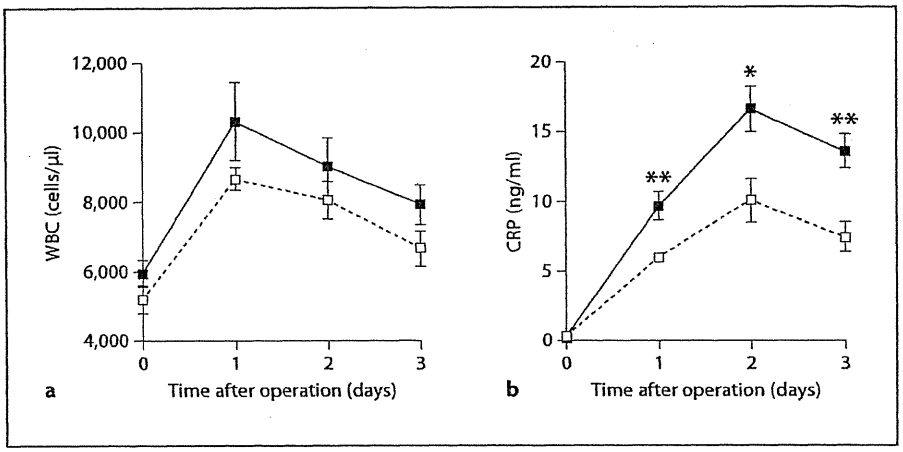

Fig. 1. Changes in white blood cell count (WBC; **a**) and CRP levels (**b**). □ = Laparoscopic ISR; ■ = open ISR. The difference between the 2 groups in CRP levels was significant: * $p < 0.05$; ** $p < 0.01$. Each bar represents the mean ± standard error.

Table 2. Patient characteristics in the case-control study

	Laparoscopic ISR group	Open ISR group	p value
Number of patients	22	22	
Sex ratio (male:female)	16:6	16:6	1
Mean age, years	55 (34–68)	58 (35–69)	0.4334
Mean body mass index	21.8 (16.8–26.7)	22.5 (19.3–28.9)	0.1804
Prior abdominal surgery	6 (27.2)	7 (31.8)	1
Preceding local resection	7 (31.8)	4 (18.2)	0.4876
ASA (I:II)	14:8	17:5	0.1464
Pathological stage (TNM stage)			
Stage I	17	18	
Stage II	1	1	
Stage III	4	3	
I:II+III	17:5	18:4	1
Mean tumor size, mm[1]	22 (15–38)	28 (11–55)	0.1549
Median lymph nodes resected	13 (3–27)	14 (529)	0.929

Values in parentheses are ranges or percentages. [1] Preoperatively locally resected cases not included.

Table 3. Intraoperative and postoperative results

	Laparoscopic ISR group	Open ISR group	p value
Operative time, min	385 (305–500)	299 (202–475)	0.0007
Blood loss, ml	139 (45–477)	434 (76–1108)	0.0003
Conversion	0	–	–
Preservation of left colic artery (yes:no)	4:18	4:18	1.0000
Combined surgery (yes:no)	2:20	1:21	1.0000
Colonic pouch (yes:no)	4:18	4:18	1.0000
Time to liquid intake, days	1 (1–2)	3 (2–11)	<0.001
Time to solid intake, days	2 (2–3)	5 (3–12)	<0.001
Length of hospital stay, days	8 (7–10)	14 (10–40)	<0.001

Values are numbers or medians (range).

Table 4. Morbidity and mortality

	Laparoscopic ISR group	Open ISR group	p value
Mortality	0	0	
Morbidity			
Anastomotic leakage	1	1	
Wound sepsis	1	4	
Bowel obstruction	1	2	
Perianastomotic abscess	1	1	
Urinary tract infection	1	1	
Dehydration	1	2	
Mucosal prolapse	2	1	
Cholecystitis	0	1	
Total number of patients	7 (32%)	13 (59%)	0.12922

panded the indication for new procedures. In the present study, a review was performed of laparoscopic ISR for lower rectal cancer, and our results demonstrated that it is a safe procedure and provides benefits in the early postoperative period without increasing morbidity or mortality. Moreover, this is the first report to conduct a comparative study between laparoscopic and open ISR, and the findings of the current study demonstrated the feasibility and safety of laparoscopic ISR compared to open ISR for selected patients with lower rectal cancer.

ISR is a demanding technique that requires experienced colorectal surgeons, regardless of whether it is performed as open or LS, and the number of surgeons who can perform laparoscopic ISR is particularly limited. In a comparison of open and laparoscopic ISR in a relatively small number of cases, Fujimoto et al. [12] found that the complication rates of the two methods did not differ. The results of the present study are similar to their results, and moreover, we found that postoperative inflammatory reactions were significantly lower after laparoscopic ISR than open ISR, based on decreased CRP levels after laparoscopic ISR. These differences in inflammatory markers suggest that laparoscopic ISR may be less invasive than open ISR. In addition, the oncological outcomes after laparoscopic ISR were acceptable with a low recurrence rate, although we note that many of the patients who underwent laparoscopic ISR had early-stage disease. These results suggest that the indications for laparoscopic ISR can be expanded, provided that the operation is conducted by an experienced surgical team.

It is noteworthy that anastomotic leakage was relatively low after laparoscopic ISR in the present study. Anastomotic leakage after rectal cancer surgery performed by open or laparoscopic techniques with per anal hand-sewn anastomosis or the double-stapling technique (DST) can result in reoperation, morbidity, mortality, permanent stoma, prolonged hospitalization, anal stenosis and anal dysfunction, and may be associated with a higher local recurrence rate. Tension-free anastomosis with full mobilization and anastomosis at a site with good blood flow are important factors to avoid leakage. In addition, the high anastomotic leakage rate in ISR in previous reports suggests that a covering ileostomy is needed to stabilize the anastomotic region in a resting position [4–6, 9–12]. In our institution, the anastomotic leakage rate in open ISR has decreased with the accumulated experience of surgeons, and fortunately, the anastomotic leakage rate was relatively low in laparoscopic ISR. Thus, when performed by surgeons with sufficient LS skills, laparoscopic ISR can be regarded as a safe procedure.

In the previous study, Laurent et al. [19] reported that the risk of anastomotic leakage is increased in male patients with lower rectal cancer in laparoscopic LAR with DST reconstruction; therefore, they recommended open or coloanal hand-sewn anastomosis in male patients with rectal cancer. In our institution, the anastomotic leakage rate was 7.7% (3/39) in patients with low rectal cancer who underwent laparoscopic LAR with DST reconstruction. This rate was higher than that in patients who underwent laparoscopic ISR. Therefore, LS with DST reconstruction may not be the best choice in male patients or in patients in whom laparoscopic LAR with DST reconstruction is difficult, and coloanal anastomosis should be considered in these cases.

There are several limitations in the design of the study. First, the study was not randomized but was performed retrospectively, which may have caused bias. Thus, a prospective, multicenter, randomized clinical trial (RCT) is required to demonstrate that laparoscopic total mesorectal excision with ISR is a feasible procedure for very low rectal cancer; however, due to the lack of sufficient patients to perform an RCT, we chose to analyze the safety of laparoscopic ISR in a single-center study. Second, a longer follow-up is required to assess the incidences of local recurrence, cancer-free survival, and functional outcome. Third, patients who underwent preoperative adjuvant chemoradiotherapy or lateral lymph node dissection were not included because most of the patients who underwent laparoscopic ISR in the present study were in clinical stage I. Another concern for preoperative adjuvant chemoradiotherapy is that preoperative chemoradiotherapy was identified as the risk factor with the greatest negative impact on anal

function after ISR [20]. The outcomes of patients without preoperative adjuvant chemoradiotherapy in our hospital have been reported previously, and we conducted preoperative adjuvant chemoradiotherapy only in patients with clinical T4 cancer and/or involvement of lateral pelvic lymph nodes [21]. Open surgery is still our gold standard approach for patients with locally advanced rectal cancer, and the safety of the laparoscopic approach requires further examination in patients with advanced rectal cancer.

Laparoscopic ISR for lower rectal cancer provides benefits in the early postoperative period without increasing morbidity or mortality, and shows long-term benefits that are comparable to those after open ISR in selected patients with lower rectal cancer. In the absence of a large-scale RCT comparing open and laparoscopic ISR, and given the small number of institutions capable of conducting high-quality laparoscopic ISR, the safety of this procedure requires confirmation through prospective accumulation of more cases.

