Table 1 Recommendation grades

- A There is sufficient scientific evidence and it is recommended to be actively performed
- B There is scientific evidence and it is recommended to be performed
- C1 There is not sufficient scientific evidence; however, it may be considered to be performed with utmost attention
- C2 There is not sufficient scientific evidence and basically it is not recommended to be performed
- D There is scientific evidence that it may be harmful for the patient and it is recommended not to be performed

Table 2 Evidence grades

Convincing	There is enough evidence to determine that an association with cancer risk is certain and taking preventive action is recommended
Probable	There is enough evidence to determine that an association with cancer risk is almost certain and taking preventive action is generally recommended
Limited-suggestive	Although neither "convincing" nor "probable" can be determined, there is evidence suggesting an association with cancer risk
Limited-no conclusion	Data are insufficient and an association with cancer risk cannot be determined
Substantial effect on risk unlikely	There is enough evidence to determine that there is no substantial effect on cancer risk

When it is recommended to be performed in the field unless there is something exceptional, such as the presence of comorbidity, A or B is determined (classification as A or B is according to the degree of strength of recommendation for it). When the position as a guideline is neutral and the decision is left to the attending physician because there is no sufficient evidence to determine whether or not to perform at this time, C1 is determined. When it is not recommended to be performed in the field unless there is something exceptional, C2 or D is determined (classification as C2 or D is according to the degree of strength of recommendation against it).

The "epidemiology and prevention" area included many CQs that were unsuitable for recommendation grades. Therefore, the evidence grades were used (Table 2). The evidence grade was determined on the basis of guidelines in "food, nutrition and physical activity and cancer prevention: from an international perspective, second edition" published by the World Cancer Research Fund (WCRF)/American Institute for Cancer Research (AICR).

Conflict of interest

The Japanese Breast Cancer Society confirmed the situation regarding conflict of interest for the guidelines committee members, who had self-reported. These guidelines were funded solely by the Japanese Breast Cancer Society.

Breast cancer clinical practice guidelines in English

All previous breast cancer clinical practice guidelines have been described in Japanese. This time, it was decided to create and publish an English version. All CQs and recommendations of the 2013 edition created in Japanese were described, followed by the addition of commentary focusing on the differences between the guidelines in Japan and overseas. It is planned to revise the English version on a regular basis in concert with the Japanese version.

In conclusion

Breast cancer incidence is still on the rise in Japan and it afflicts many women. It is hoped that these guidelines will be utilized in clinical practice and will spread the application of more appropriate practice and help to reduce the suffering of patients as a result.

The guidelines are only "what should be fully utilized with flexibility by medical staff" and should be used taking into consideration the situation of each medical institution, patient's preferences and social norms. Therefore, it is not intended to restrict the discretion of the individual physician, and use of the material as the basis of medical conflict or malpractice is a deviation from the purpose of the guidelines.

Moreover, it is meaningless unless the guidelines are supported and used by practitioners in the field. It is essential that the guidelines accurately reflect the opinions of physicians working in the field to make the guidelines easy to use and useful.

Conflict of interest H. Mukai received research grant from Chugai Pharmaceutical Co., Ltd., Daiichi Sankyo Co., Ltd., Eisai Co., Ltd., Nippon Kayaku Co., Ltd., Novartis Pharma K. K., Pfizer Inc. and Sanofi K. K.; S. Noguchi serves as an advisor of Taiho Pharmaceutical Co., Ltd., and received honoraria from Astra Zeneca Co., Ltd., and received research grant from Astra Zeneca Co., Ltd., Chugai Pharmaceutical Co., Ltd., Novartis Pharma K. K. and Takeda Pharmaceutical Co., Ltd.; H. Iwase received honoraria from Astra Zeneca Co., Ltd., and received research grant from Astra Zeneca Co., Ltd., Takeda Pharmaceutical Co., Ltd., Taiho Pharmaceutical Co., Ltd., Takeda Pharmaceutical Co., Ltd., Taiho Pharmaceutical Co., Ltd. and Chugai Pharmaceutical Co., Ltd.; J. Kurebayashi received honoraria from Takeda Pharmaceutical Co., Ltd.; M. Toi received research grant from Taiho Pharmaceutical Co., Ltd., Chugai



¹ http://www.dietandcancerreport.org/.

Pharmaceutical Co., Ltd., Takeda Pharmaceutical Co., Ltd., Eisai Co., Ltd., Daiichi Sankyo Co., Ltd. and Novartis Pharma K. K.; Y. Tokuda received research grant from Chugai Pharmaceutical Co.,

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111 2

食道癌

宮崎達也 宗田 真 桑野博行

わが国における食道癌の罹患数は国立がん研究センターがん対策情報センターの集計によると年間約2万人である。2008年の粗罹患率は男性が27.8(人口10万対)、女性が5.0で、年齢調整罹患率は男性は増加傾向にあるが、女性は近年は増減の傾向はない。死亡数は2011年では1万1,970人、粗死亡率は男性16.5(人口10万対)で、肺、胃、大腸、肝臓、膵臓に次いで6番目、女性が2.8で10番目である。

食道癌の診断・治療ガイドラインは、日本食道疾患研究会(現・日本食道学会)が食道癌の日常診療に役立てることを目的に、2002年12月版が作成されたことに始まる。その後2回の改訂を経て2012年4月に改訂版の第3版が出版された。

欧米においては米国の2つと英国、スコットランドのガイドラインの計4つが包括的な内容で記載されている。なかでも米国立がん研究所(NCI)のPhysician Data Query(PDQ®)(http://www.cancer.gov/cancertopics/pdq/treatment/esophageal/HealthProfessional)や全米がんネットワーク(NCCN)(http://www.nccn.org/professionals/physician_gls/f_guidelines.asp)のガイドラインがインターネット上で公開され、最新の情報を加えて絶えず更新がなされている。

診断

食道癌は比較的進行するまでその臨床症状に乏しく、粘膜下層までの病変では約60%に症状は認めなかったとの報告がある。一方、筋層以深に及ぶ病変では狭窄感39%、嚥下困難22%と大部分が有症状で発見されている。粘膜下層までの病変の90%が内視鏡検査で、5%が食道造影検査で発見されているが、近年開発された画像強調内視鏡検査を用いることで食道扁平上皮癌をより効率よく発見することができる。

ほとんどが内視鏡下生検による病理学的診断を得たのちに、治療方針決定のために、①進行度診断(主病巣の壁深達度診断、リンパ節転移診断、遠隔転移診断)、②全身状態の評価、③他臓器重複癌診断が必要である。進行度診断には内視鏡、CT、超音波、MRI、FDG-PET、骨シンチグラフィを用いて総合的に診断する。全身状態は活動状態(PS)、肺機能、心機能、肝機能、腎機能、耐糖能な

