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厚生労働科学研究費補助金(効果的医療技術の確立推進臨床研究事業)
(研究科題名)進行大腸がんに対する腹腔鏡下手術の根治性に関する比較研究
分担研究報告書

平成 17 年 03 月 11 日

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研究要旨

治癒切除可能な術前深達度 T3、T4(他臓器浸潤を除く)の大腸癌患者を対象として、腹腔鏡下手術を施行した患者の遠隔成績を、現在の国際的標準治療である開腹手術の遠隔成績を対照に比較評価する。Primary endpoint は全生存期間、Secondary endpoint は無病生存期間、術後早期臨床経過、有害事象発生割合とする。

A. 研究目的

大腸癌に対する腹腔鏡下手術が、従来の開腹術に対して、低侵襲であり、癌の手術として短期成績、長期成績において劣るものではないことを RCT にて実証することが当該研究の最終目的である。今年度はようやく実施段階に入ったが、現時点で当院での登録症例はなく、今回は症例対照研究のレベルでの研究結果を虎の門病院 消化器外科の経験症例を元に報告し、分担研究報告書とする。

B. 研究方法

1996 年から 2005 年 02 月までの大腸癌腹腔鏡下手術例(以下―腹腔鏡)871 例を対象、1990 年以降の従来の大腸癌開腹手術例中、根治度 A1286 例(以下―従来法)を対照として用いた。短期成績として、腹腔鏡下手術実施率、開腹移行率、偶発症率、症例対照研究としては、短期成績は、郭清程度、リンパ節郭清個数、開腹創の大きさ、手術時間、術後合併症の頻度等を、長期成績としては、生存率、健存率、再発形式の差を検討した。また、症例の積み重ねに伴う手技上の進歩につき記載する。

C. 研究結果

大腸癌腹腔鏡下手術例の実施例は、871 例で、1999 年以降の実施率は全体では 78.1%、根治度 A では 86.1%であり、実施率は更に増加傾向にある。実施例の 92.1%が根治度 A であった。腹腔鏡下手術実施例中、開腹へ移行したもの―開腹移行率は全体では 6.3%、根治度 A では、4.2%で

あり、開腹移行率は減少傾向にある。術中偶発症は 1.7%であり、やはり減少傾向にある。根治度 A、D3 郭清例について、開腹創の大きさ(平均値)は、盲腸・上行結腸癌手術例(C&A)は従来法 11.7cm に対し、腹腔鏡 4.1cm、S 状結腸癌手術例(S)では 14.6cm と 4.9cm、直腸癌前方切除例(R)では 17.3cm と 6.4cm であった。手術時間は C&A の従来法 172 分に対し、腹腔鏡 215 分、S は 179 分と 193 分、R は 230 分と 205 分であった。根治度 A、ss,al 以深の D3 郭清率は従来法 83.3%、腹腔鏡 75.6%であり、根治度 A、D3 郭清例のリンパ節郭清個数は、C&A で、従来法 34 個、腹腔鏡 35 個、S で 23 個と 27 個、R で 26 個と 26 個であった。同一条件で白血球、体温の変動を比較したが従来法と腹腔鏡で全く差はなかったが、術後 2 日目の CRP が C&A、S、R いずれにおいても腹腔鏡で有意に減少していた。術後歩行開始、鎮痛剤の投与には差はなかったが、排ガス、食事開始時期は腹腔鏡で有意に早まった。根治度 A の術後合併症率は、全体では従来法 28.2%に対し、腹腔鏡 17.8%と有意に低く($P<0.05$)、個別合併症ではイレウスが 14.0%に対し、7.6%と有意差を認めた($P<0.05$)が、他の合併症では明確な差はなかった。長期成績は、再発形式別に見た分布は、肝、肺転移等の血行性転移、腹膜播種再発では全く差はなかった。5 年生存率は、stage II の従来法 82.3%に対し、腹腔鏡 93.0%、stage IIIa は 75.0%と 91.1%、stage IIIb は 61.5%と 65.3%、5 年健存率は、stage II は 78.9%と 83.1%、stage IIIa は 66.6%と 78.7%、stage IIIb は 56.2%と 49.0%

