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Experimental and Clinical Studies on the Operative Treatment of Sliding Esophageal Hiatal Hernia

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Introduction

Recently, in proportion to a rise in the aged population in our country, cases of esophageal hiatal hernia have gradually increased as a result of the development and wide acceptance of such techniques as X-ray examination, esophageal manometry, and esophageal endoscopy. In sliding esophageal hiatal hernia the cardia is displaced cephalad to the diaphragmatic esophageal hiatus. The esophageal spiral muscle fibers, which run almost horizontally in the distal esophagus, become flaccid. In addition, the attachment of the ascending crus of the phrenoesophageal ligament to the esophageal adventitia is displaced caudad and the angle of HIS, which is extamurally produced by entry of the esophagus into the cardia, becomes obtuse. Also, because of a decreased sensitivity of the lower esophageal sphincter (LES) to endogenous gastrin, gastroesophageal incompetence will ensue and finally will result in a reflux esophagitis more than 50 % of the cases. Many symptoms of sliding hiatal hernia are thought to be due to this reflux esophagitis and its complications.

The present experiments were made, exclusively by esophageal manometry, to clarify the roles of various components of the cardiac closing mechanism in the prevention of gastroesophageal reflux and to examine the effects of endogenous or exogenous gastrointestinal hormones, various kinds of prostaglandins, antacids, and bile or bile acids on the cardiac closing mechanism in dogs. Studies were also made on the reconstructive effects of various kinds of hiatal herniorrhaphies performed on dogs in which the components of the cardiac closing mechanism had previously been divided surgically. Moreover, 12 clinical cases with hiatal hernia in which NISSEN fundoplication had been performed at the 2nd Surgical Clinic of our University Hospital, were analyzed. Finally, an attempt was made to establish the most effective method of operative therapy for sliding hiatal hernia.

Key words : Sliding esophageal hiatal hernia, Nissen fundoplication, Esophageal manometry, Gastroesophageal reflux, Gastrin
索引語：滑脱型食道裂孔ヘルニア，Nissen 胃底部皺襞形成術，食道内圧検査，胃食道逆流，ガストリン．
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Experimental Studies

A) Materials and Methods

1) Esophageal manometry

Esophageal manometry was performed with an open-tipped catheter and the withdrawal curves were graphed. The catheter was composed of seven lumens (Argyle Arndorfer-McSteen Esophageal Motility Tube, U.S.A.). It was connected to a pressure transducer (LPU-0.1, Nihon Kohden Kogyo Co. Ltd., Tokyo, Japan), a multi-purpose polygraph (RP-45, Nihon Kohden Kogyo Co. Ltd., Japan) and a carrier amplifier (RP-5, Nihon Kohden Kogyo Co. Ltd., Japan) (Fig. 1). During esophageal manometry, bubble-free distilled water was constantly infused at a flow rate of 0.8 to 1.5 ml/min through the catheter. Esophageal manometry curves were obtained by continuous rapid pull-through. Pressures were based on an atmospheric pressure of zero and the pressure transducer was positioned at the same height as the intrathoracic esophagus. Paper velocity was adjusted to 0.75 cm/sec and calibration was performed by raising the catheter tip 30 cm from a basal zero position to make 20 levels on the paper equal to 30 cm H_2O. As a filter for the carrier amplifier, 20 Hz was selected from among the mean (2 min), 120 Hz and 20 Hz.

2) Effects of division of individual components of the cardiac closing mechanism on resting and gastrin-stimulated lower esophageal sphincter pressure (LESP)

Among the components of the cardiac closing mechanism, the phrenoesophageal ligament, the WILLIS' oblique muscle, the right crus of the diaphragm, the mucosal rosette at the esophagogastric junction, the angle of HIS, the gastric bubble and the abdominal esophageal segment, as well as the lower esophageal sphincter (LES), all functioning together,

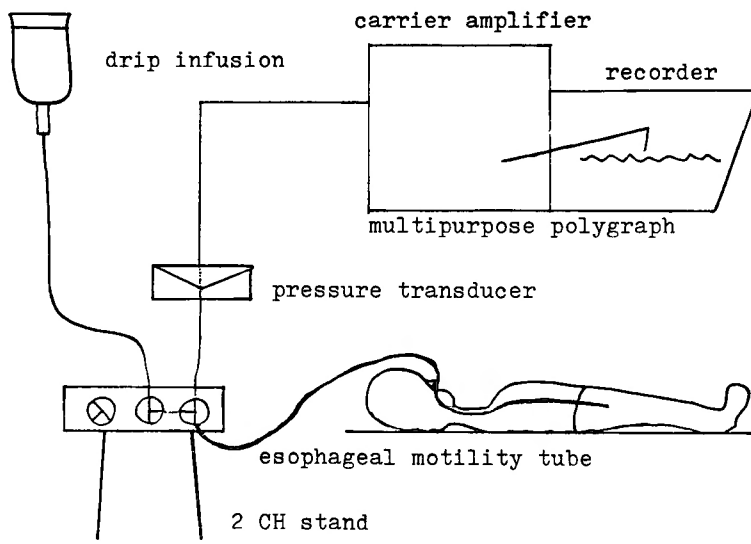

Fig. 1. Apparatus for esophageal manometry

are considered to be responsible for gastroesophageal competence. The regulatory systems of the cardiac closing mechanism are, first, the nervous supply, mainly from the vagus nerves and, secondly, the gastrointestinal hormones ; for example, gastrin and other humoral agents. Clinical reflux esophagitis is thought to occur as a result of gastroesophageal incompetence due to a disfunction in the cardiac closing mechanism.

In order to clarify which components of the cardiac closing mechanism are necessary for the maintenance of gastroesophageal competence and in order to discover how gastrin affects the cardiac closing mechanism, the following experiments were made. Among the various components, it is probable that the LES, the phrenoesophageal ligament and the WILLIS' oblique muscle can be most easily divided. Therefore, these 3 components were handled individually in the following 4 groups : (I) division of the phrenoesophageal ligament, (II) division of the phrenoesophageal ligament and the LES, (III) division of the phrenoesophageal ligament and the WILLIS' oblique muscle, and (IV) division of the phrenoesophageal ligament, the LES and the WILLIS' oblique muscle. As experimental animals, 20 adult mongrel dogs ranging from 8 to 15 kg in body weight, were used- 5 in each group. After fasting for 24 hours, water only permitted, 2 ml (100 mg) of ketamine (Park Davis Sankyo Co. Ltd., Tokyo, Japan) was injected intramuscularly. During the drowsy state, each animal was placed in a supine position on the operative board. A venous route was selected from a lower limb and an infusion of saline solution was started. This route was also utilized for the intravenous administration of various agents. After intravenous pentobarbital anesthesia (30 mg/kg) was begun, respiration was controlled with intratracheal cannulation by a respirator using room air. Anesthetic depth was kept as constant as possible with the readministration of pentobarbital (10 mg/kg). Once the ventilatory condition was properly adjusted, it was not changed during the experiment. After the first manometry was made, a laparotomy was performed through an upper midline incision. By displacement of the left lobe of the liver to the right, the esophagocardiac junction was easily visible. Subsequently, the left half of the phrenoesophageal ligament was excized, the lesser omentum was opened, and the right half of the ligament was excized. During these procedures, A. et V. gastrica sinistra and the posterior celiac branch of the vagus nerves were carefully preserved along the lesser curvature. Also, the trunks of the vagus nerves around the attachment of the ligament were not injured. However, the hepatic branches were always cut. Next, the operative divisions of the 4 groups were performed (Fig. 2). Division of the LES in Groups II and IV was performed with an extramucosal longitudinal myotomy, approximately 5 cm in length, cephalad from the attachment of the ligament, on the anterior wall of the distal esophagus along the greater curvature, the myotomy being sufficiently wide to visualize the whitish esophageal mucosa. Division of the WILLIS' oblique muscle in Groups III and IV was performed with a longitudinal myotomy, about 5 cm in length, caudal to the attachment of the ligament, on the anterior gastric wall along the greater curvature ; in Group IV, the LES and WILLIS' oblique muscle were divided in succession. After one hour, with the posterior mediastinum still open,

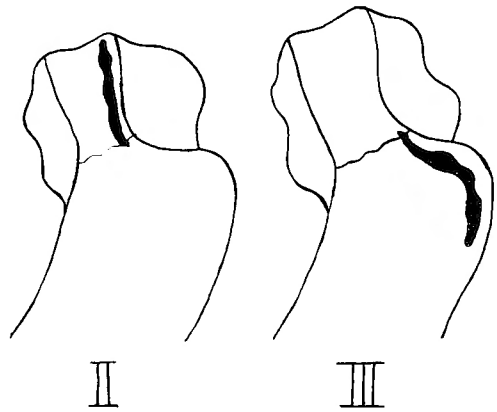

Fig. 2. Methods of division of the cardiac closing mechanism
II——Division of the phrenoesophageal ligament and LES
III——Division of the phrenoesophageal ligament and WILLIS' oblique muscle

further manometries were executed under resting and gastrin-stimulated (Tetragastrin^{R}, 5 μg/kg IV, Teikoku Zohki Co. Ltd., Japan) conditions. After NISSEN fundoplication, and another hour of rest, a final manometry was performed and the animal was sacrificed.

3) Changes in resting and gastrin-stimulated lower esophageal sphincter pressure (LESP) after the destruction of the cardiac closing mechanism (long-term experiment)

In the short-term experiments, surgical impairment of the cardiac closing mechanism was studied manometrically. Subsequently, in a long-term experiment, an attempt was made to clarify by the same operative procedures, how the LESP was influenced and how signs of esophagitis could be recognized in the distal esophageal mucosa. After the phrenoesophageal ligament, the LES and the WILLIS' oblique muscle had been divided in the same manner as in the previous short-term experiment, the phrenoesophageal ligament was reattached to the gastric serosa, approximately 2 cm caudal to its original site to close the posterior mediastinum. Esophageal manometry was performed under resting and gastrin-stimulated conditions before the operative procedures. Two months after surgery, manometry was performed again and the esophageal mucosa was carefully examined immediately after sacrifice.

Out of 15 dogs which had undergone division of three components of the cardiac closing mechanism and were alive 2 months postoperatively, 5 were studied. Out of the three dogs still alive 2 months after a laparotomy only had been performed, 2 were studied as controls.

4) Effects of intragastric instillation of alkali or acid on lower esophageal sphincter pressure (LESP) and serum gastrin level

Many reports have appeared regarding the relationship between LESP and intragastric pH in humans and animals. Although it is thought that gastrin participates in the regulation of LESP and intragastric pH, some problems still remain to be clarified. Therefore, this study examined, at regular intervals, changes in LESP and serum gastrin level by

intragastric instillation of acid and alkali.

Fifteen mongrel dogs, ranging from 8 to 15 kg in body weight, were divided into 3 groups of 5 each : (I) instillation of 0.1 N-NaOH, (II) instillation of 0.1 N-HCl and (III) instillation of saline as a control group. An upper midline incision was made, a small gastrotomy was made on the anterior wall of the antrum, a polyethylene tube for instillation of the fluids was inserted through the gastrotomy opening toward the pylorus and sutured there. The pylorus was clamped with an intestinal forceps in order to prevent duodenal efflux of the infused fluid and reflux of duodenal contents into the stomach. Cannulation through the femoral vein was also performed for blood sampling of the gastrin assay. The first esophageal manometry was performed before the operative procedure. One hour after the initial operative procedures and with additional doses of pentobarbital, manometry was performed several times until a fixed pressure value was obtained - this value being regarded as the value before instillation. The following serial manometries were all performed under the laparotomy. Instilling 0.1 N-NaOH, 0.1 N-HCl, or saline, 30 ml respectively, within one minute, through the cannula fixed to the prepylorus (closed immediately after instillation), esophageal manometry was performed every 10 minutes for 60 minutes. Additional pentobarbital was not administered during this experiment. Blood sampling, about 5 ml, for determination of serum gastrin, were taken before and 5, 10, 15, 30, 45 and 60 minutes after instillation. After clotting, blood coagula were excluded from the whole blood and residua of the blood were centrifuged at 3,000 r. p. m. for 15 minutes at room temperature. The supernatants were kept frozen in ice until measured. Gastrin determination was performed by radioimmunoassay with a CIS-kit®. A count of the radioactivity was taken for 2 minutes, 3 times and the count per minute was calculated. Graphing a standard curve, the serum gastrin levels were determined.

