ORIGINAL ARTICLE

Ten-year review of epidemiology, clinical features, and treatment outcome of achalasia in a regional hospital in Hong Kong

CME

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Objective To describe the epidemiology, clinical features, and treatment outcome of achalasia in Chinese patients.

Design Retrospective study.

Setting Major regional hospital, Hong Kong.

Patients Clinical records of patients with the diagnosis of achalasia from July 1997 to June 2007 were reviewed.

Results Thirty-two patients were diagnosed with achalasia during the study period. The mean age at diagnosis was 50 years (standard deviation, 20 years). The female-to-male ratio was 1.3:1. The main presenting symptoms were dysphagia (78%) and vomiting (50%). Nine laparoscopic and two open Heller's operations had been performed and 16 patients had undergone endoscopic dilatations. Four patients had botulinum toxin injection and four were taking calcium channel blocker (nifedipine) medications. Botulinum toxin injection and medical therapy had poor short- and long-term responses. Laparoscopic myotomy and pneumatic dilatation had comparable good short- and long-term responses.

Conclusion Achalasia affected all age-groups but there was a peak at middle age. Pneumatic dilatation and Heller's myotomy (open or laparoscopic approach) appeared able to maintain longer symptom responses than medical therapy and botulinum toxin injection.

Introduction

Achalasia is a well-recognised gastro-intestinal (GI) disorder affecting oesophageal motility, and means 'does not relax' in Greek. It was first reported in 1674 by an English physician, Sir Thomas Willis, who described an Oxford man who vomited "what ever he eats". The patient was treated with a whale bone rod with a small piece of sponge on its end inserted into the oesophagus to relieve the obstruction.[1] Achalasia is a rare disorder that had an annual incidence of approximately 0.5 to 1 cases per 100 000 in western populations; its incidence in the Chinese was lower (0.28 cases per 100 000/year).[2] There is no sex preference. It may affect patients at virtually any age, though it usually presents between the ages of 25 and 60 years.[2] Data regarding its epidemiology and effective treatment in Chinese population are scant.

Key words
Cardia; Esophageal achalasia; Esophageal sphincter, lower; Laparoscopy; Treatment outcome

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Methods

Records of all patients with a diagnosis of achalasia (International Classification of Disease Code 530.0) in Tuen Mun Hospital from 1 July 1997 till 30 June 2007 were retrieved from Clinical Management System, a computerised database utilised by the Hong Kong Hospital Authority. Our hospital is a major regional public hospital with 1405 acute beds, that served a population of 1 095 400 in the year 2006. The diagnosis of achalasia was verified and defined as the absence of peristalsis in the distal oesophagus with impaired lower oesophageal sphincter (LOS) relaxation demonstrated by manometry or typical barium swallowing features in the presence of compatible clinical features. All patients underwent upper endoscopy to rule out the possibility of pseudo-achalasia (obstruction due to malignant infiltration of LOS). Endoscopic ultrasound examination was used to exclude submucosal neoplasm if there were clinical suspicions. In-patient and out-patient records were reviewed to determine the demographic characteristics, clinical features, radiological investigations, manometry report, treatment methods and outcomes.

TABLE 1. Baseline patient characteristics and investigations carried out to confirm the diagnosis of achalasia

Characteristic/investigation	Data (n=32)
Sex (female:male)	18:14
Mean (standard deviation) age (years)	50 (20.0)
Median (range) age of symptom onset (years)	48 (13-90)
Median (range) follow-up period (months)	49 (10-120)
Investigation	
Manometric study	23 (72%)
Barium swallow	22 (69%)
Both manometry and barium swallow	16 (50%)
Computed tomography	8 (25%)
Oesophagogastroduodenoscopy	32 (100%)
Endoscopic ultrasound	5 (16%)