であった。

なお、大腸癌腹腔鏡下手術における手技上の進歩としては、①IMA 根部の郭清、②回結腸動静脈、右結腸動静脈周辺の郭清、③脾彎曲部周辺の剥離、授動、④直腸周辺の剥離、授動は腹腔鏡下手術操作の方が、より容易で確実な手技となりつつある。

D. 考察

根治度 A の腹腔鏡下手術実施率 86.1%に対し、開腹移行率 4.2%、偶発症率 1.7%は、短期的に見た腹腔鏡下手術の質としては問題がないと考えられた。また、症例の積み重ねにより実施率が増加し、開腹移行率、偶発症率は減少傾向を認めた。手術時間は C&A で有意の長期化を認めたものの、平均 43 分の延長であり、S や R では明確な延長はなく、臨床的には全体として許容範囲と考えられた。D3 郭清率、リンパ節郭清個数に差はなく、癌の手術の重要なポイントであるリンパ節郭清の質は腹腔鏡下手術においても保たれている。大腸癌腹腔鏡下手術に限らず、鏡視下手術の共通命題であるアプローチ創、つまり、開腹創の縮小化は確実に実現されている。術後合併症が腹腔鏡において有意に減少していること、排ガス、食事開始時期が短縮しているのは、低侵襲手術であることの証左と考えて良い。長期成績では、大腸癌腹腔鏡下手術における懸念材料の大きな一つである腹膜播種再発の増加はなく、また、症例対照研究とはいえ、生存率、健存率においてどの stage を見ても腹腔鏡に悪化傾向はなく、癌の手術療法の一つとしての問題点はなかったと考える。

E. 結論

大腸癌腹腔鏡下手術実施率、開腹移行率、偶発症率より見て、腹腔鏡下手術は安全、かつ、確実な手術が行われたと考える。また、症例対照研究ではあるが、短期成績では従来法より腹腔鏡が優れた結果を出しており、また、長期成績では両者に明確な差はないことより、腹腔鏡下手術は従来法と比較して、癌の手術としては劣るところはなく、低侵襲性の面で優れていることが示唆された。

今後は当該研究の症例を積み重ねていくことにより症例対象研究で得られた結果を実証していきたい。

F. 健康危険情報

なし

G. 研究発表

1. 論文発表

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その他

H. 知的財産権の出願・登録状況

1. 特許取得

なし

2. 実用新案登録

なし

3. その他

なし

研究成果の刊行に関する一覧表

書籍

著者氏名	論文タイトル名	書籍全体の編集者名	書 籍 名	出版社名	出版地	出版年	ページ
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榎本雅之、 <u>杉原健一</u>	大腸癌—進行がんに対する腹腔鏡下手術	日外会誌	105(9)	494-497	2004
國場幸均、 <u>渡邊昌彦</u> 中村隆俊、佐藤武郎 根本一彦、井原厚 大谷剛正	特集 内視鏡外科手術を安全に行うために 腹腔鏡下大腸手術を安全に行うために.	臨床外科	59(6)	687-692	2004
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Araki Y., <u>Shirozu</u> K., et al.	Clipless Hand-Assisted Laparoscopic Total Colectomy Using LigaSure Atlas ^{TS}	Kurume Medical Journal	51	105-108	2004
田中淳一、 <u>工藤進英</u> 、他	虫垂炎に対する腹腔鏡下虫垂切除術	消化器外科	27	806-815	2004
奥田準二、山本哲久、田中慶太朗、川崎浩資、 <u>谷川允彦</u>	進行直腸癌に対する腹腔鏡下低位前方切除術	臨床外科	59(13)	1535-154	2004
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<u>岡島正純</u> 、内田一徳、吉満政義 他	腹腔鏡下手術における術野展開の工夫と必要なデバイスの特徴	消化器外科	27	1521-1530	2004
<u>Yamaguchi. S, et al</u>	Laparoscopic reduction of appendiceal intussusception due to mucinous cystadenoma in an adult	JSLS	8	279-282	2004
関本貢嗣、山本浩文、池田正孝、竹政伊知朗、瀧口修司、 <u>門田守人</u>	大腸癌に対する開腹術と腹腔鏡下手術の比較 RCTの結果と欧米での評価	外科治療	92 (1)	15-21	2005
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Minimally invasive surgery for gastric tumors

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Gastric tumor, especially gastric cancer, remains one of the most common causes of cancer death in the world. The incidence of early gastric cancer has increased, however, with rapid advances in diagnostic instrumentation and the popularity of mass screening and individual examination. Because patients who have early gastric cancer have a low recurrence rate and a long survival period, attention should be directed to the quality of life (QOL) after surgery.