5) Effects of intragastric instillation of antacid on lower esophageal sphincter pressure (LESP) in dogs

There are very few studies on the effectiveness of antacids in the medical treatment of reflux esophagitis or on the effects of gastric alkalinization of antacids. Therefore, the possibility of the clinical use of antacids in cases of reflux esophagitis were studied by instilling antacid in the canine stomach and measuring the changes in the LESP. The experimental details are included in the following experiment.

6) Effects of intragastric instillation of bile on lower esophageal sphincter pressure (LESP)

Regarding the etiologies of reflux esophagitis, gastroesophageal reflux of alkaline duodenal juices after partial or total gastrectomy, pyloric insufficiency, and the direct contact of acid or pepsin in gastric juices on the esophageal mucosa, are recognized to be familiar offenders. While duodenal secretions, composed of bile and pancreatic juice, can directly damage the esophageal mucosa, it is probable that they may indirectly interfere with the cardiac closing mechanism by their reflux into the stomach, prior to a gastroesophageal reflux. In this study experiments were performed to demonstrate that reflux of duodenal

secretions, especially bile, into the stomach, can affect the cardiac closing mechanism.

Twelve mongrel dogs, ranging from 8 to 15 kg in body weight, were divided evenly into 4 groups : (I) instillation of antacid, (II) instillation of saline as a control, (III) instillation of canine gallbladder bile and (IV) instillation of 10% taurocholate. Bile was aspirated from the gallbladder of 10 dogs, frozen until use, then mixed in one bottle and used without dilution. Antacid (Maalox®, Yamanouchi Co. Ltd., Japan) was also instilled without dilution. Ten % taurocholate was prepared by dissolving 25 g of taurocholate (Nakarai Chemicals Ltd., Kyoto, Japan) in 250 ml of distilled water. Instillation of these solutions was performed in random order. Operative procedures and esophageal manometry were performed in the same manner as in Experiment 4.

7) Effects of various kinds of prostaglandins and glucagon on lower esophageal sphincter pressure (LESP)

Recently attention has been concentrated upon gastrointestinal hormones, such as gastrin, secretin, CCK-PZ, glucagon and motilin and various kinds of prostaglandins, as humoral regulating agents on the cardiac closing mechanism. Experimental studies concerning the effects of gastrin, secretin, and CCK-PZ on the cardiac closing mechanism in dogs have been carried out by SANTOKI,[53] a member of the 2nd Department of Surgery, Yamaguchi University Hospital. Therefore, this study attempted to clarify the effects of prostaglandins and glucagon on the cardiac closing mechanism.

Prostaglandin $F_{2\alpha}$ (Ono Co. Ltd., Osaka, Japan) in doses of 2.5 to 40.0 μg/kg ; prostaglandin E_1 (Sigma Chemical Co., U.S.A.) in doses of 0.25 to 32.0 μg/kg ; prostaglandin E_2 (Sigma Chemical Co., U.S.A.) in doses of 0.25 to 32.0 μg/kg ; and glucagon (Sigma Chemical Co., U.S.A.) in doses of 3.0 to 100.0 μg/kg, were given intravenously in random order. Successive doses of each drug were administered to the same dog at intervals of more than 30 minutes. Twelve mongrel dogs —that is, 5 for prostaglandin $F_{2\alpha}$, 2 for prostaglandin E_1, 3 for prostaglandin E_2 and 2 for glucagon— were used. The effects of each drug on the cardiac closing mechanism were analyzed by esophageal manometry under intravenous pentobarbital anesthesia with intratracheal cannulation. Manometry was performed by the withdrawal method immediately before and a few minutes after the administration of each dose of the drug. Although the effects of drugs on the cardiac closing mechanism should be examined continuously with a catheter tip fixed in the high pressure zone, in this study the effects were measured by a withdrawal method because of uncertainty due to displacement of the catheter tip by respiratory movement and peristalsis of the esophagus.

8) Effects of various hiatal herniorrhaphies on the destroyed cardiac closing mechanism in dogs

Although operative treatment is indicated for sliding hiatal hernia, particularly when complicated by reflux esophagitis, a variety of surgical procedures are being performed but the principles for the selection of these procedures remain unclear. One difficulty is that surgical treatment of hiatal hernia requires not only the basic measures of a hernia

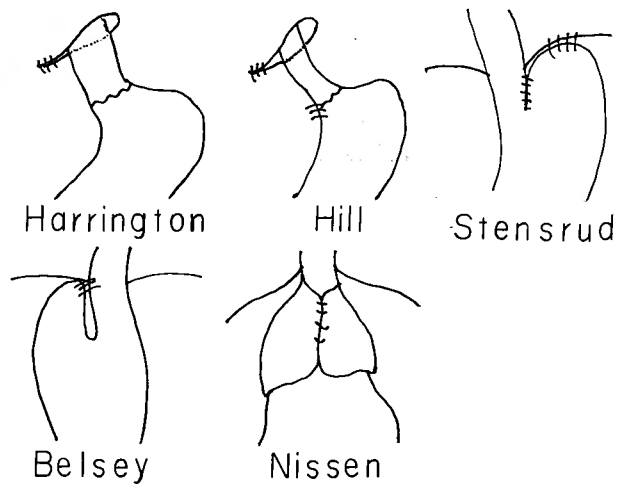

Fig. 3. Various methods of hiatal herniorrhaphies

operation—that is, reduction of the hernia content and closure of the hernia port—but also the attempt to prevent gastroesophageal reflux and to develop gastroesophageal competence. For decades, various surgical procedures have been used to produce gastroesophageal competence, but there is still a need to study and compare the reconstructive effects of these procedures for sliding hiatal hernia. In this study 5 kinds of hiatal herniorrhaphies (Fig. 3) were performed on dogs which previously had undergone division of the phrenoesophageal ligament, the LES and the WILLIS' oblique muscle, and the extent of the recovery of the cardiac closing mechanism was studied by esophageal manometry. Manometric studies were also performed under gastrin-stimulated conditions.

After laparotomy through an upper midline incision, division of the phrenoesophageal ligament, the LES and the WILLIS' oblique muscle was performed in the same manner as described in Experiment 2. Subsequently 5 kinds of hiatal herniorrhaphies were performed in random order. Fifteen mongrel dogs, divided evenly into 5 groups, were used. In the HARRINGTON method, the divided ligament was closed around the distal esophagus ; thus, the posterior mediastinum was separated again from the abdominal cavity. As an abdominal esophageal segment does not exist in dogs because of the attachment of the ligament to the stomach, a new abdominal esophagus, several cm in length, was obviously created by this method. In the HILL method, the gastroesophageal junction was sutured to the preaortic fascia in combination with the HARRINGTON maneuver. Although the BELSEY Mark IV method should be transthoracically performed, in this study an abdominal approach was used because the other 4 methods do not require thoracotomy and it was desirable to keep the experimental conditions as similar as possible when performing esophageal manometry. In the BELSEY Mark IV method, the sutures were carried to the gastric fundus, the esophagus and back to the gastric fundus.

In the NISSEN method, a 360° fundoplication around the distal esophagus using the

gastric fundus, was performed so that the area around the division of the WILLIS' oblique muscle was completely enveloped with 3～5 sutures. the most proximal one tying in the ligament.

Esophageal manometries were all performed under intravenous pentobarbital anesthesia. The first manometry was performed before the operative procedure to determine pressure value, width and the distance from the upper incisor to the high pressure zone in each dog. The second and third manometries were performed under resting and gastrin-stimulated conditions one hour after the division procedure. The fourth and fifth manometries were also performed under resting and gastrin-stimulated conditions one hour after the hiatal herniorrhaphy procedure.

B) Results

1) Pressure prefiles of esophageal manometry curves in dogs

The esophageal manometry curves are presented in Fig. 4. Respiratory fluctuations were noted but effects of heart beats were not recorded with this manometry method. Direction of the respiratory fluctuations on the curves is quite similar in the esophagus and the gastric fundus ; direction of the movement was upward on the recording paper on inspiration. It can be seen that the point of respiratory reversal occurred at 2 points and sometimes at 4. The point of respiratory reversal was always at even numbers. During pull-through from the gastric fundus to the esophagus, respiratory fluctuations gradually increased in amplitude within the high pressure zone without a change of direction and the point of respiratory reversal appeared immediately oral to the point of the peak respiratory movement. As more cephalad pull-through was made, respiratory fluctuations decreased in amplitude and abruptly reversed again around the distal esophagus. At that point, the respiratory fluctuations in the esophagus became similar to those in the stomach. When the

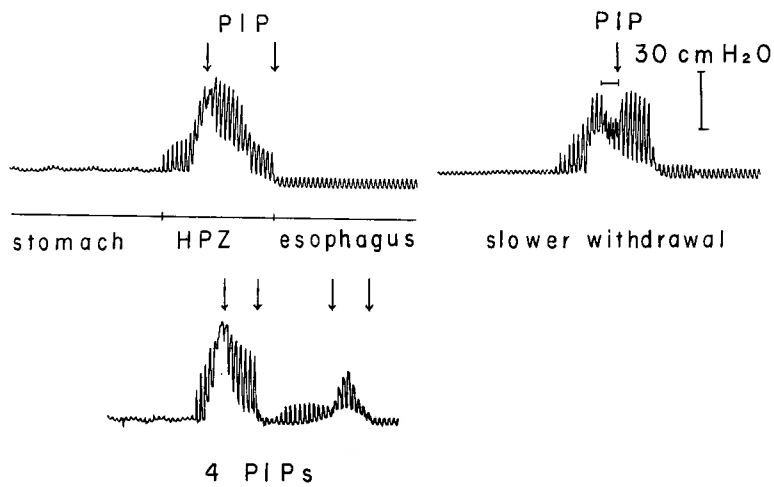

Fig. 4. Esophageal manometry curves in dogs

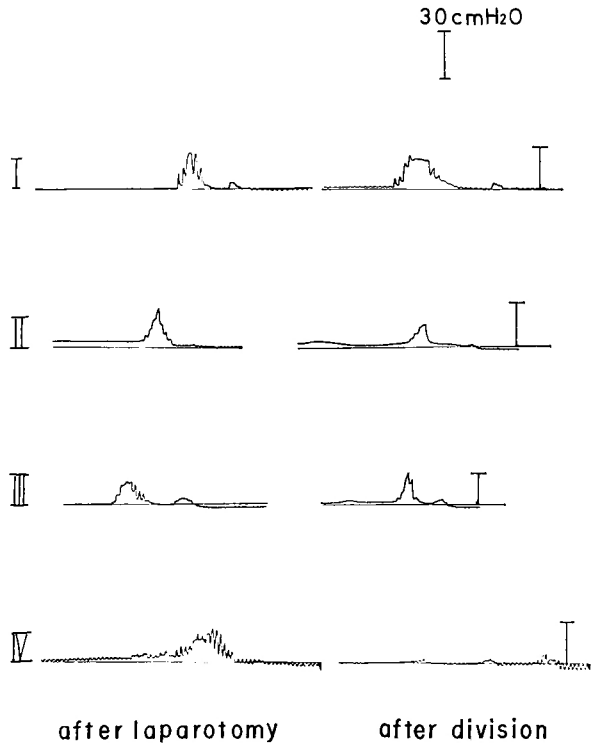

Fig. 5. Pressure profiles of the high pressure zone after division of Groups I to IV

velocity of pull-through was extremely slow, the first point of respiratory reversal became bidirectional, half-upward and half-downward, on inspiration. When respiratory reversal occurred at 4 points, the second, third, and fourth points were present just cephalad to the high pressure zone.

2) Effects of division of individual components of the cardiac closing mechanism on resting and gastrin-stimulated lower esophageal sphincter pressure (LESP)

(i) Changes in the profiles of the esophageal manometry curves caused by division procedures

Changes in the profiles of the esophageal manometry curves are depicted in Fig. 5, in which the profiles after laparotomy are compared with those after division in each group. It can be seen that the high pressure zone has almost disappeared and the curve has become flat in Group IV. However, in Group I the high pressure zone was hardly affected. Profiles of the high pressure zones in Groups II and III were affected slightly but did not show any definite tendencies. It was concluded that the LES and the WILLIS' oblique muscle must function properly in order to prevent gastroesophageal reflux.

(ii) Changes in lower esophageal sphincter pressure (LESP) caused by division procedures.

