

A Review of Factors Predicting Outcome of Pneumatic Dilation in Patients With Achalasia Cardia

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Pneumatic dilation (PD) is an effective treatment for achalasia cardia. Outcome of PD, however, varies among different studies. Recently, some groups started considering laparoscopic myotomy to be competitive to PD in treatment of achalasia considering dreaded complication like perforation following the latter therapeutic approach. Therefore, there is need to predict outcome of PD for achalasia, so that appropriate therapy, both for treatment naïve and for treatment failed patients can be chosen. Apart from age and gender, 2 investigations, namely post-PD manometry and timed barium esophagogram are most often used to predict outcome after PD. Even though there are studies available in the literature with regard to these modalities to predict outcome of PD, these are quite few in number, including small number of patients, primarily because of rarity of the disease. In this article, we review the literature predicting outcome of PD for achalasia.

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Key Words

Achalasia; Dysphagia; Esophageal dysmotility; Manometry

Introduction

Achalasia cardia is a rare primary esophageal motor disorder, which is diagnosed on the basis of esophageal manometry.¹ Typical manometry findings in achalasia are aperistalsis of esophageal body and incomplete relaxation of lower esophageal sphincter (LES).² Based on average esophageal body amplitude, achalasia is classified into classic (≤ 40 mmHg) and vigorous types (> 40 mmHg).³ Vigorous achalasia is considered as the early stage in the natural history of the disease.^{4,5} Treatment of achalasia

is usually palliative in nature.⁶ There are 3 main modes of therapy: pneumatic dilation (PD), botulinum toxin injection (both through endoscopic means) and surgery (Heller's cardiomyotomy). Endoscopic PD and surgery are effective in providing long-term remission.⁷

Pneumatic Dilation

PD is the most popular non-surgical treatment of achalasia. Moreover, it is cost-effective compared to botulinum toxin injection and surgery.⁸⁻¹⁰ PD can be performed with different dila-

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tors of variable balloon compliances. Low compliance polyethylene pneumatic dilator (Rigiflex dilator) is most widely used because of its theoretical advantages over the high compliance balloon dilator.¹¹ Most feared complication of PD is esophageal perforation. Perforation rate varies from less than 1% to 3% in various studies.¹²⁻¹⁶ Furthermore, PD is effective in 64%-87% patients.¹² Also, a proportion of initial responders experience recurrence during long-term follow-up. Therefore, it is important to predict which patient is less likely to respond or develop recurrence following an initial response for the following reasons; (1) to devise treatment strategy in a given patient, (2) to prognosticate, (3) to plan early re-intervention, if required, and (4) to help understand pathophysiology of the disease. Table 1 shows the likely predictors of outcome following PD for achalasia cardia.

The studies published in literature addressing the issue on predictors of outcome of PD (Tables 1-3) differ in type of dilator used, symptom scores used to assess the outcomes (response and

Table 1. Possible Predictors of Outcome Following Pneumatic Dilation of Achalasia Cardia

Demographic and clinical parameters
Age
Gender
Specific symptom(s)
Duration and type of achalasia
Manometry
LESP (baseline and post-PD)
Amplitude of contractions
Timed barium esophagogram
Height and width of barium column

LESP, lower esophageal sphincter pressure; PD, pneumatic dilation.

Table 2. Summary of Factors Useful to Predict Outcome of Pneumatic Dilation of Achalasia Cardia as Found in Different Studies

Author and Year	Patient number	Study type	Predictor(s)
Ponce, 1996	157	P	Age, sex, esophageal body diameter and basal LESP
Eckardt, 1992	54	P	Age, balloon diameter and post-PD LESP
Vaezi, 2004	75	R	Age, sex and timed barium esophagogram
Mehta, 2005	52	R	Age
Ghoshal, 2004	126	R	Sex and post-PD LESP
Chuah, 2009	32	P	Age

P, prospective study; R, retrospective study; LESP, lower esophageal sphincter pressure; PD, pneumatic dilation.

recurrence), treatment protocol for management of recurrence and investigations used to predict outcomes etc. In spite of such heterogeneity between the studies, these do provide valuable information, which can guide physician in planning treatment strategy.