Laparoscopic cholecystectomy has clear advantages over open surgery, including early recovery of bowel function, early hospital discharge, and decreased pain [1,2]. Therefore, laparoscopic procedures have been adopted for the treatment of gastric tumor. Since Kitano et al's first report of successful laparoscopy-assisted distal gastrectomy (LADG) for early gastric cancer in 1994 [3], the number of laparoscopic surgeries for gastric cancer has increased, and several new laparoscopic procedures for specific gastric tumors, such as gastrointestinal submucosal tumor (GIST) and malignant lymphoma, have been developed [4,5]. Several studies of the short-term outcome of these procedures have been published, but there have been few evaluations of the long-term outcome.

In this article, the authors review the literature on the present status and outcomes of laparoscopic surgery for gastric tumor, mainly gastric cancer.

Development of laparoscopic gastric surgery

Laparoscopic surgery for gastric tumor is more common in Asian countries, especially Japan, than in Western countries because of the higher

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incidence of this tumor in Asian countries; however, laparoscopic surgery for gastric tumor has not yet achieved worldwide acceptance equal to that of laparoscopic colectomy for colon cancer.

Among gastric tumors, early-stage cancers have been considered the best candidates for laparoscopic surgery, and many new laparoscopic procedures for early gastric cancer have been developed since Kitano et al [3] first reported LADG in 1994 (Table 1). These laparoscopic procedures are categorized according to the extent of lymph node dissection: laparoscopic local resection without lymph node dissection, laparoscopic gastrectomy with lymph node dissection (D1, D1 + α , and D1 + β), and laparoscopic gastrectomy with extensive lymph node dissection (D2). By the latter half of the 1990s, laparoscopic procedures were also being used to treat advanced gastric cancer.

A national survey conducted by the Japan Society of Endoscopic Surgery (JSES) showed increasing use of laparoscopic procedures to treat gastric cancer in Japan (Fig. 1) [15]. During the period 1991 to 2001, 4552 patients underwent laparoscopic surgery for gastric cancer. The use of LADG with D1 + α or β lymph node dissection has increased rapidly, and this procedure now accounts for about 75% of all laparoscopic surgeries for gastric cancer.

Since the latter half of the 1990s, there have been multiple studies of the short-term outcomes of laparoscopic surgery, but there have been few randomized controlled trials or studies of long-term outcomes.

Laparoscopic local resection for gastric cancer

There are two procedures for laparoscopic local resection of early gastric cancer: laparoscopic wedge resection (LWR) by a lesion-lifting method, and intragastric mucosal resection (IGMR) [4,16].

Indications

Laparoscopic local resection is used to treat early gastric cancer without lymph node metastasis that is not a candidate for endoscopic mucosal resection (EMR) because of tumor size or location. Lymph node metastasis occurs in 2% to 5% of mucosal cancers and in 15% to 20% of submucosal cancers. Despite many reports, the pathological characteristics of early gastric cancer without lymph node metastasis remain controversial. Hyung and colleagues [17] observed that when lymphatic or blood vessel invasion was absent, there was no lymph node metastasis if the tumor was smaller than 2.5 cm and histologically differentiated, or smaller than 1.5 cm and histologically undifferentiated, regardless of the depth of gastric wall invasion. The Japanese Gastric Cancer Association guidelines define early gastric cancer without lymph node metastasis as mucosal cancer less than 2.0 cm in diameter, histologically differentiated, and without ulceration [18].