Changes in LESP are graphed and tabulated in Fig. 6 and Table 1. Table 1 shows the

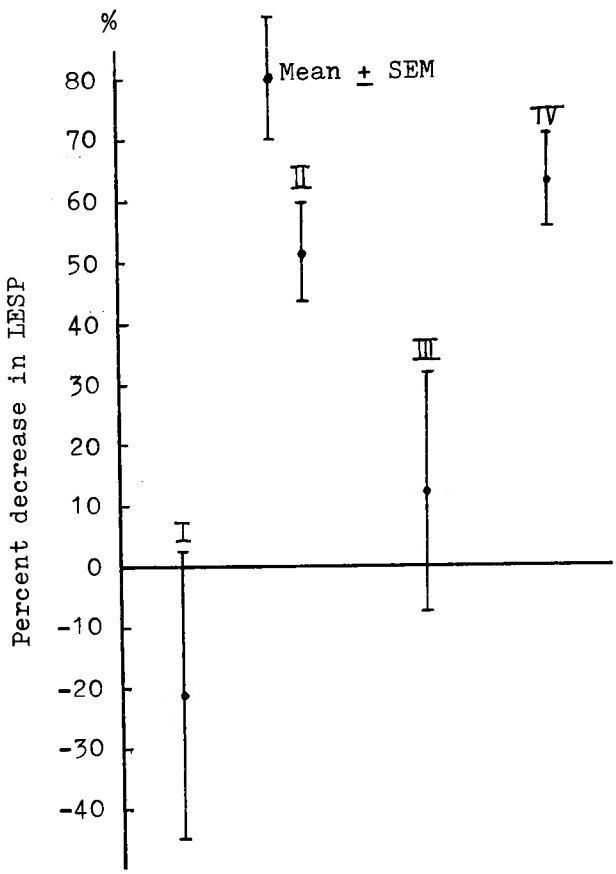

Fig. 6. Percentage decreases in LESP after division of Groups I to IV

Table 1. Changes of LESP after division in Groups I to IV
Results are expressed as the mean ± SEM. N refers to the number of animals studied

	N	after laparotomy (cm H_2O)	after division (cm H_2O)	difference[a] (cm H_2O)	percent decrease[b] (%)
I	5	24.1±2.78	27.2±3.18	−3.1±4.95	−21.16±23.89
II		33.1±4.80	15.0±2.14	18.1±5.15	51.2±7.99
III		34.8±9.54	26.8±5.22	8.0±6.79	12.1±19.61
IV		24.2±2.63	8.7±1.56	15.5±2.55	62.9± 7.64 (Mean±SEM)

a : Pressure differences between pressure value after laparotomy and after division
b : Percentage of pressure differences for pressure value after laparotomy

pressures after laparotomy and after division, the differences and their percentages. As depicted in Fig. 6, the LESP rather tended to increase in Group I, but decreased in Groups II, III, and IV, decreasing greatly in Groups II and IV, the groups in which the LES had been divided. By statistical analysis, significant differences were found ($p<0.05$) among all the groups except between II and III and II and IV. It was concluded that the

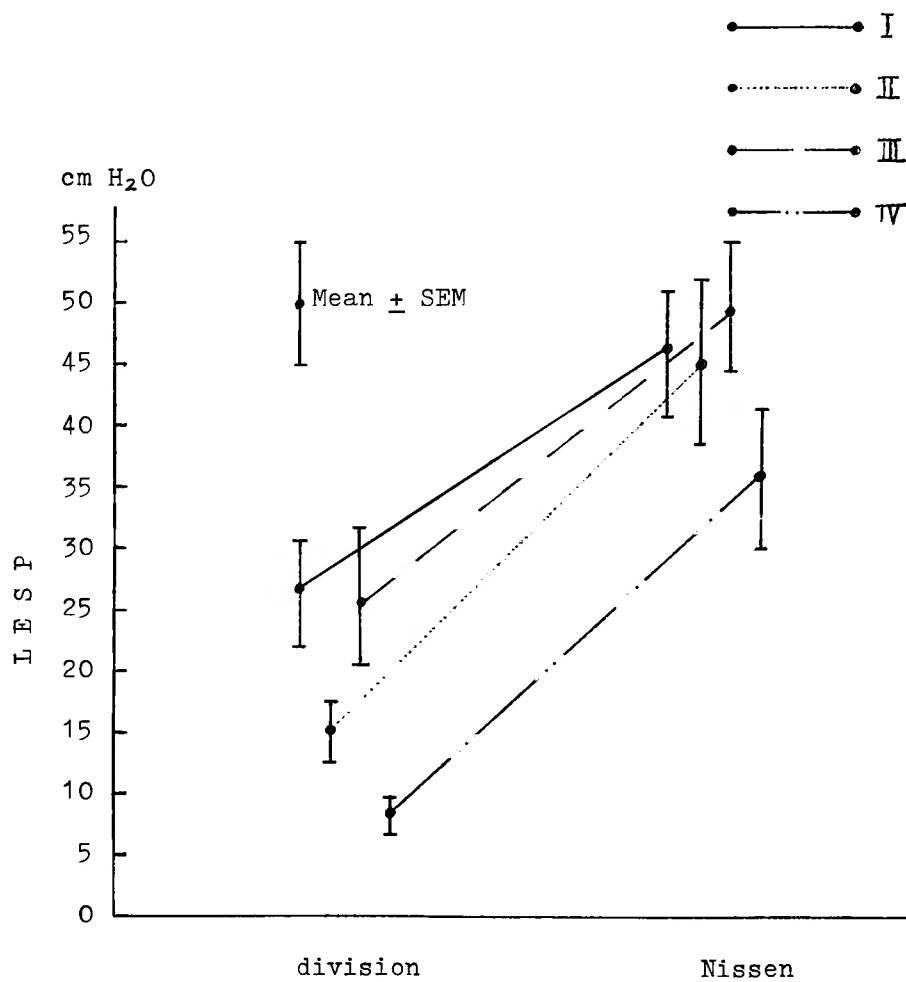

Fig. 7. Changes of LESP after NISSEN fundoplication in Groups I to IV

Table 2. Changes of LESP after NISSEN fundoplication in Groups I to IV

	N	after division (cm H_2O)	Nissen fundoplication (cm H_2O)	difference (cm H_2O)	percent increase (%)
I	5	27.2±3.18	45.7±4.91	18.5±5.53	78.3±29.36
II		15.0±2.14	45.4±6.19	30.3±6.60	227.1±71.72
III		26.8±5.22	49.1±6.58	22.3±7.67	126.6±67.55
IV		8.7±1.56	36.9±6.76	28.1±6.98	376.0±94.17
					(Mean±SEM)

LES, primarily, is related to production of the high pressure zone, the WILLIS' oblique muscle playing only a minor role and the phrenoesophageal ligment having hardly any role in LESP.

(iii) Changes in lower esophageal sphincter pressure (LESP) by NISSEN fundoplication Table 2 and Fig. 7 depict the changes in LESP after NISSEN fundoplications were performed

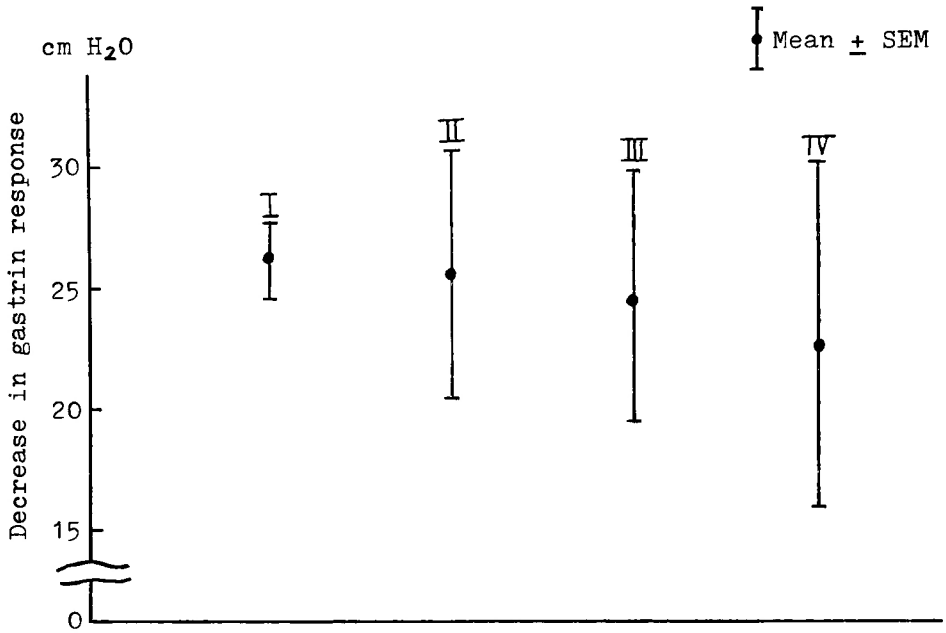

Fig. 8. Changes of responses to tetragastrin® after division

Table 3. Changes of responses to tetragastrin® after division

	N	after laparotomy (Δcm H_2O)	after division (Δcm H_2O)	difference (cm H_2O)	percent decrease (%)
I	5	37.0±1.94	9.7±2.50	27.4±1.11	25.2±5.44
II		35.4±6.21	10.2±4.48	25.2±6.59	30.3±12.99
III		34.7±1.93	9.9±3.91	24.8±5.73	29.7±12.13
IV		26.3±7.65	4.0±0.98	22.3±8.63	23.8±14.93
					(Mean±SEM)

following division procedures. After NISSEN fundoplication, LESP ranged from 30 to 50 cm H_2O and bore no relationship to division procedures in any of the groups. It was concluded that the reconstructive effects of NISSEN fundoplication were similar in all groups, even though different components were divided.

(iv) Responses of the components of the cardiac closing mechanism to exogenous gastrin

In all 4 groups responses of the components of the cardiac closing mechanism to exogenous gastrin are compared in Table 3 and Fig. 8. The pressure increases ranged from 25 to 35 cm H_2O after laparotomy, but ranged from 4 to 10 cm H_2O after division procedures in all 4 groups. Significant differences in responses were not found. It remains unclear what component of the cardiac closing mechanism is most responsive to exogenous gastrin.

3) Changes in resting and gastrin-stimulated lower esophageal sphincter pressure (LESP) after destruction of the cardiac closing mechanism (long-term experiment)

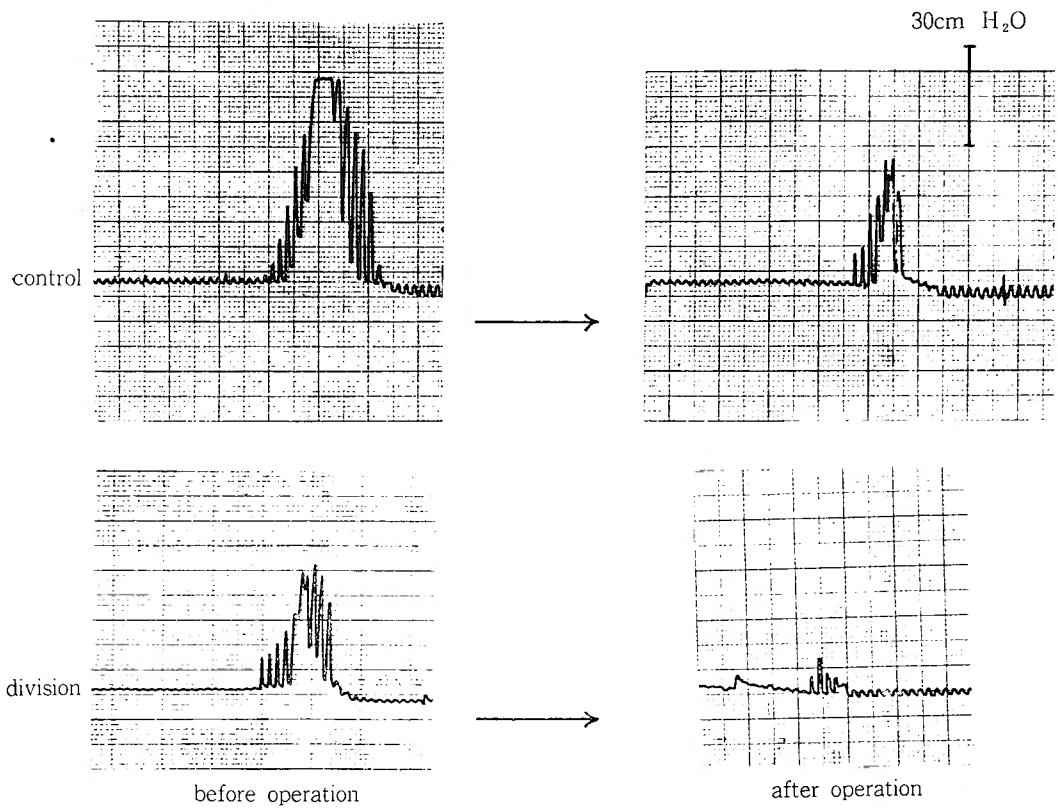

Fig. 9. Profiles of esophageal manometry curves after division of the phrenoesophageal ligament, LES and WILLIS' oblique muscle (long-term experiment)

