-in or referred, will be enrolled in the study. Baseline demographics and disease characteristics that could serve as prognostic and predictive variables of outcome will be collected at study entry. After a patient is identified as having an AS needing dilation, he will be followed before, during, and after their dilation procedures to compare the efficacy and safety of bougie with balloon dilators and to determine how patient and procedural factors affect rates of adverse events. Dependent variables will be obtained from the pre-procedural and procedural forms and include risk factors previously identified as being present in previous reports in EA children undergoing esophageal dilation (e.g. the presence of long gap EA). Post-procedural forms and adverse event forms will be utilized to capture and report the primary outcome variables.

UPDATE 2019

Site assessment and feasibility questionnaire study has been done in the frame of the study on esophageal dilation in EA patients. 101 centers all over the world have indicated to be interested in participating in the study. Further center interested in being a part of the study should send an email to renato.tambucci@opbg.net and luigi.dalloglio@opbg.net indicating hospital and contact details.

IRB approval process of the study protocol is still ongoing, the expected date for protocol approval is September/October 2019.



eCRF for data collection have been created by using the electronic data capture system REDCap which is hosted on OPBG (Rome) infrastructure and is subject to the same security and backup regimen as other systems (e.g. the network file servers). The access to REDCap will be via a user account created by the system administrator and will be provided as soon as participant centers will complete the ethical committee approval of the project.

3 Dilatation and EA : results of a survey (Chantal Ten Kate, Rotterdam),

The aim of the survey was to give an overview of the experience with different esophageal dilatation methods in stricture management worldwide. Between November 2018 and March 2019 an online questionnaire was sent to all ESPGHAN, NASPGHAN, INoEA and EUPSA members.

Responses of 115 centers (60% European) were investigated. Endoscopies are mostly performed by a pediatric gastroenterologist. Oesophageal dilatation was mostly performed by balloon dilatation (68%, 17% bougienage, 15% both techniques). In case of balloon dilatation, in 33% a guidewire was routinely used and in 5% the dilatation was radiologically guided. The balloon was insufflated with water or natrium chloride (n=49), contrast fluid (n=46) or air (n=16). The time of insufflation was standardized in a protocol in 59 centres (60.3%), with a median duration of 60 seconds (range 5-300). There were no well-designed protocols available for the chosen diameter of the dilatator.

The majority (68%) only performed dilatation in symptomatic patients, whereas 32% managed the strictures with routine dilatations to prevent symptoms. In case of recurrent strictures, preferred adjuvant treatments were intralesional steroids in 47% and topical mitomycin C in 31%.

In conclusion, there is a large diversity in the management of anastomotic strictures and a lack of consensus. Future research would require a large prospective study to investigate the most effective method with the aspiration to reach consensus for a new guideline.

NB: We recently started started STEPS-EA trial. This will be the first randomized controlled trial with intralesional steroid injections in children with esophageal atresia, to prevent recurrent anastomotic strictures. Due to the rarity of this disease, we believe it is essential to collaborate in such projects. If you are interested to participate or would like more information, please send an email to steps.ea@erasmusmc.nl!

4 Fundoplication outcomes using HRIM of Esophagus in EA patients (Taher Omari/Usha Krishnan)

Infants and children with oesophageal atresia commonly present with swallowing dysfunction or dysphagia. Dysphagia can lead to a range of significant consequences such as aspiration pneumonia, malnutrition, dehydration and food impaction. As EA patients often have severe gastroesophageal reflux disease, they are often referred for anti-reflux surgery, fundoplication. However due the inherent esophageal dysmotility in these patients, fundoplication can often worsen their pre-existing dysphagia. It would be very useful to be able to predict which EA patient is more likely to have a significant worsening of their dysphagia post fundoplication surgery in order to be able to identify those EA patients who would benefit from fundoplication compared to those in whom it should be potentially avoided.