どについて評価する。食道癌は同時性の重複 癌の頻度が約10%あるので、頭頸部癌、胃癌 を中心に全身の重複癌の精査を行う。

管理·治療(図)

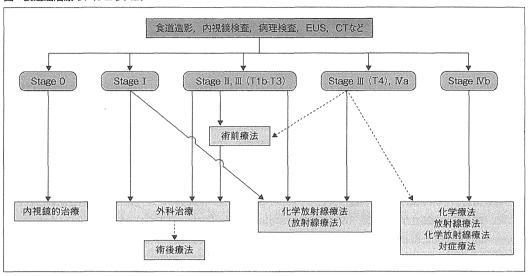
(1) 内視鏡的治療

壁深達度が粘膜層(T1a)のうち、EP、 LPM病変はリンパ節転移の頻度が低いため 内視鏡的切除術の適応となる。粘膜切除が3/ 4周以上に及ぶ場合、粘膜切除後の瘢痕狭窄 の発生が予測されるため十分な術前説明と狭 窄予防が必要である。

(2) 外科治療

食道癌の発生部位、占居範囲、壁深達度、 転移の有無、患者の全身状態、治療する施設 などにより治療方針はさまざまであるが、手 術療法は中心的な治療である。胸部食道癌は 頸・胸・腹の広範囲にリンパ節転移がみられ ることが多く、右開胸を行いリンパ節郭清と ともに胸腹部食道は全摘し、頸部、胸部、腹

図 食道癌治療のアルゴリズム



注) 進行度は食道癌取扱い規約第10版に基づく

(日本食道学会:食道癌診断・治療ガイドライン 2012年4月版 2012)

部の3領域のリンパ節を含めた切除範囲とすることが一般的である。

低侵襲性、根治性、遠隔治療成績などに関して研究段階ではあるが、体腔鏡を用いた食道切除・再建術が多くの施設で一般的になされるようになった。また、根治的化学放射線療法(50Gy以上)後の癌遺残または再発に対するサルベージ手術は合併症の発生率や在院死亡率(7~22%)が高いが、代替となる有効な治療がないことから慎重な判断のうえで行われている。

(3) 化学療法

食道癌治療における化学療法は、おもに術前後の補助化学療法と放射線治療との併用による化学放射線療法など、手術や放射線などとの併用で使用される。切除可能なStage Ⅱ・Ⅲ胸部食道癌に対する術前化学療法+根治手術がわが国における標準的治療として位

置づけられている。

(4) 化学放射線療法

化学放射線療法は食道癌治療において非外科治療を行う場合の標準的な治療である。根治を目指した化学放射線療法の対象症例はT1-3N0-3M0(UICC TNM分類2009年版)の切除可能症例、切除不能のT4N0-3M0、および所属リンパ節ではないリンパ節(M1)転移例である。

経過・予後

日本食道学会全国登録による初発食道癌の 予後は、Stage別累積 5 年生存率で、cStage 0:77.8%、cStage II:74.4%、cStage II: 49.5%、cStage III:30.7%、cStage IVA:14.8 %、cStage IVB:11.5%である。

[参考文献]

●日本食道学会 編:食道癌診断・治療ガイドライン 2012年4月版. 金原出版. 東京, 2012.

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ORIGINAL ARTICLE - GASTROINTESTINAL ONCOLOGY

Feasibility and Nutritional Impact of Laparoscopy-assisted Subtotal Gastrectomy for Early Gastric Cancer in the Upper Stomach

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ABSTRACT

Background. Laparoscopy-assisted total gastrectomy (LATG) is commonly performed for early gastric cancer (EGC) in the upper stomach; however, the incidence of anastomotic complications remains high, and postoperative nutritional status is not satisfactory. This study aimed to evaluate the feasibility and nutritional impact of a novel surgical procedure, laparoscopy-assisted subtotal gastrectomy (LAsTG).

Methods. This was a retrospective study of 167 patients with EGC in the upper stomach. Of these, 57 patients underwent LAsTG, while 110 patients underwent LATG. Postoperative change in body weight, and serum concentration of albumin (Alb) and total protein (TP) were compared between the LAsTG and LATG groups. Analysis of covariance (ANCOVA) was used to assess the influence of potential confounding factors.

Results. Frequency of anastomotic complications was significantly higher in the LATG group (16.3 %) than in the LAsTG group (5.3 %, P=0.040). Postoperative recovery of body weight at 12 months after surgery was significantly better in the LAsTG group (89.8 \pm 1.4 %) than in the LATG group (82.1 \pm 1.0 %, P<0.001). By ANCOVA, adjusted mean differences of Alb and TP at 12 months after surgery between the LAsTG and LATG groups were 0.226 g/dl (95 % CI 0.141–0.312; P<0.001) and 0.380 g/dl (95 % CI 0.265–0.495; P<0.001); thus,

the surgical procedure was significantly associated with the postoperative Alb and TP levels.

Conclusions. LAsTG could be a better choice than LATG for EGC in the upper stomach as a result of improvements in the incidence of anastomotic complications and post-operative nutritional status.

The incidence of early gastric cancer (EGC) in Japan continues to increase; it now accounts for more than 50 % of all patients with gastric cancer. There have been many reports on the feasibility and safety of laparoscopy-assisted distal gastrectomy (LADG) for the treatment of EGC. 2-10 Recently, cases of EGC in the upper third of the stomach have increased, and laparoscopy-assisted total gastrectomy (LATG) or proximal gastrectomy (LAPG) has been applied as minimal invasive surgery. 11 However, these surgical procedures carry a high level of technical difficulty, especially in reconstructions accompanied by esophagojejunostomy. 12-16 Reported postoperative anastomotic complication rates are also higher for LATG than for LADG, and such complications lead to postoperative nutritional disorder. 12 Meanwhile, restoration of the food passage by straight esophagojejunostomy after total gastrectomy is accompanied by intestinal-esophageal reflux, with its associated detrimental effect on esophageal mucosa and persistent weight loss, and occasionally by severe dumping syndromes; all of which seriously affect quality of life (QOL).17-20

In some patients with EGC in the upper body of the stomach, there is still some distance from the tumor to the esophagogastric junction (EGJ). For these selected cases, we previously reported a novel surgical procedure, laparoscopy-assisted subtotal gastrectomy (LAsTG) with very small remnant stomach.^{21,22} In the present study, we

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evaluated the feasibility and nutritional impact of LAsTG compared to LATG.

