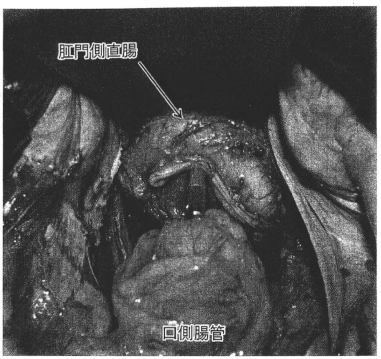

図 11　Double stapling technique（DST）

かけて肛門挙筋が明らかになる．最後に背側正中で anococcygeal raphe から続く hiatal ligament を切離すると，前壁以外の直腸が肛門挙筋に取り囲まれていることがわかり，十分に腹側に授動できるようになる．

11 直腸切離

腸管切離は，①操作部位への適度な緊張をかけるため，②術野の汚染を必要最低限とするため，③吻合部に緊張がかからない吻合を行うための適切な腸管長を確認するために，すべての剝離・授動操作が終了した後に行っている．最初に直腸切離を行う．前述したように，RS 癌・Ra 癌では 3 cm 以上，Rb 癌では 2 cm 以上の直腸間膜内肛門側進展は稀であり[3]，RS 癌・Ra 癌では腫瘍下縁から 3 cm，Rb 癌では 2 cm の部位を切離線とする．前壁では，Denonvillier 筋膜を電気メスで切離し，つぎに直腸間膜の脂肪織をクーパー剪刃とケリー鉗子を用いて丁寧に直腸壁との間を剝離し，結紮・切離を繰り返し切離線の部分で行い，直腸間膜を全周にわたって切離し，直腸壁を露出させる．

腫瘍下縁で直腸直角鉗子をかけて，肛門より生理食塩水とイソジン®加生理食塩水で直腸洗浄を行う．この目的は，腸管内糞便の除去と吻合部再発予防のための遊離癌細胞の除去である．リニア・ステイプラーを使用して直角鉗子の肛門側の直腸切離線で直腸を閉鎖し，メスで直腸を切離する．

12 S 状結腸の切離

切除直腸を術野外に誘導し，S 状結腸の切離を行う．吻合を DST で行うため，結腸切離線の口側に巾着縫合をおき，結腸切離を行う．

吻合前に，必ず次の 2 点を確認しておく．

①術野全体の止血の確認．精嚢周囲や仙骨前面の止血を確認し，また郭清した IMA 周囲の止血も確認しておく．

②摘出標本剝離面での癌の露出の有無，直腸周囲リンパ節転移状況，そして腸管内腔を切開し，癌の位置，性状を確認する．肉眼的深達度や肛門側断端までの距離が適切であるかを判定する．

13 吻合（図 11）

口側結腸にアンヴィルヘッドを挿入し，巾着縫合糸を結紮して結腸を閉鎖し，アンヴィルヘッドを装着する．会陰側より肛門括約筋を用手的に十分拡張させ（約 3 指分），肛門側からサーキュラー・ステイプラー本体を挿入する．この際肛門皮膚を巻き込まないように注意が必要である．直腸切離端のステイプラー・ライン中央後壁に rod を誘導する．低位での吻合の場合，直腸前壁側は男性では前立腺，女性では膣があるため，十分な剝離が困難な場合があり，可動性の自由度が少ない．一方，後壁側は直腸肛門輪まで剝離されているため，自由度が高く，rod はやや後壁に出したほうがよい．

口側結腸に装着したアンヴィルヘッドと接合し，周囲組織を挟み込まないよう注意しながら

結合させ，吻合する．打ち抜かれた腸管組織が口側，肛門側ともに完全な ring になっていることを確認する．また，肛門側の ring はリニア・ステイプラー・ラインを含んでいることも確認する．基本的に dog ear の補強は行っていない．

最後に骨盤腔に少量の生理食塩水を満たし，肛門側より太い尿道カテーテルを挿入し，空気を送り込み，吻合部の air leak test を行う．ドレーンは左側腹壁から腹膜下を誘導して，仙骨前面，吻合部後面に留置する．

14 側方郭清

側方郭清に関しては，別項に詳細が書かれているので割愛する．

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特集　直腸(Rb)癌の謎

II [各　論]
(4) 直腸進行癌の特性
——とくに直腸 Rb の進行癌

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要　旨　直腸癌は結腸癌に比べて再発率が高いことが知られている．とくに，肺，局所，吻合における再発頻度が結腸癌より直腸癌において多いのが特徴である．また，下部直腸癌では直腸間膜内のリンパ節のみならず，腸骨血管系に沿った側方リンパ節に転移する症例が存在することが特徴である．下部進行直腸癌に対する標準的治療法として本邦では total mesorectal excision(TME)もしくは tumor specific mesorectal excision(TSME)にて側方郭清を追加する施設が多いが，欧米では術前放射線化学療法後に TME を施行する．また，治療法の選択に際しては，患者の術後の QOL を十分考慮する必要がある．

Key words：下部直腸癌，側方リンパ節転移，側方郭清

はじめに

直腸癌は結腸癌に比べて，再発率が高いことが知られている[1]．それは，直腸癌，とりわけ下部直腸癌の解剖学的特性により，局所再発が多いことに関係している．また，治療の面では，直腸癌の手術は結腸癌の手術に比べて難易度が高く，手技に習熟することが必要である．本稿では，下部直腸癌の特徴および治療法について詳述する．

I 直腸癌の特徴

1．再発頻度

大腸癌研究会の多施設共同研究における結腸癌ならびに直腸癌の再発頻度を**表**に示した．この研究では，参加 14 施設において大腸癌治癒切除術が施行された 5,230 例を対象にその再発の特徴を明らかにしている(観察期間の中央値は 6.6 年)[1]．結腸癌および直腸癌での再発率はそれぞれ 14.1 %，24.3 %(P<0.0001)であった．また，TNM 分類の各病期においても，結腸癌より直腸癌の再発率のほうが有意に高いことが明らかと

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1883-2342/10/JCOPY

表　ステージ別・臓器別の結腸癌・直腸癌の再発率

	再発頻度(%)		P値
	結腸癌 (N=3,583)	直腸癌 (N=1,647)	
TNM stage			
Stage I	2.7	5.7	0.0056
Stage II	12.1	16.7	0.0091
Stage III	24.3	43.2	<0.0001
初発再発臓器			
肝臓	7.0	7.3	有意差なし
肺	3.5	7.5	<0.0001
局所	1.8	8.8	<0.0001
吻合部	0.3	4.2	0.0052
その他	3.6	4.2	有意差なし

なった(表).

