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ORIGINAL ARTICLE

Epidemiology and practice patterns of achalasia in Taiwan: A nationwide population-based cohort study

Kai-Liang Lin[a,b,c], Wei-Yu Lin[d], Yen-Po Wang[a,b,c,e,*], Jiing-Chyuan Luo[a,b,c], Ming-Chih Hou[a,b,c], Hui-Chu Lang[d], Ching-Liang Lu[a,b,e,*]

[a]Endoscopy Center for Diagnosis and Treatment, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan, ROC; [b]Division of Gastroenterology, Department of Medicine, Taipei Veterans General Hospital, Taipei, Taiwan, ROC; [c]Faculty of Medicine, School of Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan, ROC; [d]Institute of Hospital and Health Care Administration, National Yang Ming Chiao Tung University, Taipei, Taiwan, ROC; [e]Institute of Brain Science, School of Medicine, National Yang Ming Chiao Tung University, Taipei, Taiwan, ROC.

Abstract

Background: Achalasia is a rare disease of gastrointestinal motility characterized by impaired esophageal peristalsis and reduced esophageal sphincter relaxation. However, data on its epidemiology and outcomes in Taiwan are limited. This study aimed to assess the incidence, characteristics, and clinical management of achalasia in Taiwan.

Methods: Patients who were newly diagnosed with achalasia between 2001 and 2013 were recruited from the Taiwan National Health Insurance Research Database. The study obtained data on the age, sex, urbanization, socioeconomic status, area of residence, diagnostic methods, and interventional management of the patients. Incidence, diagnostic modalities, treatment methods, malignancy, and mortality outcomes were analyzed.

Results: In total, 206 new achalasia cases were identified. The mean annual incidence in Taiwan was 1.64 (95% confidence interval, 1.22-2.05) per 100 000 persons. The mean age of the patients at diagnosis was 51.8 years. The age-specific incidence of achalasia peaked in patients aged between 70 and 80 years and above 80 years. For achalasia diagnosis, endoscopy, computed tomography (CT), barium studies, and manometry were performed in 123 (59.71%), 97 (47.09%), 49 (23.79%), and 11 patients (5.34 %), respectively. During long-term follow-up, seven patients (3.39%) developed esophageal cancer, and 39 patients (18.93%) died. The median survival was 10.65 years after achalasia diagnosis, with a 10-year survival rate of 76.22%.

Conclusion: This is the first population-based epidemiological study on achalasia in Taiwan, revealing the incidence of achalasia before the era of high-resolution manometry. Clinicians should be vigilant about the development of esophageal cancer and mortality during long-term follow-ups. There is also room to enhance the utilization of various diagnostic tools for achalasia.

Keywords: Achalasia; Dysphagia; Epidemiology; Incidence

1. INTRODUCTION

Achalasia is a rare esophageal motility disorder that presents with symptoms, such as dysphagia, food regurgitation, belching, heartburn, and chest pain. It is characterized by impaired relaxation of the lower esophageal sphincter (LES) with absent or spastic esophageal peristalsis.[1] The suggested pathogenesis of achalasia involves inflammation and degeneration of inhibitory ganglion cells in the esophageal smooth muscle, although the precise cause remains unknown.[2] The predominant theory of achalasia has been assumed to be autoimmunity, with viral infections triggering inflammatory targets on esophageal neurons.[3] The insidious nature of achalasia presents substantial challenges for its diagnosis and significantly impacts quality of life.[4]

The global pooled incidence has been estimated to be 0.78 cases per 100 000 person-years (95% confidence interval [CI], 0.64-0.93).[5] However, the incidence varies between countries. In the United States, an administrative claims database study showed a rising trend in achalasia incidence, ranging from 10.5 to 26 per 100 000 person-years,[6] while a medical center-based study in the Chicago area reported stable incidence rates, ranging from 0.77 to 1.35 per 100,000 person-years.[7] England's national patient databases revealed an incidence of 1.53 to 1.99 per 100 000 person-years,[8] while South Australia reported a higher incidence of 2.3 to 2.8 person-year in 2017.[9] Compared with South Australia, the incidence of achalasia was relatively lower in Asian countries. In Japan, the incidence ranged from

