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Published in:
Journal of pediatric gastroenterology and nutrition

DOI:
10.1097/MPG.0000000000002221

Published: 01/04/2019

Citation for pulished version (APA):
European Society for Paediatric Gastroenterology, Hepatology and Nutrition Motility Working Group, van Lennep, M., van Wijk, M. P., Omari, T. I. M., Salvatore, S., Benninga, M. A., & Singendonk, M. M. J. (2019). Clinical Management of Pediatric Achalasia: A Survey of Current Practice. *Journal of pediatric gastroenterology and nutrition*, *68*(4), 521-526. https://doi.org/10.1097/MPG.0000000000002221

Clinical Management of Pediatric Achalasia: A Survey of Current Practice

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ABSTRACT

Objectives: Pediatric achalasia is a rare neurodegenerative disorder of the esophagus that requires treatment. Different diagnostic and treatment modalities are available, but there are no data that show how children can best be diagnosed and treated. We aimed to identify current practices regarding the diagnostic and therapeutic approach toward children with achalasia.

Methods: Information on the current practice regarding the management of pediatric achalasia was collected by an online-based survey sent to members of the European and North American Societies for Pediatric Gastroenterology Hepatology and Nutrition involved in pediatric achalasia care.

Results: The survey was completed by 38 centers from 24 countries. Within these centers, 108 children were diagnosed with achalasia in the last year (median 2, range 0–15). Achalasia was primarily managed by a pediatric gastroenterologist (76%) and involved a multidisciplinary team in 84% of centers, also including a surgeon (87%), radiologist (61%), dietician (37%), speech pathologist (8%), and psychologist (5%). Medical history taking and physical examination were considered most important to establish the diagnosis (50%), followed by (a combination of) manometry (45%) or contrast swallow (21%). Treatment of first choice was Heller myotomy (58%), followed by pneumatic dilation (46%) and peroral endoscopic myotomy (29%).

Conclusion: This study shows a great heterogeneity in the management of pediatric achalasia amongst different centers worldwide. These findings stress the need for well-designed intervention trials in children with achalasia. Given the rarity of this disease, we recommend that achalasia care should be managed in centers with access to appropriate diagnostic and treatment modalities.

Key Words: contrast swallow, Heller myotomy, high-resolution manometry, management, pediatric achalasia, peroral endoscopic myotomy, pneumatic dilation

(*JPGN* 2019;68: 521–526)

What Is Known

- Achalasia is a rare neurodegenerative disorder of the esophagus that requires treatment.
- Different diagnostic and treatment modalities are available, but there are no data that show how children should best be diagnosed and/or treated.

What Is New

- This study shows a great world-wide heterogeneity in the diagnostic work-up and treatment of pediatric achalasia amongst different centers actively involved in achalasia care.
- These findings stress the need for well-designed intervention trials in children with achalasia to determine optimal management and facilitate evidence-based clinical guideline development.

Achalasia is a neurodegenerative esophageal motility disorder characterized by progressive symptoms of dysphagia, regurgitation, failure to thrive, and anorexia (1). These symptoms result from slow or absent bolus transit through the esophagus, caused by incomplete lower esophageal sphincter relaxation and failure of esophageal peristalsis.

In children, achalasia is most often diagnosed after the age of 7 years, with an estimated annual incidence of pediatric onset achalasia ranging from 0.10 to 0.18/100.000 (1,2). Achalasia is often misdiagnosed due to a symptom profile overlapping with gastroesophageal reflux disease (GERD), rumination syndrome, and eating disorders. In young children, younger than 7 years, symptoms are even more specific (1).

Received July 24, 2018; accepted October 30, 2018.

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Supplemental digital content is available for this article. Direct URL citations appear in the printed text, and links to the digital files are provided in the HTML text of this article on the journal's Web site (*www.jpgn.org*).

Although this article is produced by the ESPGHAN Motility Working Group it does not necessarily represent ESPGHAN policy and is not endorsed by ESPGHAN.

The authors report no conflicts of interest.

