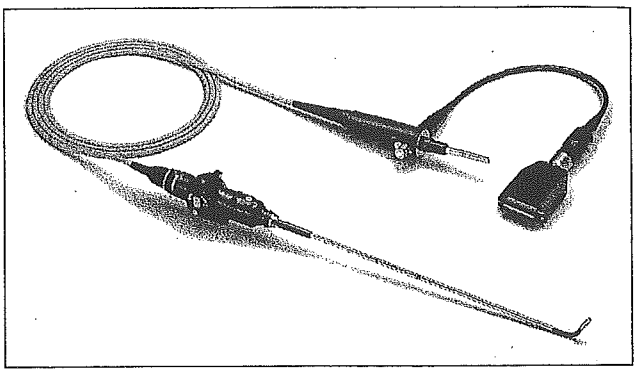

図1. 5mm径フレキシブル電子式腹腔鏡(オリンパス社製LTF VP)

ほとんど差がみられない.

またその先端の角度により0°の直視鏡から30°, 45°, 70°の斜視鏡があり, 一般的には直視鏡や30°の斜視鏡がよく使用されている. 45°の斜視鏡は30°に比べより見下ろしを必要とする場合に有用であり, 腹腔鏡補助下幽門側胃切除術(LADG)のNo.8aリンパ節などの郭清に有用という報告もある. 10mmの0°の直視鏡の視野角は約76°とかなり制限されるが, 30°の斜視鏡では180°回転させることにより152°の視野角が得られるようになるといわれている[2].

2. 電子式腹腔鏡

電子式腹腔鏡はその先端にCCDカメラが装着されており, 画像を電気信号にかえて伝達する腹腔鏡である. 前述した光学式腹腔鏡は画像を忠実に, カメラヘッドと呼ばれるCCDカメラに伝達する役目を行うためのものであり, その仕組みは大きく異なる. 一般的に先端部分が彎曲可能なフレキシブルタイプが使用されている.

以前は彎曲可能な部分が4cmと長く, 観察対象物が近すぎるとトロカールから彎曲部分が出ないため彎曲しての観察ができなかった. また径が10mmのものしかなく, 5mmポートからの使用もできなかった. 最近オリンパス社からそれらの問題を改善したEndoEyeフレキシブルビデオスコープ(LTF VP)が発売されている(図1). これは外径5.4mmと5mmポートから使用可能であり, 先端から2.5cmの部分で彎曲し, 上下・左右の彎曲角度も100°となっている. 従来のフレキシブルスコープとの比較では視野や画質で遜色なく, 彎曲角度やポートの利便性に優れていると報告されている[4]. また単純に比較はできないものの, 30°の斜視硬性鏡の視野角152°に対し5mmのこのフレキシブルスコープの視野角は280°と計算され, 視野角の大きさがフレキシブルスコープの強みといえる. 欠点としては操作がやや煩雑であり, 彎曲を使った視野の確保に慣れる必要があり, スコピストの技術の習得が不可欠である.

II. CCDカメラ

CCD電荷結合素子とは1970年代に開発され, 光の強さを電気信号に変換して出力する半導体集積回路(IC)である. 現在家庭用ビデオカメラにも使用されており, 腹腔鏡下手術の分野においてはこのCCDチップを一つ用いた1CCDカメラと三つ用いた3CCDカメラが一般に使用されている. 1CCD方式では一つのCCDにて色の3原色である赤, 青, 緑に対応するようになっているため, 1原色に対する素子数は1/3となる. それに対し3CCD方式ではプリズムを用いて光を3原色に分解し, 一つのCCDが一つの原色に対応するため, 1チップのすべての素子を1原色に使用することが可能である. そのため3CCDカメラはより鮮明な画像を得ることが可能であり, 水平解像度も1CCDカメラでは500ライン程度に対し, 3CCDカメラでは700～1,100ラインとなっている.

光学式腹腔鏡タイプのカメラヘッド部分のCCDカメラはKarl Storz社(図2), Stryker社(図3)ともに3CCDカメラである. それに対し, オリンパス社のフレキシブル電子式腹腔鏡はその先端にCCDカメラが装着されており1CCDカメラとなっている(図1). 腹腔鏡のタイプが違うために単純に比較はできないものの, 3社の最新機種を表2で比較してみた. 総素子数や解像度では1CCDカメラは3CCDカメラに劣るものの小型軽量化可能であり, 現在フレキシブルタイプでは1CCDカメラが主流となっている. また1CCDカメラは3CCDカメラより一般に安価であり,

図2. 光学式腹腔鏡用の3 CCDカメラシステム(Karl Storz社製IMAGE1)

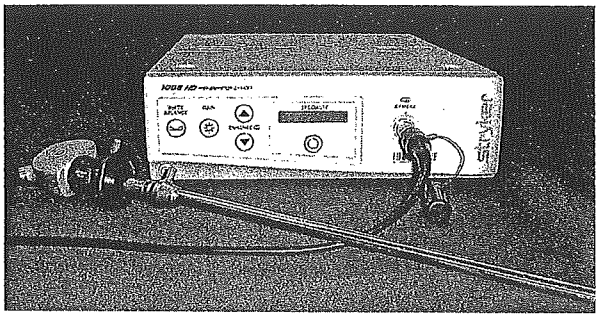

図3. 光学式腹腔鏡用の3 CCDカメラシステム(Stryker社製1088HD)

表2. CCDカメラ装置の比較

製品名 (会社名)	IMAGE1	TRICAM SL	1088HD	OTV-S7
	(Karl Storz社)		(Stryker社)	(オリンパス社)
撮像素子(CCD)	3 CCD	3 CCD	3 CCD	1 CCD
サイズ	1/4インチ×3	1/4インチ×3	1/3インチ×3	1/4インチ
総画素数	38万画素×3	41万画素×3	131万画素×3	41万画素
走査方式	インターレース方式	インターレース方式	プログレッシブ方式	インターレース方式
水平解像度	700ライン	750ライン	1,100ライン	480ライン
カメラヘッド重量	175 g	195 g	190 g	360 g (腹腔鏡を含む)
オートクレイブ対応	×	○	×	×
光学ズーム	○	○	×	×
電子ズーム	×	×	○	○
価格(定価) [腹腔鏡を含み光源は除く]	630万円	530万円	530万円	330万円

実際に腹腔鏡からCCDカメラ，カメラ本体までの1セット価格が1CCD方式のオリンパス社のものが他の2社のものに比べ定価で約200～300万円程度安価である．結局機種選定にあたっては，3CCDの画質をとるか1CCDの値段や操作性をとるかということと思われる．

III. 光源装置

消化管内視鏡もそうであるが，腹腔鏡にもカメラ装置とは別に光を送ることだけを目的とする光源を必要とする．腹腔鏡の光源には自然光(太陽光)に近い波長分布と十分な明るさが必要とされ，以前ではメタルハロゲンランプも使用されていたが，現在300Wのキセノンランプが主流である．光源装置はCCDカメラとセットで購入することが多いが，価格は各社であまり差がなく，定価で100万～150万円程度である．

