

# World Journal of *Gastroenterology*

*World J Gastroenterol* 2017 May 14; 23(18): 3195-3378



**EDITORIAL**

- 3195** Liver transplantation for intermediate hepatocellular carcinoma: An adaptive approach

*Biolato M, Marrone G, Miele L, Gasbarrini A, Grieco A*

- 3205** Immune response to vaccines in children with celiac disease

*Anania C, Olivero F, Spagnolo A, Chiesa C, Pacifico L*

**REVIEW**

- 3214** Inflammatory bowel disease in liver transplanted patients

*Filipek Kanizaj T, Mijic M*

- 3228** Platelets in liver disease, cancer and regeneration

*Kurokawa T, Ohkohchi N*

**ORIGINAL ARTICLE****Basic Study**

- 3240** Thiopurine use associated with reduced B and natural killer cells in inflammatory bowel disease

*Lord JD, Shows DM*

- 3252** Hepatitis B virus X protein induces hepatic stem cell-like features in hepatocellular carcinoma by activating KDM5B

*Wang X, Oishi N, Shimakami T, Yamashita T, Honda M, Murakami S, Kaneko S*

- 3262** Artificial liver support in pigs with acetaminophen-induced acute liver failure

*He GL, Feng L, Cai L, Zhou CJ, Cheng Y, Jiang ZS, Pan MX, Gao Y*

- 3269** Effects of sleeve gastrectomy plus trunk vagotomy compared with sleeve gastrectomy on glucose metabolism in diabetic rats

*Liu T, Zhong MW, Liu Y, Huang X, Cheng YG, Wang KX, Liu SZ, Hu SY*

- 3279** Wall shear stress in portal vein of cirrhotic patients with portal hypertension

*Wei W, Pu YS, Wang XK, Jiang A, Zhou R, Li Y, Zhang QJ, Wei YJ, Chen B, Li ZF*

**Case Control Study**

- 3287** Risk of progression of Barrett's esophagus in patients with cirrhosis

*Apfel T, Lopez R, Sanaka MR, Thota PN*

### Retrospective Study

- 3295 Clinical significance of hypoechoic submandibular gland lesions in type 1 autoimmune pancreatitis  
*Takano S, Fukasawa M, Kadokura M, Shindo H, Takahashi E, Hirose S, Fukasawa Y, Kawakami S, Sato T, Enomoto N*
- 3301 Benefit of neoadjuvant concurrent chemoradiotherapy for locally advanced perihilar cholangiocarcinoma  
*Jung JH, Lee HJ, Lee HS, Jo JH, Cho IR, Chung MJ, Park JY, Park SW, Song SY, Bang S*
- 3309 Ling classification describes endoscopic progressive process of achalasia and successful peroral endoscopy myotomy prevents endoscopic progression of achalasia  
*Zhang WG, Linghu EQ, Chai NL, Li HK*

### Observational Study

- 3315 Disruptive behavior in the workplace: Challenges for gastroenterology fellows  
*Srisarajivakul N, Lucero C, Wang XJ, Poles M, Gillespie C, Zabara S, Weinshel E, Malter L*
- 3322 Correlation of endoscopic disease severity with pediatric ulcerative colitis activity index score in children and young adults with ulcerative colitis  
*Kerur B, Litman HJ, Stern JB, Weber S, Lightdale JR, Rufo PA, Bousvaros A*
- 3330 Stress and sleep quality in doctors working on-call shifts are associated with functional gastrointestinal disorders  
*Lim SK, Yoo SJ, Koo DL, Park CA, Ryu HJ, Jung YJ, Jeong JB, Kim BG, Lee KL, Koh SJ*

### Prospective Study

- 3338 *In vivo* and *ex vivo* confocal endomicroscopy of pancreatic cystic lesions: A prospective study  
*Krishna SG, Modi RM, Kamboj AK, Swanson BJ, Hart PA, Dillhoff ME, Manilchuk A, Schmidt CR, Conwell DL*
- 3349 Chronological age when healthcare transition skills are mastered in adolescents/young adults with inflammatory bowel disease  
*Stollon N, Zhong Y, Ferris M, Bhansali S, Pitts B, Rak E, Kelly M, Kim S, van Tilburg MAL*

### Randomized Controlled Trial

- 3356 Low-FODMAP diet reduces irritable bowel symptoms in patients with inflammatory bowel disease  
*Pedersen N, Ankersen DV, Felding M, Wachmann H, Végh Z, Molzen L, Burisch J, Andersen JR, Munkholm P*

### EVIDENCE-BASED MEDICINE

- 3367 Antimicrobial susceptibility testing before first-line treatment for *Helicobacter pylori* infection in patients with dual or triple antibiotic resistance  
*Cosme A, Montes M, Ibarra B, Tamayo E, Alonso H, Mendarte U, Lizasoan J, Herreros-Villanueva M, Bujanda L*