DOI: 10.1097/MPG.0000000000002221

In adults, high-resolution esophageal manometry (HRM) is considered the gold standard for diagnosing achalasia (3). HRM criteria for diagnosing pediatric achalasia are, however, based on normative data established in adults, whereas in children it was shown that at least some HRM metrics are age dependent (4,5). In children, the lack of normative data makes it hard to establish validated HRM criteria and consequently, to reliably diagnose achalasia (6,7). Intraluminal impedance can be measured concurrently with HRM (ie, high-resolution impedance manometry [HRIM]) without additional burden for the patient (8). Although only performed in research setting, novel pressure-impedance variables can evaluate esophageal bolus transport to the EGJ (bolus presence time) and esophageal emptying through the EGJ (bolus flow time) and may therefore improve both diagnosis and assessment of therapeutic effects (9). Achalasia therapy is aimed at improving esophageal emptying by reducing lower esophageal sphincter tone either pharmacologically, endoscopically, or surgically. Randomized controlled intervention trials are lacking in pediatric achalasia and the optimal therapy is therefore unknown. Guidelines for pediatric achalasia rely upon a combination of data obtained from studies in adults and expert opinion (10).

For adult achalasia, the American College of Gastroenterology guidelines recommend delivery of treatment together with objective postprocedural investigations in high-volume centers in a multidisciplinary team setting to help identify recurrence early and improve patient outcome (11). A recent survey enrolling specialist surgeons throughout the UK showed that adult achalasia patients were discussed in a multidisciplinary team meeting in only 15% of units and routine postintervention investigations were only performed by a third of responders (12). One third of centers surveyed did not have access to diagnostic HRM.

We hypothesized that diagnosis and therapeutic management of children with achalasia would vary widely among different centers worldwide. In the present study, we therefore aimed to identify current practices regarding the diagnostic and therapeutic approach toward children with achalasia via a Web-based questionnaire, focusing on the diagnosis, management of recurrent disease, and postprocedural objective assessment during follow-up.

METHODS

Data Collection

Data regarding management of pediatric achalasia were collected by an online-based survey (Supplemental File 1, Supplemental Digital Content, *http://links.lww.com/MPG/B521*) sent to pediatric gastroenterologist members of the motility working groups of the European and North American Societies for Pediatric Gastroenterology Hepatology and Nutrition. Participants indicating that their center had *no* clinical experience with achalasia were not eligible for participation. Given the rarity of the disease, there was otherwise no set of minimum number of patients required to participate.

The survey was created by the authors and reviewed independently by 2 consultant pediatric gastroenterologists. The survey questions addressed topics spanning diagnosis, management of (recurrent) disease, and new treatment methods. Both closed and open-ended responses were included in the survey instrument. The survey was left open for a period of 9 months (March 2017–November 2017) to maximize response rates and reminders were sent out on a monthly basis. To avoid inclusion bias, only 1 representative of each institution was allowed to participate. In case the questionnaire was accidentally filled out by multiple respondents of the same institution, only the first responder was included for analysis. This study does not involve human study subjects and was therefore not reviewed by our local institutional review board.

RESULTS

The survey was completed by 44 respondents from a total of 58 pediatric gastroenterologists approached (68% response rate). Respondents were from 38 centers (24 countries, Fig. 1); hence, 6 were excluded to avoid duplication. The majority of respondents (n = 36, 95%) were from a tertiary referral center, whereas only 2 respondents (5%) were from a secondary referral center. In the centers surveyed, 108 pediatric patients were diagnosed with achalasia over the last year (median 2, range 0–15). Achalasia was primarily managed by a pediatric gastroenterologist (76%) and

FIGURE 1. Overview of countries with participating centers depicted in red.