光学式腹腔鏡では光源からのライトケーブルの接続部分(スロット)はカメラヘッドの接続部分(アイピース)と90°の関係になっている．ライトケーブルの劣化が光量減少の原因となることもあるので，定期的に点検しておく必要がある．また通常のライトケーブルは熱をもつので，腹腔鏡と接続せずライトケーブルを放置しておくと患者の火傷の原因になるので注意が必要である．それに対してフレキシブル電子式腹腔鏡ではライトケー

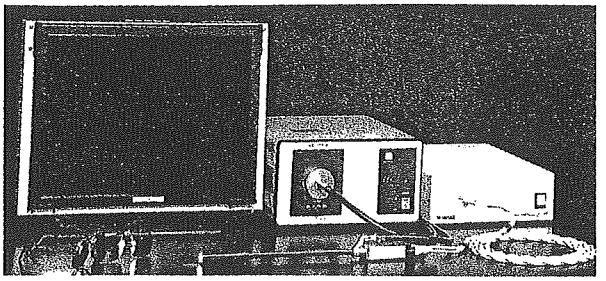

図4. 三次元画像装置一式(新興光器製作所)

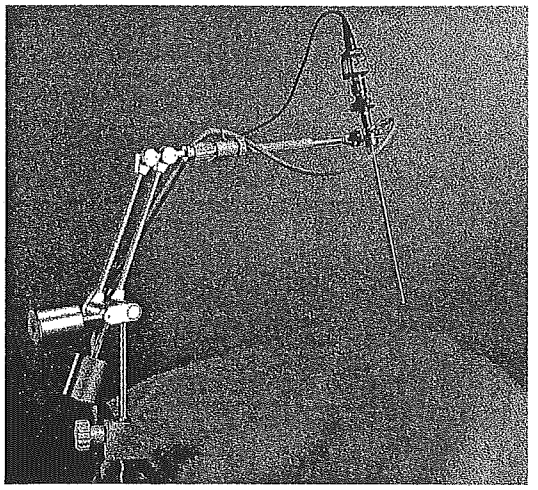

図6. サージカルテレスコープホルダー
(オリンパス社製SH-1)

ブルは一体化しており，逆に差し込み式となっている．

IV. 三次元画像装置

通常のモニターによる画像は二次元画像であり，遠近感，立体感に乏しく，腹腔鏡下手術をむずかしくしている原因の一因をなしている．この欠点を改善するために三次元(3D)画像装置が開発されている．3D画像装置の原理は視差をもつ二つの光学視管から得られる画像をそれぞれ別のCCDで結像させる2眼2カメラ方式と，1本の光学視管の接眼部で光を分割し二つのCCDで結像させる1眼2カメラ方式がある[5]．いずれの方式でも左右別々の画像をモニター上に交互に表示し，特殊メガネ(偏向メガネ)を使用することにより立体視が可能となる．わが国では2眼2カメラ方式を用いて新興光器製作所で開発・改良され，

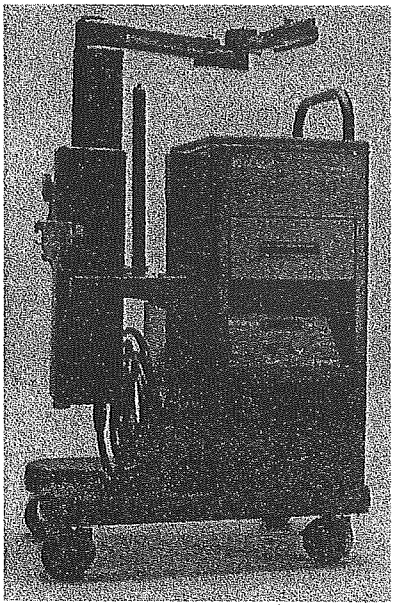

図5. AESOPシステム(ケーテック社)

立体内視鏡，CCDカメラ，立体液晶モニター，光源までの1セットの定価は930万円である(図4)．比較的高価なものとなっているが，リアルタイムに安定した立体画像を得ることが可能となっている[6]．

またわが国においてface mounted display (head mounted display)を用いた3D画像装置の開発も行われていたが[7]，手元がみえないなどの術野外の視野の問題や重量による術者の疲労の問題から開発は現在中断している．

V. 腹腔鏡保持装置

腹腔鏡下手術には経験あるスコピストの存在が不可欠とされるが，ロボット工学の技術を駆使し，スコピストにかわり腹腔鏡を保持するために開発された機器がある．米国Computer Motion社が開発したボイスコントロール(音声認識)システムであるAESOP(automated endoscopic system for optimal positioning)システムである(図5)[8]．AESOPシステムはZEUS Robotic Surgical Systemの一部にも組み込まれているが，ZEUSがわが国で現在個人輸入とされているのに対し，AESOPシステムはすでに薬事で承認されており，定価2,500万円で販売されている(ケーテック

社)．実際の手術ではAESOPのロボットアーム部分(重量18 kg以下)は本体部分から切り離され，手術台に迅速に固定され，術者の声によりスムースで確実なスコープの動きが可能となっている．

またオリンパス社もロボット工学の技術ではないものの，腹腔鏡の確実な保持と移動を可能とするサージカルテレスコープホルダーを開発している(図6)．カウンターバランス方式により腹腔鏡のスムースな動きと安定が可能であり，スコピストなしでの腹腔鏡下手術を可能とする．定価は40万円である．

おわりに

現在わが国で使用可能な腹腔鏡下手術の光学機器について概説した．最近の進歩として，5 mm径のフレキシブルビデオスコープ，3D画像装置，AESOPシステムがあげられる．より安全で確実な腹腔鏡下手術が可能になるように，今後のさらなる光学機器の開発に期待したい．

[製造・販売元連絡先]

1) エム・シー・メディカル(株)：〒160-8355　東京都新宿区西新宿7-5-25　西新宿木村ビル(TEL 03-5330-7860/FAX 03-5330-7867)
2) オリンパスメディカルシステムズ(株)：〒163-0914 東京都新宿区西新宿2-3-1　新宿モノリス(TEL 03-5330-7860/FAX 03-5330-7867)
3) 日本ストライカー(株)メドサージ事業部：〒113-0033　東京都文京区本郷3-22-5(TEL 03-5805-8930/FAX 03-5805-8939)
4) (有)新興光器製作所：〒113-0033　東京都文京区本郷2-12-2(TEL 03-3811-4194/FAX 03-3814-2608)
5) (株)ケーテック：〒104-0032　東京都中央区八丁堀3-5-7　NRE八重洲ビル(TEL 03-3552-1194/FAX 03-3552-6995)