PATIENTS AND METHODS

Patients

From January 2009 to March 2012, Japaroscopy-assisted gastrectomy was performed in 879 patients with preoperatively diagnosed EGC at our institution. The staging of the tumor was classified according to the Japanese classification of gastric carcinoma, 3rd English edition.²³ LAsTG was performed in 57 patients with EGC who fulfilled the following criteria: (1) EGC diagnosed as cT1N0; (2) tumor located in the upper third of the stomach or the tumor lesion involving the upper third of the stomach (tumor located on the greater curvature was excluded); (3) a certain distance remaining from the oral margin of tumor to EGJ but <3 cm. 21,22 For patients who would receive LAsTG, an extra preoperative gastroscopy was performed wherein the proximal margin (approximately 2 cm to the tumor) was marked by clips and was confirmed by biopsy to be cancer negative. In the same time period, LATG was performed in 110 patients with cT1N0 EGC in the upper stomach; the disease was not amenable to LAsTG. Meanwhile, the patients undergoing LAPG were excluded from this study because such procedure was performed for EGC in the fornix or the cardia, and such subjects could never be the candidates for LAsTG as a result of the tumor location.

Surgical Procedure of LAsTG

Modified D2 lymphadenectomy (D1+No. 8a, 9, and 11p) was performed according to the 2010 Japanese gastric cancer treatment guidelines, version 3.²⁴

The detailed surgical procedure of LAsTG has been described in our previous report.21 Briefly, the left gastroepiploic vessels were divided from the root, and the lymph nodes of station 4sb were totally resected. Several distal branches of the short gastric artery were also divided, preserving at least one branch near the cardia. The posterior gastric artery was also preserved. The final blood supply of the remnant stomach would be from the left inferior phrenic artery and one or two branches of the short gastric artery and posterior gastric artery. After mobilization of the stomach and lymph node dissection, intraoperative gastroscopy was performed to confirm the location of the tumor and the preoperatively placed clips. The location of clips and EGJ were marked by suturing in the outer wall, and a safe gastric resection line was marked with dye. The stomach was transected with endoscopic linear staplers, leaving a very small remnant stomach.

Reconstruction in LAsTG

An OrVil tube (Covidien, Mansfield, MA, USA) with 25-mm anvil was transorally introduced into the remnant stomach and was extracted through the hole until the anvil reached the greater curvature of the gastric stump. The specimen was removed thorough the intraumbilical 3-cm minilaparotomy incision. Then the proximal margin and some enlarged lymph nodes of stations 2 and 4sa were sent for frozen pathology; all were confirmed as negative for cancer. Jejunojejunostomy (Y-anastomosis) was performed extracorporeally to create the R-Y limb. A 25-mm circular stapler (Premium Plus CEEA stapler; Covidien Japan) was inserted into the limb of the jejunum, then introduced into the abdominal cavity. The anvil and circular stapler were connected, and gastrojejunostomy was performed laparoscopically with a hemidouble stapling technique. The jejunal stump was closed with an endoscopic linear stapler, and the antecolic R-Y reconstruction was completed.

Reconstruction in LATG

LATG was performed as previously described. ¹³ Esophagojejunostomy was performed using a modified lift-up method, which reduces the difficulty of anvil insertion by lifting up the nasogastric tube connected to the anvil head, and then the antecolic R-Y reconstruction was completed.

Clinical Analyses and Surgical Outcomes

The following clinical data were obtained from medical records: age, gender, body mass index (BMI), American Society of Anesthesiologists physical status (ASA-PS), history of abdominal surgery, previous treatment with endoscopic submucosal dissection (ESD), and clinical T stage of patients. Surgical findings such as operation time, estimated blood loss, conversion to open surgery, number of retrieved lymph nodes, and residual tumor (R) were also recorded. The following data were recorded to evaluate early postoperative outcomes: postoperative mortality, postoperative hospital stay, and postoperative complications within 3 months after surgery, including anastomotic complications (anastomotic leakage, anastomotic stricture, and anastomotic bleeding) related to gastrojejunostomy in LAsTG and esophagojejunostomy in LATG, pancreatic fistula, duodenal stump leakage, intra-abdominal bleeding, intra-abdominal abscess, and ileus. Postoperative complications were classified according to the Clavien-Dindo classification of surgical complications, and complications of grade IIIa and above were reviewed.²⁵

2030 T. Kosuga et al.

Follow-Up and Postoperative Nutritional Status

Mean follow-up time of the 167 patients was 27.9 months. To evaluate postoperative nutritional status, change in body weight and serum concentrations of Alb and TP at 3, 6, and 12 months after surgery were measured. Endoscopic gastroesophageal reflux was evaluated at 12 months after surgery according to the Los Angeles classification.

Statistical Analysis

For comparing the background characteristics between the LAsTG and the LATG groups, χ^2 -test and Student's t test were used for categorical variables and continuous variables, respectively. Postoperative change in body weight, and Alb and TP were compared between the two groups by Student's t test. In addition, the influence of potential confounding factors was assessed using analysis of covariance (ANCOVA) for Alb and TP at 12 months after surgery. In the ANCOVA model, the following factors were modeled as potential confounding factors: preoperative value of Alb and TP, age, gender, BMI, ASA-PS, previous abdominal operation, clinical T stage, and previous treatment with ESD. Statistical analyses were performed with SAS version 9.3 and JMP 8 (SAS Institute, Cary, NC, USA). All P values cited are two-sided, and significance levels were set at 5 %.

RESULTS

Patient Characteristics

Table 1 details the characteristics of patients undergoing LAsTG and LATG. No significant differences were observed in BMI, ASA-PS, previous abdominal operation,

and pretreatment with ESD between the two groups. Mean age was smaller for LAsTG group compared to LATG group, and the LAsTG group contained more females than the LATG group. With respect to the clinical T stage, the proportion of cT1a (M) was higher in LAsTG patients than in those treated by LATG.

Operative and Early Postoperative Outcomes

Operative and early postoperative outcomes of patients undergoing LAsTG and LATG are summarized in Table 2. Mean operation times and mean estimated blood loss were significantly less in the LAsTG group than in the LATG group. No LAsTG patient needed conversion to open surgery, while 2 patients (1.8 %) in the LATG group needed conversion to open procedure because of the troubles during the intracorporeal esophagojejunostomy. There were fewer retrieved lymph nodes in LAsTG patients than in the LATG group, and R0 resection was performed in all patients. Although the mean postoperative hospital stay in the LAsTG group was shorter than that for patients undergoing LATG, the difference was not significant between groups. No mortality was recorded for the LAsTG group, while 1 patient (0.9 %) who underwent LATG died 32 days after surgery of surgical complications associated with pancreatic fistula. The overall postoperative complication rate was 12.3 % in the LAsTG group, and 22.7 % in the LATG group. There were no significant differences between the groups in the complication rate regarding pancreatic fistula, duodenal stump leakage, intra-abdominal bleeding, intra-abdominal abscess, and ileus. However, frequency of anastomotic complications was significantly higher in the LATG group (16.3 %) than in the LAsTG group (5.3 %).

