—**Original**—

Validity of the Cutoff Value for Integrated Relaxation Pressure Used in the Starlet High-Resolution Manometry System

Noriyuki Kawami, Shintaro Hoshino, Yoshimasa Hoshikawa, Nana Takenouchi, Yuriko Hanada, Tomohide Tanabe, Osamu Goto, Mitsuru Kaise and Katsuhiko Iwakiri

Department of Gastroenterology, Nippon Medical School, Graduate School of Medicine, Tokyo, Japan

Background: In a previous study that used the Starlet high-resolution manometry system to assess integrated relaxation pressure (IRP) in healthy adults, the predicted cutoff value was about 26 mm Hg. However, some patients with achalasia have an IRP value of <26 mm Hg. This study examined the validity of the Starlet IRP cutoff value in patients with achalasia.

Methods: Among 37 patients with achalasia, the percentage of patients with a Starlet IRP value ≥26 mm Hg was calculated. Patients were then classified as IRP-high (IRP ≥26 mm Hg) and IRP-low (IRP <26 mm Hg), and the groups were compared in relation to basal lower esophageal sphincter (LES) pressure, Chicago classification achalasia subtype, and esophagography subtype.

Results: Twenty (54%) of the 37 patients had an IRP of ≥26 mm Hg. Basal LES pressure was significantly higher in the IRP-high group than in the IRP-low group. Chicago classification Type II achalasia was most common in the IRP-high group, whereas Type I was most common in the IRP-low group. No significant difference was noted in the distribution of esophagography subtypes between groups.

Conclusions: It is difficult to determine an IRP cutoff value with Starlet. When diagnosing achalasia with Starlet, comprehensive assessment must consider findings other than IRP values. In addition, IRP was associated with Chicago classification type. (J Nippon Med Sch 2019; 86: 322–326)

Key words: integrated relaxation pressure, Starlet, achalasia, high-resolution manometry

Introduction

Achalasia, a primary esophageal motility disorder, is characterized by disappearance of peristalsis in the esophageal body and incomplete relaxation of the lower esophageal sphincter (LES). Esophageal manometry is indispensable for diagnosing esophageal motility disorders such as achalasia and is also used for evaluation of the pathophysiology of gastroesophageal reflux disease[1,2]. The recent development of a high-resolution manometry (HRM) system with 36 channels spaced at 1-cm intervals has enabled detailed evaluation of esophageal motility function. In conventional manometry, LES relaxation is assessed with a sleeve sensor. However, in HRM, pressure can be measured by using channels at 1-cm intervals; therefore, LES relaxation can be evaluated with 7 pressure sensors spaced 1 cm apart (6 cm width) as a virtual sleeve sensor (eSleeve).

In HRM, integrated relaxation pressure (IRP) is a parameter for evaluating LES relaxation and is a function that automatically calculates mean minimum LES pressure within a specified period of time (which does not have to be continuous)[3]. The Chicago classification uses 4-s IRP (the mean minimum LES pressure for 4 s) as a parameter of LES relaxation[4]. The 95th percentile of 4-s IRP in healthy adults was 14.7 mm Hg[3]; thus, a value of ≥15 mm Hg was defined as incomplete LES relaxation. The sensitivity and specificity of this cutoff value for diagnosis of achalasia were reported to be 98% and 96%, respectively[4]. However, studies have reported that measured values vary in relation to the HRM equipment

Correspondence to Noriyuki Kawami, MD, PhD, Department of Gastroenterology, Nippon Medical School, Graduate School of Medicine, 1–1–5 Sendagi, Bunkyo-ku, Tokyo 113–8603, Japan
E-mail: s5038@nms.ac.jp
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Table 1 Clinical characteristics and demographic data of patients with achalasia

Number of subjects	37
Age, years	59 (45 - 73)
Gender, male/female	15/22
IRP (mm Hg)	28.3 (17.6 - 35.9)
Basal LESP (mm Hg)	39.0 (28.4 - 54.0)
Chicago classification subtype I/II/III	15/14/8
Esophagogram subtype ST/Sig/aSig	25/12/0

median (interquartile range), IRP: integrated relaxation pressure, LESP: lower esophageal sphincter pressure, ST: straight, Sig: sigmoid, aSig: advanced sigmoid

used[5–7]. The Chicago classification was developed by using data from the ManoScan (Medtronic plc, Dublin, Ireland) HRM system; however, IRP cutoff values for diagnosis of incomplete LES relaxation by other HRM systems have not been established. Starlet (Starmedical Inc., Tokyo, Japan) is the only HRM system approved by the Pharmaceuticals and Medical Devices Agency in Japan. It uses a Unisensor catheter (Unisensor AG, Atticon, Switzerland), and a previous study reported that the 95th percentile for 4-s IRP in healthy adults was about 26 mm Hg[6]. When the incomplete LES relaxation cutoff value is set to this value, the sensitivity of achalasia diagnosis is unclear. We have often encountered achalasia patients with a Starlet IRP of <26 mm Hg.