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Review Article

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Laparoscopic Gastrectomy for Cancer

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Key Words
Laparoscopy-assisted distal gastrectomy · Early gastric cancer · Surgical outcome

Abstract
There are three procedures for the management of early gastric cancer (EGC): laparoscopic wedge resection (LWR), intragastric mucosal resection (IGMR), and laparoscopic gastrectomy. LWR or IGMR can be applied to treat EGC without the risk of lymph node metastasis. However, owing to the recent technical advances in endoscopic mucosal resection for EGC, the use of laparoscopic local resection for these lesions has gradually decreased. On the other hand, laparoscopic gastrectomy with lymph node dissection, such as laparoscopy-assisted distal gastrectomy, is widely accepted for the treatment of EGC with the risk of lymph node metastasis. To establish the acceptability of laparoscopic gastrectomy with D2 lymph node dissection against advanced gastric cancers, safe techniques and new instruments must be developed. The following advantages of laparoscopic surgery for the treatment of gastric cancer have been well demonstrated: clinical course after operation, pulmonary function, immune response. In the future, laparoscopic surgeons have to design and implement education and training systems for standard laparoscopic procedures, evaluate clinical outcomes by multicentric randomized control trial studies, and clarify the oncological aspects of laparoscopic surgery in basic studies.

Introduction

Gastric cancer has been one of the most common causes of cancer death in the world. Recently, the detection of early gastric cancer (EGC) has been increasing and new treatment strategies for gastric cancer have been developed. The 5-year survival rate of patients with EGC who underwent surgical treatment has reached 90% or more in Japan [1–3]. On the basis of the low incidence of node involvement in most EGC patients, current surgical trends for EGC have shifted from surgery with extended lymph node dissection to minimally invasive surgery, thereby providing a better postoperative quality of life.

Laparoscopic surgery has become popular as a minimally invasive procedure. The following advantages of laparoscopic surgery for the treatment of gastrointesti-

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nal disease including EGC have been well demonstrated: clinical course after operation, pulmonary function, immune response [4–7]. For the management of patients with EGC, laparoscopic gastrectomy has been widely accepted in Japan. Recently, the use of laparoscopic gastrectomy for advanced gastric cancer has been attempted. In this article, the authors review the literature on the indications, techniques, outcomes, and future perspective of laparoscopic gastrectomy for gastric cancer.

Early Gastric Cancer

Incidence of Lymph Node Metastasis

The most important factor influencing the survival of patients with EGC is the status of lymph node metastasis [8–11]. The incidences of lymph node metastasis in large series of EGC range from 1 to 3% for tumors confined to the mucosa [10, 12, 13] and from 11 to 20% for tumors invading the submucosa [12–14]. Lymph node metastasis is rare in patients with mucosal cancer, and is restricted mostly to the perigastric nodes in patients with node-positive EGC [12, 13, 15–17].

Endoscopic Mucosal Resection for Early Gastric Cancer

Although endoscopic mucosal resection (EMR) is a useful procedure for EGC without a risk of lymph node metastasis, a successful EMR requires the en bloc resection of the EGC. The Japanese Gastric Cancer Association issued the first version of its gastric cancer treatment guidelines in 2001. These guidelines indicate EMR for intestinal-type mucosal cancers that lack ulcerative findings and that are <2 cm in diameter, regardless of tumor morphology [18]. Recently, several new devices for endoscopic submucosal dissection (ESD) have been developed, such as an insulation-tipped diathermic knife [19], a hook knife [20], a flex knife [21], and a triangle-tipped knife [22]. ESD enables us to completely remove a large lesion as a single fragment. However, as the frequency of complications during ESD is reported to be relatively higher than conventional EMR [19], endoscopists should obtain the skills needed to carry out ESD safely. When ESD is safely and commonly performed, all intestinal-type mucosal cancers without ulcerative findings will be indicated for ESD.

Laparoscopic Gastrectomy for Early Gastric Cancer

Current Trends in Laparoscopic Gastrectomy

There are three procedures for the management of EGC: (1) laparoscopic wedge resection (LWR) [23, 24], (2) intragastric mucosal resection (IGMR) [25], and (3) laparoscopic gastrectomy (totally laparoscopic, laparoscopy-assisted, and hand-assisted). Since our first experience doing laparoscopy-assisted distal gastrectomy (LADG) by a Billroth I reconstruction for a patient with EGC in 1991 [26], a national survey conducted by the Japan Society of Endoscopic Surgery (JSES) showed increasing use of laparoscopic procedures for EGC in Japan. During the period from 1991 to 2004, 7,827 patients underwent laparoscopic surgery for gastric cancer [27]. Along with the societal recognition of the significance of minimally invasive surgery for EGC, the popularity of LADG with lymph node dissection has increased rapidly, and this procedure now accounts for about 83% of all laparoscopic surgeries for gastric cancer in Japan. LADG was reported to have several advantages over open surgery, including earlier recovery and better patient's quality of life [4–7].

Several recent studies have evaluated the validity of the sentinel node (SN) concept for the treatment of gastric cancer as well as malignant melanoma or breast cancer [28–31]. Now, two major, well-designed, large-scale clinical trials to clarify the validity of the SN concept for gastric cancer have been conducted by two Japanese groups: the Japan Clinical Oncology Group and the Japan Society of Sentinel Node Navigation Surgery. Although laparoscopic detection and sampling for SNs of gastric cancer is believed to be more technically difficult than open surgery [28], the SN navigation concepts must contribute to the choice of surgical treatments for EGC, including EMR and laparoscopic surgery.

Indication of Laparoscopic Gastrectomy for Early Gastric Cancer

Most early cancers are located only in the gastric wall, and local resection of the gastric wall is adequate for complete clearance. Theoretically, laparoscopic local resection, such as LWR or IGMR, can be applied to treat EGC without the risk of lymph node metastasis. However, owing to the recent technical advances in EMR for EGC, the use of laparoscopic local resection for these lesions has gradually decreased. On the other hand, laparoscopic gastrectomy with lymph node dissection, such as LADG, has been widely accepted to treat EGC with the risk of lymph node metastasis [32].

Since it is difficult to diagnose lymph node metastasis preoperatively, the risk for it is estimated by the tumor size, the depth of cancer invasion, the presence of ulceration, and the histological type. On the basis of pathological findings in a large number of surgically resected specimens, the Japanese Gastric Cancer Association guidelines recommend the following optimal lymph node dissection levels for EGC: D1+α (perigastric lymph node dissection) for mucosal cancer, for which EMR is not indicated and for histologically differentiated submucosal cancer of <1.5 cm in diameter; D1+β for preoperatively diagnosed submucosal cancer without lymph node metastasis (N0), for which D1+α is not indicated, and for early cancer <2.0 cm in diameter with only perigastric lymph node metastasis (N1); D2 for early cancer >2.0 cm in diameter, with lymph node positive. According to these guidelines, lymph node dissection is performed in LADG.