*Address correspondence. Dr. Yen-Po Wang, Endoscopy Center for Diagnosis and Treatment, Taipei Veterans General Hospital, 201, Section 2, Shi-Pai Road, Taipei 112, Taiwan, ROC. E-mail address: ulnafu@gmail.com; ypwang@vghtpe.gov.tw, Prof. Ching-Liang Lu, E-mail address: cllu@vghtpe.gov.tw

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The data supporting the findings of this study are available in this article. The raw data supporting the findings in the study area are available from the corresponding author upon request.

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0.81 to 1.37 per 100 000 person-years in 2019 based on data from an insurance claims database.[10] Similarly, the National Healthcare Database of Korea reported a low annual incidence of 0.39 per 100 000 in 2014.[11] A prospective study in Singapore, using conventional manometry, reported an even lower incidence of 0.29 per 100 000 in 1999.[12] These disparate findings highlighted the need for further epidemiological research to clarify patterns and risk factors specific to different populations. Moreover, epidemiological data for the Chinese population are limited, with only a single regional hospital-based case study available that was conducted in Hong Kong in 2010.[13]

Another significant concern in managing achalasia is the risk of esophageal malignancy arising from chronic mucosal inflammation.[14] Studies suggested that prolonged food stasis may cause mucosal irritation, potentially predisposing patients to malignancy.[15] Thus, regular surveillance is essential for timely detection of malignant changes. Treatment options for achalasia have evolved over the decades, including pneumatic balloon dilation, endoscopic botulism injection therapy, surgical esophagomyotomy, and minimally invasive peroral endoscopic myotomy (POEM).[16] However, data about nationwide management patterns and malignancy risk of achalasia patients in Taiwan are lacking.

Thus, a better understanding of the incidence of achalasia can aid in the planning and management of patients with related symptoms. This study aimed to assess the incidence trends, diagnostic modalities, treatment patterns, malignancy, and mortality outcomes in patients with achalasia in Taiwan.

2. METHODS

2.1. Study design and data source

This nationwide retrospective cohort study utilized the Taiwan National Health Insurance Research Database (NHIRD), which included a sampling dataset of 1 million subjects, to identify the patients diagnosed with achalasia. The NHIRD contains registration files and medical claims data covering nearly 99.9% of the population in Taiwan.[17] It provides demographic details, such as age, sex, and urbanization, and clinical information, including diagnostic tests, medications, and interventional management.

2.2. Study population

Patients who were newly diagnosed with achalasia (International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM] code 530.0) between 2001 and 2013 were enrolled. These patients were identified as having at least four outpatient clinic visits or at least one hospitalization record that confirmed the diagnosis. They were followed up longitudinally until death or until December 31, 2013, whichever occurred first.

Given healthcare accessibility and practice patterns in Taiwan, we also performed a sensitivity analysis of achalasia incidence using various case definitions to minimize overestimation and underestimation. The case definitions included: (1) at least one inpatient diagnosis of achalasia, (2) at least one inpatient diagnosis or at least two outpatient diagnoses of achalasia, (3) at least one inpatient diagnosis or at least three outpatient diagnoses of achalasia, and (4) at least one inpatient diagnosis or at least four outpatient diagnoses of achalasia. This allowed us to evaluate the incidence of achalasia using different definitions.

2.3. Patient characteristics

We collected comprehensive demographic and clinical data from the patients diagnosed with achalasia, including age, sex, level of urbanization, socioeconomic status, and area of residence. The diagnostic tests involved in achalasia diagnosis were analyzed using the National Health Insurance (NHI) claim codes, including upper gastrointestinal tract endoscopy (upper gastrointestinal tract panendoscopy or esophageal endoscopy), barium studies (barium esophagography or swallowing video fluorography), computed tomography (CT), conventional manometry, and other tests (nuclear medicine scintigraphy and 24 hours esophageal pH monitoring). For interventional management, endoscopic esophageal dilation or surgical myotomy (thoracoscopic or laparoscopic esophagomyotomy and esophageal myomectomy) was performed. Esophageal cancer within this cohort was tracked using ICD-9-CM code 150. xx.

