図3 回結腸動静脈幹の同定と把持①

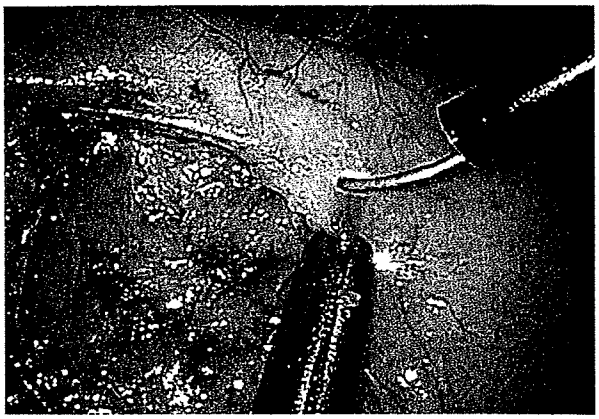


図4 後腹膜下筋膜の同定と剝離

図5 回結腸動静脈幹の把持②
Endo clinch から endo mini retractor にかけかえる.

図6 回結腸静脈のクリッピング・切離

部，そして根部郭清を行う場合には左側腹部に追加する(図2).

手術手技

腹腔内の検索を行った後，大網を横行結腸頭側へ挙上する．大網が上行結腸へ癒着している症例が時々あるが，このような症例では，癒着している大網をできるだけ剝離しておく.

メ　モ

内側アプローチか外側アプローチかこの手術が導入された当初は，内側アプローチ派と外側アプローチ派との間で，活発な議論がかわされた．最近では，進行癌に対しては内側アプローチが主流のようである．しかしながら，内側アプローチで開始しても，途中で正しい層がわからなくなった場合は，あまり固執せずに，外側アプローチに切り替えるようにしている.

1．回結腸動静脈幹の同定

回腸末端の腸間膜を広げ，内側アプローチのランドマークである回結腸動静脈幹を求める．肥満症例で，回結腸動静脈幹がわかりにくい場合には，回腸末端の Treves fold(びらびら)を把持して右尾側へ牽引してやると，回結腸動静脈が膨隆して明らかとなる．Endo Clinch(Tyco 社)で回結腸動静脈幹を把持し，これを腹側へ牽引する(図3).

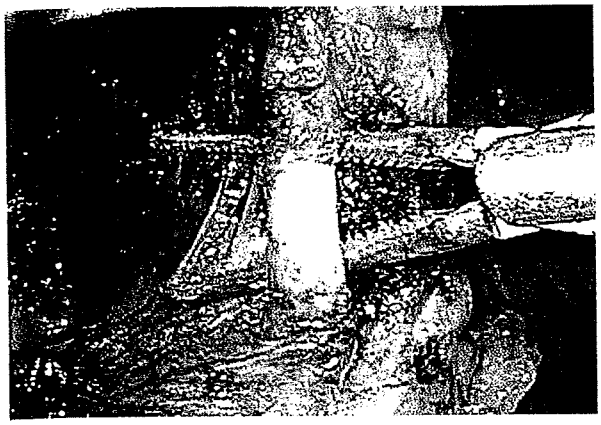


図7 回結腸動脈のクリッピング・切離

2．後腹膜下筋膜の同定・剝離

回結腸動静脈幹左側の腹膜を切開し，後腹膜下筋膜を露出し，筋膜の前面を十二指腸に向けて剝離する(図4)．十二指腸前面で後腹膜下筋膜が剝離できたならば，十二指腸水平部尾側の薄くなった腹膜を切開し，回結腸動静脈幹を把持しているEndo Clinchから Endo mini retract にかけかえる．これは traumatic な鉗子である Endo Clinch によって，転移のあるリンパ節からの癌細胞散布の危険性を減らすためである(図5)．

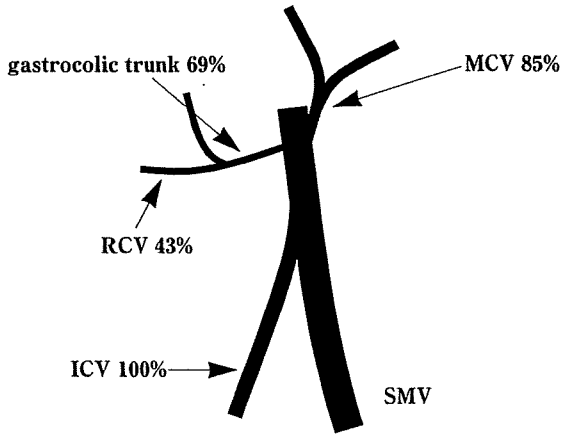
3．回結腸動静脈の処理

腹膜の切開を回結腸動静脈幹根部に向けて延長する．この時ランドマークとなるのは，上腸間膜静脈本幹である．本幹を確認し，リンパ節を郭清しつつ回結腸静脈の根部を露出し，クリッピング後，切離する(図6)．回結腸動脈も同じ高さでクリッピングするが(図7)，回結腸動脈はSMVの腹側を走行する場合と背側を走行する場合があり，注意が必要である(図8)．

4．Surgical trunk の郭清

Surgical trunk の前面を露出し，頭側に向けて剝離をすすめる．Surgical trunk 前面に沿って剝離する限り，安全である(図9)．超音波凝固切開装置や，へら型電気メスと剝離鉗子を用いて剝離する．Surgical trunk に流入する右結腸静脈が存在すれば，これをクリッピングし，切離する．右結腸静脈は約70%の症例で，また，右結腸動脈は約70～90%の症例で欠如する(図8)．