Surgical Techniques of LADG

The techniques of LADG are described below [26]. The essentials for LADG with D1+α lymph node dissection for gastric cancer are as follows: (1) Under general anesthesia, a 10-mm Hg pneumoperitoneum is created and a laparoscope is inserted through the subumbilical incision. (2) Four cannulas for grasping and dissecting instruments are placed in the upper abdomen. (3) The greater omentum and gastrocolic ligament are dissected laparoscopically outside the epigastric arcade. (4) The right gastroepiploic vessels are cut to facilitate dissection of the lymph nodes at the subpyloric portion. (5) The lesser omentum is opened and the suprapyloric lymph nodes are dissected after the right gastric artery and vein are divided between clips. (6) The stomach is fully mobilized, and the left gastric artery and vein are divided using clips. (7) The left cardiac and superior gastric lymph nodes are dissected down to the distal portion of the stomach. (8) A 5-cm long upper laparotomy is made just below the xiphoid, and the mobilized stomach is pulled out through this minilaparotomy wound. The distal two-thirds of the stomach is resected using staplers. (9) Billroth I gastroduodenostomy is carried out through the minilaparotomy wound, with the same handsewn technique as used for conventional open surgery.

Comparison of Short-Term Outcome between LADG and Conventional Open Gastrectomy for EGC

Several studies about the short-term outcome of LADG for EGC have been reported. With regard to operative findings, several studies have demonstrated a longer operation time and lower blood loss for LADG than for open distal gastrectomy (ODG) [33]. But, the learning curves of surgical teams suggested that training reduced the operation time for LADG [5, 34].

There have been several comparative studies of surgical morbidity between LADG and ODG. Most of those studies demonstrated the same or lower incidence of complications associated with LADG as with ODG [5, 33, 34]. 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. Even in obese patients, morbidity and length of hospital stay were not increased, although LADG required a longer operating time for obese patients than for non-obese patients [35, 36].

Several studies on the lower invasiveness of LADG relative to ODG demonstrated several advantages of LADG, as follows. Prospective and retrospective analyses by a single institution showed earlier recovery of bowel function after LADG than after ODG [6, 37]. Also, in several studies, pain was reported to be significantly less after LADG than after ODG [6, 7]. LADG offers particular advantages to elderly patients with EGC, including rapid return of gastrointestinal function, fewer complications, and a shorter hospital stay [38]. Other short-term advantages of LADG were demonstrated by a randomized trial with a small sample at a single institution, which revealed better postoperative pulmonary function after LADG than ODG because there was less pain after the former [39].

Regarding the cost, a case-controlled study reported that LADG is less expensive than conventional open gastrectomy because the hospital stay is shorter [40, 41].

Evaluation of Long-Term Results of LADG

Although most retrospective published studies were composed of a small number of patients and showed short-term follow-up [39, 42–46], there have been few studies about the long-term outcome of LADG [47]. Indeed there is only one prospective randomized trial (RCT) about the long-term outcome of LADG. Huscher et al. [48] reported 5-year postoperative results by RCT with a small series comparing LADG with ODG for gastric cancer. Those authors found no significant difference in operative morbidity or mortality, 5-year overall, or disease-free survival between the two groups. In the near future, a multicenter randomized controlled trial is needed to confirm the long-term advantages of LADG for gastric cancer.

Other Laparoscopic Gastrectomies for EGC

Laparoscopic distal, proximal, and total gastrectomies are performed according to the location of the tumor, as with open surgery. Laparoscopic proximal and total gastrectomies are indicated for EGC located at the upper stomach [49–53]. In both of these procedures, how to make reconstruction laparoscopically is a problem. Furthermore, to preserve the function of the gastric remnant after gastrectomy, a laparoscopic pylorus-preserving gastrectomy without injuring vagal nerves such as the pyloric or hepatic branch was tried [54].

Advanced Gastric Cancer

D2 lymph node dissection in which the lymph nodes in the first (perigastric) and second (along the celiac artery and its branches) tiers are dissected is widely accepted in Japan for the treatment of advanced gastric cancer. A study of Japanese experience found that 30–40% of patients with metastasis in even second-tier lymph nodes who underwent D2 lymph node dissection have survived more than 5 years [55]. However, surgeons in the USA and other Western countries rarely perform extensive prophylactic lymphadenectomy, because two European randomized trials (RCT) showed no survival advantage of D2 over D1. Since these trials also compared D1 and D2 and showed high operative mortality in the latter – exceeding 10% – the British NHS Cancer Guidance officially discourages the use of D2 in clinical practice [56, 57].

According to the JSES survey, D1+α lymph node dissection was performed in 67% and D2 lymph node dissection in 23% of LADGs for gastric cancer in Japan. Several investigators reported low mortality and morbidity in laparoscopic D2 lymph node dissection [58–60]. More recently, RCT by Huscher et al. [48] demonstrated the feasibility and safety of laparoscopic subtotal gastrectomy with D2 lymph node dissection for advanced gastric cancer. However, laparoscopic D2 lymph node dissection requires a learning curve, as does conventional open surgery. To establish the acceptability of laparoscopic gastrectomy with D2 lymph node dissection against advanced gastric cancers, safe techniques and new instruments must be developed.

Future Aspects

To establish laparoscopic surgery as a standard treatment for gastric cancer, several issues must be resolved. The first is the prevalence of standard techniques, and the development of education and training systems is important. Recently, several training machines and animal training centers for getting better laparoscopic techniques have been developed. In addition, the JSES has started to design a Board Certification Examination for laparoscopic procedures. Thus, with the aim of popularizing laparoscopic surgery, education and training in standard laparoscopic techniques continue to develop.

The second issue is the evaluation of long-term outcome of laparoscopic gastrectomy for gastric cancer. Since laparoscopic gastrectomy for gastric cancer has been shown to be potentially superior in short-term outcome to open surgery, multicenter, large-scale randomized trials are required in order to establish laparoscopic gastrectomy not only for EGC but also for advanced gastric cancer.

Third, the oncological aspects of the influence of CO_2 pneumoperitoneum should be elucidated. So far, the effects of CO_2 pneumoperitoneum on cancer growth and progression, including lymph node metastasis and both hematogenous and peritoneal dissemination, have been reported in animal models [61–63]. CO_2 pneumoperitoneum in laparoscopic surgery has been reported to be inferior to laparotomy in open surgery regarding the activation of the spread of cancers except liver metastasis [64]. To better evaluate the oncological aspects of laparoscopic surgery, further examination of the effects of CO_2 pneumoperitoneum on cancer progression are needed.