The first large prospective study was done by Ponce et al¹⁷ in which 157 patients with achalasia underwent PD with Witzel dilator. Patients who had post-PD lower esophageal sphincter pressure (LESP) < 10 mmHg had a better outcome than others. Using Bayes' theorem, a predictive model was constructed including 5 most discriminating values: age < 20 years, male sex, diameter of esophageal body < 3 cm, basal pressure of esophageal body > 15 mmHg and LESP > 30 mmHg. Jackknife method was used to validate the model. The limitation of this study was lack of use of conventional statistics including multivariate analysis. Furthermore, Witzel dilator has high compliance balloon that is no longer in use.

Mehta et al¹⁸ reported a retrospective study on 52 patients using Rigiflex balloon in whom 81% responded to PD. On univariate analysis, non-responders were younger in age (< 40 years), had high baseline LESP (> 50 mmHg) and reduced mid-esophageal contractions (amplitude < 30 mmHg). There was no significant difference in response rates with respect to gender. On multivariate analysis, only young age was associated with poor response, though patients with high baseline LES pressure showed a trend towards poor response. Esophageal manometry was not repeated after PD in this study.

From our center, we reported a retrospective study on 126 patients who had undergone PD for achalasia.¹² On univariate analysis, regurgitation, chest pain, pulmonary symptoms and male gender were associated with non-response. Post-PD reduction in LESP by more than 50% was associated with good response. On multivariate analysis, male gender was the only fac-

Table 3. Summary of Studies Predicting Outcome of Pneumatic Dilation of Achalasia Cardia

Predictors	Outcome
Old age (> 45 yr)	Favorable
Male gender	Poor
Large balloon size	Favorable
Post-PD LESP < 10 mmHg	Favorable
Post-PD LESP reduction by > 50%	Favorable
Complete emptying in TBE	Favorable

PD, pneumatic dilation; LESP, lower esophageal sphincter pressure; TBE, timed barium esophagogram.

tor, which was associated with worse outcome. This is the largest study in which a low compliance dilator (Rigiflex) was used. But, post-PD manometry was not done in all the patients in this study.

Eckardt et al^{19,20} reported outcome of management of 54 patients with achalasia cardia with PD. Symptom score and LESP were assessed at baseline and at 4 weeks after PD. Follow-up assessment of symptom score was done at 2 yearly intervals for a median of 13.8 years. Of 35 patients who had relapse, 32 relapsed within 5 years. Long-term outcome was significantly better in patients with age older than 40 years and post-PD LESP < 10 mmHg. Even though this study was prospective with long-term follow-up, the authors have used Brownie Mchardy dilator (high compliance balloon) which is not being used now-a-days.

Farhoomand et al²¹ reported a retrospective analysis of 75 patients who underwent PD with Rigiflex dilator. Symptom scoring and timed barium esophagogram were done in all the patients at baseline and at 1 month after PD. Among the patients who had undergone PD with 30 mm balloon, retreatment was required less often compared to the patients who had undergone PD with 35 and 40 mm balloon. Especially, early failure rate (within 3 months) was high among those who had undergone PD with 30 mm balloon compared to those in whom larger balloon diameter was used. Also, 22 of 25 patients who had early failure were men. Multivariate Cox proportional hazards model revealed that younger men (< 45 years) required additional therapy more frequently compared to older men and also the difference in response rate between male and female became narrower as age advanced. Thus they concluded that failure was commoner among young men who had undergone PD with 30 mm balloon. Similar to their previous study in which complete barium emptying in timed barium esophagogram was found to strongly correlate with symptomatic improvement, including long-term remission, this study also showed that those who did not require re-treatment more often had complete barium emptying after PD.²² Post-PD manometry was not done in this study. The authors suggested that male patients with achalasia should be treated with 35 mm balloon for even the first session of PD as 30 mm balloon often failed in them and post-PD timed barium esophagogram predicted long-term outcome after PD. A prospective study by Chuah et al²³ on 32 patients managed with Rigiflex dilator also concluded that age more than 45 years was the only significant factor predicting favorable outcome.