TABLE 1 Characteristics of patients undergoing LAsTG and LATG

Characteristic	LAsTG $(n = 57)$	LATG $(n = 110)$	P
Age (years) ^a	62.2 ± 11.4 (35–85)	65.7 ± 10.5 (39–85)	0.047
Gender (M/F)	37 (64.9)/20 (35.1)	92 (83.6)/18 (16.4)	0.006
BMI (kg/m²) ^a	$22.6 \pm 3.2 \ (15.5 - 31.8)$	$23.2 \pm 3.3 \ (16.4-38.8)$	0.267
ASA-PS (1/2/3)	18/39/0	31/77/2	0.550
Previous abdominal operation, n (%)	9 (15.8)	28 (25.5)	0.154
Previous treatment with ESD, n (%)	13 (22.8)	25 (22.7)	0.991
Clinical T stage ^b			0.019
Tla(M)	17 (29.8)	16 (14.5)	
T1b(SM)	40 (70.2)	94 (85.5)	

LAsTG laparoscopy-assisted subtotal gastrectomy, LATG laparoscopy-assisted total gastrectomy, BMI body mass index, ASA-PS American Society of Anesthesiologists physical status, ESD endoscopic submucosal dissection

^a Values are expressed as n (%), mean \pm standard deviation (range), or n

b According to the Japanese classification of the gastric carcinoma, 3rd English edition

TABLE 2 Surgical outcomes of patients undergoing LAsTG and LATG

Variable	LAsTG $(n = 57)$	LATG $(n = 110)$	P
Operation time (min) ^a	289.3 ± 49.7 (154–418)	312.9 ± 65.0 (192–516)	0.017
Estimated blood loss (ml) ^a	$51.0 \pm 61.4 (5-390)$	$128.2 \pm 143.0 \ (10-700)$	< 0.001
Conversion to open surgery	0 (0)	2 (1.8)	0.306
R0 resection	57 (100)	110 (100)	man.
No, of retrieved lymph nodes ^a	$39.1 \pm 9.8 (23-67)$	$50.0 \pm 16.5 (22-97)$	< 0.001
Morbidity	7 (12.3)	25 (22.7)	0.104
Anastomotic complication	3 (5.3)	18 (16.3)	0.040
Leakage	0 (0)	4 (3.6)	
Stricture	2 (3.5)	14 (11.8)	
Bleeding	1 (1.8)	0 (0)	
Pancreatic fistula	1 (1.8)	3 (2.7)	0.697
Duodenal stump leakage	1 (1.8)	1 (0.9)	0.634
Intra-abdominal bleeding	0 (0)	2 (1.8)	0.306
Intra-abdominal abscess	1 (1.8)	0 (0)	0.164
Ileus	1 (1.8)	1 (0.9)	0.634
Mortality, n (%)	0 (0)	1 (0.9)	0.470
Postoperative hospital stay (days) ^a	$13.9 \pm 8.4 (8-54)$	$17.8 \pm 17.2 (8-158)$	0.106

^a Values are expressed as n (%) or mean \pm standard deviation (range)

Follow-Up and Postoperative Nutritional Status

The mean follow-up time of the 57 patients undergoing LAsTG was 27.9 months (range 9.7–48.1 months), and none of them developed cancer recurrence in distant organs, remnant stomach, or lymph nodes.

Figure 1 shows the pre- and postoperative mean levels of Alb and TP in patients undergoing LAsTG and LATG. Although mean baseline Alb and TP levels were not significantly different between the two groups, Alb and TP levels at 3, 6, and 12 months after surgery were significantly higher in the LAsTG group than in the LATG group. Table 3 show the ANCOVA for Alb and TP at 12 months after surgery. Adjusted mean difference in Alb level between the LAsTG and LATG groups was 0.226 g/dl (95 % CI 0.141-0.312), thus both the surgical procedure and preoperative values of Alb and age were significantly associated with the postoperative Alb levels. Meanwhile, the adjusted mean difference in TP between the LAsTG and LATG groups was 0.380 g/dl (95 % CI 0.265-0.495), thus the surgical procedure and preoperative value of TP were significantly associated with the postoperative value

Change in body weight and the incidence of endoscopic gastroesophageal reflux at 12 months after LAsTG and LATG are summarized in Table 4. Postoperative recovery of body weight at 12 months after surgery was significantly better in the LAsTG group (89.8 \pm 1.4 %) than in the LATG group (82.1 \pm 1.0 %, P < 0.001). LosAngeles Grade B or more severe reflux esophagitis was

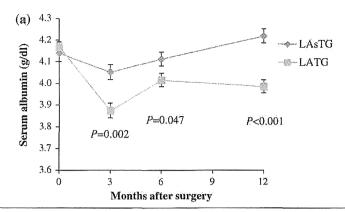
observed in 9 patients (8.2 %) in the LATG group, while such severe reflux esophagitis was not observed in the LAsTG group.

DISCUSSION

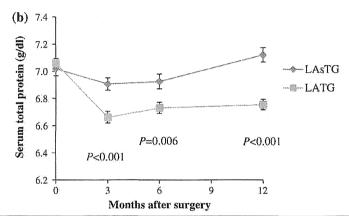
EGC has a low recurrence rate and long survival time after surgical treatment, thus current interest has been focused on postoperative QOL in patients with EGC. Although LATG or LAPG have been performed as minimally invasive operations for the treatment of EGC in the upper stomach, QOL after these procedures is not satisfactory because of the high rate of complications that substantially affects QOL such as anastomotic stricture and reflux esophagitis. ²⁶

Expanding the indication for LATG has not been without its challenges even in the hands of those with considerable experience in LADG, mainly due to the difficulties in esophagojejunostomy, in particular creating the purse-string sutures to the esophageal stump and inserting the anvil into the esophageal lumen within the confinements of the limited space in the upper abdominal cavity. ^{12–16} Actually, in this series, 2 patients (1.8 %) undergoing LATG needed conversion to the open procedure because of the esophageal injury during intracorporeal anvil placement into the esophagus. On the other hand, none of the patients undergoing LAsTG needed conversion to open procedure, and thus the intracorporeal gastrojejunostomy by using the OrVil system could be safely performed.