TABLE 1. Diagnostic investigations performed in the work-up of pediatric achalasia: overall results and results per continent

	Europe (n = 17)	Asia (n = 8)	North America (n = 6)	Australia (n = 4)	South America (n = 2)	Africa (n = 1)	Total (n = 38)
Number of investigations (median, range)	3 (1–5)	2.5 (2–4)	3 (2–5)	3 (3–5)	3	2	3 (1–5)
Contrast swallow (n, %)	14 (82%)	7 (88%)	5 (83%)	4 (100%)	2 (100%)	1 (100%)	33 (87%)
Blood draw (n, %)	6 (35%)	2 (25%)	2 (33%)	2 (50%)	0 (0%)	0 (0%)	12 (32%)
Manometry (n, %)	15 (88%)	1 (14%)	4 (80%)	4 (100%)	2 (100%)	0 (0%)	28 (74%)
Conventional (n, %)	2 (12%)	0 (0%)	0 (0%)	0 (0%)	2 (100%)		4 (11%)
HRM (n, %)	12 (71%)	2 (25%)	2 (33%)	2 (50%)	1 (50%)		19 (50%)
HRIM (n, %)	2 (12%)	0 (0%)	5 (83%)	3 (75%)	0 (0%)		10 (26%)
EGD (n, %)	14 (82%)	8 (100%)	4 (67%)	3 (75%)	2 (100%)	1 (100%)	32 (84%)
pH-MII (n, %)	5 (29%)	2 (25%)	0 (0%)	1 (25%)	0 (0%)	0 (0%)	8 (21%)
EndoFLIP (n, %)	0 (0%)	0 (0%)	2 (33%)	0 (0%)	0 (0%)	0 (0%)	2 (5%)

EGD = esophagogastroduodenoscopy; HRIM = high-resolution impedance manometry; HRM = high-resolution manometry; pH-MII = pH-impedance measurement.

a multidisciplinary team was involved in 84% of centers. The multidisciplinary teams further included surgeons (87%), radiologists (61%), dieticians (37%), speech pathologists (8%), and psychologists (5%). Only 2 centers reported the existence of an achalasia patient support organization (Italy and United States of America). Ten centers (26%), from 8 different countries, indicated that their institution made use of a standardized (locally used) protocol to diagnose and manage pediatric achalasia.

Diagnosis

Diagnostic investigations reported in the 38 centers are listed in Table 1. All centers used a standard contrast swallow and/or manometry to diagnose achalasia. Of 33 centers utilizing contrast swallows, all employed a *timed contrast swallow* protocol and 8 (24%) indicated that this was the ''most important'' diagnostic investigation they used. Of 28 centers utilizing manometry, most (89%) were using HRM or HRIM, and 17 of them (61%) indicated that manometry was the ''most important'' diagnostic test they used. The disease-specific Eckardt score was being used by 6 (16%) respondents to survey symptom severity (13). Twenty-five centers (68%) used a combination of all 3 investigations. Two North American centers used EndoFLIP to measure EGJ distensibility as part of their diagnostic evaluation.

Treatment

The nominated ''treatment of first choice'' of available therapies was usually Heller myotomy (n = 19/33, 58%) or pneumatic dilation (n = 11/24, 46%). Peroral endoscopic myotomy (POEM) was rarely indicated as a first treatment choice (n = 4/11, 29%). Two respondents indicated they prefer pharmacological therapy (drug not specified) and 1 preferred botulinum toxin injection (n = 1, 4%). Some respondents indicated that patient age (47%) and/or achalasia subtype (24%) would influence their primary choice of the available treatments. Subsequent questions regarding the way of *how* age would change management were left unanswered. Respondents indicated that achalasia type III would influence their primary choice of treatment and 6 of 11 (55%) of the respondents that answered this question would consider POEM as a first-line treatment option next to Heller myotomy. Overall characteristics of the different treatment options split out by continent are displayed in Table 2.

TABLE 2. Overall characteristics of the different treatment options, split out by continent