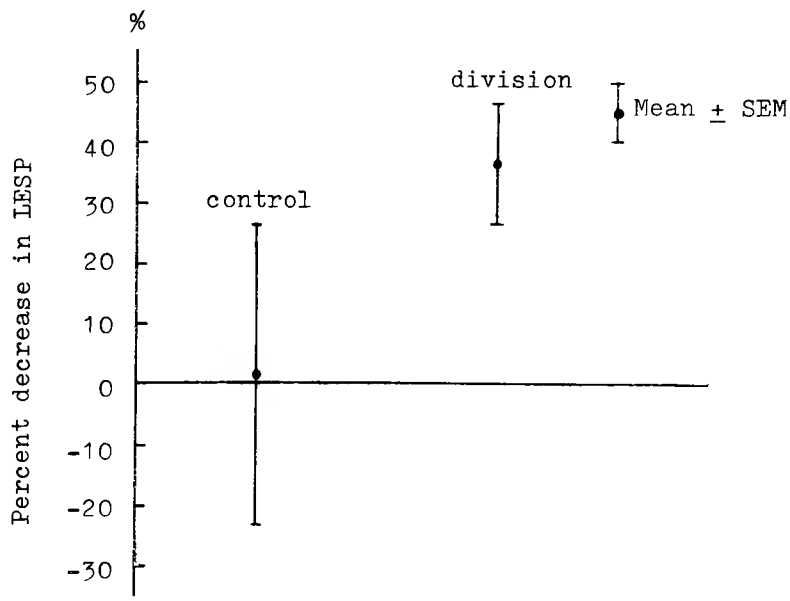

Fig. 10. Percentage decreases of LESP after division of the phrenoesophageal ligament, LES and WILLIS' oblique muscle(long-term experiment)

Table 4. Changes of LESP after division of the phrenoesophageal ligament, LES and WILLIS' oblique muscle (long-term experiment)

	before operation (cm H_2O)	2M. after operation (cm H_2O)	difference (cm H_2O)	percent decrease (%)
Division Group	33.6	24.3	9.3	27.7
	40.0	35.1	4.9	12.2
	33.9	22.3	11.6	34.2
	23.5	15.0	8.5	36.2
	40.0	11.3	28.7	71.8
Control Group	18.2	22.5	−4.3	−23.6
	63.0	46.4	16.6	26.3

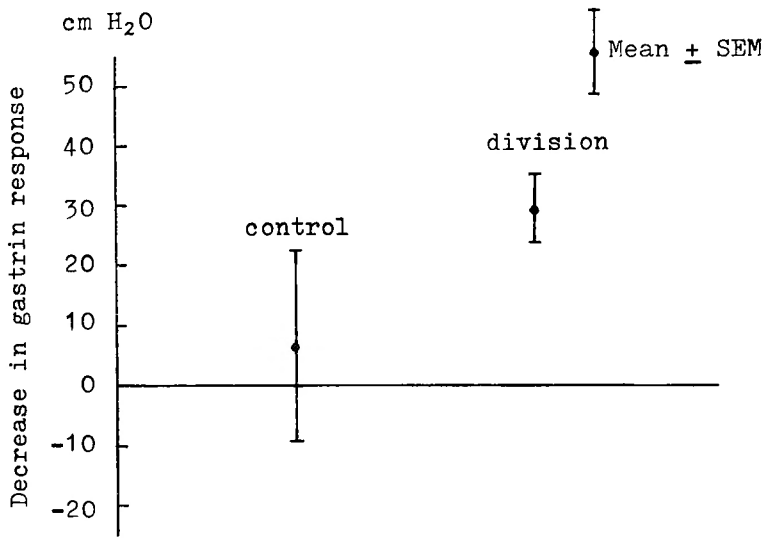

Fig. 11. Changes of responses to tetragastrin after division of the phrenoesophageal ligament, LES and WILLIS' oblique muscle (long-term experiment)

Table 5. Changes of responses to tetragastrin® after division of the phrenoesophageal ligament, LES and WILLIS' oblique muscle (long-term experiment)

	before operation (△cm H_2O)	2M. after operation (△cm H_2O)	difference (cm H_2O)	percent decrease (%)
Division Group	67.5	25.4	42.1	62.4
	60.5	44.6	15.9	26.3
	66.0	43.4	22.6	34.2
	66.0	40.7	25.3	38.3
	67.2	28.2	39.0	58.0
Control Group	67.5	45.0	22.5	33.3
	57.6	67.2	−9.6	16.7

(i) Changes in LESP over a two-month period

Profiles of the manometry curves were unchanged for the relationship between the high pressure zone and the points of respiratory reversal as depicted in Fig. 9. Changes in percentage of decrease of the LESP tended to decrease in the division group in comparison

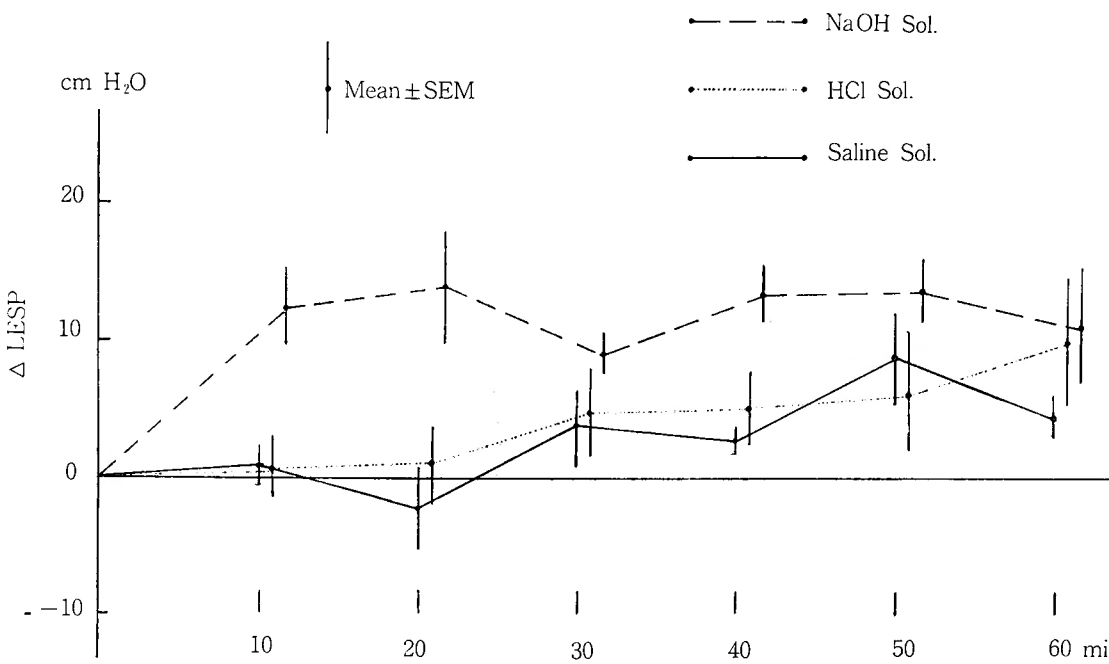

Fig. 12. Changes of LESP following instillation of NaOH, HCl and saline solutions

with the control group. A significant difference between the 2 groups was not found because of the small numbers in each group as shown in Fig. 10 and Table 4.

(ii) Changes in responses of the component of the cardiac closing mechanism to gastrin

In the division group, responses of the components of the cardiac closing mechanism to exogenous gastrin tended to decrease but not significantly, as shown in Fig. 11 and Table 5.

4) Effects of intragastric instillation of alkali or acid on lower esophageal sphincter pressure (LESP) and serum gastrin level

(i) Changes in lower esophageal sphincter pressure (LESP) over a 60-minute period

Changes in the LESP over a 60-minute period caused by intragastric instillation are expressed as differences from the pressure values before instillation in Fig. 12. Although remarkable findings were not seen for 60 minutes after instillation in either the saline or the HCl groups—no significant differences were found between them—, the LESP in the NaOH group increased significantly 10 and 20 minutes after instillation. In comparison with the saline group, pressure increases were larger in the NaOH group 10, 20 and 40 minutes after instillation. It was concluded that LESP increased in response to gastric alkalinization by instillation of a NaOH solution.

(ii) Changes in serum gastrin level over a 60-minute period

Serum gastrin levels tended to increase from 30 to 60 minutes after instillation but did not show a significant increase in the NaOH group as graphed in Fig. 13. Moreover,

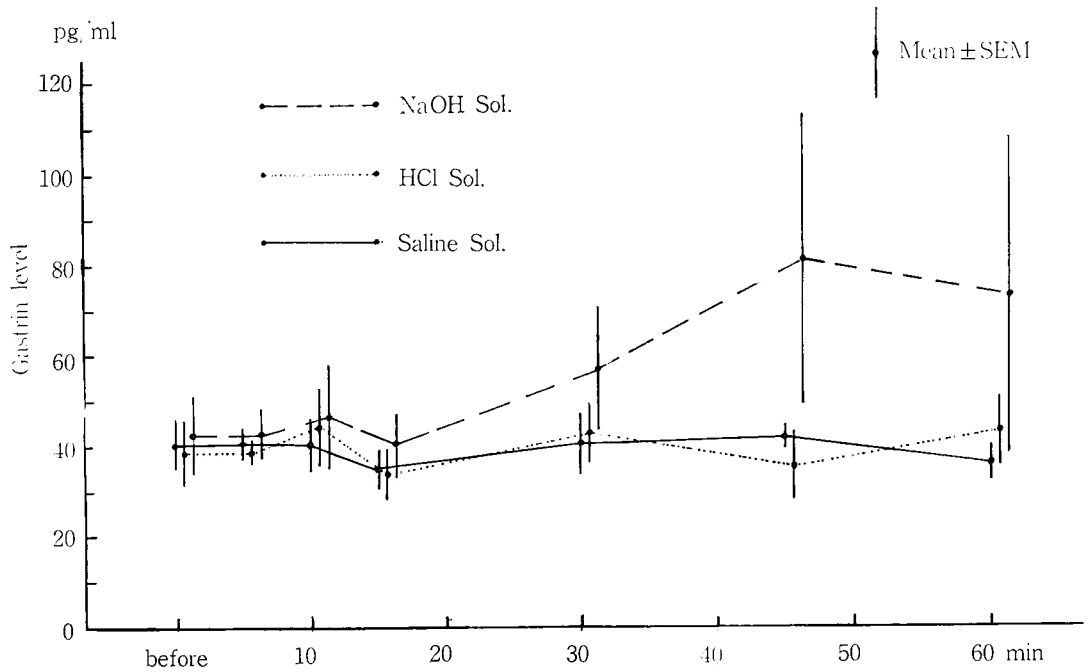

Fig. 13. Changes of serum gastrin levels following instillation of NaOH, HCl and saline solutions

