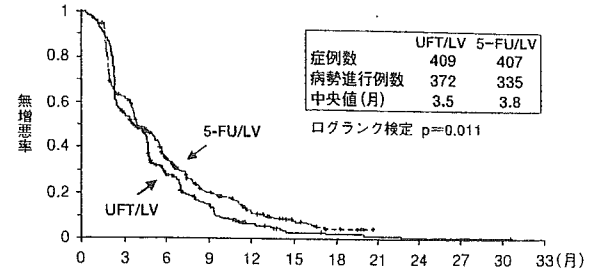
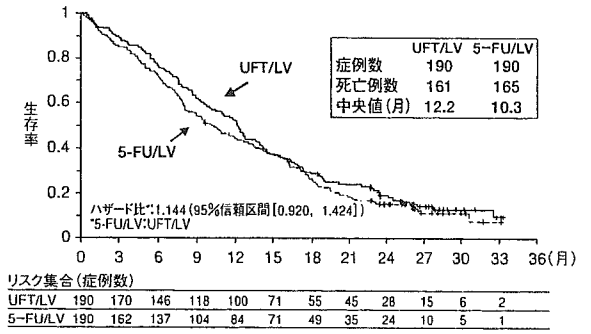


無増悪生存曲線

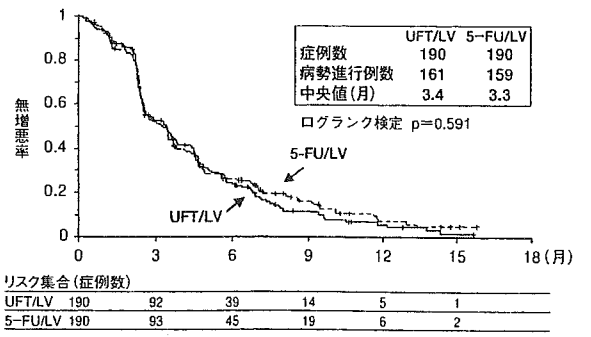
2)病勢進行までの期間の優越性検証を主目的とした試験の結果は以下のとおりで、病勢進行までの期間はUFT/LVと5-FU/LVで有意差は認められなかった。

	生存期間		病勢進行までの期間	
	UFT/LV[注10]	5-FU/LV[注11]	UFT/LV	5-FU/LV
例 数	190	190	190	190
中央値（月） [95%信頼区間]	12.2 [10.4,13.8]	10.3 [8.2,13.0]	3.4 [2.6,3.8]	3.3 [2.5,3.7]
ハザード比[注12] [95%信頼区間]	1.144 [0.920,1.424]		0.941 [0.753,1.175]	
層併合ログランク検定[注13]	p=0.227		p=0.591	

注10) LV：90mg/日とUFT：300mg/㎡/日（テガフール相当量）を併用連日28日間経口投与し、その後7日間休薬を1クールとする
注11) LV：20mg/㎡/日と5-FU：425mg/㎡/日を週5日間連日静脈内投与し、その後30日間休薬を1クールとする
注12) 5-FU/LVに対するUFT/LVのハザード比
注13) 層別因子：前補助療法の有無、ECOG PSの0対1,2
なお、本試験における5-FU/LVは国内で承認されているレボホリナート・フルオロウラシル療法の用法・用量と異なる



生存曲線



無増悪生存曲線

【薬効薬理】

1. *in vitro*試験[5]

ヒト結腸癌細胞（COLO205）に対して、レボホリナートとして0.006μM濃度のホリナートを用いた*in vitro*試験で、フルオロウラシルの抗腫瘍効果増強作用が認められている。

2. *in vivo*試験（併用投与による抗腫瘍効果増強作用）[6,7]

ヒト結腸癌細胞（KM20C、KM12C、Co-3）を移植したヌードマウスに対し、ホリナート（20mg/kg/day）とテガフール・ウラシル（テガフール20mg/kg/day）の併用でテガフール・ウラシル単独投与群に比較して抗腫瘍効果増強作用を示す。

