学 位 論 文 の 要 旨

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学 位 論 文 名　Radially Asymmetric Gastroesophageal Acid Reflux in the Distal Esophagus: Examinations with Novel pH Sensor Catheter Equipped with 8 pH Sensors

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論 文 内 容 の 要 旨

INTRODUCTION

Reflux esophagitis can be divided into 2 types; low-grade (grades A and B in the Los Angeles classification) and high-grade (grades C and D), based on the form of the mucosal breaks. We previously investigated the precise location of esophageal mucosal breaks in patients with grade A, B, or C esophagitis. Those with high-grade esophagitis (grade C) had mucosal breaks mainly in the posterior wall of the distal esophagus, whereas those with low-grade esophagitis (grades A and B) had mucosal breaks mainly in the right anterior wall of the distal esophagus. The aim of the present study was to investigate radial patterns of acid exposure in the distal esophagus and determine whether radially asymmetric acid exposure is a possible cause of radially asymmetric distribution of the lesions. We examined gastroesophageal acid reflux patterns in patients with gastroesophageal reflux disease (GERD) as well as healthy subjects using our novel pH sensor catheter.

MATERIALS AND METHODS

The experimental protocol was approved by the Ethics Committee of Shimane University School of Medicine. Written informed consent was obtained from the enrolled subjects and the study was performed according to the World Medical Association Declaration of Helsinki.

Four healthy volunteers, 5 patients with non-erosive reflux disease (NERD), and 10

patients with reflux esophagitis were enrolled in this study. Enrolled patients with reflux esophagitis consisted of 7 with grade A and 3 with grade B esophagitis.

We have developed a novel pH sensor catheter equipped with 8 pH sensors radially arrayed at the same level. It is equipped with 2 radiopaque marks, which are used to identify rotation of the catheter under fluoroscopic imaging and the position of each radially arrayed sensor. Eight-channel pH data can be simultaneously recorded by connecting the catheter to 4 portable digital recorders.

Following a 4-hour fast, the pH sensor catheter was inserted transnasally into the esophagus of each subject. The pH sensors were positioned 2 cm above the upper limit of the lower esophageal sphincter (LES). One hour after insertion of the device, the subjects consumed a high-calorie meal within 20 minutes. Subsequently, post-prandial gastroesophageal reflux was monitored for 3 hours with the subject in a sitting position, because healthy individuals, as well as patients with NERD or low-grade esophagitis, mainly experience gastroesophageal reflux during daytime post-prandial periods when they are in an upright posture. To ensure uniformity of the position and rotation of the catheter, fluoroscopic imaging was performed before and after pH monitoring. The number of acid reflux episodes, acid clearance time, and percent time at pH <4.0 during the 3-hour post-prandial period were separately calculated from data provided by each pH sensor.

RESULTS AND DISCUSSION

Using our novel 8-channel pH sensor catheter, we successfully examined radial acid exposure in the distal esophagus in all 19 study subjects without any adverse events. No positional alteration or rotation of the catheter was observed under fluoroscopic imaging either before or after pH monitoring in any of the subjects.

The maximal numbers of acid reflux episodes detected by the 8 arrayed sensors during the 3-hour post-prandial period in healthy subjects, patients with NERD, and patients with reflux esophagitis were 9.5 (0-33), 57 (26-100), and 45.5 (6-98), respectively (p = 0.037), while the maximal acid clearance times were 16.8 (0-61.8), 57.4 (19.5-207.3), and 98.4 (36.4-546.8) seconds, respectively (p = 0.029), and maximal percent times at pH <4.0 were 2.4% (0-3.9%), 23.5% (5.8-43.2%), and 27.9% (2.1-95.8%), respectively (p = 0.018).

When the radial distribution of acid exposure in the distal esophagus was analyzed, patients with NERD and those with reflux esophagitis showed acid exposure predominantly on the right wall of the distal esophagus. On the other hand, radial variations of acid exposure were not observed in the healthy subjects. In the majority of patients with reflux esophagitis, the

direction of longer acid exposure coincided with the locations of mucosal breaks. In addition, the mean percent time at pH <4.0 in locations of mucosal breaks was significantly greater than in others ($p = 0.013$).

The results of the present study clarified that patients with GERD have radially asymmetric acid exposure that is predominant on the right wall of the distal esophagus. In addition, they revealed that the direction of longer acid exposure is associated with the locations of mucosal breaks in patients with low-grade esophagitis.

The mechanism related to acid exposure occurring most frequently on the right wall of the distal esophagus in patients with low-grade reflux esophagitis has not been elucidated. The most important antireflux barrier is the LES, and radial intraesophageal pressure in the LES may not be symmetrical. Indeed, a number of investigators have measured LES pressure and found that the highest level of sphincter pressure occurred in the area of the left wall of the esophagus, indicating that the radial LES pressure profile is asymmetrical and lower in the right wall. The low level of LES pressure generated by the right wall, which has a weak antireflux barrier, may be an important factor in this mechanism.

The high level of intraesophageal pressure in the LES is produced by a combination of muscular contractions by the distal esophagus and external compression, which are mainly exerted by the crural diaphragm. The radial muscular thickness and architecture of the distal esophagus are reported to be non-uniform, as muscle thickness is greatest toward the greater curvature side and lower toward the lesser curvature. The crural diaphragm encircles the distal end of the esophagus and forms the esophageal hiatus, which is primarily composed of muscles from the right crus of the diaphragm. During the inspiratory phase, contraction of the crural diaphragm compresses the distal end of the esophagus, possibly from the left wall. Thus, sphincter pressure generated by muscular contractions of the distal esophagus and external compression may be an important mechanism by which radial intraesophageal pressure in the LES is higher in the left wall and lower in the right.

CONCLUSION

We successfully examined radial acid exposure in the distal esophagus using our novel 8-channel pH sensor catheter. Our findings clarified a radial asymmetric pattern of acid exposure in the distal esophagus of patients with GERD and also revealed that the direction of longer acid exposure is associated with mucosal break location.