


ORIGINAL ARTICLE

Retrospective study on symptoms and treatment modalities used and short-term follow up of achalasia cardia in Indian setting

Mayank Jain,*  Neha Baijal,[†] Melpakkam Srinivas,[‡] Rajiv Baijal,[§] Nitesh Pratap,[¶] Vatsal Bachkaniwala,^{||} P Ganesh^{||} and Jayanthi Venkataraman^{‡,||}

*Arihant Hospital and Research Centre, Indore, [†]Maulana Azad Medical College, [‡]Pushpavati Singhania Hospital and Research Centre, New Delhi, [§]Gleneagles Global Health City, ^{||}Sri Ramachandra Medical College, Chennai and [¶]Krishna Institute of Medical Sciences, Secunderabad, India

Key words

Achalasia, esophagus, dilatation, motility.

Accepted for publication 13 March 2020.

Correspondence

Mayank Jain, Senior Consultant, Department of Gastroenterology, Arihant Hospital and Research Centre, Indore 452009, India.

Email: mayank4670@rediffmail.com

Declaration of conflict of interest: None.

Abstract

Background: Achalasia cardia is a rare esophageal motor disorder that is frequently diagnosed late.

Aim: The aim of this study was to study the symptoms, treatment given, and response to treatment in patients with achalasia cardia in an Indian setting.

Materials and methods: This retrospective study included all patients diagnosed with achalasia cardia on high-resolution esophageal manometry, using Chicago Classification v 3.0. On follow up, patients were contacted by telephone, and details of the treatment given and response were recorded in a predesigned pro forma. We excluded overseas patients, postoperative cases of achalasia, and those in whom the manometry catheter could not be passed across the gastroesophageal junction.

Results: A total of 452 patients (260 males, median age 44.5 years) were included in the study cohort. The major symptoms included dysphagia for solids and liquids (428, 94.7%), regurgitation (360, 79.6%), naso-oral regurgitation (182, 40.3%), weight loss (322, 71.3%), and chest pain (158, 35%). Type 2 achalasia (229, 50.6%) was the most common subtype, followed by type 3 (154, 34.1%). Chest pain was more common in type 3, and weight loss and naso-oral regurgitation were more common in type 2 achalasia. A majority of patients underwent Heller's myotomy and pneumatic dilatation. Of 280 patients for whom treatment details were available, 98% reported good response to endoscopic/surgical management.

Conclusion: The predominant symptoms of achalasia cardia vary per the manometric subtype. Heller's myotomy and pneumatic dilatation are the most commonly used treatment options. Response to treatment is good. The choice of treatment modality was likely influenced by financial reasons and availability of local expertise.

Introduction

Idiopathic achalasia cardia is a rare esophageal motor disorder. It is subclassified into three major subtypes based on high-resolution esophageal manometry (HREM) findings. Pneumatic dilatation, per oral endoscopic myotomy (POEM), and Heller's myotomy are the three recommended modalities for relief of symptoms.^{1,2} A recent Indian study noted that a majority of these patients are diagnosed late.³ Urban residence, primary presentation to a gastrointestinal specialist, and severity of disease-related symptoms are more likely to lead to an early diagnosis.³

Majority of the Indian data on this rare disorder are limited to single-center experiences.⁴⁻⁶ However, in clinical practice, the choice of treatment modality used depends on multiple factors such as availability of expertise for POEM, financial constraints, and accessibility to referral centers. Thus, the present multicenter

study was undertaken to study the response to different modalities of treatment offered to patients with achalasia cardia. The study was planned to highlight the real-world practice scenario in the management of achalasia cardia in an Indian setting.

Materials and methods

A pro forma was designed and circulated among consultants working in gastrointestinal motility units of five referral centers across India. These centers included Arihant hospital and Research Centre, Indore; Gleneagles Global Health City, Chennai; Pushpavati Singhania Hospital and Research Centre, New Delhi; Krishna Institute of Medical Sciences, Secunderabad; and Sri Ramachandra Medical College, Chennai. Participation was voluntary.

All centers use 16-channel water perfusion HREM systems (Ready stock, Australia), and reporting was carried out using the same software (Hebbard, Australia). Patients with a confirmed diagnosis of achalasia cardia between January 2012 and May 2019 by HREM⁷ were included in the study. Reports classified as achalasia by Chicago classification 2.0 were reclassified using the CC v 3.0.⁷ All patients had undergone assessment using esophagogastroduodenoscopy to rule out secondary/pseudoachalasia.

For details on follow up, patients were contacted by telephone, and details of treatment received and response to the treatment were recorded using Eckardt score. Hospital records were also scrutinized for follow-up details.