Table 1
Development of laparoscopic gastrectomy

Year	First author	Operation	Report
1994	Kitano S [3]	Laparoscopy-assisted Billroth-I gastrectomy (LADG)	Surg Endosc Laparosc Percutan Tech
1995	Watson DI [6]	Laparoscopic Billroth-II gastrectomy	Br J Surg
	Uyama I [7]	Laparoscopy-assisted proximal gastrectomy	Surg Laparosc Endosc
1997	Taniguchi S [8]	Laparoscopic pylorus-preserving gastrectomy	Surg Laparosc Endosc
1999	Uyama I [9]	Laparoscopic total gastrectomy (D2) (for advanced cancer)	Gastric Cancer
	Ohki J [10]	Hand-assisted laparoscopic distal gastrectomy	Surg Endosc
	Kitano S [11]	Laparoscopy-assisted proximal gastrectomy, reconstruction by gastric tube	Surg Today
2001	Goh PM [12]	Laparoscopic radical gastrectomy (D2) (for advanced cancer)	Surg Endosc Laparosc Percutan Tech
	Uyama I [13]	Laparoscopic side-to-side esophagogastrostomy after proximal gastrectomy	Gastric Cancer
2002	Mochiki E [14]	Laparoscopically assisted total gastrectomy with jejunal interposition	Surg Endosc

Therefore, Ogami and coauthors, who developed LWR, proposed the following indications for LWR: preoperatively diagnosed mucosal cancer, elevated lesions less than 25 mm in diameter, or depressed lesions less than 15 mm in diameter without ulcer formation [4]. The pathological indications for IGMR are the same as those of LWR. The method chosen depends on

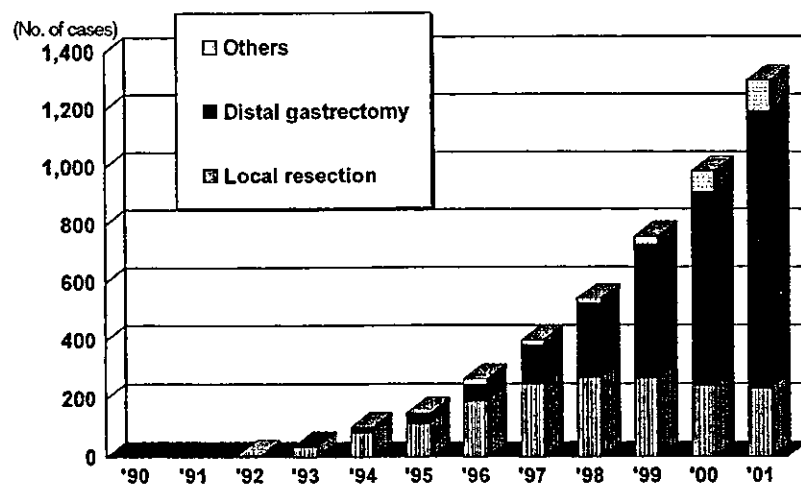


Fig. 1. Laparoscopic surgery was implemented for gastric cancer in 1991. The number of procedures totaled 4500 through 2001. (From Japan Society for Endoscopic Surgery. Nationwide survey on endoscopic surgery in Japan. Journal of Japan Society for Endoscopic Surgery 2002;7:500 [in Japanese]; with permission).

the location of the tumor. LWR is applied for cancer located on the anterior wall, lesser curvature, or greater curvature of the stomach; IGMR is applied for cancers on the posterior wall of the stomach or near the cardia or pylorus.

Techniques of laparoscopic wedge resection and intragastric mucosal resection

In both LWR and IGMR, intraoperative endoscopic observation is required to localize the cancer.

Laparoscopic wedge resection

LWR is performed as follows [4]:

- (1) The gastric wall around the cancer is identified under both endoscopic and laparoscopic observation.
- (2) The abdominal wall and gastric wall in the vicinity of lesion are pierced using a 12-G sheathed needle, and a small metal rod with a fine wire is introduced into the stomach through the outer sheath.
- (3) After retracting the metal rod to lift the cancerous lesion, wedge resection at a sufficient distance from the metal rod is performed using a laparoscopic stapler.

Intragastric mucosal resection

IGMR consisted of the following procedures [16]:

- (1) Three balloon trocars are placed in the gastric lumen, penetrating the abdomen and stomach wall.
- (2) The stomach is insufflated with CO₂, and surgical instruments are introduced.
- (3) Mucosal resection is performed with the use of forceps, electrocautery, and laser under both laparoscopic and endoscopic observation.
- (4) After the resected specimen is extracted endoscopically, each trocar site in the stomach is closed under laparoscopic surgery.

