Pediatric Achalasia in the Netherlands: Incidence, Clinical Course, and Quality of Life

Marije Smits, MSc[1], Marinde van Lennep, BSc[1], Remy Vrijlandt[1], Marc Benninga, MD, PhD[1], Jac Oors[1], Roderick Houwen, MD, PhD[2], Freddy Kokke, MD, PhD[2], David van der Zee, MD, PhD[3], Johanne Escher, MD, PhD[4], Anita van den Neucker, MD, PhD[5], Tim de Meij, MD, PhD[6], Frank Bodewes, MD, PhD[7], Joachim Schweizer, MD, PhD[8], Gerard Damen, MD, PhD[9], Olivier Busch, MD, PhD[10], and Michiel van Wijk, MD, PhD[1]

Objective To assess incidence and clinical course of Dutch patients with achalasia diagnosed before 18 years of age as well as their current symptoms and quality of life (QoL).

Study design Retrospective medical chart review and a cross-sectional study assessing current clinical status using the Eckardt score and reflux disease questionnaire. General QoL was measured using Kidscreen-52 for patients <18 years of age or to 36-Item Short Form Health Survey for patients ≥18 years of age.

Results Between 1990 and 2013, 87 children (mean age 11.4 ± 3.4 years, 60% male) diagnosed with achalasia in the Netherlands were included. Mean incidence was 0.1/100 000/y (range 0.03-0.21). Initial treatment was pneumodilation (PD) in 68 (79%) patients and Heller myotomy (HM) in 18 (21%) patients. Retreatment was required more often after initial PD compared with initial HM (88% vs 22%; $P < .0001$). More complications of initial treatment occurred after HM compared with PD (55.6% vs 1.5%; $P < .0001$). Three esophageal perforations were seen after HM (16.7%), 1 after PD (1.5%). Sixty-three of 87 (72%) patients were prospectively contacted. Median Eckardt score was 3 (IQR 2-5), with 32 patients (44.5%) having positive scores suggesting active disease. Reflux disease questionnaire scores were higher after initial HM vs PD (1.71 [0.96-2.90] vs 0.58 [0-1.56]; $P = .005$). The 36-Item Short Form Health Survey (n = 52) was lower compared with healthy population norms for 7/8 domains. Kidscreen-52 (n = 20) was similar to population norms.

Conclusions Pediatric achalasia is rare and relapse rates are high after initial treatment, especially after pneumodilation, but with more complications after HM. Symptoms often persist into adulthood, without any clinical follow-up. QoL in adulthood was decreased. *(J Pediatr 2016;169:110-5)*.

Achalasia is a severe motor disorder of the esophagus, characterized by the absence of peristalsis and a defective relaxation of the lower esophageal sphincter.[1] In childhood, symptoms are often atypical and vary with age.[2] The incidence in children is estimated to range from 0.1-0.18/100 000 children per year.[3,4] The gold standard for diagnosis is esophageal high resolution manometry (HRM).[5] No curative treatment is available, but symptoms can be relieved by mechanical disruption of the lower esophageal sphincter with balloon pneumodilation (PD) or (open or laparoscopic) Heller myotomy (HM). Scarce data is available evaluating efficacy, complication rate, and long-term outcome of PD and HM in children.[1]

This study retrospectively reviews all registered cases of pediatric achalasia in the Netherlands (1990-2013) in academic centers and prospectively describes their current achalasia associated symptoms and related quality of life (QoL).

Methods

We retrospectively reviewed medical files of Dutch children diagnosed with achalasia before 18 years of age between January 1990 and December 2013. Including patients of all 8 Dutch academic centers treating pediatric achalasia ensured inclusion of all cases. Academic centers covered the entire Dutch pediatric population. Patient files were retracted from medical as well as insurance

DSQoL	Disease-specific QoL	HRQoL	Health-related QoL
EoE	Eosinophilic esophagitis	PD	Pneumodilation
GER	Gastroesophageal reflux	POEM	Peroral endoscopic myotomy
HM	Heller myotomy	QoL	Quality of life
HMF	HM with fundoplication	RDQ	Reflux disease questionnaire
HRM	High resolution manometry	SF-36	36-Item Short Form Health Survey

From the [1]Department of Pediatric Gastroenterology and Nutrition, Emma Children's Hospital, Academic Medical Center, Amsterdam, the Netherlands; [2]Department of Pediatric Gastroenterology, Wilhelmina Children's Hospital, [3]Department of Pediatric Surgery, University Medical Center, Utrecht, the Netherlands; [4]Department of Pediatric Gastroenterology, Sophia Children's Hospital, Erasmus MC, Rotterdam, the Netherlands; [5]Department of Pediatric Gastroenterology, University Medical Center, Maastricht, the Netherlands; [6]Department of Pediatric Gastroenterology, Vrije Universiteit MC, Amsterdam, the Netherlands; [7]Department of Pediatric Gastroenterology, Beatrix Children's Hospital, University Medical Center-Groningen, Groningen, the Netherlands; [8]Department of Pediatric Gastroenterology, Willem-Alexander Children's Hospital, University Medical Center, Leiden, the Netherlands; [9]Department of Pediatric Gastroenterology, Radboud University Nijmegen Medical Center, Nijmegen, the Netherlands; and [10]Department of Surgery, Academic Medical Center, Amsterdam, the Netherlands

The authors declare no conflicts of interest.

http://dx.doi.org/10.1016/j.jpeds.2015.10.057

claim databases. The departments of pediatric gastroenterology and pediatric surgery provided medical records of patients with achalasia. Patients transferred to a nonacademic hospital after their initial diagnoses were included as well. Date of diagnosis was defined as the date the diagnostic test that led to the diagnosis was performed, or when this date was unavailable, we used the date of the report that included these test results.