3. 作用機序

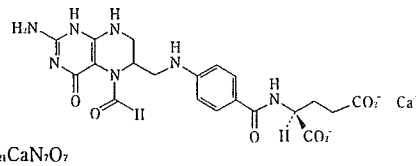
テガフール・ウラシルはフルオロウラシルのプロドラッグであるテガフールにフルオロウラシルの分解阻害作用を有するウラシルをモル比1：4（テガフール：ウラシル）で配合した抗悪性腫瘍剤である。ホリナートの光学活性体（*l*体）であるレボホリナートはBiochemical Modulationによりフルオロウラシルの抗腫瘍効果を増強させる。フルオロウラシルは活性代謝物であるフルオロデオキシウリジン一リン酸（FdUMP）が、チミジル酸合成酵素（Thymidylate synthase：TS）と結合し、TS活性を阻害することにより、チミジル酸合成を抑制しDNA合成を阻害する。レボホリナートは細胞内で還元され、5,10-CH_2-THFとなる。この5,10-CH_2-THFはFdUMP、TSと強固な三元複合体（Ternary complex）を形成し、TSの解離を遅延させることにより、フルオロウラシルの抗腫瘍効果を増強させる。従って、ホリナートとテガフール・ウラシルの併用により、テガフールの分解産物であるフルオロウラシルの抗腫瘍効果が増強される。

【有効成分に関する理化学知見】

一般名：ホリナートカルシウム（Calcium Folinate）〔JAN〕
（別名：ロイコボリンカルシウム）

化学名：Monocalcium *N*-[4-[(2-amino-5-formyl-1,4,5,6,7,8-hexahydro-4-oxopteridin-6-yl)methylamino]benzoyl]-L-glutamate

構造式：



分子式：$C_{20}H_{21}CaN_7O_7$
分子量：511.50
性　状：本品は淡黄色～黄色の粉末で、におい及び味はない。
本品は水に極めて溶けやすく、酢酸（100）に溶けやすく、エタノール(95)又はジエチルエーテルにほとんど溶けない。
本品は光によって徐々に変化する。

【承認条件】

結腸・直腸癌に対するホリナート・テガフール・ウラシル療法の有効性及び安全性の更なる明確化を目的とした十分なサンプルサイズを持つ無作為化比較試験を国内で実施すること。

【包装】

〔PTP〕42錠（21錠×2）
84錠（21錠×4）

【主要文献及び文献請求先】

＜主要文献＞
1) Shirao, K. et al. : J. Clin. Oncol., 22(17)3466(2004)
2) Douillard, J. Y., et al. : J. Clin. Oncol., 20(17) : 3605(2002)
3) Carmichael, J., et al. : J. Clin. Oncol., 20(17) : 3617(2002)
4) Damle, B., et al. : Clin. Cancer Res., 7 : 517(2001)
5) 大鵬薬品工業株式会社社内資料
6) 大鵬薬品工業株式会社社内資料
7) 大鵬薬品工業株式会社社内資料

＜文献請求先＞
ワイス株式会社　メディカルコミュニケーショングループ
〒104-0031　東京都中央区京橋一丁目10番3号
TEL　03-3561-8720

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大阪市中央区道修町四丁目1番1号

腹腔鏡下手術

これは困ったぞ，どうしよう！

亀田総合病院特命院長補佐・主任外科部長・
内視鏡下手術センター長　加納宣康　編著

中外医学社

C3 直腸切除術

Q1 剥離層がうまく同定できない．何を目安にしたらいいのだ？

A S状結腸を充分に挙上して，直腸間膜右側を緊張させる．右総腸骨動脈を確認し，その腹側の直腸間膜を切開し，鈍的に剥離すると，そこは直腸固有筋膜と骨盤筋膜の間の粗な部分であり，その層を頭側尾側に広げると剥離すべき層になる（図1，2）．腸間膜を充分に牽引することがコツである．