To characterize the complex interactions of bolus flow and motor function between mouth, pharynx and esophagus, a detailed understanding of normal and abnormal deglutition is required through the use of adequate and objective assessment techniques. As clinical symptoms do not correlate well with conventional assessment methods of motor function such as radiology or manometry but do correlate with bolus flow, the current state of the art diagnosis involves high-resolution manometry combined



with impedance measurements to characterize the interplay between esophageal motor function and bolus clearance. Using a novel pressure flow analysis (PFA) method as an integrated analysis method of manometric and impedance measurements, it is possible to calculate a “Dysphagia Risk Index”. The “Automated Impedance Manometry” parameters are currently available free through an online platform called, “Swallow Gateway”. It is possible for any centre from around the world to download there high resolution impedance manometry study done on an EA patient into this online portal and derive important data including the “Dysphagia Risk Index” to order to make rational therapeutic decisions regarding outcomes of fundoplication in EA patients. This “Swallow Gateway” platform was awarded the ESPGHAN Networking grant in 2018. Several members of the ESPGHAN EA WG already use this platform including Dr Usha Krishnan, Dr Michiel VanWjik, Dr Nathalie Rommel.

5 Potential projects for 2020 (Michaela Dellenbaum, Usha Krishnan)

5.1

- Prospective multicentre study involving centres which have a standardised follow up program for EA adolescents at transition of care
- Generic and disease specific EA QOL questionnaires
- Correlate with objective data on GI and Respiratory status
- GI
- GERD: pH/Impedance testing, Gastroscopy
- Esophageal function: HRIM where available (?use Swallow Gateway)
- Growth and Nutrition: Weight and Height z scores/?nutritional markers in blood tests
- Respiratory
- Lung Function Testing, FeNO, Lung Clearance Index (MBW), +/-CT Chest, Exercise Tolerance
- Assess readiness for transition by looking at clinical status, psychosocial functioning and condition specific QOL in 11-18 year olds

5.2

- Longitudinal prospective study on LGEA patients
- 2-18yrs
- EA Qol Questionnaires
- Evaluate relationship between
- Different methods of treating LGEA and QOL
- Relationship between clinical status (as measured by pH/Impedance, gastroscopy, +/- HRIM where available) and disease specific and generic QOL in LGEA patients
- Evaluate at 5yrs, 10yrs and 15yrs prior to transition

B. Educational activities

(i) Educational Events

(one table per event – please just copy and paste the tables as often as needed)

Full Event Name	ESPGHAN monothematic conference on the esophagus
Location	Lille
Date	3, 4 th Oct
Organizer	F Gottrand
Email Organizer	
EPP	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



UEG Training Support	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
more information if available	

Full Event Name	5th INoEA international conference on EA
Location	Rome
Date	24 to 28th June
Organizer	L Dall'Oglio
Email Organizer	
EPP	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
UEG Training Support	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
more information if available	>250 attendees 110 abstracts Hands on activities and simulators www.esophagealatresia-roma2019.it

(ii) E-Learning

(one table per project – please just copy and paste the tables as often as needed)

Full Project Name	
Project Timeline	
Project Leader	
more information if available (applied for UEG support? Etc)	

C. WG Publications / Guidelines / Position Papers

(i) Completed

(one table per publication – please just copy and paste the tables as often as needed)

Publication ID <i>(to be filled in by Office)</i>	
Full Publication Title	Can Patients With Neonatal Digestive Diseases Be Protected From Unnecessary Radiation?
Authors	Gottrand F, Avni F.
Publication Type	<input type="checkbox"/> Guideline <input type="checkbox"/> Position Paper <input type="checkbox"/> Update of existing paper <input checked="" type="checkbox"/> Other
Journal, Year, Volume, Page Numbers	J Pediatr Gastroenterol Nutr. 2018 Feb;66(2):187.
More information if available	Editorial to warn about the risk of unnecessary radiation exposure in children with EA and other neonatal digestive malformations

Publication ID <i>(to be filled in by Office)</i>	
Full Publication Title	Oesophageal atresia
Authors	van Lennep M, Singendonk MMJ, Dall'Oglio L, Gottrand F, Krishnan U,