FIG. 1 a Mean Alb levels at baseline and at 3, 6, and 12 months after surgery in patients undergoing LAsTG and LATG. b Mean TP levels at baseline and at 3, 6, and 12 months after surgery in patients undergoing LAsTG and LATG



	Baseline	3M after surgery	6M after surgery	12M after surgery
Alb in LAsTG (g/dl)	4.140 ± 0.040	4.052 ± 0.035	4.113 ± 0.032	4.220 ± 0.033
Alb in LATG (g/dl)	4.170 ± 0.022	3.875 ± 0.034	4.016 ± 0.031	3.987 ± 0.031



	Baseline	3M after surgery	6M after surgery	12M after surgery
TP in LAsTG (g/dl)	7.019 ± 0.053	6.907 ± 0.046	6.925 ± 0.054	7.120 ± 0.053
TP in LATG (g/dl)	7.060 ± 0.034	6.662 ± 0.043	6.731 ± 0.041	6.754 ± 0.038

Lee et al. 12 found a higher postoperative complication rate with LATG compared to LADG, especially that of anastomotic stricture. While the Japanese multi-institutional phase II trial to evaluate the safety of LADG (JCOG0703) has demonstrated no differences in the incidence of anastomotic complications between LADG and open distal gastrectomy, anastomotic stricture rate in LATG is reported higher compared to open total gastrectomy. 8,12-16 Extensive dissection around the distal esophagus with an ultrasonically activated coagulation device in a magnified view and inappropriate tension of the anastomotic site with intracorporeal anastomosis might be contributing to the higher incidence of anastomotic stricture in LATG. In the present study, the frequency of anastomotic complications was significantly lower in LAsTG patients than in those undergoing LATG, confirming that LAsTG has advantages over LATG in the incidence of postoperative anastomotic complications.

LAsTG showed a significant advantage over LATG with regard to the postoperative nutritional status, and severe reflux esophagitis was not observed in LAsTG while it was observed in 9 patients (8.2 %) in the LATG group. It has been well documented that distal gastrectomy is superior to total gastrectomy in terms of postoperative QOL and nutritional status, even though there have been no data demonstrating whether it also applies to our LAsTG in which very small remnant stomach is preserved.²⁷⁻³² An et al.²⁶ compared surgical results between proximal gastrectomy and total gastrectomy and found that proximal gastrectomy was associated with a markedly higher rate of anastomotic stenosis and reflux esophagitis and provided no benefit in terms of postoperative weight loss despite conserving half of the stomach. In this series, postoperative dietary intake was better after LAsTG than LATG even though the volume of the remnant stomach in LAsTG was extremely small

TABLE 3 Data for ANCOVA

Characteristic	Coefficient	95 % confidence	interval	Р
Alb at 12 months after surgery	од о	МАКА МЕТОРОППИТУ (УПОС СОСТОСТВЕНИЕ СОСТОСТВЕНИЕ СОСТОСТВЕНИЕ СОСТОСТВЕНИЕ СОСТОСТВЕНИЕ СОСТОСТВЕНИЕ СОСТОСТВЕ	TO THE CONTRACT OF THE CONTRAC	
Surgery (LATG = 0 , LAsTG = 1)	0.226	0.141	0.312	< 0.001
Preoperative value of Alb	0.448	0.285	0.612	< 0.001
Age (per year)	-0.008	-0.012	-0.003	0.001
Sex (male $= 1$, female $= 0$)	-0.087	-0.186	0.011	0.084
BMI	0.004	-0.009	0.017	0.516
ASA-PS2 (reference level: 1)	-0.059	-0.158	0.039	0.240
ASA-PS3 (reference level; 1)	0.006	-0.354	0,365	0.976
Previous abdominal operation	0.084	-0.011	0.179	0.084
Clinical T stage $(T1a = 0, T1b = 1)^a$	0.084	-0.021	0.188	0.118
Previous treatment with ESD	-0.011	-0.106	0.085	0.826
TP at 12 months after surgery				
Surgery (LATG = 0 , LAsTG = 1)	0.380	0.265	0,495	< 0.001
Preoperative value of TP	0.551	0,402	0.700	< 0.001
Age (per year)	-0.003	-0.008	0.003	0.313
Sex (male $= 1$, female $= 0$)	-0.084	-0.218	0.049	0,218
BMI	-0.013	-0.030	0.004	0.148
ASA-PS2 (reference level: 1)	-0.008	-0.142	0.126	0.906
. ASA-PS3 (reference level: 1)	0,303	-0.189	0.795	0.230
Previous abdominal operation	0.060	-0.068	0.189	0.359
Clinical T stage $(T1a = 0, T1b = 1)^a$	0.119	-0.022	0.260	0.100
Previous treatment with ESD	-0.108	-0.238	0.022	0.105

^a According to the Japanese classification of the gastric carcinoma, 3rd English edition

TABLE 4 Change in body weight and incidence of endoscopic gastroesophageal reflux at 12 months after LAsTG and LATG

Variable	LAsTG $(n = 57)$	LATG ($n = 110$)	P
Body weight (%) ^a	89.8 ± 1.4	82.1 ± 1.0	< 0.001
Reflux esophagitis ^b	0 (0)	9 (8.2)	0.026

 $^{^{\}rm a}$ Values are expressed as n (%) or mean \pm standard deviation

(data not shown). Therefore, maintaining an antireflux mechanism by preserving the lower esophageal sphincter or relatively maintained serum concentration of ghrelin rather than a reservoir function may contribute to the improved nutritional status in LAsTG. 33–35

Preserving a very small gastric remnant for EGC in the upper stomach raises some concerns about the oncological safety. LAsTG is recommended if the indication followed by accurate diagnosis is strictly confirmed. We set up a safe resection margin of 2 cm for EGC regardless of the histologic type of tumor according to the Japanese gastric cancer treatment guidelines. The tumor location and the safe proximal resection margin were confirmed by preoperatively placing clips based on biopsy and by using intraoperative gastroscopy. Nevertheless, it is advisable to do frozen pathology as complementary diagnostic

information, even though we should take into consideration the possibility of false negative. Total gastrectomy should be performed with no hesitation if the proximal margin is suspected to be cancer-positive, but we did not have such cases in this series.

The other concern is metastasis to lymph node stations 2 and 4sa. However, according to the Gastric Cancer Data Base in our hospital (1946–2004), the percentage of positive lymph node metastasis on station 2 or 4sa in the cases with EGC located in the upper third of the stomach or EGC involving the upper third of the stomach was extremely low (0.4 or 0.1 %, respectively). It would become even lower when the cases with EGC located in the cardia or the fornix, which are close to these stations, are excluded from the indication of LAsTG. Furthermore, we pick up some enlarged nodes on these stations, and confirm all of these

^b Grade B or more severe reflux esophagitis according to the Los Angeles classification

are cancer-negative by frozen pathology. So far, none of the 57 patient undergoing LAsTG have developed cancer recurrence.

In conclusion, LAsTG become a valuable surgical procedure in selected patients with EGC located in the upper stomach because it has distinct advantages over LATG in the incidence of anastomotic complications and the post-operative nutritional status. However, this is a retrospective study on a small sample size. Therefore, the results of the present study should be validated by prospective studies with large sample sizes, and oncological safety should be verified by long-term follow-up.

DISCLOSURE The authors declare no conflict of interest.