Present status

Although LWR is popular in Japan for early gastric cancer, it is more commonly performed worldwide for the treatment of GIST. IGMR is not as popular in Japan or elsewhere because of the technical difficulty of the procedure.

According to the JSES [15], LWR was performed in Japan in 1428 cases and IGMR in 260 cases during the period 1991 to 2001. Endoscopic submucosal dissection (ESD), a recently developed EMR method [19], enables endoscopic en-bloc dissection of larger lesions. The use of LWR

may decrease as the use of ESD increases. Kitagawa's report [20] of the usefulness of sentinel node navigation before LWR will likely increase the use of LWR with sentinel node navigation.

Evaluation of laparoscopic wedge resection and intragastric mucosal resection

There are few reports on the short- and long-term outcomes of laparoscopic local resection. The reported outcomes are summarized in Table 2. In Ohgami's series of 111 cases [4] (LWR, $n = 93$; IGMR, $n = 18$), there were no major complications or mortality, and patients were discharged uneventfully in 4 to 8 days. There were no conversions to open surgery. The resected specimens had sufficient surgical margins horizontally (LWR, 15 ± 5 mm; IGMR, 8 ± 4 mm) and vertically. There were two recurrences (1.8%), both of which were found near the staple line 2 years after surgery and successfully treated by open gastrectomy and laser irradiation. Shimizu et al [21] reported the short-term outcome of 24 laparoscopic local resections (LWR, $n = 20$; IGMR, $n = 4$). One LWR and one IGMR were converted to open surgery. Operation time was 144 ± 34 and 298 ± 106 minutes for LWR and IGMR, respectively, and blood loss was 56 ± 94 and 33 ± 58 g, respectively. One patient suffered a complication (bleeding) after IGMR, and there were no complications after LWR. Hospital stay was 12 ± 4 and 16 ± 3 days after LWR and IGMR, respectively. In Kobayashi and coworkers [23] department, 18 laparoscopic local resections (LWR, $n = 11$; IGMR, $n = 7$) were performed. Four patients in the IGMR group were converted to open surgery. Histologic examination showed submucosal invasion in five patients, one of whom consequently underwent open gastrectomy.

Further evaluation of the outcomes of laparoscopic local resection is necessary; however, laparoscopic local resection seems to be safe and

Table 2
Evaluation of laparoscopic local resection for cancer

First author	Report	Cases (LWR/IGMR)	Advantage of LWR
Ohgami M.	Nippon Geka Gakkai Zasshi (2000) [4]	93/18 (case)	No major complication Sufficient surgical margin Recurrence in two cases
Shimizu S.	J Am Coll Surg (2003) [21]	20/4 (case)	Detailed histological examination Faster postoperative recover Fewer complications
Kobayashi T.	Surg Endosc Laparosc Percutan Tech (2003) [22]	11/7 (case)	Curative operation Safe procedures

curative when the appropriate indications are used. Precise preoperative and postoperative diagnosis is important.

Laparoscopic gastrectomy for gastric cancer

LADG is the most popular method of laparoscopic gastrectomy. The indications for proximal and total gastrectomy have recently been challenged.

Indications for laparoscopy-assisted distal gastrectomy

LADG for gastric cancer can be performed with perigastric lymph node dissection (D1 + α), additional lymph node dissection along the common hepatic artery (D1 + β), and extended lymph node dissection (D2). The extent of lymph node dissection necessary for the treatment of submucosal cancer is still controversial. Omote et al reported no lymph node metastasis from tumors of less than 300 μ m submucosal invasion and less than 3 cm in diameter [23]. Oizumi and coauthors [24] and Fujii and associates [25] found no metastasis in patients who have submucosal tumor less than 1 cm in diameter. Hyung and coauthors [17] proposed that D2 lymph node dissection is indicated for differentiated submucosal cancers of more than 2.5 cm in diameter and for undifferentiated submucosal cancers of more than 1.5 cm. Yasuda et al [5] showed that submucosal cancers measuring 1 to 4 cm in diameter were sometimes positive for lymph node metastasis but rarely for extragastric lymph node metastasis, and concluded that D1 + α is the optimal lymph node dissection level for these submucosal cancers. The Japanese Gastric Cancer Association guidelines determine the optimal lymph node dissection level for early gastric cancer on the basis of preoperative diagnosis, as follows: D1 + α for mucosal cancer for which EMR is not indicated and for histologically differentiated submucosal cancer less than 1.5 cm in diameter; D1 + β for submucosal cancer without preoperatively diagnosed lymph node metastasis (N0) for which D1 + α is not indicated, and for early cancer less than 2.0 cm in diameter with preoperatively diagnosed perigastric lymph node metastasis (N1); D2 for early N1 cancer more 2.0 cm in diameter, early cancer with extended lymph node metastasis (N2 +), and advanced cancer.