2. 再発部位

前述の多施設共同研究において，再発部位についても検討された．治癒切除術が施行された結腸癌の初発再発部位としては肝臓がもっとも多く，以下，肺，局所と続いていた．一方，直腸癌の初発再発部位としてもっとも多かったのは局所であり，続いて肺，肝臓，吻合部の順であった．なお，この研究において直腸S状部癌は結腸癌に含まれている．そして表に示したように，大腸癌治癒切除術施行後の再発部位として肺，局所，吻合部は有意に直腸癌の術後に多く認められることがわかった．

3. 側方リンパ節転移

直腸癌，とくに腹膜翻転部より肛門側に腫瘍がある下部直腸癌では，結腸癌や上部直腸癌で認められる中枢側の腸間膜リンパ節への転移のみならず，腸骨血管系に沿うリンパ節，すなわち側方リンパ節への転移を認めることが最大の特徴である．Sugiharaらの報告によると，側方郭清を施行した直腸癌患者のうち，13.9％に側方リンパ節転移を認めた[2]．また，下部直腸癌のうち腫瘍の壁深達度がA以深の場合，18.1％に側方リンパ節転移を認め，直腸間膜内リンパ節転移を認めた症例では，23.5％に側方リンパ節転移を認めたとある．さまざまな臨床病理学的因子のうち，性別(女性)，腫瘍の局在(下部直腸)，腫瘍の壁深達度(SS，A以深)が側方リンパ節転移の独立した危険因子であった．

以上のことより，大腸癌治療ガイドラインにおいては，壁深達度A以深の下部直腸癌に対して側方郭清を施行することが推奨されている[3]．ただし，側方リンパ節転移のうち，90％以上は内腸骨リンパ節(263P，263D)もしくは閉鎖リンパ節(283)に存在する[4]．

II 下部直腸進行癌の治療法

Milesが1908年に直腸癌に対する系統的切除術として腹会陰式直腸切断術を発表し，すでに100年以上が経過したが，現在でも腹会陰式直腸切断術は下部直腸癌の標準的手術の一つである[5]．その後，肛門を温存するために種々の術式が考案されたが，1980年にKnightとGriffenによって器械を用いたdouble stapling techniqueが紹介され[6]，その後の括約筋温存手術が広く普及するようになった．しかしながら，直腸癌術後の局所再発率が高いことが問題であったため，1982年英国のHealdらによって，total mesorectal excision (TME)という概念が提唱された[7]．これは，直腸および直腸間膜を直腸固有筋膜に包まれた状態で切除し，なおかつ直腸間膜は肛門挙筋に至るまで全切除するというものである．このTMEの導入によって直腸癌術後の局所再発率は低下し，患者の予後の改善に寄与した[8]．さらに欧米では直腸癌術後の局所再発を制御する目的で，周術期の放射線療法が導入された．これにより直腸癌術後の局所再発率は低下したものの，術前放射線療法による予後改善効果は一つの臨床試験でしか明らかにされておらず[9]，他の臨床試験では予後改善効果は認められなかった[10]．

大腸癌治療ガイドラインでは，直腸癌における

直腸間膜肛門側の切離長は2 cmを目安とすることが記載されている．すなわち，distal marginを2 cm確保した上で肛門括約筋を温存できれば吻合可能であるが，それ以外の場合には腹会陰式直腸切断術が避けられないことになる．distal marginを2 cm確保できれば，TMEを施行せずtumor specific mesorectal excision(TSME)で十分ということにもなる．一方，より低位の直腸癌に対しても内肛門括約筋切除術(intersphincteric resection；ISR)を施行することで，永久的人工肛門造設を回避できる症例が近年報告されている[11)~14)]．この術式では，内肛門括約筋は切除するが，外肛門括約筋を温存することによって肛門機能の温存をはかる術式である．ただし，症例は慎重に選択する必要があり，当科では高齢者などで術前より肛門機能が低下している場合には適応から除外している．

欧米における下部進行直腸癌に対する標準的治療法がTME＋術前放射線化学療法であるのに対して，本邦の手術療法は独自の進歩をとげてきた．本邦では，直腸癌に対する系統的かつ十分なリンパ節郭清のため，1970年代後半より側方郭清を伴う拡大郭清が導入され，広く行われるようになった[15)]．一方で，拡大リンパ節郭清により骨盤内自律神経系が切除され，性機能障害や排尿障害が高率に併発し，患者のquality of life(QOL)を著しく損なう結果となった．そこで自律神経系を温存する術式が考案された．土屋らは，一定の条件下で骨盤内自律神経温存術を行い，局所再発率や5年生存率に差がない一方，性機能障害や排尿障害が減少すると報告した[16)]．現在，下部進行直腸癌に対して予防的側方郭清を行う場合には，当科では基本的に自律神経を全温存している．

また，これまで述べた手術手技は従来は開腹手術ですべて行われていたが，現在では腹腔鏡補助下に行う施設も増えている．

おわりに

下部直腸癌を中心に，その特徴と治療法について概説した．下部直腸癌はその解剖学的特性より，oncologic outcomeのみではなく，術後の患者のQOLまで考慮して治療法を決定する必要がある．

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Summary

Characteristics of lower rectal cancer

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Recurrence rates after curative resection for rectal cancer are higher than those for colon cancer. Pulmonary, local, and anastomotic recurrences of rectal cancer are more common than those of colon cancer. Low rectal cancer often exhibits lateral pelvic lymph node metastasis as well as lymph node metastasis in the mesorectum. In Western countries the standard treatment for low rectal cancer is total mesorectal excision (TME) with preoperative chemoradiotherapy. However, TME with pelvic sidewall dissection is the standard treatment in Japan. Treatment for patients with low rectal cancer should be selected in relation to postoperative quality of life.

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Key words : lower rectal cancer, lateral pelvic lymph node metastasis, pelvic sidewall dissection

Legend to Table

Table Recurrence rates between patients with colon cancer and those with rectal cancer according to the TNM stage and the recurrence sites

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ORIGINAL ARTICLE

Comparison of short, long-term surgical outcomes and mid-term health-related quality of life after laparoscopic and open resection for colorectal cancer: a case-matched control study

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Abstract
Background A multicenter randomized study is high quality, but it is also true that there are differences between institutions. The quality of treatment is consistent in a single center so comparisons in a retrospective study can be matched for many variables.
Methods This single-center study examined short-term and long-term outcomes for colorectal cancer in 258 patients who underwent laparoscopic resection (LC) and 258 matched open resection (OC) cases. The health-related qualities of life (HRQOL) at 1–2 years after the operations in 62 patients (35 LC and 27 OC) were compared by SF-36.
Results The conversion rate was 5.0%. Mean follow-up periods in LC and OC were 62.3 and 62.1 months, respectively. Operation time was longer in LC than in OC, although the difference was not significant in the later period. Bleeding and postoperative stay were reduced in LC. The morbidity rate was 18.6% in LC and 26.4% in OC. The 5-year overall survival in LC and OC were 94.6% vs. 92.0% for stage I, 95.2% vs. 91.8% for stage II, and 80.9%

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vs. 79.1% for stage III, respectively. The corresponding 5-year disease-free survival were 94.0% vs. 88.4%, 92.1% vs. 84.0%, and 64.3% vs. 65.4%, respectively. Recurrence rates did not differ between groups. In the analysis of HRQOL scores, role physical, bodily pain, social functioning, role emotional, and physical component summary scores in LC were better than in OC.

Conclusions In LC for colorectal cancer, short-term outcomes except operation time and mid-term HRQOL were better than in OC, and there were no adverse effects relating to long-term outcomes.

Keywords Case-matched study · Colorectal cancer · Laparoscopic resection · Health-related quality of life

Introduction

The use of laparoscopic resection (LC) for colon cancer has been prevalent worldwide since the early 1990s [1] but has become increasingly important in recent years, as studies have shown that its outcomes are better than or equal to those of open abdominal surgery (OC) for colon cancer [2–5]. Some randomized multicenter studies have compared short-term or long-term outcomes of LC and OC for colon cancer. However, the conversion and mortality rates in these studies have been relatively high because of differences in the techniques used at each institution. Although the results appear to be consistent in a large-scale multicenter study, differences have been reported in short-term outcomes depending on the number of cases at registration [6]. There is the potential for meta-analyses to give inconsistent results if the methodological quality is poor, even for randomized controlled trials (RCTs) [7]. Case-control studies are thought to provide weaker evidence than randomized studies, but enable sample characteristics to be better controlled. Several such studies have compared LC and OC for colorectal cancer [8–12]. Most have shown no adverse oncologic outcomes in either the short term or the long term. However, the sample sizes in these studies have been small or limited, and the case-selection criteria have tended to be poorly defined.