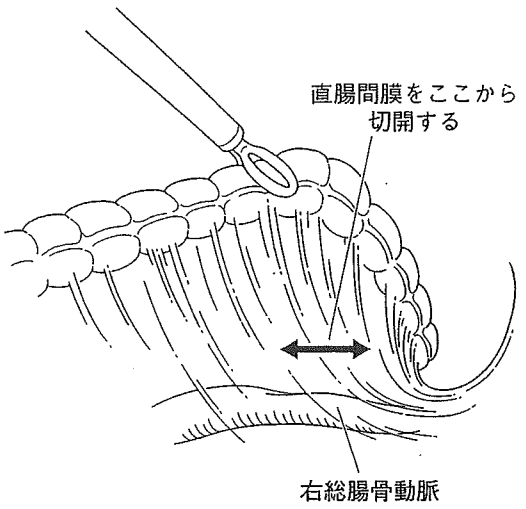

図1 正しい剥離層の見つけ方（内側アプローチ）

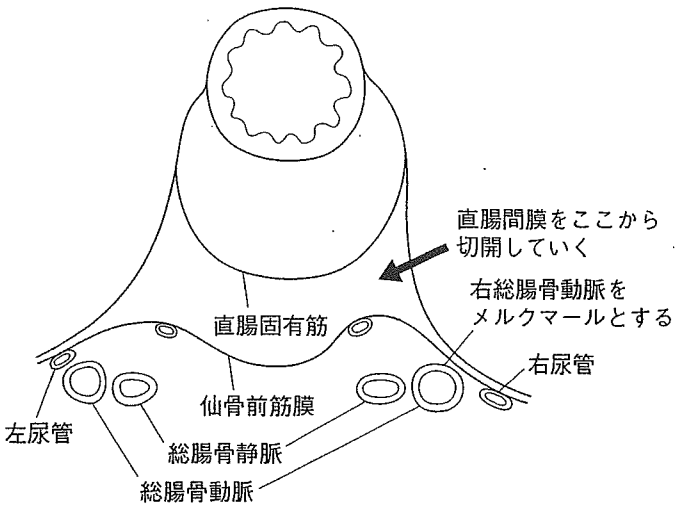

図2 正しい剥離層の見つけ方（断面図）

Q2 尿管が同定できない．どうしよう！

A 内側アプローチでは上記の剥離層を腹部大動脈前面から左側の方へ広げていくと，左総腸骨動脈と交叉する左尿管を容易に確認できる（図3）．外側よりのアプローチではToldtのfusion fasciaに沿って内側に剥離を進めると後腹膜下筋膜の背側に尿管を透見できる（図4）．

Q3 尿管に熱が伝わって一部白くなっている．どうしよう！

A 尿管の一部が白くなっている程度では問題はないと思われるが，尿管表面の血管が障害され，循環障害がある場合や尿管が全周にわたり変性している場合は狭窄や穿孔の危険があるので，要注意である．泌尿器科に依頼して，膀胱鏡下に尿管スプリントを留置する．

Q4 尿管が一部切れてしまった．どうしよう！

A 泌尿器科に依頼して吻合し，尿管スプリントを留置する．尿管の挫滅が強かったり，尿管の循環障害が合併していると，障害された尿管の切除を要することがあるので，経験豊かな泌尿器科医のアドバイスが必要である．

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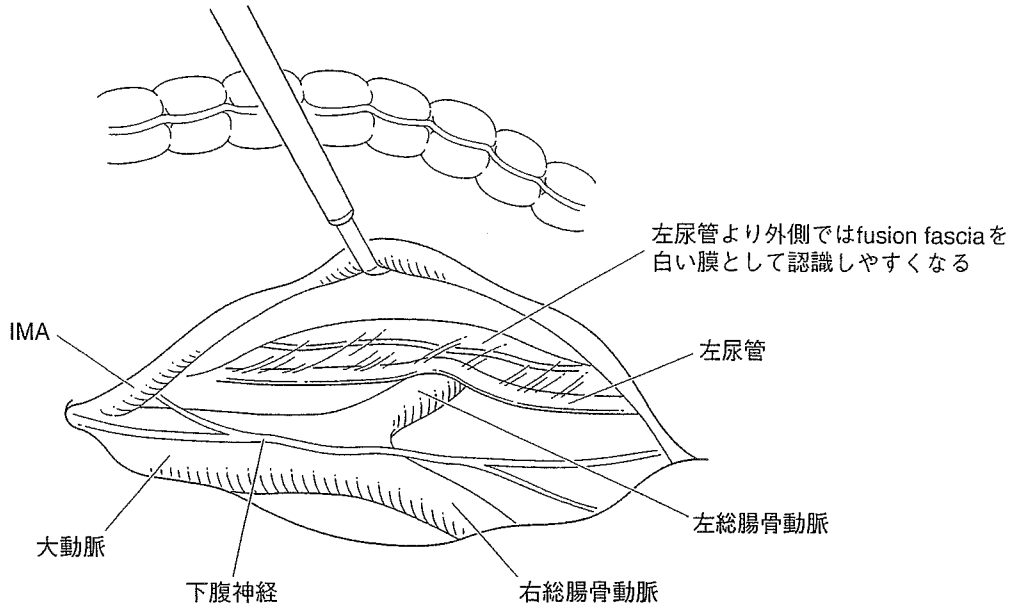

