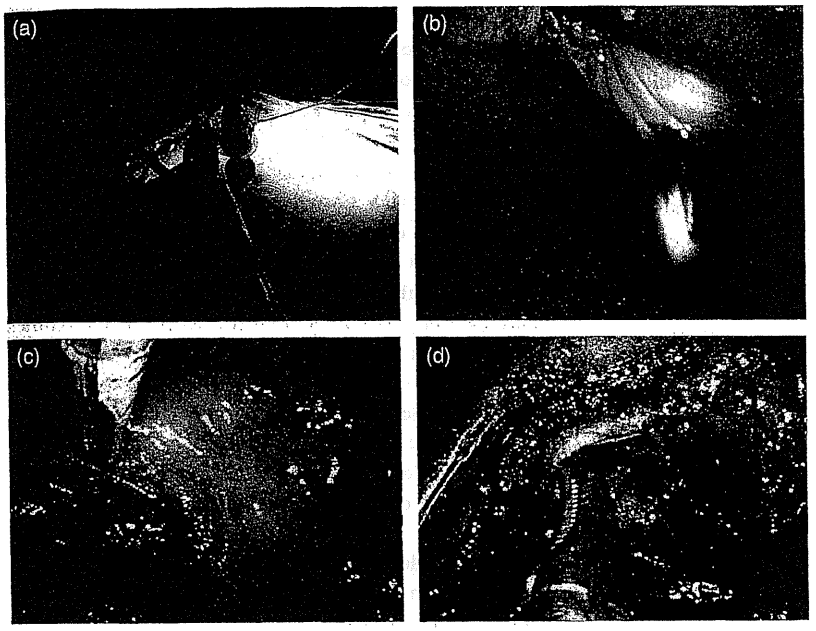

Figure 1 (a) Placement of the three ports on the umbilical incision. (b) Insertion of second umbilical port under laparoscopic guidance. (c) Ileocolic vein. (d) The exteriorized branch of the inferior mesenteric artery.

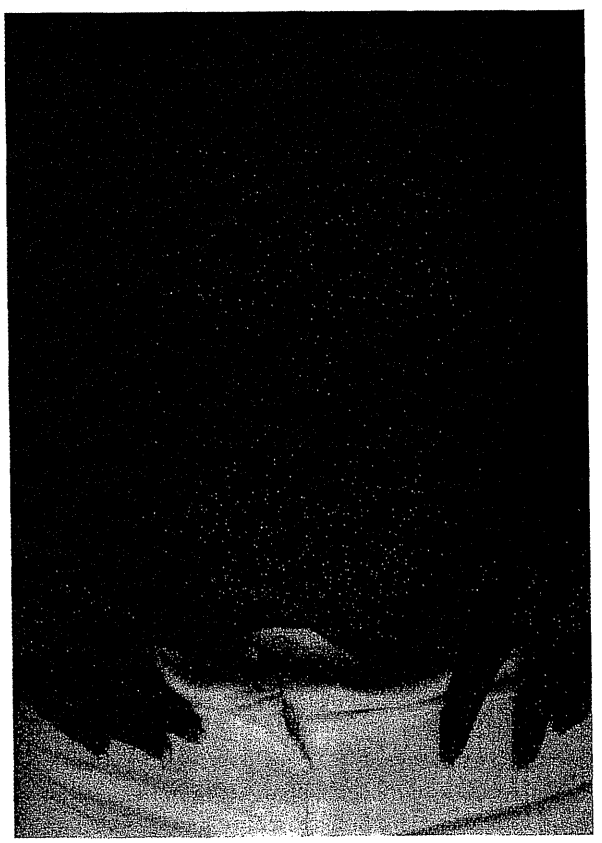

Figure 2 View of the postoperative scar 6 weeks after surgery (Patient 4).

an attempt to reduce the number and size of the ports used for laparoscopic surgery, SILS and NOTES have recently been devised as new laparoscopic procedures for cholecystectomy and appendicectomy (6,7). However, there have been few reports of application of these advanced approaches to gastric or colorectal surgery (9–11). In this article we have reported finding that SILSOID colectomy was safe and feasible. Moreover, the additional techniques or training required for SILS, NOTES and robotic surgery might not be needed. Also, SILSOID colectomy can be performed using standard operating room equipment with a few modifications. Thus, SILSOID colectomy is a more reasonable and economical alternative to conventional LC than SILS or NOTES is.

SILSOID colectomy may have some advantages in terms of rapid postoperative recovery and less postoperative morbidity because it involves less parietal trauma and a lower risk of morbidity associated with insertion of ports (i.e., port-orifice infection, hemorrhage, incisional hernia) (12). An assessment of the impact of SILSOID colectomy on quality of life is warranted, because the benefits of this procedure were not evaluated in our patients.

Pure SILS is likely to be restricted in the movement of a forceps because of the conflict against the laparoscope. However, since the length of the incision for SILSOID colectomy is about 4 cm, and the distance between the three ports is greater than in pure SILS, there was little restriction of forceps movement. In our cases, SILSOID colectomy could be completed without special training of cross-technique, which was an un-physiological technique often required in pure SILS. Intraoperative bowel injury was not experienced and surgical outcomes, including number of harvested lymph nodes and length

of resected bowel, were also acceptable, suggesting that SILSOID is feasible. Thus, SILSOID colectomy seemed to be very useful and an important step toward expanding the potential indications for SILS.

Despite some modifications of the SILSOID colectomy technique, it required a longer operative time because of some limitations in surgical techniques and instruments. This procedure does not avoid the confliction of forceps and laparoscope, and requires specialized skill in laparoscopic surgery and patience to overcome some difficulties. Because SILS has been adapted to abdominal surgery recently, a useful training system has not been established, and the development of new surgical instruments has been progressing. Although our study demonstrated that SILSOID colectomy was feasible, this procedure should be performed by experts due to these problems.

In conclusion, in our experience, SILSOID colectomy is a safe and feasible procedure that can be performed with conventional and clinically available instrumentation. Although further assessment is needed, this procedure shows promise of becoming an alternative to conventional LC and pure SILS colectomy.

Acknowledgment

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外科的治療・内視鏡的治療

大腸癌におけるロボット手術—現状と展望—

Current status of robotic surgery for colorectal cancer and its future perspectives

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Key words：大腸癌，ロボット手術，da Vinci，腹腔鏡下手術，直腸癌

はじめに

腹腔鏡下大腸切除術が導入されてから約20年が経過した．腹腔鏡下手術の利点として，小さな創，腸管蠕動の早期回復，痛みの軽減，在院期間の短縮などがあげられる．小さな創は更に小さく，そして究極的にはscarless surgeryとして，NOTES(natural orifice transluminal endoscopic surgery)や，実際的にはSPS(single port surgery)が最近では脚光を浴びている．

一方，腹腔鏡下手術の欠点として2次元画像であること，直線的で，自由度の少ない鉗子操作，そして助手任せのカメラなどがあげられる．これらの欠点を克服するために，1990年代により良い操作性を求めてロボットが登場するに至った．人間に代わる本当の意味でのロボットではなく，'主人と奴隷'の関係にあるシステムで，da Vinci，ZEUSがそうである．

本稿では，主にda Vinciを用いたロボット手術の現状と展望について述べる．

1. ロボット手術の特徴

da Vinciは遠隔手術機器として，NASAと米国国防省により遠隔地で負傷した兵士を手術する目的で開発された．前述したごとくda Vinciは完全自動能をもったロボットではなく，外科医にロボットの機能をコントロールさせる'主人と奴隷'型システムである．

