Table III. List of 44 down-regulated proteins in CRC tissues and trancriptomic expression data.

Down-regulated proteins in CRC tissues	Symbol	Entrez Gene ID	Average of 12 CRCs Log_2T/N ratio - proteomics	Average of 180 CRCs Log_2T/N ratio - transcriptomics
α1 acid glycoprotein	ORM1	5004	1.19	-0.29
ADP ribosylation factor like 10C	ARL8B	55207	-0.97	-0.06
Aldehyde dehydrogenase 2	ALDH2	217	-0.84	-0.05
ATP synthase, H^+ transporting, mitochondrial F0 complex, subunit d	ATP5H	10476	-1.44	-0.57
ATP binding cassette transporter subfamily A member 12	ABCA12	26154	-1.09	-0.18
Calreticulin	CALR	811	-0.54	0.11
Carbonic anhydrase II	CA2	760	-1.90	-2.65
Carbonyl reductase 1	CBR1	873	-0.60	0.05
Cathepsin S	CTSS	1520	-0.81	-0.77
Collagen type 12 α-1	COL12A1	1303	-0.69	0.23
Creatine kinase-B	CKB	1152	-0.67	-1.58
Cysteine rich protein 1	CSRP1	1465	-0.92	-0.13
Dynein light chain 1	DYNLL1	8655	-0.89	-0.04
Endoplasmic-reticulum-lumenal protein 29	ERP29	10961	-0.72	-0.16
Endoplasmic-reticulum-lumenal protein 46	TXNDC5	81567	-1.10	-0.35
Enoyl CoA hydratase 1	ECHS1	1892	-1.18	-0.44
Eukaryotic translation elongation factor 2	EEF2	1938	-0.95	0.27
Eukaryotic translation initiation factor 3 subunit 6	EIF3S6	3646	-1.61	0.27
FHL1 (skeltal muscle LIM-protein)	FHL1	2273	-1.16	-0.37
Gelsolin isoform a	GSN	2934	-0.98	-0.68
Glucosamine-fructose-6-phosphate aminotransferase 1	GFPT1	2673	-0.83	-0.19
GTP-binding protein Rab1	RAB1A	5861	-0.64	-0.46
Haptoglobin	HP	3240	-1.04	-0.10
Heterogeneous nuclear ribonucleoprotein A2 /B1	HNRPA2B1	3181	-0.72	0.02
Hydroxymethylglutaryl-CoA synthase, mitochondrial	HMGCS2	3158	-1.44	-0.94
Isocitrate dehydrogenase 1	IDH1	3417	-2.91	-0.57
JM5 protein	WDR45	11152	-0.64	0.25
Major vault protein	MVP	9961	-0.56	-0.14
Myeloperoxidase	MPO	4353	-0.55	-0.04
Myozenin 3	MYOZ3	91977	-0.73	-0.22
NADH Ubiquinone oxidoreductase subunit B13	NDUFA5	4698	-1.15	-0.50
Normal mucosa of esophagus specific 1	C15orf48	84419	-1.34	-1.88
Olfactomedin 4	OLFM4	10562	-0.61	-0.49
Phosphoenolpyruvate calboxykinase 2	PCK2	5106	-0.68	-0.55
Phosphoglycerate mutase 1	PGAM1	5223	-1.59	-0.02
Proline arginine-rich end leucine-rich repeat protein	PRELP	5549	-1.40	-0.12
Protein kinase C and casein kinase substrate in neurons 2	PACSIN2	11252	-0.66	-0.16
Pyridoxine 5-prime-phosphate oxidase	PNPO	55163	-1.72	-0.11
Ras associated protein Rab5B	RAB5B	5869	-0.70	-0.11
Retinoblastoma binding protein 4, 7	RBBP4/RBBP7	5928/5931	-0.70	0.02
Succinate dehydrogenase complex, subunit A, flavoprotein	SDHA	6389	-0.71	-0.35
Transferrin	TF	7018	-0.85	-0.11
UDP-glucose dehydrogenase	UGDH	7358	-0.83	-1.03
Valosin containing protein	VCP	7415	-0.95	-0.09
Villin 1	VIL1	7429	-2.18	-0.30

Discussion

The recent availability of platform technologies for high throughput transcriptomics and proteomics has led to integrated approaches to cancer research. Integrated analysis of global scale transcriptomics and proteomics data can provide important insights into the biological mechanisms underlying complex physiological processes (19). However, it is difficult to accurately evaluate their correlation using the conventional correlation coefficient analysis, which deals with a fold change

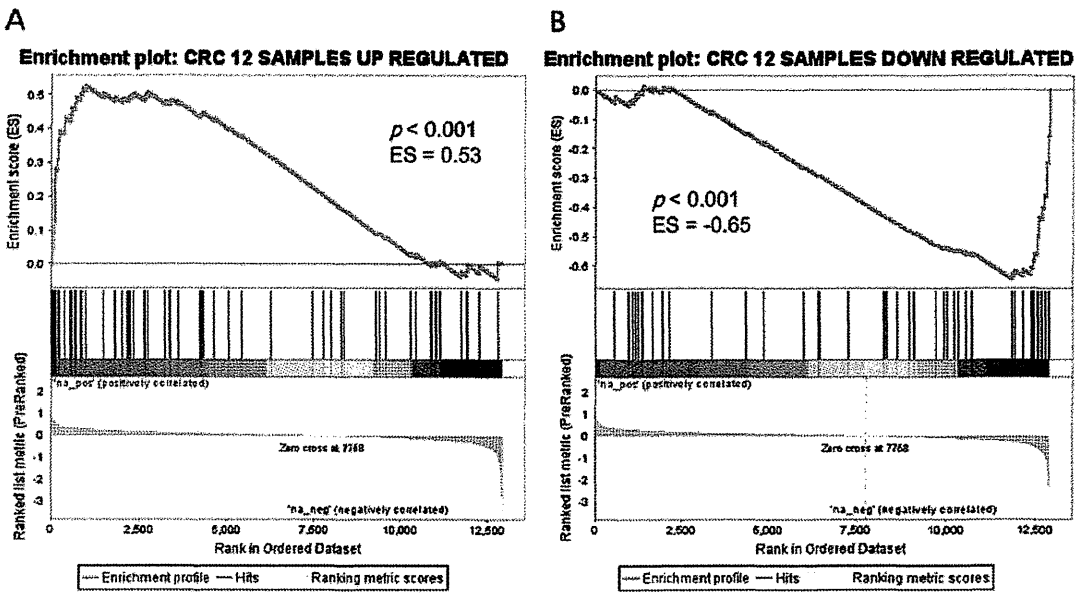

Figure 3. Enrichment plots for (A) 53 up-regulated proteins and (B) 44 down-regulated proteins in 12 CRC tissues. Top, the running enrichment score for the protein set, as the analysis sweeps through the entire ranked list organized on the basis of their magnitude of differential gene expression in 180 CRC tissues. The score at the peak of the plot is the enrichment score (ES) for the protein set. Middle, members of the protein set appear in a ranked list of genes. Bottom, the value of the ranking metric along the list of ranked genes.

Table IV. Significantly enriched genomic pathways of the KEGG database.

KEGG pathways	Size	NES	NOM P-val	FDR q-val	NBS up-regulated proteins
ECM receptor interaction	73	2.44	<0.001	<0.001	HSPG2, VTN
Ribosome	59	2.40	<0.001	<0.001	RPL13, RPL27A, RPL4, RPS18, RPS29
Cell communication	99	2.13	<0.001	<0.001	
Focal adhesion	167	1.97	<0.001	0.003	VTN, ZYX
Toll-like receptor signaling pathway	78	1.78	<0.001	0.028	
RNA polymerase	18	1.76	0.006	0.029	
Cell cycle	100	1.67	0.004	0.068	
Proteasome	22	1.65	0.023	0.071	PSMD3
WNT signaling pathway	117	1.56	<0.001	0.120	
Aminoacyl-tRNA biosynthesis	36	1.47	0.040	0.225	
Folate biosynthesis	36	1.42	0.050	0.245	
Cytokine cytokine receptor interaction	187	1.42	0.014	0.232	

GSEA was performed using gene sets from KEGG database. List of the top 12 gene sets enriched in the ranked gene list of 180 CRCs with nominal P-value <0.05. The gene list is sorted by FDR q-val in ascending order. ES; enrichment score, NES; normalized enrichment score, FDR; false discovery rate.

level in individual gene and protein expression. Most recent studies have either failed to find a correlation between protein and mRNA abundance (6) or have observed only a weak correlation (9,12). The reason is that the correlation between protein abundance and mRNA expression level depends on various biological processes and technical factors. With regard to biological processes, transcription and translation do not have a linear and simple relationship (20). Regulatory proteins and sRNAs also act as translational modulators (21). The half-live of an individual protein and the protein turnover are undoubtedly influencing the correlation between mRNA and protein expression to a considerable degree (22).