本症例では，右結腸動脈をクリッピング・切離している(図10)．中結腸静脈および胃結腸静脈幹



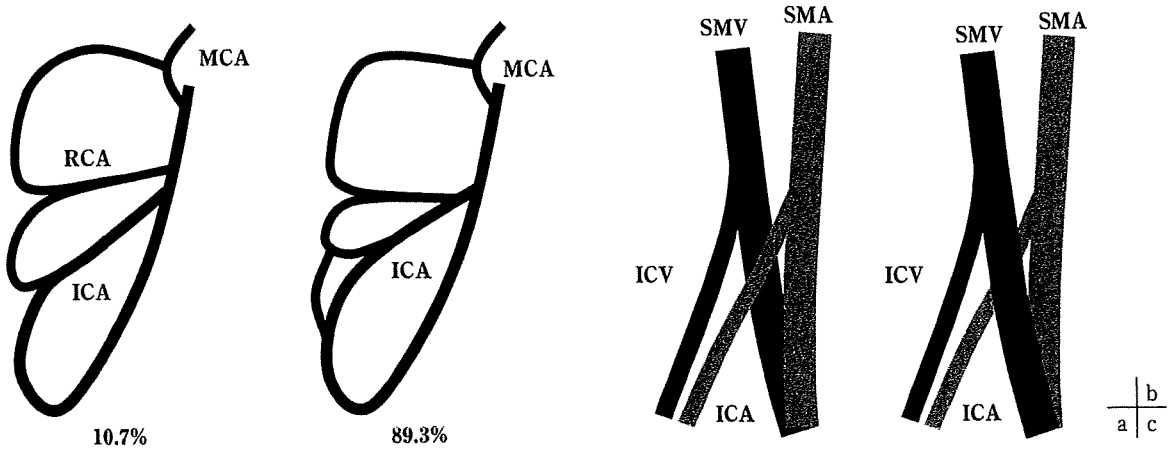


図8 右側結腸の血管系解剖

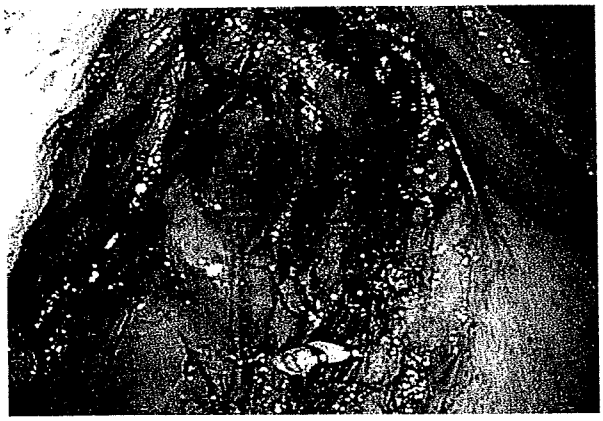


図9 Surgical trunk の郭清

図10 右結腸動脈のクリッピング・切離

図11 副右結腸静脈のクリッピング・切離

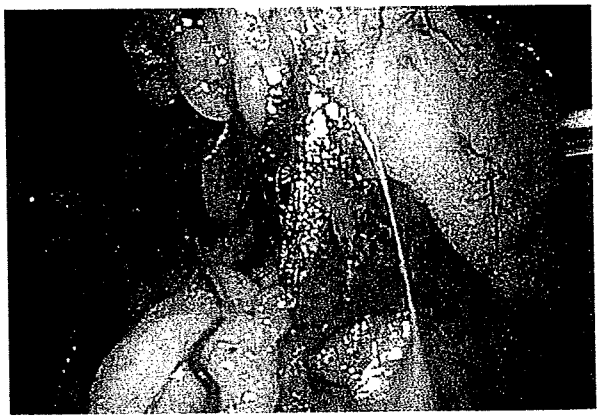


図12 肝彎曲部の剝離・授動

の流入部を確認しておく．この時点で，副右結腸静脈が確認できれば，クリッピング・切離してもよい(図11)．

5．結腸間膜の剝離授動

助手に，切離した回結腸動静脈幹を腹側に把持させ，さらにもう1本の鉗子を用いてできる限り面の状態で腸間膜を腹側に牽引させて，腸間膜を後腹膜下筋膜から可能な限り剝離する．この時，助手の鉗子の先でガーゼを束ねて把持させると，鉗子がすべらずに，また余計な損傷がなくてよい．正しい層がわかりにくくなったら，その時点で剝離をやめ，授動した腸間膜背側にガーゼを挿入しておく．

6．上行結腸・横行結腸の剝離授動

肝彎曲部を左尾側に牽引し，肝結腸間膜を切開し，後腹膜下筋膜の前面の層を保持しながら剝離授動する(図12)．内側アプローチで十分に剝離されていれば，外側の腹膜を切開するだけで，前もって挿入しておいたガーゼと貫通する．結腸右半切除術では，横行結腸左側で網嚢を開放し，膵下縁を確認しておく．

7．横行結腸間膜の処理

大網を横行結腸頭側に挙上した後，横行結腸を2本の鉗子で腹側に牽引し，横行結腸間膜を展開する．腫瘍の局在に応じて，どの血管を処理するかを見定め，間膜のうすい所を切開する．中結腸静脈や，胃結腸静脈幹から分岐することが多い副

図13 中結腸静脈のクリッピング・切離

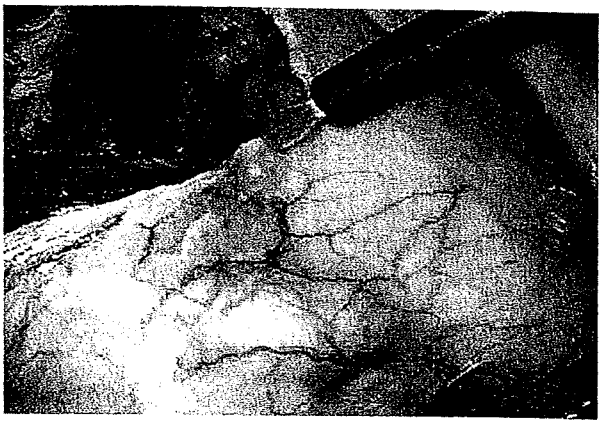


図14 回盲部の剝離・授動

右結腸静脈はクリッピングし切離する．動脈も症例に応じて，中結腸動脈右枝などをクリッピング，切離する(図13)．上腸間膜動脈(SMA)，同静脈(SMV)は，回結腸動静脈を除いて，分岐のパターンが複雑であるので，術前に3D-CTによる血管系の情報が有用である．

8．回盲部の剝離授動

上行結腸の剝離線を尾側に延長し，回盲部を剝離授動する．体位を頭低位にし，助手に虫垂根部を把持させて回盲部を頭側に牽引する．回腸終末部の腸間膜と後腹膜の移行部のラインを大動脈分岐部に向けて切開する(図14)．右側結腸の剝離・授動の目安は，回盲部が肝臓まで余裕で届いていることである．この操作ではカメラポートを下腹部正中のポートにすると，カメラ操作が楽である．

9．切除・吻合

腸管の剝離・授動および血管処理が終了したならば，小切開創に創縁保護のためのプロテクターをかけ，病変部腸管を体外に誘導する(図15)．Lap discのままでは，discの厚さ(高さ)のために，病変部の露出が制限される．中結腸静脈系の血管を腹腔内で処理しておかないと，病変部を体外に露出する際に，静脈が避けて思わぬ大出血をきたすことがあるので注意する．切除・吻合にはわれわれは，器械吻合を用いたfunctional end-to-end anastomosis(FEEA)を好んで行っている[4]．吻合は術者が慣れた方法で，手早く確実に行うことが重要であると考えている．手早く行うのは，吻合後に吻合部が浮腫をきたして，露出した腸管を体内に還納できなくなるのを防ぐためである．もし浮腫をきたして還納できない場合には，躊躇なく，小切開創を少し延長する．また，われわれは腸間膜欠損部は修復していない．

図15 郭清終了図

10．再 気 腹

吻合が完了したならば，露出した腸管を体内に還納し，再びlap disc miniを用いて再気腹する．腸管露出時や還納時の思わぬ出血がないか，また腸管の捻れがないか，腸管が腹膜欠損部をくぐっていないかなどをチェックする．ドレーンをトロッカー部より挿入留置する．小切開創以外は

5 mm トロッカー刺入部なので，スキンステープラーのみで閉鎖している．

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Results of a multicenter study of 1,057 cases of rectal cancer treated by laparoscopic surgery