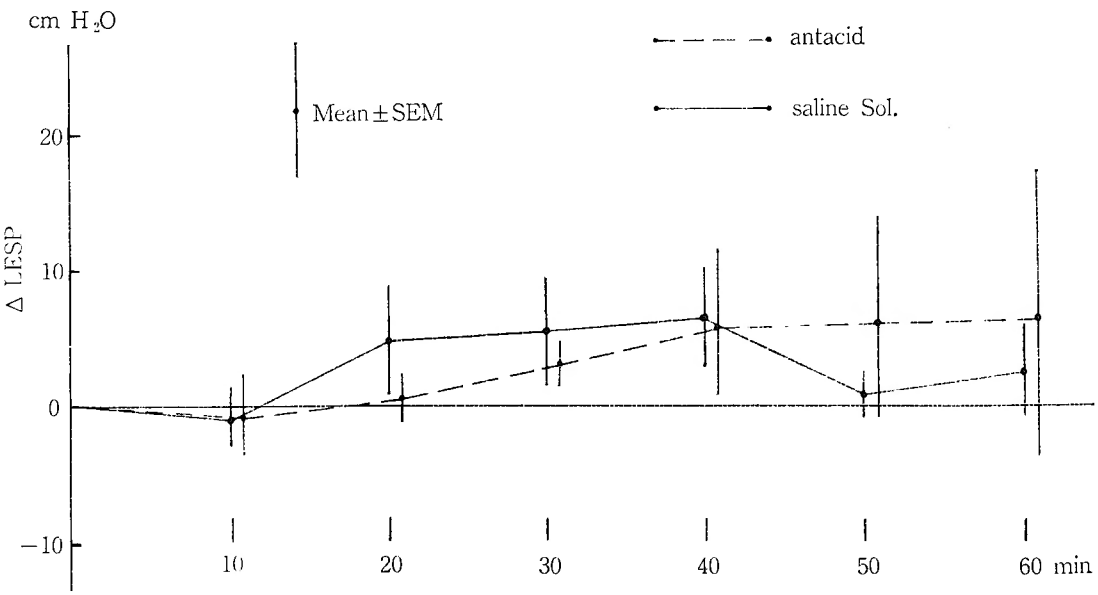

Fig. 14. Changes of LESP following instillation of antacid

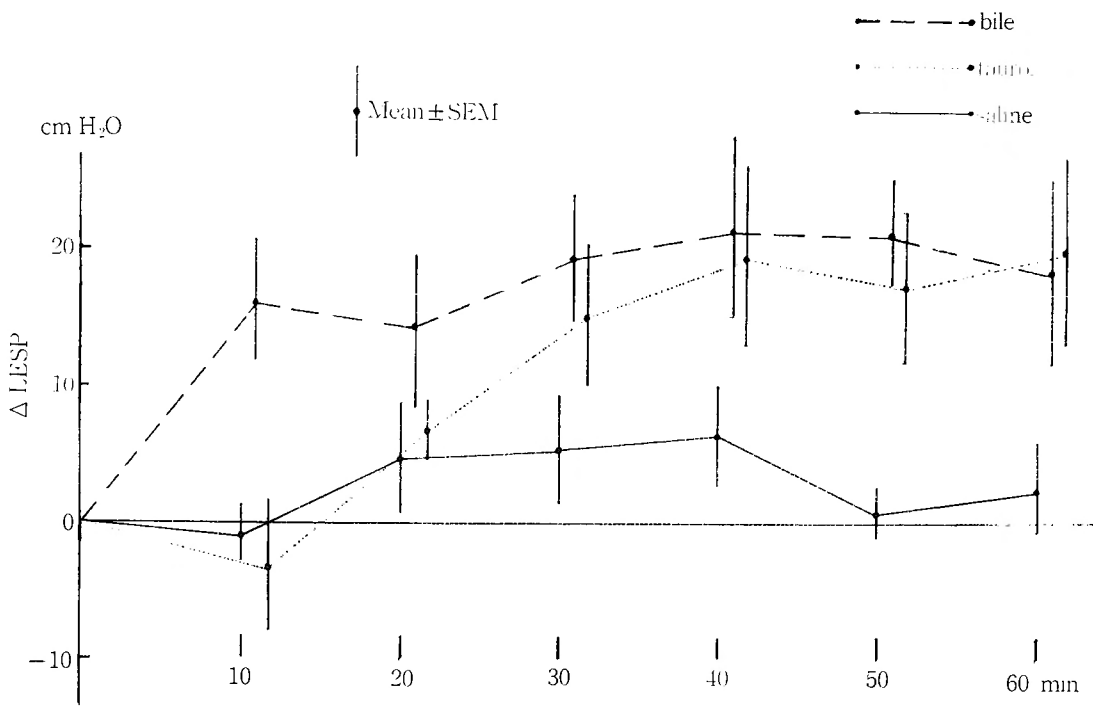

Fig. 15. Changes of LESP following instillation of bile, taurocholate and saline solutions

significant differences were not found between the NaOH and saline groups or between the HCl and saline groups. It was concluded that serum gastrin level was not significantly changed by gastric alkalinization or by acidification.

5) Effects of intragastric instillation of antacid on lower esophageal sphincter pressure (LESP) in dogs

Changes in the LESP were studied for 60 minutes after instillation of antacid. It tended to increase after 20 minutes but the change was not statistically significant as shown in Fig. 14. There was no significant increase in the antacid group at any time interval in comparison with the saline group. It was found that intragastric alkalinization by antacid did not increase the LESP.

6) Effects of intragastric instillation of bile on lower esophageal sphincter pressure (LESP)

(i) Instillation of bile

The LESP began to increase 20 minutes after instillation and increased significantly 40 and 60 minutes after instillation as depicted in Fig. 15. Moreover, the LESP increased significantly 50 and 60 minutes after instillation in comparison with the saline group. It was concluded that the LESP was increased by intragastric instillation of bile.

(ii) Instillation of 10 % taurocholate

The LESP tended to increase 10 minutes and increased significantly 40 minutes after

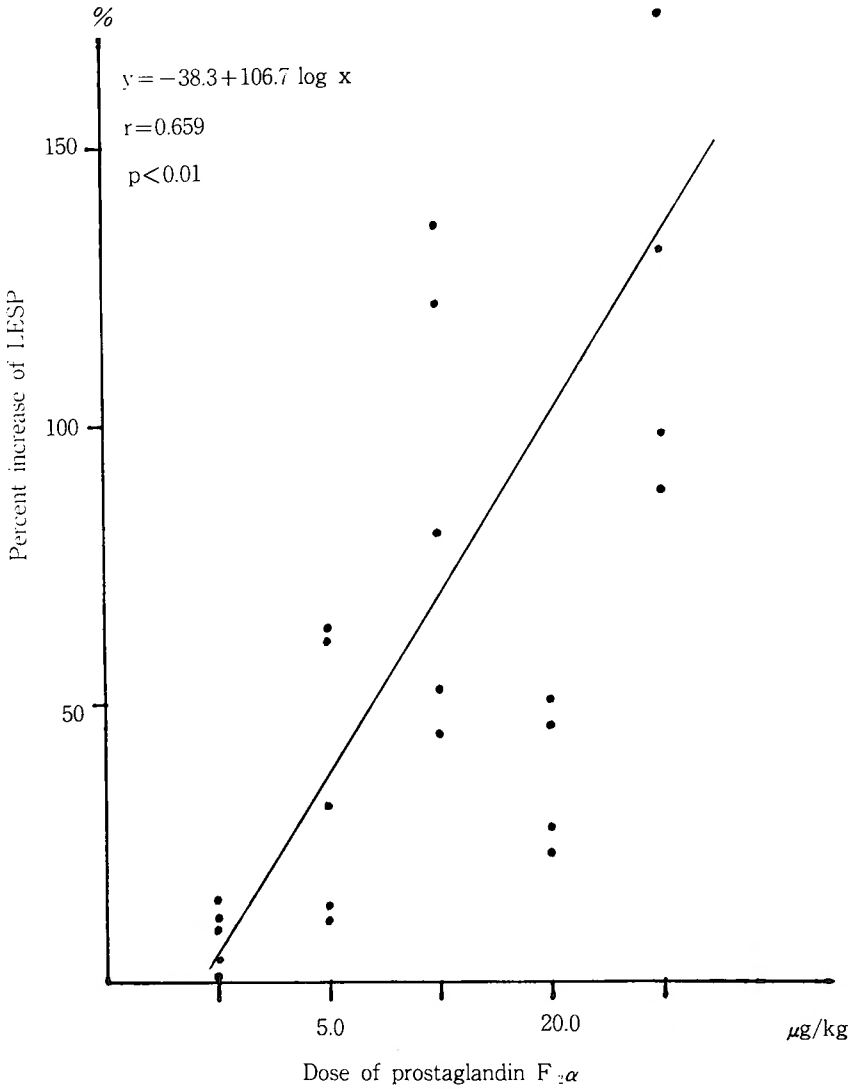

Fig. 16. Responses of the cardiac closing mechanism to prostaglandin $F_{2\alpha}$

instillation in the taurocholate group as depicted in Fig. 15. The LESP in this group increased significantly 10, 40 and 50 minutes after instillation in comparison with the saline group; that is, the changes in the taurocholate group were similar to those in the bile group except 10 minutes after instillation. It was concluded that the LESP was increased by intragastric instillation of 10 % taurocholate.

7) Effects of various kinds of prostaglandins and glucagon on lower esophageal sphincter pressure (LESP)

(i) Effects of prostaglandin $F_{2\alpha}$

In Fig. 16, changes in the LESP by prostaglandin $F_{2\alpha}$ are expressed as percentages

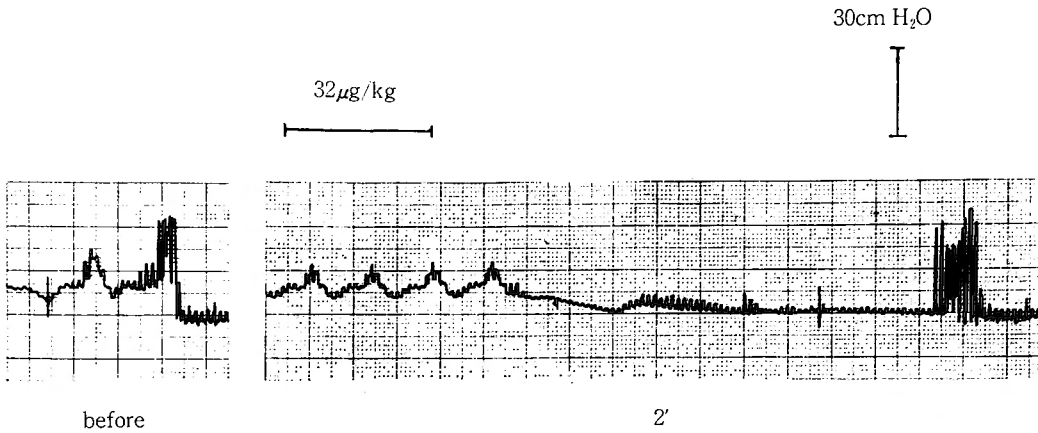

Fig. 17. Responses of the cardiac closing mechanism to prostaglandin E_1 (32μg/kg)

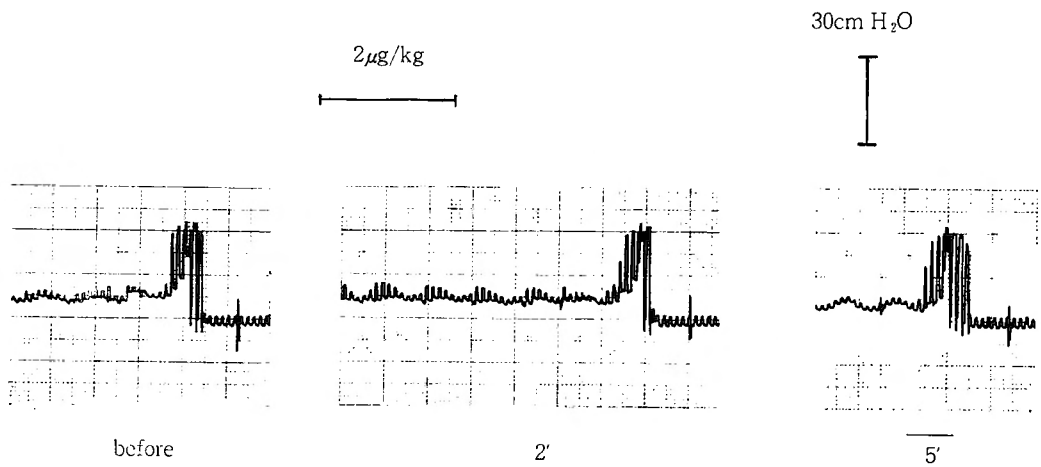

Fig. 18. Responses of the cardiac closing mechanism to prostaglandin E_2 (2 μg/kg)

of the pressure values before administration. The LESP increased significantly with every dose from 2.5 to 40.0 μg/kg.

(ii) Effects of prostaglandin E_1

The LESP was not influenced by any dose of prostaglandin E_1. For example, when the dose of 32 μg/kg was given, the LESP was hardly changed 2 minutes after administration in comparison with the pressure value before administration. However, the fundic pressure decreased after administration of prostaglandin E_1 as shown in Fig. 17.