**CASE REPORT**

- 3374** Severe esophageal injury after radiofrequency ablation - a deadly complication

*Katz-Agranov N, Nevah Rubin MI*

## ABOUT COVER

Editorial board member of *World Journal of Gastroenterology*, Ballarin Roberto, PhD, Assistant Professor, Doctor, Surgeon, Hepatobiliopancreatic Oncologic Surgery and Liver Transplant Center, University of Modena, Modena 41100, Italy

## AIMS AND SCOPE

*World Journal of Gastroenterology* (*World J Gastroenterol*, *WJG*, print ISSN 1007-9327, online ISSN 2219-2840, DOI: 10.3748) is a peer-reviewed open access journal. *WJG* was established on October 1, 1995. It is published weekly on the 7<sup>th</sup>, 14<sup>th</sup>, 21<sup>st</sup>, and 28<sup>th</sup> each month. The *WJG* Editorial Board consists of 1375 experts in gastroenterology and hepatology from 68 countries.

The primary task of *WJG* is to rapidly publish high-quality original articles, reviews, and commentaries in the fields of gastroenterology, hepatology, gastrointestinal endoscopy, gastrointestinal surgery, hepatobiliary surgery, gastrointestinal oncology, gastrointestinal radiation oncology, gastrointestinal imaging, gastrointestinal interventional therapy, gastrointestinal infectious diseases, gastrointestinal pharmacology, gastrointestinal pathophysiology, gastrointestinal pathology, evidence-based medicine in gastroenterology, pancreatology, gastrointestinal laboratory medicine, gastrointestinal molecular biology, gastrointestinal immunology, gastrointestinal microbiology, gastrointestinal genetics, gastrointestinal translational medicine, gastrointestinal diagnostics, and gastrointestinal therapeutics. *WJG* is dedicated to become an influential and prestigious journal in gastroenterology and hepatology, to promote the development of above disciplines, and to improve the diagnostic and therapeutic skill and expertise of clinicians.

## INDEXING/ABSTRACTING

*World Journal of Gastroenterology* (*WJG*) is now indexed in Current Contents<sup>®</sup>/Clinical Medicine, Science Citation Index Expanded (also known as SciSearch<sup>®</sup>), Journal Citation Reports<sup>®</sup>, Index Medicus, MEDLINE, PubMed, PubMed Central, Digital Object Identifier, and Directory of Open Access Journals. The 2015 edition of Journal Citation Reports<sup>®</sup> released by Thomson Reuters (ISI) cites the 2015 impact factor for *WJG* as 2.787 (5-year impact factor: 2.848), ranking *WJG* as 38 among 78 journals in gastroenterology and hepatology (quartile in category Q2).

## FLYLEAF

### I-IX Editorial Board

## EDITORS FOR THIS ISSUE

Responsible Assistant Editor: *Xiang Li*  
Responsible Electronic Editor: *Cui-Hong Wang*  
Proofing Editor-in-Chief: *Lian-Sheng Ma*

Responsible Science Editor: *Yuan Qi*  
Proofing Editorial Office Director: *Jin-Lei Wang*

NAME OF JOURNAL  
*World Journal of Gastroenterology*

ISSN  
ISSN 1007-9327 (print)  
ISSN 2219-2840 (online)

LAUNCH DATE  
October 1, 1995

FREQUENCY  
Weekly

### EDITORS-IN-CHIEF

**Damian Garcia-Olmo, MD, PhD, Doctor, Professor, Surgeon**, Department of Surgery, Universidad Autonoma de Madrid; Department of General Surgery, Fundacion Jimenez Diaz University Hospital, Madrid 28040, Spain

**Stephen C Strom, PhD, Professor**, Department of Laboratory Medicine, Division of Pathology, Karolinska Institutet, Stockholm 141-86, Sweden

**Andrzej S Tarnawski, MD, PhD, DSc (Med), Professor of Medicine, Chief Gastroenterology**, VA Long Beach Health Care System, University of California, Irvine, CA, 5901 E. Seventh Str., Long Beach,

CA 90822, United States

### EDITORIAL BOARD MEMBERS

All editorial board members resources online at <http://www.wjgnet.com/1007-9327/editorialboard.htm>

### EDITORIAL OFFICE

Jin-Lei Wang, Director  
Yuan Qi, Vice Director  
Ze-Mao Gong, Vice Director  
*World Journal of Gastroenterology*  
Baishideng Publishing Group Inc  
7901 Stoneridge Drive, Suite 501,  
Pleasanton, CA 94588, USA  
Telephone: +1-925-2238242  
Fax: +1-925-2238243  
E-mail: [editorialoffice@wjgnet.com](mailto:editorialoffice@wjgnet.com)  
Help Desk: <http://www.f6publishing.com/helpdesk>  
<http://www.wjgnet.com>

### PUBLISHER

Baishideng Publishing Group Inc  
7901 Stoneridge Drive, Suite 501,  
Pleasanton, CA 94588, USA  
Telephone: +1-925-2238242  
Fax: +1-925-2238243  
E-mail: [bpoffice@wjgnet.com](mailto:bpoffice@wjgnet.com)  
Help Desk: <http://www.f6publishing.com/helpdesk>

<http://www.wjgnet.com>

PUBLICATION DATE  
May 14, 2017

### COPYRIGHT

© 2017 Baishideng Publishing Group Inc. Articles published by this Open-Access journal are distributed under the terms of the Creative Commons Attribution Non-commercial License, which permits use, distribution, and reproduction in any medium, provided the original work is properly cited, the use is non commercial and is otherwise in compliance with the license.