	Terheggen-Lagro SWJ, Omari TI, Benninga MA, van Wijk MP.			
Publication Type	<input type="checkbox"/> Guideline	<input type="checkbox"/> Position Paper	<input type="checkbox"/> Update of existing paper	<input checked="" type="checkbox"/> Other
Journal, Year, Volume, Page Numbers	Nat Rev Dis Primers. 2019 Apr 18;5(1):26.			
More information if available	Review on the topic written my members of EA WG			

(ii) in progress

(one table per publication – please just copy and paste the tables as often as needed)

Publication ID <i>(to be filled in by Office)</i>				
Full Publication Title				
Publication Timeline and Status of Paper				
Publication Leader				
Publication Type	<input type="checkbox"/> Guideline	<input type="checkbox"/> Position Paper	<input type="checkbox"/> Update of existing paper	<input type="checkbox"/> Other
More information if available				

(iii) future topics considered in 2019

(one table per publication – please just copy and paste the tables as often as needed)

Full Publication Title	EA: Transition to adulthood			
Publication Timeline and Status of Application for Paper	WG just started to work			
Publication Leader	U Krishnan			
Publication Type	<input type="checkbox"/> Guideline	<input checked="" type="checkbox"/> Position Paper	<input type="checkbox"/> Update of existing paper	<input type="checkbox"/> Other
More information if available	Non only EA WG member but also INoEA members (Australia, Canada, USA...)			

D. Financial Report / YTD Budget for 2019: Will be added by EPGHAN Office

All in Euros	Allocated	Used so far
Expenses	Will be added by EPGHAN Office	Will be added by EPGHAN Office
Activity 1		
Activity 2		
Activity 3		
Activity 4		
Activity 5		
Activity 6		
Activity 7		
Activity 8		
TOTAL Expenses 2019		
Income	Please also add funding from other sources if applicable	
Activity 1		



Activity 2		
Activity 3		
Activity 4		
Activity 5		
TOTAL Income 2019		

Additional comments on financial report:

Outlook on Planned Activity for 2020

A. Working Group meetings (date and any main points/activities)

(one table per meeting – please just copy and paste the tables as often as needed)

Meeting	Annual meeting of EA WG
Location	Copenhagen
Date	
Main Points / Activities	Progress of the networking project on EoE in EA (retrospective and prospective database) Progress of the project dilatation in anastomotic stenosis comparison bougie/savary New projects Progress on position paper on transition in EA

B. Proposed Educational activities

(i) Educational Events

(one table per event – please just copy and paste the tables as often as needed)

Full Event Name	
Location	
Date	
Organizer	
Email Organizer	
Applied for EPP	<input type="checkbox"/> Yes <input type="checkbox"/> No
Applied for UEG Training Support	<input type="checkbox"/> Yes <input type="checkbox"/> No
more information if available	

(ii) Scientific Symposia planned for the Annual Meeting

(one table per project – please just copy and paste the tables as often as needed)

Full Symposia Name	Since this is the World congress not sure there will be room for WG symposium?
Project Leader	
more information if available	

C. Proposed Publications / Guidelines / Position Papers

(one table per publication – please just copy and paste the tables as often as needed)



Full Publication Title				
Publication Timeline and Status of Application of Paper				
Publication Leader				
Publication Type	<input type="checkbox"/> Guideline	<input type="checkbox"/> Position Paper	<input type="checkbox"/> Update of existing paper	<input type="checkbox"/> Other
More information if available				

D. Financial Report / Budget for 2020:

- Kindly attach or copy paste your submitted budget request for 2020
10000 euros for organizing a face to face meeting on transition in EA patients. This is an initiative of INoEA (international network on EA) in which several members of the EA WG are strongly involved. This money will support transportation and hosting members participating to this project (including in addition to pedGI, family support group representative, adult doctors, nurses...)
Additional request: 5000 € for shipping fees of samples to Dr Marc Rothenberg lab in the US (Cincinnati). This is an ancillary project of the prospective register on EoE in EA patients to collect samples for metabolomics/epigenetics in these patients to better understand the mechanisms of EoE in EA patients (the network was funded by espghan, which did not include the epigenetic analysis).

- Additional comments on financial report:

- Any other issues that may be of interest
Final Modifications of the EA-WG terms of reference have been approved by the members during Glasgow meeting