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Abstract
Background The aim of this study was to clarify the feasibility of laparoscopic surgery for rectal cancer retrospectively in 28 centers throughout Japan.
Methods Between May 1994 and February 2006, 1,057 selected patients with rectal cancer underwent laparoscopic surgery. All the data regarding the patient details, and operative and postoperative outcome were collected retrospectively.
Results Mean follow-up was 30 months. Procedures included anterior resection in 938, abdominoperineal resection in 107, Hartmann's procedure in 10, and others in two patients. Conversion to open procedures occurred in 77 patients (7.3%). Postoperative surgical complications developed in 235 patients (22.2%), including anastomotic leakage in 84 (9.1%). Median length of postoperative hospital stay was 15 days (7–271 days). Patients with upper rectal cancer had shorter hospital stay than those with lower rectal cancer (14 versus 18 days, $p < 0.01$). Tumor–node–metastases (TNM) stage included 83(7.9%) stage 0, 495 (46.8%) stage I, 197 (18.6%) stage II, 230 (21.8%) stage III, and 52 (4.9%) stage IV. Recurrence was developed in 67 patients (6.6%) of the 1,011 curatively treated patients. Local recurrence occurred in 11 patients (1.0%). There was no port-site metastasis. Of the 1,011 curatively treated patients, the 3-year disease-free survival rate was 100% in stage 0, 94.6% in stage I, 82.1% in stage II, and 79.7% in stage III.
Conclusions Laparoscopic surgery is feasible and safe in selected patients with rectal cancer, with favorable short-term and mid-term outcome.

Keywords Rectal cancer · Laparoscopic surgery · Short-term outcome · Multicenter study

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The role of laparoscopic surgery has gained acceptance in the treatment of benign diseases, but it remains controversial in the treatment of malignancies, because of concerns about adequacy of lymphadenectomy, the extent of resection, early findings of port-site metastasis, and the lack of long-term results [23]. There are some retrospective and prospective comparative studies reporting on the feasibility and favorable outcome of laparoscopic surgery for colorectal cancer including earlier return of bowel motility [6, 9, 17, 27], less postoperative pain [6, 27], and shorter hospital stay [6, 8, 9, 27]. Recently, results of large

randomized controlled trials comparing laparoscopic with conventional open surgery have been published, demonstrating that laparoscopic surgery for colon cancer was equivalent to open surgery in terms of postoperative complications and long-term outcome [4, 11, 18]. After the publication of these trials, laparoscopic surgery for colon cancer has been recognized as an alternative treatment to open surgery.

However, these studies did not include rectal cancer because of technical difficulties including anastomotic techniques, except the Conventional versus Laparoscopic-Assisted Surgery in Patients with Colorectal Cancer (CLASICC) trial, which included rectal cancer and showed impaired short-term outcomes in patients undergoing laparoscopic anterior resection for rectal cancer, and concluded that the routine use of laparoscopy for rectal cancer is not justified. There are some reports about the feasibility of laparoscopic surgery for rectal cancer, however, these studies included only a small number of patients, and the role of laparoscopy for rectal cancer remains to be defined [1, 2, 19, 22, 24].

This retrospective, multicenter study was conducted to clarify the feasibility, safety, and short-term and mid-term surgical outcomes of laparoscopic surgery for rectal cancer. To the best of our knowledge, the present study is the first retrospective study that included the data of more than 1,000 patients with rectal cancer undergoing laparoscopic surgery.

Patients and methods

This multicenter study was conducted by 28 institutions which are members of the Japan Society of Laparoscopic Colorectal Surgery. The study group consisted of patients who underwent laparoscopic surgery for rectal cancer in those 28 institutions during the period between May 1994 and February 2006. All of the surgeons were skillful both in the open and laparoscopic colorectal surgery, and had experienced at least 30 laparoscopic surgeries for colorectal cancer.

Indications for laparoscopic surgery for colorectal cancer have expanded gradually throughout Japan, based on the preoperative diagnosis of the tumor. Therefore, the indications for laparoscopic surgery for rectal cancer varied amongst the institutions, and the patients were selected at the surgeons' discretion. In the majority of institutions, indications were limited to T1 or T2 tumors in the rectum, and patients with bulky tumors, those with a previous history of extensive adhesions, those with bowel obstruction, and those who did not consent to laparoscopic surgery were excluded. No hand-assisted laparoscopic procedures were included in the present study.

Tumor location was defined according to the *General Rules for Clinical and Pathological Studies on Cancer of the Colon, Rectum, and Anus* edited by the Japanese Society for Cancer of the Colon and Rectum [16]. When the tumor was located between the inferior margin of the second sacral vertebra and the peritoneal reflection, the location was recorded as the upper rectum. When the tumor was located below the peritoneal reflection, its location was recorded as the lower rectum. The location of the tumor was determined by pelvic computed tomography (CT) scan, colonoscopy, and/or barium enema preoperatively and confirmed during surgery.

The extent of lymphadenectomy and site of ligation and division of the inferior mesenteric vessels were decided by the surgeon in charge. Conversion to open surgery was defined as incision longer than 8 cm. In laparoscopic low anterior resection, the rectum was transected laparoscopically using laparoscopic linear staplers or through a small laparotomy, at the surgeon's discretion. A diverting stoma was also fashioned at the surgeon's discretion.

Clinical data including sex, age, body mass index (BMI), tumor location from anal verge, location of the tumor, laparoscopic procedures, size of tumor, distal margin, lymph node resected, and pTNM stage were collected retrospectively and reviewed. Operative and postoperative data including operative time, blood loss, length of incision, intraoperative complications, reasons for conversion to open surgery, time until resumption of liquid and solid intake, length of postoperative hospital stay, morbidity, 30-day mortality, and reason for reoperation were also collected retrospectively, and data regarding oncologic follow-up were collected at the time of the present study.

Statistical differences in categorical variables were analyzed by the chi-square test, and differences in continuous variables were analyzed by Student's *t*-test. The Kaplan–Meier method was used to calculate survival rates.

Results

Between May 1994 and February 2006, 1057 patients with rectal cancer underwent laparoscopic surgery. The patient details are summarized in Table 1. Of these, 655 (62%) patients had tumors in the upper rectum, and 402 (38%) in the lower rectum. Five patients received preoperative radiotherapy; the reasons for radiotherapy were not described. Forty-nine patients (4.6%) had previously undergone tumor removal by transanal or endoscopic resection. Stage 0 or I disease was present in 578 (54.7%) patients. Anterior resection with double stapling technique was performed in 888 (84.0%) patients and hand-sutured coloanal anastomosis was performed in 107 patients (10.1%) patients, whereas abdominoperineal resection or

Table 1 Patient details

Number of patients	1,057
Sex (male/female)	665/392
Age (years)[a]	62.9 ± 11.7
BMI (kg/m^2)[a]	22.9 ± 3.2
Location of tumor	
Upper rectum	655
Lower rectum	402
Preoperative radiation	5 (0.5)
Previous tumor removal	49 (4.6)
Type of tumor	
Well/moderate	1023 (96.8)
Poor	11 (1.0)
Others	23 (2.2)
TNM stage	
0	83
I	495
II	197
III	230
IV	52
Procedures	
Anterior resection with double stapling technique	888 (84.0)
Anterior resection with sutured coloanal anastomosis	107 (10.1)
Abdominoperineal resection	50 (4.7)
Hartmann's procedure	10 (0.9)
Others	2 (0.2)
Diverting ileostomy	116

[a] Values are mean ± standard deviation; BMI, body mass index

Numbers in parentheses are percentages

Hartmann's procedure was performed in only 60 (5.6%) patients. A diverting ileostomy was fashioned in 20 (3.0%) patients in the upper rectum and 96 (23.9%) patients in the lower rectum. Conversions to open procedures occurred in 77 (7.3%) patients; the reasons for the conversions are shown in Table 2. Intraopearative complications occurred in 52 (4.9%) patients, including trouble in anastomosis in 17, uncontrollable bleeding in 15, injuries to other organs in 10, and others in 10. Operative and postoperative outcome are shown in Table 3. Operative time was significantly shorter and blood loss was significantly less for upper rectal cancer than for lower rectal cancer (250 versus 300 min, $p < 0.001$; 56 versus 150 ml, $p < 0.01$). Median length of postoperative hospital stay was 15 days (7–271 days). Patients with upper rectal cancer had shorter hospital stay than those with lower rectal cancer (14 versus 18 days, $p < 0.01$). Mean number of dissected lymph nodes was 15, which did not differ between the upper and lower rectal cancers.

