Pneumatic balloon dilation in pediatric achalasia: efficacy and factors predicting outcome at a single tertiary pediatric gastroenterology center

Giovanni Di Nardo, MD,1 Paolo Rossi, MD,1 Salvatore Oliva, MD,1 Marina Aloi, MD,1 Denis A. Cozzi, MD,2 Simone Frediani, MD,2 Adriano Redler, MD,3 Saverio Mallardo, MD,1 Federica Ferrari, MD,1 Salvatore Cucchiara, MD, PhD1

Rome, Italy

Background: The use of pneumatic dilation (PD) is well established in adults with achalasia; however, it is less commonly used in children.

Objective: To evaluate the efficacy of PD in pediatric achalasia and to define predictive factors for its treatment failure.


Setting: Academic tertiary referral center.

Patients: Twenty-four patients with achalasia were enrolled from January 2004 to November 2009 and were followed for a median of 6 years.

Intervention: PD was performed with the patients under general anesthesia.

Main Outcome Measurements: Efficacy and safety of PD. Follow-up was performed by using the Eckardt score, barium swallow contrast studies, and esophageal manometry at baseline; 1, 3, and 6 months after dilation; and every year thereafter. A Cox regression model was used to identify independent predictors of failure after the first PD.

Results: The PD success rate was 67%. In 8 patients, the first PD failed, but the parents of one patient refused a second PD and requested surgery. Of the 7 patients who underwent repeated treatment, the second PD failed in 3 (43%). Overall, only 3 of the 24 patients underwent surgery (overall success rate after a maximum of 3 PDs was 87%). Multivariate analysis showed that only older age was independently associated with a higher probability of the procedure success (hazard ratio [HR] 0.66; 95% CI, 0.45-0.97).

Limitations: Small sample size, single-center study.

Conclusions: PD is a safe and effective technique in the management of pediatric achalasia. Young age is an independent negative predictive factor for successful clinical outcome. (Gastrointest Endosc 2012;76:927-32.)

Achalasia is a rare primary esophageal dysmotility disorder, with an estimated annual incidence in children of 0.11 cases per 100,000 pediatric patients. It is characterized by functional obstruction of the esophagus because of failed relaxation of the lower esophageal sphincter (LES) in combination with absent peristalsis of the distal esophagus.1,3 The imbalance between defective inhibitory innervation and apparently spared excitatory (cholinergic/tachykinergic) neuronal components is thought to play a major role in the pathogenesis of esophageal motor ab-

Abbreviations: HR, hazard ratio; LES, lower esophageal sphincter; PD, pneumatic dilation.

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Current affiliations: Department of Pediatrics, Pediatric Gastroenterology and Liver Unit (1), Pediatric Surgical Unit (2), Department of Surgical Science (3), “Sapienza” University of Rome, Rome, Italy.

Reprint requests: Salvatore Cucchiara, MD, PhD, Department of Pediatrics, Pediatric Gastroenterology and Liver Unit, Sapienza University of Rome, Viale Regina Elena 324, 00161 Rome, Italy.
normalities and LES dysfunction. Although the exact etiology of neuronal alterations in primary achalasia remains unknown, several lines of evidence indicate that infectious, immune, and genetic factors may play important roles in the mechanisms of this neuropathy. The distinctive symptoms of achalasia are dysphagia for solids and liquids, regurgitation of undigested food, respiratory symptoms (nocturnal cough, aspiration), retrosternal pain, and weight loss.

All therapeutic options focus on reducing the pressure gradient across the LES because no treatment can restore muscular activity. This can be achieved by pharmacological agents, injected endoscopically (botulinum toxin) or taken orally (Ca<sup>2+</sup> channel blockers and nitrates), but the clinical effects of these agents are short-lived. Alternatively, LES pressure can be reduced by pneumatic dilation (PD) or by surgical myotomy, which are considered the main procedures for treating achalasia. Many authors consider PD the first choice in adults because of its high degree of effectiveness and low degree of morbidity and mortality, with the additional advantage of a short hospital stay and lower instrumental cost. Surgery is usually reserved for patients who do not respond to PD.

Knowing the possible predictive response factors for PD is very useful in selecting patients who could benefit from surgery early on. Several adult studies found that older age, female sex, a long history of symptoms before diagnosis, high pretherapeutic LES pressure, a postdilation LES pressure of less than 10 mm Hg, limited contrast retention on postdilation barium esophagram, and a higher number of repeated baseline PD dilations were associated with a favorable outcome for PD. All of these studies were performed in adults, and often retrospectively. Experience with pediatric patients is limited to small retrospective series, and possible predictive response factors have never been studied in the pediatric age group.