Thus, laparoscopic surgeons have to design and implement education and training systems for standard laparoscopic procedures, evaluate clinical outcomes by multicentric RCT studies, and clarify the oncological aspects in basic studies. Laparoscopic surgeons expect that laparoscopic gastrectomy with minimal invasiveness will become a worldwide standard procedure for the treatment of gastric cancer.

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された治療としての下大腸癌手術

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KEY WORDS

はじめに

1991年，Jacobsら[1]が世界ではじめて腹腔鏡下大腸切除術を報告して以来，腹腔鏡下手術は従来の開腹手術と比べ低侵襲で整容性に優れており，低侵襲治療としての位置づけを確立しながら，この10年余りで急速に普及してきた[2]。一方，早期癌から進行癌へその適応拡大がすすむにつれ，port site recurrenceなどの癌に対する腹腔鏡下手術の影響が懸念されるようになり，1990年半ばより各国で開腹手術と腹腔鏡下手術のランダム化比較試験(RCT)が開始され始めた。本稿では，大腸癌に対する開腹手術と腹腔鏡下手術との国内外で施行されているRCTに基づいたエビデンスを示すとともに，標準治療としての腹腔鏡下手術の現時点での位置づけと今後の展望について概説する。

Ⅰ．大腸癌に対する腹腔鏡下手術の現況

1．日本内視鏡外科学会アンケート調査結果

わが国における大腸癌に対する腹腔鏡下手術の現況は，日本内視鏡外科学会の2年に1度行っている全国アンケート調査結果[3]に基づくと，2003年までに施行された腹腔鏡下手術の症例数は年々増加しており，総手術症例数は17,200例を超え，2003年の1年間では4,000例に及び，そのなかで進行癌の比率は55％を占めるに至っている(図1)。わが国のこのような普及の背景には，2002年の腹腔鏡下手術の保険適応拡大が主な要因の1つと考えられる。

2．厚生労働省多施設共同班研究報告

わが国の大腸癌に対する腹腔鏡下手術の治療成績について，平成13～16年度厚生労働省がん研究助成金「がんに

おける体腔鏡手術の適応拡大に関する研究(北野班)」における多施設共同研究(retrospective multicenter study)のなかで報告されている[4][5]。この班研究は，わが国の腹腔鏡下手術の先進的な17施設が参加し，1993年から2002年8月までの大腸癌に対する腹腔鏡下手術施行2,036症例を集計し，安全性と根治性を解析している。これによると登録症例の癌進行度の割合は，stage Ⅰ；53%，stage Ⅱ；16%，stage Ⅲ；26%，stage Ⅳ；5%である。開腹移行(conversion)は，結腸癌の4.8%，直腸癌の4.4%，開腹移行理由は，適応を超えた癌の過進展が約半数，術中の出血や他臓器損傷が約3割という内訳である。結腸癌の治療成績では，術中合併症は1.4%，術後合併症は12.6%の頻度，根治手術1,367例中61例(4.5%)に再発を認め，その形式は，肝が2.4%と最も多く，腹膜が0.4%，肺が0.4%，リンパ節が0.3%，局所が0.2%という内訳である。5年生存率は，stage Ⅰ，Ⅱ，Ⅲの順に，95%，86%，74%を示している(図2-1)。直腸癌では，術中合併症が3.6%，術後合併症は14.1%の頻度で，根治手術476例中30例(6.3%)に再発を認め，その形式は，肝が2.7%と最も多く，肺0.6%，腹膜1.1%，局所0.8%，リンパ節0.7%という内訳であった。5年生存率は，stage Ⅰ，Ⅱ，Ⅲの順に，95%，85%，80%を示している(図2-2)。このRetrospective multicenter studyの報告から，わが国の結腸癌および直腸癌の治療成績は，合併症・再発率・再発形式・5年生存率のいずれも従来の開腹手術と比較してほぼ同等と考えられる。

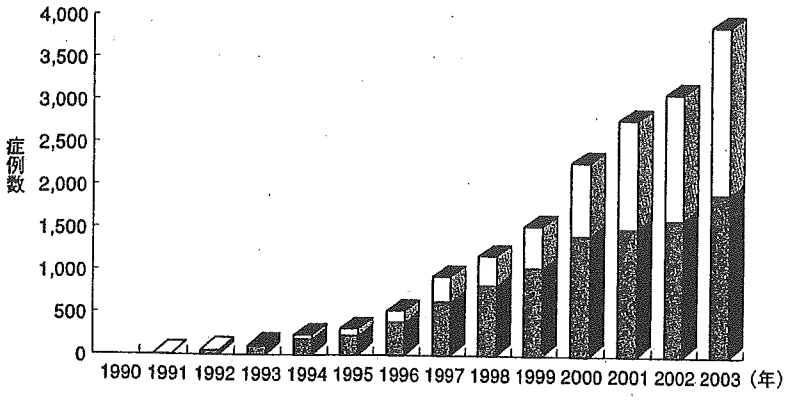

図1．大腸癌に対する腹腔鏡下手術の動向
(第7回日本内視鏡外科学会全国アンケート調査)
▩：早期大腸癌，□：進行大腸癌

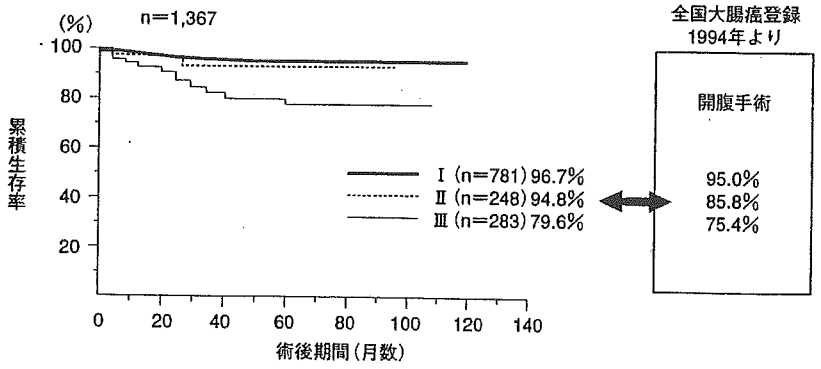

図2-1．結腸癌に対する腹腔鏡下手術の遠隔成績(TNM staging別)
追跡調査期間：3～125ヵ月(中央値32ヵ月)　(文献[5]引用改変)

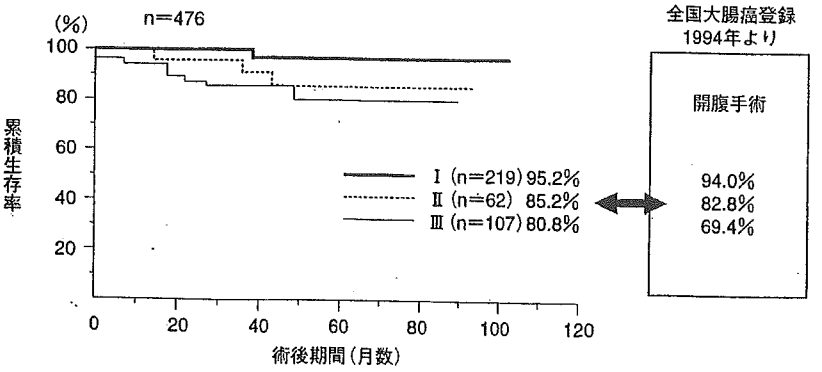

図2-2：直腸癌に対する腹腔鏡下手術の遠隔成績(TNM staging別)
追跡調査期間：3～120ヵ月(中央値28ヵ月)
(文献[5]引用改変)

