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ORIGINAL ARTICLE

Therapeutic efficacy of laparoscopic Heller-Dor surgery for chest pain in patients with achalasia: a single institutional experience

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Abstract

Background Chest pain reduces the quality of life of patients with achalasia. Although laparoscopic Heller-Dor surgery (LHD) is a standard surgical treatment for achalasia, its therapeutic efficacy for chest pain is not clear. The present study evaluated the therapeutic efficacy of LHD for chest pain and tried to identify factors associated with the relief of chest pain.

Methods The study included 244 patients with preoperative chest pain who underwent LHD as the first surgical intervention. The questionnaire-based symptom frequency score was multiplied by the severity score, and the calculated metric was defined as the symptom score. The study population was stratified, by the change in the chest pain symptom score, into Complete Remission (CR), Partial Remission (PR), and No Remission (NR) groups, which were compared for patient background and surgical outcome. Multivariate analysis was also performed to determine factors associated with the relief of chest pain.

Results As for preoperative clinicopathological conditions, the CR subgroup was older ($p=0.0169$) with fewer previous balloon dilatations ($p=0.009$). Although no difference was detected in the surgical outcome, the NR group had higher postoperative symptom scores for both difficulty in swallowing and vomiting and a lower score for patient satisfaction with surgery ($p=0.0141$). Multivariate analysis detected two factors associated with CR: disease duration over 60 months and less than two previous balloon dilatations.

Conclusions LHD improved chest pain symptoms in 90% of patients with achalasia. The patients who achieved relief of chest pain were characterized by disease duration over 60 months and less than two previous balloon dilatations.

Keywords Achalasia · Surgical outcome · Chest pain · Noncardiac chest pain

Abbreviations

LHD	Laparoscopic Heller-Dor
CR	Complete remission
PR	Partial remission
NR	No remission
LES	Lower esophageal sphincter
QOL	Quality of life
TBE	Timed barium esophagogram
St	Straight type
Sig	Sigmoid type
BMI	Body mass index
OL	Overall length of LES
AL	Abdominal length of LES

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Introduction

Achalasia is characterized by lower esophageal obstruction due to impaired relaxation of the lower esophageal sphincter (LES). Thus, a representative symptom of achalasia is a difficulty in swallowing, which accompanies chest pain in many cases and partly contributes to a significant decrease in the quality of life (QOL) of patients with achalasia [1]. Although the mechanism of chest pain is unclear, strong contraction of the esophageal muscle layer seems to be a cause, as the pain is often described as a squeezing feeling in the chest [2]. Myotomy is expected to improve the symptom by inducing rupture of the circular muscle in the lower esophageal region, resulting in complete or partial relief of chest pain after surgery in many cases. However, the same surgical procedure under similar pathological conditions does not improve chest pain in some cases. We, therefore, compared preoperative conditions relative to the extent of chest pain improvement in patients who underwent

laparoscopic Heller-Dor (LHD) surgery for achalasia and characterized the patients who achieved postoperative remission of chest pain using multivariate analysis.

Materials and methods

Patients

Esophageal radiography and pressure manometry were used for the diagnosis of achalasia. Of 543 patients who underwent LHD as the first surgical intervention between July 1996 and May 2017, 406 (75%) were available for a questionnaire-based symptom survey before and at 3 months after the surgery. Of these, 244 patients with chest pain [60%; 112 males (46%); mean age 42.8 years] were included in the present study (Fig. 1).

Methods

Before and at 3 months after the surgery, patients were surveyed by questionnaire for the frequency and severity of chest pain, difficulty in swallowing, vomiting, and heartburn. The frequency (0 = none, 1 = 2–3 times per month, 2 = 2–3 times per week, 3 = every day, 4 = every mealtime) and severity (0 = none, 1 = mild, 2 = moderate, 3 = severe, 4 = extremely severe) were rated on a 5-point scale. The calculated metric by multiplying the frequency score and the severity score was defined as the symptom score (0–16 points) [3]. Based on the symptom scores before and after surgery, the percent improvement was calculated using the formula: [{(preoperative symptom score—postoperative symptom score)/preoperative symptom score)} × 100]. The study population was then stratified by the percent improvement into 100% improvement (Complete Remission, CR), less than 100% improvement (Partial Remission, PR), and no improvement (No Remission, NR) subgroups, which were compared for patient background, preoperative pathological condition, surgical outcome, and postoperative course. The level of satisfaction with the operation was also rated on a 5-point scale (5 = highly satisfied, 4 = satisfied, 3 = somewhat satisfied, 2 = unsatisfied, 1 = highly unsatisfied) in the postoperative symptom survey questionnaire [4].

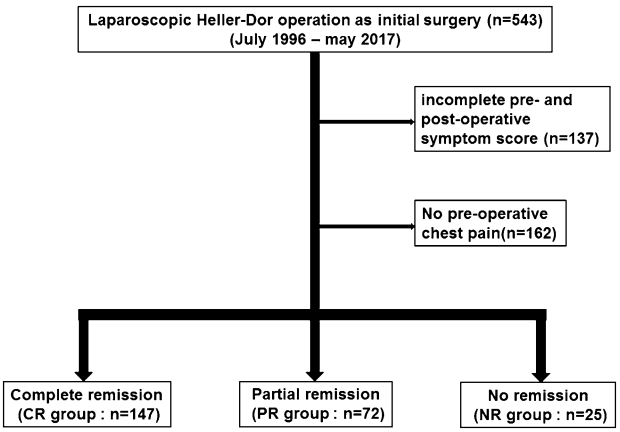

Fig. 1 The patient selection. Of the 545 patients with esophageal achalasia who underwent laparoscopic Heller-Dor surgery as the first surgical intervention, excluding 139 without pre- and postoperative sufficient symptom scores and 162 with no preoperative chest pain, 244 were selected and were divided into three groups by the degree of improvement in chest pain after LHD

Preoperative pathological condition was evaluated by barium swallow for the type and degree of dilation. The type of dilation was classified based on the morphology of the lower esophagus into two categories: straight type (St) and sigmoid type (Sig). The degree of dilation was classified into 3 grades: Grade 1 (up to 3.5 cm in maximum diameter), Grade II (3.5–6.0 cm), and Grade III (over 6.0 cm) [5].