Techniques of laparoscopy-assisted distal gastrectomy

To identify the oral margin of cancer lesion, endoscopic clipping before surgery is performed. There are several modified techniques of LADG, but the most common techniques in LADG with D1 + α lymph node dissection consisted of the following procedures [3]:

- (1) After CO₂ pneumoperitoneum is created, the four trocars are placed at the upper abdomen.

- (2) Under laparoscopic procedures, the greater and lesser omentums and the gastrocolic ligament are dissected.
- (3) The right gastroepiploic vessels are cut to dissect the subpyloric lymph nodes (number 6).
- (4) The suprapyloric lymph nodes are dissected after cutting of the right gastric artery (number 5).
- (5) The left gastric vessels are divided, and the left cardiac and superior gastric lymph nodes are dissected (numbers 1, 3, 7).
- (6) After mobilization of the stomach and D1 + α lymph node dissection under laparoscopic procedures, a 5-cm laparotomy is made below the xyphoid.
- (7) The duodenum and the distal portion of the stomach are exteriorized through this minilaparotomy.
- (8) The distal gastrectomy with D1 + α lymph nodes is performed with a linear stapler.
- (9) Usually, the reconstruction by Billroth-I method is performed.

Present status of laparoscopy-assisted distal gastrectomy

There are three types of laparoscopic gastrectomy: the totally laparoscopic procedure, the laparoscopy-assisted procedure, and the hand-assisted laparoscopic procedure. The laparoscopy-assisted procedure is the most popular because the resected specimen can be pulled out of the abdominal cavity through the small laparotomy incision.

Laparoscopic distal, proximal, and total gastrectomy are performed according to the location of the tumor and depth of invasion, as in open surgery. In Asian countries, LADG is the most frequently used procedure. In Japan, the JSES survey showed that 2600 patients underwent LADG for gastric cancer during the period 1991 to 2001 [15]. Pylorus-preserving gastrectomy and vagus-preserving gastrectomy techniques have recently been developed for early gastric cancer.

Because laparoscopic gastrectomy was developed as a treatment for early gastric cancer, it is most often performed with D1 + α lymph node dissection. According to the JSES survey [15], D1 + α lymph node dissection was performed in 67% and D2 lymph node dissection in 23% of LADGs in Japan.

Evaluation of laparoscopy-assisted distal gastrectomy

The results of LADG have been investigated since 1995. There have been several case-controlled studies comparing LADG with open gastrectomy, and a few randomized controlled studies on the short-term outcome of LADG (Table 3). We have seven studies about outcome and evaluation of LADG to date. All studies, showed some advantages, including early recovery, less pain, and less invasiveness in LADG.

Table 3
Evaluation of LADG for cancer

First author	Report	Cases (LADG/DG)	Advantage of LADG
<i>Short-term clinical outcome</i>			
Kitano S	Surg (2002) [26]	14/14 (RCT)	Less pain, less impaired pulmonary function
Adachi Y	Arch Surg (2000) [27]	49/53 (case)	Less surgical trauma, less impaired nutrition
Yano H	Gastric Cancer (2001) [28]	24/35 (case)	Less pain, shorter hospital stay
			Shorter times to the first passing of flatus, first walking, restarting of oral intake
Reyes CD	Surg Endosc (2001) [29]	18/18 (case)	Shorter hospital stay, less pain
Mochiki E	World J Surg (2002) [30]	24/31 (case)	Earlier return to bowel function, shorter hospital stay
Migoh S	Hepato-gastro (2003) [31]	10/17 (case)	Shorter hospital stay, rapid recovery of bowel function
Weber KJ	Surg Endosc (2003) [32]	12/13 (case)	Lower rate of postoperative complication
<i>Immunofunction</i>			
Fujii K	Surg Endosc (2003) [33]	10/10 (case)	Earlier start of liquid diet, lower level of serum CRP
Cost			Earlier return to bowel function, shorter hospital stay
Adachi Y	Surg Endosc (2001) [34]	48/43 (case)	Preservation of postoperative Th1 cell function
<i>Patient's QOL (questionnaire)</i>			
Adachi Y	Ann Surg (1999) [35]	41/35 (case)	Less expensive
Goh PMY	Surg Endosc (1997) [36]	16 surgeons	Better patient
			Superior to the open techniques (10 of 16 surgeons)