食道弛緩不能症的流行病學、臨床症狀及治療結果：香港一所分區醫院的十年經驗

目的 描述食道弛緩不能症華籍患者的流行病學、臨床症狀及治療結果。

設計 回顧研究。

安排 香港一所主要分區醫院。

患者 1997年7月至2007年6月期間被確診患上食道弛緩不能症的病人病歷紀錄。

結果 研究期間共32位病人患上食道弛緩不能症。病人確診時平均年齡50歲（標準差：20歲），男女比例為1比1.3。病發時主要症狀為吞嚥困難（78%）及嘔吐（50%）。進行了9次腹腔鏡及2次赫勒手術。16人曾進行內鏡下氣囊擴張治療。4人曾接受肉毒毒素注射，另4人服用鈣離子阻斷劑藥物。以短期或長期效果而言，肉毒毒素注射及服用藥物都有較差的治療反應。相反，腹腔鏡肌肉切開術和氣囊擴張術治療失弛緩症則有較佳的治療效果。

結論 食道弛緩不能症的影響遍及所有年齡組別的病人，尤其多見於中年人士。與藥物及肉毒毒素注射比較，氣囊擴張術及赫勒肌肉切開術（開腹或腹腔鏡）似乎能維持較長遠的治療效果。

Statistical analyses

All continuous data were expressed as means or medians with standard deviations (SDs) or maximal and minimal ranges, respectively. Demographic data and symptoms were analysed with respect to different treatment modalities, namely pneumatic dilatation, operative and non-invasive treatments. The differences among three groups were analysed by the Chi squared or Kruskal Wallis tests, for categorical or continuous variables, respectively. The number of hospital admissions and hospitalised days in the pneumatic and operative groups were compared by the Mann-Whitney *U* test. Factors affecting the LOS pressure were analysed by the Chi squared test. The data were compiled and analysed using the Statistical Package for the Social Sciences (Windows version 11.5; SPSS Inc, Chicago [IL], US). All P values were two-sided, and P values of less than 0.05 were considered statistically significant.

Results

Thirty-two patients were newly diagnosed with achalasia during the study period. One patient was excluded because she was referred from another hospital for further follow-up after an operation for achalasia. There were 18 females and 14 males (ratio, 1.3:1). The mean age at diagnosis was 50 (SD, 20) years. The commonest age of symptom onset was 41 to 50 years. Twenty-three (72%) of the patients underwent manometric examination but four failed the test due to lack of cooperation, vomiting, or large amounts of food residue in oesophagus. The median LOS pressure was 36 mm Hg (range, 11-60 mm Hg). Twenty-two (69%) of the patients underwent barium swallows and all showed typical features of achalasia including smooth tapering of the lower oesophagus resembling a 'bird's beak' and a dilated oesophagus. Sixteen (50%) patients underwent both manometry as well as a barium examination. Eight (25%) patients had computed tomography (CT) of the thorax at which a dilated oesophagus with food residue suggestive of achalasia was noted. Five (16%) patients had an endoscopic ultrasound to exclude pseudo-achalasia (Table 1).

Eleven (34%) of the patients underwent operative management (two had open Heller's myotomies and nine were laparoscopic); in nine of them this was the initial treatment offered, whilst two were offered laparoscopic myotomy after a poor response to nifedipine. Sixteen (50%) of the patients underwent 20 sessions of pneumatic dilatation, which was the initial treatment in 12 of them. Eight episodes of dilatation were offered as second- or third-line treatment after failed previous treatments (surgery, pneumatic dilation, nifedipine or botulinum toxin injections). Four (13%) patients were taking medical treatment (nifedipine 5 or 10 mg sublingually before meals). Four (13%) of the patients underwent botulinum injections. Two (6%) of the patients were treated conservatively by insertion of a feeding tube, both of whom were bed-ridden and unable to communicate due to mental retardation or chronic psychosis. One patient refused any kind of treatment; she was 84 years old and died of aspiration pneumonia 26 months after presentation (Fig 1).