2.4. Statistical analysis

Descriptive statistical analyses were performed using SAS 9.3 software (SAS Institute Inc., Cary, NC). Frequency distributions, means, and SDs were used to describe patient demographics and clinical characteristics. The incidence of achalasia was calculated by identifying the newly diagnosed cases within the study period. The incidence of achalasia was determined by dividing the number of incident achalasia cases by the total sampled population. Incidence was annualized to facilitate temporal trend analysis and comparison with other regions. Incidence is presented as cases per 100 000 person-years, with estimates calculated in aggregate and by age-sex strata. The age-adjusted incidence rate was calculated by the direct method using the 2000 WHO world standard population.[18]

2.5. Ethics statement

The study protocol adhered to the ethical guidelines of the Declaration of Helsinki and was reviewed and approved by the Institutional Review Board (IRB) of Taipei Veterans General Hospital. In accordance with the NHIRD policy and patient confidentiality regulations, informed consent was waived by the IRB as the participants in the data were all de-identified and permanently unlinked.

3. RESULTS

3.1. Study population demographics

A total of 206 new achalasia cases were identified in the NHIRD database between 2001 and 2013. Among these patients, 109 (52.91%) were female. The average age at diagnosis was 51.8 years, with an SD of 20.18 years. A total of 175 (84.95%) patients resided in urban areas, and 111 patients (53.88%) were classified as having low socioeconomic status. The full demographics are shown in Table 1.

Sensitivity analysis was conducted to define the case definitions of achalasia. Using at least one inpatient diagnosis as a criterion, 71 new achalasia cases were identified. Considering Taiwan's healthcare characteristics, we further used either a one-time inpatient diagnosis or two to four separate outpatient diagnosis codes as diagnostic criteria, which resulted in the identification of 705, 315, and 206 new cases, respectively. To avoid overestimation, we chose at least one inpatient diagnosis or at least four separate outpatient diagnoses as the case definitions of achalasia for this study.

3.2. Incidence of achalasia

The mean annual incidence of achalasia in Taiwan was 1.64 per 100 000 person-years, with a 95% CI of 1.22 to 2.05, ranging from 0.81 to 3.05 per 100 000 person-years (Table 2). The mean incidence rates for male and female patients were 1.75 and 1.52 per 100 000 person-years, respectively. The annual incidence of newly diagnosed achalasia during the study period is shown in Table 2. The highest number of new cases occurred in individuals aged 40 to 49, but the peak age-specific incidence

Table 1

Demographic data of the newly diagnosed patients with achalasia (2001-2013)

	Patient numbers (n = 206)	%
Age (mean, SD)	51.18, 20.18	
Sex		
Female	109	52.91
Male	97	47.09
Urbanization		
Urban	175	84.95
Suburban	24	11.65
Rural	5	2.43
Missing value	2	0.97
Socioeconomic status		
Low	111	53.88
Middle	46	22.33
High	49	23.79
Area		
North	104	50.49
Middle	64	31.07
South	34	16.5
East	4	1.94

was observed in those aged 70 to 80 years and older. The age distribution of patients during the 2001–2013 study period is detailed in Table 3.

3.3. Diagnosis pattern

Various tests have been used to diagnose achalasia. Endoscopy, the most commonly used method, was performed in 123 patients (59.71%). CT scan was performed in 97 patients, and barium studies were performed in 49 (23.79%). Manometry was performed in 11 patients (5.34%). Less frequently used tests included nuclear medicine scintigraphy and 24-hour pH tests, which were used in three (1.46%) and two patients (0.97%), respectively. Detailed information regarding the tests used to diagnose achalasia is presented in Table 4.

3.4. Interventional management trend for achalasia

Among the treatment approaches, balloon dilation was performed in 12 patients, whereas laparoscopic myotomy was performed in 17 patients, indicating a preference for surgical intervention over balloon dilation.