Abbreviation: QOL, quality of life.

There are currently no adequate data to determine the long-term outcome of LADG.

Short-term outcome

Operative findings. Reports of operation time for LADG differ. Mochiki et al [30] reported a longer operation time for LADG than for open distal gastrectomy (DG) (199.8 versus 238 minutes, $P = 0.002$). In contrast, Adachi and coauthors [27] and Yano and colleagues [28] reported no significant difference in operation time between the procedures. The operation time seems to depend on the learning curve of the surgical team; however, most studies found significantly decreased blood loss with LADG in comparison to DG. This may result from the use of laparoscopic coagulating shears under the amplified operative field in LADG.

There have been several comparative studies of morbidity associated with LADG and DG. Adachi and coworkers [27] reported the same rate of complications with LADG as with DG; however, Mochiki and associates [30] found that postoperative ileus was less frequent with LADG than with DG (2% versus 19%, $P = 0.003$). Yano et al [28] showed that the morbidity rate with LADG was lower than with DG (4.2% versus 11.4%, $P < 0.05$). In addition, there have been a few reports about outcomes in case series. Asao and colleagues [37] reported no serious complications in their series. Fujiwara and coauthors [38] warned of a high incidence (14%) of anastomotic leakage with LADG, despite the use of a circular stapler.

According to the JSES survey, the morbidity and mortality associated with LADG were 9.7% and 0%, respectively. These results suggest that LADG is a safe procedure.

Histological findings in resected specimens. The curability of LADG is discussed in terms of the resected margin and the number of dissected lymph nodes. Weber et al [32] reported that all resected margins were free of tumor in 12 laparoscopic surgery cases. Adachi and colleagues [27] indicated that the proximal margin of resected specimens was the same with LADG as DG (6.2 versus 6.0 cm).

Most comparative studies of the number of dissected lymph nodes found no significant difference between LADG with D1 + α and DG with D1 + α lymph node dissection. Furthermore, Miura et al [39] showed that LADG with D2 resection yielded a sufficient number of nodes for adequate TNM classification (> 15 nodes) in 86% of patients, suggesting that LADG may be appropriate for more advanced cancer. Thus, the histological findings indicate that LADG is as much curative procedure for early gastric cancer as open gastrectomy.

Postoperative course. It is difficult to assess the effect of reduced invasiveness of LADG on the postoperative course, because there is no

objective measure. Many reports, however, confirm that the less invasive procedure, in comparison to open surgery, is associated with rapid return of gastrointestinal function, shorter hospital stay, and less pain. In a randomized controlled trial, Kitano and associates [26] identified several advantages of LADG, including lower Visual Analog Scale (VAS) pain score and decreased impairment of pulmonary function as determined by Forced Vital Capacity (FVC) and Forced Expiratory Volume in 1 Second (FEV1). In a case-controlled study, Adachi and colleagues [27] found decreased leukocyte counts on days 1 and 3, decreased granulocyte counts on day 1, and decreased levels of serum of C-reactive protein (CRP), interleukin-6, and albumin on day 1 or 3. Furthermore, weight loss with LADG was less than that with Distal Gastrectomy (DG), suggesting reduced nutritional impairment after LADG. Migoh and coworkers [31] also observed a lower serum CRP level on postoperative day 3 with LADG (4.2 versus 9.4, $P < 0.05$). Fujii et al [31] examined the immune responses after LADG, and found that LADG contributed to the preservation of postsurgical Th1 cell-mediated immune function. Goh and coauthors [36] surveyed surgeons worldwide, and found that laparoscopic gastrectomy was considered superior to open surgery by 10 of 16 surgeons because of faster recovery, less pain, and better cosmesis. In another questionnaires-based study, Adachi and colleagues [35] found that patients reported a better postoperative QOL after LADG than after DG.