Clinical features

The main presenting symptoms of these patients were dysphagia (25 patients), vomiting (16), weight

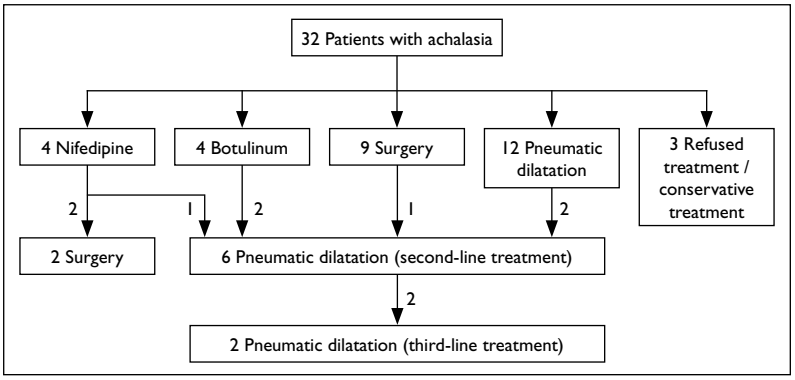

FIG 1. Treatment flowchart

loss (10), and food regurgitation (10). Four (13%) patients presented with extra-GI symptoms; three had a chronic cough, and one had recurrent pneumonias (Fig 2).

Manometric results

Twenty-three (72%) patients had manometric tests. In four patients, the test failed due to lack of cooperation, vomiting, or large amounts of food residue in the oesophagus. All of them showed aperistalsis over distal third of oesophagus and impaired LOS relaxation. The median LOS pressure was 36 mm Hg (range, 11-60 mm Hg). Six patients showed hypertensive LOS pressures (≥46 mm Hg), and 13 were normo-tensive (10-45 mm Hg). There were no difference in age, gender, and presenting symptoms between patients with high and normal pressures.

Treatment response

Response to treatment was defined as no clinical symptom recurrence, or radiological or manometric evidence of recurrence at the time of study closure. Four patients received botulinum injection, but only one appeared to respond. Two underwent subsequent pneumatic dilatation and one refused further treatment. Four patients received nifedipine therapy, none of whom appeared to respond. Three patients underwent surgical treatment or pneumatic dilatation. One patient refused further treatment. Patients treated medically, including those with botulinum injections, were categorised as having non-invasive therapy. Treatment failure was less likely in patients undergoing pneumatic dilatation or surgery than in the non-invasive group (Fig 3, Table 2).

Treatment morbidity and mortality

There was no complication associated with nifedipine treatment and injections. The total number of disease-related hospital admissions and hospitalised days were recorded in patients in invasive category, but those who switched from one modality of treatment to another were excluded. Patients in both treatment categories had similar numbers of admissions and hospitalised days (Table 3). There was only one treatment-related complication; one patient suffered oesophageal perforation after pneumatic dilatation and underwent operative repair. Thus, in this series of pneumatic dilatations, the risk of perforation was 1 in 20 (5%). Two patients died before the end of the study period; one was an 84-year-old woman who refused all forms of treatment and died of aspiration pneumonia, and the other was a 93-year-old woman who failed botulinum injection treatment but responded to pneumatic dilatation. The latter died of pneumonia 32 months after the final pneumatic dilatation. One patient developed symptomatic gastro-oesophageal reflux after an open Heller's operation; her symptoms abated following oral therapy with a proton pump inhibitor.

Discussion

Achalasia affected males and females equally, and at all ages but most often in persons aged 40 to 49 years