Esophageal pressure was evaluated using infusion-type conventional manometry until September 2012, and thereafter with high-resolution manometry. The manometric parameters analyzed in this study included lower esophageal sphincter (LES) pressure, full length and abdominal length of the lower part of the esophagus, and relaxation rate of the LES.

Clearance rate of the lower part of the esophagus

Timed barium esophagography (TBE) was performed before and after the surgery to evaluate esophageal clearance in the lower part of the esophagus at each time point. TBE is a procedure described by de Oliveira et al. [6] for use in the evaluation of clearance in esophageal achalasia; patients are instructed to take 200 mL of 45% (w/w) diluted barium as quickly as possible and monitored for the height and width of the barium column after 1, 2, and 5 min in the standing frontal view to assess esophageal clearance over time. The height of the barium column was also measured immediately after barium intake (at baseline) for objective evaluation of clearance improvement after the surgery. The clearance rate was calculated based on the measurements at 1, 2, and 5 min post-intake as follows: the clearance rate (%) at × minutes post-intake was defined as [{(height of barium column at baseline—height of barium column at × minutes post-intake)/(height of barium column at baseline)} × 100].

Factors associated with complete relief of postoperative chest pain

To determine the factors associated with CR, data were summarized and analyzed to identify patient background factors, preoperative pathological factors, and operative factors. The data were summarized and categorized into

subgroups for background factors (age, sex, body mass index (BMI), duration of chest pain symptoms, weight loss status, oral medication status, previous balloon dilatations), pathological factors (esophageal pressure manometry parameters, type and degree of dilation, and maximum transverse diameter of the esophagus), and surgical factors (operative time, intraoperative hemorrhage volume, and intraoperative complications). All these parameters were analyzed using a logistic regression model to identify factors associated with CR of chest pain.

Statistical analysis

The median and interquartile range of each continuous data were provided, and box-whisker plot was adapted in figures. Three-group comparison was performed using the Kruskal–Wallis test for continuous data and Chi-square test or Fisher's exact test for categorical data. To detect potential factors associated with CR of postoperative chest pain, univariate logistic regression analysis and stepwise multivariate logistic regression analysis were performed. The 95% confidence interval (CI) and odds ratio (OR) were calculated. All statistical analyses were performed using STATA 12.1 (Stata Corp., TX, USA), and P values < 0.05 were considered statistically significant.

Results

Patient background

The background characteristics of the patients with and without preoperative chest pain are presented in Table 1. The patients with preoperative chest pain were significantly young and mild condition of disease compared to the patients without preoperative chest pain (Table 1).

The study population consisted of 112 male (46%) and 132 female with a median age of 42 years. All but one subject complained of difficulty in swallowing. The subjects were classified into CR group (147 subjects, 60%), a PR group (72 subjects, 30%), and an NR group (25 subjects, 10%), confirming the overall symptom improvement in 90% of the subjects. In the comparison of preoperative patient background and pathological conditions among the three groups, differences were observed in age, previous balloon dilatations, and the type of dilation ($P = 0.0169$, $P = 0.009$, and $P = 0.02$, respectively) but not in sex, BMI, duration of chest pain symptoms, oral medication history, or parameters of esophageal manometry (Table 2).

Preoperative symptom score

Preoperative chest pain score was significantly different among CR, PR, and NR groups at 4 (2–6), 6 (4–8), and 3 (2–4), respectively ($P = 0.0001$), and the PR group had

Table 1 Patients' characteristics

Parameter	Patients with chest pain ($n = 244$)	Patients without chest pain ($n = 162$)	P
Background			
Age	42.0 (31.0–52.0)	50.5 (39.0–63.0)	< 0.0001
Sex (M:F)	112:132	92:70	0.032
BMI (kg/m^2)	20.3 (18.4–22.5)	20.3 (18.6–22.5)	0.732
Length of disease (months)	48 (24–120)	60 (24–120)	0.1445
Body weight loss (patients (%))	125/222 (56%)	77/150 (51%)	0.345
Pre-Op medication (patients (%))	68/224 (30%)	41/145 (28%)	0.669
Pre-Op dilatation (patients (%))	43/239 (18%)	36/156 (23%)	0.217
Manometry			
LESP (mmHg)	41.3 (30.0–54.4)	37.5 (25.6–52.4)	0.1966
OL (cm)	3.2 (2.5–4.0)	3.2 (2.5–4.0)	0.6117
AL (cm)	2.0 (1.4–2.6)	2.0 (1.1–3.0)	0.8479
Relaxation of LES (%)	52.2 (30.2–74.0)	55.8 (33.7–76.0)	0.8802
Barium study			
Type (St/Sg/unknown)	208/33/3	119/39/4	0.005
Grade(I/II/III/unknown)	38/143/60/3	20/83/56/3	0.08
Maximum width (mm)	49 (40–58)	52 (42–64)	0.0195

BMI body mass index, *LES* lower esophageal sphincter, *OL* overall length of LES, *AL* abdominal length of LES

Table 2 Comparison of patients' characteristics by status of postoperative chest pain

	CR ($n=147$)	PR ($n=72$)	NR ($n=25$)	P
Background				
Age (years)	44 (33–56)	38.5 (30–47.5)	39 (28–49)	0.0169
Sex (M:F)	60:87	38:34	14:11	0.14
BMI (kg/m^2)	20.3 (18.3–22.5)	20.4 (19.1–22.0)	19.8 (18.1–22.2)	0.6453
Length of disease (months)	60 (21–120)	48 (24–96)	36 (12–84)	0.2757
Body weight loss (patients (%))	74/130 (57%)	33/67 (49%)	18 (72%)	0.144
Pre-op medication (patients (%))	36/129 (28%)	22/70 (31%)	10 (40%)	0.471
Pre-op dilatation (patients (%))	18/144 (13%)	16/70 (23%)	9 (36%)	0.009
Manometry				
LESP (mmHg)	41.3 (29.1–53.3)	39.7 (31–56.3)	45.6 (37.3–59.8)	0.7119
OL (cm)	3.25 (2.7–4.0)	3.2 (2.1–4.3)	3.1 (1.9–3.75)	0.6795
AL (cm)	2.0 (1.5–2.7)	2.0 (1.2–2.4)	2.35 (1.8–2.8)	0.2421
Relaxation of LES (%)	50.6 (25.7–68.0)	51.4 (34.4–78.0)	68.5 (55.0–82.0)	0.5739
Barium study				
Type (St/Sg/unknown)	117/27/3	68/4/0	23/2/0	0.02
Grade(I/II/III/unknown)	23/90/31/3	13/38/21/0	21/15/8/0	0.454
Maximum width (mm)	47 (40–55)	50 (40–60)	55 (45–63.5)	0.1692

BMI body mass index, *LES* lower esophageal sphincter, *OL* overall length of LES, *AL* abdominal length of LES

the highest symptom score of chest pain among the three groups. There was no difference in difficulty in swallowing, vomiting, or heartburn (Fig. 2a–d).