This study examined the validity of the Starlet IRP cutoff value for diagnosis of incomplete LES relaxation and analyzed the clinical characteristics of achalasia in relation to IRP value.

Materials and Methods

Participants

This retrospective study analyzed data from 37 patients with achalasia (15 men, age 59 [45-73] years). Achalasia was suspected because of patient symptoms and esophagogastroduodenoscopic findings of esophageal rosette[8] and retention of fluid and food debris in the dilated esophagus. Achalasia was diagnosed with HRM (**Table 1**). Patients who had undergone endoscopic balloon dilatation, surgery, or peroral endoscopic myotomy and those with secondary achalasia were excluded. This study was conducted in accordance with the provisions of the Helsinki Declaration and was approved by the Ethics Committee for Human Research of Nippon Medical School (No. 29-03-913).

HRM

HRM studies using the Starlet HRM system were performed after at least a 6-h fast. The HRM system has a catheter with 36 solid-state sensors at 1-cm intervals (Unisensor catheter). The catheter was placed transnasally and positioned to record from the hypopharynx to the stomach. The manometric protocol included a 5-min period to assess basal LES pressure and 10 swallows of 5 mL of water at 30-s intervals with the patient in supine position. In addition, a multiple rapid swallowing (MRS) test, in which 2 mL of water was swallowed 10 times consecutively at 2- to 3-s intervals, was performed[9–11].

Achalasia was diagnosed based on the Chicago classification v3.0, as follows. If there was no peristalsis, panesophageal pressurization, or premature contraction, and IRP was ≥26 mm Hg, achalasia was diagnosed; if IRP was <26 mm Hg, MRS was performed. In addition, if intraesophageal pressure was higher during than before MRS, and end-expiratory LES nadir pressure during MRS was >3 mm Hg higher than the gastric baseline[10], achalasia was diagnosed (**Fig. 1**). On HRM, achalasia was classified into 3 subtypes (types I-III) based on the Chicago classification v3.0[4].

Esophagography

Esophagography was performed in all patients, and achalasia was classified into 2 subtypes (straight and sigmoid) on the basis of the Descriptive Rules for Achalasia of the Esophagus in the Japanese Classification of Achalasia (4th Edition). Sigmoid achalasia with acute angulation was classified as advanced sigmoid achalasia[12].

Sensitivity of Diagnosis of Achalasia and Comparison of the IRP-High and IRP-Low Groups

The sensitivity of the diagnosis of achalasia was calculated when the cutoff value for incomplete LES relaxation was set at 26 mm Hg. In addition, patients were classified as IRP-high (IRP ≥26 mm Hg) and IRP-low (IRP <26 mm Hg), and the groups were compared in relation to basal LES pressure, HRM achalasia subtype, and esophagography subtype.

Statistical Analysis

Age, IRP, and basal LES pressure are expressed as median (interquartile range). The Mann-Whitney U test was