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トレーニングシステムと技術認定の動向

日本内視鏡外科学会技術認定制度の現況；消化器・一般外科領域

JSES Endoscopic Surgical Skill Qualification System : General and Gastroerterological Surgery

小西 文雄[*, *5] 木村 泰三[**, *5] 森 俊幸[***, *5] 松田 公志[*4, *5]
Fumio Konishi *Taizo Kimura* *Toshiyuki Mori* *Tadashi Matsuda*

●要旨●本邦における安全かつ十分な治療となる腹腔鏡下手術が発展することを目的として，2004年に日本内視鏡外科学会における技術認定制度が発足した。本制度は，消化器・一般外科のみならず，呼吸器外科，小児外科，産科婦人科，泌尿器科，整形外科などの領域における内視鏡外科手術技術を高い基準に従って評価し，後進を指導するに足る所定の基準を満たした者を認定することを目的としている。この技術認定制度は，未編集の匿名化されたビデオを審査員が見て申請者の技術を審査するという世界に類をみない手術手技の技術認定制度である。2004～2009年全体の合格率の平均は，44.9%であった。この合格率は，本制度では比較的厳しい評価による技術認定を施行していることを示している。本制度が，「後進を指導するに足る所定の基準を満たした者を認定する」ことを目的としていることから考えると，この合格率はほぼ適切なものと考えられる。

● key words：内視鏡外科手術，手術技術，技術認定

はじめに

腹腔鏡下手術は1990年に胆嚢摘出術が開始されて以来，めざましく発展した。腹腔鏡下手術件数は年々増加し，2009年の日本内視鏡外科学会（JSES）のアンケート調査によると，2009年には6万件にもおよぶ腹腔鏡下手術が集計されている[1)]。腹腔鏡下胆嚢摘出術は，1990年代の半ばでプラトーとなり，その後は徐々に増加している。これに対して，腹腔鏡下大腸切除や胃切除は難易度が高く，最近になって著しい増加傾向にある。一般的に，内視鏡外科手術は技術的な難易度が高く，十分に習熟した外科医が手術を施行するか手術を指導する必要がある。腹腔鏡下手術によって重篤な合併症をきたすことがあってはならない。技術修練を目的として，日本内視鏡外科学会や関連研究会は，腹腔鏡下手術一般あるいは各種の腹腔鏡下手術について技術講習会を積極的に開催してきた。さらに，本邦における安全かつ十分な治療となる腹腔鏡下手術が発展することを目的として，2004年に日本内視鏡外科学会における技術認定制度が発足した。本制度は，消化器・一般外科のみならず，呼吸器外科，小児外科，産科婦人科，泌尿器科，整形外科などの領域における内視鏡外科手術技術を高い基準に従って評価し，後進を指導するに足る所定の基準を満たした者を認定することを目的としている[2)]。この技術認定制度は，未編集の匿名化されたビデオを審査員が見て申請者の技術を審査するという世界に類をみない手術手技の技術認定制度である。

本制度においては，2004年に第1回の技術認定がなされ，その後2009年まで計6回の認定がなされた。消化器・一般外科領域では，臓器別に応募することになっており，胃，大腸，食道，胆道，脾臓，副腎，腎臓，乳腺，甲状腺，ヘルニアの各臓器に区分されている。筆者は，本制度発足から4年間大腸領域審査の責任者を担当し，さらに昨年より消化器・一般外科領域技術認定の責任者の命を受け，消化器・一般外科全体の技術認定に携わってきた。本稿では，日本内視鏡外

* 自治医科大学附属さいたま医療センター一般・消化器外科教授
** 富士宮市立病院名誉院長
*** 杏林大学医学部外科教授
*4 関西医科大学泌尿器科教授
*5 日本内視鏡外科学会技術認定制度委員会

表1　JSES 技術認定合格率（2004～2009年）

年	受験者	合格者	合格率（%）
2004	422	214	50.7
2005	269	129	48.0
2006	217	88	40.6
2007	203	90	44.3
2008	258	120	46.5
2009	213	70	33.0
合計	1582	711	44.9

表2　JSES 技術認定臓器別合格率（2004～2009年）

	受験者	合格者	合格率（%）
胆道	634	300	47.3
食道	80	36	45.0
胃	345	156	46.5
大腸	429	174	40.6
脾臓	31	16	51.6
内分泌　他	62	31	50.0

科学会技術認定制度の発足時から本制度に関与してきた者として，内容の変遷，審査結果とその妥当性と今後の方向性について述べる。

応募数の推移

消化器・一般外科領域の応募数は，第1回（2004年）が422名と多数であったが，第2回以後はおよそ200～270名の間で推移している。臓器別にみた応募者数の合計（2004～2009年）は，胆道がもっとも多く634名であり，大腸429名，胃345名の順である。食道，内分泌，ヘルニアは，それぞれ100名に満たない応募者数であった（表1，2）。

各領域における応募ビデオの基準と問題点

1. 提出ビデオ基準の推移

第1回および第2回（2004～2005年）は，提出ビデオの手術としては，胃や大腸では疾患や術式を特定せず，腹腔鏡下手術を広く受け付けた。その結果，とくに大腸領域では，大腸癌の手術のみならず，炎症性腸疾患，直腸脱に対する直腸固定術，虫垂切除術など，広い範囲の手術が提出された。大腸領域ではじめの1年間に応募された手術の約8割が大腸癌手術であったがその他の手術も2割あり，大腸癌手術以外の手術で応募された場合には，審査基準に見合った均一な審査が困難であった。そこで，第3回目（2006年）以後は，応募ビデオの手術内容をさらに限定し，S状結腸あるいは直腸癌で，D2あるいはD3郭清がなされ，かつ腹腔内で吻合が施行された症例に限定した。最終的には，対象症例は，S状結腸癌，直腸S状部癌に限定する，D2以上のリンパ節郭清を施行した症例，腹腔内吻合がなされた症例，という規定となった[3)4)]。このように，応募ビデオの手術を限定することによって，審査の均一性が保たれるようになった。胃の領域でも同様の変更がなされ，癌に対する幽門側胃切除，幽門保存胃切除に限定する，体外操作は腹腔鏡カメラによるものでもよいので収録すること，時間制限は設けない，などの規定となった。胆道に関しては，簡単な胆嚢摘出術は90点満点，困難な胆嚢摘出術と総胆管結石手術は100点満点，胆嚢摘出術は3時間以内，総胆管結石手術は4時間以内とする，両手法（術者の左右の手で操作）で行われた手術，という規定が設けられている。

表３　JSES 技術認定臓器別合格率の推移（%）

	2004年	2005年	2006年	2007年	2008年	2009年
胆道	63	45	36	39	43	38
食道	25	56	33	67	75	40
胃	43	57	49	45	43	37
大腸	35	38	42	47	50	25
脾臓	43	40	50	100	100	0
内分泌　他	43	69	50	50	40	17
全体	51	48	41	44	47	33

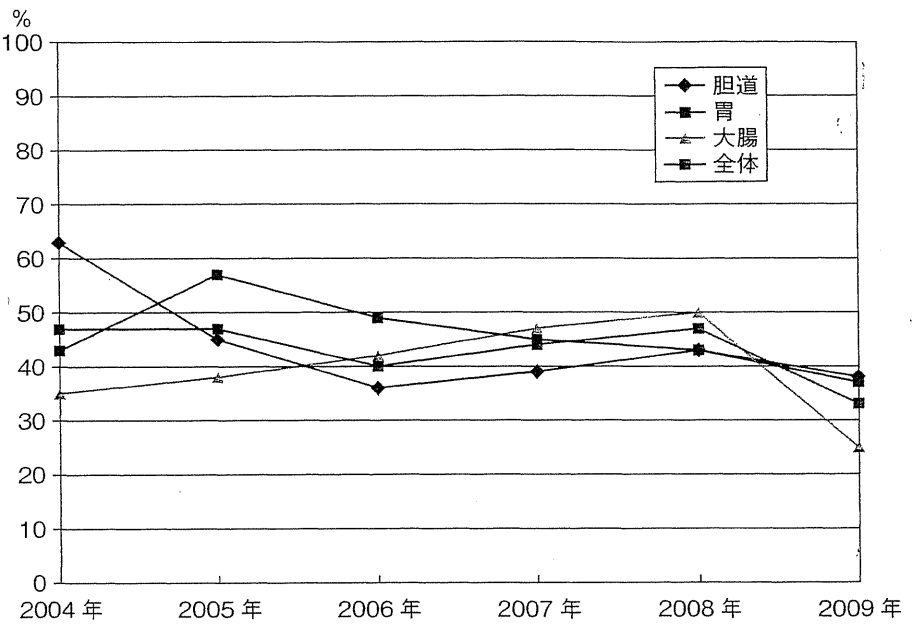

図１

HALS（hand assisted laparoscopic surgery）は腹腔鏡下手術の１つの方法として位置づけるが，HALS のビデオでは腹腔鏡下手術の評価が困難である。したがって，HALS 施行例のビデオは受け付けないことになっている[4]。

内視鏡外科手術の技術認定は，これらの規定に該当する症例に対して独力で標準的な手術を安全かつ確実に施行できるか否かを判定するものであり，技術的困難症例に対する技術を競うものではない点を強調しておきたい。