Preoperative clearance rate in the lower esophagus

In a comparison of clearance rate in the lower part of the esophagus, as calculated from preoperative TBE data, no difference was seen among the 3 groups after 1 or 2 min, but the clearance rate varied among the three groups after 5 min, with a lower clearance rate noted in the CR group (Fig. 3).

Surgical outcomes

No difference was observed in the operative time, intraoperative hemorrhage volume, or intraoperative mucosal damage among the three groups (Table 3).

Postoperative course

There was no statistical difference among the three groups in the postoperative timing of meal resumption or postoperative hospital stay. There was no difference in postoperative reflux esophagitis frequency, acid suppressant usage frequency, postoperative dilation procedure rates, or reoperation rates among the three subgroups (Table 3).

Postoperative symptom scores and patient satisfaction

Based on the questionnaire survey conducted at 3 months postoperatively, the chest pain score was 0 (0–0), 2 (1–3), and 4 (3–6) in the CR, PR, and NR groups, respectively. The difficulty in swallowing in the three groups was 0 (0–1), 1 (0–2), and 2 (0–4) and the vomiting score was 0 (0–0), 0 (0–0), and 0 (0–2), respectively, demonstrating a statistical difference among the three groups ($P=0.0004$ and $P=0.0357$, respectively). The symptom score was not different among the three groups (Fig. 4a–d). To demonstrate the improvement in each symptom after surgery, the post/preoperative symptom ratio in each group was calculated. The post/preoperative symptom ratio was significantly different among three groups in chest pain, difficulty in swallowing and vomiting ($P=0.0001$, $P=0.0003$ and $P=0.0411$, respectively) (Fig. 5a–d). The patient satisfaction scores were 5 (5–5), 5 (4–5), and 5 (4–5), respectively, exhibiting a statistical difference among the three groups ($P=0.0141$, Fig. 6a). In addition, more than four of satisfaction score defined satisfied level of surgery, and the ratio of patients' satisfaction were calculated. The ratio of patients' satisfaction were 97.8, 90.0, and 80.0%, respectively (Fig. 6b).

Postoperative clearance rate in the lower esophagus

The clearance rate in the lower esophagus was also calculated from the postoperative TBE data in the same manner

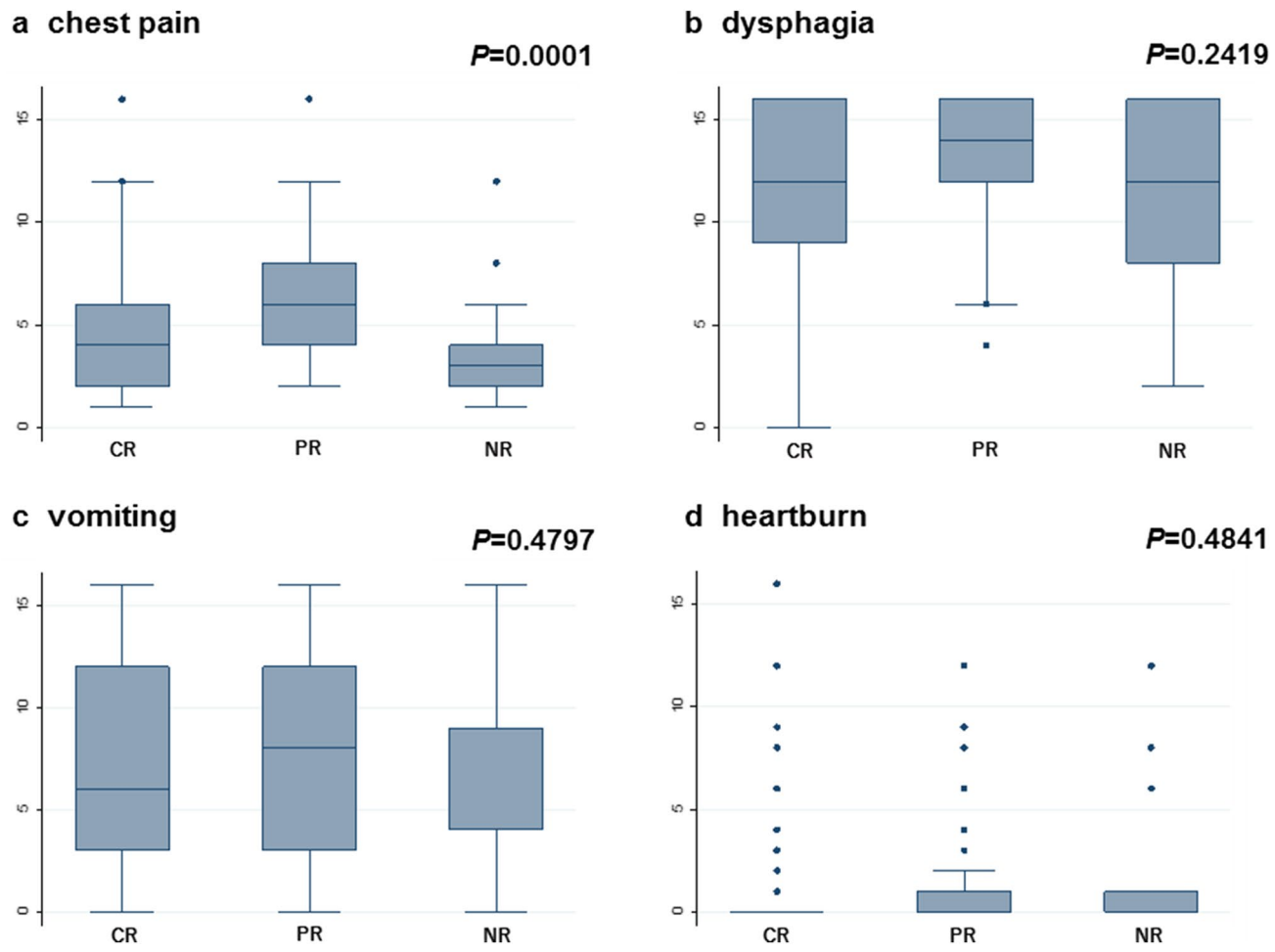

Fig. 2 Symptom scores in the preoperative questionnaire: (**a**) chest pain, (**b**) difficulty in swallowing,(**c**) vomiting, and (**d**) heartburn. Although the score of chest pain was significantly different among the three groups ($p < 0.05$), there were no difference in the other preoperative symptom scores among the three groups

