

The Functional Relationships between Hiatal Hernia and Reflux Esophagitis

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The purpose of this research was to investigate functional studies by which the hiatal hernia (HH) may be relevant to a reflux esophagitis (RE). Group I consisted of healthy controls who were endoscopically normal (n=21). Group II consisted of patients with hiatal hernia but no reflux esophagitis (n=8). Group III had patients with hiatal hernia with reflux esophagitis (n=9). Group IV had patients with reflux esophagitis but no hiatal hernia (n=16). Esophageal manometry, ambulatory 24 hour intraesophageal pH monitoring, acid clearance test, and gastric emptying scan were performed in each of the patients. The contraction amplitude at 3cm above the lower esophageal sphincter did not differ significantly among the four groups, but the mean lower esophageal sphincter pressure was significantly decreased in group II. The DeMeester score in ambulatory 24 hour intraesophageal pH monitoring was significantly higher in group III compared with the controls. No significant difference among the groups was found with respect to acid clearance. Total and proximal gastric emptying times ($T_{1/2}$) were significantly delayed in group III. We found that hiatal hernia combined with delayed gastric emptying may bear a relationship to the multifactorial origins of reflux esophagitis, and we suggest a rationale for using prokinetic agents as the therapeutic regimen in patients with HH complicated by RE.

Key Words: Hiatal hernia, reflux esophagitis, gastroesophageal reflux

Hiatal hernia (HH) has been defined as a circular extension of the gastric mucosa 2 cm or more above the diaphragmatic hiatus (DeMeester *et al.* 1981). An incompetent lower esophageal sphincter (LES) may result from poor anchoring of the esophagus within the abdomen because of HH, with consequent shortening of the intraabdominal segment of the sphincter exposed to the positive pressure environments. Also, the extrasphincteric anti-

reflux mechanisms can be disrupted when stomach herniates into the chest through the diaphragmatic hiatus (Sloan *et al.* 1992). In several endoscopic studies HH was found in 63~84% of the patients with reflux esophagitis (RE) (Wright and Hurwitz, 1979; Berstad *et al.* 1986; Petersen *et al.* 1991). The association between RE and HH is generally accepted as being significant, and this relationship appears fairly established (Wright and Hurwitz, 1979; Berstad *et al.* 1986; Petersen *et al.* 1991). However, functional data between them are still debatable. Therefore, we have undertaken an investigation of functional studies which may indicate that HH is relevant to RE in Korean patients.

MATERIALS AND METHODS

This study was carried out prospectively in

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the four groups of subjects at the Department of Internal Medicine, Yonsei Medical Center between March 1st, 1994 and February 28, 1995. The presence of a HH was determined by endoscopic studies revealing a gastric pouch lined with rugal folds above the crural impression and measuring at least 2 cm between the crura and the squamous columnar junction, with the patient resting in the left lateral position and breathing quietly (Mittal *et al.* 1987). No special respiratory maneuvers were employed to increase abdominal pressure and encourage herniation. Esophagitis was defined as a gross mucosal injury ranging from red longitudinal streaks with associated friability to erosions or ulcerations in the distal esophagus (Kobayashi and Kasugai, 1974). Patients were excluded if jaundice, previous gastric operation, or adjacent gastric or esophageal malignancy was present. Group I consisted of 21 healthy controls (mean age, 40.1 yrs.; M/F=7:14) who were endoscopically normal. Group II consisted of 8 patients with HH but no RE (mean age, 41.1 yrs.; M/F=2: 6). Group III had 9 patients with HH and RE (mean age, 44.4 yrs.; M/F=6: 3). Group IV had 16 patients with RE but no HH (mean age, 39.3 yrs.; M/F=6: 10). Each of the patients were given an esophageal manometry, a 24 hour ambulatory intraesophageal pH monitoring, an acid clearance test, and a gastric emptying scan.