2. 応募に必要な経験症例数

最低経験症例数は，第１回～第６回まで変わりなく，また，今後もおそらく改変はないと思われる。胆嚢摘出術，虫垂切除術，ヘルニア手術などの比較的簡単な手術であれば50例，大腸切除，胃切除などの難易度の高い手術であれば20例が最低必要とされた症例数である。これらは，術者あるいは指導的助手として携わった手術件数である。審査員の経験と審査結果からして，これらの症例数が最低の応募者の経験症例数として妥当であろうと考えている。胆道領域では，手術手技の難易度が比較的低い胆嚢摘出術が主体となる。従って，50例の経験症例の中に５例の，胆嚢摘出術に限らず高難易度手術を含むことが定められている[2]。

審査過程

1. ビデオ審査

2004年の技術認定制度発足前には，審査員全員が集合し，それぞれの臓器責任者がサンプルビデオを見

表4　審査員間の一致係数 Cohen's weighted kappa value

k値	一致の強さ
負値	accidental agreement
<0.20	poor
0.21～0.40	acceptable
0.41～0.60	fair
0.61～0.80	good
0.81～1.00	excellent

（絶対値評価ではない）

ながら審査基準の説明を行い，一定の基準で審査がなされるようにした。未編集のビデオを見て審査することは，審査員の時間的および労力的にかなりの負担を負うこととなっている。応募者1人あたり審査員2名でビデオの審査を行っているが，消化器・一般外科以外の領域と同様，応募者の氏名は終始ブラインドとし，また，2名の審査員もお互いに名前は伏せてビデオ審査を行っている。共通項目および臓器の合計点数で70点以上を合格としているが，2名の審査員で合否が割れたものについては，第3の審査委員がビデオを審査して最終決定するか，あるいは，数名の審査員が再度当該ビデオを見て最終決定を行っている。毎年の審査結果における合格率や2名の審査委員間での判定の一致率を審査委員会にて検討し，各臓器別に「コンセンサスミーティング」を繰り返して行って，審査委員間の審査の不一致を低下させるように努力している。

2. 異議申し立て

今まで，不合格という審査結果に対して異議申し立てが少数あった。すべて綿密な再調査を行い審査に誤りがないかを確認している。その結果，複数のビデオを1本にダビングした際の画面のずれが生じていたものを除き，すべて審査委員会の判定が正当であることが確認され，その旨を申請者に伝えている。

審査結果

審査結果は，本学会誌に公表しているとおりである。全体の年度別合格率は，33.0～50.7%であった（表1）。2004～2009年全体の臓器別合格率は，40.6～51.6%とそれほど臓器間で差がなかった（表2）。年次別，臓器別に合格率の推移を分析すると，発足当初の2年間は主な臓器別合格率が不安定であったが2006～2008年の3年間は，胆道，胃，大腸とも35～50%の間で推移しており，比較的安定した合格率の推移であった。一方，2009年の合格率は低下し，胆道38%，胃37%，大腸25%と全体的に低下していた（表3，図1）。この2009年における合格率の低下の原因は不明であるが，この結果を受けて現在各臓器別にビデオ審査の検討委員会が開催されており，審査基準の再確認と一致率の向上を目指している。

2名の審査委員間での一致率

本技術認定制度は，2名の審査員が同一のビデオを見て審査し，合格・不合格が2名の審査委員で一致した場合はその判定を最終判定とし，不一致であった場合は，第3の審査員の判定を待って決定するかあるいは，複数の審査員でビデオを再審査して合議により最終決定を行っている。

本技術認定制度では，審査基準を共通基準60点および臓器別基準を40点の合計100点で，70点以上を合格としている。審査基準は共通基準および臓器別基準が詳細に規定されており，審査員が審査基準に従った判定を行っている。2名の審査員での一致係数（Cohen's weighted kappa value）[5]を求めて，審査の一致率を検討した。Cohen's weighted kappa valueは，0.21～0.40以上であれば受け入れられる程度（acceptable）の一致率であり，0.41～0.60であれば比較的良好（fair）な一致率であるとされている（表4）。応募者数の多い胆道，大腸，胃のCohen's weighted kappa valueをみると，2004年と2005年はややばらつきがあったが，2006～2008年は0.2～0.4の間で推移していた。2009年は，0.23～0.26であり，"acceptable"の範囲ではあるが，2008年以前と比較して一致率の低下を認めている（表5）。この原因は不明であるが，引き続き各臓器担当の審査委員の間でビデオの画像をreviewして，審査基準に則った客観的な

表５　２名の審査員間での一致率 Cohen's weighted kappa value（2004～2009年）

	2004年	2005年	2006年	2007年	2008年	2009年
胆道	0.18	0.35	0.29	0.20	0.25	0.23
食道	0.36	0.28	0.30	0.62	0.40	—
胃	0.37	0.59	0.34	0.28	0.21	0.28
大腸	0.40	0.37	0.40	0.37	0.31	0.26
合計	0.31	0.40	0.36	0.38	0.29	0.26

表６　合格・不合格と合併症率（2004～2008年）

	合併症率（%）		*p* 値
	合格者	不合格者	
胆道	3.2±5.9	3.7±7.7	0.871
食道	11.0±11.8	9.7±11.6	0.6538
胃	4.7±5.9	7.6±1.0	0.0284
大腸	4.4±6.4	6.6±7.9	0.0048
合計	4.3±6.8	6.5±8.4	0.0096

評価がなされるように努め，一致率の向上を目指している。

合併症率と合否の関係

2004～2008年の応募者における，術中および術後の合併症と合格・不合格の関係を臓器別に示したのが，表6である。胃および大腸では，合格者における合併症率は不合格者における合併症率より有意に低率であり，本技術認定制度が適切に技術認定を行っていることの１つの傍証であろうと考えられた。食道では応募者が少なく対象症例に variation があること，また，胆道ではほとんどが胆嚢摘出術であり，胆嚢摘出術は提出ビデオ症例に難度のバリエーションが大きかったために差が出なかったものと考えられた[6]。

これまでの技術認定の審査における問題点と今後の方針

2004～2009年全体の合格率は44.9%であった（表1）。この合格率からは，本制度では比較的厳しい評価による技術認定を施行していることになる。本制度が，「後進を指導するに足る所定の基準を満たした者を認定する」ことを目的としていることから考えると，この合格率はほぼ適切なものと考えられる。癒着が高度な症例や肥満例などでは，難易度が高く，従って減点が多くなる。審査ビデオは，困難症例ではなくて標準的な手術が施行された症例を提出することをお勧めする。本技術認定は，内視鏡外科手術技術のコンテストでははく，後進を指導するに足る安全で確実な内視鏡外科の技術を認定するものであることを忘れてはならない。

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ORIGINAL ARTICLE—ALIMENTARY TRACT

Characteristics of recurrence after curative resection for T1 colorectal cancer: Japanese multicenter study

Hirotoshi Kobayashi · Hidetaka Mochizuki · Takayuki Morita · Kenjiro Kotake · Tatsuo Teramoto · Shingo Kameoka · Yukio Saito · Keiichi Takahashi · Kazuo Hase · Masatoshi Oya · Koutarou Maeda · Takashi Hirai · Masao Kameyama · Kazuo Shirouzu · Kenichi Sugihara

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Abstract
Background Because the rate of recurrence after curative resection for T1 colorectal cancer is low, the characteristics of recurrence remain obscure. This multicenter study attempted to clarify the characteristics of recurrence after curative resection for T1 colorectal cancer.

Methods We analyzed the associations between recurrence and various clinicopathological features in 798 patients who had undergone curative resection alone for T1 colorectal cancer at 14 hospitals between 1991 and 1996.
Results The rate of lymph node metastasis (LNM) in patients with T1 colorectal cancer was 10.5% (84/798), and 18 (2.3%) of the 798 patients developed recurrence during the median follow-up of 7.8 years. The recurrence rates in patients with colon cancer with and without LNM were 3.6

All authors are members of the Study Group of the Japanese Society for Cancer of the Colon and Rectum (JSCCR) on Postsurgical Surveillance of Colorectal Cancer.