### SPECIAL STATEMENT

All articles published in journals owned by the Baishideng Publishing Group (BPG) represent the views and opinions of their authors, and not the views, opinions or policies of the BPG, except where otherwise explicitly indicated.

### INSTRUCTIONS TO AUTHORS

Full instructions are available online at <http://www.wjgnet.com/bpg/gerinfo/204>

ONLINE SUBMISSION  
<http://www.f6publishing.com>

## Retrospective Study

# Ling classification describes endoscopic progressive process of achalasia and successful peroral endoscopy myotomy prevents endoscopic progression of achalasia

Wen-Gang Zhang, En-Qiang Linghu, Ning-Li Chai, Hui-Kai Li

Wen-Gang Zhang, En-Qiang Linghu, Ning-Li Chai, Hui-Kai Li, Department of Gastroenterology, Chinese PLA General Hospital, Beijing 100853, China

**Author contributions:** Zhang WG analyzed the data and wrote the manuscript; Chai NL acquired the data; Linghu EQ and Li HK made a classification of all the achalasia patients in the present study according to Ling classification.

**Institutional review board statement:** The study was carried out under the ethics committee approval from the Chinese PLA General Hospital (Beijing, China).

**Informed consent statement:** Informed consent was waived due to the retrospective nature of this study.

**Conflict-of-interest statement:** We declare that we have no financial or personal relationships with other people or organizations that can inappropriately influence our work.

**Data sharing statement:** No additional data are available.

**Open-Access:** This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

**Manuscript source:** Unsolicited manuscript

**Correspondence to:** En-Qiang Linghu, MD, Department of Gastroenterology, Chinese PLA General Hospital, No. 28, Fuxing Road, Haidian District, Beijing 100853, China. [linghuenqiang@vip.sina.com](mailto:linghuenqiang@vip.sina.com)  
Telephone: +86-13501233558  
Fax: +86-10-66937485

Received: January 4, 2017

Peer-review started: January 5, 2017

First decision: January 19, 2017

Revised: February 1, 2017

Accepted: March 30, 2017

Article in press: March 30, 2017

Published online: May 14, 2017

## Abstract

### AIM

To verify the hypothesis that the Ling classification describes the endoscopic progressive process of achalasia and determine the ability of successful peroral endoscopic myotomy (POEM) to prevent endoscopic progression of achalasia.

### METHODS

We retrospectively reviewed the endoscopic findings, symptom duration, and manometric data in patients with achalasia. A total of 359 patients (197 women, 162 men) with a mean age of 42.1 years (range, 12-75 years) were evaluated. Symptom duration ranged from 2 to 360 mo, with a median of 36 mo. Patients were classified with Ling type I ( $n = 119$ ), II a ( $n = 106$ ), II b ( $n = 60$ ), II c ( $n = 60$ ), or III ( $n = 14$ ), according to the Ling classification. Of the 359 patients, 349 underwent POEM, among whom 21 had an endoscopic follow-up for more than 2 years. Pre-treatment and post-treatment Ling classifications of these 21 patients were compared.

### RESULTS

Symptom duration increased significantly with increasing Ling classification (from I to III) ( $P < 0.05$ ), whereas lower esophageal sphincter pressure decreased with increasing Ling type (from I to III) ( $P < 0.05$ ). There was no difference in sex ratio or onset age among the Ling types, although the age at time of diagnosis was

higher in Ling types IIc and III than in Ling types I, IIa, and IIb. Of the 21 patients, 19 underwent high-resolution manometry both before and after treatment. The mean preoperative and postoperative lower esophageal sphincter pressure were 34.6 mmHg (range, 15.3-59.4 mmHg) and 15.0 mmHg (range, 2.1-21.6 mmHg), respectively, indicating a statistically significant decrease after POEM. All of the 21 patients were treated successfully by POEM (postoperative Eckardt score  $\leq 3$ ) and still had the same Ling type during a mean follow-up period of 37.8 mo (range, 24-51 mo).

## CONCLUSION

The Ling classification represents the endoscopic progressive process of achalasia and may be able to serve as an endoscopic assessment criterion for achalasia. Successful POEM (Eckardt score  $\leq 3$ ) seems to have the ability to prevent endoscopic evolution of achalasia. However, studies with larger populations are warranted to confirm our findings.