それは自由度の高い，人間の手首に似た角度で曲がる鉗子や持針器，そして助手に依存しないカメラを備えたアームをもつカートと，外科医が操作するための双眼鏡がついたコンソールから成り立っている(**図1**)．外科医はこの双眼鏡を通して，術野の3次元画像を見ることができ，あたかも患者の腹腔内に自らが入っていくような感覚になる．da Vinciのもう一つの利点は，通常の真っ直ぐな腹腔鏡下手術用鉗子では不可能な，人間の手首のような自在な動きをする鉗子と持針器が備わっているために，操作性が向上している点である(**表1**)．更に，手の振せんや心臓の拍動などと同期させる振せんフィルターと動作スケーリングを備えていることにより，安定した精度の高い画像が得られる点である．これらは心臓のバイパス手術では特に有用である．

他の利点は，術者の身体的緊張やストレスが軽減され，術者の疲労が少なくなる点である．通常の腹腔鏡下手術では，術者は不自然な姿勢での手術を余儀なくされるため，術者の身体的疲労はロボット手術に比べるとはるかに高い．Pigazziらは腹腔鏡下total mesorectal excision(TME)とロボットTMEで，術者の疲労を比較

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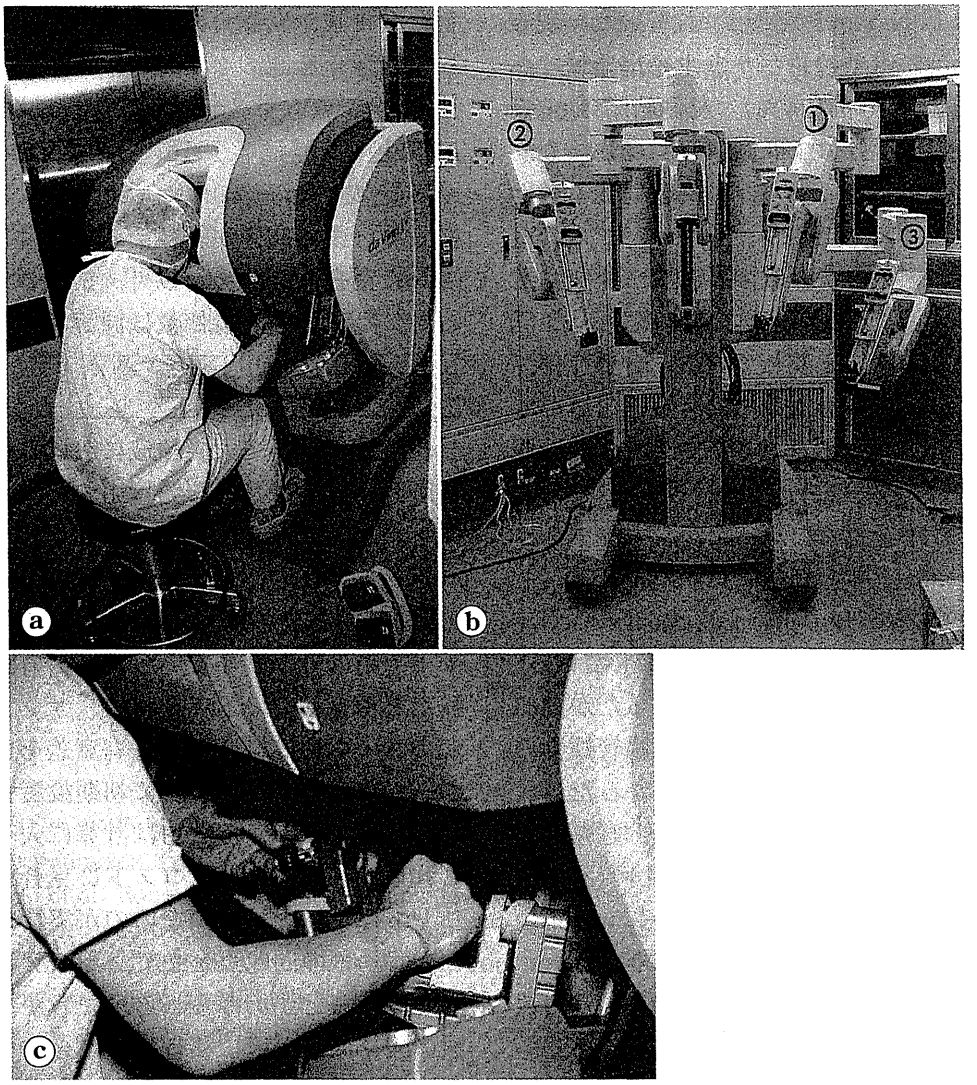

図1 da Vinci(藤田保健衛生大学 花井恒一氏のご厚意により提供)
a. コンソールボックス, b. 本体, c. コンソールボックス(拡大).

表1 ロボット手術の利点と欠点

利点
3次元画像
自由度の高い優れた操作性
振せんフィルターと動作スケーリング
術者の身体的緊張の軽減
欠点
高額な費用(初期費用, メインテナンスも含めて)
巨大で重いシステム
限られた術野
触覚の欠如

し, ロボットTMEで身体的ストレスが少ないことを報告している[1]. このようにda Vinciは骨盤腔などの狭い空間にアプローチして操作するのに有用であり, 特に縫合操作を必要とする手技で特に有用であるため, 泌尿器科領域において前立腺摘出に多く用いられている.

2. 大腸領域における役割

2001年にロボット補助下の腹腔鏡下結腸切除が報告されて以来, 20ほどの論文が報告されている. Mirnezamiらによると, 17論文中288人の患者がロボット大腸手術を受けた[2]. このうち151人(52%)が悪性腫瘍であり, 1つの

報告を除いてda Vinciが使用されていた．現在ではda Vinciが唯一のロボット手術用器械である．右側結腸は70例（24％），左側結腸は86例（30％），骨盤内手技は126例（44％）であった．ほとんどが症例報告であるが，比較研究も数件報告されている．

このうち症例数の多いものとして，イタリアのD'Annibaleらが53例のロボット手術と53例の腹腔鏡下手術を比較している．合併症率，出血量，リンパ節郭清個数には有意差を認めず，また，在院日数はロボット手術群で2.5日，腹腔鏡群で3日であった[3]．また，実際の手術時間に関しては差を認めなかったが，セットアップ時間はロボット群で有意に長かった．

同じイタリアのSpinoglioらも50例のロボット手術と161例の腹腔鏡下手術を比較している[4]．手術時間はロボット群で有意に長かったが（383分対266分，$p<0.001$），在院日数や腸管蠕動の回復などの短期成績には差を認めなかった．

米国のPigazziらは39例のロボット直腸切除を施行した．手術時間は285分で，1例（2.6％）が開腹手術に移行した[5]．6例（15％）にmajor合併症を認め，うち4例は縫合不全であった．

直腸癌だけに限った報告の中で最も症例数が多いのが韓国のBaikらによるものである．Baikらは，まずpilot randomised trialを行い，36例の患者をロボットTME群と腹腔鏡下TME群に振り分けた[6]．手術時間，ヘモグロビン変化，移行率は両群で差を認めなかった．また，在院日数はロボット群で有意に短かった（6.9日対8.7日，$p<0.001$）．Baikらは更に症例数を増やし，randomiseではないがprospectiveに，腹腔鏡下低位前方切除術57例とロボット低位前方切除術56例とを比較した[7]．手術時間には差を認めなかったが，開腹移行率，重篤な合併症率は腹腔鏡群で有意に高率で，在院日数も腹腔鏡群で有意に長かった．また，TME標本を肉眼的に判定したqualityはロボット群で有意に高かった．