3.5. Risk of esophageal carcinoma and mortality in patients with achalasia

Among the 206 achalasia patients diagnosed between 2001 and 2013, seven (3.39%) developed esophageal cancer, and 39 (18.93%) died during the follow-up period. The annual incidence of esophageal carcinoma in patients with achalasia was calculated to be 490 per 100 000 person-years. The median survival time after achalasia diagnosis was 10.65 years (standard error = 0.258), with a 10-year survival rate of 76.22% (Fig. 1).

4. DISCUSSION

This study presents the first epidemiological analysis of achalasia in the general population of Taiwan. Our data revealed an average incidence of 1.64 cases per 100 000 person-years, a rate lower than that in Australia, comparable to those observed in Western countries and Japan, but higher than in other East Asian nations, including Korea and Singapore.[10–13] It also exceeded the global pooled incidence.[5] Although previous meta-analyses have reported an overall upward trend in the incidence of achalasia,[5] the current study suggests a relatively steady incidence within Taiwan. The slight difference in the crude incidence rates between 2001 and 2013 may reflect variations in diagnostic practices or actual changes in disease epidemiology. The trend observed in our study may partly reflect the limited use of diagnostic tools before the approval of high-resolution manometry by Taiwan's National Health Insurance. In addition, the introduction of the Chicago Classification in 2009 as the standard for diagnosing esophageal motility disorders likely reduced the misclassification of other esophageal motility disorders as achalasia and minimized missed cases. Finally, advancements in identifying secondary causes, such as pseudoachalasia, may have improved the accurate diagnosis of primary achalasia, thereby contributing to the observed reduced incidence. The majority of diagnosed individuals resided in urban areas (84.95%), suggesting better access to medical facilities in these regions.

The age distribution at diagnosis was broad. Our study indicated that achalasia was typically diagnosed in middle age, affecting both sexes almost equally, and peaking among those aged 70 to 80 years and older. These findings were consistent

Table 2

Yearly incidence of the newly diagnosed patients with achalasia (2001-2013)

	Number of incident cases (n = 206)			Incidence (per 100 000 persons)		
Year	Male	Female	Total	Male	Female	Total
2001	14	7	21	3.00	1.49	2.25
2002	15	11	26	3.21	2.35	2.78
2003	15	14	29	3.20	2.90	3.05
2004	7	8	15	1.49	1.65	1.57
2005	13	5	18	2.62	0.99	1.80
2006	5	6	11	1.02	1.19	1.11
2007	3	8	11	0.62	1.59	1.11
2008	5	3	8	1.03	0.60	0.81
2009	10	4	14	2.06	0.80	1.42
2010	2	7	9	0.41	1.41	0.91
2011	8	13	21	1.65	2.61	2.14
2012	7	6	13	1.44	1.21	1.32
2013	5	5	10	1.03	1.01	1.02

Table 3

Age distribution of the newly diagnosed patients with achalasia (2001-2013)

	Number of incident cases (n = 206)		
Age group (y)	Male	Female	Total
0–9	2	7	9
10–19	3	4	7
20–29	7	4	11
30–39	11	11	22
40–49	24	24	48
50–59	20	16	36
60–69	24	10	34
70–79	12	14	26
≥80	6	7	13

Table 4

Tests used in the diagnosis of achalasia

	n	%
Endoscopy	123	59.71
Manometry	11	5.34
Nuclear medicine scintigraphy	3	1.46
24 h pH tests	2	0.97
Radiologic examination	49	23.79
Computed tomography	97	47.09

with those of previous studies demonstrating that the incidence of achalasia increases with age.[19–21] The higher incidence in older age groups could indicate an aging Taiwanese population, delayed diagnosis, and age-related idiopathic degeneration of inhibitory myenteric neurons in the LES.[22,23] A study has shown that older patients with achalasia have higher basal LES pressures, and a linear correlation between age and residual LES pressures has also been observed.[24] Traditionally, elderly people are less likely to seek medical attention, resulting in underdiagnoses and a delay in diagnosis in this age group. However, with the implementation of the NHI program in 1995 and increased health awareness in Taiwan, an increasing number of elderly patients are receiving appropriate medical care. Rapid population aging with declining birth rates in Taiwan,[25] similar to the other parts of Asia, also contributes to the higher incidence in the elderly.