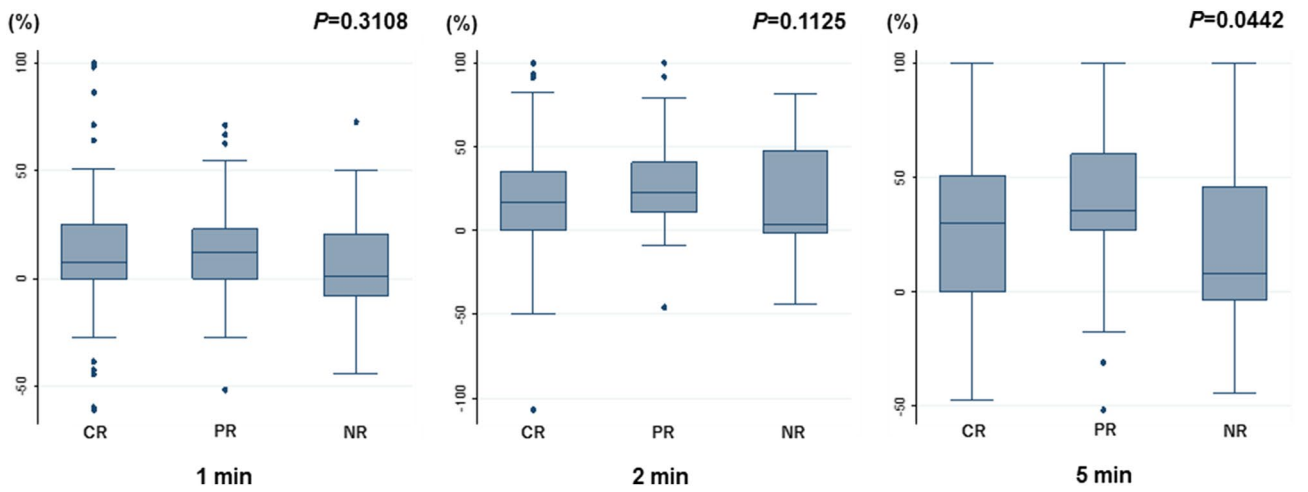

Fig. 3 The clearance rate of barium at the lower part of the esophagus calculated by preoperative TBE. The clearance rate in 5 min was significantly different among the three groups ($p < 0.05$), and the lowest score of the clearance rate was in NR group

Table 3 Surgical outcome and postoperative course

	CR ($n=147$)	PR ($n=72$)	NR ($n=25$)	P
Surgical outcome				
Operative time (min)	171 (141–203)	166 (134–195)	170 (145–201)	0.8582
Estimated blood loss (ml)	0 (0–0)	0 (0–0)	0 (0–0)	0.6097
Injury of mucosa (patients (%))	20 (14%)	11 (15%)	2 (8%)	0.724
Postoperative course				
Diet intake (days)	2 (2–2)	2 (2–2)	2 (2–2)	0.147
Post-op. hospitalstay (days)	4 (4–4)	4 (4–4)	4 (4–4)	0.6533
Required anti-acid medication (patients (%))	15 (10%)	12 (17%)	5 (20%)	0.207
Post-op. reflux esophagitis (patients(%))	24 (16%)	15 (21%)	3 (12%)	0.585
Post-op. dilatation (patients (%))	0	1 (1%)	1 (4%)	0.071
Redo (patients (%))	2 (1%)	0	1 (4%)	0.303