**Key words:** Ling classification; Achalasia; Progression; Peroral endoscopic myotomy; Endoscopy

© The Author(s) 2017. Published by Baishideng Publishing Group Inc. All rights reserved.

**Core tip:** Achalasia is a progressive disease, as verified by manometric and radiographic findings. Thus, we speculated that this progressive process could be visualized by endoscopy. We have proposed the Ling classification for achalasia on the basis of the endoscopic morphological severity of the esophagus. This study supports the hypothesis that the Ling classification portrays the progressive process of achalasia. Preliminary evidence suggests that successful peroral endoscopic myotomy (POEM) has the ability to prevent endoscopic progression of achalasia. Moreover, this study suggests that the Ling classification may serve as a criterion for endoscopic assessment of achalasia and will be useful for long-term endoscopic follow-up of post-POEM achalasia.

Zhang WG, Linghu EQ, Chai NL, Li HK. Ling classification describes endoscopic progressive process of achalasia and successful peroral endoscopy myotomy prevents endoscopic progression of achalasia. *World J Gastroenterol* 2017; 23(18): 3309-3314 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v23/i18/3309.htm> DOI: <http://dx.doi.org/10.3748/wjg.v23.i18.3309>

## INTRODUCTION

Achalasia is a rare esophageal motility disorder characterized by symptoms of dysphagia, regurgitation, weight loss, and chest pain<sup>[1,2]</sup>. Achalasia is a progressive disease, as demonstrated by manometric and radiographic findings<sup>[3]</sup>. Thus, it can be inferred

that there is also a progressive process of achalasia as revealed by endoscopy. Dr. En-Qiang Linghu has proposed the Ling classification for achalasia based on the endoscopic morphological severity of the esophagus. We hypothesized that the Ling classification could be used to describe the endoscopic progressive process of achalasia.

Peroral endoscopic myotomy (POEM) has been shown to be an effective and safe procedure for achalasia and is quickly becoming one of the first-line therapies for achalasia<sup>[4-6]</sup>. However, it remains unclear whether this procedure can prevent endoscopic progression of achalasia. Criteria to assess long-term endoscopic follow-up of post-POEM achalasia are still lacking. The present study aimed to verify the hypothesis that the Ling classification depicts the endoscopic progressive process of achalasia and to determine the ability of successful POEM to prevent the endoscopic evolution of achalasia.