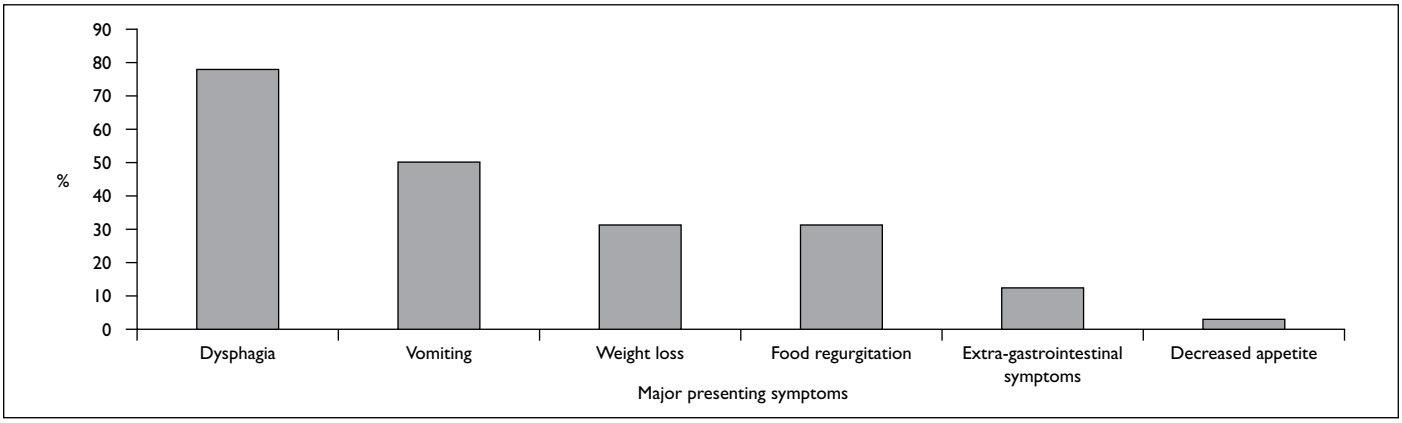

FIG 2. Major presenting symptoms

old. In contrast to British studies,[3,4] our patients did not show a higher rate in older subjects.[3]

In our patients the main presenting symptoms were similar to those reported in the literature, which included dysphagia in 78%, followed by vomiting in 50%, food regurgitation in 31%, weight loss in 31%, and diminished appetite in 3%. However, four (13%) patients complained of extra-GI symptoms, three of whom had a persistent cough and one had recurrent severe pneumonias. Two of these four patients were unable to communicate due to chronic psychosis and mental retardation. In all four patients, achalasia was suspected after thoracic X-rays and CT and confirmed by manometry or barium study. Extra-GI symptoms, particularly pulmonary manifestations, were quite common. Up to 30% complained of nocturnal cough and 8% had bronchopulmonary symptoms.[5] A few case reports have indicated pulmonary symptoms as the leading symptoms of achalasia.[6-8] Most of these were in children as they may not articulate their GI symptoms. In our series, two middle-aged patients had recurrent chest complaints, whilst typical GI symptoms were absent. Physicians should be aware of achalasia as a possible differential diagnosis in patients with unexplained pulmonary symptoms.

In this series, those having pneumatic dilatation and Heller's myotomy (open or laparoscopic) were able to maintain longer symptomatic responses than those after medical therapy and botulinum toxin injection. There was no statistically significant difference in treatment response among those having pneumatic dilatation or Heller's myotomy, which was also concordant with other retrospective comparative studies.[8] Intra-operative mucosal perforation was a well-known complication for myotomy, with the reported rate being 10%.[9] In our series, all cases were performed by the same senior surgeon, who is experienced in laparoscopic myotomy. No intra-operative complication was reported and no procedure was converted to an open approach, but our small sample size may have underestimated the true complication rate.

The addition of fundoplication reduces pathological reflux by 13 to 38%, without influencing postoperative subjective or objective dysphagia outcomes.[10,11] No fundoplication was performed in our cases and only one (13%) patient reported acid reflux for which an oral proton pump inhibitor was prescribed. The cumulative rates of heartburn and reflux disease reported in the literature were 22% after the abdominal approach and 10% following transthoracic surgery.[12] In one series however, no preoperative predictor of postoperative acid reflux could be identified.[13]

Whether to offer achalasia patients initial pneumatic dilatation or to proceed directly to surgery continues to be debated. Intra-operative complications such as mucosal perforation were more common in those having pneumatic dilatation or botox injections. Postoperative complications, such as severe dysphagia and pulmonary complications, were also more common after pneumatic dilatation. Though pneumatically dilated patients were more prone to short-term operative failures,[14] long-term outcomes were similar to those offered surgery as first-line treatment.[15]