最近の直腸癌に限った報告では，Bianchiらは25例のロボットTMEと25例の腹腔鏡下TMEを比較している[8]．手術時間，開腹移行率，術後合併症，在院日数，リンパ節郭清個数などには有意差を認めなかった．また，Parkらは低位直腸癌（AV 1–8 cm）に対するロボットTME 41例と，腹腔鏡下TME 82例をcase matchさせて比較した[9]．ロボット群で手術時間が有意に長く，また病変が経肛門もしくは経腟に摘出された割合が高かった以外，術後合併症，在院日数，リンパ節郭清個数は同等であった．

3. 問題点と将来展望

現時点において大腸領域におけるロボット手術が今ひとつ普及しない理由の一つとして，コストがあげられる．Delaney[10]やRawlings[11]らはロボット大腸手術と腹腔鏡下大腸手術を比較して，トータルの病院支出はすべての手技でロボット手術の方が高額であったが，有意差はなかったと報告している．それは，サンプルサイズが小さいために統計学的に有意差を検出できなかったためであろう．更に初期投資費用とメインテナンスにかかる費用は計算に入っておらず，これらを勘案すると，コストに見合うだけのメリットは見いだせていないのが実情である．

もう一つの問題点として，システム自体が巨大で重いことがあげられる．患者が術中緊急事態に陥り開腹手術に移行するときにも，患者に近づくのも容易でない．また，術野が骨盤内に限定している泌尿器科では問題とならないが，術野が複数にまたがる大腸手術では，ロボットアームが干渉してしまう．このため，直腸癌に対する前方切除術では，脾彎曲の授動を通常の腹腔鏡で行い，骨盤内操作をロボットで行うhybrid手術が多く行われている．最近，脾彎曲の授動から骨盤内操作を1回のセットアップで行う方法も報告されている[12,13]．コスト削減と器械の縮小化が今後の課題の一つである．

現在のロボット手術においても欠如しているのは，触覚である．組織の硬さ，柔らかさを目で見て判断しているため，ロボットのアームが視野外に出てしまうと，組織損傷を感じることはできない．触覚をもった鉗子の開発が森川らによってなされており[14]，第23回日本内視鏡外科学会総会でもデモンストレーション展示され

た．将来的には触覚をもった鉗子を備えたロボットが望まれる．

おわりに

大腸癌に対するロボット手術はまだ発展途上ではあるが，症例を選べば安全に施行可能であることは明らかである．しかしながら，通常の腹腔鏡下手術と比べて臨床的に真に有用であるのかは，今後大規模なRCT(randomised controlled trial)により証明されなくてはならない．現在，直腸癌に対する世界規模での多施設RCTが計画中である．

また，コストも含めた検証は必須であろう．メインテナンスコストを考慮すると，たとえRCTでロボット手術の方が有用であることが証明されたとしても，日本の現状では保険適用とすべきではないと思われる．

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Evaluation of factors affecting the difficulty of laparoscopic anterior resection for rectal cancer: "narrow pelvis" is not a contraindication

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Abstract
Background This study aims to evaluate the clinical and anatomical factors, particularly pelvic dimensions that influence the difficulty of performing laparoscopic anterior resection for rectal cancer.
Methods We studied 50 consecutive patients who underwent laparoscopic anterior resection with double-stapling technique (DST) anastomosis for rectal cancer between January 2006 and February 2010. Staging was performed by computed tomography. Five pelvic dimensions (anteroposterior and transverse diameters of pelvic inlet and outlet, and pelvic depth) were measured using three-dimensional volume-rendering images. We also examined a number of other clinical characteristics, including gender, history of laparotomy, body mass index (BMI), operator, tumor location, tumor depth, nodal involvement, and tumor diameter. Univariate and multivariate analyses were performed to determine the predictive significance of these variables on surgical difficulty based on operative time and intraoperative blood loss.
Results Males had significantly shorter pelvic inlets and outlets and significantly greater pelvic depth than females. However, gender did not significantly affect surgical outcomes, although males did tend to experience greater blood loss. Maximum tumor diameter ($p = 0.014$), BMI ($p = 0.001$), operator ($p < 0.001$), and tumor location ($p = 0.009$) were independent predictors of operative time, which, in turn, was related to intraoperative blood loss ($p < 0.001$).
Conclusions Maximum tumor diameter, BMI, operator experience, and tumor location can be used to predict the operative time required to complete laparoscopic anterior resection with DST anastomosis for rectal cancer, with no correlations between pelvic dimensions and operative time. The difficulty of the procedure was not related to patients' pelvic dimensions, which led us to conclude that "narrow pelvis" is not a contraindication for this surgery. Based on these results, we suggest that laparoscopic anterior resection should be performed by experienced surgeons in patients with large tumors, high BMI, and/or extraperitoneal rectal cancer.

Keywords Laparoscopic anterior resection · Rectal cancer · Body mass index · Pelvic dimension · Narrow pelvis · Volume-rendering image

Laparoscopic procedures for rectal cancer have been reported to be safe and effective for a number of reasons, including relatively low levels of pain and blood loss, early resumption of bowel movement, and short postoperative hospital stay [1–6]. Additionally, randomized studies have shown that laparoscopic total mesorectal excision (TME) and lymph node dissection are productive surgical techniques with survival and recurrence rates comparable to those of open procedures [4, 6–8]. However, while laparoscopic surgery is the standard treatment for colon cancer, it is not commonly performed in cases of rectal cancer because it is technically challenging and may be associated with disadvantages such as long

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operative time [1, 2, 4] and increased rate of positive surgical margins [9].

Rectal surgery is performed through a narrow and funneling bony inlet, which makes access and visualization difficult in the deep pelvis. Even in the relatively simpler open approach, it is difficult to maintain a clear surgical field, to recognize precise anatomy, and to accurately perform rectal mobilization and excision while preserving urogenital functions. Recent studies have suggested that the quality of open rectal surgery is influenced not only by the surgeon's skill but also by the patient's clinical and anatomical factors, such as gender, tumor height, and pelvic size [10–12]. Similar relationships possibly influence the outcomes when using the laparoscopic approach, but evaluation of the influence of such clinical and anatomical factors on laparoscopic rectal surgery has been limited [13, 14]. The purpose of this study is to evaluate the influence of various clinical and anatomical factors, particularly pelvic dimensions, on operative time and intraoperative blood loss, which were selected as dependent variables to represent the level of difficulty in performing laparoscopic anterior resection with double-stapling technique (DST) anastomosis for rectal cancer.

Patients and methods

Patients

We studied 50 consecutive patients who underwent laparoscopic anterior resection with DST anastomosis for rectal cancer located below the inferior edge of the S2 vertebra between January 2006 and February 2010.

The indications for laparoscopic surgery were rectal cancer without involvement of the lateral lymph nodes or invasion of the adjacent organs, as determined by computed tomography (CT) and pelvic magnetic resonance imaging (MRI) during preoperative examinations. An additional indication was evidence of metastatic disease that could not be curatively resected using open surgery.

In Japan, preoperative radiotherapy or chemotherapy is not routinely administered in the treatment of rectal cancer; it is currently being used in clinical trials or mainly in patients with locally advanced, very low tumors to increase the chance of sphincter-preserving surgery. In this study, no patients underwent preoperative radiotherapy or chemotherapy.