Esophageal manometry

Esophageal manometry was performed to determine the basal lower esophageal sphincter pressure (LESP) and the amplitude of peristalsis in the distal esophagus with a four-channel continuous perfusion catheter. The manometric orifices in the 4 lumen catheter were 5 cm apart at a 90° angle (outer diameter 4.5 mm; internal diameter of each, 0.8 mm). A pneumohydraulic capillary infusion system (Arndorfer Medical Specialties Inc., Greendale, WI, USA) was used for continuous infusion of each lumen at a rate of 0.5 mL/min. Each manometric catheter was connected to a transducer and its pressure profiles were recorded (PC Polygraf HR, Synetics Medical, Stockholm, Sweden) and analyzed by a

Polygram Upper GI Edition, Version 5.06C2 (Gastrosoft Inc., Stockholm, Sweden). A station-pull through technique was used to measure the LESP. The assembly was then positioned with the distal opening at 3 cm above the LES, and other openings were situated at 8, 13, and 18 cm above the sphincter, respectively. Contractile activity in the body of the esophagus was evaluated in response to swallowing 5 ml of water. All patients fasted and were off of all medications known to alter the LESP 48 hours before the study. Patients were kept in a supine position with the head of the bed elevated approximately 15° during the course of the manometry.

Ambulatory 24 hour intraesophageal pH metry

Ambulatory 24 hour intraesophageal pH monitoring was carried out in both the patients and the control subjects. A microcrystalline antimony electrode (calibrated in buffers of pH 7.01 and 1.07) was positioned 5 cm above the manometrically determined upper border of the LES. The electrode and a silver chloride skin electrode was connected to a digitrapper (Synetics Medical, Stockholm, Sweden). The data was analyzed with the EsopHogram program (Gastrosoft Inc., Stockholm, Sweden). An episode of acid gastroesophageal reflux was determined to have begun when the pH fell below 4, and was determined to have ended when the pH rose to above 5. The data was analyzed for the percentage of total reflux time, the percentage of upright and supine reflux, the total number of reflux episodes, the total number of reflux episodes longer than five minutes, and the longest reflux episode. These reflux parameters were used to evaluate the Johnson and DeMeester score (Johnson and DeMeester, 1974).

Esophageal acid clearance test

The esophageal acid clearance was evaluated by means of a pH probe positioned 5 cm above the previously determined LES. With the subject in the left lateral decubitus position, a bolus of 15 ml of 0.1 N HCl was instilled over a 30 second period via a polyvinyl

catheter with a port located 5 cm proximal to the pH probe. Swallowing was standardized by instructing the subject to take a dry swallow every 30 seconds after instillation of the acid bolus until the esophageal pH rose to above 5.0.

Gastric emptying scan

The gastric emptying time was assessed by scintigraphy (Collins *et al.* 1983). After an overnight fast of at least 10 hours, the subjects ingested a test meal. A standard test meal consisted of a scrambled egg to which had been added 400 uCi 99mTc-pertechnetate, one slice of toast, followed by 150 ml of orange juice. The total caloric content of the meal was 250 kcal. Immediately after ingestion of the test meal, data was obtained in a dynamic mode for at least 90 minutes, with a 1 minute frame using a dual-headed gamma camera (ADAC, Millpitas, CA, USA) equipped with low energy, high resolution parallel hole collimators. The determination of the regions of interest for the proximal and total stomach has been described previously by Collins *et al.* (1991). The proximal stomach region was defined as the 'reservoir' area seen in all subjects for at least the first few minutes after ingestion of the test meal, and an imaginary line of proximal stomach was drawn immediately below this region. Anterior and posterior gastric emptying curves from each part were obtained, and the 50% emptying time ($T_{1/2}$) was calculated using the arithmetic mean of each scan data to correct the gamma ray attenuation.

Statistics

All values were expressed as mean \pm standard deviation. The statistical significance of the values was determined by the Kruskal-Wallis test with multiple comparisons. A *p* value of less than 0.05 was considered to be significant.