There was only one randomised controlled trial that compared laparoscopic myotomy and pneumatic dilatation in the treatment of achalasia.[16] It showed that the former was superior to endoscopic balloon

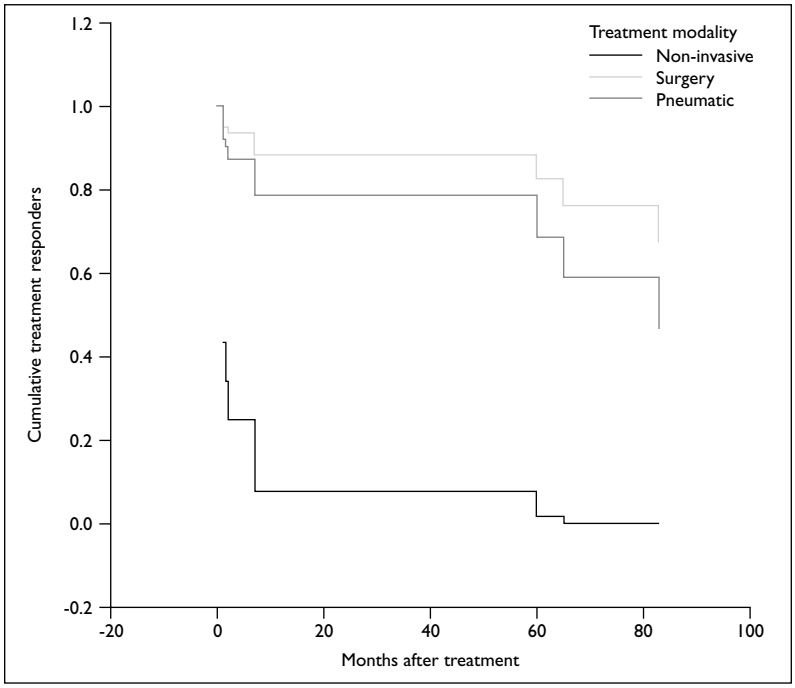

FIG 3. Treatment response according to modality of treatment
Significant test was calculated by Cox regression analysis

TABLE 2. Comparison of failure rates after different treatment modalities

Treatment modalities	Hazard ratio	95% Confidence interval
Pneumatic vs surgery	0.5	0.1-2.7
Pneumatic vs non-invasive	0.1	0.03-0.48
Surgery vs non-invasive	0.5	0.07-0.28

TABLE 3. Number of hospital admissions and days in hospital per year

Patient group	Median (range)	
	No. of admissions/year	Hospitalised days/year
Surgically managed	0.88 (0.53-2.40)	2.7 (1.4-7.3)
Pneumatically dilated	0.95 (0.26-12.50)	2.3 (0.8-54.0)
P value*	0.32	0.38

* Mann-Whitney *U* test

dilatation in the first 12 months in terms of cumulative treatment failures. Conversely, cost-effectiveness studies showed that pneumatic dilatation was in this respect. The main costs for laparoscopic myotomy were the operative costs.[17,18] In our series, the surgical myotomy and pneumatically dilated patients had similar number of hospital admissions/year (0.88 vs 0.95) and days in hospital/year (2.7 vs 2.3). The laparoscopic patients incurred higher operative costs.

Limitations and strengths

This was a retrospective study, such that recall bias could not be avoided. The methods used to diagnose achalasia were heterogeneous; 72% of the patients were diagnosed manometrically and 28% solely by barium studies. Pneumatic dilatation technique varied depending on the operator. The dilatation time ranged from few seconds to minutes. No post-treatment manometric or barium studies were conducted to monitor response and progress.

Although there was previous local report on the long-term results on endoscopic balloon dilatation in patients with achalasia,[19] ours is the first local study to compare outcomes after different modalities of treatment (medical, endoscopic, and surgical) with long follow-up.