## MATERIALS AND METHODS

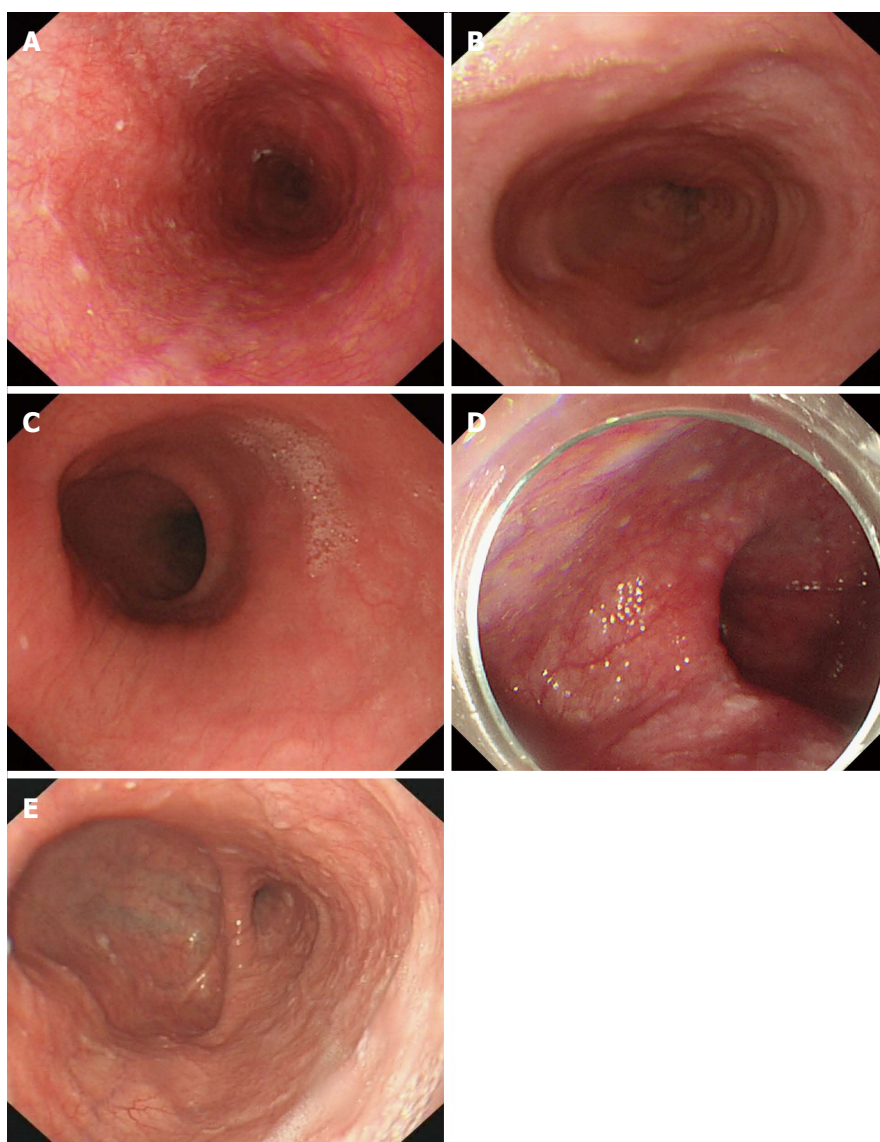
### Patients

A total of 359 patients (197 women and 162 men) with a mean age of 42.1 years (range, 12-75 years) were evaluated. High-resolution manometry (HRM), endoscopy, and barium swallow were performed to confirm the diagnosis of achalasia. The duration of symptoms ranged from 2 to 360 mo, with a median of 36 mo. Patients were classified with Ling type I, IIa, IIb, IIc, or III, according to the Ling classification<sup>[7]</sup>. Duration of symptoms and lower esophageal sphincter pressure (LESP) were compared among the five Ling types. Of the 359 patients, 349 underwent POEM, among whom 21 had an endoscopic follow-up for more than 2 years. Pre-treatment and post-treatment Ling types of the 21 patients with long-term follow-up were compared.

### Ling classification

Dr. Linghu proposed the Ling classification in 2011 and published it in 2013<sup>[7]</sup>. The Ling classification includes three types: type I, no multi-ring, crescent-like structure or diverticulum structure; type II, the presence of multi-ring or crescent-like structure but without diverticulum structure; and type III, the presence of diverticulum structure. Type II was further classified into three subtypes: IIa, IIb and IIc. The criteria for classifying Ling type II subtypes were as follows: Ling IIa, the presence of multi-ring structure; Ling IIb, the presence of crescent-like structure and the midpoint of its inner edge not larger than 1/3 of the esophageal lumen; Ling IIc, the presence of crescent-like structure and the midpoint of its inner edge over 1/3 of the esophageal lumen (Figure 1). The endoscopy reports of all 359 patients were collected and classified according to the diagnostic information by two endoscopists (Li HK and Linghu EQ), according





**Figure 1** Typical pictures of Ling classification. A: Ling I; B: Ling II a; C: Ling II b; D: Ling II c; E: Ling III.

to the criteria mentioned above. Of note, both endoscopists were blinded to the other data collected from each patient.

### **Duration of symptoms**

The duration of symptoms for each of the 359 patients was collected from medical records. The definition used for the appearance of symptoms was dysphagia or chest pain for  $\geq 4$  d of the week. All patients had been inquired about case history based on the definition mentioned above.

### **HRM**

HRM was performed using the following protocol: a 36-channel, solid-state catheter system with high-fidelity circumferential sensors at 1-cm intervals (Manosacn; Sierra Scientific Instruments Inc, Los Angeles, CA, United States) was advanced through the nasal canal. Studies were performed with patients in a supine position after

at least a 6-h fast. Pressure data of 10 wet swallows were recorded and analyzed using a dedicated computerized analysis system.

### **POEM procedure and follow-up**

During the procedure, patients were kept in the supine position with the right shoulder elevated. General anesthesia was administered while the patient's respirations, blood pressure, oxygen saturation, and electrocardiogram were monitored. An additional cap attached at the top of the endoscope was required. Then, POEM was performed as follows. First, a submucosal injection of methylene blue saline solution (1:10000) was administered, and a mucosal incision was made at the right posterior esophageal wall, approximately 6-10 cm from the gastroesophageal junction (GEJ). Then, a submucosal tunnel was established, passing over the GEJ and about 2-3 cm into the proximal stomach. Myotomy started at 2 cm



**Table 1** Demographic characteristics of patients presenting with achalasia *n* (%)

Characteristic	Value
Sex, female/male ( <i>n</i> )	197/162
Age (yr), mean (range)	42.1 (12-75)
Duration of symptoms (mo), median (range)	36 (2-360)
Lower esophageal sphincter pressure (mmHg), mean (range)	33.0 (0.7-72.4)
Ling classification	
I	119 (33.1)
II a	106 (29.5)
II b	60 (16.7)
II c	60 (16.7)
III	14 (3.9)

distal to the incision and extended 2-3 cm into the stomach. After complete hemostasis and ensuring that an endoscope could easily pass the cardia of the stomach, the mucosal incision was sutured with approximately 5 hemostatic clips.

Patients were scheduled for a follow-up visit at 3 mo, 6 mo, and 1 year postoperatively, and yearly afterwards. Endoscopy, HRM, and 24-h esophageal pH monitoring were required at each follow-up.