In this study, we assumed that development of a sophisticated statistical approach was essential to overcome these limitations. To assess the correlation between mRNA and protein expression, we tried the novel approach of GSEA that deals with entire genes represented by an array as ranked gene list ordered by phenotypic correlation (14,23). As expected, the conventional Spearman rank coefficient showed only a weak correlation. In GSEA, when differentially expressed proteins were treated as

a collective set, significant concordance was observed with primary tumor gene expression data.

In the present study, NBS method also plays a role in improving the precision of correlation analysis. This method is based on stable isotope labeling of tryptophan residues by NBS reagents. As previously described (15,24), this novel method has two major advantages: it reduces the number of peptides by selecting NBS-labeled tryptophan-containing peptides from bulk tryptic digests and a special matrix is used for MALDI-TOF MS measurements that can detect NBS-labeled peptides with high sensitivity. Therefore, this method could improve proteome mining by increasing the dynamic range of detection, and it shows potential for quantitative proteome analysis (25,26).

As a following step, GSEA enabled us to identify 12 potentially regulated genetic pathways in CRC. Cell-ECM (extracellular matrix) interaction is an essential mechanism in several biological processes, such as cell proliferation, migration, differentiation, apoptosis, as well as carcinogenesis (27,28). CRC cells invade the stroma as coherent cell nests instead of single cells (29,30). Of the molecules within ECM interaction pathway, HSPG2 and VTN were revealed as potential key modulators by NBS-based proteomics. HSPG2, the large prominent heparan sulfate proteoglycan of extracellular matrices, is known as a component that may participate in ECM interaction (31). Within the matrix, vitronectin can support cellular adhesion through interactions with integrins (32). In addition, vitronectin is a major component of the stroma of primary hepatocellular carcinoma and metastatic hepatic tumors including colorectal hepatic metastases (32,33).

The ribosome pathway is essential for protein synthesis. The increased overall ribosome biogenesis is a well-known common feature of active proliferation, and the proliferation rate of tumor cells is higher than that of normal ones (34). Ribosomal proteins (RPs) showed different expression patterns: not all RPs increased in the same tumor or tissue, and the same RP was expressed differentially in different tumors or different stages of diseases (35). In our study, of the molecules within Ribosomal proteins, RPL13, RPL27A, RPL4, RPS18, and RPS29 were up-regulated at the protein level. Previous studies on CRC revealed extraribosomal functions for these proteins including self-translation regulation, development regulation, and tumor suppressor gene regulation (36,37).

The assumption of GSEA is that functional gene sets with significantly high expression coherence suggest putative functionality. It must be noted that annotated functions of gene sets with higher expression coherence do not always directly correspond with the actual biological functions (38). Nonetheless, several physiological cellular responses require simultaneous participation of gene products, and genes with central roles are likely to have similar regulatory control and expression patterns (39,40). Comparative analysis also showed that coexpression patterns of many functionally related genes are conserved across diverse species (41). Thus, most gene sets with significantly high expression coherence, if not all, might represent key molecular functions of the corresponding expression profiles.

In conclusion, we performed an integrated analysis of mRNA and protein expression data in CRC. Overall, significant correlation was observed between changes in mRNA and protein levels that were consistent with the expectation that a substantial proportion of changes in protein would be a consequence of changes in mRNA levels rather than post-transcriptional effects. Our identified regulatory signatures of mRNA and protein levels might be able to enhance the understanding of carcinogenesis and cancer proliferation and lead to the elucidation of novel molecular targets in the clinical field.

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Clinical outcomes of laparoscopic surgery for advanced transverse and descending colon cancer: a single-center experience

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Abstract
Background The role of laparoscopic surgery in management of transverse and descending colon cancer remains controversial. The aim of the present study is to investigate the short-term and oncologic long-term outcomes associated with laparoscopic surgery for transverse and descending colon cancer.
Methods This cohort study analyzed 245 patients (stage II disease, $n = 70$; stage III disease, $n = 63$) who underwent resection of transverse and descending colon cancers, including 200 laparoscopic surgeries (LAC) and 45 conventional open surgeries (OC) from December 1996 to December 2010. Short-term and oncologic long-term outcomes were recorded.
Results The operative time was longer in the LAC group than in the OC group. However, intraoperative blood loss was significantly lower and postoperative recovery time was significantly shorter in the LAC group than in the OC group. The 5-year overall and disease-free survival rates for patients with stage II were 84.9% and 84.9% in the OC group and 93.7% and 90.0% in the LAC group, respectively. The 5-year overall and disease-free survival rates for patients with stage III disease were 63.4% and 54.6% in the OC group and 66.7% and 56.9% in the LAC group, respectively.
Conclusion Use of laparoscopic surgery resulted in acceptable short-term and oncologic outcomes in patients with advanced transverse and descending colon cancer.

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Keywords Laparoscopic colon surgery · Colon cancer · Transverse colon cancer · Descending colon cancer · Survival rate

Since publication of the first report of laparoscopic surgery for colon cancer in 1991 [1], utilization of the procedure has steadily increased. Benefits of laparoscopic surgery relative to open surgery include improved cosmesis, improved short-term outcomes, reduced surgical trauma, reduced requirements for narcotic analgesia, earlier return of bowel function, and shorter postoperative hospital stay [2–4]. However, due to an insufficient body of clinical evidence, laparoscopic surgery for colon cancer has not yet replaced the conventional open surgery as the standard of care.

Although the safety and oncologic efficacy of laparoscopic surgery for treatment of colon cancer have been demonstrated in many randomized controlled trials [5–13], patients with transverse colon and descending colon cancer were excluded from many of these trials, mainly due to the difficulty in determining the appropriate operative procedure and the extent of lymphadenectomy [14]. Several recent studies have described the feasibility and safety of laparoscopic surgery for transverse and descending colon cancer [15–19]. However, there are few reports that describe the long-term outcomes associated with this management strategy.

In our institution, laparoscopic surgery was performed in more than 1,000 patients with colon cancer up to December 2008. Thus, the goal of this study is to investigate the short-term and oncologic long-term outcomes associated with laparoscopic surgery for transverse and descending colon cancer.

Patients and methods

The first laparoscopic resection for colon cancer at our institution was performed in 1996. At that time, laparoscopic colectomy was indicated only for early-stage cancer. Gradually, the indication for this procedure was expanded to more advanced stages of cancer. Further, with standardization of the surgical system, more than 90% of colorectal resections were ultimately performed laparoscopically. Conversion to conventional open surgery was performed at surgeon discretion. Between December 1996 and December 2008, 1,236 patients underwent surgery for colon cancer (laparoscopic surgery, $n = 1{,}009$: conventional open surgery, $n = 227$). Of these, 245 resections were performed for cancers of the transverse and descending colon without synchronous double malignancies. All patients underwent comprehensive assessment with blood testing, serum carcinoembryonic antigen measurement, colonoscopy, pathologic confirmation, barium or air enema, computed tomography (CT), and chest X-ray before surgery. If tumor localization was unclear, preoperative colonoscopic India ink tattooing and clipping was performed. The procedure for lymphadenectomy was determined based on depth of tumor invasion according to the Japanese Classification of Colorectal Carcinoma [20]. The laparoscopic nontouch isolation technique (i.e., the median-to-lateral approach) was utilized whenever possible. The study was approved by the institutional ethics of research committee, and informed consent was obtained from each patient.

Study design

This cohort study analyzed 245 patients (stage II disease, $n = 70$; stage III disease, $n = 63$) who underwent resection of the transverse and descending colon cancer, including 200 laparoscopic surgeries (LAC) and 45 conventional open surgeries (OC) from December 1996 to December 2010. Short-term outcomes and oncologic long-term outcomes were assessed among patients with stage II (70 cases) and stage III (63 cases) disease.