Conclusion

Achalasia affected all age-groups but there was a peak at middle age. The pneumatic dilatation and Heller's myotomy (open or laparoscopic approach) appeared to maintain longer symptomatic responses than medical therapy and botulinum toxin injections.

References

1. Kraichely RE, Farrugia G. Achalasia: physiology and etiopathogenesis. Dis Esophagus 2006;19:213-23.
2. Ho KY, Tay HH, Kang JY. A prospective study of the clinical features, manometric findings, incidence and prevalence of achalasia in Singapore. J Gastroenterol Hepatol 1999;14:791-5.
3. Mayberry JF, Atkinson M. Studies of incidence and prevalence of achalasia in the Nottingham area. Q J Med 1985;56:451-6.
4. Mayberry JF, Atkinson M. Variations in the prevalence of achalasia in Great Britain and Ireland: an epidemiological study based on hospital admissions. Q J Med 1987;62:67-74.
5. Vantrappen G, Hellemans J, Deloof W, Valembois P, Vandenbroucke J. Treatment of achalasia with pneumatic dilatations. Gut 1971;12:268-75.
6. Hirata M, Kohno K, Murakami S, et al. A case of recurrent aspiration pneumonia by achalasia [in Japanese]. Nihon Kokyuki Gakkai Zasshi 2002;40:149-53.
7. Kugelman A, Berkowitz D, Best LA, Bentur L. Upper airway obstruction as a presenting sign of achalasia in childhood. Acta Paediatr 2000;89:356-8.
8. Gockel I, Junginger T, Bernhard G, Eckardt VF. Heller myotomy for failed pneumatic dilation in achalasia: how effective is it? Ann Surg 2004;239:371-7.
9. Bessell JR, Lally CJ, Schloithe A, Jamieson GG, Devitt PG, Watson DI. Laparoscopic cardiomyotomy for achalasia: long-term outcomes. ANZ J Surg 2006;76:558-62.
10. Richards WO, Torquati A, Holzman MD, et al. Heller myotomy versus Heller myotomy with Dor fundoplication for achalasia: a prospective randomized double-blind clinical trial. Ann Surg 2004;240:405-15.
11. Falkenback D, Johansson J, Oberg S, et al. Heller's esophagomyotomy with or without a 360 degrees floppy Nissen fundoplication for achalasia. Long-term results from a prospective randomized study. Dis Esophagus 2003;16:284-90.
12. Vaezi MF, Richter JE. Current therapies for achalasia: comparison and efficacy. J Clin Gastroenterol 1998;27:21-35.
13. Rosen MJ, Novitsky YW, Cobb WS, Kercher KW, Heniford BT. Laparoscopic Heller myotomy for achalasia in 101 patients: can successful symptomatic outcomes be predicted? Surg Innov 2007;14:177-83.
14. Smith CD, Stival A, Howell L, Swafford V. Endoscopic therapy for achalasia before Heller myotomy results in worse outcomes than Heller myotomy alone. Ann Surg 2006;243:579-86.
15. Gockel I, Junginger T, Bernhard G, Eckardt VF. Heller myotomy for failed pneumatic dilation in achalasia: how effective is it? Ann Surg 2004;239:371-7.
16. Kostic S, Kjellin A, Ruth M, et al. Pneumatic dilatation or laparoscopic cardiomyotomy in the management of newly diagnosed idiopathic achalasia. Results of a randomized controlled trial. World J Surg 2007;31:470-8.
17. Karanicolas PJ, Smith SE, Inculet RI, et al. The cost of laparoscopic myotomy versus pneumatic dilatation for esophageal achalasia. Surg Endosc 2007;21:1198-206.
18. Kostic S, Johnsson E, Kjellin A, et al. Health economic evaluation of therapeutic strategies in patients with idiopathic achalasia: results of a randomized trial comparing pneumatic dilatation with laparoscopic cardiomyotomy. Surg Endosc 2007;21:1184-9.
19. Chan KC, Wong SK, Lee DW, et al. Short-term and long-term results of endoscopic balloon dilation for achalasia: 12 years' experience. Endoscopy 2004;36:690-4.