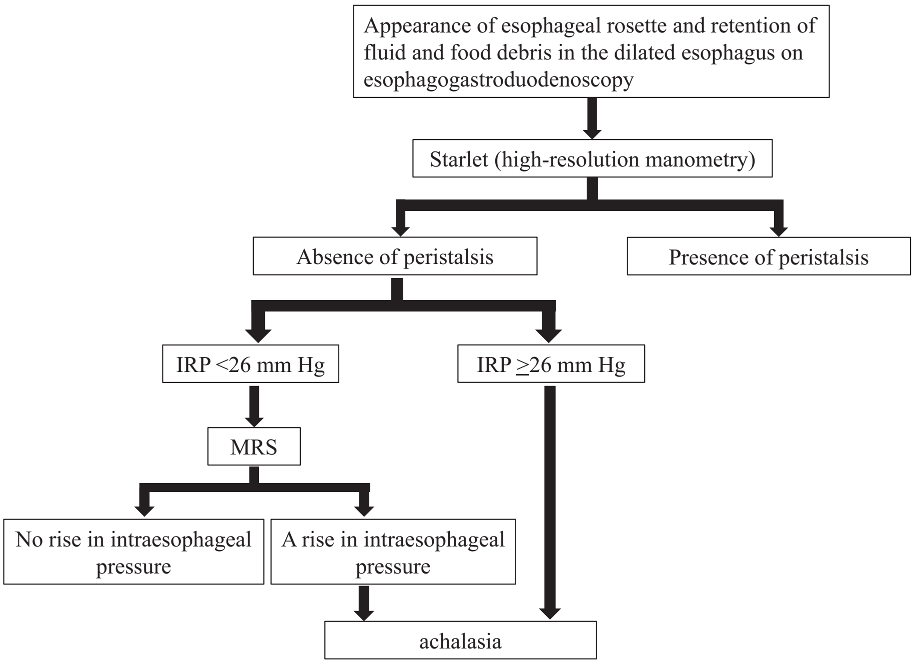

Fig. 1 Flow chart for diagnosis of achalasia.
IRP, integrated relaxation pressure; MRS, multiple rapid swallowing.

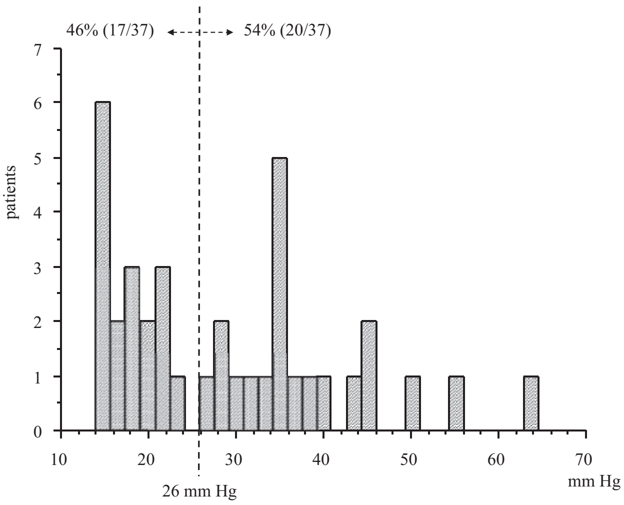

Fig. 2 Distribution of integrated relaxation pressures (IRP) in 37 patients with achalasia.

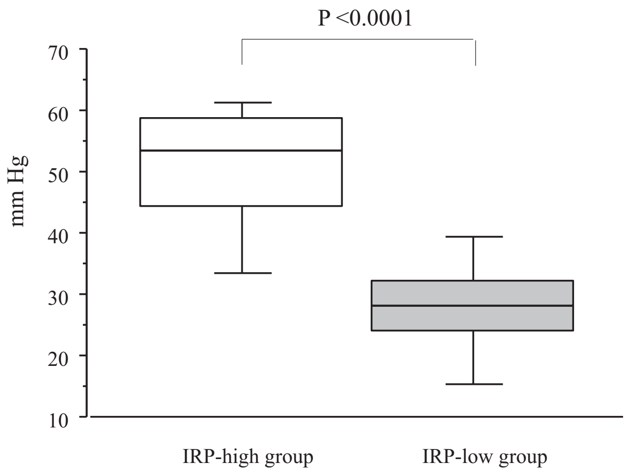

Fig. 3 Basal lower esophageal sphincter pressures in the integrated relaxation pressure (IRP)-high and IRP-low groups.
Data are presented as median (interquartile range).

used to compare basal LES pressure in the 2 groups. Classification of achalasia subtype by HRM and esophagography was evaluated with the chi-square test, and a P value of <0.05 was considered significant.

Results

Twenty (54%) of the 37 patients had an IRP of ≥26 mm Hg (**Fig. 2**). The sensitivity of achalasia diagnosis was 54% when the cutoff value for incomplete LES relaxation was set at 26 mm Hg.

Basal LES pressure was 53.4 mm Hg (44.4-58.7) in the IRP-high group, which was significantly higher than the value of 28.0 mm Hg (24.0-32.1) in the IRP-low group (P <0.0001) (**Fig. 3**). The most frequent Chicago classification achalasia subtype was Type II in the IRP-high group (Type I/II/III: 3/12/5) and Type I in the IRP-low group (Type I/II/III: 12/2/3); the difference was significant (P= 0.0016) (**Fig. 4**). No significant difference was noted in the distribution of esophagography subtypes between groups (subtype: straight in 15 and sigmoid in 5 in the IRP-high group; straight in 10 and sigmoid in 7 in the

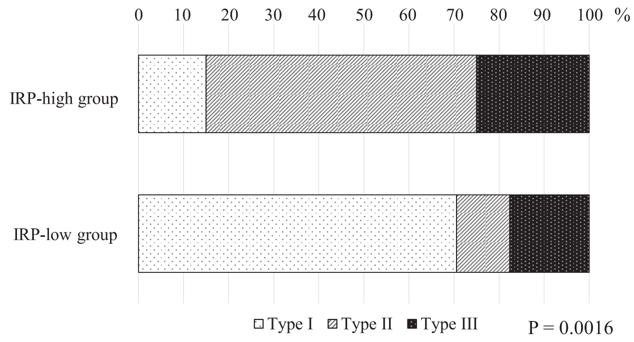

Fig. 4 Achalasia subtypes, according to the Chicago classification, in the integrated relaxation pressure (IRP)-high and IRP-low groups.