Moreover, there are few large-sized randomized studies of mid-term health-related quality of life (HRQOL) in colorectal cancer patients, and the results are controversial [5, 13, 14].

The current study analyzed our experience with LC for colorectal cancer over the past 15 years. Patients undergoing LC were matched to cases undergoing conventional OC in terms of several characteristics, including physical status. We compared the short-term and long-term outcomes for cases undergoing LC and OC for colorectal cancer in a single-center study. The mid-term HRQOL at 1–2 years after the operations was compared and assessed using the SF-36 Health Survey Questionnaire Second Japanese Version [15].

Patients and methods

Data for cases treated in our department were registered prospectively from 1992 and included patient characteristics, surgical outcomes, and long-term outcomes. Between June 1993 and March 2008, a total of 2,521 patients underwent resection for colorectal cancer at Yokohama City University Hospital, Japan. Among these, 570 patients underwent LC, the use of which for early colon cancer was initiated at our institution in June 1993.

Until March 2000, surgical indications for this technique were limited to a preoperative diagnosis of colon cancer with invasion through the muscularis mucosa into the submucosa (T1), no lymph node involvement (N0), and a non-bulky tumor. However, as our experience increased, the indications were gradually extended in April 2000 to include cancer with invasion through the submucosa into the muscularis propria (T2) and no lymph node invasion (N0). In April 2002, indications included cancer with invasion of the surrounding structures or with tumor cells on the free external surface of the bowel (T4) with the involvement of one to three nodes (N1) but excluding adjacent organ infiltration. In April 2005, cancer with the involvement of four or more nodes (N2) was included. Surgical indications for rectal cancer were extended to T2 N0 in 2001 and were expanded to include invasion through the muscularis propria into the subserosa but not to any neighboring organs or tissues (T3) and N1 for upper rectal cancer in 2007. In total, 246 patients underwent LC in the 12-year period up until 2004; the number increased rapidly after 2005, with 324 patients undergoing LC over a period of 3 years and 3 months. In most cases, the decision to use the LC or OC technique was made with the patient's informed consent, after the attending physician had presented the latest evidence concerning LC.

In order to compare outcomes, the LC and OC groups were matched in terms of the following variables: gender, age (within 10 years), American Society of Anesthesiologists (ASA) score (within one point), operative year, tumor location (right side of the colon, transverse colon, left side of the colon, upper rectum, and lower rectum), operative procedure (right-sided colectomy, transverse colectomy, left-sided colectomy, anterior resection of the rectum, abdominoperineal resection, and intersphincteric resection of the rectum), and International Union Against Cancer Tumor–Node–Metastasis (TNM) stage (0, I, IIA, IIB, IIIA, IIIB, IIIC, or IV). The exclusion criteria were as follows: emergency surgery, adjacent organ infiltration, histological

types other than adenocarcinoma, simultaneous multiple cancers, and follow-up of the surviving patient for <1 year. The operation was carried out according to the standard radical cure procedure described in the seventh edition of the *Japanese General Rules for Clinical and Pathological Studies on Cancer of the Colon, Rectum and Anus* [16]. Specifically, all operations were colectomies with dissection of the intestinal lymph nodes and the middle lymph node along the feeding blood vessels. In cancers classified as T2 or above, lymph node dissection around the root of the main feeding vessel was also performed. The same procedures were used for the lymph node dissections in the LC and OC cases. For rectal cancer, pelvic sidewall lymph node dissection was excluded for cases classified as T2 or below. All the operations in both groups were performed by a team from the same colorectal cancer treatment specialty. Operations enforced by the general surgeon and emergency operations were excluded. Three surgeons up to 1999 and four surgeons from 2000 onwards worked as colorectal cancer treatment specialists. There were replacements in personnel, and the surgeon's experience ranged from 3 to 13 years. The operations were performed by eight surgeons in total. All colorectal surgeons performed both the open and the laparoscopic surgery.

The oncologic outcomes of the surgery were compared between the LC and OC groups using the following variables: the proximal margin (millimeters), the distal margin (millimeters), and the number of harvested lymph nodes. The latter variable was compared in each respective cancer location. The distal margin in rectal cancer was also compared. The histopathological workup was described in detail. After excision of the specimen, the surgeon removed the lymph nodes from the mesocolon, and it was submitted to the pathology department. The pathologic diagnosis was made using hematoxylin–eosin staining.

Short-term results were defined as the operative results and the complications that occurred within 30 days after the operation. The following short-term results were recorded for all patients: the operation time (minutes), the operative blood loss (milliliters), the blood transfusion rate (percent), the details and rates of mortality and morbidity within 30 days, and the duration of the postoperative stay (days). Mortality was defined as death that occurred prior to leaving the hospital after the operation. Morbidity was defined by adverse events classified as grade 1 or above according to version 3.0 of the *Common Terminology Criteria for Adverse Events* [17]. These data were compared between the LC and OC groups. The years before 2004 were categorized as the earlier period, and those after 2005 were categorized as the later period. There were many limitations of the indication for LC in 1993–2004. It was expanded to include T4a and N2 in colon cancer after 2005, and the number of cases also increased. The learning curve rose with an increase in the number of cases. The LC and OC groups were compared in each of these periods. The short-term outcomes were also analyzed according to tumor location.

Long-term was defined as the period of more than 5 years after the operation. The long-term outcomes were evaluated according to the 5-year overall survival and the 5-year disease-free survival in the respective TNM stages, and the initial cancer recurrence rate in patients with curative resection (R0) except for stage IV. Curative resection (R0) was defined as having no vestigial remnant of cancer in histology [16]. The initial recurrence pattern was defined as local recurrence, peritoneal recurrence, or distant organ metastases (such as liver, lungs, and bones). Port-site recurrence was also included. The survival rates were calculated from the time of resection of the primary lesion to the date when either death or recurrence occurred. Survival was also compared according to the tumor location.

The postoperative follow-up methods were as follows: patients at stages 0 and I were followed-up with outpatient examinations and tumor-marker measurements once a year for 5 years; if an abnormality was detected, computed tomography (CT) and/or colonofiberscopy were performed. Patients at stage II were examined by CT and tumor-marker measurements every 6 months for 2 years, then once a year for the next 5 years. Patients at stage III were examined by CT and tumor-marker measurements every 4 months for 3 years, and then once a year for the next 5 years.

Postoperative adjuvant chemotherapy was administered to patients at stage III and high-risk stage II who were 75 years old or less, except in cases where this approach was rejected by the patient. The cases who received adjuvant chemotherapy before 1999 were excluded from the analysis because the adjuvant chemotherapies were not uniform. Beginning in 2000, intravenous 5-fluorouracil/leucovorin therapy was performed for stage III colonic cancer. Each course of treatment was 500 mg/m^2 5-Flourourcil and 75 mg/kg body weight 5-fluorouracil/leucovorin weekly for 6 weeks, followed by 2 weeks rest. Three courses of treatment were performed. In stage II colonic cancer, oral uracil-tegafur (UFT) was administered for 5 days per week at 500–600 mg/day. UFT therapy was performed for 52 weeks. No radiation therapy was administered. Neoadjuvant chemoradiotherapy was not performed on all rectal cancers, as neoadjuvant chemoradiotherapy for rectal cancer is not a standard treatment in Japan.