Data for age, gender, history of laparotomy, body mass index (BMI), tumor location, tumor size, tumor staging, operative time, amount of blood loss, conversion to open surgery, pathology, 30-day morbidity, and mortality were collected prospectively. Tumors were staged according to the sixth tumor–node–metastasis (TNM) classification of the International Union against Cancer (UICC) on the basis of the histological findings of the surgical specimens.

Surgical procedures

The surgeries were performed by an experienced expert surgeon (T.Y.) or by trainees with 3–6 years of experience, operating under the expert's supervision.

Anterior resection is used for the treatment of early cancer located just above the dentate line and advanced cancer located >1 cm above the dentate line; these criteria enable the acquisition of adequate distal margin after rectal transection. Here, patients were placed in Lloyd–Davis position with the head and right side of the bed lowered. First, a 12-mm camera port was inserted below the umbilicus using the open method. After creation of a pneumoperitoneum, four working ports were inserted: a 5-mm port in the right and left upper abdominal quadrants each, and a 12-mm port in the right and left lower abdominal quadrants each. The mesocolon was mobilized using the mediolateral approach, and the inferior mesenteric artery was divided near its origin in order to achieve wide lymphadenectomy. This permitted TME, except in cases of intraperitoneal rectal cancer, where tumor-specific mesorectal excision (TSME) was performed instead. The rectum was transected intracorporeally using an Endo-Cutter (Ethicon Endo-Surgery, Cincinnati, OH, USA) and anastomosed with DST. No diverting stoma was created.

Pelvimetry

All patients underwent abdominopelvic CT (Aquilion 16; Toshiba Medical Systems Corporation, Tochigi, Japan). In most cases, the slice interval was adjusted to 5 mm. Sequences were volume-rendered using a DICOM 3D viewer, INTAGE Realia (KGT Inc., Tokyo, Japan). Volume-rendering (VR) images were obtained from the extracted volume data using INTAGE Volume Player (KGT Inc., Tokyo, Japan). A single observer (S.O.) blinded to all clinical information regarding the patients made all measurements in the VR images. Five pelvic dimensions were measured: anteroposterior and transverse diameters in the pelvic inlet (the axis from the superior aspect of the pubis symphysis to the sacral promontory and the longest lateral axis in the iliopectineal line), anteroposterior and transverse diameters in the pelvic outlet (the axis from the inferior aspect of the pubis symphysis to the tip of the coccyx and the distance between the tips of the ischial spines, i.e., interspinous distance), and the pelvic depth (the distance between the sacral promontory to the tip of the coccyx) (Fig. 1).

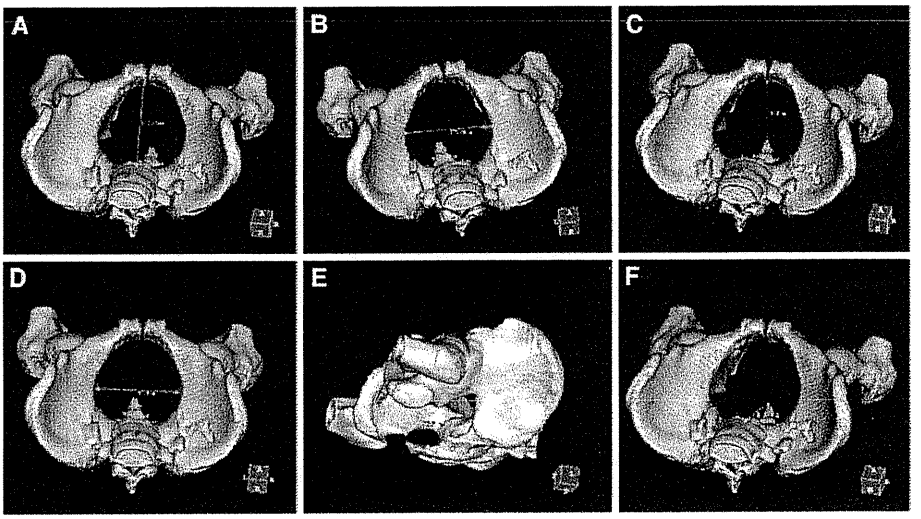

Fig. 1 Anteroposterior (**A**) and transverse (**B**) diameters in the pelvic inlet, anteroposterior (**C**) and transverse (**D**, **E**) diameters in the pelvic outlet, and length of pelvic depth (**F**) were measured using three-dimensional VR images

Statistical analysis

The sample size was calculated to detect moderate correlation (correlation coefficient: $|r| = 0.4$) with α of 0.05 (two-sided) and β of 0.2 (power of 80%), suggesting a total study population of 47 patients. All statistical analyses were performed using SPSS version 15.0 (Statistical Package for Social Sciences™; SPSS, Inc., Chicago, IL, USA). Statistical significance was defined as $p < 0.05$. Where appropriate, we used Fisher's exact test, chi-square test, Student's t test, Welch's test, or Pearson's product-moment correlation coefficient to investigate relationships between patients' clinical and anatomical characteristics and surgical difficulties. Multivariate analysis was performed using a multiple linear regression model with a stepwise method (significance level to enter = 0.05; significance level to stay = 0.1).

To assess intraobserver variation, measurements of the pelvic dimensions of 10 patients were repeated after an interval of 4 weeks, with the observer blinded to the initial results [10, 14]. According to the Pearson's product-moment correlation coefficient, the intraobserver variation was 0.946. The two sets of measurements were highly correlated ($p < 0.001$), indicating that they accurately described pelvic anatomy.

Results

Patient and tumor characteristics are summarized in Table 1. Anastomosis height was significantly greater in males than in females ($p = 0.014$). All five pelvic dimensions differed significantly between male and female patients. Females had significantly longer measurements for the pelvic inlet and outlet (all $p < 0.003$), while males had significantly greater pelvic depth ($p < 0.001$). Overall, this indicated that male pelvises were significantly narrower and deeper than female pelvises.

Although males tended to experience more blood loss during surgery ($p = 0.11$), there were no significant differences between the genders in surgical outcomes (Table 2). In no case was there conversion to open surgery, death or positive circumferential resection margins (CRM). Complications were identified in two male patients: one wound infection and one anastomotic leakage. The overall morbidity rate was 4%, and the anastomotic leakage rate was 2%.

Univariate analysis showed that age ($p = 0.012$), BMI ($p = 0.009$), operator ($p = 0.006$), and maximum tumor diameter ($p = 0.003$) were significantly associated with operative time (Table 3). Although operative time tended to increase as anteroposterior pelvic inlet diameter decreased ($p = 0.151$) and pelvic depth increased ($p = 0.103$), these relationships were not significant.

Stepwise linear regression analysis showed that the optimal model for predicting operative time included maximum tumor diameter, BMI, operator, and tumor location ($p < 0.001$, Table 4). Operative time increased as maximum tumor diameter and BMI increased, but decreased with an expert performing the operation and for intraperitoneal tumor location. Operative time, in turn, was the only factor significantly associated with blood loss ($p < 0.001$); no other variables had any relationship with blood loss.