		Europe (n = 17)	Asia (n = 8)	North America (n = 6)	Australia (n = 4)	South America (n = 2)	Africa (n = 1)	Total (n = 38)
Heller myotomy	Availability (n, %)	15 (88%)	7 (88%)	6 (100%)	4 (100%)	1 (50%)	0 (0%)	33 (78%)
	Therapy of first choice (n, %)	6/15 (40%)	5/7 (71%)*	4/5 (67%)*	3 (75%)	1/1 (100%)*	0 (0%)	19/33 (58%)
	Fundoplication as part of the procedure (n, %)	7/14 (50%)*	3/7 (43%)*	4 (67%)	2 (50%)	1/1 (100%)*	NA	17/33 (52%)
Pneumatic dilation	Availability (n, %)	12 (71%)	4 (50%)	4 (67%)	3 (75%)	1 (50%)	0 (0%)	24 (63%)
	Therapy of first choice (n, %)	7/12 (58%)	1/4 (25%)	1/4 (25%)*	1/3 (33%)	1/1 (100%)	0 (0%)	11/24 (46%)
	Videofluoroscopic control (n, %) initial series always with 2 dilatations (n, %)	8/12 (67%)*	2/4 (50%)*	4/4 (100%)*	2/3 (67%)*	1/1 (100%)	NA	17/24 (71%)
		2/11 (18%)*	2/3 (67%)*	0/4 (0%)*	1/2 (50%)*	1/1 (100%)		6/24 (25%)
Peroral endoscopic myotomy	Availability (n, %)	7 (41%)	1 (13%)	3 (50%)	0 (0%)	0 (0%)	0 (0%)	11 (29%)
	Therapy of first choice (n, %)	3/7 (43%)	1 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	4/11 (36%)
Botulinum toxin	Availability (n, %)	12 (71%)	7 (88%)	5 (83%)	2 (50%)	1 (50%)	0 (0%)	24 (63%)
	Therapy of first choice (n, %)	1/12 (8%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1/24 (4%)
Pharmacological therapy†	Therapy of first choice (n, %)	0 (0%)	1 (13%)	0 (0%)	0 (0%)	0 (0%)	1 (100%)	2 (5%)

*Valid percentage (ie, missing data excluded from analysis).
†Pharmacological therapy of choice not further specified.

Pneumatic Dilation

Pneumatic dilation was available in 24 (63%) centers with 17 (71%) of these routinely using fluoroscopic control. Pneumatic dilations were performed by pediatric gastroenterologists (n = 18, 48%), pediatric surgeons (n = 3, 8%), adult gastroenterologists (n = 1, 3%), or intervention radiologists (n = 2, 5%; missing data, n = 14, 37%).

Initial dilation was performed with a balloon size ranging from 25 to 35 mm and repeated to up to 4 times in case of persisting symptoms with a maximum balloon size of 40 mm. Six respondents (25%) indicated to always perform an initial session of 2 dilations, regardless of clinical symptoms.

In case of symptom recurrence postdilation, the majority of respondents indicated that they would then consider Heller myotomy (n = 28, 71%), whereas 6 (16%) would perform POEM and 5 (13%) would repeat the dilation. None of the respondents considered botulinum toxin injection for the management of symptom recurrence postdilation.

Heller Myotomy

Heller myotomy was available in 33 (87%) centers, however, was reported to have been performed in only 12 (32%) centers over the last 3 years. A fundoplication would routinely be performed as part of the operation in 17 (52%) centers. The procedure was mostly performed by a pediatric surgeon (n = 26, 79%) or by a pediatric surgeon working together with an adult surgeon (n = 6, 18%). In 1 center, Heller myotomy was solely performed by an adult surgeon (n = 1, 3%). In case of symptom recurrence post-Heller myotomy, respondents indicated that they would then dilate (n = 20, 53%), repeat the myotomy surgically (5, 13%), endoscopically (8, 21%), or use botulinum toxin injection (8, 21%).

Peroral Endoscopic Myotomy

POEM was available in 11 (29%) centers in Europe (n = 7), North America (n = 3), and Asia (n = 1) and was reported to have been performed in 6 (55%) of these (16% of all centers) over the last 3 years. The procedure was most often performed by an adult gastroenterologist (n = 9, 82%). A pediatric gastroenterologist performed the procedure in 2 centers (n = 2, 18%). Centers that did not offer POEM indicated a lack of expertise with the procedure as the main reason it was not available.

Follow-up

Postprocedural follow-up varied from no follow-up to follow-up until time of transition to continuing care by an adult gastroenterologist. Most respondents (84%) indicated they conducted a follow-up as a routine. Follow-up was by Eckardt score and quality of life questionnaires (9, 24%), timed contrast swallow (26, 68%), and HRM/HRIM (15, 38%).