Laparoscopic procedures

For transverse colon lesions, proximal ligations of the right or left branch or the root of the middle colic vessels were conducted, and lymphadenectomy was performed simultaneously using the median-to-lateral approach. Mobilization was performed from the hepatic and/or splenic flexures. For the hepatic side, if the root of the middle colic vessels was clearly identified, the vein was divided just before the point at which it drained into the gastrocolic trunk of Henle.

For descending colon lesions, the left branch of the middle colic, left colic and sigmoid colic pedicles were identified, and lymphadenectomy was performed simultaneously with proximal ligations of the tumor-feeding vessels. The mesentery of the descending colon was gently mobilized from the ligament of Treitz by the median-to-lateral approach. The omental bursa was entered, and the mesentery of the transverse colon was dissected from the inferior border of the pancreas. The bowel loop of transverse or descending colon was delivered under a wound protector through a 3- to 5-cm incision and was divided from the marginal vessels. The anastomosis was performed extracorporeally using the functional end-to-end method.

Postoperative follow-up

For follow-up, patients with stage I and II disease underwent assessment of serum carcinoembryonic antigen levels (at 3-month intervals during the first year and at 6-month intervals thereafter), chest and abdominopelvic CT (at 6-month intervals), and colonoscopy (at 1-year intervals) in addition to routine outpatient visits. Patients with stage III disease underwent assessment of serum carcinoembryonic antigen levels (at 4-month intervals during the first 2 years and at 6-month intervals thereafter), chest and abdominopelvic CT and colonoscopy at the same interval in addition to routine outpatient visits. Patients with stage III disease received adjuvant chemotherapy with 5-fluorouracil plus leucovorin per standards of care.

Statistical analysis

Statistical analysis was performed using JMP 8 (SAS Institute Inc., Cary, NC, USA) for Windows. Student's t test, Mann–Whitney U test and the χ^2 test were used to compare continuous and categorical variables, respectively, with two-sided $p < 0.050$ indicating significance. Patient survival analysis was performed using Kaplan–Meier survival curves with log-rank statistics.

Results

Laparoscopic surgery versus conventional open surgery

Patient demographics and pathologic variables are summarized in Table 1. Gender, age, body mass index (BMI), and American Society of Anesthesiology (ASA) classification were not significantly different when comparing the OC group and the LAC group. According to the tumor–node–metastasis (TNM) classification, the proportion of patients with advanced stage was higher in the OC group than in the LAC group, mainly because LAC was initially

Table 1 Characteristics of patients ($n = 245$) with transverse or descending colon cancer

	OC ($n = 45$)	LAC ($n = 200$)	p value[a]
Gender (male/female)	26:19	110:90	0.734[b]
Age, years (mean, range)	64 (29–84)	65 (24–90)	0.570
BMI, kg/m^2 (mean, range)	21 (16–34)	22 (16–32)	0.102
ASA classification			0.034[b]
I	15	70	
II	20	116	
III	7	14	
IV	2	0	
Tumor classification			<0.001[b]
0	2	20	
I	2	65	
II	15	55	
III	19	44	
IV	7	16	

OC Conventional open surgery, *LAC* laparoscopic surgery, *BMI* body mass index, *ASA* American Society of Anesthesiologists

Clinical stage is classified by UICC-7 staging

[a] Student's t test

[b] χ^2 test

used only for early-stage cancers. Therefore, short-term outcomes and oncologic long-term outcomes were investigated in patients with stage II (70 cases) and stage III (63 cases) disease. Patient demographics and pathologic variables of these cases are summarized in Table 2. Patients with stage II disease undergoing OC included 3 right hemicolectomies, 4 left hemicolectomies, and 8 transverse colectomies, while patients with stage III disease undergoing OC included 1 right hemicolectomy, 6 left colectomies, and 12 transverse colectomies. By contrast, patients with stage II disease undergoing LAC included 15 right hemicolectomies, 21 left hemicolectomies, and 19 transverse colectomies, while patients with stage III disease undergoing LAC included 11 right hemicolectomies, 23 left colectomies, and 10 transverse colectomies. Five (9.1%) patients with stage II disease required conversion to open surgery (bleeding, $n = 3$; surgical technique, $n = 1$; massive invasion, $n = 1$). Six (13.6%) patients with stage III disease required conversion to open surgery (adhesion, $n = 2$; massive invasion, $n = 2$; bleeding, $n = 1$; surgical technique, $n = 1$). All patients underwent D3 lymphadenectomy according to the Japanese Classification of Colorectal Carcinoma [20]. Gender, age, BMI, ASA classification, tumor size, number of dissected lymph nodes, and tumor differentiation were not significantly different when comparing the OC group and the LAC group. According to the TNM classification, the proportion of patients with pathologic T (pT) category was higher in the OC group than in the LAC group, likely because of the exclusion criteria utilized for this study. However, in terms of pathologic N (pN) category, there was no significant difference between the OC and the LAC group.

Table 3 presents the short-term outcomes of patients with stage II or stage III disease who underwent OC or LAC for transverse and descending colon cancer. The median operative time in patients with stage II disease was longer in the LAC group (230 min) than in the OC group (165 min; $p = 0.012$), and the median operative time in patients with stage III disease was also longer in the LAC group (245 min) than in the OC group (202 min; $p = 0.038$) with stage III. In patients with stage II disease, the median blood loss was significantly lower in the LAC group (10 ml) than in the OC group (100 ml; $p < 0.001$), and in patients with stage III disease, the median blood loss was also significantly lower in the LAC group (10 ml) than in the OC group (155 ml; $p < 0.001$). The duration until start of solid food after surgery was shorter in the LAC group (5 days) than in the OC group (7 days; $p = 0.026$) in patients with stage II disease and was also shorter in the LAC group (4 days) than in the OC group (7 days; $p < 0.001$) in patients with stage III disease. The median hospital stay after surgery was shorter in the LAC group (15 days) than in the OC group (29 days; $p < 0.001$) in patients with stage II disease and was also shorter in the LAC group (7 days) than in the OC group (31 days; $p < 0.001$) in patients with stage III disease.

Table 4 summarizes the mortality and morbidity in each group. There were no perioperative deaths in patients with stage II disease. In patients with stage III disease, two patients died postoperatively: one from severe sepsis and septic shock in the LAC group, and one from liver failure with liver cirrhosis in the OC group. There was no significant difference in morbidity when comparing groups.

Table 5 summarizes the oncologic outcomes for the various groups. For patients with stage II disease, the median (range) follow-up period was 64 (10–154) months in the OC group and was 61 (12–128) months in the LAC group. For patients with stage III, the median (range) follow-up period was 53 (24–167) months in the OC group and 44 (9–145) months in the LAC group.

The 5-year overall and disease-free survival rates in patients with stage II disease were 84.9% and 84.9% in the OC group and 93.7% and 90.0% in the LAC group, respectively (Fig. 1A, B). The 5-year overall and disease-free survival rates in patients with stage III disease were 63.4% and 54.6% in the OC group and 66.7% and 56.9% in the LAC group, respectively (Fig. 2A, B). The number of recurrences did not differ significantly between the LAC group and the OC group (2 versus 0; $p = 0.322$) in patients

Table 2 Patient demographics and characteristics of transverse and descending colon cancer in patients with stage II or stage III disease

	Stage II			Stage III		
	OC (15)	LAC (55)	*p* value[b]	OC (19)	LAC (44)	*p* value[b]
Gender (male/female)	9:6	27:28	0.452[c]	9:10	22:22	0.848[c]
Age, years[a]	67 (51–84)	66 (24–90)	0.654	63 (29–81)	65 (44–83)	0.701
BMI, kg/m^{2a}	21 (16–26)	22 (16–32)	0.975	22 (16–29)	21 (16–32)	0.528
ASA classification			0.353[c]			0.470[c]
I	5	22		7	18	
II	8	29		10	23	
III	1	4		1	3	
IV	1	0		1	0	
Tumor size, cm[a]	5.4 (2.5–7.6)	4.8 (1.4–8.7)	0.316	5.0 (3.2–11.2)	4.2 (1.0–10)	0.119
Lymph nodes[a]	19 (7–27)	15 (3–33)	0.132	14 (5–41)	16 (5–35)	0.711
pT category			0.860[c]			0.008[c]
T1	0	0		0	2	
T2	0	0		1	5	
T3	14	52		14	37	
T4	1	3		4	0	
pN category			–			0.566[c]
N0	15	55		0	0	
N1	0	0		17	37	
N2	0	0		2	7	
Tumor differentiation			0.071[c]			0.098[c]
Well	8	37		9	18	
Moderate	5	17		7	25	
Poor	2	0		3	1	
Mucinous	0	1		0	0	