Discussion

In this study, multivariate analysis showed that larger maximum tumor diameter, higher BMI, trainee performing

Table 1 Patients' clinical and anatomical characteristics

	Male ($n = 30$)	Female ($n = 20$)	p Value
Age (years)	66 (60, 79)	70 (58, 75)	0.93
Previous laparotomy (no.)	9	9	0.43
BMI (kg/m^2)	21.5 (18.7, 22.6)	21.4 (18.0, 23.4)	0.87
Operator			0.82
Expert (no.)	17	12	
Trainee (no.)	13	8	
Tumor location of lower edge			0.20
Intraperitoneal (no.)	19	9	
Extraperitoneal (no.)	11	11	
Tumor depth			0.81
Tis/T1/T2 (no.)	19	12	
T3/T4 (no.)	11	8	
Nodal involvement			0.75
N0 (no.)	22	13	
N1/N2 (no.)	8	7	
Maximum tumor diameter (cm)	4.0 (1.8, 5.2)	3.3 (2.0, 4.1)	0.38
Procedure			0.72
High anterior resection (no.)	2	1	
Low anterior resection (no.)	28	19	
Anastomosis height from anal verge (cm)	6.0 (4.0, 6.8)	4.0 (4.0, 5.0)	**0.014**
Pelvic dimensions			
Inlet			
Anteroposterior (cm)	11.0 (10.3, 11.8)	11.9 (11.5, 12.7)	**<0.001**
Transverse (cm)	12.3 (11.9, 12.7)	12.9 (12.4, 13.3)	**0.002**
Outlet			
Anteroposterior (cm)	10.0 (9.4, 10.3)	10.6 (10.1, 11.4)	**0.003**
Transverse (cm)	9.7 (9.1, 10.0)	11.1 (10.7, 11.9)	**<0.001**
Depth (cm)	12.4 (11.4, 12.7)	11.2 (10.0, 11.8)	**<0.001**

All continuous variables are described as median (first quartile, third quartile)

Bold font in table means that the p-values were statistically significant

Table 2 Surgical outcomes in relation to gender

	Male ($n = 30$)	Female ($n = 20$)	p Value
Operative time (min)	305 (271, 325)	277 (254, 333)	0.26
Blood loss (ml)	25 (8, 58)	5 (0, 23)	0.11
Complication (no.)	2	0	0.66
Anastomotic leakage (no.)	1	0	0.84
Conversion (no.)	0	0	na
Mortality (no.)	0	0	na
Positive CRM (no.)	0	0	na

CRM circumferential resection margin

the operation, and extraperitoneal tumor location were significantly associated with longer operative time in laparoscopic anterior resection with DST anastomosis for rectal cancer, while pelvic dimensions had no correlations with operative time. Furthermore, operative time was the only factor significantly associated with intraoperative blood loss. The present findings are valuable in suggesting that pelvic dimensions were not definitive factors as compared with maximum tumor diameter, BMI, operator experience, and tumor location in predicting the difficulty of performing this procedure.

Interest in pelvimetry began with attempts to predict cephalopelvic disproportion in pregnant women prior to labor. Pelvimetry has been utilized for patients with rectal cancer, using MRI [10–12] and CT [13, 14] images; in these cases, measurements were made on two-dimensional reconstructed (axial and sagittal) images. However, these cross-sectional images only permit measurement of distances between points that exist in the same orthogonal coordinate axis. We preferred the use of three-dimensional VR images, because they allow precise measurements along any axis and can be especially beneficial in cases with anatomically strained pelvis or mismatched alignments between patients and imaging devices. The precision and sensitivity of this technique were demonstrated by its ability to correctly indicate that male pelvises are narrower and deeper than female pelvises, as well as by the strong correlation between the two sets of

Table 3 Correlations between operative time and operative parameters

Variable	*p* Value
Gender (male versus female)	0.131
Age	**0.012**
Previous laparotomy	0.430
BMI	**0.009**
Operator (expert vs. trainee)	**0.006**
Tumor location (intraperitoneal versus extraperitoneal)	0.338
Tumor depth (Tis/T1/T2 vs. T3/T4)	0.247
Nodal involvement (N0 vs. N1/N2)	0.471
Maximum tumor diameter	**0.003**
Anastomosis height from anal verge	0.338
Pelvic dimensions	
Inlet	
Anteroposterior	0.151
Transverse	0.250
Outlet	
Anteroposterior	0.481
Transverse	0.324
Depth	0.103

Bold font in table means that the *p*-values were statistically significant

4 Variables included in the final stepwise linear regression model explaining variations in operative time

	B	*β*	*p* Value
Intercept	190.871		<0.001
Maximum tumor diameter (cm)	8.075	0.289	0.014
BMI (kg/m^2)	6.828	0.382	0.001
Operator (expert)	–66.755	–0.576	<0.001
Tumor location (intraperitoneal)	–42.945	–0.373	0.009
$R^2 = 0.463$			
Model utility test: $p < 0.001$			

measurements in the intraobserver variation test ($r = 0.946$, $p < 0.001$).

In this study, we chose to evaluate cases of rectal cancer that underwent laparoscopic anterior resection with DST anastomosis, because intracorporeal rectal transection and anastomosis is one of the most difficult procedures in laparoscopic rectal surgery and therefore should be considered separately from cases that undergo abdominoperineal resection or intersphincteric resection with transanal hand-sewn anastomosis. We selected operative time and intraoperative blood loss as dependent variables representing technical difficulties during this procedure. Other variables, including complications, anastomotic leakage, conversion, mortality, and positive CRM, occurred at such low rates that they could not be analyzed. This indicates that the procedure can be performed safely and without morbidity or conferring any oncologic disadvantage.

It is not immediately clear why anastomosis height was significantly greater in males than in females. Unlike previous authors [13, 15], we did not find that operative outcome differed significantly between the two genders. These results may partly be explained by the fact that pelvic procedures can be completed more easily in wider and shallower female pelvises, but may also be disrupted by the presence of the uterus.

Patients in this study had BMI ranging from 12.0 to 27.8 kg/m^2; these values are lower than those in Western populations. Nevertheless, our results agreed with previous reports that found a positive association between operative time and BMI [14]. This is likely associated with greater mesorectal volume, which restricts the pelvic working space for the procedures. Therefore, visceral fat may be an even better predictor of surgical difficulty than BMI [16, 17]. Further, larger maximum tumor diameter reflects larger tumor volume, which again restricts the pelvic working space. Space can also be restricted by the location of tumors; i.e., when tumors are positioned extraperitoneally, surgeons have a narrower space in which to perform rectal dissection, transection, and anastomosis, since the pelvic width becomes narrower as one approaches deeper into the pelvis. Thus, cumulatively, higher BMI, larger maximum tumor diameter, and extraperitoneal tumor location impact operative time by limiting pelvic free space for the procedures and reducing visibility, maximum retraction, and access to the depths of the pelvis via the pelvic inlet.

In keeping with our previous finding, operative time was longer when procedures were performed by trainees [18]. Pelvic space cannot be expanded by pneumoperitoneum, as can be done in the upper abdomen, and limited working space directly affects the difficulty of safe and quick access, required to optimize visibility and retraction. We presume that these issues do not present as great a problem to expert surgeons because they have more experience in creating an appropriate surgical field and obtaining a good view for identifying and dissecting anatomical structures even in a limited pelvic working space.

Although pelvic depth tended to correlate with operative time, we did not find any significant patterns linking pelvic dimensions with operative outcomes. These results are contrary to those previously reported elsewhere [13, 14]. We hypothesize that this is because BMI, maximum tumor diameter, and tumor location have greater effect on pelvic working space than do pelvic dimensions. Additionally, this study included cases of both intraperitoneal and extraperitoneal rectal cancer, while a similar previous study focused only on extraperitoneal rectal cancer [14]. Furthermore, the procedures in our study were performed by both experts and trainees, rather than experts only [14].

Thus, these differences in inclusion criteria may explain why we did not detect any significant correlations between pelvic dimensions and operative time.