RESULTS

Mean LESP was significantly decreased in group II (HH but no RE) (15.4 ± 4.7 mmHg)

compared with group I (healthy controls) (23.8 ± 6.6 mmHg). Though statistically not significant, there was a decreased level of LESP in group III (HH with RE) (17.6 ± 6.9 mmHg) compared with the controls. LESP was not significantly different between the two groups of patients with HH. The contraction amplitude at 3 cm above LES was 87.0 ± 29.5 , 49.4 ± 12.9 , 66.9 ± 35.3 , 79.6 ± 34.3 mmHg in group I, II, III, and IV (RE but no HH), respectively, and did not differ significantly among the groups (Table 1). The DeMeester score in ambulatory 24 hour intraesophageal pH monitoring was 5.3 ± 3.5 (range; 0.2~10.8), 10.7 ± 12.2 (range; 0.6~27.8), 37.2 ± 36.9 (range; 3.4~122.9), 12.3 ± 9.0 (range; 5.2~28.7) for groups I, II, III, and IV, respectively. The score was significantly higher in group III compared with group I ($p < 0.05$). Clearance of acid from the esophagus (swallows to reach pH=5.0) was 7.5 ± 2.5 (range; 4~11), 8.3 ± 2.6 (range; 6~11), 14.4 ± 7.4 (range; 8~26), and 10.3 ± 5.1 (range; 4~21) for groups I, II, III, and IV, respectively. No significant difference among the groups was found with respect to acid clearance, but group III showed a delayed trend in acid

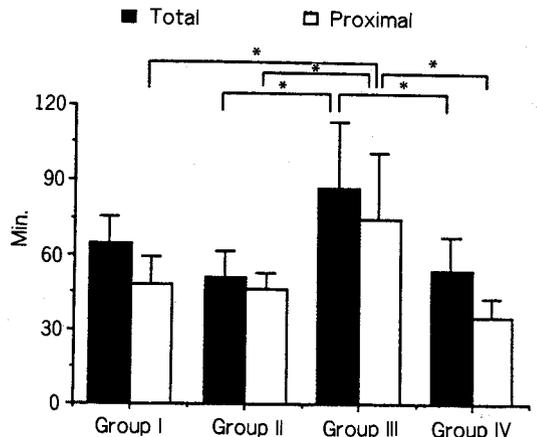


Fig. 1. Comparison of gastric emptying times ($T_{1/2}$). Total and proximal stomach $T_{1/2}$ were significantly delayed (total $T_{1/2}$, 87.0 ± 26.4 min.; proximal $T_{1/2}$, 75.0 ± 25.8 min.) in group III (*: $P < 0.05$). Group I; healthy controls, Group II; HH without RE, Group III; HH with RE, Group IV; RE without HH.

Table 1. Comparison of esophageal pressure profiles

	Group I	Group II	Group III	Group IV
LESP(mmHg)	23.8±6.6	15.4±4.7*	17.6±6.9	20.4±6.4
Mean±SD	24	15	14	19
Median	11~36	8~22	7~38	11~33
Range				
Contraction amplitude(mmHg)	87.0±29.5	49.4±12.9	66.9±35.3	79.6±34.3
Mean±SD	86.5	44.9	66.1	76.3
Median	38.1~138.5	35.9~67.1	25~134.1	2~176
Range				

*: $P < 0.05$ compared with Group I.

Group I; healthy controls, Group II; HH without RE, Group III; HH with RE, Group IV; RE without HH

clearance. Gastric emptying time determined by total stomach $T_{1/2}$ and proximal stomach $T_{1/2}$ are shown in Fig. 1. Total and proximal stomach $T_{1/2}$ were significantly delayed (total $T_{1/2}$, 87.0 ± 26.4 min.; proximal $T_{1/2}$, 75.0 ± 25.8 min.) in group III.

DISCUSSION

In an endoscopic study (Berstad *et al.* 1986), 42% of the patients with HH did not have esophagitis, whereas 63% of the patients with RE had hernia. They found that RE was significantly related to HH. Although it appears that HH often contributes to gastroesophageal reflux (GER), HH is neither necessary nor sufficient for the development of RE. In other words, the association between RE and HH is generally accepted as being significant, although there is still debate in terms of their functional relationships. Present results showed that patients with HH complicated by RE revealed abnormal acid GER and impaired gastric emptying, whereas patients with HH but no esophagitis revealed no abnormal functional studies except lower resting LESP. The DeMeester score in ambulatory 24 hour intrasophageal pH monitoring was significantly higher in patients with HH complicated by RE compared with the controls, whereas the score was not significantly elevated in either the patients with HH but no RE, or those with RE but no HH.