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ORIGINAL ARTICLE

Potentially fatal complications for elderly patients after laparoscopy-assisted distal gastrectomy

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Abstract

Background The safety of surgery for gastric cancer in the elderly has been shown previously. However, potentially fatal complications based on an established severity grading system were not well described, and associated risk factors have not been assessed. The present study sought to examine severity-dependent postoperative complications after laparoscopy-assisted distal gastrectomy (LADG) in elderly patients and risk factors of potentially fatal postoperative complications.

Methods The study included 189 patients aged 70 years or older and who underwent LADG for early gastric cancer. Patient characteristics, perioperative outcomes, postoperative complications including severity assessment using the Clavien-Dindo classification, and risk factors related to postoperative complications were analyzed.

Results The overall complication rate was 24.9 % (47/189). The most frequent complication was abdominal fluid collection (9 cases, 4.8 %). Severe complications classified as grade III or above in the Clavien-Dindo grading system were found in 20 (10.6 %) patients. Multivariate analysis identified preoperative serum albumin concentration (odds ratio, 5.200; 95 % CI, 1.706–15.850),

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Roux-en-Y reconstruction (odds ratio, 3.611; 95 % CI, 1.103-11.817), and simultaneous cholecystectomy (odds ratio, 5.008; 95 % CI, 1.378-18.201) as independent predictors of a higher rate of severe postoperative complications after LADG in elderly patients.

Conclusion The incidence of severe complications after LADG in the elderly was quite acceptable considering the risks associated with radical surgery with extensive lymphadenectomy. Preoperative serum concentrations of albumin (<4.0 g/dl), Roux-en-Y reconstruction, and simultaneous cholecystectomy are independent risk factors for severe postoperative complications in these patients.

Keywords Laparoscopic surgery · Gastrectomy · Elderly · Postoperative complication · Risk factor

Introduction

Several recent studies on open gastric surgery have shown that gastrectomy in the elderly is safe and that, because of improved surgical techniques and perioperative management, old age alone should not be a contraindication to surgery [1-3].

In Japan and Korea, the superiority of laparoscopyassisted gastrectomy (LAG) for early gastric cancer compared with conventional open gastrectomy has been confirmed by both randomized and nonrandomized clinical studies, with advantages including less intraoperative bleeding, less pain, and shorter postoperative hospital stays [4-12]. Reported postoperative complication rates are comparable between LAG and conventional open gastrectomy cases.

In contrast, laparoscopic surgery usually requires a pneumoperitoneum, which can disrupt respiratory or

2 Springer

cardiovascular performance during the operation[13–15], and these effects could be more significant in elderly patients with a higher likelihood of preoperative comorbidities and reduced functional capacities [16, 17]. Although several studies found no significant difference in the incidence of postoperative complications between elderly and younger patients undergoing LAG [18–21], severity of complications was poorly defined in most of these studies.

This study therefore sought to analyze postoperative complications after LADG in elderly patients using the Clavien–Dindo severity grading system and to examine the risk factors for these complications relative to severity.

Patients and methods

Patient clinical data

From April 2005 to March 2010, 1001 patients underwent LAG for gastric cancer with curative intent in the Department of Gastroenterological Surgery, Cancer Institute Hospital, Tokyo, Japan. Of these, 280 were aged 70 years or older and 189 underwent LADG. For each patient, surgery was either performed or supervised by one of two experts in laparoscopic surgery. The study was approved by an Institutional Review Board. All enrolled patients provided written informed consent.

Clinical classification of tumor depth (cT) and nodal involvement (cN) was determined by preoperative evaluations, including barium radiography, upper gastrointestinal tract endoscopy, computed tomography, and endoscopic ultrasonography. All tumors were diagnosed histologically as adenocarcinomas. Preoperatively diagnosed intramucosal or submucosal carcinoma without lymph node metastasis (cT1, cN0) was designated as suitable for LADG.

Preoperative evaluation of general condition

We examined the results from chest X-rays, laboratory tests, electrocardiogram (ECG) readings, and respiratory function tests using spirometry in all patients to assess preoperative cardiopulmonary function and other comorbidities. Patients were classified according to the American Society of Anesthesiologists (ASA) Classification of Physical Status guidelines so that patient comorbidity could be assessed objectively. Neither LAG nor conventional open gastrectomy was indicated in our hospital for patients with cardiac (greater than New York Heart Association class I), pulmonary (greater than Hugh–Jones grade III), hepatic (Child classes B and C), or renal insufficiencies consequent to a lack of adequate support from specialists in these fields.

Surgical procedures

LADG was performed under a pneumoperitoneum that was created by injection of carbon dioxide (10–12 mmHg). However, an intraperitoneal pressure of 8 mmHg was sometimes selected if a lower cardiopulmonary reserve was expected. A total of five ports (each 5–12 mm) were inserted, and LADG with perigastric and suprapancreatic lymph node dissection was conducted as reported previously [22–26]. Extracorporeal reconstruction was performed using a 4- to 5-cm upper midline incision with Billroth-I reconstruction after LADG. Alternatively, intracorporeal reconstruction was performed with Roux-en-Y reconstruction if the remnant stomach was too small to enable Billroth-I reconstruction.

The following parameters were recorded: patient age and gender, body mass index (BMI), ASA physical status (ASA-PS), peripheral blood count and biochemical findings, nutritional status, tumor characteristics, operation time, estimated intraoperative blood loss, postoperative complications, and length of postoperative hospital stay. BMI was calculated using preoperative physical measurements, and the severity of complications was graded using the Clavien–Dindo classification of surgical complications [27, 28]. In this study, complications of grade I or above in the Clavien–Dindo classification were defined as overall complications.

Statistical analysis

All data are presented as mean \pm standard deviation. Factors that might affect postoperative complications were evaluated by univariate and multivariate logistic regression analysis. Statistical analyses were performed using SPSS version 11.0 (SPSS, Chicago, IL, USA). Significance was established at P < 0.05.

Results

Clinicopathological findings

Table 1 summarizes the patient characteristics. Of the 189 patients, 121 (64.0 %) patients had preoperative comorbidities classified as ASA-PS class 2 or 3. Past history of abdominal surgery including appendectomy was observed in 54 (28.6 %) patients.