### Statistical analysis

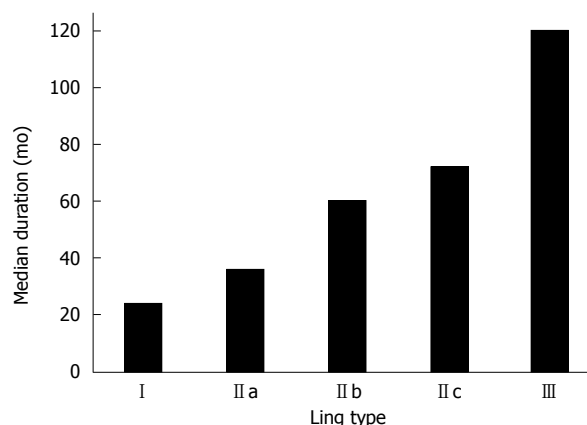
All statistical analyses were performed using SPSS software version 17.0. Variables are expressed as mean or median. The Kruskal-Wallis test or single factor analysis of variance was used to compare the onset age, age at time of diagnosis, duration of symptoms, and LESF among the five Ling types.  $\chi^2$  test was used to compare the sex ratio among the five Ling types. All reported *P*-values are two-tailed, with *P*-values < 0.05 considered statistically significant.

## RESULTS

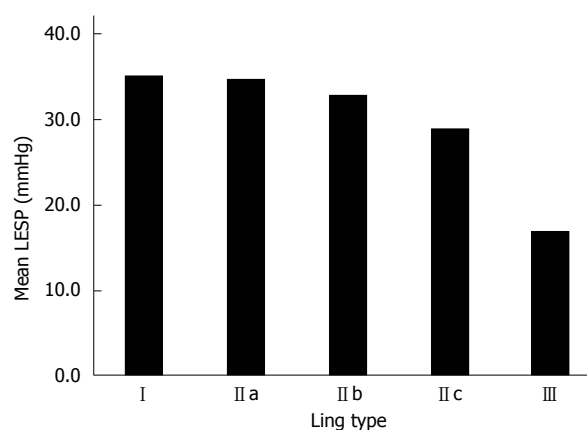
As shown in Table 1, a total of 359 patients (197 women and 162 men) with a mean age of 42.1 years (range, 12-75 years) were evaluated. The duration of symptoms ranged from 2 to 360 mo, with a median of 36 mo. Of the 359 patients, 119 were classified with Ling I, 106 with Ling II a, 60 with Ling II b, 60 with Ling II c, and 14 with Ling III.

The duration of symptoms increased significantly when the Ling classification increased (from I to III) (*P* < 0.05), as shown in Figure 2. LESF decreased with increasing Ling classification (from I to III) (*P* < 0.05) as shown in Figure 3. There was no difference in sex ratio or onset age among the Ling types, although the age at time of diagnosis was higher in Ling types II c and III than in Ling types I, II a, and II b (Table 2).

Of the 359 patients, 349 underwent POEM, among whom 21 had an endoscopic follow-up longer than 2 years. The demographics and treatment outcomes of the 21 patients (9 women, 12 men) with a post-POEM follow-



**Figure 2** Symptom duration increased significantly when the Ling classification increased (from I to III) (*P* < 0.05).



**Figure 3** Lower esophageal sphincter pressure decreased when the Ling classification increased (from I to III) (*P* < 0.05). LESF: Lower esophageal sphincter pressure.

up more than 2 years are shown in Table 3. Of the 21 patients, 8 were classified with Ling type I preoperatively, 7 with Ling type II a, 5 with Ling type II b, and 1 with Ling type III. Of the 21 patients, 19 had HRM both before and after treatment. The mean preoperative and postoperative LESF were 34.6 mmHg (range, 15.3-59.4 mmHg) and 15.0 mmHg (range, 2.1-21.6 mmHg), respectively, indicating a statistically significant decrease after POEM. All of the 21 patients were treated successfully by POEM (postoperative Eckardt score ≤ 3) and still had the same Ling type during a mean follow-up period of 37.8 mo (range, 24-51 mo).

## DISCUSSION

Achalasia is a progressive disorder as measured by manometric and radiographic findings<sup>[3]</sup>. Thus, there should exist a progressive process of achalasia as visualized by endoscopy. We have previously proposed the Ling classification for achalasia based on the endoscopic morphological severity of the esophagus<sup>[7]</sup>. Therefore, we hypothesized that the Ling classification can be used to assess the endoscopic progressive

**Table 2** Comparison of symptom duration, lower esophageal sphincter pressure, and dysphagia score among Ling classifications

Ling type	I	II a	II b	II c	III	P value
<i>n</i>	119	106	60	60	14	
Onset age (yr), mean	35.3	38.9	36.1	36.4	32.9	> 0.05
Age at time of diagnosis (yr), mean	38.5	42.8	43.8	46.4	45.4	< 0.05
Sex (female/male)	65/54	60/46	32/28	35/25	5/9	> 0.05
Duration (mo), median	24	36	60	72	120	< 0.05
LESP (mmHg), mean	35	34.7	32.8	28.9	16.9	< 0.05

LESP: Lower esophageal sphincter pressure.