Mid-term was defined as the period between 12 and 24 months after the operation. HRQOL at 12–24 months after the operation was assessed using the SF-36 Health Survey Questionnaire Second Japanese Version. A question

regarding the period until recovering to daily life besides the SF-36 was added to the questionnaire. Self-administered questionnaires were mailed to the patient's home with the agreement, and questionnaires that were returned were analyzed. SF-36 scores were based on the Japanese National Reference value [15]. They were compared for eight different health-related quality items that consisted of physical functioning (PF), role physical (RP), bodily pain (BP), general health (GH), vitality (VT), social functioning (SF), role emotional (RE), and mental health (MH). The Physical and Mental Component Summaries (PCS, MCS) that were calculated from these eight items were compared. Additionally, the periods until recovering to daily life were compared.

Statistical analysis The statistical analysis was performed with the SPSS software package (version 11.0J for Windows; SPSS Inc., Chicago, IL, USA). The continuous variables were compared between groups using the Student's *t* test. Pearson's Chi-squared test or Fisher's exact test was used to compare discrete variables. Survival curves were produced using the Kaplan–Meier method. Statistically significant differences between the groups were determined by the log-rank test. A p value <0.05 was considered statistically significant (two-tailed test).

Results

During the 15-year study period, 258 of the 570 patients who underwent LC for colorectal cancer were matched to patients who underwent conventional OC. Among these, 252 underwent operations during the earlier period, and 264 patients underwent operations during the later period. The number of registrations and the number of patients with advanced cancer increased annually based on the extension of the surgical indications for LC (Table 1). However, this ceased after 2006, because we participated in the multicenter Japan Clinical Oncology Group Randomized Controlled Trial to Evaluate Laparoscopic Surgery for Colorectal Cancer (JCOG 0404) [18]. The demographic characteristics of both groups are shown in Table 2. The numbers of patients in each category of gender, operative year, operative procedure, tumor location, and TNM stage were the same in both groups, due to the matched control study design. Most of the other demographic data showed similar patterns between the two groups. Approximate values were used for age, ASA score, body surface area, and body mass index. The mean follow-up period of surviving patients was 62.1±31.3 months (range, 14–161 months) for the LC group and 62.3±30.5 months (range, 14–164 months) for the OC group (p=0.961).

Table 1 Number of registered patients and tumor–node–metastasis staging in every year

	TNM stage								Total
	0	I	IIA	IIB	IIIA	IIIB	IIIC	IV	
1993		4							4
1994	4	2	2						8
1995		2					2		4
1996	2	4			4				10
1997		12			2				14
1998	2	4							6
1999	1	7							8
2000	1	15	2		4	4	2		28
2001	2	18	4			8	2		34
2002		10	12		4	8			34
2003	4	20	10			6	4		44
2004	2	30	10		2	8	4	2	58
2005	2	20	24	2	4	14	10	4	80
2006		18	24	4	6	18	6	2	78
2007		40	28	2	6	14	10	2	102
2008			2		2				4
Total	20	206	118	8	34	80	40	10	516

Postoperative adjuvant chemotherapy was administered to 69 patients (26.7%) in the LC group and 60 patients (23.3%) in the OC group (p=0.416). The use of adjuvant chemotherapy did not differ significantly based on stage between the LC and OC groups (stage II, 7.9% vs. 4.8%, respectively, p=0.717; stage III, 77.9% vs. 70.1%, respectively, p=0.358; and stage IV, 80.0% vs. 60.0%, respectively, p=1.000). There were two patients in stage II and eight patients in stage III before 1999 who did not receive adjuvant chemotherapy.

There were ten stage IV patients. The sites of metastasis were three liver cases and two lung cases in LC, and four liver cases and one lung case in OC. In the LC group, two patients had liver metastases, and one patient had lung metastasis excised from 1 to 2 months after the colectomies. They received adjuvant systemic chemotherapy (5-fluorouracil/leucovorin) and have been living for 28–54 months. One patient with multiple liver metastases received systemic chemotherapy (Irinotecan/5-fluorouracil/leucovorin) and died of cancer 47 months later. One patient with lung metastases wanted only supportive care and died of cancer 22 months later. In the OC group, two patients had liver metastases excised 1 month after the colectomies. One patient has been living for 31 months without chemotherapy. The other had cancer relapses to the bone throughout the body and died of cancer 25 months later, although he received systemic chemotherapy (5-fluorouracil/leucovorin). Two patients with multiple liver metastases received systemic chemotherapy

Table 2 Patient demographics

Variable	Laparoscopic	Open	*P*
Mean age (years, mean ± SD)	64.8±9.8	65.8±10.5	0.266
Gender			
Female	100	100	1.000
Male	158	158	
American Society of Anesthesiologists score (mean ± SD)	1.50±0.60	1.53±0.63	0.475
Body surface area (m^2, mean ± SD)	1.59±0.19	1.58±0.18	0.627
Body mass index (kg/m^2, mean ± SD)	22.6±3.5	23.1±3.6	0.451
Tumor location			1.000
Right-sided colon	53	53	
Transverse colon	16	16	
Left-sided colon	110	110	
Upper rectum	63	63	
Lower rectum	16	16	
Operative procedure			1.000
Right colectomy	53	53	
Transverse colectomy	16	16	
Left-sided colectomy	110	110	
Anterior resection of rectum	77	77	
Intersphincteric resection of rectum	1	1	
Abdominoperineal resection of rectum	1	1	
TNM stage			1.000
0	10	10	
I	103	103	
IIA	59	59	
IIB	4	4	
IIIA	17	17	
IIIB	40	40	
IIIC	20	20	
IV	5	5	
Follow-up period of survival (months, mean ± SD)	62.1±31.3	62.3±30.5	0.961
Postoperative adjuvant chemotherapy	69 (26.7%)	60 (23.3%)	0.416
Stage II	5 (7.9%)	3 (4.8%)	0.717
Stage III	60 (77.9%)	54 (70.1%)	0.358
Stage IV	4 (80.0%)	3 (60.0%)	1.000

SD standard deviation

(Irinotecan/5-fluorouracil/leucovorin) and died of cancer 7 and 48 months later, respectively. One patient with lung metastases wanted only supportive care and died of cancer 7 months later.

In total, 13 patients underwent conversion from LC to OC, and the conversion rate was 5.0%. These included 11 cases of technical problems, eight cases in which the operative view could not be obtained (because of obesity in five patients and a narrow pelvis in three patients), two cases in whom bleeding could not be controlled, one case due to problems with the separation device, two cases based on progression of the cancer, and one case due to T3 in the operative finding, because the indication for LC was limited to T1 in 1995. The other case was diagnosed as peritoneal metastasis, so the peritoneal nodule was excised. However, it was not metastasis.

Oncologic outcome of surgery The mean number of lymph nodes harvested was 24.1±13.4 (range, 1–92) in the LC group and 25.2±15.3 (range, 1–107) in the OC group (p+ 0.408; Table 3). Because the indication for LC was expanded to include advanced colon cancer in the latter term, the number of harvested lymph nodes was more in the latter than in the first term. There were no differences between LC and OC in harvested LN number at first and latter term, so there was no difference of the background (Table 3). There was no significant difference between the groups with respect to cancer location. The mean proximal margin and mean distal margin was 111±54 and 84± 63 mm, respectively, in the LC group and 118±66 and 83± 58 mm, respectively, in the OC group (p=0.239, p=0.864, respectively). The mean distal margin for rectal cancer was

Table 3 Oncologic outcome of surgery

Variable	Laparoscopic	Open	*P*
Number of lymph nodes harvested (mean ± SD)	24.1±13.4	25.2±15.3	0.408
Term			
First (mean ± SD)	20.4±11.4	23.5±15.1	0.063
Latter (mean ± SD)	27.7±14.3	26.7±15.4	0.606
Location			
Right-sided colon (mean ± SD)	28.0±13.9	28.5±13.9	0.851
Transverse colon (mean ± SD)	18.6±13.4	20.0±14.9	0.776
Left-sided colon (mean ± SD)	23.0±14.4	22.2±15.5	0.672
Upper rectum (mean ± SD)	25.5±10.7	28.1±15.1	0.273
Lower rectum (mean ± SD)	18.6±11.6	26.6±15.0	0.102
Proximal margin (millimeter, mean ± SD)	111±54	118±66	0.238
Distal margin (millimeter, mean ± SD)	84±63	83±58	0.864
Distal margin in rectal cancer (millimeter, mean ± SD)	43±24	37±24	0.164

43±24 mm in the LC group and 37±24 mm in the OC group (p=0.164). In both groups, the circumferential margins were negative in all patients.