Clinical stage is classified by UICC-7 staging

OC Conventional open surgery, *LAC* laparoscopic surgery, *BMI* body mass index, *ASA* American Society of Anesthesiologists, *Well* well-differentiated adenocarcinoma, *Moderate* moderately differentiated adenocarcinoma, *Poor* poorly differentiated adenocarcinoma, *Mucinous* mucinous adenocarcinoma

Lymph nodes is number of lymph nodes removed

[a] Values expressed as median (range)

[b] Mann–Whitney *U* test

[c] χ^2 test

Table 3 Intraoperative and postoperative results of surgeries for transverse or descending colon cancer

	Stage II			Stage III		
	OC (15)	LAC (55)	*p* value[a]	OC (19)	LAC (44)	*p* value[a]
Operative time (min)	165 (130–460)	230 (130–525)	0.012	202 (105–305)	245 (150–465)	0.038
Blood loss (ml)	100 (40–660)	10 (10–1050)	<0.001	155 (10–660)	10 (10–450)	<0.001
Days to diet	7 (5–34)	5 (2–22)	0.026	7 (4–34)	4 (3–36)	<0.001
Hospital stay (day)	29 (12–72)	15 (8–53)	<0.001	31 (10–75)	7 (14–156)	<0.001

OC Conventional open surgery, *LAC* laparoscopic surgery

Values expressed as median (range)

[a] Mann–Whitney *U* test

with stage II disease or between the LAC group and the OC group (11 versus 7; $p = 0.346$) in patients with stage III disease. There was no port-site recurrence or wound recurrence in either group, and there was no significant difference in the site of recurrence when comparing the groups.

Table 4 Mortality and morbidity associated with surgery for transverse or descending colon cancer

	Stage II			Stage III		
	OC (15)	LAC (55)	*p* value[a]	OC (19)	LAC (44)	*p* value[a]
Mortality	0	0	–	1	1	0.517
Morbidity	5	11	0.069	6	7	0.163
SSI	2	8		2	6	
Leakage	1	1		2	1	
Ileus	2	0		1	0	
Colitis	0	2		0	0	
Duodenal ulcer	0	0		1	0	

OC conventional open surgery, *LAC* laparoscopic surgery, *Mortality* within 30 days after surgery, *SSI* surgical-site infection

[a] χ^2 test

Table 5 Five-year oncologic outcomes of patients who underwent surgery for transverse or descending colon cancer

	Stage II			Stage III		
	OC (15)	LAC (55)	*p* value[a]	OC (19)	LAC (44)	*p* value[a]
Overall survival (%)	84.9	93.7	0.240	63.4	66.7	0.819
Disease-free survival (%)	84.9	90.0	0.489	54.6	56.9	0.890
Recurrence rate (%)	0	3.6	0.322[b]	37	25	0.346[b]
Recurrence site	0	2	–	7	11	0.432[b]
Liver	0	0		2	7	
Lung	0	1		2	1	
Local	0	1		3	3	

OC conventional open surgery, *LAC* laparoscopic surgery, *Recurrence site* site of first recurrence

[a] Log-rank statistics

[b] χ^2 test

Discussion

Several randomized controlled trials have demonstrated that laparoscopic surgery for colon cancer (excluding those with transverse or descending colon cancer) can achieve favorable short-term outcomes and oncologic outcomes that are similar to open surgery [5–13]. Other recent studies of laparoscopic surgery have also demonstrated the feasibility and safety of the procedure for transverse and descending colon cancers [15–19]. However, the oncologic outcomes of patients undergoing laparoscopic resection of transverse and descending colon cancer have not yet been studied.

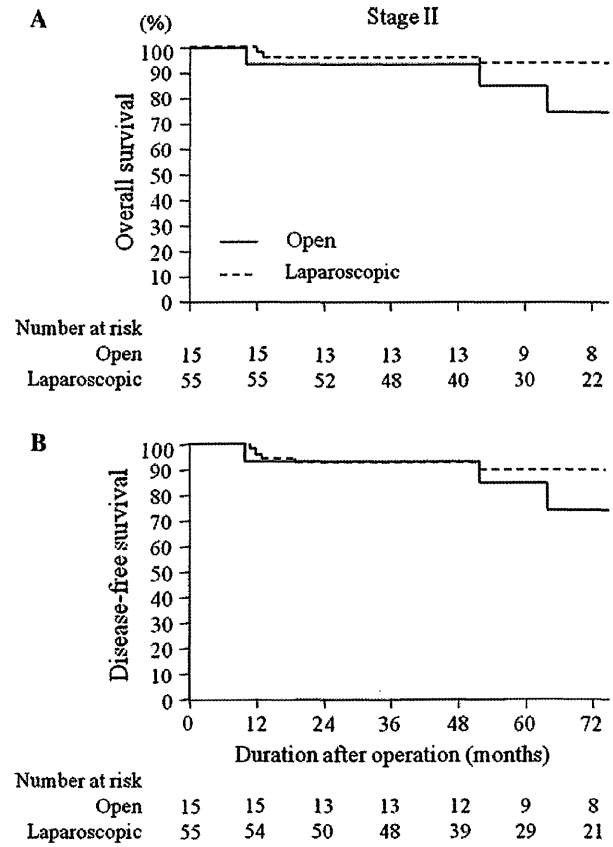

Fig. 1 Kaplan–Meier curves of patients with stage II disease undergoing laparoscopic surgery or conventional open surgery: **A** overall survival rate and **B** disease-free survival rate. There was no statistically significant difference in survival between the two groups

Certainly, there are some difficulties when utilizing laparoscopic resection for transverse and descending colon cancer, as described in previous studies [15–19]; for example, mobilization, extent of resection, and details of lymphadenectomy may vary according to the precise location of the tumor in patients with transverse and descending colon cancer. In addition, resection of transverse and descending colon cancers that are adjacent to other critical structures, including the pancreas, duodenum, spleen, and the base of the mesenteric vessels, can result in major complications in case of dissection in the wrong plane. Therefore, thorough appreciation of the intricacies of venous anatomy at the gastrocolic trunk of Henle at the level of pancreas along the right plane is required when conducting this procedure. Jamali et al. [14] reported that a high-grade technique was required for splenic flexure mobilization, because of the requirement for extensive posterior dissection with simultaneous preservation of the vascular supply to the hind gut via the marginal artery as well as preservation of retroperitoneal structures, such as

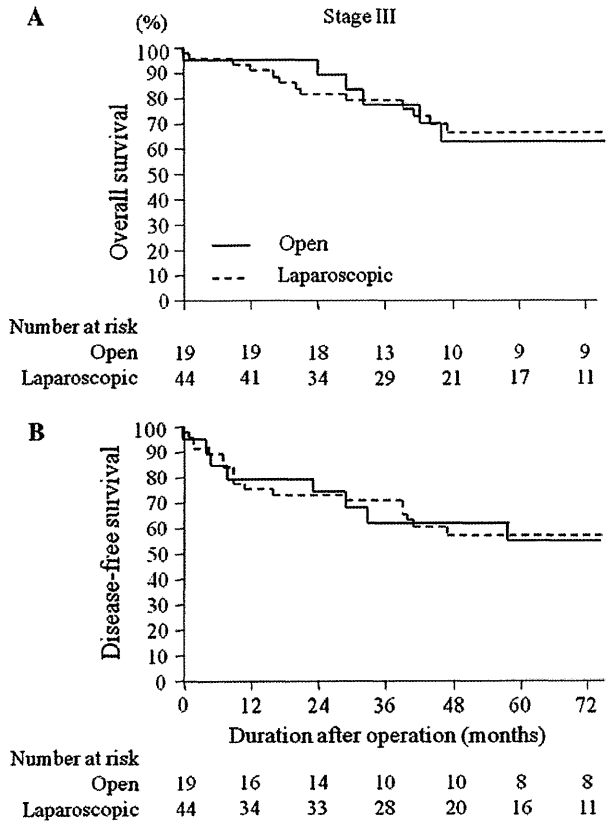

Fig. 2 Kaplan–Meier curves of patients with stage II disease undergoing laparoscopic surgery or conventional open surgery: **A** overall survival rate and **B** disease-free survival rate. There was no statistically significant difference in survival between the two groups