As different centers used different protocols, only details of the procedure done and symptom relief were noted. The protocols for pneumatic dilatation (size of balloon and number of procedures), radiological and HREM assessment postintervention, use of medications such as sorbitrate or calcium channel blockers postintervention, and use of antireflux procedures post-Heller's myotomy varied between the different centers. Thus, these factors were not considered for analysis.

Exclusion criteria were: age < 18 years, overseas, postoperative cases of achalasia, and those cases in whom manometry catheter could not be passed across the gastroesophageal junction.

The data collected were analyzed for the following (Fig. 1)

1. Demographic trends, symptoms, and HREM findings
2. Treatment details (available for 280 patients)—all treatment modalities were explained to patients by the attending doctors. Based on the available local expertise and cost, the decision regarding undergoing a particular intervention was made by the patient.
3. Symptom relief after intervention (with at least 6 months' follow up) —available for 80 patients

Statistical analysis. Data was entered in a Microsoft Excel sheet and interpreted as median, range, and percentages. Comparison of medians was carried out using the Mann–Whitney U test, and for proportions, the chi square test was used. Pre- and post-intervention symptom scores were compared using a paired t test

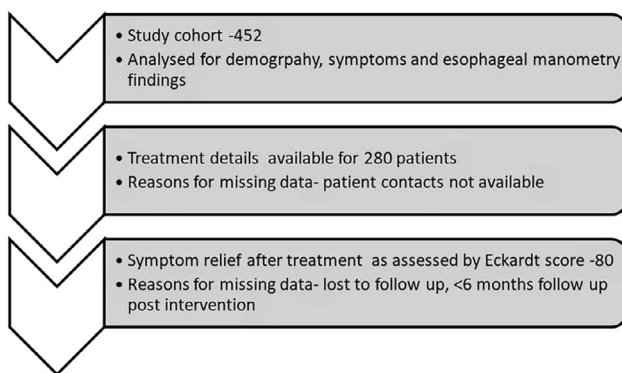


Figure 1 Flowchart highlighting data analysis in the present study.

in a subset of patients. A p value of <0.05 was considered statistically significant. Statistical analysis was performed using SPSS version 20.

The study was approved by the Institutional Ethics Committee of the respective hospitals.

Results

Demography, symptoms, and HREM findings. The study cohort consisted of 452 patients (260 males, median age 44.5 years). The median duration of symptoms was 3 years (0.2–20 years). The common clinical symptoms at presentation included dysphagia for solids and liquids (428, 94.7%), regurgitation (360, 79.6%) including naso-oral regurgitation (182, 40.3%), weight loss (322, 71.3%), and chest pain (158, 35%).

The most common type of achalasia cardia was type 2 (229, 50.6%), followed by type 3 (154, 34.1%) and type 1 achalasia (69, 15.3%). The differences in symptomatology in the three types of achalasia are seen in Table 1. Type 3 achalasia was common in older patients (median age 49.5 years), often presenting with chest pain. Type 2 achalasia patients had significant weight loss ($P = 0.004$) and naso-oral regurgitation ($P = 0.004$). In Type 1 achalasia, the median integrated relaxation pressure (IRP) was significantly low (18.4, $P = 0.03$). Eckardt score was similar in the three subtypes (Table 1).

Treatment details and follow up. Treatment details were available for 280 patients (62%). A majority had undergone Heller's myotomy (122, 43.6%), followed by pneumatic dilatation (76 patients; 27.1%): single session in 30 cases and multiple sessions in 46 patients. Three patients (1%) received botulinum toxin injection, and POEM was performed in 32 (11.4%). Nineteen patients (6.8%) were on nifedepine or sorbitrate. Twenty-eight cases (10%) did not pursue medical/surgical treatment and were receiving alternative medications for symptom control. The treatment modalities used in various subtypes of achalasia are highlighted in Table 2. Significantly higher proportions of patients with types 1 and 2 achalasia underwent pneumatic dilatation. Heller's myotomy and POEM were more frequent in those with type 3 achalasia. As noted in Table 3, a majority of the patients who underwent endoscopic/surgical treatment felt better after treatment (246/252, 98%).

Symptom relief after intervention (with at least 6 months' follow up). This was assessed for 80 cases that had >6 months' follow up. Eckardt score was calculated and compared with preprocedure score. Postprocedure Eckardt score showed significant improvement posttreatment (preintervention score 7 vs postintervention score 3, $P = 0.02$).