Our study has certain limitations. The sample size of this study was small, although the study was not statistically underpowered. However, future examinations with larger sample size would elucidate our results further. Additionally, other variables, including complications, anastomotic leakage, conversion, mortality, and positive CRM, should be examined to generalize the present findings.

In summary, our results indicate that "narrow pelvis" is not a contraindication for laparoscopic resection of rectal cancer. We also recommend that this procedure be performed by experienced surgeons in patients with large tumors, high BMI, and/or extraperitoneal rectal cancer.

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大腸癌治療における地域連携—QOL向上のために—

Local communication in the treatment of colorectal cancer—for the improvement of quality of life—

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Key words：クリティカルパス，病診連携

はじめに

大腸癌患者のQOL向上を目指した地域連携は，その進展に応じて四段階に分けることができると考える．第一段階は，自覚症状出現，または検診(便潜血検査)陽性判明の時点から大腸内視鏡検査，更に治療機関への患者の受け渡しの段階である．第二段階は，内視鏡的摘除手術などの治療後，フォローアップまたは補助療法を'かかりつけ医'とともに行う段階である．第三段階は，再発あるいは切除不能進行癌に対して外来化学療法を行う段階で，最近では特に内服薬併用のプロトコールが増えているため，'かかりつけ薬局'との連携も必要となっている．第四段階は，病院などでの治療が困難となった時期で，自宅あるいは自宅の近くの施設にて緩和ケアを行う段階である．いずれの段階でも情報が遺漏なく伝達され，患者のスムーズな受け渡しが行われることがQOL向上につながる．

これら各段階の連携を推進するのは，病院においては地域医療連携部，緩和ケアチーム，外来点滴センターなどであり，地域においては医師会，薬剤師会，訪問看護ステーションなどであるが，それぞれの段階で関与の程度が微妙に異なり，ややもすれば患者主体の医療がないがしろにされることもある．大切なことは，これら背景の異なる各部門，各職種を緩やかにまとめあげ，患者を中心としたチーム医療を実践するリーダーシップである．

本稿では，吹田市地域における取り組みを紹介しながら，大腸癌における地域連携について考察したい．

1. 第一段階：発見から診断，治療まで —'早期発見パス'の導入—

大腸癌の早期発見に検診(便潜血検査)が有用であることは周知されている．老人保健法による検診受診者は該当者の18.8％で，この向上には受診方法や費用負担など，国の施策の改善も求められる．ここで問題としたいのは，便潜血陽性となって大腸内視鏡を受ける率が60％以下にとどまっていることである[1]．患者の拒否などを除けば，病院または内視鏡専門医のいる診療所への連携がスムーズでないことがうかがわれる．この原因としては以下の点が挙げられる．

(1) 患者に最も近く，便利な医療機関を紹介したいが，医療機関ごとに予約形式や前処置の方法などが異なるため，煩雑である．

(2) 高齢化に伴い，抗血小板薬や抗凝固薬を

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服用している患者が多く，大腸内視鏡前にそれらを中止することの判断は，リスクとベネフィットを勘案して慎重に行うべきである．中止時期の基準は学会などのガイドラインで明らかになっているが，その責任の所在があいまいなことが多い．

(3) 大腸内視鏡の結果，癌もしくは腺腫が発見され，治療が必要となった場合の患者への説明や治療機関への転送に関して，あらかじめ患者と紹介元の同意を得ておく必要があるが，これも検査予約の段階ではあいまいである．

そこで，これらの問題点を解決するために，(1)については地域の病院，内視鏡専門診療所共通の申し込み用紙を作成，(2)と(3)については予約時にチェック項目を盛り込むこととし，'かかりつけ医'，病院内視鏡担当医，内視鏡専門診療所との合意のもとに，医師会主導で'早期発見パス'を作成した．

'早期発見パス'は，通常のクリティカルパスとは異なり，いわば地域共通の検査説明書兼情報提供書である．大腸内視鏡検査の前処置や検査の概略を，患者，医療機関共通の用紙によって説明することで，'かかりつけ医'の負担を減らすことができる．また，先述したあいまいな点について予約時に明らかにしておくことで，大腸癌発見時には迷うことなく結果説明を行い，患者の希望する治療機関に転送することができる．こうして，大腸癌が発見されたときに，結果が正確に伝えられなかったり，治療開始が遅れることを防止できる．また，抗血小板薬や抗凝固薬の中止に伴う合併症も未然に予防できると考える．すなわち，内服の中止は，原則的に処方医の確認を取ってから行うこととし，中止してもよい場合と中止せずにヘパリン置換などを行う方がよい場合を，予約時に明確にするようにした．

いまだに多くの患者は'大腸内視鏡は痛くて苦しい'という固定観念をもっており，一度受けた患者は'もう二度と受けたくない'というケースも散見される．これらを払拭して，便潜血陽性患者の二次検診受診率を向上させるには，内視鏡専門医の技術の向上もさることながら，気軽に大腸内視鏡を受診できる連携システムの構築が重要であると考えている．'早期発見パス'がその一助になることを期待している．

2. 第二段階：治療後のフォローアップ
—'地域連携パス'の導入—

大腸癌は，五大癌の中でも比較的予後が良く，再発の早期発見が予後改善に寄与することが知られている．したがって，手術後のフォローアップが計画的に，過不足なく行われることが重要である．大腸癌治療ガイドラインにもフォローアップ(ここではサーベイランスと呼ばれる)の目安が掲載されているが，Stage Iのmp癌およびStege II，IIIの大腸癌は，通常5年間のサーベイランスを目安とするとされている[2]．

著者らは，地域医師会('かかりつけ医')と病院(手術担当医)の共同作業で大腸癌の術後フォローアップパスを作成し，2008年9月より全国に先駆けて実施してきた．実施に先立って地元医師会会員対象にアンケートを行った(**図1**)．その結果，Stage IIIについては，使い慣れない抗癌剤処方に不安を抱く診療所が多く，時期尚早と判断した．そこで，多くの診療所が安全に共同フォローアップに参加できるように，術後補助化学療法の不要であるStage IおよびIIに限定した．術後患者にフォローアップのスケジュールや手術所見などを記載した手帳('大腸パスポート'，**図2**)を渡し，病院と'かかりつけ医'を交互に訪問するよう指導した．

具体的には，6カ月に1回のCT検査と採血を病院で行って結果を説明，その中間に3カ月程度の間隔で腫瘍マーカーを含む採血を'かかりつけ医'で行う．'かかりつけ医'は異常があれば病院に報告し，必要に応じて患者を受診させる．

地域連携パスの効用であるが，'かかりつけ医'側の利点としては，病診連携が構築されていることへの安心感から，患者からの信頼感が増すことがあげられる．病院側の利点であるが，現在は病院を受診する回数をほとんど減らしていないため，病院医師の負担は変わっていない．しかしながら，将来は地域連携パスが繁用され