Table 2 Reasons for conversions to open surgery

Trouble in anastomosis	15 (19.5)
Advanced disease	12 (15.6)
Narrow pelvic cavity	12 (15.6)
Adhesion	10 (13.0)
Obesity	7 (9.1)
Bleeding	5 (6.5)
No visualization of the location of tumor	5 (6.5)
Injury to other organs	3 (3.9)
Others	8 (10.4)
Total	77

Numbers in parentheses are percentages

Postoperative surgical and nonsurgical complications were seen in 278 (26.3%) patients (Table 4). Incidence of anastomotic leakage, which was the most common postoperative complication, was 9.1%. Of these, 36 patients were reoperated. There was no mortality within 30 days after surgery.

Curative surgery was performed in 1011 cases (95.6%). The reasons for noncurative surgery were liver metastasis in 28 cases, lung metastasis in 9, peritoneal dissemination in 6, and other metastases in 9 cases. The mean follow-up

Table 3 Operative and postoperative outcomes

Operative time (min)[a]	270 (122–780)
Blood loss (ml)[a]	90 (0–1800)
Time to oral intake (days)[a]	2 (1–70)
Time to first stool (days)[a]	4 (0–31)
Length of stay (days)[a]	15 (6–270)

[a] Values are median (range)

Table 4 Postoperative complications

Surgical complications, *n* (%)	235 (22.2)
Anastomotic leakage	84 (9.1)[a]
Wound infection	71 (6.7)
Bowel obstruction	38 (3.6)
Bleeding (including bleeding from anastomotic site)	15 (1.4)
Abscess	11 (1.0)
Others	16 (1.5)
Nonsurgical complications (%)	43 (4.1)
Urinary	16 (1.5)
Peripheral nerve	13 (1.2)
Pulmonary	6 (0.6)
Liver	2 (0.1)
Others	6 (0.6)
Mortality	0 (0)

[a] Patients undergoing Hartmann's procedure or abdominoperineal resection were excluded

Numbers in parentheses are percentages

Table 5 Recurrences and 3-year disease-free survival

Site of recurrence (%)	72
Lung	23 (31.9)
Liver	21 (29.2)
Local	11 (15.3)
Peritoneum	4 (5.7)
Others	13 (5.6)
Three-year disease-free survival (%)	
TNM stage	
0	100
I	94.6
II	82.4
III	79.7

Numbers in parentheses are percentages

period was 906 days (5–4,185 days). Recurrence was developed in 67 patients (6.6%) of the 1,011 curatively treated patients. The site of the first recurrence was the liver in 21 cases, the lung in 23, the local in 11, the peritoneum in 4, and other sites in 13 cases. The recurrence was detected during the first year in 22 patients and during the second year in 28 patients. There was no port-site metastasis. Of the 1,011 curatively treated patients, the 3-year disease-free survival rate was 100% in stage 0, 94.6% in stage I, 82.1% in stage II, and 79.7% in stage III (Table 5).

Discussion

The present study showed that laparoscopic surgery for rectal cancer is safe and feasible, with a low conversion rate, and provided favorable short-term and mid-term outcome. Conversion to open surgery occurred in 77 patients (7.3%), which was low compared with previously published data (10–30%) [1, 4, 5, 11, 12]. A low conversion rate was also reported by a few specialized centers [19, 26]. One of the reasons for the low conversion rate may be that the present study included a selected group of patients with rectal cancer, i.e., mainly early rectal cancer, which means that bulky, advanced tumors were not included. A bulky tumor in the narrow male pelvis is one of the reasons for conversion. Another reason might be that very few Japanese patients were overweight, the mean body mass index in the present study being less than 23 kg/m^2. The other reason might be that the definition of conversion was an incision more than 8 cm, which was liberal. Some procedures can be carried out with an incision of 8 cm in thin patients under direct vision, however, length of incision was the only parameter that could be collected in a multicenter, retrospective study. Conversion itself is not necessarily a negative event, but the appropriate incidence of the conversion is difficult to determine, however, the authors think that good selection of patients is reasonable and justified, considering that the patients with conversion had a higher incidence of postoperative complications than those without conversion in other studies [13].

The overall morbidity in the present study was 26%, which compares favorably with the published data of 53% in open procedures [3]. The most common postoperative complication was anastomotic leakage, with an incidence of 9.1%, which is consistent with published reports that report incidence in the range from 7% to 17% [5, 19, 20, 24]. Several risk factors have been reported be associated with postoperative complications, especially anastomotic leakage, including male sex, obesity, and the level of anastomosis [21, 23]. There are several reports on higher anastomotic leak rates after total mesorectal excision than in conventional surgery [3, 14]. Although some authors reported leak rates less than 5% after total mesorectal excision [26], others reported leak rates as high as 10–20% [3, 10]. The incidence of anastomotic leakage in laparoscopic rectal surgery seems to be higher than that in open surgery, however, there are some reports showing no differences in leak rates between the laparoscopic and open procedures [11, 20].

One technical factor could be one of the reasons for the higher leakage rates in laparoscopic rectal surgery. In the double stapling technique, the circular stapler used in laparoscopic procedures is basically the same as in open procedures, whereas the linear staplers are different. Some surgeons in the present study group used laparoscopic linear staplers through a suprapubic port to transect the rectum intracorporeally. Although articulated staplers are now available, at least two, or sometimes three or four, linear staplers are needed, thus resulting in an unduly long staple line. An unduly long staple line could be a reason for the higher leakage rate, although there are no data regarding the number of linear staplers used and the incidence of anastomotic leakage. Some surgeons in this group attempted to use a conventional linear stapler such as the TA stapler (Tyco, USA), Roticulator (Tyco, USA) or Access (Ethicon Endo-Surgery Inc., Cincinnati, USA), for open procedures through a small incision under direct view, which is sometimes difficult because it provides poor visualization of the deep narrow pelvis through a small incision. Recently, a new curved cutter stapler has become available, and its application to laparoscopic anterior resection might be a good alternative [15].

A diverting ileostomy was fashioned at the surgeon's discretion in the present study. The incidence of a diverting stoma for the lower rectum was 23.9% in the present study, which may be somewhat high. Some surgeons routinely fashion a diverting ileostomy for laparoscopic anterior

resection for rectal cancer [18]. The presence of a stoma does not prevent the development of anastomotic leakage, however, it can prevent a subsequent disaster.