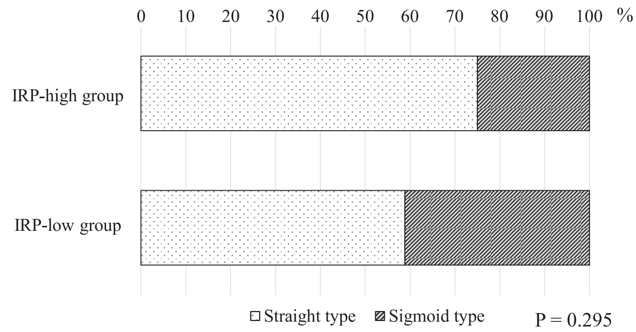

Fig. 5 Achalasia subtypes, as determined by esophagography, in the integrated relaxation pressure (IRP)-high and IRP-low groups.

IRP-low group) (P=0.295) (**Fig. 5**).

Discussion

A previous study reported that the 95th percentile of IRP for the Starlet system was 26 mm Hg in healthy adults[6]; thus, when the cutoff value was set at an IRP of 26 mm Hg, the specificity for incomplete LES relaxation was 95%. However, in the present study, the percentage of achalasia patients with an IRP of <26 mm Hg in the Starlet system was high, 46% (16/35). That is, when the cutoff value for incomplete LES relaxation was set at 26 mm Hg, the sensitivity of for achalasia diagnosis was 54%. In the ManoScan HRM system, when an IRP of 15 mm Hg was used as the cutoff value for incomplete LES relaxation, the sensitivity and specificity of the diagnosis of achalasia were high: 98 and 96%, respectively[3]. Therefore, although a small number of patients with achalasia have an IRP of <15 mm Hg[13], we believe that it is useful to use 15 mm Hg as the cutoff value for incomplete LES relaxation with ManoScan. With Starlet, however, the present results suggest that it is difficult to define a clear cutoff value. A possible reason for this, other than differences in race or other participant characteristics, is the catheter type used. ManoScan catheters contain 12 concentrically arranged sensors per channel and show the mean pressure for each sensor[14]. The pressure channels of the Unisensor catheter used in the Starlet HRM system are ball-shaped. One pressure sensor is located in the ball-shaped channel[5], so that the maximum pressure applied to the channel is shown as the IRP value. In addition, differences in catheter hardness and thickness result in varying IRP values. These differences in the characteristics of catheters and sensors may have complicated the identification of definite cutoff values for IRP in healthy persons and achalasia patients. When diagnosing achalasia with the Starlet system, IRP values should be evaluated in conjunction with MRS, a complementary test involving 2-mL water swallows at 2-3 s intervals[9–11]. During successive swallows at short intervals, LES remains relaxed. After the last swallow, primary peristalsis occurs, and LES relaxation is terminated. In the presence of incomplete LES relaxation, multiple rapid swallows result in intraesophageal fluid retention, which increases intraesophageal pressure. Thus, the MRS test evaluates the maximal LES relaxation function[10].

Analysis of the association between IRP and HRM achalasia subtype showed that Types I and II were most common in the IRP-low and IRP-high groups, respectively, and that the difference was significant. Type II is generally more frequent than Type I in patients with early achalasia, when nerves of the inhibitory system are impaired while nerves of the excitatory system are preserved, which results in elevated basal LES pressure and IRP. In contrast, Type I is more common in patients with advanced achalasia, when impairment of both inhibitory and excitatory nerves leads to decreased basal LES pressures and IRP[15–17].

Although the distribution of esophagography subtype did not differ between groups, the percentage of patients with sigmoid achalasia was higher in the IRP-low than in the IRP-high group, perhaps because more patients had advanced achalasia in the former group and sigmoid achalasia is more frequent when the disease has progressed.

In conclusion, the results suggest that it is difficult to use Starlet to determine the optimal IRP cutoff value for diagnosis of incomplete LES relaxation, a characteristic of achalasia. When diagnosing achalasia with the Starlet HRM system, clinicians should measure IRP and confirm an increase in intraesophageal pressure during MRS testing. In addition, we observed an association between IRP and achalasia subtype in the Chicago classification.

Conflict of Interest: The authors declare that they have no conflict of interest.

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