the ureters and the tail of pancreas. Further, surgeons may have comparatively less experience in dealing with this procedure because the incidence of transverse and descending colon cancer is low. Thus, laparoscopic transverse colectomy and left colectomy are more difficult than sigmoid colectomy and right colectomy, which often limits their use for cancers of the transverse and descending colon, especially for those with advanced cancer. In our institution, laparoscopic surgery has been utilized in more than 200 patients with transverse and descending colon cancer. The present study characterized the short-term outcomes and oncologic long-term outcomes after resection for advanced cancer of transverse and descending colon in patients with stage II or stage III disease undergoing OC or LAC. Gender, age, BMI, ASA, and tumor size were similar in both groups. Operative time was longer in the LAC group than in the OC group, likely because of anatomical and technical difficulties. However, blood loss was significantly lower and the postoperative course of recovery was significantly shorter in the LAC group than in the OC group. The morbidity and mortality were not significantly different when comparing the two groups. Further, the number of dissected lymph nodes and the incidence of intraoperative injury were not significantly different when comparing the two groups, nor were there differences in the number of recurrences, overall survival, or disease-free survival. These data indicate that laparoscopic surgery for advanced transverse and descending colon cancer resulted in favorable short-term outcomes (i.e., lower blood loss, shorter postoperative stay) and similar oncologic long-term outcomes when compared with conventional open surgery. Thus, laparoscopic surgery is an acceptable management strategy for advanced colon cancer regardless of tumor location.

Successful laparoscopic surgery for transverse and descending colon cancer requires an advanced technique. Thus, acquisition of general laparoscopic skills is required to perform this fairly complex procedure. Since the number of patients requiring this specific procedure is relatively low, one way to gain this experience is through the development of laparoscopic skills when performing simpler, more common procedures, such as sigmoid colectomy and right colectomy. This experience may attenuate the otherwise steep learning curve needed to successfully achieve more complex laparoscopic procedures, thereby reducing the operative time, need for conversion to open procedures, and complication rate.

In conclusion, laparoscopic resection for transverse and descending colon cancer appears safe and feasible and produces acceptable short-term and oncologic long-term outcomes. Curative resection for advanced transverse and descending colon cancer is technically possible; however, the present data were derived from single-institution experience and were not generated in a prospective manner. Laparoscopic surgery for colon cancer has not yet replaced conventional open surgery as the standard, mainly because there is insufficient clinical evidence. Further, there are also controversies regarding the level of difficulty of the individual procedure, the lack of data regarding oncological long-term outcomes after curative resection, and hospital costs. However, the favorable results seen in several randomized controlled trials of the safety and oncologic efficacy of this procedure for advanced colon cancer have resulted in increased utilization of the procedure. Confirmation of the value of laparoscopic surgery for colon cancer in prospective randomized controlled trials may result in increased demand for laparoscopic procedures from physicians and patients. In our institution, the chief and senior surgeons are actively trained in laparoscopic colon surgery. Indeed, with standardization of the surgical system and gradual expansion of the indications, more than 90% of colon surgeries in 2010 were performed laparoscopically at our institution. Since the demand for laparoscopic surgery for colon cancer is expected to

increase, chief and senior surgeons as well as young surgeons starting will gradually increase. Regardless, we believe that laparoscopic surgery may become the gold standard for management of colon cancer, regardless of stage or tumor location.

Disclosures Authors M. Yamamoto, J. Okuda, K. Tanaka, K. Kondo, N. Tanigawa, and K. Uchiyama have no conflicts of interest or financial ties to disclose.

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Ⅲ 虫垂・結腸の手術

3. 結腸癌手術
a) 結腸右半切除術に必要な局所解剖*

山口茂樹　石井利昌　田代　浄
諏訪宏和　近藤宏佳　鈴木麻未**

はじめに

本邦で行われる結腸右半切除術の多くが結腸癌に対するものであるため，腸管切除とともにリンパ節郭清が必要となる．右側結腸の血管系は分岐形態の症例差が大きく，また損傷による術中出血は大きなトラブルとなるので，外科解剖の熟知が必要である．最近では欧州からもcomplete mesocolic excision（CME）の有用性が報告され，中枢郭清が注目されている．本稿では，リンパ節郭清を伴う腹腔鏡下結腸右半切除術の術式，局所解剖について解説するが，開腹手術においても局所解剖の理解は同様である．

Ⅰ．術式の概要

❶ 回結腸動静脈根部郭清

いわゆる内側アプローチでは，回結腸血管を挙上し間膜切開，その背側にいたって十二指腸を確認し，間膜を剝離・授動する．回結腸血管の走行を確認して，根部の郭清を静脈中心に行い，動静脈は順次切離する．

❷ 結腸授動

膵前筋膜を温存しつつ，結腸間膜の授動を頭側方向へすすめる．十二指腸と膵頭部から結腸間膜を十分剝離し，さらに右腎周囲脂肪織を筋膜におおわれたまま背側に落として授動が完了する．結腸外側の腹膜付着部を切離すると，右半結腸は遊離した状態になる．

❸ 右結腸動静脈根部郭清

Surgical trunkを露出しつつ，回結腸血管の次の分枝である右結腸動静脈を切離する．しばしば右結腸動脈（right colic artery：RCA）および右結腸静脈（right colic vein：RCV）は欠損する．その場合，上行結腸は回結腸動脈（ileocolic artery：ICA）または中結腸動脈（middle colic artery：MCA）から栄養され，回結腸静脈（ileocolic vein：ICV）または中結腸静脈（middle colic vein：MCV），あるいは胃結腸静脈幹（gastrocolic trunk：GCT）からドレナージされる．

❹ 中結腸動静脈根部郭清

癌の占居部位を確認し肛門側腸管切離部位を設定し，含まれる血管を切除・郭清する[1]．明らかなリンパ節腫大がなければ，MCA右枝の分岐部で切離することが多い．横行結腸を頭側に反転させて処理し，左から動脈，静脈の順に切離する．

❺ Gastrocolic trunkの処理

上腸間膜静脈（superior mesenteric vein：SMV）に流入する結腸枝の中で，右胃大網静脈（RGEV）や前上膵十二指腸静脈（ASPDV）と共通幹を形成するものがGCTである．予防的郭清では結腸枝のみを切離する．結腸枝のほとんどが上行結腸や肝彎曲からの流出静脈であり，合流形態が複雑なので損傷に注意する．

キーワード：右側結腸癌，surgical trunk，gastrocolic trunk

* Surgical anatomy for right hemicolectomy

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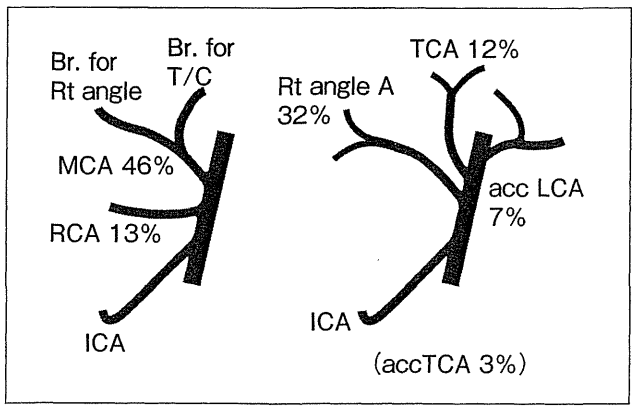


図1. 右側結腸の動脈の解剖（文献2より引用）
Br. for Rt angle：肝彎曲枝，Br. for T/C：横行結腸枝，Rt angle A：肝彎曲動脈，acc LCA：副左結腸動脈，acc TCA：副横行結腸動脈