Surveillance of Gastroesophageal Reflux Disease

Thirty-seven percent of respondents (n = 14) prescribed antireflux therapy to *all* patients postintervention and 11% (n = 4) respondents indicated that they would do this postmyotomy only. The need for antireflux therapy was guided by symptom occurrence and/or endoscopy/pH-impedance results in 21% (n = 8) of centers, respectively. Eleven (29%) centers routinely perform endoscopy for the surveillance of postintervention GERD, whereas 2 centers (5%) indicated they would perform pH-impedance monitoring.

Within Center Discrepancy

Six participants represented duplicate responses of already included centers and were excluded to avoid inclusion bias. Retrospective analysis of these duplicate pairs revealed large within center discrepancy on all domains.

DISCUSSION

In this study, we evaluated current practices regarding the diagnostic and therapeutic approach toward children with achalasia. Although the management of pediatric achalasia usually involved a multidisciplinary team, protocols were not standardized and clinical decision making around diagnostic investigations, therapeutic approach, and management strategies varied widely amongst centers worldwide.

Esophageal manometry was available in most centers but was only considered by half to be the most important diagnostic investigation. These findings are consistent with a survey conducted by the International Pediatric Endosurgical group, where 73% requested a manometry before intervention (14). Access to and experience with HRM remains a limitation in pediatric practice despite the fact that HRM is now considered the best test for diagnosing and subtyping achalasia in adult patients. In this survey, only a third of respondents would change their first-line treatment strategy depending on achalasia subtype. It is noteworthy that only 3 respondents answered the subsequent question on *how* HRM subtype would influence their treatment. As recently proposed by our group, HRM should ideally be globally implemented in the diagnostic work-up of pediatric achalasia as it has the potential to improve therapeutic management (9). Consensus regarding standard operating procedures and diagnostic criteria for esophageal manometry in children is, however, lacking (15).

Among therapies for achalasia, dilation is considered the standard against which other therapies can be compared in adults. Although dilation is effective in the short term, children often experience recurrence of symptom requiring reintervention (1,16–18). Adult series showing dilation and Heller myotomy are equally effective, also show that younger adults (<40 years) have the shortest clinical response to dilation and only modest improvement after repeat dilation (19). In growing children suffering from achalasia, potentially facing a lifetime of repeated therapy, this is specifically relevant as we found that less than a third of the respondents considered dilation to be the optimal treatment approach. Methodology with regards to size of the balloon and number of initial dilations also varied widely amongst these centers.

Our survey confirms that Heller myotomy is generally considered the preferred first-line treatment for children with achalasia (14,21), which is also reflected by the adult literature (12). A recent systematic review assessing safety and efficacy of Heller myotomy in children found no difference in the incidence of postoperative GERD in patients with or without fundoplication performed at the time of Heller myotomy (20). In our survey, concomitant fundoplication was performed by half of the respondents and postoperative pH-impedance measurement studies or endoscopies were only seldomly performed to objectively assess postoperative reflux control. Our survey did not assess the incidence of GERD after Heller myotomy. Further prospective studies are needed to evaluate postmyotomy GERD and determine whether postoperative surveillance strategies are required.

None of the centers were using botulinum toxin injection as a first-line treatment choice. This is consistent with literature reports of only a modest, transient benefit after botulinum toxin injection in children (22,23). Almost a quarter of centers would, however, consider it in cases of symptom recurrence post-Heller myotomy.

This finding appears to contrast with a recent review indicating botulinum toxin injections were performed only in 0.3% (1/49) of patients requiring reintervention post-Heller (20). Despite adult management guidelines not recommending dilation as salvage therapy after myotomy, our survey and a recent survey amongst pediatric surgeons in the UK, indicated that more than half of respondents would consider dilation in cases of recurrence of symptoms post-Heller (11,12).