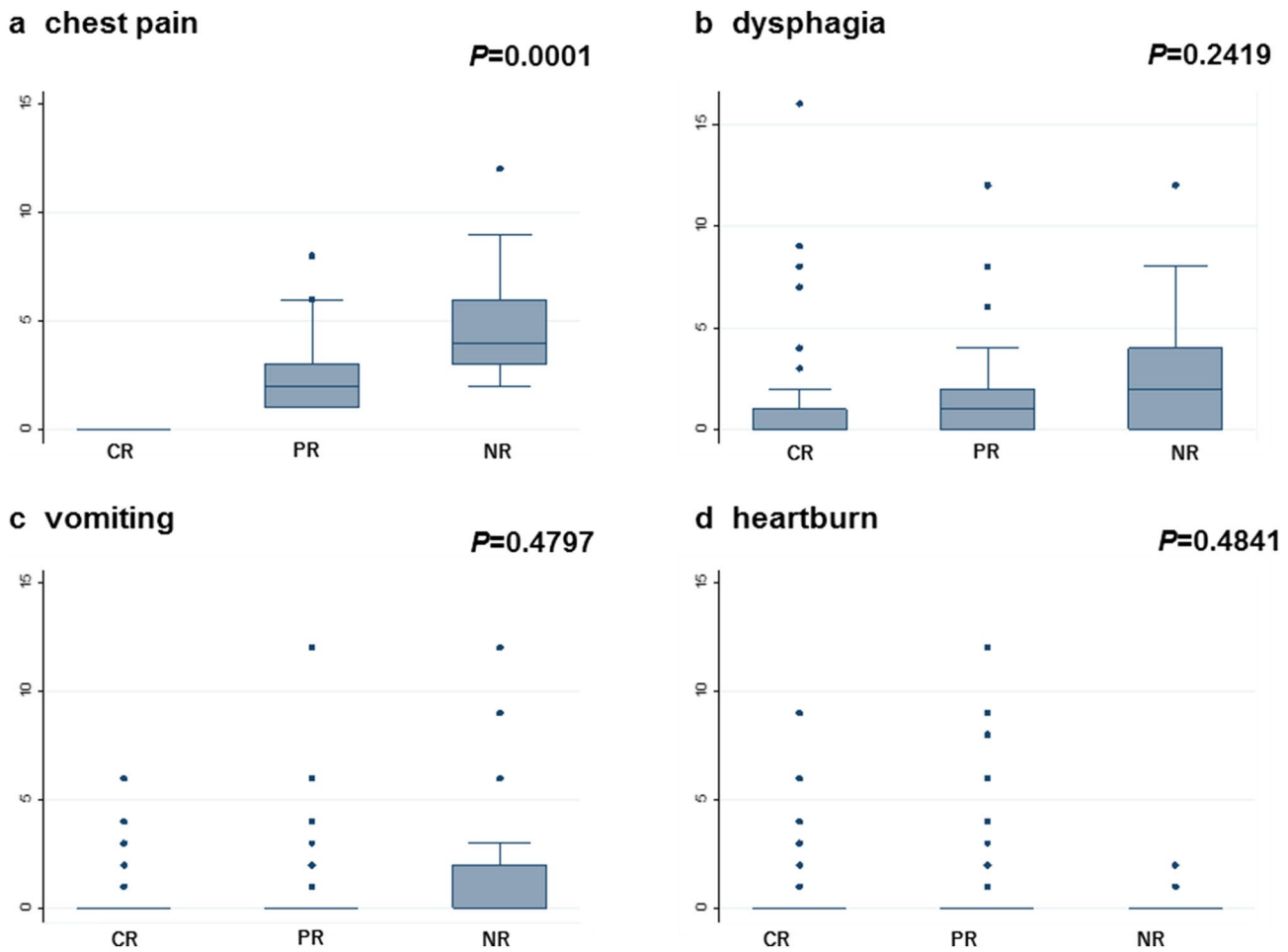

Fig. 4 Symptom scores in the postoperative questionnaire: (**a**) chest pain, (**b**) difficulty with swallowing, (**c**) vomiting, and (**d**) heartburn. There were significant difference in chest pain, difficulty in swallowing, and vomiting among the three groups after surgery ($p<0.05$, each). In postoperative symptom scores, only heartburn failed to demonstrate a difference among the three groups ($p=0.1607$)

as that for preoperative calculation. The postoperative TBE-based clearance rate was not different among the three groups (Fig. 7).

Factors associated with complete remission of postoperative chest pain

In univariate analysis, age 60 years or older [odds ratio

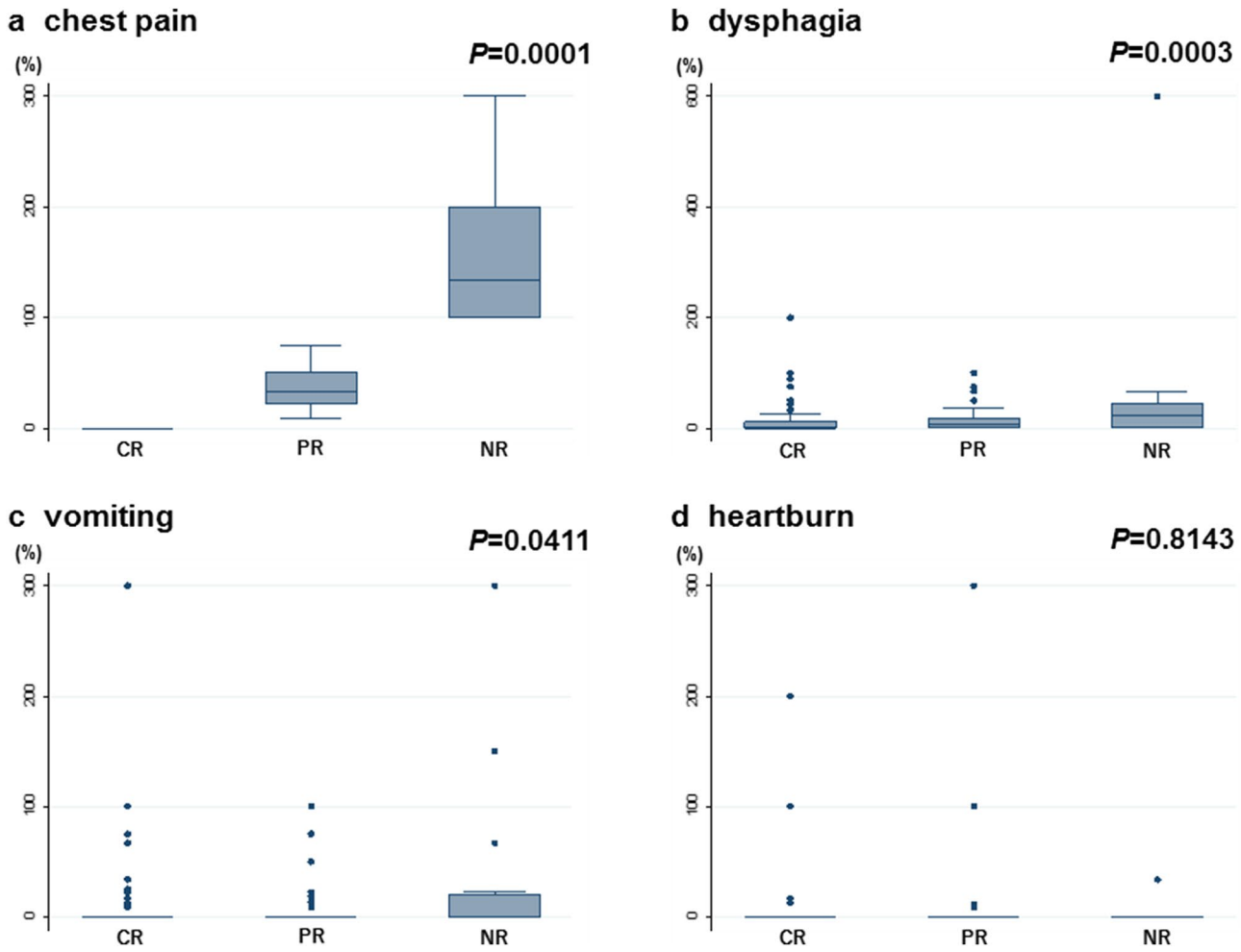

Fig. 5 Post/Preoperative symptom ratio: (**a**) chest pain, (**b**) difficulty with swallowing, (**c**) vomiting, and (**d**) heartburn. Chest pain, difficulty in swallowing, and vomiting were significantly improved after surgery among the three groups ($p < 0.05$, each)