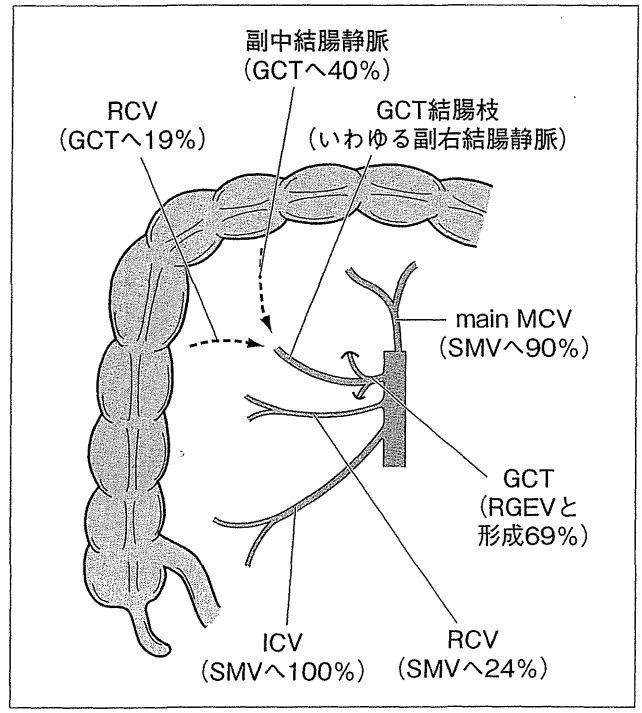
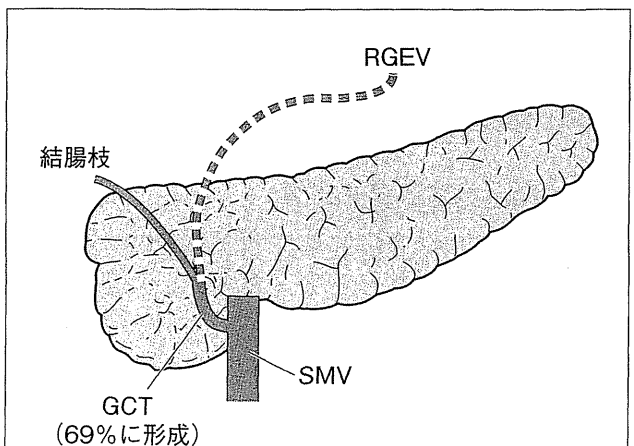


図2. 右側結腸の静脈の解剖（文献3より引用）



結腸枝＝副右結腸静脈	
上行結腸から	
RCV	28 %*
横行結腸から	
main MCV	18 %
副中結腸静脈	58 %*

*重複あり

図3. GCTの結腸枝（文献3より引用）

❻ 結腸切離と吻合

手縫いの端々吻合，器械による機能的端々吻合のうち，慣れた方法で行う．機能的端々吻合は器械のコストはかかるものの，手術時間が短く術者による差も少ないとともに，大きな吻合口が得られる．

Ⅱ．手術（手技）のポイントとなる局所解剖図

❶ 右側結腸の動脈の解剖（図1）
❷ 右側結腸の静脈の解剖（図2）
❸ Gastrocolic trunkの結腸枝（図3）
❹ 右側結腸の動静脈の相関関係（図4）
❺ 右側結腸間膜と周囲臓器（図5）

Ⅲ．手術（手技）のポイントとなる局所解剖図の解説

❶ 右側結腸の動脈の解剖

上腸間膜動脈（superior mesenteric artery：SMA）から分枝して回盲部を栄養するICAは，ほぼ全例に1本のみ存在する．分岐位置は十二指腸前面から下縁あたりが多い．時に上行結腸を栄養する分枝がICAの根部付近から分かれることがあり注意を要するが，これはICAの上行結腸枝と呼ぶべきものである．RCAはSMAから直接分岐

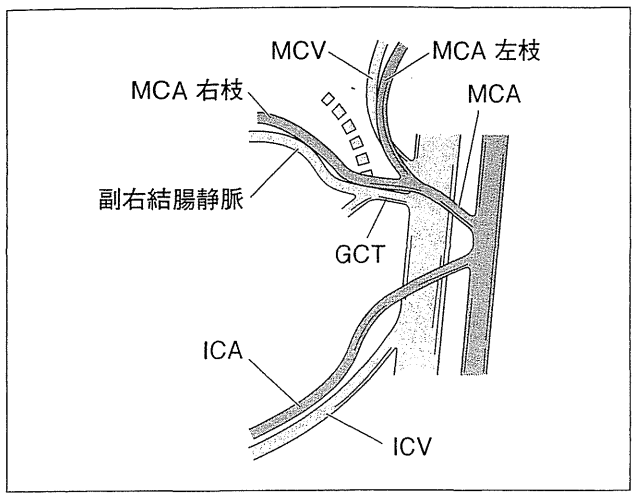


図4. 右側結腸の動静脈の相関関係

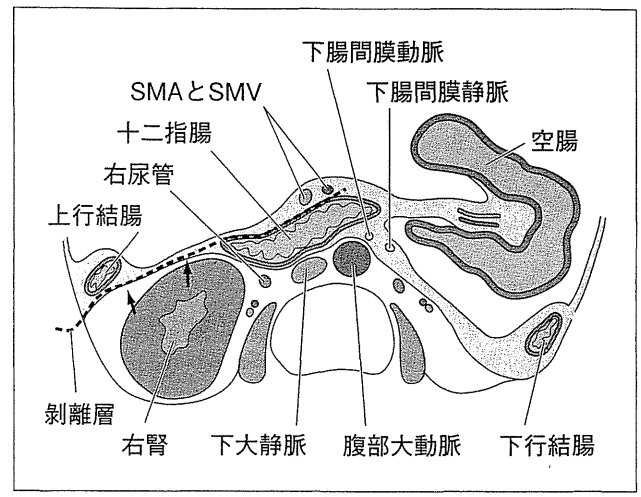


図5. 右側結腸間膜と周囲臓器
矢印：腹膜下筋膜に沿って剝離

して上行結腸を栄養する．実際には30％程度の存在率で，比較的細いことが多い．MCAはもっとも個人差の大きい動脈である．一般に2分岐して右枝，左枝と呼ばれるが，向かう方向は右枝が肝彎曲方向，左枝が横行結腸中間部方向のものが多いとされる[2]．MCA右枝・左枝分岐までの長さも個人差が大きく，各々独立してSMAから分岐するものもある．さらに左側横行結腸を栄養する副中結腸動脈が40％程度，またSMAから下行結腸を栄養する副左結腸動脈が7％程度存在するといわれている．

❷ 右側結腸の静脈の解剖

回盲部から流出するICVは，ICAに伴走してSMVに流入する．動脈同様1本のみ存在するが，上行結腸からの分枝がICV根部近くに流入することがあることも動脈に似る．上行結腸から流出するRCVがSMVに直接流入するものは24％，後述するGCTに流入するものは19％である[3]．40％では副中結腸静脈を介して横行結腸からGCTに流入する．

MCVの数は1本38％，2本50％，3本12％であるが，もっとも太いMCVがSMVに直接流入するものが90％である．2本目のMCVとしてもっとも多い副中結腸静脈は横行結腸肝彎曲寄りからGCTに入るものであるが，後述する動静脈の相関関係からはしばしばこの静脈がMCA右枝領域をカバーしている．

❸ Gastrocolic trunkの結腸枝

GCTは上行結腸または横行結腸からの静脈がRGEVやASPDVと合流して共通幹を形成したもので，SMVに合流する．69％にRGEVとの共通幹を形成するGCTがみられ，この結腸枝は一般に副右結腸静脈と呼ばれている．この副右結腸静脈を厳密にみると，58％は横行結腸からの副中結腸静脈，28％は上行結腸からのRCV本幹，そして残りがMCV本幹で構成されており，本来解剖学的にはそのように命名されるべきである．しかしながら術中には頻度の低いMCV本幹以外は正確な認識が困難であり，外科的には副右結腸静脈と総称で呼ばざるをえない．またGCTの結腸枝は短く，無理な牽引で容易に損傷するため，術中操作ではもっとも注意を要する部位の一つである．

❹ 右側結腸の動静脈の相関関係

右結腸の血管処理をいっそう複雑にしているのが動脈，静脈の相関関係である．一般に伴走する動静脈には同じ名称が与えられるものであるが，ここでは異なる場合が出てくる．もっとも典型的な例を図4に示す．RCA欠損は70％程度と多数を占める．その場合の多くはMCAが上行結腸を栄養している．またGCTは69％に存在しており，この結腸枝は前述のように副右結腸静脈と呼ばれる．副右結腸静脈は動脈に伴走しないこともあるが，伴走する場合は図4のようにMCA右枝を伴うことが多く，異なった命名の血管が伴走することになる．

❺ 右側結腸間膜と周囲臓器

結腸右半切除で授動・切除すべき右側結腸間膜

はSMA，SMVより右側に存在し，血管根部付近では膵頭部および十二指腸の前面に生理的に癒着している．尾側は下大静脈の前面，すぐ外側には尿管と性腺血管が存在する．十二指腸外側には右腎が存在する．肝彎曲の頭側には肝右葉と胆嚢があり，大網とともに結腸に癒着している場合は副損傷に注意して剝離する．