Over the last decade, POEM has emerged as a therapy for achalasia with adult series suggesting that POEM is very effective. It shares the advantages of both dilation (no skin incisions, decreased pain, less blood loss, low morbidity) and surgical myotomy (durable surgical myotomy and single procedure). Emerging data have shown that POEM requires a shorter operative time and leads to earlier discharge due to faster recovery and lower complication rates. Although the vast majority of respondents would not consider POEM as a primary treatment option for achalasia *overall*, this differed when it considered type III achalasia. This finding is well in line with results from adult literature, reporting POEM to be most successful in this subtype. POEM in children was shown to be feasible and (a limited number of uncontrolled) studies show that it is very effective and safe on the short term (24–27). The largest series of 27 children (age 6–17 years) reported feasibility of 96.3% and treatment success (defined as Eckardt symptom score $\leq$3) in all cases with mean follow-up of 25.6 months (range 15–48 months) (27). Our current study shows that only a few centers have access to POEM at this time. Although large randomized controlled trials with long-term follow-up are needed to confirm efficacy and safety on the long term, there may be potential for a shift in standard treatment given the promising short-term results of the procedure.

In terms of follow-up, we found a large variation in the assessment of results of treatment in terms of effective symptom management and occurrence of complications. Based on the current survey, only a quarter of centers used the Eckardt score as part of their follow-up management. Although the Eckardt score is considered to be a fair measure of achalasia symptom severity overall, a recent study identified the evaluation of the item ''weight loss'' to be an apparent weakness of the Eckardt score, decreasing its reliability (28). The evaluation of weight loss is even more challenging to assess in the pediatric achalasia population as children are expected to *grow* and secondly, ''catch-up'' growth is also to be expected during the refeeding period if a child has been ill or severely undernourished (29). All in all, a validated disease specific symptom questionnaire tailored to the pediatric population may well be helpful to better monitor therapeutic efficacy and tailor treatment decision in case reintervention is required. Also, a disease-specific quality of life measure has been developed and validated for use in children (30). Despite the availability of this questionnaire since 2010, in the present survey only less than a quarter of centers, however, evaluated quality of life as part of their follow-up. Quality of life has shown to be significantly reduced in pediatric achalasia patients and children who are affected pose a significant management challenge (31). Assessment of quality of life before and after intervention is therefore critical to inform counseled discussions and help manage expectations.

This study is the first to assess clinical management of pediatric achalasia globally. A high response rate and good representation of centers worldwide was accomplished, even given the rarity of the disease. To avoid inclusion bias, responses of 6 participants were excluded as these represented duplicate responses of already included centers. Retrospective analysis of these duplicate pairs revealed large within-center discrepancy on all domains, even on the preferred diagnostic and therapeutic modalities and thus further confirms the heterogeneity described above.

A strength of this study is that we included data on emerging techniques such as EndoFLIP and POEM and questions regarding follow-up and patients in need for reintervention. A limitation of this study is that availability of diagnostic investigations was not surveyed. This would have been informative to know; however, data cannot be retrieved in retrospect. Unfortunately, we could not provide an actual overview of *order* of procedures performed in the different centers, as questions were rather posed in a way to determine *importance* of diagnostic and therapeutic interventions. Second, we reached relatively low response rates on questions regarding patient-tailored treatment decisions, and on questions regarding dilation regimens. A possible explanation for the low response rate on dilation regimens may be that dilation was not performed by the pediatric gastroenterologist, who may thus not have been aware of the applied regimens. This was indeed the case in all 3 respondents who reported that a pediatric surgeon performed the pneumatic dilations. Nevertheless, missing data were equally distributed between pediatric, adult gastroenterologists, and intervention radiologists. Last, the questionnaire was send out to pediatric gastroenterologist members of the motility working groups of the ESPGHAN-NASPGHAN; however, a majority of respondents is European. Although these working groups are open for members from other continents, this approach could have induced selection bias. Response bias is a systematic error inherent to this type of research and we have made every attempt to minimize this by sending out reminders on a regular basis.

In conclusion, our study shows a lack of uniformity in the diagnostic and therapeutic management and follow-up of pediatric achalasia amongst and even within different centers worldwide. These findings stress the need for well-designed intervention trials in children with achalasia to determine optimal management and facilitate evidence-based clinical guideline development. Despite the current lack of such trials, we recently proposed a diagnostic and therapeutic management algorithm based upon expert opinion and available pediatric and adult data as a first step toward uniform and improved management of pediatric achalasia (8). Given the rarity of this disease, we recommend that achalasia care should be managed in centers with access to appropriate diagnostic and treatment modalities and that treatment decisions should best be made by a multidisciplinary team of experienced consultants.

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