The Medical Ethical Committee of the Academic Medical Center, Amsterdam, the Netherlands and participating centers approved the study protocol. After review of the medical files, patients received a written notice on the cross-sectional part of this study. Patients provided information on current achalasia treatment and follow-up. All parents or guardians of children <18 years of age signed informed consent prior to filling out the questionnaires.

Patient characteristics, diagnostic investigations, treatment, and treatment outcome were extracted. All follow-up visits during childhood were taken into account.

Initial treatment and relapse treatment options were categorized into: (1) 1 or 2 PDs within 14 days (PD); (2) open or laparoscopic HM; or (3) open or laparoscopic HM with fundoplication (HMF). Treatment success was defined as a documented statement of the treating physician that the patient was symptom free. Relapse was defined as documented recurrence of symptoms, requiring retreatment >14 days after initial diagnosis.

All patients were approached by telephone. Patients were asked to fill out 4 questionnaires, either by means of a structured telephone interview or by self-administration in an online format built for this study. The questionnaires included Eckardt score (positive if >3)[6] or reflux disease questionnaire (RDQ, positive if reported mild heartburn and/or regurgitation occurring ≥2 day per week or moderate/severe heartburn and/or regurgitation ≥1 day per week[7,8]), general QoL (Kidscreen-52 if patients were <18 years of age,[9] 36-Item Short Form Health Survey [SF-36] if patients were ≥18 years of age[10]), and disease-specific QoL (DSQoL if patients were <18 years of age,[11] health-related QoL [HRQoL][12] if patients were ≥18 years of age). Kidscreen-52 and SF-36 were compared with healthy reference standards.

Data Analyses

Yearly incidence and prevalence were calculated as previously described[13] using the death and birth rates up to 2012 from the Dutch Governmental Database (Central Bureau voor de Statistiek), and trends were assessed using Poisson regression analysis.[14] Prevalence was calculated over 2012.

Age-adjusted body mass index z-scores (SDS) were calculated using Dutch reference data.[15]

For assessment of the relationship between balloon size and treatment success, cases without documented clinical follow-up after PD were excluded. All normally distributed data are presented with mean and SD. All other data is displayed as median and IQR. Specific statistic tests were based on the distribution of the data (parametric/nonparametric). Association between balloon size and treatment success was assessed using the χ^2 test for trends. A P value of <.05 was considered statistically significant.

Results

Between 1990 and 2013, 87 children, (52 [60%] boys) were diagnosed and treated for achalasia in the Netherlands. Data on clinical course was available for all except one patient (file contained only 1 letter confirming diagnosis), whom was only included for incidence/prevalence calculations. Mean achalasia incidence from 1990 to 2012 was 0.1/100 000 (range 0.03/100 000-0.21/100 000) children per year. No significant increase was shown over the study period (P = .216, 1.021 95% CI 0.988-1.055). In 2012, the prevalence of pediatric achalasia was 0.9/100 000 children (n = 31 children with achalasia).

Symptoms and Diagnostic Testing

In 13 patients (15%), an erroneous diagnosis was documented prior to the diagnosis of achalasia: asthma (n = 2), eosinophilic esophagitis (EoE, n = 4), gastroesophageal reflux (GER) disease (n = 3), anorexia nervosa (n = 1), functional stricture of the esophagus (n = 1), unspecified mental problems (n = 1), and cystic fibrosis (n = 1) (**Table I**). In patients with and without documented manometry (**Figure 1**; available at www.jpeds.com), success rate without retreatment was comparable (27% vs 27.8%).

Treatment: Choices, Success, and Complications

After diagnosis, 68 patients (79%) were initially treated with PD and 18 (21%) with HMF or HM without fundoplication (**Figure 2**; available at www.jpeds.com). After the initial treatment, recurrence of symptoms requiring retreatment occurred in 65 (75%) and >1 relapse in 47 patients (54%). Recurrence of symptoms occurred significantly more often in patients initially treated with PD compared with HM or HMF (61/68 = 90% vs 4/18 = 22%, P < .0001). Median number of overall retreatments was equal for boys and girls, (2 [0-2] vs 2 [1-3] respectively, P = .134), as was the success percentage at first clinical visit after treatment (24.6% vs 28.6%, P = .941).

Balloon sizes were documented in 136/209 PDs and subsequent treatment success in 123/136. In 10 of 12 patients who underwent PD with balloons 18-30 mm, no treatment success was reached; in the other 2 treatment success was not documented. Rate of success increased significantly (P = .009) with increasing balloon size from 3.6% (30 mm balloon, n = 83) to 6.1% (35 mm, n = 33) and 37.5% (40 mm, n = 8).

Complications occurred in 62% after HM or HMF and in 2% after a single PD, with higher complication rates after HM or HMF vs PD after initial as well as after relapse treatments (initial treatment 10/18 vs 1/68 P < .0001 and relapse treatment 3/135 vs 20/22, P < .0001; **Table II**). Nine of 11 esophageal perforations occurred after HM or HMF. Complications after PD occurred only when ≥35 mm balloons were used.