Perioperative outcomes

Postoperative short-term outcomes are listed in Table 2. Among 20 patients who underwent simultaneous cholecystectomy, 12 had gallstones, whereas the other 8 patients



550 K. Kumagai et al.

Table 1 Characteristics of elderly patients undergoing laparoscopyassisted distal gastrectomy (LADG)

Characteristic	Value
Number of cases	189
Age, years (median) (range)	76 (70–90)
Sex ratio (M:F)	124:65
Body mass index (kg/m²)	22.2 ± 3.4
ASA-PS (1/2/3)	68/106/15
Previous Iaparotomy	54 (28.6)
Location	
Upper	11 (5.8)
Middle	86 (45.5)
Lower	92 (48.7)
Hemoglobin (g/dl)	13.0 ± 1.4
CRP (g/dl)	0.22 ± 0.47
Albumin (g/dl)	4.1 ± 0.3
Prealbumin (mg/dl)	24.8 ± 5.0
Lymphocytes (cells/µl)	1829 ± 701
PNI	49.8 ± 4.8
Pretreatment (ESD)	27 (14.3)

Data are presented as mean \pm SD. Values in parentheses are percentages

ASA-PS American Society of Anesthesiologists physical status, PNI prognostic nutritional index, ESD endoscopic submucosal dissection

Table 2 Perioperative data for LADG in the elderly

Variable	Value
Operation time (min)	218 ± 60
Blood loss (ml)	76 ± 182
Reconstruction	
Billroth-I	160 (84.7)
Roux-en-Y	29 (15.3)
Combined surgery	
Cholecystectomy	20 (10.6)
Lymph node dissection	
D1+	163 (86.2)
D2	26 (13.8)
Median postoperative hospital stay (days)	11 (7–55) ^a

Data are presented as mean \pm SD. Values in parentheses are percentages

had normal gallbladders and underwent cholecystectomy to prevent gallstone formation or cholecystitis.

Postoperative complications

Postoperative morbidity and mortality outcomes are listed in Table 3. The overall complication rate was 24.9 % (47/189), with the most frequent complication being

Table 3 Postoperative complications after LADG in the elderly

Complication	Number (of 189)
Overall complications	47 (24.9)
Grade I	8 (4.2)
Grade II	19 (10.1)
Grade IIIa	16 (8.5)
Leakage	5 (2.7)
Stricture	5 (2.7)
Abdominal fluid collection	3 (1.6)
Intraabdominal bleeding	1 (0.5)
Anastomotic bleeding	1 (0.5)
Superficial SSI	1 (0.5)
Grade IIIb	3 (1.6)
Bowel obstruction	2 (1,1)
Enteric injury	1 (0.5)
Grade IVa	1 (0.5)
Subdural hematoma	1 (0.5)

Each grade based on the Clavien-Dindo grading system. Values in parentheses are percentages

SSI surgical site infection

abdominal fluid collection including pancreatic fistula (9 cases, 4.8 %). Complications classified as grade III or above in the Clavien–Dindo grading system occurred in 20 (10.6 %) patients. No postoperative mortality was observed in this study. The most frequent severe complication was anastomotic or stump leakage (5 cases, 2.7 %) and anastomotic stricture (5 cases, 2.7 %).

Risk factors of postoperative overall complications

Overall complications after LADG in the elderly correlated significantly with age (75 years old or more), preoperative comorbidity (ASA-PS class 2 or 3), preoperative serum albumin (less than 4.0 g/dl), and preoperative serum prealbumin (less than 22 mg/dl) by univariate analysis (Table 4). Multiple logistic regression analysis identified ASA-PS (odds ratio, 2.754; 95 % CI, 1.207–6.284; P = 0.016) and preoperative serum albumin (odds ratio, 2.224; 95 % CI, 1.089–4.538; P = 0.028) as the independent predictors of a higher postoperative complication rate (Table 5). Preoperative serum prealbumin was not used in multivariate analysis because of the possible strong correlation with preoperative serum albumin concentration.

Risk factors of postoperative severe complications

Subgroup analysis of severe postoperative complications was performed in the same way. Preoperative serum albumin concentration (less than 4.0 g/dl) and simultaneous cholecystectomy were significantly correlated by



^a Value in parentheses is a range

Table 4 Univariate analysis of risk factors for overall and severe postoperative complications after LADG in the elderly

Variables	Overall complications	Overall complications		Severe complications (Dindo, III, IV, and V)	
	Percent (no./total no.)	P	Percent (no./total no.)	P	
Sex	raping personal transfer to the second control of the second cont	COSTANTINIS (COSTANT) (COSTANTINIS COSTANTINIS (COSTANTINIS COSTANTINIS COSTANTINIS COSTANTINIS COSTANTINIS CO		ad to efficient y com _{and y company} parameters a selective de l'Administrative anticoncompany action de mate	
Male	27.4 (34/124)	0.264	12.9 (16/124)	0.161	
Female	20.0 (13/65)		6.2 (4/65)		
Age (years)					
70–74	17.3 (14/81)		8.6 (7/81)		
75–	30.6 (33/108)	0.039	12.0 (13/108)	0.455	
Operation time (min)					
>218	26.2 (22/84)	0.707	13.1 (11/84)	0.318	
≤218	23.8 (25/105)		8.6 (9/105)	*	
Blood loss (ml)					
>76	25.7 (9/35)	0.898	11.4 (4/35)	0.857	
≤76	24.7 (38/154)		10.4 (16/154)		
BMI (kg/m²)					
<18.5	33.3 (8/24)	0.283	20.8 (5/24)	0.071	
≥18.5	23.2 (38/164)		8.5 (14/164)		
Comorbidity (ASA-PS)					
Class 1	13.2 (9/68)		8.8 (6/68)		
Class 2 and 3	31.4 (38/121)	0.007	11.6 (14/121)	0.557	
Previous laparotomy					
Yes	27.8 (15/54)	0.559	11.1 (6/54)	0.881	
No	23.7 (32/135)		10.4 (14/135)		
Hemoglobin (g/dl)					
<10	40.0 (2/5)	0.437	40.0 (2/5)	0.055	
≥10	24.5 (45/184)		9.8 (18/184)		
CRP (g/dl)					
cki (g/di) ≥1	25.0 (1/4)	0.928	0 (0/4)	0.778	
<1	27.0 (40/148)		11.5 (17/148)		
Albumin (g/dl)					
<4.0	36.7 (22/60)	0.012	21.7 (13/60)	0.002	
≥4.0	19.4 (25/129)		5.4 (7/129)		
Prealbumin (mg/dl)					
<22	35.7 (15/42)	0.043	9.5 (4/42)	0.943	
≥22	19.8 (22/111)		9.9 (11/111)		
Lymphocyte (cells/µl)					
<1500	23.7 (14/59)	0.742	11.9 (7/59)	0.739	
≥1500	26.0 (33/127)		10.2 (13/127)		
Pretreatment (ESD)					
No	23.5 (38/162)		9.9 (16/162)		



552

Table 4 continued

Variables	Overall complications		Severe complications (Dindo III, IV, and V)	
	Percent (no./total no.)	P	Percent (no./total no.)	P
Yes	33.3 (9/27)	0.275	14.8 (4/27)	0.443
Reconstruction				
Billroth-I	23.8 (38/160)		8.8 (14/160)	
Roux-en-Y	31.0 (9/29)	0.405	20.7 (6/29)	0.062
Lymph node dissection	on			
D1+	24.5 (40/163)		10.4 (17/163)	
D2	26.9 (7/26)	0.794	11.5 (3/26)	0.865
Cholecystectomy				
No	23.7 (40/169)		8.9 (15/169)	*
Yes	35.0 (7/20)	0.272	25.0 (5/20)	0.035
Location				
Upper	45.5 (5/11)	0.116	27.3 (3/11)	0.080
Others	23.6 (42/178)		9.6 (17/178)	