いわゆる内側アプローチでは，回結腸血管の尾側で腹膜を切開し，腸間膜を切離して十二指腸を確認する[4]．回結腸動静脈を切離後，膵前筋膜に沿って結腸間膜を膵頭部および十二指腸から剝離する．外側方向に剝離をすすめると自然に右腎の前に出て，そのまま腹膜下筋膜に沿って剝離できる．さらに尾側方向に剝離すれば，尿管や性腺血管もおのずと背側に温存される．

内側からの剝離で結腸外側の切離は容易なことが多いが，肝下面は時に大網が癒着していることがある．十二指腸前面ですでに剝離した腔に入ることができれば，癒着した大網を順次凝固切離できる．容易に背側に入れなければ，肝，胆嚢から丹念に癒着を剝離した後に，背側の腔に入って肝彎曲の授動を完了する．

おわりに

結腸右半切除のポイントは，個人差の大きい血管系の理解と処理手順の定型化，結腸間膜の十分な剝離による膵頭部，十二指腸からの授動である．特にGCT周囲の解剖を理解し，副損傷を起こさないことが肝要である．

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特集 主題Ⅰ：早期大腸癌の診断と治療の進歩

Ⅳ．大腸SMおよびMP癌のリンパ節転移

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大腸SM癌に対しては内視鏡的治療および腸切除＋リンパ節郭清が施行されている．また，MP癌に対しては腸切除＋リンパ節郭清が施行されており，大腸癌治療ガイドラインによるとSM癌に対するリンパ節郭清はD2，MP癌に対してはD2ないしD3が推奨されている．今回，自験大腸SM癌およびMP癌症例，大腸癌全国登録症例，報告からSM癌およびMP癌のリンパ節転移率，リスクファクター，郭清範囲などを検討した．SM癌に対するD2郭清，MP癌に対するD2ないしD3郭清は妥当であり，中分化・低分化MP癌に対してはD3を施行すべきと考える．

索引用語：大腸SM癌，大腸MP癌，リンパ節転移

はじめに

近年，大腸癌治療は内視鏡診断学や臨床病理学の進歩，薬剤，医療機器などの開発，腹腔鏡手術の普及，臨床試験の推進により急速に変化している．本邦における大腸癌治療においては2005年に大腸癌治療ガイドラインが作成され，内視鏡的治療，手術治療方針，化学療法などが記載されている．最新の2010年版では大腸SM癌に対する内視鏡的切除後の追加腸切除の適応について垂直浸潤距離1,000 μm以上，脈管侵襲陽性，低分化腺癌・印環細胞癌，簇出grade 2，3のうち，いずれかでも認めればリンパ節郭清を伴う追加腸切除を考慮するとされている．手術治療ではM癌にはリンパ節転移はないので，リンパ節郭清の必要はないが，術前深達度診断の精度もありD1郭清を行ってもよいとされ，SM癌では約10%のリンパ節転移があること，中間リンパ節転移も少なくないことから，D2郭清が必要であるとされている．また，MP癌の手術治療では少なくともD2郭清が必要であり，主リンパ節転移が少なからずあること，および術前深達度診断の精度の問題から，D3郭清を行ってもよいと記載されている[1]．このように大腸早期癌に対する術前深達度診断はいまだ課題があり，今回，自験大腸pSM癌に加えてpMP癌に対するリンパ節転移状況を検討し，また，諸家の報告から大腸SM癌およびMP癌のリンパ節転移状況や治療方針について述べてみたい．

1．自験大腸pSM，pMP癌のリンパ節転移状況（表1）

2004年4月から2012年3月までに当院で切除した大腸pSM癌およびpMP癌はおのおの132例，146例であった．pSM癌のリンパ節郭清はD1が22例，D2が77例，D3が33例に施行され，pMP癌ではD1が10例，D2が54例，D3が82例に施行されていた．pSM癌のリンパ節転移は9.1%に認めた．部位別にみると結腸およびRSでは6.6%，直腸では14.6%であった．pMP癌のリンパ節転移は16.4%に認めた．結腸およびRSでは11.1%，直腸では23.1%に認めた．リンパ節転移程度はpSM癌ではpN1が8.3%，pN2が0.8%であった．pMP癌ではpN1が13.7%，pN2が2.7%でありpN3症例は認めなかった．リンパ節転移個数はpSM癌ではリンパ節転移1個が7例（5.3%），2個が4例（3%）で，7個が1例（0.8%）であった．pMP癌では1個が7例（4.8%），2個が11例（7.5%），3個が2例（1.4%），4個が1例（0.7%），8個が1例（0.7%）であった．pSM癌で7個，pMP癌で8個転移を認めた症例はともに術後補助化学療法を施行し5年無再発生存中である．組織型別ではpSM癌では高分化腺癌104例中7.7%，中分化腺癌27例中40.7%，低分化腺癌

表1　大腸pSM癌，pMP癌のリンパ節転移（自験例）

	pSM	pMP
部位別リンパ節転移		
C+RS	6.6%（6/91）	11.1%（9/81）
R	14.6（6/41）	23.1（15/65）
リンパ節転移程度		
N1	8.3%（11/132）	13.7%（20/146）
N2	0.8（1/132）	2.7（4/146）
リンパ節転移個数		
1	5.3%（7/132）	4.8%例（7/146）
2	3.0（4/132）	7.5（11/146）
3	0（0/132）	1.4（2/146）
4	0（0/132）	0.7（1/146）
5～	0.8（1/132）	0.7（1/146）
組織型別リンパ節転移		
高分化	7.7%（8/104）	10.9%（6/55）
中分化	40.7（3/27）	19.3（16/83）
低分化	100（1/1）	50.0（1/2）
粘液	—	20.0（1/5）
その他	—	0（0/1）
治療法別リンパ節転移		
内視鏡的ポリープ切除後手術	3.2%（1/31）	—
直接手術	10.8%（11/101）	16.4%（24/146）
計	9.1%（12/132）	16.4%（24/146）

C: colon, RS: rectosigmoid, R: rectum

表2　大腸SM，MP癌のリンパ節転移（大腸癌全国登録2000～2002年度症例2）

	n0	n1	n2	n3	n4
結腸SM（n=1,018）	88.3	7.5	1.9	0	0
直腸SM（n=679）	80.3	6.5	2.1	0.1	0.4
結腸MP（n=1,029）	77.7	15.6	3.3	0.8	0.2
直腸MP（n=1,151）	72.9	18.2	3.6	1.4	0.3

表3　大腸SM癌のリンパ節転移率

報告者	SM癌症例数	対象	リンパ節転移率
太田[3]	198	A	11.6%
浅井[4]	113	A	12.4%
渡部[5]	59	B	15.3%
前田[6]	112	A	5.3%
江頭[7]	182	B	9.3%
長谷川[8]	156	A	9.6%
Nascimbeni[9]	353	B	13.0%
Yamamoto[10]	301	A	6.3%
Tominaga[11]	155	B	12.3%
Sohn[12]	48	B	14.6%
Tateishi[13]	322	B	14.3%
工藤[14]	391	A	11.0%

A：内視鏡切除例＋手術切除例
B：はじめから腸切除が施行された例

1例中100%，また，pMP癌では高分化腺癌55例中10.9%，中分化腺癌83例中19.3%，低分化腺癌2例中50%，粘液癌5例中20%のリンパ節転移を認め，分化度が低分化になるにつれてリンパ節転移率の増加を認めた．大腸pSM癌の内視鏡的ポリープ切除の有無とリンパ節転移では内視鏡的ポリープ切除後手術症例31例中1例に，直接手術例では101例中10.8%のリンパ節転移を認めた．内視鏡的ポリープ切除後に手術を施行しリンパ節転移を認めた症例は，S状結腸の12×8×12mmのIspおよび14×12×12mmのIsp病変に対して内視鏡的ポリープ切除を行い，前者の病理診断は高分化腺癌，深達度SM（SM浸潤距離1,400μm），ly0，v0，budding（+），後者は中分化腺癌，深達度SM（SM浸潤距離2,000μm），ly0，v1，budding（−）であり，1,000μm以上のSM浸潤，静脈侵襲，budding（+）を認めたため手術適応と判断して腹腔鏡下S状結腸切除D2を施行した症例で，傍結腸リンパ節転移1個を認めた．6ヵ月間の補助化学療法を施行し，現在術後1年6ヵ月無再発生存中である．