H. Kobayashi (✉) · K. Sugihara
Department of Surgical Oncology, Graduate School, Tokyo Medical and Dental University, 1-5-45 Yushima, Bunkyo-ku, Tokyo 113-8519, Japan
e-mail: h-kobayashi.srg2@tmd.ac.jp

H. Mochizuki
Department of Surgery, National Defense Medical College, Tokorozawa, Japan

T. Morita
Department of Surgery, School of Medicine, Hirosaki University, Hirosaki, Japan

K. Kotake
Department of Surgery, Tochigi Cancer Center, Tochigi, Japan

T. Teramoto
Division of General and Gastroenterological Surgery, Department of Surgery (Omori), School of Medicine, Toho University, Tokyo, Japan

S. Kameoka
Department of Surgery II, Tokyo Women's Medical University, Tokyo, Japan

Y. Saito
Department of Surgery, International Medical Center of Japan, Tokyo, Japan

K. Takahashi
Department of Surgery, Tokyo Metropolitan Komagome Hospital, Tokyo, Japan

K. Hase
Department of Surgery, Self-Defense Forces Central Hospital, Tokyo, Japan

M. Oya
Department of Surgery, Cancer Institute Hospital, Tokyo, Japan

K. Maeda
Department of Surgery, Fujita Health University, Toyoake, Japan

T. Hirai
Department of Gastroenterological Surgery, Aichi Cancer Center Hospital, Nagoya, Japan

M. Kameyama
Department of Surgery, Osaka Medical Center for Cancer and Cardiovascular Diseases, Osaka, Japan

K. Shirouzu
Department of Surgery, Kurume University School of Medicine, Kurume, Japan

and 1.3%, respectively ($p = 0.19$). These rates in patients with cancer of the rectum were 25.0 and 1.1% ($p < 0.0001$). Among various parameters, histological grade ($p < 0.0001$), location ($p = 0.025$), LNM ($p < 0.0001$), and venous invasion ($p = 0.0013$) were risk factors for recurrence. Among them, LNM ($p = 0.0008$) and histological grade ($p = 0.041$) were independent risk factors for recurrence after curative resection for T1 colorectal cancer. Time to recurrence was more likely to be shorter for patients with, than without nodal involvement. In patients with an unfavorable histological grade, all recurrences developed within 1 year.

Conclusions The recurrence rate after curative resection for node-negative T1 colorectal cancer was very low. The effectiveness of surveillance to detect recurrence after curative resection for T1 colorectal cancer should be validated in further studies.

Keywords Lymph node metastasis · Lymph node ratio · Venous invasion · Histological grade · Relapse

Introduction

Colorectal cancer is the second leading cause of cancer death in Japan, as well as in the United States [1], and its frequency is rapidly increasing in Japan [2, 3]. The most promising treatment for colorectal cancer is curative resection, and colorectal cancer is detected earlier thanks to advances in screening technology. Some T1 colorectal cancers can be treated by endoscopic mucosal resection or endoscopic submucosal dissection [4–7]. In Japan, endoscopic resection is indicated for patients with T1 colorectal cancer, of which the depth of submucosal invasion is <1000 μm [8]. Lymph node metastasis (LNM) is an important risk factor for recurrence in colorectal cancer [9], the rate of which is around 10% in T1 colorectal cancer [10, 11]. Therefore, radical resection is necessary for patients with a risk of LNM, even if invasion is limited to the submucosal layer. Currently, unfavorable histological grade, depth of submucosal invasion ≥1000 μm, lymphovascular invasion, and tumor budding are parameters for radical resection in patients with T1 colorectal carcinoma in Japan [8, 12]. However, the rate of recurrence after radical resection for T1 colorectal cancer is low. Therefore, the characteristics of recurrence in these patients remain obscure. The standard surveillance schedule after curative resection for colorectal cancer in Japan comprises serum tumor marker measurements every 3 months for the first 3 years and every 6 months for the next 2 years, computed tomography (CT) for chest and abdomen every 6 months for the first 3 years and every 12 months for the next 2 years, and colonoscopy every 1–2 years. This schedule seems to be rather intensive for T1 cancer. This multicenter study examined the characteristics of recurrence after curative resection for T1 colorectal cancer.

Patients and methods

Patients

We enrolled 798 patients with T1 colorectal cancer who had undergone curative resection with lymph node dissection between January 1991 and December 1996 at 14 hospitals that are members of the Study Group of the Japanese Society for Cancer of the Colon and Rectum (JSCCR) on Postsurgical Surveillance of Colorectal Cancer. All patients were followed up until December 2003. Although this study was a retrospective one, these data were prospectively collected in each institution. The local ethics committees approved this study. None of these patients had received preoperative radiotherapy or neoadjuvant chemotherapy. Patients with T1 cancer who were treated by endoscopic mucosal resection (EMR) or transanal resection (TAR) were excluded. Other exclusion criteria were cancers associated with inflammatory bowel disease or familial adenomatous polyposis.

Specimens were examined by pathologists of each institution. Sections were made every 3 mm.

The anatomical definition of the rectum was as follows: the upper rectum is located between the lower border of the second sacral vertebra and the peritoneal reflection, which is equivalent to 8 cm from the anal verge; and the lower rectum is between the peritoneal reflection and the upper border of the anal canal.

Resection for recurrence was considered in the absence of a medical contraindication to surgery, when technically feasible.

Most of the patients with LNM were administered with oral 5-fluorouracil or uracil-tegafur (UFT) as adjuvant chemotherapy for 1 year during the period of this study.

Preoperative investigations included barium enemas, colonoscopy, chest X-rays, ultrasonography (US) and/or CT of the liver, and blood tests for carcinoembryonic antigen (CEA). Most institutions established a 5- to 10-year follow-up period comprising serum tumor marker measurements every 3–6 months for the first 3 years and every 6 months for the next 2 years, hepatic imaging (US and/or CT) and chest X-rays every 6 months, annual pelvic CT for rectal cancer, and colonoscopy every 1–2 years.

We investigated risk factors for LNM, recurrence, and survival after radical resection for T1 colorectal cancer and evaluated recurrence sites and treatment.

Statistical analysis

Data were statistically analyzed using the StatView statistical package (StatView 5.0;Abacus Concepts,, Berkeley, CA, USA). All data are expressed as means ± standard deviation. Lymph node metastasis and recurrence rates were investigated using the χ^2 method for independence according to each parameter. Independent risk factors were determined by logistic regression analysis. Actuarial patient survival was calculated using the Kaplan–Meier method. Overall survival rates in all groups were compared using the log-rank test. Independent prognostic factors were determined using the Cox proportional hazard model. Statistical significance was established at $p < 0.05$ for all results.

Results

Lymph node metastasis

Table 1 shows the clinicopathological features of the patients. T1 rectal cancer was more likely to have a histological type other than well-differentiated adenocarcinoma, and was more likely to have lymphatic invasion and venous invasion than T1 colon cancer. The rates of LNM in T1 colorectal cancer, T1 cancer of the colon, and T1 cancer of the rectum were 10.5, 9.6, and 13.1%, respectively (Table 2). There was no difference in the rate of LNM between upper and lower rectal tumors (12.0 and 13.9%, respectively) in this study. Of the 798 patients, 714 (89%) were N0, 77 (10%) were N1, and 7 (1%) were N2. On univariate analysis, risk factors for LNM in T1 colorectal cancer were histological grade of poorly differentiated adenocarcinoma or mucinous carcinoma ($p < 0.0001$), lymphatic invasion ($p < 0.0001$), and venous invasion ($p < 0.0001$). Multiple logistic regression analysis revealed that unfavorable histological grade ($p = 0.0053$) and lymphatic invasion ($p < 0.0001$) were independent risk factors for LNM in T1 colorectal cancer.

The numbers of harvested lymph nodes in patients with node-positive and node-negative T1 colorectal cancer were 17 ± 14 and 13 ± 10, respectively ($p = 0.013$). The number of LNMs in patients with T1 colorectal cancer was associated with the lymph node ratio; namely, the ratio of metastatic to examined lymph nodes ($p < 0.0001$, Table 3). There was no N2 in patients with a lymph node ratio of less than 0.05.

Table 1 Clinicopathological characteristics of 798 T1 colorectal cancer patients who underwent curative surgery

Clinicopathological features	Colon (%)	Upper rectum (%)	Lower rectum (%)	*p* Value
Age (years)	60 ± 10	61 ± 10	60 ± 10	0.67
Gender				
Male	379 (64.9)	48 (52.2)	76 (62.3)	
Female	205 (35.1)	44 (47.8)	46 (37.7)	0.067
Primary site				
Cecum	17 (2.1)	92 (11.5)	122 (15.3)	
Ascending colon	71 (8.9)			
Transverse colon	58 (7.3)			
Descending colon	41 (5.1)			
Sigmoid colon	306 (38.3)			
Rectosigmoid	91 (11.4)			
Pathology				
Well-differentiated	422 (72.6)	57 (62.0)	75 (61.5)	
Moderately differentiated	153 (26.3)	35 (38.0)	42 (34.4)	
Poorly differentiated	4 (0.7)	0	3 (2.5)	
Mucinous	2 (0.3)	0	2 (1.6)	0.012
Unknown	3			
Lymph node metastasis				
Absent	528 (90.4)	81 (88.0)	105 (86.1)	
Present	56 (9.6)	11 (12.0)	17 (13.9)	0.32
Lymphatic invasion				
Absent	340 (61.9)	43 (48.9)	64 (53.3)	
Present	209 (38.1)	45 (51.1)	56 (46.7)	0.026
Unknown	35	4	2	
Venous invasion				
Absent	434 (79.9)	63 (70.8)	77 (64.2)	
Present	109 (20.1)	26 (29.2)	43 (35.8)	0.0005
Unknown	41	3	2	