Values in parentheses are percentages

univariate analysis with complications classified as grade III or above using the Clavien–Dindo grading system (Table 4). Factors with relatively small P values (P < 0.1) in the univariate analysis were selected as covariables in the multivariate analysis, which identified preoperative serum albumin concentration (odds ratio, 5.200; 95 % CI, 1.706–15.850; P = 0.004), Roux-en-Y reconstruction (odds ratio, 3.611; 95 % CI, 1.103–11.817; P = 0.034), and simultaneous cholecystectomy (odds ratio, 5.008; 95 % CI, 1.378–18.201; P = 0.014) as independent predictors of a higher rate of severe postoperative complications (Table 5). Location of the tumor was not used in multivariate analysis because of the possible strong correlation with reconstruction method.

Discussion

Several previous studies indicating the feasibility of LAG in the elderly concluded that LAG produces an incidence rate of postoperative complications in the elderly similar to that in younger patients [18–21]. However, the definition of complication severities after LAG in the elderly was not strictly defined in these previous reports. Severe postoperative complications can easily become fatal in elderly patients as the result of age-related decline in immune functions, which could increase the prevalence and severity of infectious diseases in elderly patients [29–32]. Therefore, we analyzed postoperative complications depending

on their severity and studied risk factors for severe complications in elderly LADG cases.

K. Kumagai et al.

The incidence of complications classified as grade III or above in the Clavien–Dindo grading system was approximately 10 % in our cohort. This rate was relatively low and satisfactory compared with previous studies [18, 19, 21], especially considering that we performed radical surgery involving modified D2 lymph node dissection with curative intent. Median postoperative hospital stay (range) was 11 (7–55) days, which did not seem to be different from previously reported postoperative stay after LADG in all age groups, although statistical analysis was not performed [33].

Reported risk factors for complications following extended lymphadenectomies for gastric cancer are age, operation time, total gastrectomy, and pancreatectomy [34]. In this study, we identified ASA-PS (class 2 and 3) and preoperative serum albumin (<4.0 g/dl) as independent risk factors of overall complications with LADG in elderly patients. We also identified preoperative serum albumin (<4.0 g/dl), Roux-en-Y reconstruction, and simultaneous cholecystectomy as independent risk factors of complications classified as grade III or above in the Clavien-Dindo system. A feature of the Clavien-Dindo classification is that different risk factors could be identified for complications of different severity in the same population. We did not include surgical experience as a variable in the analyses although it is reported to be one of the independent risk factors of postoperative complication in LAG [35]. The



Table 5 Multivariate analysis of risk factors for overall and severe postoperative complications after LADG in the elderly

Variables	Overall complications				Severe complications (Dindo III, IV, and V)			
	OR	95 % CI		P	OR	95 % CI		P
		Lower	Upper			Lower	Upper	
Age (years)	A COLORA DE LA CALLACTE DE LA CALLAC							
70–74	1							
≥75	1.519	0.719	3.211	0.274				
Comorbidity (ASA-P	S)							
Class 2 and 3	2.754	1.207	6.284	0.016				
Class 1	1							
Albumin (g/dl)								
<4.0	2.224	1.089	4.538	0.028	5.200	1.706	15.850	0.004
≥4.0	1				1		×	
BMI (kg/m ²)								
<18.5					2.836	0.794	10.133	0.109
≥18.5					1			
Hemoglobin (g/dl)								
<10					3.698	0.486	28.140	0.206
≥10					1			
Reconstruction								
Roux-en-Y					3.611	1.103	11.817	0.034
Billroth-I					1			
Cholecystectomy								
Yes					5.008	1.378	18.201	0.014
No					1			

OR odds ratio

reason for this non-inclusion is that operator selection is a potential risk of bias because difficult cases tended to be operated by experts and some of the relatively easy cases are done by trainees, particularly in this cohort.

ASA-PS classification is a reported predictive factor of postoperative complications after major abdominal surgeries for colorectal and pancreatic disease [36–38]. ASA-PS class 2 defines "a patient with mild systemic disease" such as controlled hypertension, diabetes without systemic effects, and cigarette smoking without chronic obstructive pulmonary disease [39]. The results of this study suggested that such a mild comorbidity could be a risk factor for postoperative complications, specifically in elderly patients with reduced functional capacities.

Preoperative albumin level is recognized as the best predictor of postoperative morbidity and mortality in various kinds of operations [40–43]. Prealbumin, also known as transthyretin, is a rapid-turnover protein that could provide a sensitive indicator of nutritional status [44, 45]. In elderly patients, major surgeries under the condition of poor nutritional status could be fatal. To prevent the postoperative complications conferred by a malnutrition

status in the elderly, pre- or postoperative immune-nutritional therapy for LADG would be an interesting topic for future study.

We previously reported that Roux-en-Y reconstruction in LADG is an independent risk factor for complications classified as grade III or above for all ages [33]. Roux-en-Y reconstruction in LADG was thought to confer the potential for complications such as internal hernia, duodenal stump leakage, and stricture of the jejunojejunostomy if some procedures to prevent these complications were not applied. In other words, they are regarded as preventable if the potential risks are understood and prophylactic procedures such as closure of mesenteric defects, invagination of the staple line of the duodenal stump, and temporary intracorporeal fixation of the jejunojejunostomy before extracorporeal jejunojejunal anastomosis are applied [33].

We identified simultaneous cholecystectomy during LADG as an independent risk factor of severe postoperative complications, including intraabdominal bleeding, intraabdominal fluid collection, and duodenal stump disruption, although these complications are not necessarily directly related to the cholecystectomy procedure.



Operation time for the patients with simultaneous cholecystectomy (273 \pm 80 min) was 62 min longer than that for the patients who did not undergo that procedure (211 \pm 53 min, P=0.003), and the difference was much greater than empirically expected. In our previous study of LADG for all ages, simultaneous cholecystectomy was not identified as an independent risk factor of postoperative complications classified as grade III or above [33]. Excessive surgical stress could also be a risk factor of postoperative complications after LADG in the elderly, indicating that prophylactic cholecystectomy during LADG in elderly patients should be avoided.

In conclusion, the incidence of severe complications after LADG in the elderly was quite acceptable considering the risks associated with radical surgery with extensive lymphadenectomy. Preoperative serum concentrations of albumin, Roux-en-Y reconstruction without procedures to prevent complications specific to this method, and simultaneous cholecystectomy are independent risk factors for severe postoperative complications in these patients.

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