Even though, some studies evaluated duration of dysphagia and type of achalasia as possible parameters predicting outcome, they were not found important in predicting outcome even in uni-

variate analysis.^{12,17-19} Post-PD manometry and timed barium esophagogram are the 2 most widely used investigations to predict the outcome after PD. Manometry studies have used various criteria to predict the outcome such as post-PD LESP < 10 mmHg and reduction of LESP by more than 50% of baseline LESP.

Andersson et al²⁴ reported a prospective study, in which 51 patients with achalasia were randomized into 2 treatment groups, namely PD and laparoscopic myotomy. Timed barium esophagogram was done at baseline and after treatment. The median follow-up time after the post-treatment timed barium esophagogram was 18 months. They found a significant correlation between barium emptying at 1 minute and symptom scores at the end of follow-up period in both the groups. Patients with less than 50% improvement in this parameter after treatment had a 40% risk of treatment failure on follow-up.

The recently introduced high resolution manometry displays spatiotemporal plots of esophageal body and LESPs.^{25,26} It also helps us to understand the segmental functional anatomy of esophageal body and LES, which contributes to our understanding of various subsets of achalasia and possibly their difference in response to various modes of treatment. Till now, this attractive research tool has not been studied for predicting the outcome of PD in achalasia.

Why Is Pneumatic Dilation Less Effective in Men? —

Explanation for worse outcome of PD among men is unknown. However, one may hypothesize that LES muscles might be stronger among men than women that might be responsible for worse outcome among them. LES tone might be more in younger men than in older men, thus further explaining less favorable outcome in young men. However, this needs to be studied further.

Why Is Old Age a Favorable Predictor? —

Apart from some of the above discussed studies, there are many other studies in literature which concluded old age as a predictor of favorable outcome.²⁷⁻³⁰ Though, the exact reason for this is not known, there are various hypotheses to explain this finding.

Anatomically, LES has 2 components, namely clasp fibers encircling the gastroesophageal junction medially and gastric sling fibers present on left lateral side. In PD, only the clasp fi-

bers are targeted. Hence, it is possible that gastric sling fibers, unaffected by PD, contribute to residual LES tone in these patients after PD. As discussed previously, this tone is likely to be higher in younger patients, thus explaining poor response in young patients.³¹ Patients with long-standing symptoms often interpret mild improvement in esophageal emptying as dramatic relief from dysphagia.³² Older patients perceive less pain compared to their younger counterparts when balloon is distended in esophagus.³³ Also, older patients are expected to have weaker LES muscles that might be easily torn during PD.

Clinical Implications

Young men having persistently high LESP and poor esophageal emptying after PD might be better treated by laparoscopic myotomy rather than persisting with repeated PDs. Similarly, old women after PD having low (or > 50% reduced) LESP and good esophageal emptying may be offered repeated PD in the unlikely event of recurrence. Thirty-five mm instead of 30 mm balloon should be tried for first PD, particularly in males.

Need for Future Research

A prospective study with large number of patients and long-term follow-up is needed. Both timed barium esophagogram and manometry, especially high resolution manometry should be done at baseline and post-PD, so that they can be compared in their value in predicting outcome. Strong statistical methods will add to the strength of evidence.

Conclusion

PD is an effective alternative to surgery. The response to PD depends on age and gender of the patient and size of the balloon used for PD. The long-term response can be predicted with the help of post-PD manometry and timed barium esophagogram. Balloon size has to be chosen according to the gender. Further prospective studies with larger numbers are needed.

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