This study, performed in pediatric patients with achalasia, aimed to assess the efficacy and safety of PD and to define predictive factors for symptom recurrence requiring repeated PD and surgery.

**PATIENTS AND METHODS**

Twenty-four patients (11 female patients; mean age 10 years; range 5-17 years) with a diagnosis of achalasia who were treated in our unit from January 2004 to November 2009 were prospectively included in this study. The diagnosis of achalasia was made based on clinical symptoms, a barium esophagogram, and the absence of peristalsis and impaired relaxation of the LES (lowest pressure of ≥10 mm Hg during swallow-induced relaxation) at esophageal manometry.

Exclusion criteria were (1) short duration of follow-up (<12 months), (2) parents of patients who refused PD and requested surgery, (3) patients who did not attend the control sessions, and (4) patients receiving an initial diagnosis and/or balloon dilation in another center. The patients were not treated with drugs that could alter the dilation results.

**Take-home Message**

- Pneumatic dilation (PD) can be used as first-line therapy in pediatric achalasia because of its safety and efficacy.
- The study results show that most children can be eligible for repeat PD; however, some patients, such as those patients younger than 6 years of age, may be referred for surgery earlier if they experience a recurrence.

**Endoscopic training before enrollment**

The first author (G.D.N.) completed 2 years of training at an adult GI endoscopy center. During the second year, he began to perform endoscopy in pediatric patients. During this period, he routinely performed balloon dilation for different conditions; in particular, he acquired experience in the use of the Rigiflex dilator (Rigiflex; Microvasive, Boston Scientific, Natick Mass) in both adult and pediatric achalasia patients (22 PDs in 16 patients, 3 pediatric and 13 adult; these pediatric patients were not enrolled in the study). Dr Oliva completed 2 years of training at an adult GI endoscopy center. During the second year, he began to perform endoscopy in pediatric patients. During this period, he performed 18 PDs in 12 adults with achalasia. He was actively involved in the study under the supervision of Dr. Di Nardo, who acquired additional experience in pediatric therapeutic endoscopy. In addition, Drs Di Nardo and Oliva were supervised by Dr Cucchiara, who is the Head of the Pediatric Gastroenterology and Liver Unit of the University of Rome and has 30 years of experience in motility GI disorders and pediatric diagnostic and operative endoscopy.

The study was approved by our Ethics Committee.

**Evaluation of symptoms**

Clinical manifestations evaluated by history (dysphagia, regurgitation, chest pain, and weight loss) were recorded by using a scoring system of 0 to 3 for each of them. The following clinical stages were established in accordance with Eckardt scoring system: 0 (scores of 0-1), I (scores of 2-3), II (scores of 4-6), and III (scores >6). The clinical stage of all patients was monitored at baseline; 1, 3, and 6 months after dilation; and every year thereafter. Patients in clinical stages 0/1 were considered to be in clinical remission and those in stages II/III in treatment failure.

**Radiological evaluation**

The maximum caliber of the esophageal body was measured before dilation, 6 months after dilation, and every year thereafter by using barium esophagrapy. Achalasia was classified into 3 groups based on the maxi-
mum diameter of the esophageal body (<35 mm, 35-59 mm, >60 mm).

Esophageal manometry

Esophageal manometry was performed after an 8-hour overnight fast and a semiliquid diet the day before using a dent-sleeve catheter perfused with distilled water at a rate of 0.5 mL/min by using a low-compliance pump connected through a separate pressure transducer (Medtronic AB, Kista, Sweden) to an 8-channel polygraph (Medtronic). The manometric endoscope was passed through the nose to the gastric cavity, and, with the patient in the dorsal decubitus position, the LES was located by manually drawing the endoscope back at 1-cm intervals. During this procedure, the LES resting pressure and relaxation as well as esophageal body motility occurring in response to 10 wet swallows were recorded. The basal LES pressure, reported in millimeters of mercury (mm Hg), was determined by the difference between the maximum value of end-expiratory pressure and expiratory fundic pressure. Relaxation of the LES was recorded. The basal LES pressure, reported in millimeters of mercury (mm Hg), was determined by the difference between the maximum value of end-expiratory pressure and expiratory fundic pressure. Relaxation of the LES after swallowing a 5-mL bolus of water was considered normal if it reached 80% of the basal pressure.

Endoscopic dilation: technique and evaluation of efficacy

Pneumatic dilations were performed with the patients under general anesthesia by using a polyethylene balloon system (Rigiflex; Microvasive, Boston Scientific).