(iii) Effects of prostaglandin E_2

As with the administration of prostaglandin E_1, the LESP was also hardly influenced by any dose of prostaglandin E_2. In Fig. 18, which shows the manometry curves for the dose of 2 μg/kg, the LESP was not influenced 2 or 5 minutes after administration.

(iv) Effects of glucagon

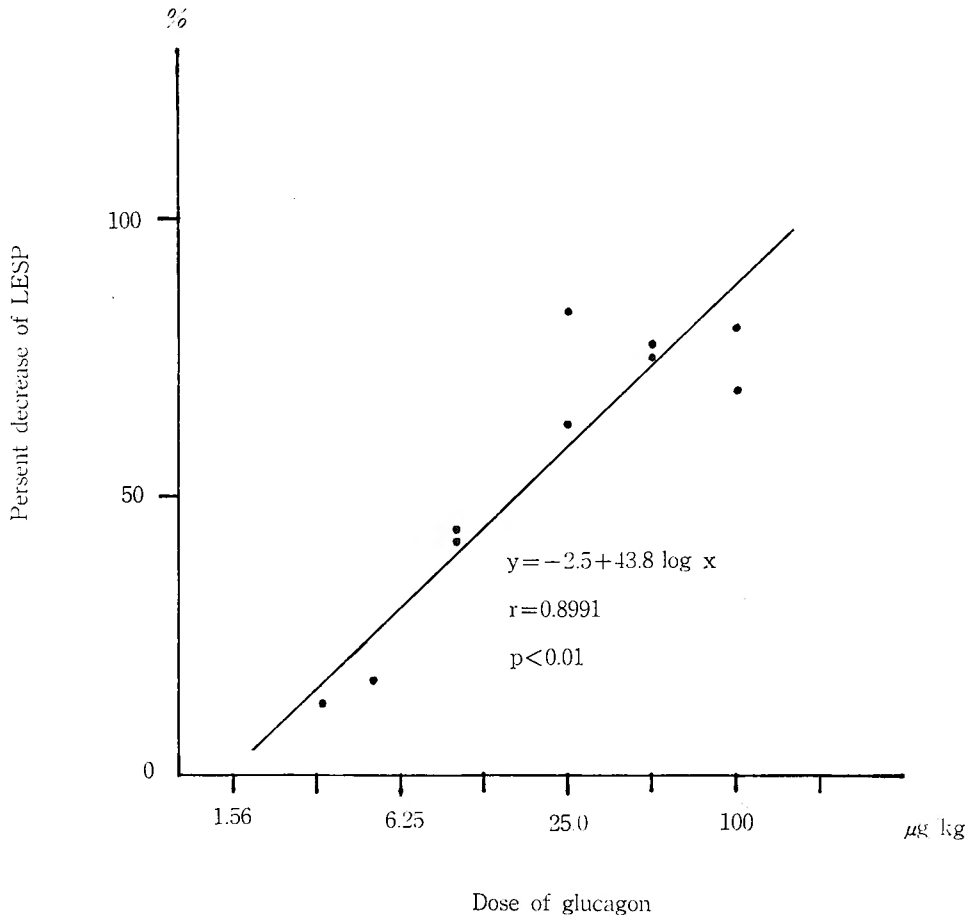

Fig. 19. Responses of the cardiac closing mechanism to glucagon

In Fig. 19, changes in the LESP are shown by percentages of pressure value before administration. A linear relationship was found between the dose given and the percentage increase in LESP. In summary, LESP decreased with every dose of glucagon.

8) Effects of various hiatal herniorrhaphies on the destroyed cardiac closing mechanism in dogs

(i) Changes in profiles of the high pressure zone

A high pressure zone with high amplitude was reconstructed by the NISSEN and BELSEY Mark Ⅳ methods, after the high pressure zone had been almost flattened by division of the phrenoesophageal ligament, the LES and the WILLIS' oblique muscle as depicted in Fig. 20. However, reconstructive effects on the high pressure zone were not remarkable by the HARRINGTON and HILL methods; a high pressure zone with two phases occurred by approximating the crus of the diaphragm. With the STENSRUD method, a specific profile of manometry curves was not seen particularly in the high pressure zone.

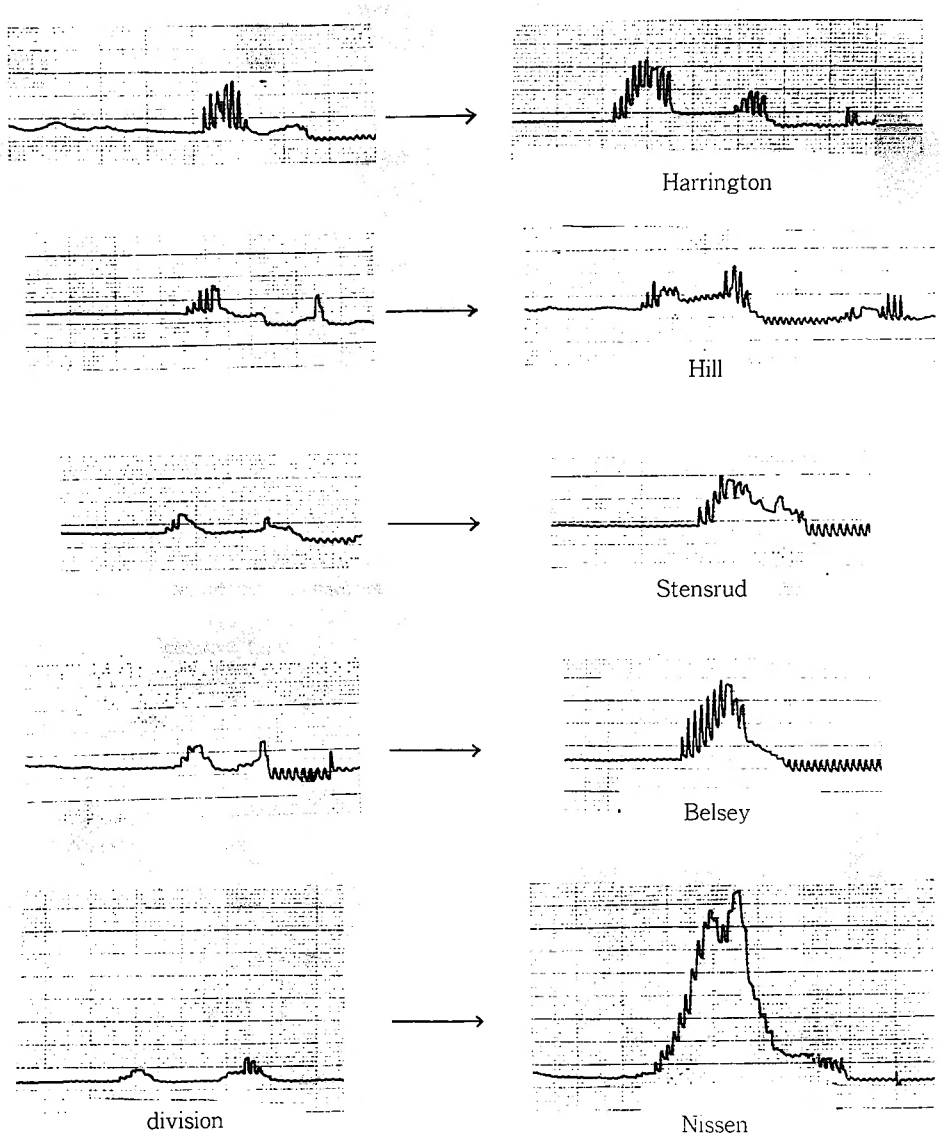

Fig. 20. Esophageal manometry curves after performance of various methods of hiatal herniorrhaphies

(ii) Changes in LESP

Differences between the LESP after hiatal herniorrhaphies and after division of the ligament, the LES and the WILLIS' oblique muscle, in Fig. 21, showed the reconstruction of the high pressure zone. Although the reconstructive effects of the HILL and HARRINGTON methods were not remarkable, significant increases in the LESP were found with the STENSRUD, BELSEY Mark Ⅳ and NISSEN methods. The greatest increase in the LESP was noted with the NISSEN method, less with the Stensrud and BELSEY Mark Ⅳ methods, and the least with the HARRINGTON and HILL methods.

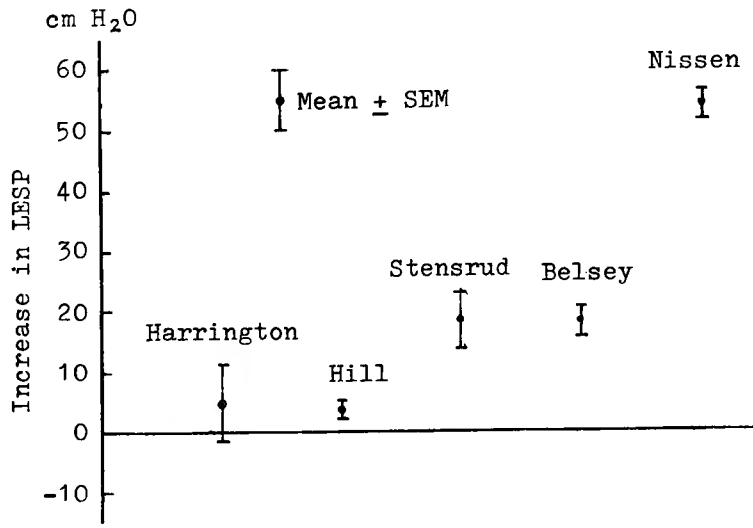

Fig. 21. Changes of LESP after performance of various methods of hiatal herniorrhaphies

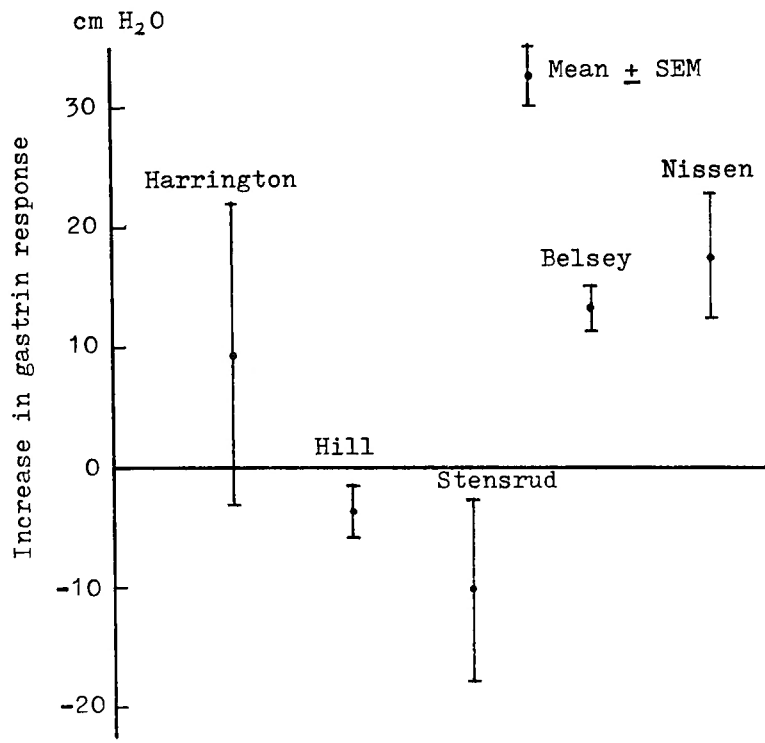

Fig. 22. Changes of responses to tetragastrin[R] after performance of various methods of hiatal herniorrhaphies

Table 6. Associated disorders in our cases of hiatal hernia

Esophageal diverticula	1
Esophageal cancer	1
Esophagocardial cancer	3
Gastric cancer	1
Gastric cancer (postoperative)	2
Cholelithiasis	1
Cholelithiasis with cancer of the gallbladder	2
Duodenal ulcer	1
Diverticula of the colon	0
Kyphoscoliosis	7
Obesity	2
Not recognized	8

Table 7. Endoscopic classification of our cases of hiatal hernia

Discoloring type	11
Erosive and/or ulcerative type	4
Uneven type	3
Malignant	4
Not performed	5
	27

Table 8. X-ray classification of our cases of hiatal hernia

Sliding type	21
Paraesophageal type	0
Mixed type	1
Malignant	5
	27

Table 9. Subjective symptoms in 21 cases primarily diagnosed as "Hiatal Hernia"

Heart burn	6
Dysphagia	11
Retrosternal pain	3
Epigastralgia	3
Hematemesis	3
Asymptomatic	4

Table 10. Complications in 21 cases primarily diagnosed as "Hiatal Hernia"

Reflux esophagitis	18
Esophageal ulcer	2
Esophageal stricture	3
Hemorrhage	3
Perforation	0
Anemia	3
Pulmonary complications	0
Not recognized	5

Table 11. Details of treatment in 21 cases primarily diagnosed as "Hiatal Hernia"

Medical or no treatment	4
Esophagofundectomy	3
Harrington operation	1
Hill operation	1
Nissen operation	12
	21

(iii) Responses of the component of the cardiac closing mechanism to exogenous gastrin

Responses to gastrin after division of the ligament, the LES and the WILLIS' oblique muscle and after hiatal herniorrhaphies were compared as differences in pressure increases as shown in Fig. 22. Although significant differences were not found among the 5 kinds of hiatal herniorrhaphies, the tendency for an increased response was found in the NISSEN and BELSEY Mark IV methods.