One may criticize the relatively long postoperative hospital stay of 14 days in the present study. Because most Japanese insurance schemes cover the complete cost of hospitalization, there is still little incentive for early discharge. As a result, length of hospital stay is not yet a major concern for both patients and surgeons, which is a completely different situation from that in Western countries.

This study had several limitations in that it included only selected patients with rectal cancer because the indications for laparoscopic surgery expanded gradually as the authors gained experience, and the indications differed among the institutions. Patients with far advanced rectal cancer were not included and, when surgery was indicated, open procedures were adopted. Therefore, this study was not intended to be a strict comparison of open with laparoscopic procedures, and the mid-term or long-term outcome may be irrelevant. Neoadjuvant therapy has not been established and surgery is the first choice for rectal cancer in our country. Another study on preoperative chemoradiation for lower rectal cancer is now running. In the next study, preoperative chemoradiation may be a choice of treatment for lower rectal cancer. Only five patients receiving preoperative radiation or chemoradiation were included, and the feasibility of laparoscopy in these patients should also be evaluated in the future. Although the incidence of anastomotic leakage was 9.1% in the present study, which was comparable to other studies, the incidence of a diverting stoma was high. A prospective phase II study is being conducted by the authors' group to elucidate this matter, and a randomized controlled trial should be conducted to clarify the benefits of laparoscopic surgery for rectal cancer; however, the authors believe that the findings of the present study are of value in proposing the future studies.

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先人のコツ①
直腸診－基本的態度－

山口高史

Point

① 便秘，下痢，出血など排便に関する症状のある患者には必ず直腸診を行おう
② 不必要な苦痛を与えないように，やさしく丁寧に診察しよう
③ 便潜血検査のために直腸診をするのではない．視診，触診，便の観察が大事である
④ 直腸内を奥まで手首，腕，体を使って隈なく観察しよう

はじめに

直腸診で診察すべき点は多く，肛門，直腸，前立腺（子宮頸部，膣），ダグラス窩などそれぞれの専門的診断となると奥が深い．しかし一般医に求められるのは異常の検知である．**直腸診の経験を積み正常を知ると異常に気づくようになる．**必要な症例には積極的に直腸診を行うようにしよう．

1 直腸診の流れ

① 体位は左側臥位で右示指の腹で診察する
② 直腸診の前に肛門部の視診も行う
③ 指診はゼリーをたっぷりつけてゆっくりと
④ 肛門管，直腸内を奥まで隈なく触診する
⑤ ダグラス窩など腹腔内も観察する
⑥ 指についた便を観察する
⑦ 肛門を拭くなど後始末も大切

見逃されるポイント

① 直腸癌発見までに直腸診がされていない
② 直腸診はやっているが直腸癌を発見できていない
③ 診察が荒く患者に不要な苦痛を与えている

2 ミスの原因と対処法

・以前から痔があるという患者の申告を信用して肛門出血があっても直腸診をしていない，貧血で内視鏡検査はするが直腸診はしていないなどが見られる

→ 対処法：直腸診は患者も医者も嫌なものだが，専門医でなくても簡単，安全にできる手技である．排便症状，貧血のある場合には必ず行う

・外来の直腸診では内視鏡検査前のクリーンな直腸と違い，便塊などのために進行癌でも存在診断すら難しいこともある

→ 対処法：便をかき分け時間をかけて丁寧に直腸全周にわたって診察するしかない

・診察の際に少量のゼリーで一気に直腸内に指を挿入し患者がのけぞっている．診察は短く便性状も見ずに便潜血反応検査を行う．診察後は肛門を拭きもせず終了，などを見かける

→ 対処法：**荒っぽく診察すると所見がとりにくくなる．直腸診に対する意識を変え，やさしく丁寧に診察する**

3 直腸診のコツ

1）体位のコツ

基本は左側臥位だが前方が触りにくいので手首だけでなく腕，体を使って全周性に診察する（図1 A）．非常に診察しにくい患者や前方を主に診察したければ砕石位にするとよい（図1 B）．

2）挿入のコツ

ゼリーをたっぷりつけてゆっくりと．キシロカイン®ゼリーはすべりが非常によく有用（肛門でのアナフィラキシーは非常に稀）．指をゆっくり挿入し肛門管入口でいったん止まるくらいの感じ（図2）．もう一度ゼリーをつけなおすこともある．なお，しっかり診察する場合指サックでは手に便やゼリーがついてしまうので**普通の手袋がよい．**

3）病変を見過ごさないコツ

便塊が充満している場合などは便塊をかき分けてしっかり診察する．全周性に，指が届くかぎり奥まで診察．直腸内に入っても丁寧に触ったり押したりする．荒っぽく触診すると何も病