Discussion

The present study highlights that, in an Indian setting, dysphagia, regurgitation, and weight loss are the most common symptoms of achalasia. Chest pain is noted in one-third of cases, predominantly in those with type 3 achalasia; regurgitation and weight loss were more frequent in type 2 achalasia. The median duration

Table 1 Comparison of demography, symptom profile, and IRP between the subcategories of achalasia cardia

Parameters	Type 1 (<i>n</i> = 69)	Type 2 (<i>n</i> = 229)	Type 3 (<i>n</i> = 154)	<i>P</i> value
Age	43 (18–77)	43 (15–78)	49.5 (13–85)	0.02
Males	36 (52.2%)	130 (56.7%)	94 (61%)	0.44
Duration of disease (in years)	2 (0.3–14)	3 (0.2–20)	3 (0.3–12)	0.34
Symptoms				
Dysphagia	61 (88.4%)	215 (93.9%)	152 (98.7%)	
Regurgitation	49 (71%)	192 (83.8%)	119 (77.3%)	
Naso-oral regurgitation	30 (43.5%)	124 (54.1%)	75 (48.7%)	0.004
Chest pain	20 (29%)	60 (34.1%)	78 (50.6%)	
Weight loss	47 (68.1%)	183 (80%)	92 (59.7%)	
Symptom severity				
Eckardt score	6 (2–10)	6.5 (2–10)	6 (2–10)	0.35
Manometry parameters				
Median IRP (range)	18.4 (16.5–54.8)	26.2 (15.9–70.7)	27.2 (16–69.5)	0.03

Table 2 Treatment modalities used in various subcategories of achalasia cardia

	Heller's myotomy	Pneumatic dilatation	POEM	Medications/Botulinum toxin	<i>P</i> value
Type 1 (36)	16 (44.5%)	16 (44.5%)	2 (5.5%)	2 (5.5%)	0.005
Type 2 (<i>n</i> = 116)	53 (45.7%)	43 (37%)	10 (8.6%)	10 (8.6%)	
Type 3 (<i>n</i> = 100)	53 (53%)	17 (17%)	20 (20%)	10 (10%)	

Table 3 Details of follow up in various treatment modalities used

Intervention	Duration of follow up	Good relief in symptoms	Recurrence
Heller's myotomy (<i>n</i> = 122)	2.6 years (15 days to 5 years)	119 (97.5%)	None
Pneumatic dilatation (<i>n</i> = 76)	2.6 years (28 days to 4 years)	74 (97.4%)	46 required repeat dilatation
Per oral endoscopic myotomy (<i>n</i> = 32)	1.1 years (56 days to 2.2 years)	31 (96.9%)	None
Drugs (<i>n</i> = 19)	12–48 days	11 (57.9%)	—

of symptoms is 3 years, and symptoms vary as per the subtype of achalasia.

Type 2 achalasia is the most common variant, followed by types 3 and 1. IRP was higher in patients with type 3 achalasia. These findings are similar to previous Indian studies.⁸ Heller's myotomy and pneumatic dilatation were commonly used treatment options with good symptom response, especially for dysphagia.

The available data on management in achalasia cardia from India is based on single-center experiences. These centers offer specialized high-end diagnostic and therapeutic endoscopy procedures.^{9,10} However, the scenario in routine gastroenterology practice depends on multiple factors such as patient's financial status, limited access to specialized treatment, local expertise, and willingness to undergo specific procedures. We noted that Heller's myotomy was the most common treatment modality used, followed by pneumatic dilatation. All forms of treatment—medication based, surgical, or endoscopic—resulted in symptom improvement. A majority of the patients undergoing pneumatic dilatation required at least two sessions.

Earlier Indian studies have shown that male gender is associated with poor response to dilatation.⁶ As 98% of our

patients had good treatment response, and data were not complete in those with treatment failure, the predictors of nonresponse could not be assessed. Postdilatation Lower Esophageal Sphincter (LES) pressure measurement may be used to guide follow up and treatment.¹¹ In three cases, botulinum toxin injection was used. In one case, it was used to treat recurrence of symptoms postpneumatic dilatation, and in the remaining two cases, comorbid state precluded other therapeutic options. An earlier Indian study has shown that botulinum toxin is as good as pneumatic dilatation in achieving initial improvement in dysphagia of achalasia cardia. It is reported to be effective in patients with tortuous megaesophagus and previous failed pneumatic dilatation. However, symptoms recur within a year.¹²

There are striking variations in demographic trends and symptoms in patients with achalasia cardia across different countries. This suggests the possible role of environmental factors in the causation of disease.¹³ Studies from the West have shown that dysphagia is the most frequent symptom of achalasia. Regurgitation and heartburn are also frequent in these patients. The prevalence, severity, and duration of chest pain does not correlate with the manometry finding of vigorous achalasia.¹⁴ Pandolfino

et al. noted that type II achalasia was the most common subtype in their cohort and more likely to respond to any treatment modality. Type III and pretreatment esophageal dilatation were predictive of negative treatment response.¹⁵

We firmly believe that the choice of treatment modality used in the management of achalasia cardia is greatly influenced by the associated expenditure. Prior to diagnosis, there is a financial burden because of medical tests and decreased work productivity. The treatment is usually expensive, with major costs incurred in those undergoing Heller's myotomy and POEM. These modalities are available at a cost ranging from \$1200 to \$2000 USD across Indian centers. Pneumatic dilatation is cheaper (\$150–250 USD per session), but symptoms tend to recur in a majority of the patients, and then, they may require repeat dilatation or definitive surgery. In the centers where the study was conducted, the money spent on treatment was primarily from patients' pockets, and this greatly influenced the choice of treatment modality used. Apart from this, long-term follow up is needed after treatment to identify recurrence of symptoms or development of reflux and malignancy.