図3　内側アプローチでの尿管の見つけ方

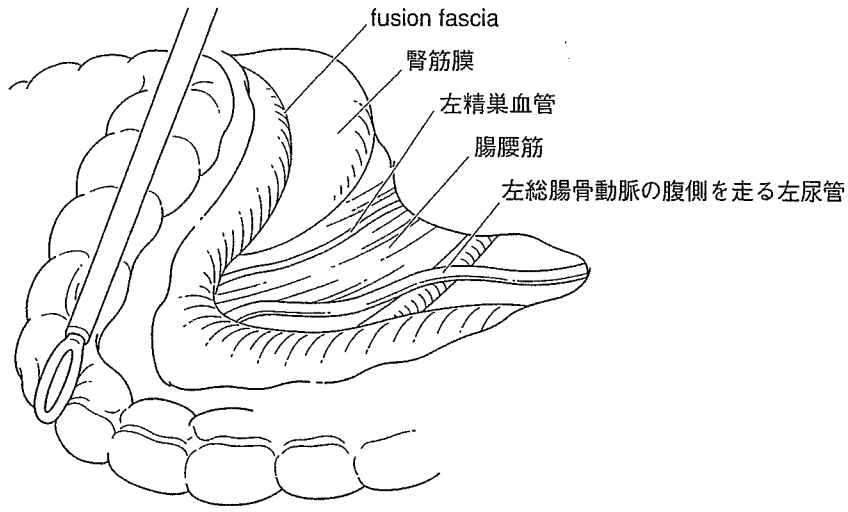

図4　外側アプローチでの尿管の見つけ方

Q5　**脂肪が多くて閉口する．経験豊富な人たちはどうやっているのだろう？**

A　肥満のために開腹移行することはほとんどないが，肥満者でいちばん困難なことは，腹壁が厚いためにトロカーを刺入したあとのトロカーの角度の自由度（可動範囲）が制限されることである．腹腔内での操作は正しい剥離層で手術を進める限り，時間はかかっても不可能なことはない．良好な視野を得るためには，トロカーを追加する．ハンドアシストを考慮する．

Q6　**重力を使って腸管を移動させて術野を作れというが，いったいどこまで傾けてもいいものだろう？　安全な固定方法は何か？**

A　鏡視下専用の手術台ではなくてもかなりのティルトは可能である．われわれは下肢をレビテータで固定し，特注の（現在は製品化されている）側板を使用している（図 5）．手術台のティルトだけに頼らず，トロカーの追加やハンドアシストも考慮する．

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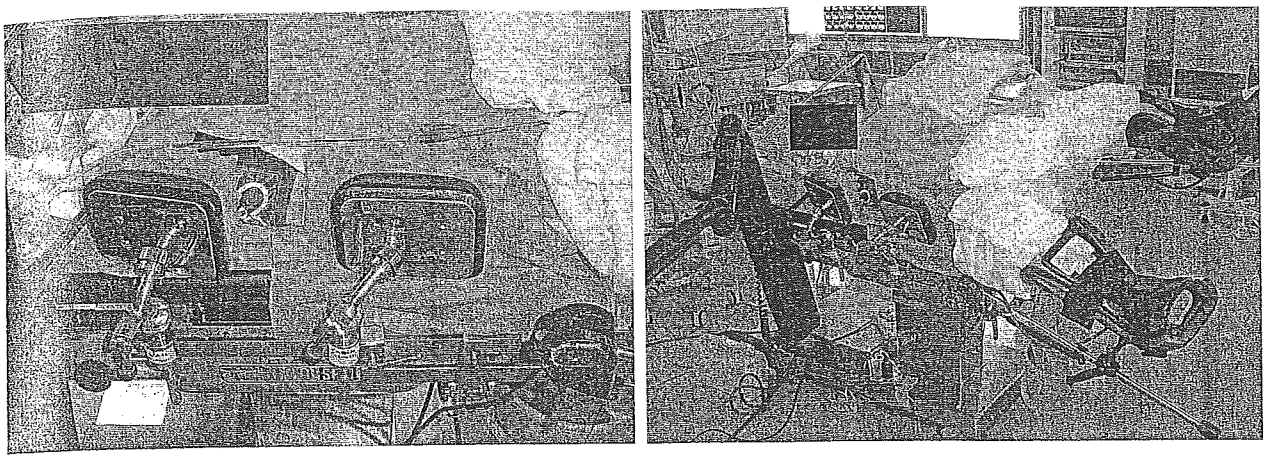

図5　特注の側板による患者の保持

Q7　直腸を endostapler で切ったが，緊張がかかった状態で切ったので，一部が開いていないか心配だ．どうしよう！

A　リークテストを行う．口側を腸鉗子や綿テープでクランプし，肛門より空気を注入する．もし，リークが認められたら，さらに肛門側を再切除できる場合はステープラで再度縫合切離する．下部直腸で再度の切除が困難な場合は，経肛門的手縫い吻合に変更する．

Q8　直腸を引っ張って剥離しているうちに一部穴があいた．どうしよう！

A　さらに肛門側を剥離して穿孔部の肛門側でステープラを使って直腸を切離する．下部直腸で穿孔してしまい，上記の対応ができない場合は，直腸を切離してしまい，経肛門的に手縫い吻合する（超低位前方切除とする）．