Table 2 Risk factors for lymph node metastasis in T1 colorectal cancer

	Univariate analysis			Multivariate analysis		
	LNM (+) (%)	LNM (−) (%)	*p* Value	Odds ratio	95% CI	*p* Value
Gender						
Male	45/503 (8.9)	458/503 (91.1)	0.058			
Female	39/295 (13.2)	256/295 (86.8)				
Location						
Colon	56/584 (9.6)	528/584 (90.4)	0.15			
Rectum	28/214 (13.1)	186/214 (86.9)				
Histological grade						
Well or Mod	78/784 (9.9)	706/784 (90.1)	<0.0001	1		
Poorly or Muc	5/11 (45.5)	6/11 (54.5)		7.58	1.82–31.25	0.0053
Lymphatic invasion						
Absent	8/437 (1.8)	429/437 (98.2)	<0.0001	1		
Present	35/285 (12.3)	250/285 (87.7)		5.13	2.87–9.09	<0.0001
Venous invasion						
Absent	21/549 (3.8)	528/549 (96.2)	<0.0001	1		
Present	22/167 (13.2)	145/167 (86.8)		1.46	0.86–2.48	0.16

LNM Lymph node metastasis, *CI* confidence interval, *Mod* moderately, *Muc* mucinous

Table 3 Recurrence and survival rates according to lymph node ratio

	Lymph node ratio (total positive/total examined)				*p* Value
	<0.05	0.05–0.19	0.2–0.39	0.4–1.0	
Lymph node metastasis					
N1	10	50	15	2	<0.0001
N2	0	1	3	3	
Recurrence rate (%)	0 (0/10)	11.8 (6/51)	11.1 (2/18)	20 (1/5)	0.11
5-Year overall survival (%)	100	90	83.3	80	–

Recurrence

Cancer recurred in 18 (2.3%) of the 798 patients during a median follow-up of 7.8 ± 3.5 years. The rates of recurrence of T1 cancer of the colon and rectum were 1.5 and 4.2%, respectively ($p = 0.02$). The recurrence rates among patients with T1 colon cancer with and without LNM were 3.6 and 1.3% ($p = 0.19$), and the recurrence rates in patients with T1 rectal cancer with and without LNM were 25 and 1.1%, respectively ($p < 0.0001$). The most frequent sites of recurrence were the liver and the lung in T1 colon and rectal cancers, respectively (Table 4). Most T1 colorectal cancers recurred at a single site during a median of 1.9 years (range, 0.3–4.4 years). T1 colorectal cancer recurred sooner in patients with than in those without nodal involvement, although the difference did not reach statistical significance ($p = 0.28$, Fig. 1). In patients with nodal involvement, cancer recurred in 78% of them within 1 year. On the other hand, most cancer did not recur within 1 year in patients with T1 colorectal cancer without LNM. The patients with unfavorable histological grade ($p = 0.033$) or LNM ($p = 0.0044$) were more likely to have a recurrence within 1 year (Table 5).

Table 4 Recurrence sites of T1 colorectal cancers

	Colon ($n = 9$)	Rectum ($n = 9$)	*p* Value
Number of recurrence sites			
Single	7	7	>0.99
Multiple	2	2	
Recurrence site			
Liver	6	1	0.17
Lung	1	3	
Local	1	2	
Other	3	4	

Other recurrence sites included bone and distant lymph nodes

The patients with a high lymph node ratio were more likely to develop recurrence, although there was no significant difference according to whether the ratio was high or low (Table 3). There was no recurrence in patients with a lymph node ratio of less than 0.05 in this study.

Risk factors for recurrence

Univariate analysis revealed that tumor location ($p = 0.025$), histological grade ($p < 0.0001$), LNM ($p < 0.0001$), and

venous invasion ($p = 0.0013$) were risk factors for recurrence (Table 6). Among them, multivariate analysis revealed that histological grade ($p = 0.041$) and LNM ($p = 0.0008$) were independent risk factors for recurrence after curative resection for T1 colorectal cancer.

Treatment for recurrence

Table 7 shows the details of the 18 patients with recurrence after curative resection for T1 colorectal cancer. Most of the liver metastases were detected by liver imaging such as CT or US. Pulmonary metastasis was detected by CEA or chest X-ray. Seven (39%) of the 18 patients underwent surgical resection for recurrence, and the procedure was curative in 6 of them (pulmonary metastasis, $n = 3$; liver metastasis, $n = 1$; supraclavicular LNM, $n = 1$; lateral pelvic LNM, $n = 1$). Three of the 6 patients who underwent curative resection for metastasis to the liver, lung, and lateral pelvic lymph nodes did not develop re-recurrence. Five patients received chemotherapy, and 6 did not receive any treatment for recurrence.

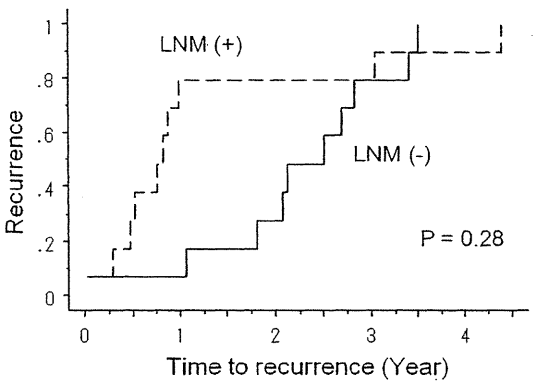

Fig. 1 Cumulative appearance rate of recurrence after curative resection for T1 colorectal cancer in patients with and without lymph node metastasis (*LNM*)

Prognosis after curative resection for T1 colorectal cancer

The 5-year overall survival rates after curative resection for T1 colon cancer in patients with and without LNM were 92.7 and 94.1%, respectively (Fig. 2a, $p = 0.49$). These rates in the patients with T1 rectal cancer with and without LNM were 82.1 and 93.8%, respectively (Fig. 2b, $p = 0.0018$). Table 8 shows the prognostic factors for patients after curative resection for T1 colorectal cancer. Univariate analysis showed that LNM ($p = 0.021$) and venous invasion ($p = 0.0099$) were factors indicating a poor prognosis, and the Cox proportional hazard model also revealed that these were independent factors indicating a poor prognosis ($p = 0.032$ and 0.030, respectively).

Discussion

The prognosis of T1 colorectal cancer is relatively good, and it is often treated by endoscopic resection or local excision.

Table 5 Time-dependent analysis of recurrence

	Univariate analysis			Multivariate analysis		
	Rec within 1 year	Rec 1 year or later	*p* Value	OR	95% CI	*p* Value
Gender						
Male (11)	4	7				
Female (7)	4	3	0.39			
Location						
Colon (9)	3	6				
Rectum (9)	5	4	0.34			
Histological grade						
Well or Mod (15)	5	10		1		
Poorly or Muc (3)	3	0	0.033	270964	0–	0.98
Lymph node metastasis						
Absent (9)	1	8		1		
Present (9)	7	2	0.0044	15.9	1.1–250	0.042
Lymph invasion						
Absent (8)	3	5				
Present (10)	5	5	0.60			
Venous invasion						
Absent (8)	2	6				
Present (10)	6	4	0.14			

The values given in parentheses are the total numbers

Rec Recurrence, *OR* odds ratio, *CI* confidence interval, *Mod* moderately, *Muc* mucinous

Table 6 Risk factors for recurrence in T1colorectal cancer

	Univariate analysis			Multivariate analysis		
	Rec (+) (%)	Rec (−) (%)	*p* Value	Odds ratio	95% CI	*p* Value
Gender						
Male	11/503 (2.2)	492/503 (97.8)	0.86			
Female	7/295 (2.4)	288/295 (97.6)				
Location						
Colon	9/584 (1.5)	575/584 (98.5)	0.025	1		
Rectum	9/214 (4.2)	205/214 (95.8)		1.74	0.63–4.85	0.29
Histological grade						
Well or Mod	15/784 (1.9)	769/784 (98.1)	<0.0001	1		
Poorly or Muc	3/11 (27.3)	8/11 (72.7)		6.21	1.08–35.6	0.041
Lymph node metastasis						
Absent	9/714 (1.3)	705/714 (98.7)	<0.0001	1		
Present	9/84 (10.7)	75/84 (89.3)		6.02	2.11–17.2	0.0008
Lymphatic invasion						
Absent	8/437 (1.8)	429/437 (98.2)	0.16			
Present	10/285 (3.5)	275/285 (96.5)				
Venous invasion						
Absent	8/549 (1.5)	541/549 (98.5)	0.0011	1		
Present	10/167 (6.0)	157/167 (94.0)		2.29	0.80–6.57	0.12