How do we explain the functional relationships between the two in view of their mechanisms? First, HH has been found to be associated with LES incompetency. Some have found that HH is associated with a decreased LESP (DeMeester *et al.* 1981), and that this LES hypotension predisposes to GER. We found significantly decreased LESP in patients with HH but no RE, but there was no significantly decreased LESP in patients with HH complicated by RE. We cannot explain this discrepancy exactly but it may be partly due to disease heterogeneity. For example, we did not measure the size of the HH identified in groups II and III, and this could account for some of the discrepancies in the measured characteristics, especially the LESP. Relatively high LESP in patients with RE in our study indicates that a majority of Korean patients do not have a mechanically defective LES. This may explain partly why the prevalence of RE in Korea is relatively low compared with that of the Western countries.

As for acid clearance, it has been known to be one of the important mechanisms against the development of RE (Sloan and Kahrilas, 1991). This occurs generally as a 2 step process, that is, volume clearance by peristaltic contraction, and acid neutralization by saliva. HH has been reported as an impaired esophageal acid clearance (Mittal *et al.* 1987). During acid clearance, a small amount of acid is trapped in the HH sac and refluxes into the esophagus during subsequent swallows when there is relaxation of the LES. These repeat-

ed episodes of acid reflux from the HH account for the delayed acid clearance observed in GER patients with HH (Mittal *et al.* 1987). Whether this finding is a primary abnormality or is secondary to disturbed motility is unknown. But, another study found that acid clearance time was significantly prolonged in patients with nonreducing HH, and that the efficiency of esophageal emptying was progressively impaired both in patients with reducing hernias (61% success rate) and in those with nonreducing hernias (32% success rate), suggesting a mechanism whereby some subgroups of HH may be involved in the pathogenesis of reflux disease (Sloan and Kahrilas, 1991). We did not find any significant differences among the groups with respect to acid clearance, except that there was a delayed trend in patients with HH complicated by RE. If we were to have graded the esophagitis in groups III and IV, there could have been a better analysis with respect to the measured characteristics (e.g., more severe grades of esophagitis had poorer acid clearance), but unfortunately, none of the group III and IV patients was above stage III of Savary and Miller (1978). We therefore were not able to stratify the esophagitis grades in these two patient groups. In addition, we did not find any significant differences in the peristaltic amplitudes in distal esophagus among the 4 groups.

Finally, delays in gastric emptying of liquid and semi-solid meals have been found to be common in patients with gastroesophageal reflux disease (GERD) and RE (Maddern *et al.* 1985; Collins *et al.* 1986), and abnormalities in gastric emptying have been reported in up to 60% of patients with GERD (McCallum *et al.* 1981; Maddern *et al.* 1985). Gastric emptying time was significantly delayed in patients with moderate/severe esophagitis as opposed to patients with mild esophagitis (Cogliandolo *et al.* 1992). Gastric emptying is determined by the coordinated function of at least two physiologically distinct compartments of the stomach (Read and Houghton, 1989). The proximal stomach accommodates food, that is, functions as a reservoir and regulates the transfer of food to the distal compartment. Therefore, the persistence of the gastric

reservoir may increase the exposure of the esophagus to gastric juice by accentuating significant gastric content to reflux, and may increase the likelihood of reflux episodes by increasing the number of spontaneous relaxations of the LES. In addition, delayed clearance of bile and pancreatic secretion which pass intermittently across the pylorus may allow alkaline reflux into the stomach. Our results revealed that gastric emptying was significantly delayed in both the total and the proximal compartment of the stomach in patients with HH complicated by RE.

In conclusion, low LESP, normal acid clearance, and normal gastric emptying were observed in patients with HH but no RE, and delayed acid clearance and delayed gastric emptying were observed in patients with HH complicated by RE. HH combined with delayed gastric emptying may bear a relationship to the multifactorial origins of RE, and we suggest a rationale for using prokinetic agents as therapeutic regimen in patients with HH complicated by RE.

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