Short-term outcomes There was no mortality in either group (Table 4). There was a significant difference in the operation time between the LC and OC groups (255±77 vs. 210±85 min, respectively, p<0.001). The analysis according to time period showed that a difference of 78 min during the earlier period (p<0.001) was shortened to 16 min during the later period and was no longer significant (p=0.100). The analysis according to tumor location revealed significant differences at all sites except for the transverse colon (p=0.074). The overall amount of bleeding differed significantly (125±214 vs. 254± 266 g in the LC and OC groups, respectively, p<0.001) and differed significantly for all periods and locations (Table 4), except for the right side of the colon (p= 0.486). The analysis of total patient morbidity within 30 days revealed that the rate was significantly lower in the LC group than in the OC group (18.6% vs. 26.4%, respectively, p=0.045). However, there were no significant differences between the two periods at each location. The analysis of morbidity showed that the digestive disorder rate was lower in the LC group than in the OC group (p=0.030). There was no significant difference in the rate of bowel obstruction (2.3% vs. 5.8%, respectively, p=0.072) or respiratory disorder (0.4% vs. 2.3%, respectively, p=0.122), although both tended to be lower in the LC group. The estimated rate of anastomotic leakage in cases with reconstruction after rectal cancer was similar between the LC and OC groups (9.0% vs. 12.8%, respectively, p= 0.609). The overall duration of postoperative stay differed significantly among all periods and locations, except for the transverse colon (p=0.660). The duration of postoperative stay in the LC group was shorter than that in the OC group (11.7±8.4 vs. 16.4±10.3 days, respectively, p< 0.001) and differed significantly for all periods and locations (Table 4), except for the transverse colon (p= 0.660). In both groups, most of the short-term outcomes were improved in the later period compared with the earlier period, with the exception of the morbidity rate in the LC group.

Long-term outcomes The 5-year overall survival rates for the LC and OC groups were 94.6% vs. 92.0%, respectively, for stage I (log-rank test, p=0.249, Fig. 1a), 95.2% vs. 91.8%, respectively, for stage II (p= 0.521, Fig. 1b), and 80.9% vs. 79.1%, respectively, for stage III (p=0.822, Fig. 1c). The corresponding 5-year disease-free survival rates were 94.0% vs. 88.4%, respectively, for stage I (p=0.139, Fig. 2a), 92.1% vs. 84.0%, respectively, for stage II (p=0.328, Fig. 2b), and 64.3% vs. 65.4%, respectively, for stage III (p=0.629, Fig. 2c). Based on the analysis of tumor location, there was no significant difference in overall and disease-free survival at all stages (Table 5).

R0 with the exception of stage IV was performed in 253 patients in both groups. In total, 27 patients (10.7%) in the LC group and 28 patients (11.1%) in the OC group showed recurrence (p=0.100). One patient in the LC group had a port-site recurrence accompanied by peritoneal metastases 25 months after surgery. This patient had stage IIIC rectosigmoid cancer that involved massive lymph node metastases; there was a metastasis in 30 of 36 dissected lymph nodes. The patient underwent chemotherapy after the first recurrence but died of peritoneal and lung metastases 47 months postoperatively. There was no difference in the recurrence pattern including repetition between the two groups (Table 6). There was no difference in the causes of death between the two groups (Table 6).

Table 4 Short-term outcomes

Variable	Laparoscopic	Open	*P*
Operative time (minutes, mean ± SD)	255±77	210±85	<0.001
Term			
First (1993–2004; minutes, mean ± SD)	298±68	220±74	<0.001
Latter (2004–2008; minutes, mean ± SD)	217±63	201±93	0.100
Location			
Right-sided colon (minutes, mean ± SD)	226±76	179±57	0.001
Transverse colon (minutes, mean ± SD)	261±100	204±63	0.067
Left-sided colon (minutes, mean ± SD)	251±73	203±94	<0.001
Upper rectum (minutes, mean ± SD)	265±63	222±68	<0.001
Lower rectum (minutes, mean ± SD)	326±82	298±105	0.410
Blood loss (gram, mean ± SD)	125±214	254±266	<0.001
Term			
First (gram, mean ± SD)	167±207	279±250	<0.001
Latter (gram, mean ± SD)	88±214	232±279	<0.001
Location			
Right-sided colon (gram, mean ± SD)	125±296	157±122	0.486
Transverse colon (gram, mean ± SD)	95±70	179±122	0.030
Left-sided colon (gram, mean ± SD)	104±142	212±208	<0.001
Upper rectum (gram, mean ± SD)	118±167	346±359	<0.001
Lower rectum (gram, mean ± SD)	325±390	521±338	0.141
Blood transfusion (%)	0 (0%)	8 (3.1%)	0.007
Mortality rate (%)	0	0	1.000
Morbidity within 30 days	48 (18.6%)	68 (26.4%)	0.045
Term			
First	22 (17.5%)	34 (27.0%)	0.095
Latter	26 (19.7%)	34 (25.8%)	0.304
Location			
Right-sided colon	10 (18.9%)	17 (32.1%)	0.180
Transverse colon	2 (12.5%)	6 (37.5%)	0.220
Left-sided colon	20 (18.2%)	19 (17.3%)	1.000
Upper rectum	11 (17.5%)	19 (30.2%)	0.142
Lower rectum	5 (31.3%)	7 (43.8%)	0.716
Surgical site infection	25 (9.7%)	22 (8.5%)	0.650
Bowel obstruction	6 (2.3%)	15 (5.8%)	0.072
Respiratory disorder	1 (0.4%)	6 (2.3%)	0.122
Circulatory disorder	1 (0.4%)	2 (0.8%)	1.000
Digestive disorder	0 (0%)	6 (2.3%)	0.030
Anastomotic leakage	10 (3.9%)	13 (5.0%)	0.671
Anastomotic leak in rectal cancer	7 (9.0%)	10 (12.8%)	0.609
Duration of postoperative stay (days, mean ± SD)	11.7±8.4	16.4±10.3	<0.001
Term			
First (days, mean ± SD)	12.7±9.2	17.8±10.7	<0.001
Latter (days, mean ± SD)	10.9±7.6	15.2±9.7	<0.001
Location			
Right-sided colon (days, mean ± SD)	9.8±3.7	16.6±11.6	<0.001
Transverse colon (days, mean ± SD)	14.3±16.2	16.4±9.0	0.660
Left-sided colon (days, mean ± SD)	10.8±5.3	14.7±9.3	<0.001
Upper rectum (days, mean ± SD)	12.8±11.1	17.6±10.3	0.013
Lower rectum (days, mean ± SD)	18.5±10.6	22.6±11.4	0.305