(OR) = 4.3; 95% confidence interval (CI) = 1.6–11.6; $P = 0.0004$], 60 months or longer duration of chest pain (OR = 1.8; 95% CI = 1.0–3.0; $P = 0.034$), and less than two previous balloon dilatations (OR = 4.3; 95% CI = 1.7–10.9; $P = 0.002$) among patient background factors as well as sigmoid type dilation (OR = 3.5; 95% CI = 1.4–8.8; $P = 0.008$) among pathological factors were identified as statistically significant (Table 4). In stepwise multivariate logistic regression analysis identified 60 months or longer duration of chest pain (OR = 2.0; 95% CI = 1.1–3.7; $P = 0.023$) and less than two previous balloon dilations (OR = 4.1; 95% CI = 1.5–11.3; $P = 0.005$) were determined to be statistically significant independent factors associated with complete relief of postoperative chest pain (Table 4).

Discussion

Achalasia is a characteristic primary disease of esophageal motor dysfunction, which manifests mainly as difficulty in swallowing and vomiting due to impaired relaxation of the lower esophageal sphincter [7, 8]. It is well known that associated symptoms, such as insufficient oral intake and reflux during sleep, significantly compromise the QOL of patients with achalasia. Severe noncardiac chest pain, which is often mistaken for ischemic heart disease, also contributes partly to decreased QOL [9–11]. Although the mechanism of chest pain in achalasia is unclear, involvement of spasm of the esophageal muscle layer, pain

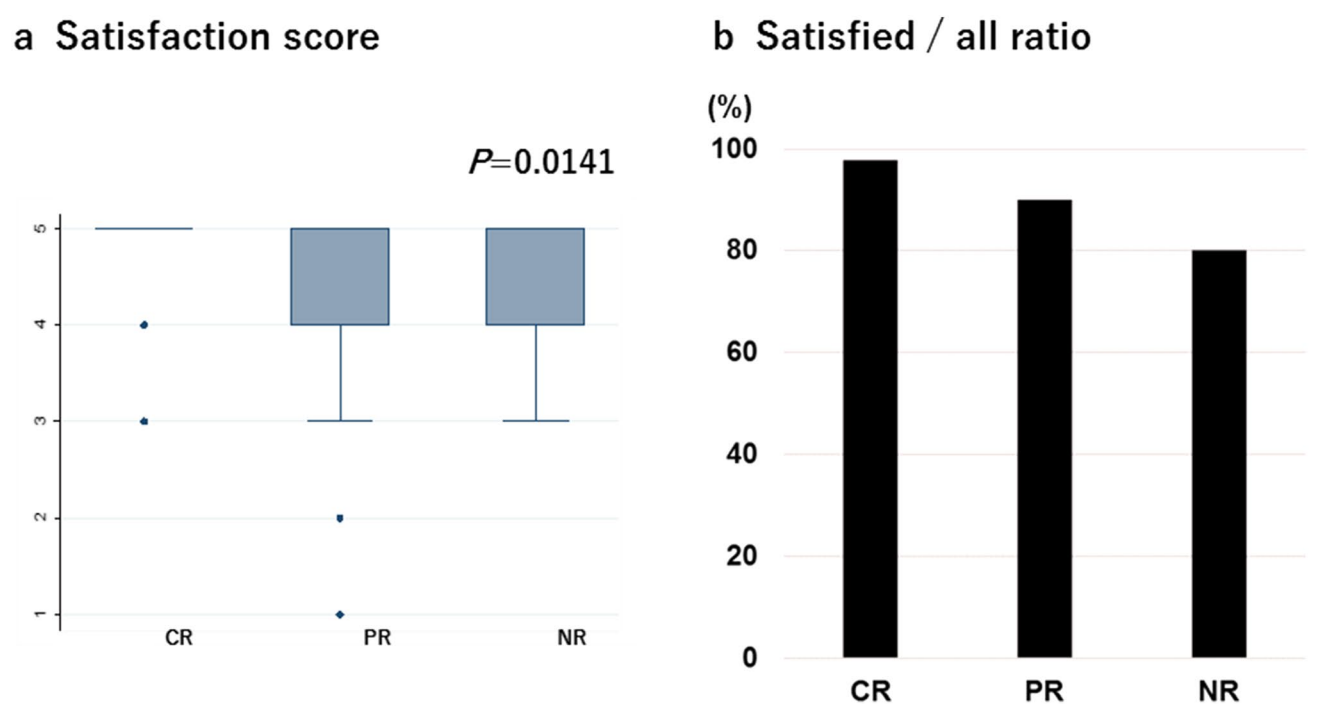

Fig. 6 Patient satisfaction. The patient satisfaction scores were statistically different among the three groups ($P=0.0141$) (**a**). In particular, NR group had significantly lower score than that the CR group ($p<0.05$). The ratio of satisfaction for surgery was 97.8% in CR group, 90.0% in PR group and 80.0% in NR group (**b**)