**Table 3** Demographics and treatment outcomes of the 21 patients with a post-peroral endoscopic myotomy follow-up for > 2 years *n* (%)

Characteristic	Value
Sex, female/male ( <i>n</i> )	9/12
Age (yr), mean (range)	43.8 (16-62)
Duration of symptoms (mo), median (range)	36 (6-120)
Endoscopic follow-up (mo), mean (range)	37.8 (24-51)
Manometry follow-up rate	19 (90.5)
Lower esophageal sphincter pressure (mmHg), mean (range)	
Pre-treatment	34.6 (15.3-59.4)
Post-treatment	15.0 (2.1-21.6)
Ling classification	
I	8 (38.1)
II a	7 (33.3)
II b	5 (23.8)
II c	0 (0)
III	1 (4.8)
Treatment success rate (Eckardt score ≤ 3)	21 (100)

process of achalasia. The present study provided evidence supporting this hypothesis by comparing the duration of symptoms and LESP among the different Ling types.

Shiino *et al*<sup>[3]</sup> published a study in which patients with achalasia were divided into four groups according to the duration of symptoms: less than 5 years; 5 to 10 years; 10 to 15 years, and 15 years or longer. This study found that the tortuosity of the esophagus, as measured by the maximal angle of the esophageal axis on radiography, was significantly greater in patients with a longer duration of symptoms ( $P < 0.02$ ). Henderson<sup>[8]</sup> classified achalasia into three stages according to the degree of esophageal dilatation on X-ray. Stage 1 has a diameter less than 4 cm, stage 2 has a diameter of 4-6 cm, and stage 3 has a diameter greater than 6 cm. A greater degree of esophageal dilation was shown to be related to the duration of symptoms. The present study found that duration of symptoms increased significantly for every type using the Ling classification (from I to III) ( $P < 0.05$ ). Given that morphological severity of the esophagus increases from Ling type I to Ling type III, the results of the present study are compatible with both Yutaka's and Henderson's studies. However, while these previous studies were based on radiography, the present study was able to evaluate the endoscopic progressive

process of achalasia by direct visualization.

LESP decreased with increasing Ling classification (from I to III) ( $P < 0.05$ ). Shiino *et al*<sup>[3]</sup> reported that LESP decreased as the duration of symptoms increased, although the results were not significant. Given that the present study confirmed the association between longer duration of symptoms and increasing Ling classification (from I to III) ( $P < 0.05$ ), the results of the present study and Yutaka's support each other. However, the association between decreasing LESP with increasing symptom duration still requires to be confirmed by a further prospective study.

POEM was first reported as a treatment for achalasia in 2010<sup>[9]</sup> and has developed rapidly since then. Despite the evidence that POEM is effective and safe, it remains unclear whether the esophageal morphology in achalasia patients changes postoperatively. In the present study, a total of 21 patients had an endoscopic follow-up period more than 2 years after POEM. All 21 patients had their achalasia successfully treated (Eckardt score ≤ 3) and still had the same Ling type throughout a mean follow-up period of 37.8 mo (range, 24-51 mo), suggesting that POEM may prevent the endoscopic progression of achalasia. However, the sample size (21 patients) of our analysis was relatively small because most of the 349 patients who underwent POEM at our hospital did not undergo endoscopic follow-up beyond two years postoperatively. Thus, a prospective study with a larger sample is required to further confirm the conclusions based on the results above. Another limitation is that there is a lack of criteria to assess endoscopic follow-up of post-POEM achalasia. Furthermore, given that POEM has been utilized for only 6 years, the long-term (≥ 7 years) efficacy, especially with regard to esophageal morphology changes, remains uncertain. The Ling classification may be a good choice of criteria to endoscopically assess post-POEM achalasia.

Performing POEM for advanced achalasia, such as Ling types II c-III or sigmoid-type achalasia, is more challenging. Thus, patients with achalasia should undergo POEM soon after diagnosis because of the progressive nature of the disease, which has been confirmed in previous studies and the present study<sup>[3]</sup>.

One limitation to our study was the retrospective nature of our methods; however, the Ling classification, duration of symptoms, and LESP were recorded prospectively. Another limitation was that only 21

patients had an endoscopic follow-up for more than 2 years. To the best of our knowledge, this is the first study reporting the long-term postoperative esophageal morphological changes as visualized by endoscopy in patients with achalasia.

In conclusion, the Ling classification captures the endoscopic progressive process of achalasia and might be able to serve as criteria to assess achalasia endoscopically. Successful POEM may prevent the endoscopic evolvement of achalasia. However, future longitudinal studies with larger samples are warranted.