Ⅱ．大腸癌に対する腹腔鏡下手術のエビデンス

1990年代半ばより海外ですすめられている大腸癌に対する腹腔鏡下手術と開腹手術のRCTを表1に示す。また現在まで長期成績が報告された3つのTrialの概要と結果を表2，3にまとめた。2002年のスペインのLacyらの報告[6]では，腹腔鏡下手術は再発率，癌死率，全死亡率において独立した危険減少因子であり(p＝0.04，0.02，0.006)，その差はstage Ⅲの開腹手術の治療成績不良によるものと考察されている。2004年の米国[7]，香港[8]からの報告では，腹腔鏡下手術と開腹手術との間にどのstageにおいても再発率，全生存率に差は認めず同等との結果であった。しかし，これらのRCTは症例数が少なかったり，術後補助療法の規定がなかったり，あるいは開腹移行率や合併症発生率が高いなど，わが国の医療にそのまま受け入れることは妥当ではないと考えられる。

表1．現在進行中の海外RCT(大腸癌に対する開腹手術vs腹腔鏡下手術)

国名	治験名	開始	Target accrual	
スペイン	— (Lacy AM)	1993	250	完了
香港	— (Leung)	1993	1000	完了
米国	COST (Nelson H)	1994	1200	完了
ドイツ	LAPKON (Bohm B)	1995	1200	
イギリス	CLASSIC (Guillou PJ)	1996	1000	
ヨーロッパ	COLOR (Hazebroek EJ)	1997	1200	
ニュージーランド	— (Bagshaw)	1998	1260	

表2．長期成績が報告された海外RCTの試験概要
(大腸癌に対する開腹手術vs腹腔鏡下手術)

著者	雑誌	症例	第一次エンドポイント	第二次エンドポイント
Lacy (スペイン)	Lancet (2002)	OC 101 LAC 105	癌関連生存率	全生存率 無再発生存率
Leung (香港)	Lancet (2004)	OC 200 LAC 203	全生存率 無再発生存率	—
COST (米国)	N Engl J Med (2004)	OC 428 LAC 435	再発までの期間	無再発生存率 全生存率 合併症 クオリティ・オブ・ライフ
JCOG (日本)		OC 409 LAC 409	全生存率	無再発生存率 合併症 術後早期経過 腹腔鏡下手術完遂率

OC：開腹手術，LAC：腹腔鏡下手術

Ⅲ．わが国におけるエビデンスの確立

前述の背景を受けてわが国でも，厚生労働省科学研究費補助金に基づき，Japan Clinical Oncology Group (JCOG)の臨床研究として，2004年10月より「進行大腸がんに対する腹腔鏡下手術と開腹手術との根治性に関するランダム化比較試験(JCOG 0404)」(研究代表者：北野正剛)[9]が開始されている。予定登録症例数は818例，登録期間は3年，追跡期間5年の非劣性試験である。腫瘍深達度はT3・T4(他臓器浸潤を除く)，主占拠部位は盲腸・上行結腸・

表3．長期成績が報告された海外RCTの試験結果(大腸癌に対する開腹手術vs腹腔鏡下手術)

著者	開腹移行率	合併症率	周術期死亡率	全生存率	無再発生存率
Lacy (スペイン)	11%	p＝0.001 (29% vs 11%)	p＝0.19 (2.9% vs 0.9%)	HR 0.39 95% CI 0.19～0.82	p＝0.006 (Stage Ⅲ症例)
Leung (香港)	23%	NS (24% vs 26%)	p＝0.97 (0.6% vs 2.4%)	p＝0.61 (73% vs 76%)	p＝0.45 (78% vs 75%)
COST (米国)	21%	p＝0.64 (20% vs 21%)	p＝0.40 (1.0% vs 0.5%)	p＝0.51 (85% vs 86%)	NS

S状結腸・直腸S状部の病変を対象とし，ランダム化割付因子は登録施設と腫瘍占拠部位(右側/左側)の2因子である。このRCTは海外で報告されたRCTの問題点をovercomeすべく以下のような特徴を有している。すなわち，①対象は早期癌を除外し進行癌に限定，②リンパ節郭清をD3と規定，③補助化学療法はstageⅢに対して5Fu/Lv静注療法と規定，④試験への参加施設および手術を施行する手術担当責任医の基準を設定，⑤全施行症例の手術写真を中央判定委員会にて審査，など臨床試験の高い質の確保を目指している。2005年11月現在，RCT開始後間もなく1年を迎えようとしているが，登録総数約200例の進捗状況である。

Ⅳ．大腸癌に対する腹腔鏡下手術の位置づけ

本稿で示したわが国の多施設共同班研究と海外のRCT結果に基づくエビデンスから，現時点における腹腔鏡下手術の位置づけを結腸癌と直腸癌に分けて図3に示した。結腸癌に対しては，深達度T2までは腹腔鏡下手術が受け入れられており，T3/T4に関しては根治性に関する長期成績が十分に明らかにされていないため，わが国の大規模RCTの結果が期待されるところである。一方，直腸癌においては，現時点ではT1あるいはT2までが受け入れられつつあるが直腸の切離・吻合手技の安全性や側方郭清を踏まえた適応の問題点があり，現在，腹腔鏡下大腸切除研究会(代表：渡邊昌彦教授)が中心となり直腸癌に対するphase Ⅱ study，いわゆるFeasible studyが開始されるところである。