Clinical Study of Cases with Sliding Esophageal Hiatal Hernia

Twenty-seven cases of hiatal hernia, 10 men and 17 women, were treated at the 2nd

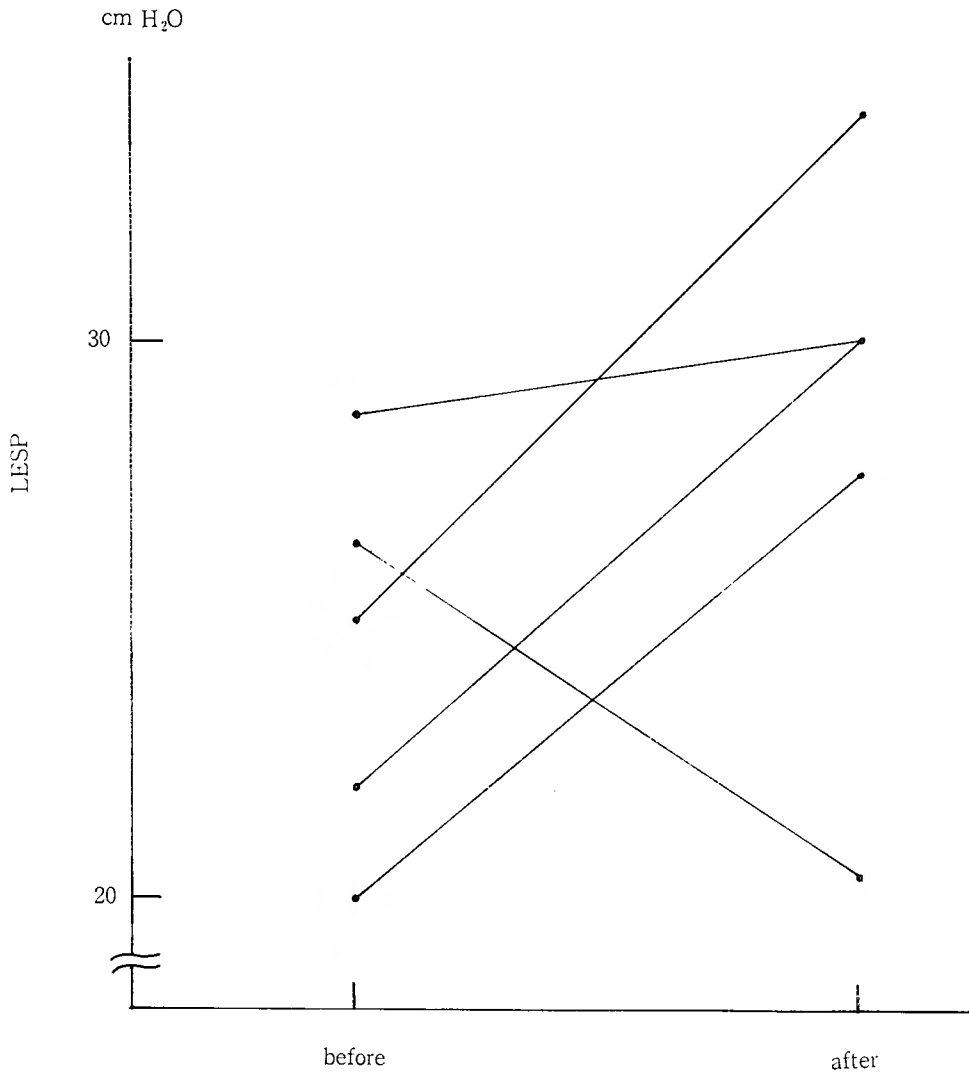

Fig. 23. Changes of LESP before and after NISSEN fundoplication

Surgical Clinic, Yamaguchi University Hospital, from September, 1970 until August, 1979. Details of the accompanying disorders in these cases are summarized in Table 6. There were no cases of Saint's triad. It is worthy to note that 7 cases with kyphoscoliosis, which is considered as one of the etiologic factors, were present. Esophagitis was diagnosed in 18 cases by esophageal endoscopy (Table 7). On X-ray, 22 cases were classified as sliding type and 1 case was classified as mixed type (Table 8). Out of the 27 cases, there were 21 who had been diagnosed as only hiatal hernia and were treated primarily for this condition.

These 21 cases were analyzed on sex, age, clinical symptoms, complications, manometric findings and treatment. Among the 21 cases, there were 7 men and 14 women, the mean

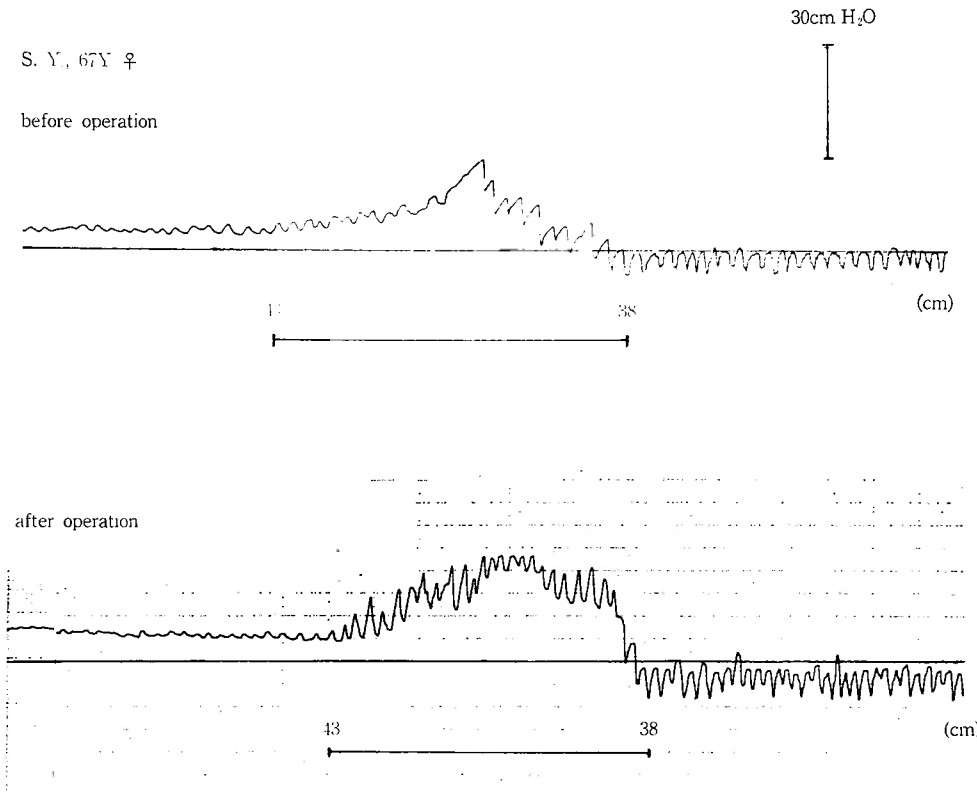

Fig. 24. One case of hiatal hernia (67 years, ♀)
Esophageal manometry curves before and after NISSEN fundoplication

age was 67.8 years ranging from 43 to 78. Clinical symptoms, primarily chief complaints, are summarized in Table 9. There were 11 cases with dysphagia among the three more frequent symptoms : that is, heart burn, dysphagia, and retrosternal pain. Regarding complications, 18 cases of reflux esophagitis and 3 cases of esophageal stricture were recognized (Table 10). Regarding details of treatment, as shown in Table 11, esophagofundectomy was performed on 3 cases, in which malignancies or severe stenosis were already present. NISSEN fundoplication exclusively was performed on all 12 cases, admitted after October, 1976, at our institution. In only 5 cases was esophageal manometry executed both before and after surgery. In all the cases except one, the LESP increased after NISSEN fundoplication as graphed in Fig. 23. The mean LESP increase in 5 cases was from 24.3 ± 1.44 cm H_2O preoperatively, to 28.4 ± 2.25 (M $\pm$SEM) cm H_2O postoperatively. A case was presented in Fig. 24 and the LESP in this case measured 25 cm H_2O before and 34 cm H_2O after surgery. Recurrence of clinical symptoms occurred in only one case, in which the HILL method had been performed ; but there were no postoperative complications, such as passage disturbance or gas bloat syndrome in any case, and there have been no recurrences in all the other cases to date.

Discussion

Methods of esophageal manometry have been experimentally and clinically studied by many investigators.[1)14)25)28)34)40)47)48)50)53)55)61)63)] It is thought at present that higher technical standards of esophageal manometry are achieved with an open-tipped catheter[47)50)] than with a balloon[63)] catheter and with an intraluminal infusion method rather than with a noninfusion method, as the pressure-sensing device. Regarding withdrawal methods, it is said that profiles of manometry curves and pressure values are more reproducible with a rapid-pullthrough[14)] than with a station-pullthrough technique. In this study the experiments were made, using the apparatus depicted in Fig. 2.

When esophageal manometry is performed in animal experiments, it is desirable to conduct it in a non-anesthetic condition. As experimental animals, the dog[56)], cat[13)], opposum and baboon have been utilized to perform esophageal manometric studies. Particularly in the oppossum and the baboon, the anatomy and physiologic functions of the esophagus are similar to those of the human esophagus and therefore, these animals are useful for manometric studies. However, in this study the mongrel dog was elected as the experimental animal and the withdrawal curves were recorded under the general anesthesia with ketamine and pentobarbital. In the basic profiles of the esophageal manometry in dogs by this method, as depicted in Fig. 4, the respiratory excurtion in the abdominal cavity was the same as in the thoracic cavity. Therefore, the respiratory reversal point in the high pressure zone was always present at two points and sometimes at four points. The reason why the respiratory excurtions in the abdominal and the thoracic cavities were in the same direction is not clear. It may have been due to the artificial respiration under general anesthesia with intratracheal intubation. The respiratory reversal point is thought to be related to the diaphragmatic hiatus ; however there is theory that the respiratory reversal point is not a fixed point but a movable one within the high pressure zone[24)]. Certainly, the "double respiratory reversal"[33)] phenomenon, which is thought to be specific to hiatal hernia, is different from that which occurred in this study in dogs, considering the profiles of the manometry curves in the abdominal and thoracic cavities.

As already stated regarding the muscular architecture of the human lower esophageal sphincter[18)38)], the esophageal muscle layer, particularly the LES, the gastric oblique muscle fibers (WILLIS), the angle of HIS and the phrenoesophageal ligament are the chief components of the cardiac closing mechanism. In dogs the phrenoesophageal ligament attaches distally to the squamocolumnar junction[51)] and therefore, the abdominal esophageal segment found in humans is not present in dogs. In this study, surgically dividing the LES, the WILLIS' oblique muscle and the phrenoesophageal ligament including the diaphragmatic crus, esophageal manometry was used to determine which component was the most important in the prevention of the gastroesophageal reflux. Profiles of the high pressure zone and the LESP were hardly affected by division of the ligament when compared with the profiles before division (Fig. 5 & 6). However the profiles of the high pressure zone

became almost flat after division of the LES, the WILLIS oblique muscle and the ligament. The LESP decreased significantly in Groups Ⅱ and Ⅳ in which division of the LES had been performed. From these experimental results it was concluded that the LES was the most important component constituting the high pressure zone and that the ligament had little relationship to the formation of this zone. However several problems remain regarding these conclusions. First, these were short-term experiments performed under anesthesia. Second, comparison was made before and after only the division procedures but investigation of the control group, which might show changes over the course of time during short-term experiments, was not performed.