Rec Recurrence, *CI* confidence interval, *Mod* moderately, *Muc* mucinous

Table 7 Details of patients with recurrence

Case	Age	Gender	Tumor location	Histological type	Nodal involvement	Time (year) to recurrene	Recurrence site	First indicator
1	59	M	Ascending colon	Well	Absent	2.0	Others	Symptom
2	61	M	Lower rectum	Well	Present	4.4	Lung	Chest X-ray
3	74	F	Lower rectum	Muc	Present	0.5	Others	Symptom
4	62	F	Sigmoid colon	Well	Absent	2.8	Liver	Imaging
5	58	M	Rectosigmoid	Well	Absent	2.1	Liver, anastomosis	Imaging
6	66	M	Upper rectum	Well	Present	0.3	Liver	CEA, imaging
7	66	M	Lower rectum	Well	Absent	2.7	Others	CEA, imaging
8	67	M	Sigmoid colon	Mod	Absent	3.5	Others	Symptom, imaging
9	58	M	Rectosigmoid	Well	Present	0.7	Liver	Imaging
10	53	F	Rectosigmoid	Well	Absent	1.8	Others	Clinical examination
11	81	M	Ascending colon	Mod	Present	0.5	Liver, Lung	CEA, imaging
12	84	F	Lower rectum	Por	Present	0.9	Others	Clinical examination
13	60	M	Lower rectum	Mod	Present	3.0	Lung	Chest X-ray
14	81	F	Upper rectum	Mod	Present	1.0	Local, Others	CEA, imaging
15	71	M	Ascending colon	Well	Absent	2.5	Liver	CEA
16	51	M	Descending colon	Well	Absent	1.0	Liver	Imaging
17	48	F	Lower rectum	Por	Present	0.8	Others	Symptom
18	67	F	Lower rectum	Well	Absent	3.4	Lung	CEA, chest X-ray

Well Well-differentiated adenocarcinoma, *Mod* moderately differentiated adenocarcinoma, *Por* poorly differentiated adenocarcinoma, *Muc* mucinous adenocarcinoma, *Others* bone and distant lymph node metastasis, *Imaging* computed tomography (CT) or ultrasonography (US), *CEA* carcinoembryonic antigen

Nevertheless, about 10% of T1 colorectal cancers metastasize to regional lymph nodes [10, 11]. Surgery with lymph node dissection is indicated for patients with T1 colorectal cancer with a risk of LNM. The features of recurrence after curative resection have remained obscure because recurrence after curative resection for T1 colorectal cancer is rare.

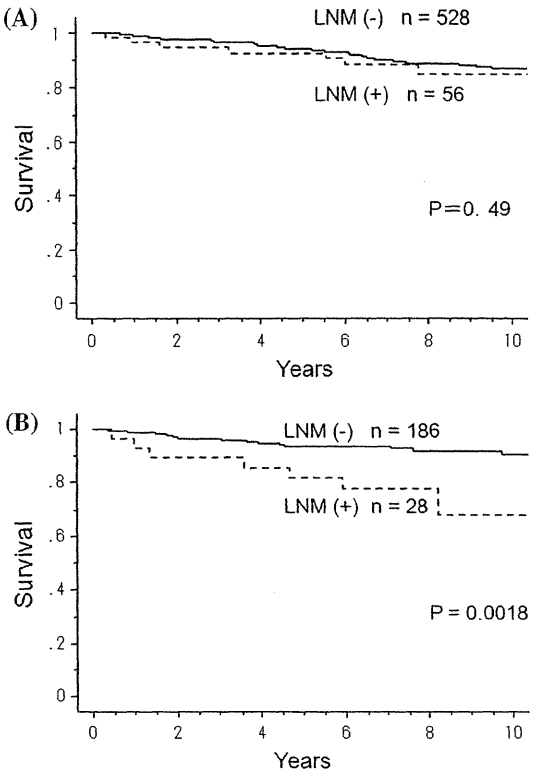

Fig. 2 Five-year overall survival curves for patients after curative resection for T1 cancer of the colon (**a**) and rectum (**b**). *Dotted* and *unbroken lines* indicate survival with and without lymph node metastasis (*LNM*), respectively

Table 8 Prognostic factors in patients with curative resection for T1 colorectal cancer

	n	Univariate analysis	Multivariate analysis		
		p Value	HR	95% CI	*p* Value
Gender					
Male	503				
Female	295	0.79			
Location					
Colon	584				
Rectum	214	0.81			
Histological grade					
Well or Mod	784				
Poorly or Muc	11	0.42			
Lymph node metastasis					
Absent	714		1		
Present	84	0.021	1.91	1.06–3.46	0.032
Lymphatic invasion					
Absent	447				
Present	310	0.34			
Venous invasion					
Absent	574		1		
Present	178	0.0099	1.70	1.05–2.76	0.030

HR Hazard ratio, *CI* confidence interval, *Mod* moderately, *Muc* mucinous

Histological grade was an independent risk factor for recurrence after curative resection for T1 colorectal cancer, as well as LNM. The recurrence rate among patients with poorly differentiated adenocarcinoma or mucinous carcinoma that invaded the submucosal layer was 27.3% in the present study. Blumberg et al. [13] have reported that a poorly differentiated tumor is a predictor of tumor-related mortality in patients with surgical resection for T1 rectal cancer. Cooper et al. [14] demonstrated that 37.5% of patients with grade III early cancer had adverse outcomes such as local and/or distant recurrence. Adjuvant chemotherapy or chemoradiotherapy might be necessary for such patients, even if they have T1 colorectal cancer. On the other hand, local resection for early distal rectal cancer is thought to be a reasonable alternative to abdomino-perineal resection or low anterior resection. However, the recurrence rate after local excision for rectal cancer was not necessarily low (6.6–18%) in previous studies [15–19]. The indication for local excision in patients with early distal rectal cancer should be determined carefully. A recent study demonstrated that the combination of gender and histological type was useful to determine the appropriate candidates for local excision for early distal rectal cancer [20].

The present study found that the most frequent sites of recurrence in T1 cancer of the colon and rectum were the liver and the lung, respectively. This is consistent with previous studies that enrolled mainly patients with advanced cancer [9, 21]. In the present study, all curative resections were performed in patients with metastasis in a single organ. The rate of curative resection for recurrence after radical resection for T1 colorectal cancer in our study was 33%, which is similar to previous findings, in which the rates of curative resection for liver and pulmonary metastasis were between 20 and 40% [9, 22, 23]. Curative resection for recurrence permanently cured 50% of the patients in our study; thus, we highly recommend curative resection for recurrence when possible.

Time to recurrence was shorter in T1 colorectal cancer patients with LNM than in those without LNM. Approximately 80% of recurrences in patients with LNM developed within 1 year, whereas most of the cancers did not recur within 1 year in those without LNM. If patients with T1 colorectal cancer do not have LNM, follow-up after initial surgery might be unnecessary, at least for the first year. In terms of the first indicator for recurrence, liver imaging such as CT or US was useful to detect liver metastasis, although a combination of CEA and chest X-ray detected all pulmonary metastases. From a comprehensive point of view, CEA

and CT from chest to abdomen seem to be useful to detect a recurrence after curative resection for T1 colorectal cancer at this moment.

The outcome after curative resection for T1 colorectal cancer in the present study was satisfactory. The 5-year overall survival rate of patients with T1 colon cancer was more than 90%, even if nodes were involved, and the prognosis after curative resection for T1 colon cancer did not differ between patients with and without LNM. This result may indicate that lymph node dissection for T1 colon cancer is more useful than that for colon cancers at other T-stages. At the same time, the good prognosis might be a result of the number of LNMs. In this study, most of the stage III patients with T1 colorectal cancer were N1. Furthermore, a recent study demonstrated that the lymph node ratio was associated with the survival rate [24]. The lymph node ratios in our study were less than those in a previous study which enrolled patients with stage II and III colon cancer. Especially, in our study, patients with a lymph node ratio of less than 0.05 did not have a recurrence, even if they had LNM. The lymph node ratio may be useful to predict the prognosis of patients with node-positive T1 colorectal cancer. On the other hand, the 5-year overall survival rate for patients with rectal cancer and LNM was 82.1%, even when tumor invasion was confined to the submucosal layer.

Lymph node metastasis (LNM) and venous invasion were independent factors for a poor prognosis in the present study. Others have reported that LNM is one of the strongest predictors of prognosis in patients with colorectal cancer [25, 26]. Venous invasion has also been reported as an independent adverse prognostic factor in T1, as well as in T2–4 tumors [14, 27–31].

The present study demonstrated that the rates of LNM in T1 cancer of the colon and rectum were 9.6 and 13.1%, respectively. These results are consistent with previous findings in which the rates of nodal involvement in T1 colorectal cancer were approximately 10% [11, 31–33 That is, surgery might have been unnecessary in almost 90% of patients who underwent radical resection for T1 colorectal cancer. Therefore, to identify a more accurate predictor of LNM in T1 colorectal cancer is important. Histological grade and lymphatic invasion were independent risk factors for LNM in T1 colorectal cancer in the present study.