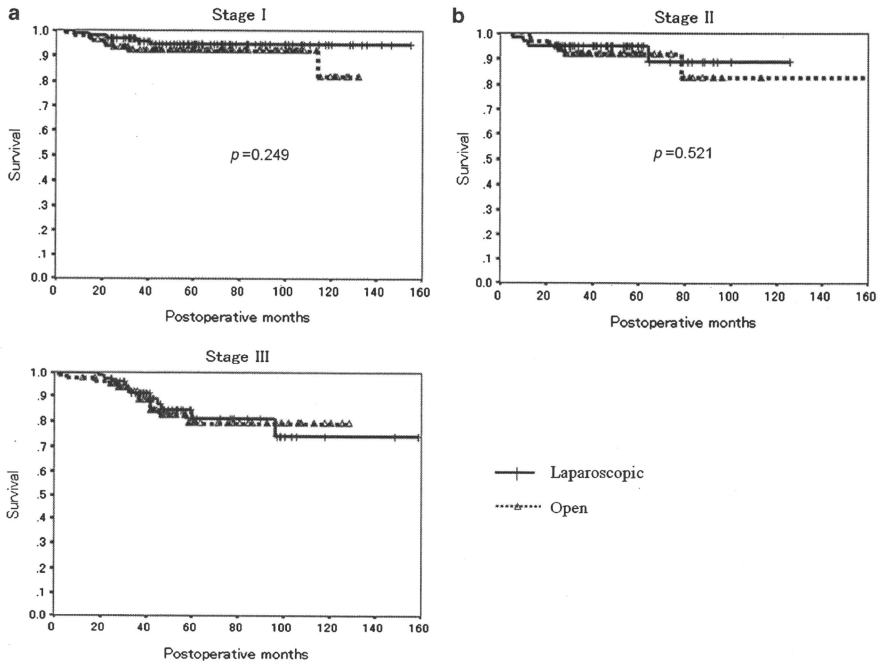

Fig. 1 There were no significant differences in overall survival at all stages

Mid-term HRQOL Seventy-eight patients 1–2 years after operation in 2007–2008 were research subjects. Of 78 patients, 62 replied to the questionnaire (79.5%). A total of 35 of 43 LC patients (81.4%) and 27 of 35 OC patients (77.1%) were analyzed. No significant differences were found between LC and OC groups in characteristics (Table 7). There were significant differences in RP (53.0±8.3 vs. 44.2±13.5, respectively, p=0.002), BP (57.3±7.4 vs. 52.7±10.3, respectively, p=0.046), SF (53.2±10.5 vs. 47.6±11.1, respectively, p=0.049), RE (53.6±6.2 vs. 45.4±12.5, respectively, p=0.002), and PCS scores (46.2±7.4 vs. 41.4±10.4, respectively, p=0.039) between the two groups (Fig. 3). There were no other statistically significant differences; however, all HRQOL scores of the LC group were better than those of the OC group. The periods until recovering to daily life did not differ significantly between the two groups; however, they tended to be shorter in the LC group (73.5±89.4 vs. 111.4±98.4 days, respectively, p=0.145). Postoperative adjuvant chemotherapy affected the period until recovering to daily life in both groups (chemotherapy, 143.1±111.5 days versus surgery alone, 68.1±77.7 days, p=0.007).

Discussion

Several reports on short-term and long-term studies and large-scale RCTs have demonstrated that LC is equal to OC in terms of morbidity and survival rates [2–5]. A retrospective large-scale multicenter study of LC in 1,495 cases of colon cancer and 541 cases of rectal cancer in Japan showed, in the short term, that the conversion rate was 4.8% for colon cancer and 4.4% for rectal cancer, 1.4% of patients experienced complications during surgery, and the morbidity rate was 11.2% [19]. Another large-scale retrospective study compared 1,092 patients who underwent sigmoid colectomy with LC and 9,511 patients who underwent sigmoid colectomy with OC and demonstrated advantages of the former in terms of a shorter postoperative hospital stay and a lower wound infection rate [20].

Significant advantages with respect to short-term results have also been shown in larger-scale studies, such as nationwide trials or those exceeding 100 centers, even when the differences have been relatively small [21, 22]. However, these large-scale examinations tend to have been limited by

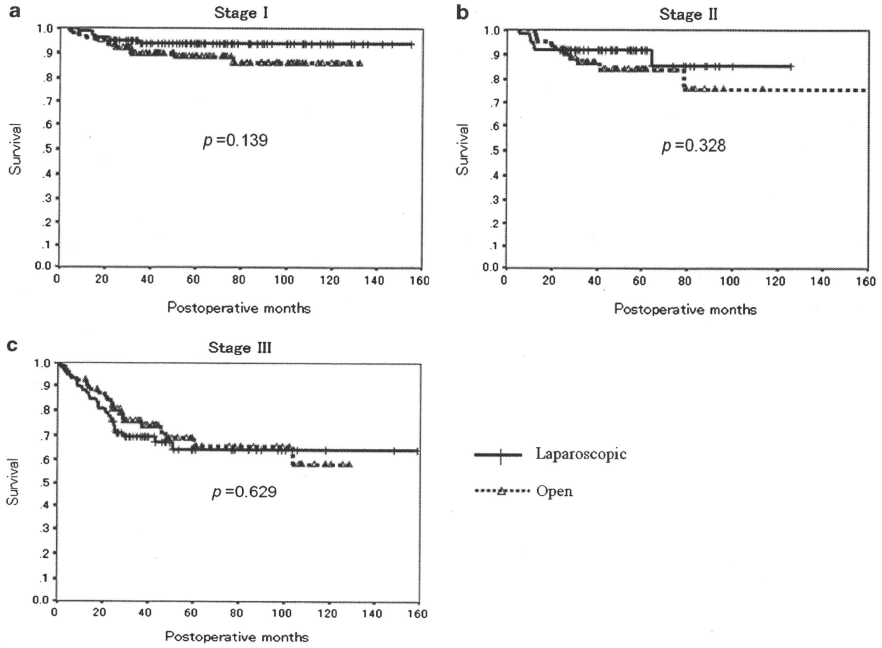

Fig. 2 There were no significant differences in disease-free survival at all stages

poorly defined registration conditions. In addition, the maintenance of quality appears to be difficult in research relating to surgical techniques. The conversion rate was comparatively high (11–23%) in some well-known RCTs [2–5]. One trial reported a mortality rate of 5%, although it was possible that the quality of the analysis was limited. By contrast, several case-matched control studies have reported comparisons between LC and OC [8–12]. In these reports, the comparisons between open and laparoscopic surgery were done with two to five matched variables, including gender, age, year of surgery, site of cancer, staging of cancer, operating procedure, and surgeon. We matched seven variables (gender, age, ASA score, operative year, tumor location, operative procedure, and TNM stage) in the present study to more carefully compare short-term and long-term results. The case-matched control study design allows the quality of the data and various conditions to be maintained. The quality of surgical techniques can also be controlled in single-facility studies. However, one limitation of this approach is the reduced number of patients, which might bias the results. In the present study, to maximize the quality of the comparison, many of the registration conditions were matched. Moreover, to include a large number of registrations, the registration period was set at 15 years. A previous case-matched control study compared 172 examples [9]. By contrast, the current study compared 258 examples, with a conversion rate of 5.0%, a morbidity rate of 18.6%, and no mortality. We therefore believe that the results of the current analysis are comparable to those of a large-scale multicenter study with advanced facilities. The use of propensity score is appropriate for matching of a case-matched control study. There is a limitation in this study because of no use of propensity score. However, there were the time-related changes in the indication for LC; it was thought that matching the backgrounds as closely as possible and comparing with OC was the most meaningful approach. The dropout rate increased because seven variables were matched.