Thus, to the extent that postoperative course reflects the effect of surgical invasion, the reduced invasiveness of LADG appears beneficial.

Cost. There has been only one study on the cost of LADG [34]. According to this study, LADG is less expensive than DG because both the postoperative recovery period and hospital stay are shorter.

Long-term outcome

There have been few reports on the long-term outcome of LADG for early gastric cancer. Kitano et al [40] successfully performed 116 LADGs for early gastric cancer over 10 years, and all patients except one, who died not of cancer but of cerebral bleeding, were alive without recurrence or port-site metastasis during a mean follow-up period of 45 months. Randomized controlled trials and case-controlled studies to compare long-term survival after LADG are warranted.

Laparoscopic surgery for other tumors

Surgeons have begun to use laparoscopic procedures to treat tumors other than early gastric cancer. These include GIST and malignant lymphoma.

*Laparoscopic surgery for gastric gastrointestinal submucosal tumor**Indications*

Leiomyoma or leiomyosarcoma is the most common type of GIST in the stomach. Leiomyosarcoma of the stomach represents about 1% to 3% of primary malignant tumors and about 20% of submucosal tumors of the stomach [41]. If lymph node dissection is necessary for surgical management of gastric leiomyosarcoma, total gastrectomy is often required because about 60% of leiomyosarcomas are located in the upper third of the stomach. Lindsay et al [42], however, reported that in a group of 50 patients, none had lymph node metastasis, suggesting that lymph node dissection was not necessary. Thus, there are few reports in which the presence of lymph node metastasis in leiomyosarcoma measuring less than 5 cm in diameter is described. Estes and associates [43] recommended wedge resection of the stomach with a tumor-free margin for the treatment of leiomyosarcoma. Also, Yoshida and coauthors [44] concluded from a retrospective study that LWR can be considered the first-line treatment for gastric leiomyosarcoma.

Present status of laparoscopic wedge resection

There are several case reports of LWR for GIST. Bouillot and colleagues [45] reviewed 65 cases of gastric GIST in 20 centers in France, and Choi et al [46] reported 32 cases of gastric GIST treated by laparoscopic surgery. The JSES survey [15] showed that in Japan, 629 cases of gastric GIST were treated with LWR and 475 with laparoscopic gastrectomy during the period 1991 to 2001; the morbidity rate was 3.2%. In Japan, a large leiomyoma is considered an indication for laparoscopic gastrectomy with lymph node dissection.

The evaluation of laparoscopic wedge resection

Although many cases of LWR for gastric GIST have been reported, only one retrospective study comparing short-term outcomes of LWR versus open wedge resection has been performed [47]. According to this study, LWR for gastric GIST has several advantages, including earlier oral intake, shorter hospital stay, and reduced use of analgesics, despite the longer operation time. Although there are not a sufficient number of studies to evaluate the short- and long-term outcomes of LWR, LWR seems to be a feasible treatment for gastric GIST.

Laparoscopic surgery for other tumors

There have been several case reports of laparoscopic surgery for other types of tumors, including nonepithelial and submucosal tumor. Yasuda and coauthors [5] applied LADG to treat a malignant lymphoma of the stomach, and Benitez et al [48] performed LWR for B-cell gastric mucosa-associated lymphoid tissue lymphoma. Harold and colleagues [49] reported using LWR for symptomatic pancreatic rests located in the stomach.

Summary

Since 1991, laparoscopic surgery has been used to treat gastric tumors, including gastric cancer and gastric GIST. Although laparoscopic gastric resection for gastric tumors has not been accepted worldwide, its use has rapidly increased in Asian countries because of earlier recovery, earlier hospital discharge, less pain, and good cosmesis without a decrease in operative curability. To establish laparoscopic surgery as a standard treatment for gastric tumors, multicenter randomized controlled clinical trials are needed to compare the short- and long-term outcomes of laparoscopic versus open means of access.

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