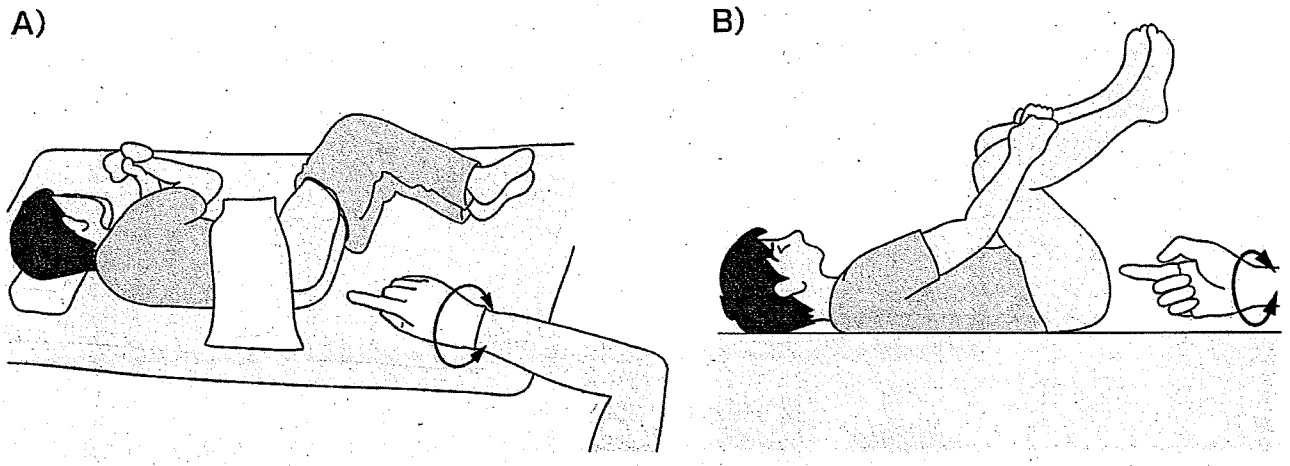

図1 直腸診時の体位
A）基本体位は左側臥位だが前方が触りにくい．手首，腕，体を使って全周性に観察する．
B）前方をしっかり診察したい場合砕石位にしてもよい．

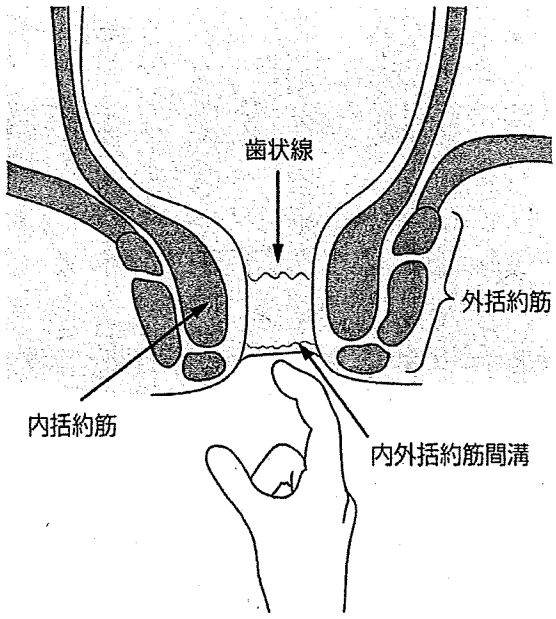

図2 直腸診時の挿入のコツ
ゼリーをたっぷりつけ指をゆっくり挿入する．肛門管入口（内外括約筋間溝）でいったん止まるくらいの感じ．

変がなくても痛みを訴えることがある．しっかり所見をとるには結構苦痛を伴うこともあるが，それ以前の段階で苦痛を与えてしまうと詳細な診察は不可能になる．**意味のある診察には時間がかかるものである．**痔のありなしを簡単に言ってはいけない．普通の視診や触診で簡単にわかるのは内痔核の脱出（脱肛）や血栓性外痔核くらいである．

4）苦痛を与えないコツ

挿入に気を使い肉体的苦痛を少なくするのはもちろんのこと，声をかけることも患者に精神的安心を与えるため重要である．診察前にはちょっと気持ち悪いですが力をぬいてくださいなどと声をかけ，診察中も，奥の方までしっかり診ているので少しつらいですがなどと時折話しかける．終了後は肛門をしっかり拭く，お疲れ様でしたと声をかけるなど**後始末も大切である．**

最後に

専門医側からみると，紹介状に直腸診の所見が記載してあるだけで感心してしまう．基本的なことだけでよいのでマスターしよう．

Profile

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進行再発大腸癌に対する全身化学療法併用肝動注の検討

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Intermittent Hepatic Arterial Infusion with Systemic Chemotherapy for Metastatic Colorectal Cancer: Yoshihito Ide[*1], Koji Mikami[*2] and Kohei Murata[*1] (*1*Dept. of Surgery, and* *2*Dept. of Radiology, Suita Municipal Hospital*)

Summary

We report 5 cases of metastatic colorectal cancer with intermittent hepatic arterial infusion (HAI) and systemic chemotherapy (CPT-11, biweekly) in 2006-2008. Two patients with poor performance status were for systemic chemotherapy, and 3 patients were initiated as third-line treatment or more. Among the 5 patients, 2 patients were recorded as PR, 2 patients were as SD, and 1 patient was as NE. Three patients are alive with a mean follow-up of 19 months. HAI is intended to have few side effects compared with the systemic chemotherapy, and the treatment methods for these cases were not indicated for any of standard chemotherapies. But HAI alone is considered as insufficient treatment for unresectable liver metastasis, because HAI cannot be proved to have an apparent survival benefit. It is possible that a combination of regional and systemic drug treatments will be more effective than systemic treatment alone for unresectable colorectal cancer.

Key words: Hepatic arterial infusion (HAI), Liver metastasis, Colorectal cancer

要旨 2006年4月～2008年12月までに当院で行われた，大腸癌肝転移に対する全身化学療法併用肝動注治療例5例をretrospectiveに検討した。5例のうちPSが悪く，肝動注をfirst-lineとして選択した例が2例，third-line以降に使用されたものが3例であった。レジメンは肝動注（5-FU毎週投与）のみから導入し，CPT-11の全身投与を隔週で追加したものが3例，初回から併用したものが2例であった。最良効果はPR 2例，SD 2例，NE 1例であった。2例が原病死し，3例が現在も治療中である［観察期間578日（407～1,050日）］。肝動注療法は副作用が少なく，FOLFOXなどの標準的な全身化学療法が適応とならない症例に対しても使用できる。局所制御率が高いものの，肝以外の病巣の制御ができないことが短所であったが，全身化学療法と併用することにより生存期間の延長も期待される。結語: 全身化学療法併用肝動注は，全身状態不良例，標準的治療無効例においても効果が期待できる治療であり，その意義は大きいと考える。

はじめに

大腸癌肝転移に対する第一の治療法は切除であるが，切除不能肝転移に対しては全身化学療法が選択される場合が多い。近年，本邦においても分子標的治療薬を含めたkey drug 5剤がそろい，全身化学療法の成績の進歩は目をみはるものがある。一方，肝動注療法は副作用が少なく，局所制御率に優れていることが知られているが，生存期間への効果は明らかではなく，現時点では標準治療とはなっていない。しかし欧米と本邦では方法，使用薬剤が異なっており，優れたIVR技術を有している本邦においては，肝動注療法はいまだ役割を失っていないと考える。特に全身化学療法を併用することにより，生存期間の延長も期待できると考えられる。当院における全身化学療法併用肝動注施行例をretrospectiveに検討し，その意義について考察する。

I. 対象，方法

2006年4月～2008年12月までに当院で行った，大腸癌肝転移に対する全身化学療法併用肝動注治療例5例を対象とした。レジメンは5-FU（1,000 mg/m^2）毎週投与（weekly high-dose 5-FU: WHF）から導入し，後にCPT-11（80～120 mg/m^2, biweekly）を追加したものが3例，初回から併用したものが2例であった。

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表 1 肝動注施行例

症例	年齢（歳）	原発巣	進行・再発	First-line	Second-line	Third-line	Fourth-line	Fifth-line
A	78	S	進行	WHF	WHF＋CPT	mFOLFOX6＋bev		
B	61	RS	進行	WHF	WHF＋CPT	mFOLFOX6＋bev	cet＋CPT	
C	60	S	再発	mFOLFOX6＋bev	FOLFIRI＋bev	WHF＋CPT	cet	
D	62	S	再発	IRIS	mFOLFOX6＋bev	FOLFIRI＋bev	WHF＋CPT	cet
E	60	Ra	進行	mFOLFOX6＋bev	IRIS＋bev	WHF＋CPT		

IRIS: S-1＋CPT-11, WHF: weekly high-dose 5-FU（肝動注）, CPT: CPT-11, bev: bevacizumab, cet: cetuximab

II. 結　果

肝動注施行例5例を示す（表1）。5例のうち，PSが悪く，肝動注をfirst-lineとして選択した例が2例（症例A，B），third-line以降に使用されたものが3例（症例C，D，E）であった。観察期間中に投与されている化学療法は3レジメン2例，4レジメン2例，5レジメンが1例であった。5-FUは中央値で12回（3～34），CPT-11は4回（2～14）投与されていた。最良効果はPR 2例，SD 2例，NEが1例であった。奏効率は40%（2/5例）で，first-lineとしては50%（1/2例），third-line以降としては33%（1/3例）であった。無増悪生存期間は治療開始後から155日（中央値，41～302日）であった。有害事象は，肝動脈閉塞1例，胆嚢炎1例，末梢神経障害（grade 3）を1例に認めた。肝動注治療の中止理由（重複あり）は有害事象によるものが2例，病状の増悪によるものが4例であった。2例が原病死（生存期間407日，504日）し，3例が現在も化学療法中である［観察期間578日（407～1,050日）］。