There are similar reports of other experiments using division[19)30)36)41)43)54)59)62)]. MEISS contended[41)], after performing a long-term experiment in which the LES, the angle of HIS, the phrenoesophageal ligament and the mucosal rosette were divided, that the LES was very important for the prevention of reflux esophagitis but that the diaphragm, the angle of HIS and the mucosal rosette were related to its prevention. INGRAM[30)] regarded an intrinsic "sphincter" and its complete vagal innervation as necessary factors and SMIDDY[59)] reported that the angle of HIS constructed by the WILLIS' oblique muscle was necessary. KURAMOTO[36)] stated that it was necessary for all three components, the LES, the WILLIS' oblique muscle and the ligament, to be intact but that the angle of HIS was not so important. Another researchers had the idea that the WIILLIS' oblique muscle was important[19)]. MICLHELSON[43)] and SASAKI[54)] stated the importance of the phrenoesophageal ligament only which is quite different from the results of this study. VANDERTOLL[62)] regarded only the LES as important.

Following the finding that the high pressure zone almost disappeared on esophageal manometry curves in the short-term experiment which divided the phrenoesophageal ligament, the LES and the WILLIS' oblique muscle, this study attempted to produce experimental esophagitis in a long-term experiment by dividing the above-mentioned three components and to ascertain its presence by esophageal manometry and by pathologic examinations after sacrifice. The results showed that the LESP tended to be lower in the division group than in the control group but not significantly so. The esophageal mucosas were almost normal with little findings of esophagitis (Fig. 9 & 10), such as erosions, ulcers and bleeding. On these points, the results of the short-term and long-term experiments were discrepant. However, VANDERTOLL[62)] et al., for example, could recognize esophagitis by a circular myotomy of the distal portion of the esophagus. MEISS[41)] found esophagitis in all cases with esophagogastrectomy. GAHAGAN[19)] produced esophagitis experimentally by resection of the oblique muscle fibers. LIPPA et al[39)]. produced esophagitis by WENDEL cadioplasty and the production of a hiatal hernia with the administration of histamine in beeswax.

Regarding control of the cardiac closing mechanism, much attention has been paid to the effects of humoral factors[22)], such as gastrointestinal hormones and prostaglandins. Although changes in the responses of the components of the cardiac closing mechanism to exogenous gastrin were studied by division in short- and long-term experiments, no definite conclusions were reached (Fig. 8 & 11). Subsequently, in order to evaluate the effects of

endogenous release of gastrointestinal hormones on the cardiac closing mechanism, the following experiments were performed in which esophageal manometry and serum level of gastrin were measured before and after intragastric instillation of HCl, NaOH and antacid solutions (Fig. 12, 13 & 14). The LESP increased significantly after instillation of the NaOH solution but was not affected by instillation of antacid. The serum gastrin level tended to increase 30 minutes or more after instillation of the NaOH solution but more slowly than the increases in the LESP. Previous reports[7)16)] contended that the LESP was decreased by acid and increased by alkali instillation. However, KLINE et al[35)]. reported that no changes in the LESP and gastrin level occurred after gastric alkalinization. Regarding the effects of antacids, CASTELL[8)] et al. reported that the LESP was significantly increased by a commercial antacid preparation. Therefore, it is probable that antacids are effective for reflux esophagitis through these two modes of action. Regarding the reasons why significant changes did not occur with antacid instillation in this study, the antacid was administered to dogs under anesthesia and it is questionable whether contact with the gastric mucosa of the antacid was sufficient.

This study found that the LESP showed a significant increase after intragastric instillation of bile and taurocholate (Fig. 15). A similar study was made by LATTINEN et al[37)]. which found that the LESP increased 20 minutes after bile instillation and that intragastric bile did not change intragastric pH. Clinically, following reflux of duodenal contents into the stomach, the LESP may be increased by the reflux and a subsequent reflux into the esophagus be prevented.

Although many reports have appeared regarding the effects of prostaglandins on the cardiac closing mechanism in oppossum[20)21)49)] and humans[10)], this study examined prostaglandins in dogs and found that after prostaglandin $F_{2\alpha}$ had been administered, the LESP increased as was found in previous reports[10)49)] (Fig. 16). However, when prostaglandin E_1 or E_2 was administered, the LESP was not affected. This was different from the results of GOYAL et al[21)]. with oppossum and may be due to an anatomical difference—the LES of dogs is composed of striated muscle, not of smooth muscle as in the oppossum. It was found that with a dose of 32μg/kg of prostaglandin E_1 (Fig. 17) only the fundic pressure decreased. It is probable that prostaglandin $F_{2\alpha}$ has its effect on striated muscle as was found in dogs (Fig. 16). DILAWARI et al[10)]. found that the LESP was increased by antiinflammatory drugs (rectal indomethacin) and suggested that it was probably due to inhibition of the endogenous synthesis of prostaglandin E_2. It is probable that when inflammation, such as reflux esophagitis, occurs, tissue synthesis of prostaglandin E_2 will increase, LESP will decrease and the esophagitis will become worse by the formation of the vicious circle.

It was found in this study that a linear relationship existed between the doses of glucagon and the percentage decreases of LESP on a semilog graph (Fig. 19). The same results had been obtained in dog experiments by JENNEWEIN et al[32)]. It was also reported that the LESP was decreased in humans[9)29)31)32)] by administration of glucagon. These results can be explained by the fact that glucagon has the same chemical structure as secretin.

HOGAN et al[29]. showed that these responses occurred without changes in blood glucose or insulin concentrations. It remains to be clarified whether endogenous glucagon can affect gastroesophageal competence under physiological conditions. It is probable that the dosage of exogenous glucagon was large and the response of the LESP was pharmacological[29] according to the results of the above-mentioned experiment.

Performing 5 kinds of hiatal herniorrhaphies—HARRINGTON[23], HILL[26], STENSRUD[60], BELSEY Mark Ⅳ[2] and NISSEN[45] methods—by an abdominal approach on dogs, in which the cardiac closing mechanism had previously been divided, reconstructive effects and responses of the components of the cardiac closing mechanism to gastrin were studied by esophageal manometry. The herniorrhaphies effected an LESP increase proportionately in the following order : NISSEN, BELSEY, STENSRUD, HILL and HARRINGTON (Fig. 21). Responses to gastrin tended to increase with the NISSEN and BELSEY methods, but not significantly (Fig. 22). The serial experiments in this study were all short-term and under anesthesia. Although these studies should be performed in long-term experiments, the short-term experiment has some advantages in that the experimental conditions can be kept more constant than in a long-term experiment. Similar reports have been relatively scarce. BOMBECK et al.[1)3)], for example, found that esophagitis improved by performing NISSEN fundoplication on 2 groups which had undergone either phrenoesophageal ligament reinsertion and esophageal hiatal widening or lower esophageal myotomy. SIEWERT et al.[5)7)] also performed fundoplication on groups of dogs which had undergone circular myomectomy or myotomy and concluded that the LESP increased and the response of the cardiac closing mechanism to pentagastrin or glucagon was preserved.

In the 2nd Surgical Clinic, Yamaguchi University Hospital, since October, 1976, Nissen fundoplication have been executed in 12 cases. Although the period of postoperative follow-up has been relatively short, postoperative complications[4)5)27)42)52)64)], such as gastric leak[5)], fundoplication disruption[52)] gastric ulceration[4)5)] and gas bloat syndrome[42)]. have not yet been encountered. However, as a matter of fact, it is difficult to study clinically the operative methods for hiatal hernia because of the restricted number of cases and the requirement of long periods of follow-up. According to reports from other institutions, comparisons between crural repair and NISSEN fundoplication[64)], among HILL, BELSEY and NISSEN[12)], and between BELSEY and NISSEN[11)44)], have been made and all concluded that NISSEN fundoplication was superior to the other methods. However, it has been pointed out that NISSEN fundoplication is accompanied by postoperative dysphagia and vomiting[12)] (50%). Moreover, clinical studies have been performed exclusively on the NISSEN fundoplication[6)15)17)46)58)]. Ellis et al[15)]. contended that reattainment of the LESP and length of the high pressure zone was obtained and that the effect of fundoplication was due to "mechanical restoration of sphincter strength" and recovery of the physiologic neural response to the increase in intragastric pressure. This study obtained the same result in 5 cases by manometry before and after fundoplication (Fig. 23). As an operative treatment for sliding hiatal hernia it is necessary to strengthen and reconstruct the cardiac closing mechanism as well as making

simple anatomical repairs. Although there are many reports that NISSEN fundoplication is the most excellent among the many operative methods, it is accompanied by some complications. Therefore it is necessary to evolve simple and more excellent operative methods.

Summary and Conclusions

In order to clarify the pathogenesis of reflux esophagitis associated with sliding esophageal hiatal hernia and to compare the effects of several operative methods for the treatment of this type of hernia, the cardiac closing mechanism was studied experimentally and clinically by esophageal manometry with an open-tipped method and the following conclusions were drawn:

1) Among the components of the cardiac closing mechanism in dogs, the LES is the most important and the WILLIS' oblique muscle is next. The phrenoesophageal ligament seems unrelated to the formation of the cardiac closing mechanism.

2) LESP was increased by intragastric instillation of alkali in dogs, but was not decreased by gastric acidification. Serum gastrin levels tended to increase after gastric alkalinization, slightly more slowly than increases in LESP.

3) LESP was increased by intragastric instillation of bile and taurocholate solutions.

4) LESP was increased by administration of prostaglandin $F_{2\alpha}$, but was not affected by administration of prostaglandin E_1 and E_2. LESP decreased after administration of glucagon.

5) Comparing 5 kinds of hiatal herniorrhaphies, LESP increased proportionately after the operation in the following order : NISSEN, BELSEY Mark Ⅳ, HILL and HARRINGTON methods. Responses to gastrin tended to increase after the NISSEN and BELSEY Mark Ⅳ methods.

6) No recurrences and no complications, such as fundoplication disruption, dysphagia and gas bloat syndrome, occurred in the 12 cases which had undergone NISSEN fundoplication at the 2nd Surgical Clinic, Yamaguchi University Hospital. The mean LESP increase was from 24.3 ± 1.44 cm H_2O preoperatively, to 28.4 ± 2.25 cm H_2O ($M \pm SEM$) postoperatively ($n=5$).

From these experimental and clinical results, it has been concluded that NISSEN fundoplication is the most excellent operative treatment at present for sliding esophageal hiatal hernia if performed by correct operative technique.

Acknowledgement

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和文抄録

滑脱型食道裂孔ヘルニア手術術式に関する実験的ならびに臨床的研究

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滑脱型食道裂孔ヘルニアに伴われる逆流性食道炎の病因を解明するとともに，このヘルニアに対する各種手術術式施行の効果を比較・検討する目的で，主としてopen-tipped methodを用いた食道内圧測定によって噴門括約機構を実験的ならびに臨床的に検討し，以下の結論を得た．

1） イヌ噴門括約機構構成因子のうちでは下部食道括約筋（LES），次いでWillis胃斜走筋がこの部の高圧帯の形成に重要であり，横隔食道靱帯はほとんど無関係であった．

2） イヌ胃内のアルカリ化によって下部食道括約筋圧（LESP）は上昇したが，酸性化では低下しなかった．血清ガストリン濃度は胃内アルカリ化により上昇傾向を示し，しかも時間的にLESPの上昇にやや遅れて出現した．

3） 胆汁またはタウロコール酸溶液の胃内注入によってLESPは上昇した．

4） Prostaglandin $F_{2\alpha}$ の投与によってLESPは上昇したが，prostaglandin E_1 または E_2 の投与では著変を示さず，またglucagon投与によってLESPは低下した．

5） 5種のヘルニア手術術式施行前後のLESPを比較・検討したところNissen, Belsey Mark Ⅳ, Stensrud, Hillおよび Harrington各術式の順により高度に上昇した．またガストリンに対する反応性は，Nissen法およびBelsey Mark Ⅳ法の施行後により著明に認められた．

6） 山口大学第2外科で施行された12例のNissen法施行例を検討したが，ヘルニアの再発，さらに嚥下困難，gas bloat syndrome，皺襞形成部裂開などの合併症はみられなかった．また食道内圧検査を施行した5例において，高圧帯圧値は術前の 24.3 ± 1.44 cm H_2O から，術後には 28.4 ± 2.25 cm H_2O に上昇した．

以上の成績から，Nissen氏胃底部皺襞形成術は現時点では，滑脱型食道裂孔ヘルニアに対する外科手術術式として最もすぐれた方法ということができる．