We generally perform the procedure in the morning, after the patient has fasted overnight. The patient is placed in the left lateral position. The endoscope is advanced into the stomach, the guidewire is placed in the stomach, and the endoscope is then removed. The balloon dilator is advanced over the guidewire and positioned across the gastroesophageal junction under fluoroscopic control. The balloon is inflated to 5 psi for 1 minute and subsequently to 10 to 12 psi, and the pressure is maintained until obliteration of the waist occurred. All patients were observed for 8 hours after the procedure. If no symptoms developed during the control period, patients were allowed to eat. If symptoms (fever, chest pain, or cough) or abnormality on chest auscultation occurred, a gastrografin swallow was performed. The first pneumatic dilation was performed with the use of a 30-mm balloon; if, 4 weeks later, the Eckardt score was greater than 3, a second dilation was performed by using a 35-mm balloon. If the Eckardt score remained greater than 3 (stages II/III), the treatment was considered to have failed. Patients with a recurrence of symptoms during the follow-up period underwent dilation again, this time by using a 35-mm balloon and, if necessary (ie, if the Eckardt score remained >3), with the use of a 40-mm balloon. A third and final series of dilations was allowed only if symptoms recurred more than 1 year after the second series.

Statistical analysis

We estimated the overall rate of success of the first dilation as the percentage of patients who did not experience a relapse during follow-up. Univariate survival analysis was performed to test whether sociodemographic (age, sex) or clinical (baseline clinical score, baseline maximum caliber of the esophageal body, basal LES pressure, and the percentage of decrease in caliber of the esophageal body and LES pressure after PD) characteristics were associated with a higher risk of treatment failure. Because of the small sample size, we limited this analysis at the first dilation. Kaplan-Meier curves were estimated, and the log-rank test was performed.

Finally, we performed a multivariate analysis to evaluate the independent effect of factors that resulted in significance on univariate analysis by using a Cox survival analysis.

RESULTS

Twenty-four patients were enrolled in the study and underwent a first PD (34 sessions of PD). Table 1 shows the demographic and clinical characteristics of the studied population. All patients were observed for at least 2 years with a median follow-up of 6 years (range 2-7 years). The first PD failed in 8 patients, corresponding to a success rate of 67% (95% CI, 0.45-0.84); parents of one patient refused a second PD and requested surgery for personal choice, whereas the treatment was repeated in the remaining 7 patients. Of the latter, PD failed in 3 patients (43%) and a third PD was needed. Of these 3 patients, PD failed again in 2 patients who then underwent surgery, whereas 1 patient had a good response (Fig. 1). Overall, only 3 of the 24 patients enrolled in the study underwent surgery (overall success rate after a maximum of 3 PDs was 87%).

The first recurrences occurred at a mean interval of 12.2 months (range 2.8-17.6 months), whereas the second recurrences occurred at 10, 12, and 14 months in each of the 3 patients, respectively.

Of a total of 34 PDs performed in 24 patients, no serious complications occurred. Postprocedural pain occurred after 4 of 34 procedures (11%). In all 4 of these patients, pain persisted for less than 24 hours and did not require the use of narcotics. The median age of children in whom the first PD failed was 6 years (SD), whereas for those who did not undergo a second PD, the median age was 12 years. We observed a significantly higher probability of first PD success among older children (log-rank test, \( P = .0048 \)) (Fig. 2), those with a higher LES pressure at baseline (log-rank test, \( P = .0134 \)), and those with a higher percentage of decrease in LES pressure after the first PD (log-rank test, \( P = .0035 \)) (Fig. 3). No differences were observed for the other evaluated parameters (sex, baseline esophageal diameter, pre-/post-PD variation in esophageal diameters).

However, the multivariate analysis showed that only older age was independently associated with a higher
probability of procedure success (hazard ratio 0.66; 95% CI, 0.45-0.97) (Table 2). Of 3 patients in whom a second PD failed, 2 were boys 5 and 6 years of age, respectively, and 1 was a 5-year-old girl. They had baseline clinical scores of 10 and 12 (in 2 of them), which is higher than the median value of the whole sample, and esophageal sphincter pressure of 70, 42, and 30 mm Hg, respectively.

**DISCUSSION**

Achalasia is a rare disorder with an annual incidence of 1 case per 100,000, of which childhood achalasia accounts for less than 5%. In adults, PD is recommended as the initial treatment because of its low morbidity, low cost, and short postprocedural hospital stay. In contrast, experience in the pediatric population is limited because of the rarity of the disease in children. A review of the literature shows that PD is successful in the majority of reported pediatric series, with success rates of 45% to 90%; this method has not gained universal acceptance in children. Azizkhan et al and Nakayama et al reported that PD was unsuccessful in children younger than 9 years of age and technically difficult to perform in children younger than 5 years of age.