The present study has several limitations such as retrospective study design and nonavailability of treatment data for all patients. Despite our best efforts, there was a high rate of missing data as many patients could not be contacted for follow up. Thus, the outcome data were only analyzed for a subset of patients who were available on follow up. A prospective study would be able to address this issue better. A majority of our patients underwent surgical treatment and pneumatic dilatation as discussed earlier. This choice of treatment is not as per international guidelines. It was influenced by local expertise, availability of the treatment modality, and patient preferences. Data regarding socioeconomic status was not available, and its impact on the choice of treatment modality could not be confirmed. We noted higher incidence of type 3 achalasia, which is probably related to referral bias. Eckardt score could not be assessed in a majority of the cases by telephonic conversation during follow up.

Despite these shortcomings, this multicenter Indian study highlights the current trends in the diagnosis and management of achalasia cardia.

References

- Patel DA, Kim HP, Zifodya JS, Vaezi MF. Idiopathic (primary) achalasia: a review. *Orphanet J. Rare Dis.* 2015; **10**: 89.
- Ramchandani M, Nageshwar Reddy D, Nabi Z *et al.* Management of achalasia cardia: expert consensus statements. *J. Gastroenterol. Hepatol.* 2018; **33**: 1436–44.
- Jain M. Achalasia cardia—A diagnosis often delayed! *Indian J. Gastroenterol.* 2019; **38**: 183–4.
- Jain M, Ware S, Bundiwal A, Sircar S, Jain AK. Etiological spectrum of motor dysphagia as per Chicago Classification—Experience at a tertiary center in Central India. *Indian J. Gastroenterol.* 2015; **34**: 186–7.
- Misra A, Chourasia D, Ghoshal UC. Manometric and symptomatic spectrum of motor dysphagia in a tertiary referral centre in Northern India. *Indian J. Gastroenterol.* 2010; **29**: 18–22.
- Ghoshal UC, Kumar S, Saraswat VA, Aggarwal R, Misra A, Choudhuri G. Long-term follow-up after pneumatic dilatation for achalasia cardia: factors associated with treatment failure and recurrence. *Am. J. Gastroenterol.* 2004; **99**: 2304–10.
- Kahrilas PJ, Bredenoord AJ, Fox M *et al.* International High Resolution Manometry Working Group, The Chicago Classification of esophageal motility disorders—V 3.0. *Neurogastroenterol. Motil.* 2015; **27**: 160–74.
- Pratap N, Kalapala R, Darisetty S *et al.* Achalasia cardia subtyping by high-resolution manometry predicts the therapeutic outcome of pneumatic balloon dilatation. *J. Neurogastroenterol. Motil.* 2011; **17**: 48–53.
- Ramchandani M, Nageshwar Reddy D, Darisetty S *et al.* Peroral endoscopic myotomy for achalasia cardia: Treatment analysis and follow up of over 200 consecutive patients at a single center. *Dig. Endosc.* 2016; **28**: 19–26.
- Nabi Z, Ramchandani M, Chavan R *et al.* Per-oral endoscopic myotomy for achalasia cardia: outcomes in over 400 consecutive patients. *Endosc. Int. Open.* 2017; **5**: E331–9.
- Ghoshal UC, Rangan M, Misra A. Pneumatic dilatation for achalasia cardia: reduction in lower esophageal sphincter pressure in assessing response and factors associated with recurrence during long-term follow up. *Dig. Endosc.* 2012; **24**: 7–15.
- Ghoshal UC, Chaudhuri S, Pal BB, Dhar K, Ray G, Banerjee PK. Randomized controlled trial of intrasphincteric botulinum toxin A injection versus balloon dilatation in treatment of achalasia cardia. *Dis. Esophagus.* 2001; **14**: 227–31.
- Mayberry JF. Epidemiology and demographics of Achalasia. *Gastrointest. Endosc. Clin. N. Am.* 2001; **11**: 235–47.
- Fisichella PM, Raz D, Palazzo F, Niponmick I, Patti MG. Clinical, radiological, and manometric profile in 145 patients with untreated achalasia. *World J. Surg.* 2008; **32**: 1974–9.
- Pandolfino JE, Kwiatek MA, Nealis T, Bulsiewicz W, Post J, Kahrilas PJ. Achalasia: a new clinically relevant classification by high-resolution manometry. *Gastroenterology.* 2008; **135**: 1526–33.