The analysis of the short-term outcomes revealed that the morbidity rate was lower in the LC group than in the OC group. This result was similar to those of previous large-scale reports [21, 22]. However, there were no significant

Table 5 Five-year overall and disease-free survival rates at respective tumor locations for patients at all stages

Location		Laparoscopic (%)	Open (%)	*P*
Right-sided colon				
Stage I	5-year OS[a]	84.0	79.3	0.666
	5-year DFS[b]	84.0	79.3	0.666
Stage II	5-year OS	94.1	94.1	0.552
	5-year DFS	94.1	88.2	0.988
Stage III	5-year OS	71.1	55.6	0.663
	5-year DFS	44.4	66.7	0.959
Transverse colon				
Stage I	5-year OS	100	85.7	0.317
	5-year DFS	100	85.7	0.317
Stage II	5-year OS	100	75.0	0.317
	5-year DFS	75.0	75.0	0.919
Stage III	5-year OS	100	66.7	0.317
	5-year DFS	66.7	66.7	0.486
Left-sided colon				
Stage I	5-year OS	100	92.2	0.066
	5-year DFS	97.4	88.9	0.085
Stage II	5-year OS	96.3	96.0	0.964
	5-year DFS	92.6	91.4	0.927
Stage III	5-year OS	85.6	90.0	0.483
	5-year DFS	62.2	77.1	0.216
Rectum				
Stage I	5-year OS	93.6	100	0.146
	5-year DFS	94.6	92.7	0.995
Stage II	5-year OS	93.3	86.2	0.276
	5-year DFS	93.3	70.6	0.078
Stage III	5-year OS	77.2	78.9	0.993
	5-year DFS	75.4	65.2	0.598

[a] Overall survival rate

[b] Disease-free survival rate

differences in specific illnesses excluding the digestive symptoms. There were no differences in the outcomes of surgical site infections (9.7% vs. 8.5%, respectively). Intestinal obstruction (2.3% vs. 5.8%, respectively) is thought to have contributed to the overall illness rates. This corresponds to grade 2 in the Clavien system [23]. It is thought to be an important result, even though it was not a significant difference (p=0.072). The LC group showed better short-term outcomes, with the exception of operation time. However, during the later period, the operation time did not differ significantly owing to a learning curve effect. It seems that the learning effect in LC also improved OC outcomes because the short-term results of OC were improved at the latter term. Only the morbidity rate of the LC group did not improve during the later stage because the number of cases of rectal cancer or advanced cancer cases increased during this period.

Table 6 The initial recurrence pattern and the causes of death

	Laparoscopic	Open	*P*
Recurrent site			
Liver	13 (5.1%)	14 (5.5%)	1.000
Lung	7 (2.8%)	8 (3.2%)	1.000
Peritoneum	4 (1.6%)	3 (1.2%)	1.000
Local	3 (1.2%)	4 (1.6%)	1.000
Lymph node	3 (1.2%)	2 (0.8%)	1.000
Bone	2 (0.8%)	0 (0%)	0.449
Port site	1 (0.4%)	0 (0%)	1.000
Causes of death			0.261
Colorectal cancer death	11 (4.3%)	9 (3.6%)	
Other cancer death	3 (1.2%)	2 (0.8%)	
Other disease	7 (2.8%)	16 (6.3%)	

Several previous studies have reported on the efficacy of oncologic resection by lymph node harvesting in LC [24–26]. Tsikitis et al. reported that the total number of lymph nodes analyzed in stage III colon cancer was not a prognostic indicator of the cancer-specific and disease-free

Table 7 Patient's demographics for research of the health-related quality of life graphics

Variable	Laparoscopic (n=35)	Open (n=27)	*P*
Mean age (years, mean ± SD)	65.7±9.0	63.7±9.7	0.424
Gender			
Female	18	12	0.618
Male	17	15	
American Society of Anesthesiologists score (mean ± SD)	1.66±0.54	1.63±0.56	0.846
Tumor location			0.503
Right-sided colon	9	6	
Transverse colon	2	2	
Left-sided colon	11	13	
Rectum	13	6	
Operative procedure			0.503
Right colectomy	9	6	
Transverse colectomy	2	2	
Left-sided colectomy	11	13	
Anterior resection of rectum	13	6	
TNM stage			0.915
0	0	0	
I	13	11	
II	9	8	
III	12	7	
IV	1	1	
Postoperative adjuvant chemotherapy	10 (28.6%)	7 (25.9%)	0.817
Research time of the health-related quality of life after surgery (months, mean ± SD)	17.6±3.7	18.2±3.6	0.509

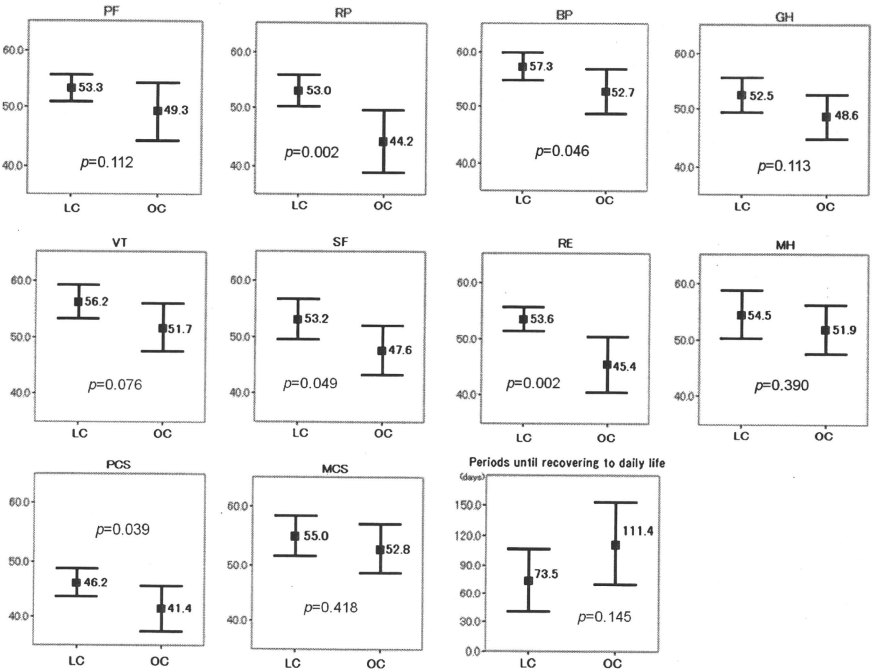

Fig. 3 Comparison of the health-related quality life scores. The *error bars* display 95% confidence interval of the mean value. There were significant differences in RP, SF, RE, and PCS scores between two groups. The scores of them in LC group were better than OC group. *PF* physical functioning, *RP* role physical, *BP* bodily pain, *GH* general health, *VT* vitality, *SF* social functioning, *RE* role emotional, *MH* mental health, *PCS* physical component summary, *MCS* mental component summary

survival rates [27]. The important factors appeared to be accurate staging, appropriate surgery, and the identification of lymph nodes in the colon cancer specimen. The surgical margin and the number of harvested lymph nodes seemed to be adequate for our comparison of LC with OC, and there appeared to be no oncological problems. In this study, the circumferential margins were negative in all patients. This may have been because the indication for LC was limited to T4 colon cancer and T2 lower rectal cancer without other internal organ infiltration.

The analysis of the long-term outcomes showed similar oncologic results for all stages, probably because numerous variables were matched in the current study. It was suggested that peritoneal metastasis may be increased due to being overlooked intraoperatively and the influence of carbon dioxide pneumoperitoneum in the laparoscopic surgery [28–31]. However, the peritoneum recurrence rate was 1.6% in LC and 1.2% in OC, and the difference was not significant. Peritoneal metastasis would be unlikely to increase if there was no inappropriate technique, such as touching of the tumor directly. There was no difference in the overall and disease-free survival of all stages. If the cancer stage and physical status of patients undergoing LC are equivalent to those of patients undergoing OC, both approaches can be seen to have similar survival benefits.