2．大腸癌研究会全国登録のおける大腸SM癌およびMP癌のリンパ節転移状況[2]（表2）

大腸癌研究会の2000年～2002年度症例大腸癌全国登録によると結腸SM癌のリンパ節転移状況はn0が88.3%，n1が7.5%，n2が1.9%であり，直腸SM癌ではn0が80.3%，n1が6.5%，n2が2.1%，n3が0.1%，n4が0.4%であった．一方，結腸MP癌ではn0が77.7%，n1が15.6%，n2が3.3%，n3が0.8%，n4が0.2%であり直腸MP癌でn0が72.9%，n1が18.2%，n2が3.6%，n3が1.4%，n4が0.3%であった．

3．大腸SM癌のリンパ節転移の報告

大腸SM癌のリンパ節転移率は5%～20%で

表4　大腸SM癌のリンパ節転移のリスクファクター

報告者	リスクファクター
下田[15]	若年，形態（Ⅱa+Ⅱc），深達度（SM3）
藤吉[16]	簇出
岡部[17]	深達度（SM1,000μ）またはSM width（4mm）
井原[18]	深達度（SM1c）
長谷[19]	深達度，組織型，脈管侵襲，簇出，INF
酒井[20]	脈管侵襲，深達度，占居部位，形態（Is, Ⅱa+Ⅱc）
井上[21]	組織型，深達度，脈管侵襲
岡部[22]	リンパ管侵襲
浅井[4]	SM垂直浸潤距離，SM水平浸潤距離，簇出，リンパ管侵襲
渡部[5]	desmoplastic reaction
江頭[7]	深達度（SM2,000μm）
工藤[14]	深達度，脈管侵襲，簇出，粘膜筋板消失
Nascimbeni[9]	SM3, lymphovascular invasion, lower third of the rectum

表5　大腸SM癌のリンパ節郭清範囲

報告者	郭清範囲
石井[23]	D2
酒井[20]	D1 + α
井上[21]	D3（SM-massive）
前田[6]	D2

表6　大腸MP癌のリンパ節転移率

報告者	症例数	リンパ節転移率
森谷[27]	131	27.5%
角田[28]	42	19.0%
安井[29]	218	26.1%
貞廣[30]	102	31.7%
渡辺[31]	91	18.7%
村瀬[32]	58	29.3%
藤田[34]	54	28%
佐藤[35]	52	21.2%

表7　大腸MP癌の郭清範囲

報告者	郭清範囲
森谷[27]	腫瘤型ではD2，潰瘍型ではD3
角田[28]	腫瘤型ではD2，潰瘍型ではD3
安井[29]	D2
渡辺[31]	腫瘤型ではD2，潰瘍型ではD3
村瀬[32]	MP1はD2，MP2，3は適宜D3（坂谷らの分類）
佐藤[35]	D2
前田[6]	D2＋サンプリング

10%程度とする報告が多い．表3は2000年以降に報告された主なSM癌のリンパ節転移率であり，内視鏡的切除例と手術症例が混在しているものをA，はじめから腸切除が施行されたものをBとしたが，内視鏡的切除後の追加腸切除例のみにおけるリンパ節転移率の報告はなかった[3-14]．また，大腸SM癌のリンパ節転移のリスクファクターに関しては深達度，組織型，脈管侵襲，簇出などを挙げているものが多い（表4）[4,5,7,9,14-22]．大腸SM癌のリンパ節郭清範囲はガイドラインではD2が推奨されているが，酒井らはn2以上の転移例は経験なくD1+αで十分とし[20]，井上はSM-massive例では局所再発例もあり，進行癌に準じたD3を行うべきとしている[21]（表5）．

3群や4群リンパ節転移陽性例も報告されているが頻度は低い[24,25]．術後再発に関しては徳永らが51例中4例（7.8%）としており，うち2例がリンパ節転移陽性例であり，中分化腺癌の再発が高いと述べている[26]．

4．大腸MP癌のリンパ節転移の報告

大腸MP癌のリンパ節転移率は20～30%とされており，約30%とするものが多い（表6）[27-32,34,35]．貞廣らは大腸MP癌の発育形態とリンパ節転移などの関係について検討を行ったが，リンパ節転移の有無で発育形態に差は見られず，組織標本の上での浸潤の程度，深度から転移を予測することは困難であると述べている[30]．MP癌のリンパ節転移率は森谷によると腫瘤型では6%，潰瘍型では34%[27]，角田によると腫瘤型では9%でn2転移に留まり[28]，潰瘍型では28%でn3転移例を認め，渡辺によると腫瘤型では15%でn1に留まり，潰瘍型では19.7%でn2以遠のリンパ節転移を認め，腫瘤型ではD2，潰瘍型ではD3を施行すべきと述べている[31]．一方，安井は

治癒切除を行ったD2群とD3群の間で術後再発率，生存率はリンパ節転移の有無にかかわらず有意な差を認めず，同様に直腸癌でも上方郭清D2群とD3群で術後の遠隔成績に有意な差はなく，下部直腸のMP癌では側方郭清の有無による予後に有意差を認めず，大腸MP癌の郭清範囲はD2で十分であるとしている[29]．佐藤らは大腸MP癌52例の検討で，リンパ節転移は21.2%であったが，すべてn1までD2でよいと述べている[35]．村瀬らはMP癌に坂谷らの分類[33]を用いて浸潤度細分類を行い，MP1はSM癌に準じたD2郭清，MP2，MP3は適宜D3郭清を追加し，特にRa以下のMP2，MP3はss(a1)，以深の進行癌と同様の対処が必要であると述べている（表7）[32]．また，Kobayashiらは臨床的T1でリンパ節転移陰性例では傍結腸リンパ節郭清が至適で，臨床的T1でリンパ節転移陽性例でも主幹動脈を超えての転移は見られず，臨床的にT2でリンパ節転移陰性例では根部リンパ節の転移は見られず，明らかなリンパ節転移陽性例では根部リンパ節を超えての転移は認めなかったと報告している[36]．

腸管傍リンパ節の郭清範囲については，大腸癌取扱い規約では5 cm，10cmルールが記載されている[37]が，Hidaらは結腸癌のリンパ節転移をclearing methodを用いて検討し，SM癌では根部リンパ節郭清は不要，口側および肛門側の郭清は3 cm必要で，MP癌では根部リンパ節と口側および肛門側の5 cmの範囲のリンパ節郭清は行うべきと述べている[38]．

5．考察

大腸早期癌に対する外科治療も大きな変貌を遂げつつあり，特に，腹腔鏡手術の普及は著しいものがある．現在の大腸癌治療ガイドラインでは術前の臨床所見あるいは術中所見によるリンパ節転移度と腫瘍の壁深達度から手術治療方針が決定されている．大腸癌のリンパ節転移診断はCT，MRI，PETCTなどの画像診断の限界や微小転移[39]の点から困難な場合があるが，5個以上のリンパ節が転移陽性でも完治したと思われる症例もあり，リンパ節転移例に対する郭清の治療効果は明らかである．一方，pSM癌の約90%，pMP癌の約70%，pSS以深癌の約50%はリンパ節転移陰性である．また，深達度診断は注しても100%の正診率は得られていない．術前リンパ節転移および深達度診断，術中リンパ節転移診断の精度が不完全である以上，治療方針はやや「oversugery」にする必要があり，現在の大腸癌治療ガイドライン[1]に示されているSM癌に対するD2郭清，MP癌に対するD2ないしD3郭清は妥当と考える．自験例ではMP癌のpN3症例は認めなかったが，中分化・低分化腺癌ではD3を施行すべきと考えている．今後，手術，郭清の縮小化を進めるためには，リンパ節転移陰性の診断法の開発が望まれる．

まとめ

大腸癌治療ガイドラインによるとSM癌に対するリンパ節郭清はD2，MP癌に対してはD2ないしD3が推奨されているが自験大腸SM癌およびMP癌症例，大腸癌全国登録症例，報告からSM癌およびMP癌のリンパ節転移率，リスクファクター，郭清範囲などを検討したところ，SM癌に対するD2郭清，MP癌に対するD2ないしD3郭清は妥当であり，中分化・低分化MP癌に対してはD3を施行すべきと考える．

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