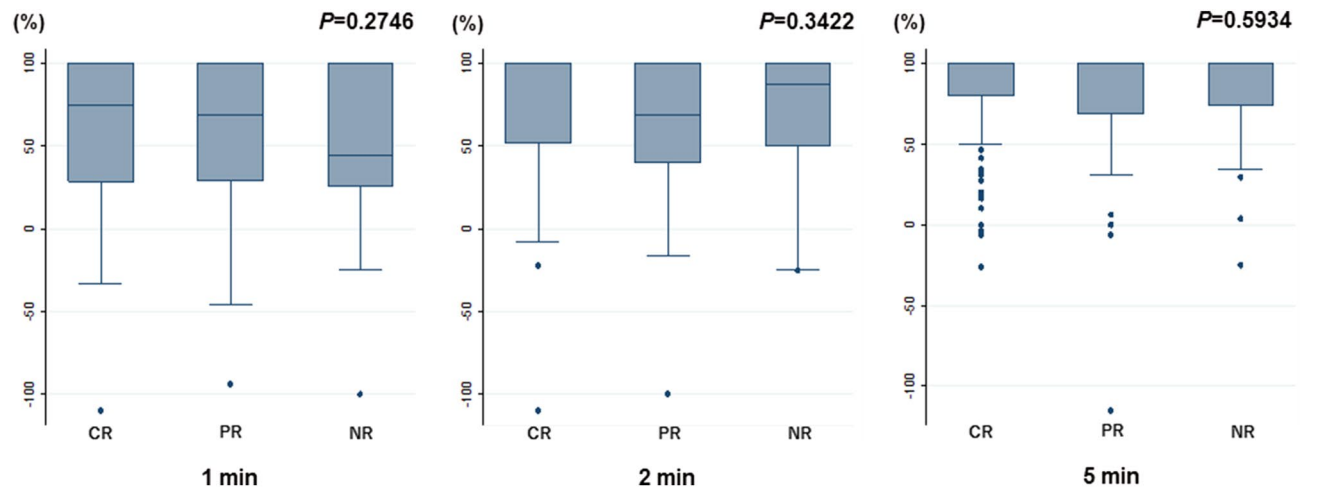

Fig. 7 The clearance rate of barium at the lower part of the esophagus calculated by postoperative TBE. There was no difference in clearance at each time point among the three groups

receptors for chemical stimuli in the esophageal mucosa, and receptors for extension stimuli have been proposed [2, 12, 13]. To date, several studies have evaluated therapeutic efficacy for achalasia from the aspect of improvement in difficulty with swallowing, but there have been limited investigations on therapeutic efficacy for chest pain, which needs to be studied further.

When we investigated the therapeutic efficacy of LHD for chest pain in patients with achalasia in 2006 [14], the sample size was limited to 66. Of these 66 patients, 24 (36%) had chest pain before the surgery. After the surgery, chest pain was completely resolved in 50%, and the symptom was improved in another 42%, indicating an overall chest pain improvement rate of 92%. Subgroup analysis revealed that

Table 4 Logistic regression analysis for independent factors associated complete remission of postoperative chest pain

Group	CR group ($n=147$)	PR and NR group (n = 97)	Univariate		Multivariate	
Predictor			OR (95% CI)	*P*	OR (95% CI)	*P*
Patient factor						
Age over 30	126 (86)	72 (74)	2.1 (1.1–4.0)	0.027		
Over 40	90 (61)	47 (48)	1.7 (1.0–2.8)	0.05		
Over 50	50 (34)	20 (21)	2.0 (1.1–3.6)	0.025		
Over 60	28 (19)	5 (5)	4.3 (1.6–11.6)	0.0004		
Male	60 (41)	52 (54)	1.7 (1.0–2.8)	0.05		
BMI over 25	13/144 (9)	7/93 (8)	1.2 (0.5–3.2)	0.685		
Over 20	79/144 (55)	65/93 (70)	1.0(0.6–1.7)	0.997		
Disease duration over 12 months	132/145 (91)	88/94 (94)	0.7 (0.3–1.9	0.473		
Over 36 months	98/145 (68)	61/94 (65)	1.1 (0.7–2.0)	0.667		
Over 60 months	79/145 (54)	38/94 (40)	1.8 (1.0–3.0)	0.034	2.0 (1.1–3.7)	0.023
Body weight loss	74/130 (57)	51/92 (55)	1.1 (0.6–1.8)	0.826		
Pre-op. medication	36/129 (28)	32/95 (34)	0.8 (0.4–1.4)	0.353		
Pre-op. dilatation	18/144 (13)	25/95 (26)	0.4 (0.2–0.8)	0.008		
Less than twice	137/144 (95)	77/94 (82)	4.3 (1.7–10.9)	0.002	4.1 (1.5–11.3)	0.005
Sigmoid type	27/144 (19)	6 (6)	3.5 (1.4–8.8)	0.008	2.8 (0.98–8.0)	0.054
Transversal diameter over 35 mm	121/144 (84)	82 (85)	1.0 (0.4–2.0)	0.915		
Over 60 mm	31/144 (22)	29 (30)	0.6 (0.4–1.2)	0.142	0.5 (0.2–1.1)	0.073
Operation factor						
Operative time over 120 min	128/146 (88)	89 (92)	0.6 (0.3–1.5)	0.316		
Over 180 min	61/146 (42)	40 (41)	1.0 (0.6–1.7)	0.933		
Over 240 min	19/146 (13)	10 (10)	1.3 (0.6–2.9)	0.525		
Intraoperative bleeding	16 (11)	14 (14)	1.3 (0.3-1.6)	0.41		
Mucosal injury	20 (14)	13 (13)	1.3 (0.5–2.2)	0.964		

() percentage, *BMI* body mass index

preoperative achalasia patients with chest pain tended to have straight rather than sigmoid morphology and tended to be younger [14].

To date, there have been contradictory reports on the therapeutic efficacy of surgical intervention for chest pain in patients with achalasia, making it a controversial issue. Echardt et al. [15] evaluated 64 patients with chest pain in a prospective study of 101 patients and reported that patients with preoperative chest pain were younger, with a shorter duration of chest pain symptoms, and that balloon dilatation and myotomy were unlikely to be effective for chest pain, even though these were very effective in relieving difficulty in swallowing. Arain et al. [16] also evaluated 64 patients among 78 who underwent surgery and reported that preoperative chest pain was observed in 66% of cases, but the operation improved chest pain in only 18% of patients. Furthermore, Wuller et al. [17] studied 157 patients who underwent LHD and evaluated 108 who took a symptom survey questionnaire before and after the operation. In their report, the proportion of patients with preoperative chest pain (69 patients, 63.8%) was not very different from that with postoperative chest pain (65 patients, 60.2%), but the frequency of chest pain was significantly decreased. Nine patients (8.3%) newly developed chest pain after the operation, but the symptom was not problematic in most of these cases. On the other hand, Perretta et al. [18] studied 211 patients with achalasia who underwent LHD. Preoperative chest pain was observed in 117 patients (55%) and was relieved in 84%, with symptom improvement in 11% after LHD, indicating high efficacy of LHD for chest pain. This rate of symptom improvement with LHD is similar to our results reported herein and in a previous study [14]. In addition, Popoff et al. [19] studied long-term improvement after laparoscopic Heller-Toupet surgery for a mean follow-up period of 5.9 years in 51 patients with achalasia and reported favorable outcomes, as demonstrated by long-term symptom improvement in 80% of cases, with prolonged chest pain in only six patients (12%).