However, the current study was limited because it was not a randomized trial. A high-quality large-scale RCT is necessary to obtain stronger evidence. The JCOG 0404 multicenter randomized study of laparoscopic versus open surgery for T3/4 colon cancer is currently ongoing, with results expected imminently [18]. We greatly anticipate a large-scale multicenter randomized study of the long-term results in advanced cancer. Additionally, the current analysis of tumor locations was less effective for lower rectal cancer and transverse colon cancer. Analyzing long-term outcomes in a single-center study appears to be

difficult for tumors of the transverse colon cancer due to the relatively small number of patients. A phase II multicenter study in stage 0 or I disease of rectal cancer was started under the direction of the Japan Society of Laparoscopic Colorectal Surgery beginning in 2008 [32]. Another multicenter study of transverse colon cancer is scheduled to begin soon by this society. The results of these clinical studies are expected to clarify the effectiveness of laparoscopic surgery.

There are few large-scale multicenter randomized studies of HRQOL after laparoscopic and open resection (OC) for colorectal cancer [5, 13, 14]. The Clinical Outcome of Surgical Therapy (COST) group analyzed HRQOL in 428 patients at 2 days, 2 weeks, and 2 months after surgery using 13 scoring items. They reported that physical pain in the hospital and HRQOL 2 months postoperatively were superior in LC compared with OC [13]. Braga analyzed HRQOL in 391 patients at 12, 24, and 48 months after surgery using the SF-36 and reported that GH, PF, and SF at 12 months and SF at 24 months were better in LC [14]. The UK Medical Research Council Conventional versus Laparoscopic-Assisted Surgery in Colorectal Cancer trial (CLASCC) Group analyzed HRQOL in 696 patients at 2 weeks and 3, 18, and 36 months after surgery using the EORTC QOL-C30 [33] and QLQ-C30 [34]. They reported no significant difference between LC and OC. In another randomized study, HRQOL at 4 months after surgery in LC was better than in OC [35]. In a retrospective study of benign bowel disease, there was no significant difference in HRQOL between LC and OC at 39 months [36]. Thus, short-term HRQOL of LC is thought to be excellent; however, the superiority of mid/long-term HRQOL of LC is controversial. Our data showed that RP, BP, SF, RE, and PCS scores in LC were significantly better than in OC. Five other items and the period until full recovery to daily life did not differ significantly; however, all mean values in LC exceeded those in OC. Moreover, nine of ten items in LC were better than the Japanese national reference value, but five were better in OC. These results suggest that mid-term QOL with LC is better than that with OC. Chiefly, physical items and mental functions were influenced because the RE score was better.

In this study, SF-36 scores were normalized to the Japanese National Reference values published in 2002 [15]. This normalization makes it easy to compare scores. Moreover, a self-administered questionnaire form was used. The response rates might lower with this type of questionnaire than with the interview type, but this method is preferred to reduce possible biases in response [14].

This study never denies high-quality RCT. We would like to send our data to a more refined research group such as COST [4]. In this study, the results obtained in a single institute, according to almost the same procedure, were compared, matching a lot of variables and matching the background. It is smaller than the RCT of the multicenter with regards to the number of cases. However, there are a lot of numbers of cases with examination in single facilities in the past case-matched report. It is thought that the conclusion is more detailed because a lot of corresponding variables were able to be put out.

Conclusion

This study demonstrated that LC outperformed OC with regard to short-term outcomes and mid-term HRQOL, with the exception of the operation time. Moreover, LC had no adverse effects in respect to long-term outcomes. LC was therefore shown to be a suitable therapy for colorectal cancer in this single-center case-matched study. However, a large-scale multicenter study is necessary for transverse colon and lower rectal cancer.

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Original Paper

Paraaortic Lymph Node Metastasis Showed CR to UFT/LV Therapy in Elderly Rectal Cancer

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KEY WORDS:
Elderly patient; Metastatic colorectal cancer; UFT/LV therapy; Para–aortic lymph node metastasis

ABBREVIATIONS:
Complete Response (CR); Uracil–tegafur (UFT); Leucovorin (LV)

ABSTRACT

Background/Aims: Intravenous chemotherapy with a combination of several drugs is commonly used to treat metastatic colorectal cancer. However, the associated adverse events can be severe. Here we report a rare case of metastatic rectal cancer in an elderly patient who got complete response for metastatic rectal cancer with oral uracil-tegafur plus leucovorin therapy.
Methodology: 77-year-old male. An abdominoperineal resection of the rectum was performed, but para-aortic lymph-node metastasis occurred. Uracil-tegafur plus leucovorin therapy was started on postoperative day 48. Each chemotherapy course comprised 400 mg/day uracil-tegafur and 75 mg/day leucovorin administered for 28 days every 35 days.
Results: After 10 courses, abdominal computed tomography indicated that a good partial response had been achieved. The para-aortic lymph-node swelling disappeared after 17 courses, indicating a complete response. During this period, no adverse events were noted. No recurrence had occurred 4 months after the complete response.
Conclusions: This case demonstrates that uracil-tegafur plus leucovorin therapy can be used safely even in elderly patients, and suggests that it is likely to be effective in treating metastatic colorectal cancer.

INTRODUCTION

Chemotherapy for metastatic colorectal cancer has rapidly diversified since the appearance of new anti-cancer drugs and molecular target agents (1). The intravenous administration of combinations of several drugs is reported to have a high response rate (2-4). However, the incidence of adverse events (AEs) associated with this approach is of concern both with prolonged treatment and in elderly patients (5-7). Improving the quality of life (QOL) is an important therapeutic goal when treating metastatic colorectal cancer, as well as the treatment efficacy, and the QOL can be decreased by AEs particularly in elderly patients. Uracil-tegafur plus leucovorin (UFT/LV) oral therapy is chiefly used as postoperative adjuvant chemotherapy in Japan (8). A phase III study of UFT/LV and fluorouracil (5-FU)/LV for the treatment of metastatic colorectal cancer in Europe reported that these combinations had similar therapeutic effects (9,10). Moreover, UFT/LV therapy has a lower incidence of AEs than 5-FU/LV therapy, is more convenient to use, and its safety has been established (11). Here we report on a case of metastatic rectal cancer in a 77-year-old man. Excision did not provide a radical cure, and UFT/LV chemotherapy was performed on an outpatient basis with the intention of maintaining the patient's QOL. A complete response (CR) was achieved 23 months after the start of treatment with no AEs.

METHDOLOGY

A 75-year-old man with a positive feces occult blood test result, was diagnosed with early cancer of the lower rectum, TisN0M0 (stage 0), in February 2004. Endoscopic mucosal resection of the tumor was performed at the Yokohama City University Gastroenterological Center, Japan. The pathohistological findings revealed a well-differentiated adenocarcinoma (Tis) with no lymphatic/venous invasion (ly0, v0) and a negative surgical margin, but the specimen was excision divided into three. Two follow-up colonofiberscopies were performed 3 and 10 months later, respectively, and no recurrence was detected. However, after 29 months, blood was present in the feces, and rectal cancer recurrence was diagnosed. The tumor was located 0.5 cm above the dentate line. An elevated lesion with an ulcer was revealed by a colonofiberscopy and a double-contrast roentgenogram of the lower rectum (**Figure 1**). Computed tomography (CT) of the body trunk revealed no lung and liver metastases, but para-aortic lymph-node swelling was observed. However, the para-aortic lymph nodes metastasis was diagnosed as negative because the swelling of them were sparsely in, preoperatively.