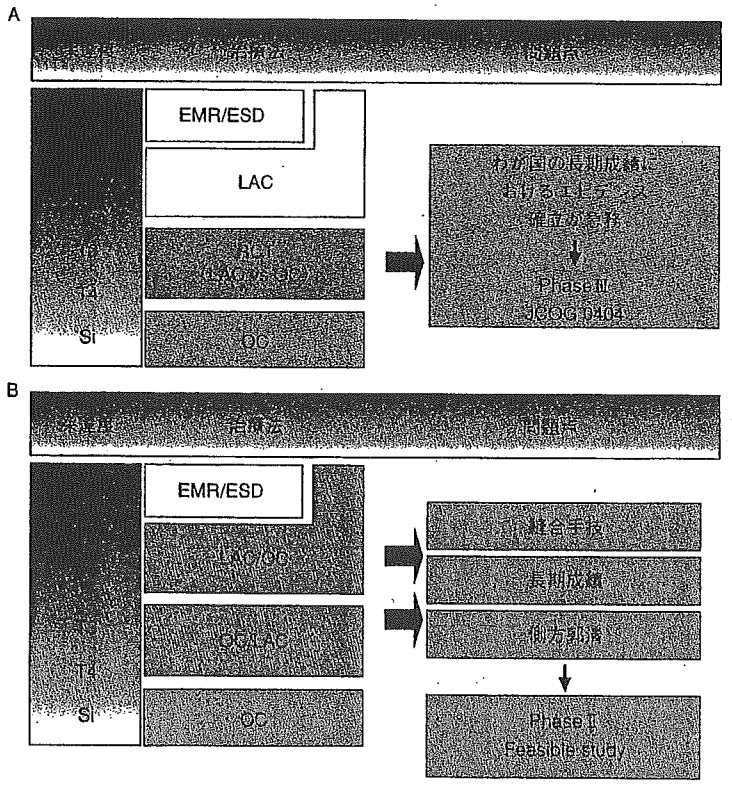

図3．外科治療における腹腔鏡下手術の位置づけ
A：結腸癌，B：直腸癌

Ⅴ．標準化への取り組み

わが国の大腸癌に対する腹腔鏡下手術の標準化への取り組みとして，前述のRCTによるEBMの確立とともに技術面における標準化への努力も行われている。

1．腹腔鏡下大腸切除研究会の取り組み

1998年に発足した本会(設立者／代表：小西文雄教授)は，標準術式の確立，講習会の開催やトレーニング法の検討，データ集積による治療成績の分析など，大腸癌研究会のプロジェクト研究としてすすめられてきた[10]。

2．内視鏡外科学会技術認定制度の発足

昨年度より，日本内視鏡外科学会において，安全な手術手技の普及を目的に，指導的立場にある内視鏡外科医を認定する制度が発足した。提出された無修正ビデオの手術手技に対して，共通項目と臓器別項目に分けて各領域ごとに厳正に審査が行われている[11]。本制度の推進により，腹腔鏡下手術の普及と手術手技の標準化がさらにすすむものと考えられる。

おわりに

大腸癌に対する外科治療は，大きく変貌しようとしている。これは「患者にやさしい低侵襲治療」を望む社会のニーズとそれを実践させうる腹腔鏡下手術の登場に帰するところが大きい。

現時点で腹腔鏡下手術は早期結腸癌において標準治療として受け入れられているが，進行結腸癌や直腸癌では，エビデンスの確立や安定した手技の点からまだ十分とはいえない状況である。今後は，わが国のRCTによるEBMの確立，講習会やアニマルラボによるトレーニングシステムの整備，学会レベルでの技術認定制度の取り組みが必要であり，さらに安全性，長期成績に加え医療経済も考慮した総合的な評価が腹腔鏡下手術の標準化に必要であろう。

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Long-term Prognostic Value of Conventional Peritoneal Cytology after Curative Resection for Colorectal Carcinoma

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Background: This study was undertaken to evaluate the long-term prognostic significance of conventional peritoneal cytology in patients with advanced colorectal carcinoma after curative resection.

Methods: A review was performed of 189 patients who underwent curative resection for pT3/T4 carcinoma of the colon and upper/middle rectum between March 1987 and December 1991. Patient outcomes were reviewed retrospectively. Peritoneal cytology was performed before manipulation of the tumor. Intraoperatively, 50 ml of saline were instilled and 20 ml were reaspirated for cytology. In all patients, Papanicolaou and Giemsa stainings were performed to detect intraperitoneal free tumor cells.

Results: The median follow-up was 103 months. Malignant cells were identified in peritoneal washings from 11 patients (5.8%). Of the 11 patients with positive cytology, six (54.5%) developed recurrence and peritoneal recurrence was observed in four (36.4%). In contrast, of the 178 patients with negative cytology, 46 (25.8%) developed recurrence and peritoneal recurrence was observed in four (2.2%). The peritoneal recurrence rate was significantly increased ($P = 0.0004$) in the patients with positive cytology. The cancer-specific 10-year survival rates for the patients with positive and negative cytology were 45.5 and 80.3%, respectively ($P = 0.0051$). Multivariate analysis (Cox proportional hazard model) revealed that peritoneal cytology (positive: $P = 0.0256$) and lymph node metastasis (pN2: $P = 0.0004$) were independent predictors of cancer-specific survival.

Conclusion: Conventional peritoneal cytology serves as a new prognostic marker after curative resection in patients with advanced colorectal carcinoma. It appears to be a useful diagnostic procedure for predicting recurrence, especially peritoneal recurrence.

Key words: peritoneal dissemination – peritoneal cytology – colorectal carcinoma

INTRODUCTION

Complete removal of the tumor is the most effective primary treatment for carcinoma of the colon and rectum. However, recurrences after curative resection of an apparently localized tumor are inevitable and it is widely accepted that the liver, lung, pelvis and peritoneum are the most common sites of recurrence and metastasis (1). Despite recent advances in the knowledge of various clinical, biological and pathological features that relate to the prognosis of colorectal carcinoma, the degree of tumor penetration into the bowel wall and lymph node involvement have been regarded as the main prognostic factors for patients with colorectal cancer, and these factors are used for prognostic classification in Dukes staging and TNM classification (2,3).

It has been reported that peritoneal cytology can be considered useful for predicting the prognosis of gastric, pancreatic and gynecological malignancies (4–6). Recently, several studies analyzed, in patients with colorectal carcinoma, the incidence of free malignant cells in the peritoneal cavity at the time of surgery and its prognostic significance by means of conventional cytology and immunocytology (7–11).

The aim of this study was to analyze the incidence and the long-term prognostic value of conventional peritoneal lavage cytology after curative resection for colorectal carcinoma at the median follow-up of 103 months.

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Table 1. Characteristics of the patients with colorectal carcinoma according to peritoneal cytology

Variable	Cytology positive ($n = 11$)	Cytology negative ($n = 178$)	*P* value
Gender			
Male	3	93	0.1292
Female	8	85	
Age (years): mean (range)	62.4 (45–78)	60.5 (23–88)	0.5481
Location			
Colon	7	118	1.0000
Rectum	4	60	
Histology			
Well	7	94	0.5478
Others	4	84	
pTNM classification			
pT3	6	99	1.0000
pT4	5	79	
pN0	2	90	0.0588
pN1+pN2	9	88	
Recurrence			
Positive	6	46	0.0739
Negative	5	132	

PATIENTS AND METHODS

PATIENTS

Between March 1987 and December 1991, intraoperative peritoneal lavage cytology was performed in 189 patients who underwent curative resection for pT3/T4 carcinoma of the colon and upper/middle rectum. Only patients with no clinically evident metastatic disease or peritoneal disseminations undergoing planned surgery for curative intent were investigated. Preoperative chemotherapy or radiation therapy was not performed in this series. Follow-up data were obtained for a median observation time of 103 months (range: 2–176 months).