The sample size of our present study is 244 patients, which is larger than that in previous reports and considered highly reliable from this perspective. Both CR and PR groups had lower scores for postoperative difficulty in swallowing and vomiting compared with the NR group. This suggests that the NR group had poor esophageal clearance

after the surgery, but no difference was seen in actual postoperative clearance measured as an objective parameter. Symptoms are subjective in nature. Thus, individuals in the NR subgroup who failed to have improved chest pain may have had a lower threshold of symptom manifestation, and more easily perceived symptoms.

Past epidemiological studies support a higher frequency of chest pain in younger patients, while the present study identified 60 months or longer duration of chest pain as an independent factor associated with chest pain relief after surgical intervention. This may be related to reduced sensory perception in the esophagus in elderly patients who suffered from long disease duration. In fact, the patients with age 50 years or older in our study were significantly higher proportion of 60 months or longer duration of chest pain compared to the patients with less than age 50 years (64% vs. 43%, $P=0.005$). Supporting data are found in a report by Rao et al. [20], who conducted a study in 22 healthy volunteers and demonstrated that the esophageal cross-sectional area in the striated muscle region/smooth muscle region with esophageal pressurization is greater in the elderly than in younger individuals, concluding that the pain threshold is significantly higher in the elderly than in younger people.

We also identified less than two previous balloon dilatations as an independent factor associated with chest pain relief after the surgery. This may be related to periesophageal fibrosis in the lower esophagus due to balloon dilatations. Periesophageal fibrosis may affect postoperative esophageal motility and perception, influencing the extent of symptom improvement. We previously reported that patients with a history of preoperative balloon dilatations had a decreased postoperative clearance rate in the lower esophagus compared with those without such a history [3]. Because reduced clearance rate is partly attributed to fibrosis in the lower esophagus, multiple balloon dilatations are expected to induce fibrosis and reduce clearance, causing chest pain due to extension stimulus of the esophagus. Thus, patients with fewer balloon dilatations may have had a higher rate of chest pain relief. We actually found lower preoperative esophageal clearance in the NR group, which is consistent with the fact that this subgroup had undergone more balloon dilatations in the past. There have been several reports on clinical investigation of the impact of balloon dilatations on esophageal tissues. Beckingham et al. [21] performed laparoscopic surgery in 10 patients who failed to achieve symptom improvement after 2–7 previous balloon dilatations. They found periesophageal fibrosis in many of these patients and submucosal fibrosis in all patients, and experienced difficulty in identifying the muscle layer and hemorrhage upon incision. Similarly, Dolan et al. [22] studied the impact of previous balloon dilation on the outcome of laparoscopic surgery in patients with achalasia, and found periesophageal fibrosis and submucosal fibrosis in six of seven patients with a history of balloon dilatations, but not in five patients who underwent laparoscopic surgery as the first surgical intervention. Balloon dilation-associated changes in the lower esophageal sphincter have also been demonstrated in animal experiments. Richardson et al. [23] conducted a study in which 18 swines were divided into three groups of six animals each and received either no treatment, botulinum toxin injection, or balloon dilatation. After 30 days post-treatment, the lower esophagus was excised for histopathological examination, and demonstrated significantly more severe inflammatory mucosal change and fibrosis in the lower esophagus of the animals treated with botulinum toxin injection or balloon dilation.

It is also interesting that the present study found the highest preoperative chest pain scores in the PR group. It seems that the extent of chest pain improvement with surgery has a limitation and the symptom may not always disappear when chest pain is severe and exceeds a certain range. Although it is hard to prove this hypothesis, the operation in the PR subgroup was effective to a certain extent but left a mild symptom, because the preoperative scores may have exceeded the range that could be reversed by the surgery.

There are several limitations to the current study. First, the study included historical cases of more than 20 years ago to achieve a sufficient sample size. Achalasia is a rare disease that occurs in one per 100,000 individuals. It is, therefore, difficult to obtain a sufficient number of patients within a relatively short period at a single institution. Nevertheless, we believe that our data are highly reliable because (1) the surgical procedure for achalasia is nearly unchanged since the time laparoscopic surgery was introduced, (2) the surgical procedure and pre-/postoperative management are very consistent, as the study was conducted at a single institution, (3) the majority of cases (216 patients, approximately 89%) were treated within the past 10 years, and (4) the surveillance method of symptom was consistent.

In addition, the patients with preoperative chest pain were selected to verify the efficacy of LHD and identify the factors associated with the remission of chest pain. It might be existed the factors of sensitive dullness for analysis. However, we performed logistic regression analysis to identify the independent factor-associated remission of postoperative chest pain, we think outcomes gained from our study could be trustable.

Finally, the current study only evaluated a single time point, based on data obtained in a symptom survey at 3 months after surgery. A survey performed after 1 year or several years in long-term follow-up may yield different results. Because the disease is benign and long-term follow-up is often difficult, we chose to evaluate patients at an early postoperative stage to ensure follow-up of all patients. We will continue accumulating long-term follow-up cases for further investigation.

Conclusions

In conclusion, LHD was effective in improving chest pain in 90% of patients with achalasia and is a treatment option expected to provide sufficient improvement of the symptom. However, the patients who had no relief of chest pain were significantly younger compared to the whole group. The present study also indicates that chest pain is likely to resolve in patients with disease duration over 60 months and those with less than two previous dilation procedures. Thus, LHD should be actively performed in these patients.

Author contributions Kazuto Tsuboi analyzed data and wrote the manuscript. Nobuo Omura supervised the study and critically revised the manuscript. Fumiaki Yano, Masato hoshino, Se-Ryung Yamamoto, Shunsuke Akimoto, Takahiro Masuda, and Hideyuki Kashiwagi collected data. Katsuhiko Yanaga critically revised the manuscript.

Compliance with ethical standards

Ethical Statement The protocol of this study has been approved by the Jikei University School of Medicine Institutional Review Board (#28-047 [8290]). All informed consent was obtained from the subjects and guardians.

Conflict of interest Drs. Tsuboi, Omura, Yano, Hoshino, Yamamoto, Akimoto, Masuda, Kashiwagi and Yanaga have no conflicts of interest or financial ties to disclose.

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