Cooper et al. [14] demonstrated that unfavorable histology such as grade III, tumor margin <1.0 mm in endoscopically resected polyps, lymphatic and venous invasion, and unfavorable tumor grade were associated with LNM [12]. Our data support these results.

In the present study, tumor location in T1 colorectal cancer was not a risk factor for LNM. However, some studies have associated tumor location with LNM. Nascimbeni et al. [10] demonstrated that the lower third of the rectum was a risk factor for LNM in T1 colorectal cancer. Another study showed that the level of invasion, configuration, and location were risk factors for LNM in early invasive colorectal cancer [34] The frequencies of LNM in T1 colon and rectal cancers in these studies were 3.8 and 9.7%, respectively. The rate of LNM in our study was somewhat higher than in previous studies, because our patients were preoperatively diagnosed with a risk of LNM and were treated with surgical resection. Recent reports indicate that the depth of submucosal invasion and tumor budding are risk factors for LNM in T1 colorectal cancer [12, 35–37. One study has shown that 42.1% of patients with T1 colorectal cancer have LNM if tumor budding is present [12]. Kurokawa et al. [38] have reported that tumor matrilysin expression is a promising biomarker predicting nodal metastasis of colorectal cancer.

We conclude that unfavorable histological grade and lymphatic invasion are risk factors for LNM in patients with T1 colorectal cancer. Thus, these patients should undergo curative resection with lymph node dissection, even if the depth of tumor invasion is limited to the submucosal layer. Lymph node metastasis (LMN) and unfavorable histological grade were independent risk factors for recurrence after curative resection for T1 colorectal cancer. The optimal surveillance schedule after curative resection for T1 colorectal cancer should be validated in further studies.

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Original Paper

Short-and Long-Term Outcomes of Laparoscopic Surgery in Patients with Pathological Stage II and III Colon Cancer

Takatoshi Nakamura[1], Hiroyuki Mitomi[2], Wataru Onozato[1], Takeo Sato[1], Atsushi Ikeda[1], Masanori Naito[1], Naoto Ogura[1], Hiroki Kamata[1], Akira Ooki[1] and Masahiko Watanabe[1]

[1]Department of Surgery, Kitasato University, School of Medicine, Kanagawa, Japan
[2]Department of Human Pathology, Juntendo University, School of Medicine, Japan

Corresponding author: Masahiko Watanabe M.D., Ph.D., F.A.C.S., Kitasato University School of Medicine Department of Surgery, 1-15-1 Kitasato, Minami-ku Sagamihara, Kanagawa 252-0374, Japan;
Tel: +81427788111, Fax: +81427455582; E-mail: n-toshi@kitasato-u.ac.jp

ABSTRACT

Background/Aims: In Japan, the safety and long-term outcomes of laparoscopic surgery for advanced colorectal cancer remains a matter of debate. We studied the safety and outcomes of laparoscopic surgery in patients with pathological stage II and III colon cancer. **Methodology:** The study group comprised 253 patients with colon cancer who underwent laparoscopic surgery from January 1998 through December 2006. We studied surgical outcomes, invasiveness, safety, recurrence rates, recurrence patterns, and long-term outcomes. **Results:** Median follow-up was 67 months (range, 7-149). Laparoscopic surgery was converted to open surgery in 5 patients (2%). Postoperative complications occurred in 23 patients (9%); wound infections were most common (11 patients, 4.3%), followed by ileus (5 patients, 1.9%). Recurrence developed in 66 patients (26%). Liver and lung metastases were the most common types of recurrence; there was no port-site recurrence. The 10-year recurrence-free survival rate and the overall survival rate were respectively 92.9% and 93.3% in stage II disease, 82.7% and 82.9% in stage IIIA and IIIB disease, and 70.3% and 68.6% in stage IIIC disease. **Conclusions:** In patients with pathological stage II and III colon cancer, laparoscopic surgery is safe, minimally invasive, and has good surgical outcomes, overall survival rates and recurrence-free survival rates. Our results suggest that laparoscopic surgery is a viable treatment option for pathological stage II and III colon cancer.

Key Words: Laparoscopic surgery, Colon cancer, Clinical outcome.

Abbreviations: Computed Tomography (CT).

INTRODUCTION

Laparoscopic surgery was first used to treat colorectal cancer in our hospital in 1995. To date, we have performed laparoscopic surgery in more than 800 patients with colorectal cancer. Recently, the indication range has been expanded and now includes advanced cancer as well as early cancer (1-3). The increased use of laparoscopic surgery is attributed to several advantages over open surgery, including less postoperative pain, a lower risk of postoperative ileus, a shorter length of postoperative hospital stay, and an earlier return to usual activities, *i.e.* a better postoperative quality of life (4,5). In patients with advanced cancer, however, opinions on the use of laparoscopic surgery are divided. Laparoscopic surgery does not allow surgeons to adequately visually inspect or palpate the peritoneal cavity, potentially leading to a less reliable intraoperative evaluation of disease stage and raising concerns about the risks of tumor cell dissemination and implantation in the peritoneal cavity, as well as port-site recurrence (6,7). Recent randomized, controlled studies of advanced colon cancer conducted in Western countries have reported that long-term outcomes after laparoscopic surgery are comparable to those after open surgery (8-12). In Japan, however, the surgical results, invasiveness and long-term outcomes of laparoscopic surgery in patients with advanced colon cancer remain largely uninvestigated. We therefore retrospectively studied short- and long-term outcomes after laparoscopic surgery in patients with pathological stage II and III colon cancer.

METHODOLOGY

From January 1998 through December 2006, we performed laparoscopic surgery in 595 patients with colon cancer. Of these patients, we studied 105 with pathological stage II disease and 148 with stage III disease (total, 253 patients; 136 men and 117 women). The median follow-up period was 67 months (range, 7-149) (**Table 1**). Laparoscopic surgery was indicated for patients in whom barium enema fluoroscopy, colonoscopy, abdominal ultrasonography and computed tomography of the chest and abdomen showed no distinct evidence of tumor invasion to other organs. Patients with ileus that did not respond to decompression were excluded from the study.

As for the technique for laparoscopic surgery, the first port was placed in a skin incision about 3cm in length, made 2 finger widths below the xiphoid process if the lesion was in the right side of the colon or 2 finger widths above the pubic bone if the lesion was in the left side of the colon. A Lap Disk (Johnson and Johnson Co., Ltd., USA) was placed at the incision site, and a 12-mm port was inserted. The abdomen was insufflated with carbon dioxide at a mean pressure of 8mmHg/hour. While examining the peritoneal cavity with a 5-mm flexible scope, a camera port and three or four 5-mm ports were placed in the subumbilical region. For right-sided colon cancer, the transection lines of the ileocolic artery, right colic artery and middle colic artery were decided on the basis of the site of the lesion and the disease stage. If invasion was T3 or deeper, the main blood vessels were transected at their origins. Transection and anastomosis of the in-

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testine were performed by extending the small abdominal incision to about 5cm. The intestine was then exteriorized, and transection and anastomosis were performed. For left-sided colon cancer, the origin of the inferior mesenteric artery was transected if the depth of invasion was T3 or deeper. If the portion of the intestine containing the lesion could be adequately elevated through the small incision, transection and anastomosis of the colon were performed extracorporeally. If the intestine could not be elevated, the mesentery was divided, and the distal colon was transected intracorporeally with the use of an automatic stapler. The portion of the colon containing the lesion was exteriorized through the small incision, and the proximal colon was transected. The tip of the automatic stapler was placed in the cut end of the intestine, and the intestine was repositioned into the peritoneal cavity. The abdomen was re-insufflated, and anastomosis was performed in the peritoneal cavity using a double-stapling technique (13).

After surgery, patients with stage III disease received adjuvant chemotherapy with an oral preparation of 5-fluorouracil for about 6 to 12 months, in principle. After discharge, patients were followed-up on an outpatient basis. In addition to physical examinations, serum carcinoembryonic antigen levels were measured (3-month to 1-year intervals), and computed tomography of the chest and abdomen (6-month intervals) and colonoscopic examinations (1-year intervals) were performed. The results of these imaging and histopathological studies were comprehensively evaluated to diagnose recurrence.

Statistical analysis was performed using the chi-square test and Mann-Whitney U test. A p value of less than 0.05 was considered to indicate statistical significance. The recurrence-free survival rate and overall survival rate were calculated with the Kaplan-Meier method. The logrank test was used to compare differences between groups.

TABLE 1. Demographic characteristics of the patients.