Q9　直腸後面の血管処理を超音波凝固切開装置でやっていたら直腸が焼けて一部白くなっている．ここで切離して大丈夫だろうか？　また，超音波凝固切開装置だけで切ると不安だが，どうしよう！　クリップを使うと吻合の時じゃまになるかもしれない．

A　下部直腸で切離する場合は，直腸の剥離には超音波凝固切開装置だけで充分である．クリップはステープラの誤動作の原因となるので，切離線近くで使用してはならない．

Q10　DST で吻合したら，吻合後に抜けなくなった．どうしよう！

A　リニアステープラをサーキュラーステープラで打ち抜けないときに起こり得る．アンビルヘッドをリリースし，ステープラ本体を抜去した後，経肛門的にステープルラインを切離して，アンビルヘッドを除去する．強引に引き抜くと吻合線を損傷する．

Q11　DST で吻合したら，帰室してから大量に下血した．どうしよう！

A　吻合線からの出血と考える．まず，止血薬の投与，冷生食での洗浄，トロンビン末の直腸内散布を行う．それでも出血が止まらない時は，内視鏡的にクリップで止血する．

〔宗像康博〕

JCLS 498-04324

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SURGICAL
CLINICS OF
NORTH AMERICA

Surg Clin N Am 85 (2005) 151–164

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 pyrorus-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

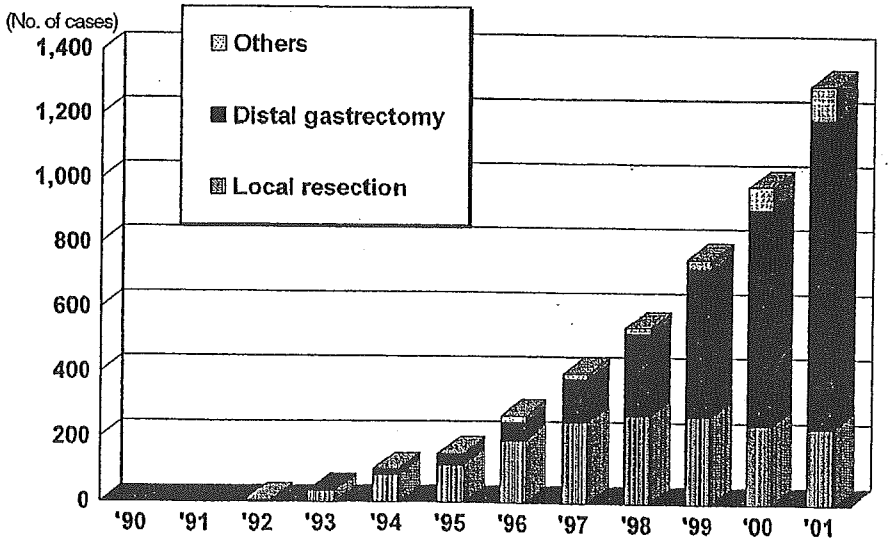

Fig. 1. Laparoscopic surgery was implemented for gastric cancer in 1991. The number of procedures totaled 4500 through 2001. (*From* Japan Society for Endoscopic Surgery. Nationwide survey on endoscopic surgery in Japan. Journal of Japan Society for Endoscopic Surgery 2002;7:500 [in Japanese]; with permission).

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. Kitagawas 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 um 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 gastroepiploric 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
Short-term clinical outcome			
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 Less pain, shorter hospital stay
Yano H	Gastric Cancer (2001) [28]	24/35 (case)	Shorter times to the first passing of flatus, first walking, restarting of oral intake Shorter hospital stay, less pain
Reyes CD	Surg Endosc (2001) [29]	18/18 (case)	Earlier return to bowel function, shorter hospital stay
Mochiki E	World J Surg (2002) [30]	24/31 (case)	Shorter hospital stay, rapid recovery of bowel function Lower rate of postoperative complication
Migoh S	Hepato-gastro (2003) [31]	10/17 (case)	Earlier start of liquid diet, lower level of serum CRP
Weber KJ	Surg Endosc (2003) [32]	12/13 (case)	Earlier return to bowel function, shorter hospital stay
Immunofunction			
Fujii K	Surg Endosc (2003) [33]	10/10 (case)	Preservation of postoperative Th1 cell function
Cost			
Adachi Y	Surg Endosc (2001) [34]	48/43 (case)	Less expensive
Patient's QOL (questionnaire)			
Adachi Y	Ann Surg (1999) [35]	41/35 (case)	Better patient
Goh PMY	Surg Endosc (1997) [36]	16 surgeons	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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