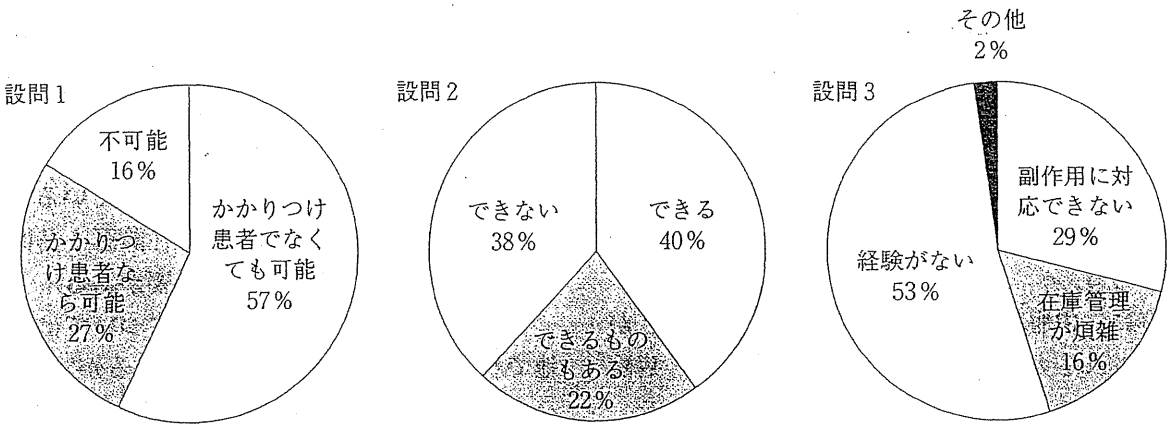

図1　医師会会員へのアンケート

設問1. 連携パスに従った大腸がん術後患者のフォローアップ(採血と簡単な検査，診察，投薬)は可能ですか？
設問2. 大腸がんの内服抗がん剤(ユーエフティ，ティーエスワン，ゼローダの3種が中心)の処方はできますか？
設問3. 前問でできないと答えた方へ，最も大きな理由は何ですか？

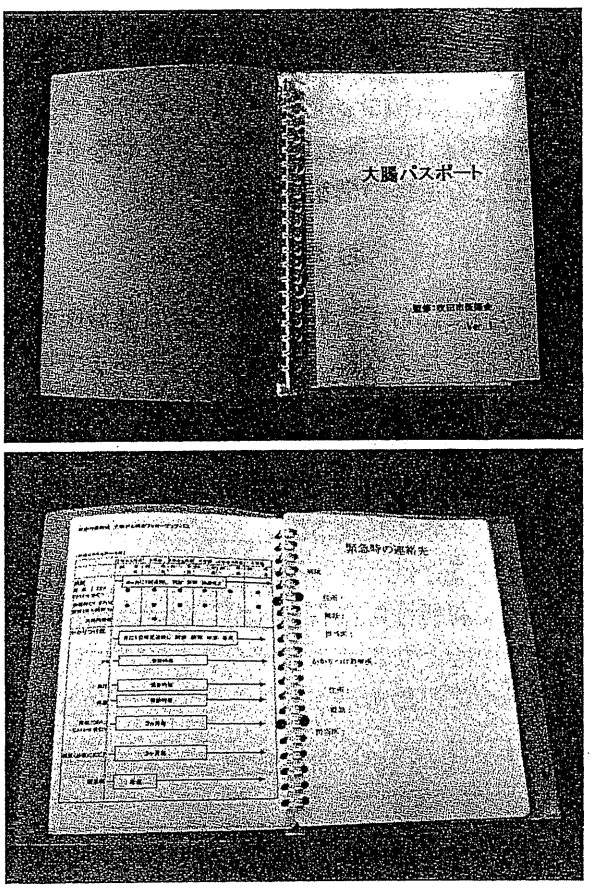

図2　'大腸パスポート'

A5サイズの患者用手帳で，術後5年間の診察・検査スケジュールを表にし，入院サマリー，検査データなどはクリアポケットに入れる．医師の記入項目は最小限にした．

るとCT結果の説明も含めてかかりつけ医に任せられるケースも増えてくると考える．その結果，病院への受診回数が減少し，ハイリスク症例を中心に効率的なフォローアップを行う結果，外来化学療法，入院治療に費やす時間が増えるものと期待される．

2010年4月から地域連携加算が導入され，癌の地域連携パスの普及は加速した．今後は患者の予後向上やマクロの医療経済への影響も評価していく必要がある．

3. 第三段階：外来化学療法 —'化学療法パス'の導入—

完治することの少ない切除不能大腸癌に対しては，外来化学療法が患者のQOL向上のために有用であることはいうまでもない．最近では特に，注射薬と内服薬の併用プロトコールが増加し，外来点滴センターのキャパシティーの問題からも，これらを選択する施設が増えている．もちろん，通院回数が少なくなることで，患者のQOLが更に向上する可能性もある．

そこで重要となるのが，内服薬が実際に調剤され，患者に手渡される院外処方薬局('かかりつけ薬局')の役割である．患者は，'かかりつけ薬局'において，内服抗癌剤の用法や副作用について，より詳細な説明を受けることが期待される．また，担当医や病院スタッフには言い

にくい要望や，質問などもなされる可能性がある．

しかしながら，現状の医療体制では，病院から‘かかりつけ薬局’への情報提供の手段がほとんど存在しない．‘かかりつけ薬局’では，処方内容から病状を推察して説明しているのが実情であろう．

特に，内服薬併用による副作用の増悪などが懸念される大腸癌化学療法レジメンでは，病院で行われた点滴治療の内容やスケジュールを，院外薬局が知っておく必要があると考えられる．更に，他院で処方されている抗凝固薬など抗癌剤以外の薬剤の影響もチェックする必要がある．

そこで，地元薬剤師会の協力を得て，‘化学療法パス’を作成した．これもA5版のクリアファイルに，患者が病院で受けている化学療法レジメンの内容，患者自身の副作用記録（日誌形式），従来のお薬手帳や血液検査結果などが挿入できるクリアポケットを綴じ込んだ．患者の個人情報が不必要に流出することは避けるべきで，病状や予後などについては記載していない．

この試みは新しいものであり，各方面から注目を集めている．ファイルされた情報は，‘かかりつけ薬局’だけでなく，‘かかりつけ医’にも参考となるはずであり，地域連携において果たす役割は大きいと予想される．今後は，患者や‘かかりつけ薬局’へのアンケートなどを行い，その結果をみて内容の改訂作業を行っていきたい．

4. 第四段階：在宅緩和ケア—地域在宅緩和ケアネットワークの構築—

病院での治療が困難となってきた段階で，早い時期から在宅ケアや緩和ケア病棟への紹介を準備することも，QOL向上に役立つと考えられる．当院では，すべての入院患者に，治療できない状態となったときに終末期をどこでどのように過ごしたいかを文書で確認しているが，その希望が自宅である場合は，往診医，訪問看護師などの手配を迅速に行う必要がある．

在宅緩和ケアのネットワークについては，各地で様々な取り組みがなされているが[3]，重要なことは，組織作りもさることながら，時間をかけた信頼関係の構築だと痛感している．また，市民講座などを通じての市民へのねばり強い啓蒙活動も必要である．

著者らも，病院医師，ホスピス医師，診療所医師，往診専門医師，訪問看護師，介護支援専門員（ケアマネージャー），薬剤師，社会福祉士（医療ソシャルワーカー），一般市民などの多職種からなる組織である‘吹田在宅ケアを考える会’を立ち上げ，年数回の会合をもちながら，顔の見える連携の構築に努めている．

おわりに

大腸癌に限らず，癌治療における地域医療は以上に述べたように，診断から終末期までのあらゆる段階で重要である．種々の診療報酬加算による誘導は，一時的には連携を促進するかのように見えるが，患者自身に利益がなければ定着しないと考えられる．

大切なことは，各医療機関がそれぞれの目先の利益や利便性に左右されず，患者および患者家族が中心となるケアを行うことを常に肝に銘じておくことであろう．

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ORIGINAL ARTICLE – COLORECTAL CANCER

Effects of Intraperitoneal Chemotherapy with Mitomycin C on the Prevention of Peritoneal Recurrence in Colorectal Cancer Patients with Positive Peritoneal Lavage Cytology Findings

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ABSTRACT

Background. The detection of intraperitoneal free cancer cells in colorectal cancer (CRC) patients is associated with a poorer prognosis. The aim of this study was to investigate the effects of intraperitoneal chemotherapy (IPC) with mitomycin C (MMC) on preventing peritoneal recurrence in CRC patients with positive peritoneal lavage cytology findings.