## COMMENTS

### Background

It has been proved that achalasia is a progressive disease, as verified by manometric and radiographic findings. Based on this knowledge, it could be speculated that there is also an endoscopic progressive process of achalasia.

### Research frontiers

The authors have proposed the Ling classification for achalasia in 2011, based on the endoscopic morphological severity of the esophagus. Therefore, they speculated that Ling classification represents the endoscopic progressive process of achalasia.

### Innovations and breakthroughs

The authors confirmed that the Ling classification describes the endoscopic progressive process of achalasia. Moreover, to the best of this knowledge, this was the first study reporting the long-term postoperative esophageal morphological changes as revealed by endoscopy in patients with achalasia.

### Applications

After being confirmed to have the ability to represent the endoscopic progressive process of achalasia, Ling classification might be able to serve as criteria to assess achalasia endoscopically.

### Terminology

Ling classification, an endoscopic classification for achalasia based on the morphological severity of the esophagus, was proposed by Professor Linghu in 2011. Peroral endoscopic myotomy, a recently developed endoscopic therapeutic technique, is performed for achalasia.

## Peer-review

The present manuscript is related to Ling classification and the endoscopic progressive process of achalasia. Besides, successful POEM seems to have the ability to prevent the endoscopic evolvement of achalasia. The study demonstrated that the Ling classification does work.

## REFERENCES

- 1 **Richter JE.** Esophageal motility disorders. *Lancet* 2001; **358**: 823-828 [PMID: 11564508 DOI: 10.1016/s0140-6736(01)05973-6]
- 2 **Boeckxstaens GE,** Zaninotto G, Richter JE. Achalasia. *Lancet* 2014; **383**: 83-93 [PMID: 23871090 DOI: 10.1016/s0140-6736(13)60651-0]
- 3 **Shiino Y,** Houghton SG, Filipi CJ, Awad ZT, Tomonaga T, Marsh RE. Manometric and radiographic verification of esophageal body decompression for patients with achalasia. *J Am Coll Surg* 1999; **189**: 158-163 [PMID: 10437837]
- 4 **Familiari P,** Gigante G, Marchese M, Boskoski I, Tringali A, Perri V, Costamagna G. Peroral Endoscopic Myotomy for Esophageal Achalasia: Outcomes of the First 100 Patients With Short-term Follow-up. *Ann Surg* 2016; **263**: 82-87 [PMID: 25361224 DOI: 10.1097/sla.0000000000000992]
- 5 **Shiwaku H,** Inoue H, Yamashita K, Ohmiya T, Beppu R, Nakashima R, Takeno S, Sasaki T, Nimura S, Yamashita Y. Peroral endoscopic myotomy for esophageal achalasia: outcomes of the first over 100 patients with short-term follow-up. *Surg Endosc* 2016; **30**: 4817-4826 [PMID: 26932548 DOI: 10.1007/s00464-016-4813-1]
- 6 **Von Renteln D,** Fuchs KH, Fockens P, Bauerfeind P, Vassiliou MC, Werner YB, Fried G, Breithaupt W, Heinrich H, Bredenoord AJ, Kersten JF, Verlaan T, Trevisonno M, Rösch T. Peroral endoscopic myotomy for the treatment of achalasia: an international prospective multicenter study. *Gastroenterology* 2013; **145**: 309-311.e1-3 [PMID: 23665071 DOI: 10.1053/j.gastro.2013.04.057]
- 7 **Li HK,** Linghu EQ. New endoscopic classification of achalasia for selection of candidates for peroral endoscopic myotomy. *World J Gastroenterol* 2013; **19**: 556-560 [PMID: 23382636 DOI: 10.3748/wjg.v19.i4.556]
- 8 **Henderson RD.** Esophageal motor disorders. *Surg Clin North Am* 1987; **67**: 455-474 [PMID: 3109043]
- 9 **Inoue H,** Minami H, Kobayashi Y, Sato Y, Kaga M, Suzuki M, Satodate H, Odaka N, Itoh H, Kudo S. Peroral endoscopic myotomy (POEM) for esophageal achalasia. *Endoscopy* 2010; **42**: 265-271 [PMID: 20354937 DOI: 10.1055/s-0029-1244080]

**P- Reviewer:** Chow WK, Lee CL **S- Editor:** Gong ZM  
**L- Editor:** Wang TQ **E- Editor:** Wang CH





Published by **Baishideng Publishing Group Inc**  
7901 Stoneridge Drive, Suite 501, Pleasanton, CA 94588, USA  
Telephone: +1-925-223-8242  
Fax: +1-925-223-8243  
E-mail: [bpgooffice@wjgnet.com](mailto:bpgooffice@wjgnet.com)  
Help Desk: <http://www.f6publishing.com/helpdesk>  
<http://www.wjgnet.com>



ISSN 1007-9327