III. 考　察

切除不能大腸癌に対する標準的治療法は全身化学療法であり，海外を主とする膨大な臨床試験結果を根拠にFOLFOX，FOLFIRIなどに分子標的治療薬を加えたいくつかの方法が広く使用されている。しかし全身状態不良のため，強力な全身化学療法の適応とならない症例や，いわゆる標準的治療がすべて使用されたものの，肝転移巣が生命予後に最もかかわる場合などには，局所治療としての肝動注を含めた治療法を選択する場合もある。

一方，肝動注療法はその高い局所制御率から汎用されてきた治療法であるが，欧米でのRCTを検討したmeta-analysisでは生存期間に対する効果が乏しく，切除不能肝転移に対するfirst-lineに選択すべきではないと結論された[1]。しかし欧米と本邦では内容，方法が大きく異なっている[2]。欧米では5-FUまたは5′-DFURの持続投与，主に開腹によるカテーテル留置であるが，日本では5-FUの間欠的持続投与，IVRによる経皮的カテーテル留置であり，特に放射線科医の高いIVR技術は日本独自のものであると考えられる。米国のガイドライン（NCCN Practice Guideline in Oncology-Ver. 2.0 2009）においては，肝動注療法はまったく登場していないが，本邦における大腸癌治療ガイドライン 医師用2009年版[3]においては，切除不能肝転移に対して全身化学療法と肝動注療法の単独または併用を考慮すると明記されており，ガイドライン改訂に伴い評価が高まっている。特に全身化学療法との併用による効果についてはいくつかの報告があるが[4,5]，KemenyらはHAIにoxaliplatinとCPT-11の全身投与を併用したphase I studyにおいて，切除不能肝転移例の47%を切除可能にconversionすることができたと報告しており[6]，今後全身化学療法単独治療を凌駕する治療法として注目できる。

しかし現時点ではHAIに全身化学療法を併用する治療法はエビデンスが不足しており，標準治療とはいい難い。そこで自験例のような適応が検討され得る。全身状態不良例，特に肝転移が全身状態に大きく影響していると考えられるような症例に対して肝動注単独から治療を開始し，全身状態が改善した後，全身化学療法を併用するというstrategyは有用であり，自験例の症例A，B[7]はそれに該当する。また，症例C，Dにおいてはoxaliplatin，CPT-11をbaseとした標準治療が無効となったものの，肝動注＋CPT-11のレジメンを施行しながら病状を制御することによって，その後使用可能となったcetuximabが導入できている。

肝転移が生命予後にかかわると考えられる症例に対する，全身化学療法併用肝動注のfirst-lineとしての意義は不明である。今後本報告のような標準治療不能例での症例を集積しながら，RCTによってエビデンスを構築していく必要がある。また，oxaliplatinや分子標的治療薬と併用することにより，より効果の高い治療法の開発も期待できる。

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Second Primary Cancer in Patients with Colorectal Cancer after a Curative Resection

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Key Words
Colorectal cancer · Second primary cancer · Extracolorectal cancer · Observed/expected ratio

Abstract
Background: Colorectal cancer (CRC) patients have an increased risk of developing other malignancies. Understanding the characteristics of the second primary cancer is important to establish an effective surveillance program. ***Methods:*** This study investigated 301 CRC patients to assess the risk factors for postoperative primary cancers arising from organs distinct from the colorectal area (extracolorectal cancers). The observed/expected ratio (O/E ratio) was calculated using the Osaka Cancer Registry, to determine the rate of increase in extracolorectal cancers. ***Results:*** The frequency of postoperative extracolorectal cancers was 12.6%. A logistic regression analysis showed only age to be an independent risk factor for postoperative extracolorectal cancer development. The O/E ratio of overall postoperative extracolorectal cancer was significantly higher than one (O/E ratio 2.6, $p < 0.01$). In each organ, the frequency of lung and gastric cancers were significantly higher than one, with O/E ratios of 3.2 and 2.7 ($p < 0.01$ and $p < 0.05$, respectively). ***Conclusion:*** The frequency of postoperative extracolorectal cancers in CRC patients was significantly higher than that in the normal population, especially for lung and gastric cancers. Clinicians should carefully follow patients for a possible recurrence of CRC and educate CRC patients with regard to the high risk of a second primary cancer.

Introduction

Colorectal cancer (CRC) is among the most common malignant disorders in Western populations, whereas cancers of the upper gastrointestinal tract (esophagus and stomach) and liver have predominated in the East. However, many Asian countries, including Japan, have experienced an increase of two- to fourfold in the frequency of CRC during the past few decades [1, 2]. The 5-year relative survival rate of approximately 50–60% [1] results in patients with one primary neoplasm who are at risk for developing a second neoplasm due to the effect of shared risk factors, either as a consequence of treatment

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for the initial cancer or because of intensified medical surveillance, thus resulting in an earlier detection of a second cancer or, due to the effect of shared risk factors.

The present study was designed to assess the risks of second primary cancers by employing a logistic regression analysis and by calculating the observed/expected (O/E) ratio using the correlative data file of the Osaka Cancer Registry, one of the world's largest cancer databases [3, 4]. Determining the frequency and the susceptible organ in second primary cancers is therefore important for the postoperative follow-up.

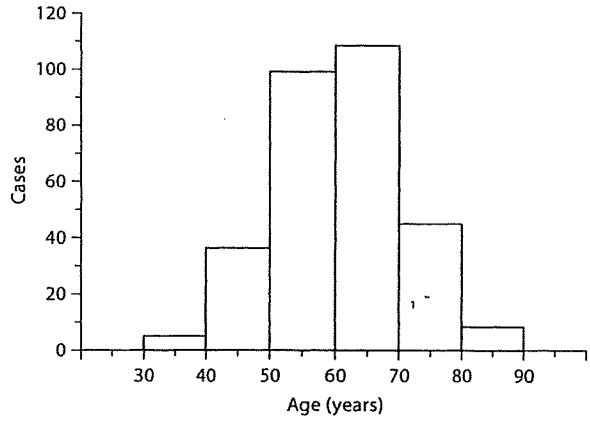

Fig. 1. Patient age distribution.