SAMPLES

Immediately after a midline abdominal incision had been made and before manipulation of the tumor, peritoneal lavage cytology was performed. Intraoperatively, 50 ml of saline were instilled into the abdominal cavity over the tumor site and 20 ml were reaspirated for cytology. The lavage solution was immediately centrifuged (1500 r.p.m. for 10 min) and cytological examination was performed after Papanicolaou and Giemsa stainings. The slides were examined by light microscopy by experienced cytologists unaware of the clinical findings. Patients with suspicious morphological evidence of malignancy by microscopy were included in the positive cytology group.

Table 2. Peritoneal cytology and type of recurrence

Type of recurrence	Cytology positive ($n = 11$)	Cytology negative ($n = 178$)	*P* value
Peritoneum	4	4	0.0004
Liver	4	28	0.0939
Lung	1	24	1.0000
Others	4	20	0.0361

PERITONEAL RECURRENCE

Peritoneal recurrence was defined as radiological or histocytological evidence of cancer recurrence in the abdominal cavity. Liver metastasis, intra-abdominal lymph node metastasis and local recurrence, defined as radiological or histocytological evidence of cancer recurrence at or in the region of primary tumor bed, were excluded.

STATISTICAL ANALYSES

The clinicopathological parameters such as gender, age, location of tumor, histology, pTNM classification and recurrence between the group with positive and negative cytology were compared using Student's *t* test and the Fisher's exact test as appropriate. Cancer-specific survival curves and disease-free survival curves were estimated using the Kaplan–Meier technique and were compared by means of the log-rank test. For cancer-specific survival, only cancer-related deaths were considered; data on the patients who had died from other causes or who were still alive at the end of the study were censored. To identify independent prognostic factors for survival, statistical analyses were performed using univariate and multivariate analysis. In the univariate analysis, cumulative survival rates were calculated using the Kaplan–Meier method and the differences in the survival curves were compared using the log-rank test. In the multivariate analysis, a Cox proportional hazards model was used to assess the impact of various factors on survival. A *P* value of <0.05 was considered significant.

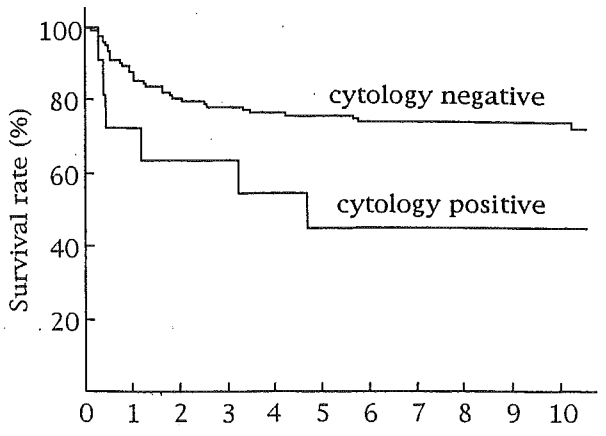
RESULTS

PATIENTS' CHARACTERISTICS

The patients' demographics are summarized in Table 1. No significant differences were observed regarding the clinicopathological parameters between the groups with positive and negative cytology.

PROGNOSIS AND TYPE OF RECURRENCE

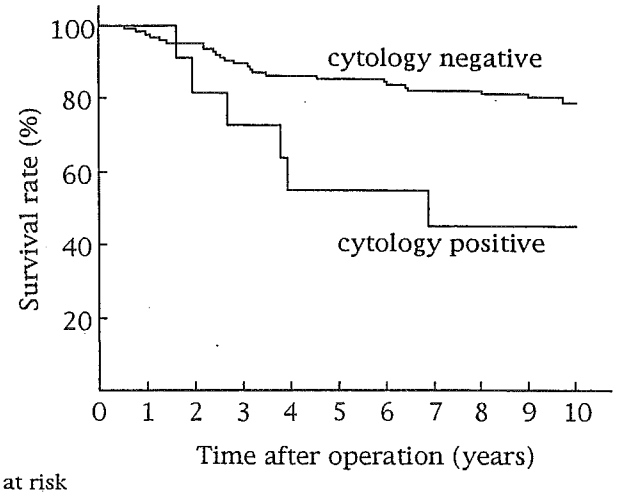
Disease-free survival rates at 5 and 10 years were both 45.5% for the positive cytology group and 75.6 and 74.3% for the negative cytology group, respectively (Fig. 1). The difference between the two groups was significant ($P = 0.0216$). Cancer-specific survival rates at 5 and 10 years were 54.5 and 45.5%



No. at risk

Negative	178	155	142	137	130	127	109	96	87	72	52
Positive	11	8	7	7	6	5	4	1	1	1	1

Figure 1. Cumulative disease-free survival curves of patients with negative and positive cytology. The difference between the two groups was significant ($P = 0.0216$).



No. at risk

Negative	178	174	168	158	147	145	127	110	97	83	63
Positive	11	11	10	8	7	6	6	6	5	5	4

Figure 2. Cancer-specific survival curves of patients with negative and positive cytology. The difference between the two groups was significant ($P = 0.0051$).

Table 3. Colorectal carcinoma: univariate analysis of prognostic factors

Variable	No. of patients ($n = 189$)	Disease-free 10-year survival (%)	*P* value	Cancer-specific 10-year survival (%)	*P* value
Gender					
Male	96	69.5	0.4829	77.1	0.9517
Female	93	75.9		79.4	
Age (years)					
≤60	93	71.9	0.9893	79.7	0.6514
>60	96	73.4		78.4	
Location					
Colon	125	74.8	0.4237	78.3	0.6965
Rectum	64	68.2		77.5	
Histology					
Well	101	69.6	0.4778	75.2	0.7039
Others	88	76.0		81.2	
pTNM classification					
pT3	105	75.7	0.4258	78.6	0.5794
pT4 (invasion negative)	76	64.1		76.3	
pT4 (invasion positive)	8	75		87.5	
pN0	92	82.3	0.0010	87.4	<0.0001
pN1	69	69.2		77.0	
pN2	28	49.7		53.1	
Peritoneal cytology					
Positive	11	45.5	0.0216	45.5	0.0051
Negative	178	74.3		80.3	

for the positive cytology group and 85.8 and 80.3% for the negative cytology group, respectively (Fig. 2). The difference between the two groups was again significant ($P = 0.0051$).

Recurrences occurred in six of 11 (54.5%) patients with positive cytology and in 46 of 179 (25.7%) patients with negative cytology (Table 1). The rate of peritoneal recurrence was significantly elevated in patients with positive cytology and the details of peritoneal cytology and type of recurrence are summarized in Table 2.