Number of patients	253
Age (years)	64 (29-88)
Male:Female	136:117
ASA score (I:II:III)	100:133:20
BMI (kg/m^2)	23 (14-38)
Tumor site	
Right colon	115 (45%)
Left colon	138 (55%)
Tumor size (cm)	4 (1-12)
Depth of tumor invasion	
T1	4 (2%)
T2	16 (6%)
T3	230 (91%)
T4	3 (1%)
Lymph node metastasis	
N0	105 (42%)
N1	119 (47%)
N2	29 (11%)
AJCC/TNM staging	
IIA	104 (41%)
IIB	1 (1%)
IIIA	23 (9%)
IIIB	97 (38%)
IIIC	28 (11%)
Follow-up period (months)*	67 (7-149)

Values are represented as medians (range). BMI, Body Mass Index; Right colon, cecum, ascending colon and transverse colon; Left, descending colon, sigmoid and rectosigmoid colon; ASA status, Physical status according to the American Society of Anesthesiologists Classification.

RESULTS

Postoperative complications occurred in 9% (23/253) of the patients. Wound infection was most common (4.3%, 11/253), followed by ileus (1.9%, 5/253). The conversion rate to open surgery was 2% (5/253). The reasons for conversion to open surgery were tumor invasion to other organs in 2 patients, adhesion in 2, and difficulty in securing an adequate field of vision because of obesity in 1 patient (**Table 2**).

Postoperative recurrence occurred in 26% (66/253) of patients. As for the type of recurrence, liver metastasis was the most common (47%, 31/66), followed by lung metastasis (21%, 14/66) and lymph-node metastasis (14%, 9/66) (**Table 3**). No patient had port-site recurrence.

The 10-year recurrence-free survival rate (**Figure 1**, p=0.003) and the overall survival rate (**Figure 2**, p=0.003) were respectively 92.9% and 93.3% in pathological stage II disease, 82.7% and 82.9% in stage IIIA plus IIIB disease, and 68.6% and 70.3% in stage IIIC disease. The differences among the 3 groups were significant.

TABLE 2. Operation time, blood loss and postoperative complications.

Operation time (min)*	195 (120-380)
Estimated blood loss (mL)	20 (0-3880)
Conversion to open procedure	5 cases (2.0%)
Postoperative complications	
Wound infection	11 cases (4.3%)
Intestinal obstruction	5 cases (2.0%)
Anastomotic leakage	4 cases (1.6%)
Intestinal bleeding	3 cases (1.1%)

*Values are represented as medians (range)

TABLE 3. Recurrence in patients with colon cancer.

Site of recurrence	Number of cases
Liver*	31 (47%)
Lung*	14 (21%)
Lymph nodes	9 (14%)
Peritoneum	7 (11%)
Anastomosis	4 (6%)
Ovary	1 (2%)

*Including 4 cases with synchronous metastasis of liver and lung. *The total number of recurrent cases was 66 (26%).

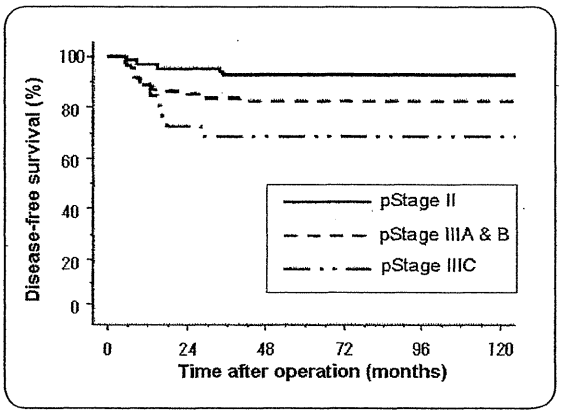

FIGURE 1. Disease-free survival according to tumor-node-metastasis stage in patients with colon cancer.

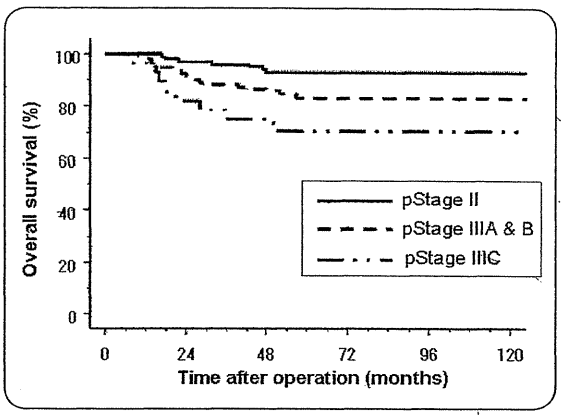

FIGURE 2. Overall survival according to tumor-node-metastasis stage in patients with colon cancer.

DISCUSSION

Our study showed that laparoscopic surgery was minimally invasive and had good surgical outcomes and a low incidence of postoperative complications in patients with pathological stage II and III colon cancer. Moreover, the 10-year recurrence-free survival rate and the overall survival rate were both good.

As for short-term outcomes, Schwenk *et al.* (14) conducted a meta-analysis of 25 randomized controlled studies. Laparoscopic surgery was found to have a longer operation time than open surgery, but was associated with less blood loss and a shorter duration of paralytic ileus after operation. Other advantages of laparoscopic surgery were better postoperative respiratory function, less postoperative pain, and fewer postoperative complications. Lourenco *et al.* (15) conducted a meta-analysis of 19 studies and reported that laparoscopic surgery was associated with a shorter hospital stay, less blood loss, less postoperative pain and an earlier return to usual activities than open surgery. However, the operation time was longer with laparoscopic surgery than with open surgery. The rate of lymph-node dissection, the resection rate of lesions and the quality of life did not differ between the 2 treatments.

As for long-term outcomes, the results of randomized controlled trials such as the Barcelona trial (8), the Clinical Outcomes of Surgical Therapy (COST) study (9), the Colon Cancer Laparoscopic or Open Resection (COLOR) trial (10), the Conventional *vs.* Laparoscopic-Assisted Surgery in Patients with Colorectal Cancer (CLASICC) trial and a prospective randomized trial conducted by Leung *et al.* (12) showed that oncological outcomes did not differ between laparoscopic surgery and open surgery. Bonjer *et al.* performed a meta-analysis of data from the Barcelona, COST, COLOR, and CLASICC trials, including a total of 1765 patients with stage I to III colon cancer (16). After excluding 229 patients, 796 underwent laparoscopic surgery and 740 underwent open surgery. The recurrence-free survival rate and the overall survival rate at 3 years did not differ significantly between the groups. Jackson *et al.* (17) conducted a meta-analysis of 10 randomized controlled trials comparing laparoscopic surgery with open surgery, including the CLASICC and COLOR trials. The study group comprised a total of 3830 patients. Patients were followed up for more than 18 months in 7 of the 10 studies. There was no difference in the recurrence rate or the overall survival rate between the laparoscopic surgery group and open surgery group.

As for long-term outcomes, randomized controlled trials such as the study by Lacy *et al.* (8) and the COAST (9) and CLASICC trials (11) demonstrated that laparoscopic surgery is superior or non-inferior to open surgery. The COLOR trial enrolled patients with T1 to T3 colon cancer and excluded those with stage IV disease. As for short-term outcomes, laparoscopic surgery was associated with less postoperative pain, earlier recovery of intestinal peristalsis and a shorter hospital stay than open surgery. The rates of postoperative complications and surgical mortality were similar in both groups, showing that laparoscopic surgery was safe. However, an intent-to-treat analysis failed to demonstrate that laparoscopic surgery is non-inferior to open surgery with respect to 3-year disease-free survival (10). The rate of conversion to open surgery was 20% among patients included in the analysis, and the number of lymph nodes removed was small. About half of patients with T4 disease were converted from laparoscopic surgery to open surgery. These results suggest that there might have been problems in the preoperative diagnosis and surgical techniques.

The current technique for laparoscopic resection of colorectal cancer is associated with several unresolved issues. Many studies, including ours, have shown that outcomes of laparoscopic surgery are generally similar to those of open surgery in patients with colorectal cancer. However, the risks of tumor cell dissemination and intraperitoneal implantation remain important concerns in patients undergoing laparoscopic surgery. Procedures that damage tumors have increased risks of the intraperitoneal dissemination of tumor cells during laparoscopic surgery. Therefore, procedures that require direct contact with tumors should be avoided whenever possible. Laparoscopic surgery has several other limitations. Firstly, laparoscopic procedures do not allow surgeons to adequately palpate or visually inspect the inside of the peritoneal cavity, negatively affecting the accuracy of intraoperative disease staging. Secondly, the effect of carbon dioxide gas on the biologic malignancy of cancer cells remains unclear. Experimentally, carbon dioxide gas has been shown to promote cancer cell adhesion and increase liver metastases (18). Thirdly, laparoscopic surgery might reduce the extent of lymph-node dissection. However, the number of removed lymph nodes after laparoscopic surgery has been reported to be similar to that after open surgery, provided that the techniques for lymph-node dissection are mastered (19,20). In our study, the number of lymph nodes removed was standard. Fourthly, port-site recur-