This is the largest prospective study in pediatric achalasia aimed at evaluating the efficacy and safety of PD as well as factors predicting outcome. In our study, 1 session of PD was clinically effective in 67% of the patients, as

### Table 1. Demographic and clinical characteristics of the enrolled patients

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Only 1 PD</th>
<th>&gt;1 PD</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total, no. (%)</td>
<td>16 (66.7)</td>
<td>8 (33.3)</td>
<td>24 (100)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>8 (50.0)</td>
<td>5 (62.5)</td>
<td>13 (54.2)</td>
</tr>
<tr>
<td>Female</td>
<td>8 (50.0)</td>
<td>3 (37.5)</td>
<td>11 (45.8)</td>
</tr>
<tr>
<td>Age at diagnosis, y</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>11.8</td>
<td>6.4</td>
<td>10.0</td>
</tr>
<tr>
<td>SD</td>
<td>2.5</td>
<td>2.2</td>
<td>3.5</td>
</tr>
<tr>
<td>Clinical score at baseline</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>9.9</td>
<td>10.8</td>
<td>10.2</td>
</tr>
<tr>
<td>SD</td>
<td>1.4</td>
<td>1.5</td>
<td>1.4</td>
</tr>
<tr>
<td>LES pressure at baseline</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>67.9</td>
<td>57.7</td>
<td>64.5</td>
</tr>
<tr>
<td>SD</td>
<td>13.2</td>
<td>21.0</td>
<td>16.5</td>
</tr>
<tr>
<td>Esophageal diameter at baseline</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>6.15</td>
<td>6.9</td>
<td>6.4</td>
</tr>
<tr>
<td>SD</td>
<td>1.4</td>
<td>0.3</td>
<td>1.2</td>
</tr>
<tr>
<td>Pre-/postdilation variation in LES pressure, %</td>
<td>48.0</td>
<td>19.0</td>
<td>38.0</td>
</tr>
<tr>
<td>Pre-/postdilation variation in esophageal diameter, %</td>
<td>37.0</td>
<td>23.0</td>
<td>32.0</td>
</tr>
</tbody>
</table>

PD, Pneumatic dilation; SD, standard deviation; LES, lower esophageal sphincter.

**Figure 1.** Study flow. PD, pneumatic dilation.
described in the majority of adult studies reporting an almost 80% success rate, with therapeutic effectiveness similar to that in patients undergoing surgery.\textsuperscript{9,31-34} In our series, we did not observe serious complications, only self-limited postprocedural pain in 11% of patients.

Recurrence of symptoms usually occurs early, mainly during the first year post-PD\textsuperscript{11} with the need for repeat dilation and/or surgery. The median time between the first and the second dilations was 12.2 months (range 2.8-17.6 months) in our patients, whereas the second recurrences occurred at 10, 12, and 14 months in 3 patients. Consequently, it is of value to know the predictive response variables to PD that affect long-lasting clinical improvement.

A first statistical analysis showed that predictive factors of failure after the first PD were young age, low basal LES pressure, and a small decrease in the LES pressure after PD. However, we observed that the last 2 factors were highly correlated, i.e., patients with a low baseline LES pressure were those exhibiting a small decrease in the LES pressure after PD. Therefore, it was not advisable to analyze the 2 variables in a multivariate model, and we performed a multivariate Cox regression analysis including only age and the percentage of decrease in the LES pressure after PD. This model shows that when controlling for age, the percentage of decrease in the LES pressure after PD was no longer significant.

Our observations suggest that the only independent predictor of PD failure is young age. A larger sample size would probably confirm these results. This is in accordance with other published adult studies in which a younger age (between 20 and 40 years) was a predictive factor for a worse response.\textsuperscript{11,20,35,36}

In conclusion, PD is a safe and effective procedure for the treatment of pediatric achalasia, with an 87% overall 6-year success rate. Young age at presentation seems to be the only independent negative predictive factor for the need for a repeat PD and surgery. This factor should be taken into account in the follow-up strategy of the pediatric patients with achalasia, leading to a stricter follow-up protocol in patients younger than 6 years of age.

Our results show that most patients can be eligible for repeat PD; however, some patients, such as those younger than 6 years of age, may be referred for surgery earlier if they experience a recurrence.

\begin{table}[h]
\centering
\begin{tabular}{|l|l|l|l|}
\hline
Covariates & HR & SE & 95\% CI \\
\hline
Pre-/postdilation variation in LES pressure, % & & & \\
\hline
\textless{}=55 & 1.0 & — & — \\
30-54 & 2.1 & 3.39 & 0.089-49.814 \\
\textgreater{}=30 & 11.64 & 14.66 & 0.986-137.435 \\
Age at diagnosis, y & 0.66 & 0.13 & 0.452-0.73 \\
\hline
\end{tabular}
\caption{Cox model analysis of time free of repeat PD after first PD}
\end{table}

\textbf{REFERENCES}