4.1. Diagnosis of achalasia

For a comprehensive diagnosis of achalasia, esophageal manometry, endoscopy, and barium esophagography are essential.[16,26] Previous studies have reported low utilization of manometry for achalasia diagnosis.[27] This may be due to the difficulty in performing manometry, particularly in patients with tortuous or sigmoid-type achalasia, where inserting the catheter into the stomach is difficult.[28] In addition, the interpretation of conventional endoscopy can be challenging, and the paucity of manometric equipment in many hospitals has also contributed to the underutilization of this diagnostic tool. In the current study, only 8.9% of the patients underwent manometry. High-resolution manometry has been shown to increase the diagnostic yield for achalasia compared with conventional manometry[29] and is also easier to interpret.[30] Since March 2021, high-resolution manometry has been approved by Taiwan's National Health Insurance, which may lead to increased future utilization. Timed barium esophagography can help identify esophageal motor function in achalasia patients and evaluate treatment efficacy.[26] Although endoscopic examination can reveal food and fluid retention, it also carries a risk of aspiration. Our study suggested that few patients underwent all three standard diagnostic tests, with many completing only one or none, often because of clinical factors, such as severe vomiting or high-risk conditions. Diagnoses based on symptoms, empirical judgments, or incomplete records were also common, especially before the Chicago Classification was introduced. A comprehensive evaluation using a multimodal approach is essential to accurately diagnose achalasia and its subtypes, and to avoid misdiagnosis of pseudoachalasia.[31]

4.2. Associated risks

An elevated risk of esophageal carcinoma is a notable concern in the management of achalasia. According to an analysis of the Taiwan Cancer Registry, the risk of esophageal carcinoma in the general population was estimated at 14.53 per 100 000 person-years in 2015, which was significantly lower than the incidence observed among the achalasia patients in our findings.[32] Previous studies in other countries have also reported an increased risk of esophageal cancer in individuals with achalasia.[8,14] This elevated risk emphasizes the importance of routine surveillance for esophageal cancer in patients with achalasia.

4.3. Treatment approaches and effectiveness

Our analysis revealed a preference for surgical interventions, such as laparoscopic Heller myotomy (LHM) over pneumatic dilation (PD). However, this study was conducted before the introduction of POEM in Taiwan, and thus did not include data on POEM. A study noted that only 40% of patients treated with a single session of PD remained in remission after 5 years.[33] In Taiwan, PD achieved short-term remission rates of 86.7%, with long-term rates of 61.7%.[34] High rates of repeated interventions were observed following esophageal dilation. Previous research has demonstrated that the 5-year cumulative efficacy of LHM surpasses that of balloon dilation (90.5% vs 47.6%).[35] Recent global trends favor less invasive treatments, such as POEM, which has shown promising clinical remission rates.[36] A Taiwan study reported 100% clinical remission rates in the short term and 95.5% at 2 years, with only 4.3% of patients experiencing symptomatic recurrence during the follow-up period.[37] For achalasia treatment, types I and II achalasia can be managed well with POEM, LHM, or PD, whereas type III achalasia is more effectively managed with POEM.[16,38] In addition to these interventions, pharmacological treatments such as nitrates, calcium channel blockers, and sildenafil play a minor role in achalasia management, offering temporary relief by reducing LES pressure through smooth muscle relaxation. They are typically reserved for patients who are unfit for or unwilling to undergo invasive procedures.[38] Similarly, botulinum toxin injection is a minimally invasive endoscopic treatment for achalasia that lowers LES pressure by inhibiting acetylcholine release with immediate success rates exceeding 90%. Although generally safe, its use is primarily limited by its short-lived efficacy (6-9 months).[39] Botulinum toxin injections remain a viable option for elderly or high-risk patients who are unsuitable for standard interventions. Evolving treatment patterns and preferences warrant further research. In addition, the accessibility of these treatments remains limited to the tertiary hospitals in Taiwan and is not reimbursed by the NHI, highlighting a potential area for policy improvement.