Patients and Methods

Patients

During the period between January 1991 and December 1996, 301 CRC patients who underwent curative surgery at Osaka Medical Center for Cancer and Cardiovascular Diseases were selected for this study. The selection criterion was that these patients had no history of cancer at the time of the CRC diagnosis. The majority of the tumors were well-differentiated adenocarcinoma (n = 172), followed by moderately differentiated adenocarcinoma (n = 117), and other carcinomas (poorly differentiated adenocarcinoma, mucinous adenocarcinoma, and signet-ring cell carcinoma; n = 12). The TNM stage [5] included 121 stage I patients, 87 stage II patients, and 93 stage III patients. None of the patients underwent either preoperative chemotherapy or irradiation. The patients included 190 males and 111 females, with a median age of 61 years (range, 33–89 years, fig. 1). Sixty-two tumors were located in the right-side colon (cecum–transverse colon), 148 in the left-side colon (descending colon–sigmoid colon), and 91 in the rectum. Forty-five patients had a familial history of cancer that included CRC. We defined metachronous and synchronous carcinomas according to the criteria used by Warren and Gates [6]; synchronous carcinoma was defined as tumors detected after an interval of less than 1 year, and metachronous carcinoma was defined as tumors detected after an interval of 1 year or longer. Nine patients had hereditary nonpolyposis colorectal cancer (HNPCC) according to the Amsterdam criteria II [7]. The patients were followed postoperatively for at least 5 years or until death. When the follow-up was interrupted, detailed information was available from the Osaka Cancer Registry. After surgery for CRC, newly detected primary cancers arising from organs distinct from the colorectal area (extracolorectal cancers) were counted as 'second primary cancer'.

Osaka Cancer Registry

The Osaka Cancer Registry is a cooperative effort of the Osaka Prefectural Department of Health and Welfare, the Osaka Medical Association, and the Osaka Medical Center for Cancer and Cardiovascular Diseases [3, 4]. The Osaka Cancer Registry registers all primary malignant neoplasms in the Osaka Prefecture, which had a population of 8.8 million people in 2000. In this system, the site of origin, histological findings, clinical stage, and primary treatments are documented for all first and subsequent primary malignant neoplasms. Follow-up information, including the last date of contact and cause of death where applicable, is also available. This registry provides the age-, period-, and gender-matched incidences in Osaka, and is reported in *Cancer Incidence in Five Continents,* because its accuracy meets the standards established by the International Agency for Research on Cancer [8].

The method for calculating the 'expected incidence' of postoperative extracolorectal cancers has been previously described [9, 10]. Person-years at risk were calculated from the date of diagnosis of the CRC until the date of diagnosis of the second primary cancer, date of death, or the closing date, December 31, 2005, whichever occurred first. The patients for whom there were no matching death certificates were assumed to be alive at the closing date. Using gender and age at surgery for each CRC patient, the expected incidence of postoperative extracolorectal cancers was estimated from the average incidence rates of the Osaka Cancer Registry database from 1999 to 2001.

The incidence of postoperative extracolorectal cancer for each patient was calculated and defined as the 'observed incidence' of postoperative extracolorectal cancers.

Diagnosis of CRC and the Follow-Up System

The preoperative diagnostic and staging procedures performed included colonoscopy, chest X-rays or CT, abdominal + pelvic CT, abdominal ultrasonography, serum tumor markers, and occult blood tests of stool and urine. The preoperative surveillance of extracolorectal cancer was not standardized, but it was performed according to the preference of the attending surgeon. Briefly, chest X-rays, abdominal ultrasonography, and occult blood tests of stool and urine were the minimum examinations performed for all patients.

After surgery, all patients were followed for at least 5 years; this included a physical examination, serum tumor marker analysis, hepatic imaging (US and/or CT), pelvic CT, chest X-ray or CT every 4–6 months for the first 3 years and every 6 months for the next 2 years, and colonoscopy every 1–2 years. Basically, only recurrence of CRC was followed and further cancer screening was not conducted, except for CRC. CRC patients are therefore ad-

Table 1. Time interval (years) and number of second primary cancers

Second primary cancer site	Time interval				Total
	0–3	3–5	5–10	>10	
Stomach	5	3	0	0	8
Lung	6	2	0	0	8
Liver	4	1	1	0	6
Gallbladder	1	1	1	0	3
Blood	1	1	1	0	3
Prostate	0	1	1	0	2
Ureter	1	0	1	0	2
Others	5	2	1	0	8
Total	23	11	6	0	40

vised to receive cancer screening not only during the follow-up but also after the follow-up.

Statistical Analysis

A statistical evaluation was performed by the Mann-Whitney U test, χ^2 test or the Fisher exact test with the use of the StatView software program (SAS Institute Inc, Cary, N.C., USA). A multivariate analysis using logistic regression modeling was also performed to determine the independent predictive factors for extracolorectal cancers. The significance of the O/E ratios was tested by a Poisson distribution analysis [11]. All data are expressed as the mean ± SD. A p value of <0.05 was considered to be statistically significant.

Results

Frequency of a Second Primary Cancer

Mean follow-up period was 6.8 ± 2.6 years. A second primary cancer was detected in 38 patients (12.6%) after a curative resection for CRC. Thirty-six of the patients had a single second primary cancer and 2 patients had two second primary cancers.

The time interval and the number of second primary cancers are summarized with some overlapping data in table 1. Of 38 patients, 13 patients had synchronous carcinoma, 24 patients had metachronous carcinoma, and one patient had both synchronous and metachronous carcinoma. The major sites of the second primary cancer were the stomach (n = 8), lung (n = 8), and liver (n = 6). The major sites were the stomach (n = 6) in males and liver (n = 2) in females. The mean interval from surgery to diagnosis of the second primary cancer was 2.5 ± 2.7 years. Twenty-three (57.5%) of 40 cancers occurred less than 3 years after the resection of CRC. Thirty-four (85.0%) of 40 cancers occurred after less than 5 years. However, 6 cancers (15.0%) were recognized more than 5 years later. There were no patients who had a second primary cancer more than 10 years later.

Table 2. Characteristics of patients with and without second primary cancers (univariate analysis)

	Second primary cancer + (n = 38)	Second primary cancer – (n = 263)	p value
Age, years	63.9 ± 9.1	59.9 ± 9.6	0.0049
Sex			
Male	29 (76%)	161 (61%)	0.0713
Female	9 (24%)	102 (39%)	
Tumor site			
Right-side colon	5 (13%)	57 (22%)	0.0896
Left-side colon	25 (66%)	123 (47%)	
Rectum	8 (21%)	83 (32%)	
Histological grade			
Well	24 (63%)	148 (56%)	0.5922
Mod	12 (32%)	105 (40%)	
Others	2 (5%)	10 (4%)	
TNM Stage			
I	13 (34%)	108 (41%)	0.1539
II	16 (42%)	71 (27%)	
III	9 (24%)	84 (32%)	
Family history of colorectal cancer			
+	2 (5%)	15 (6%)	0.9999
–	36 (95%)	248 (94%)	
Family history of all cancers			
+	7 (18%)	38 (14%)	0.4435
–	31 (82%)	225 (86%)	
Multiple colorectal cancers			
+	3 (8%)	25 (10%)	0.9999
–	35 (92%)	238 (90%)	
HNPCC			
+	1 (3%)	8 (3%)	0.9999
–	37 (97%)	255 (97%)	
Follow-up period, years	6.7 ± 3.3	6.8 ± 2.4	0.7728

Right-side colon = Cecum–transverse colon; left-side colon = descending colon–sigmoid colon; Well = well-differentiated adenocarcinoma; Mod = moderately differentiated adenocarcinoma; Others = poorly differentiated adenocarcinoma, mucinous adenocarcinoma and signet-ring cell carcinoma.

Relationship between the Second Primary Cancer and Clinicopathological Characteristics Based on a Univariate Analysis

Table 2 lists the clinicopathological characteristics of the 301 patients with and without a second primary can-