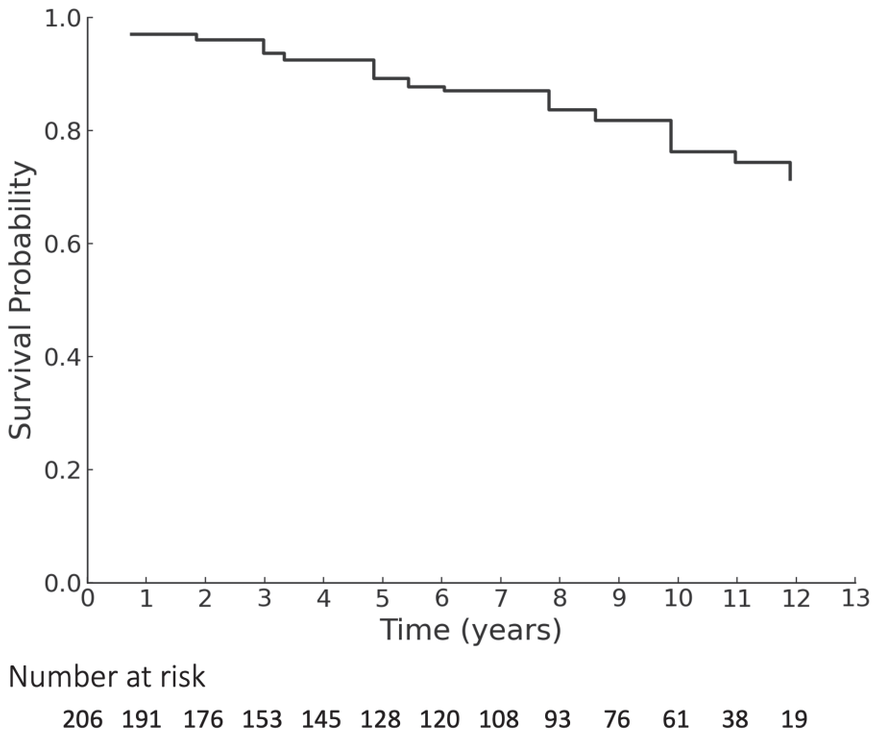

Fig. 1 Kaplan–Meier curve for survival among the patients diagnosed with achalasia.

Our study has several limitations. First, it relied on administrative claims data, which lacked the ability to review and validate diagnostic reports. This disadvantage could compromise diagnostic accuracy owing to the reliance on specific diagnostic codes and the potential inclusion of other esophageal motility diseases. Moreover, detailed clinical information, such as patients' presenting symptoms, laboratory data, clinical courses, achalasia subtypes, and complications, could not be obtained. In addition, our study was conducted before the introduction of high-resolution manometry in Taiwan. Subsequent implementation of high-resolution manometry and systematic diagnostic standards, such as the Chicago Classification, may reveal higher incidence rates. Previous meta-analyses indicated a significant increase in incidence after 2009 compared with previous years (1.48 vs 1.02 cases per 100 000 person-years). However, the rates from different periods—2000–2009 (1.45 cases per 100 000 person-years), 2010–2013 (1.51 cases), 2014–2017 (1.37 cases), and 2018–2021 (1.64 cases)—showed only slight differences.[5] Therefore, while diagnostic innovations may influence the reported incidence rates, they likely do not substantially underestimate them.

In conclusion, this is the first population-based epidemiological study of achalasia in Taiwan conducted before the era of high-resolution manometry, showing an incidence similar to that in Japan, England, and the United States. The incidence of achalasia increases with age and is higher among patients living in urban areas or those with low socioeconomic status. Clinicians should be vigilant about the development of esophageal cancer and mortality during long-term follow-ups. The findings of this study have significant implications for clinical practice and public health policies in Taiwan. In addition, there is scope to enhance the utilization of diagnostic tools, including high-resolution manometry, radiological examinations, and endoscopy, for the diagnosis of achalasia.

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