Methods. A total of 52 CRC patients who had no clinically confirmed peritoneal dissemination and whose status of peritoneal lavage cytology was positive were investigated. Conventional peritoneal lavage cytology was performed. Overall, 31 of the 52 patients (59.6%) were administered IPC with MMC. Before closure of the abdomen, 4 silicon catheters were inserted into peritoneal cavity. After closure, the perfusate (diluting 20 mg MMC with 500 ml saline) was instilled from the catheter, and all catheters were clumped. All catheters were opened 1 h later.

Results. The mean follow-up period was 83.1 months. According to univariate analyses of all 52 patients and the subgroup of 36 patients with stage II or III tumors, patients with IPC had a significantly better peritoneal recurrence-free survival and cancer-specific survival than patients who did not receive IPC ($P < 0.005$). In multivariate analysis, IPC remained an independent prognostic factor for peritoneal recurrence-free survival in all patients.

Conclusions. It appears that IPC with MMC is an effective treatment to prevent peritoneal recurrence and prolong the cancer-specific survival in CRC patients without peritoneal dissemination, but who have positive peritoneal lavage cytology. It is necessary to verify the effectiveness of IPC with MMC in a prospective trial.

The prognosis of colorectal cancer (CRC) depends on local tumor growth, lymph node involvement, and the presence of peritoneal or distant metastasis.[1] Complete removal of the tumor is the most effective treatment for CRC. However, metastases after curative resections are often unavoidable, and it is well known that the most common sites of recurrence are the liver, lung, and local.[2] For liver or lung metastases, hepatectomy or pulmonary resection have been aggressively used.[3,4] For local recurrence, aggressive surgical resection may be beneficial.[5,6] Peritoneal recurrence is less common than recurrence to other sites and therefore is prognostically less important than other sites of recurrence.[7] The detection of intraperitoneal-free cancer cells is associated with a higher recurrence rate and poorer prognosis.[8–12] Free malignant cells, which are present within the peritoneal cavity in CRC patients before surgery, may indicate early peritoneal seeding. The detection of these cells intraoperatively, through peritoneal lavage cytology, leads to identification of patients who are more likely to develop peritoneal carcinomatosis. Positive peritoneal lavage cytology in CRC patients also contributes to the identification of those who need more frequent postoperative follow-up and possibly adjuvant chemotherapy.[8,9,12]

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Peritoneal dissemination of CRC results in considerable morbidity and eventual mortality as it leads to intractable ascites, intestinal obstruction, and further tumor proliferation. Peritoneal dissemination, therefore, is a sign of the terminal stage of the disease, and most of the patients with peritoneal metastases have a very poor prognosis.[13] Surgery is usually impractical for peritoneal recurrence because of the multiplicity and microscopic size of the lesions. Thus, it is important to establish an effective prophylactic treatment for peritoneal recurrence in CRC patients. Systemic chemotherapy is inefficient because cytotoxic agents do not penetrate into the peritoneal cavity at a high enough concentration to effectively eliminate microscopic residual disease.[14] Intraperitoneal chemotherapy (IPC) has the benefit of delivering higher concentrations of cytotoxic drug locally to the site of the tumor, while minimizing systemic toxicity compared with intravenous chemotherapy. The primary use of mitomycin C (MMC) has been for the treatment of gastrointestinal carcinomas including CRC, either as a single agent or in combination with other chemotherapeutic agents. In gastric cancer, IPC with MMC prevents the peritoneal recurrence and improves the overall survival of patients.[15–17] IPC has also been used for CRC patients as an adjuvant treatment or as treatment for advanced disease.[18–20] However, the efficacy of the significance of using IPC with MMC on patient response and survival is still unclear.

The aim of this study was to investigate the significance of IPC with MMC for CRC patients with positive peritoneal lavage cytology findings. This study is a retrospective study, not a randomized-controlled trial.

PATIENTS AND METHODS

Patients

From January 1985 through December 2006, intraoperative peritoneal lavage cytology was performed in 1677 patients who underwent a resection for CRC. A total of 52 patients (3.1%) who had no clinically evident peritoneal dissemination and whose status of peritoneal lavage cytology was positive were investigated in the present study. There were 16 patients with stage IV cancer enrolled in this study. The sites of distant metastases were the liver in 13 patients, para-aortic lymph nodes in 2 patients, and lung in 1 patient. Adjuvant chemotherapy was administered to 42 patients (28 with stage II and III disease and 14 with stage IV). Also, 36 patients took oral chemotherapy with 5-fluorouracil (5-FU) derivatives, and 6 patients received intravenous chemotherapy with 5-FU and leucovorin. They did not receive combination chemotherapy such as FOLFOX or FOLFIRI. To confirm the presence or absence of distant metastases, the cancer was preoperatively staged in all patients with abdominal plus pelvic computed tomography (CT) and chest CT. The tumors were classified according to the UICC TNM system.[21]

Peritoneal Lavage Cytology

Peritoneal lavage cytology was performed using the conventional method, as described previously.[12] Briefly, peritoneal lavage cytology was performed immediately after the laparotomy before the manipulation of the tumor. Intraoperatively, 100 ml of physiological saline solution (37°C) was instilled into the Douglas cavity. The collected lavage fluid was immediately heparinized and centrifuged at 2000 rpm for 3 minutes, and the sediment was smeared on 4 glass slides. The slides were stained by the Giemsa and Papanicolaou methods and evaluated by 2 experienced cytologists who were blinded to the clinical information. A slide was classified as positive if at least 1 cancer cell was detected. A suspicion of malignancy was classified as negative.

Intraperitoneal Chemotherapy with MMC

Before closure of the abdomen, silicon catheters (typically 4) were inserted through the abdominal wall into the peritoneal cavity. The tips of the catheters were positioned bilaterally at the upper and lower abdomen. After closure of the abdomen, the perfusate (diluting 20 mg MMC with 500 ml saline (37°C)) was instilled into the abdomen from the catheter positioned in the lower abdomen, and all catheters were clamped. We did not take action particularly to promote the distribution of this drug. All catheters were opened 1 h later. In addition, there was no active attempt to remove the chemotherapy perfusate. IPC with MMC was not randomized. The surgeon performed the IPC based on the general status of patients or the degree of surgical invasiveness.

Patient Follow-up

Follow-up for recurrence included the following procedures and tests: a physical examination, serum tumor markers, hepatic imaging (ultrasound, CT, or both), abdominal plus pelvic CT, and chest x-ray or CT every 4–6 months for the first 3 years and every 6 months for the next 2 years; colonoscopy every 1–2 years. Peritoneal recurrence was defined as radiologic or histocytologic evidence of cancer recurrence in the abdominal cavity. Liver metastasis, intra-abdominal lymph node metastasis, and local recurrence, defined as radiologic or histocytologic evidence of cancer recurrence, were excluded.

Statistical Analysis

A statistical analysis was performed using the StatView version 5.0 software package (Abacus Concepts, Berkeley, CA). Associations between the clinicopathologic parameters were assessed using the chi-square test or the Fisher exact test for discrete variables. The *t* test was performed for continuous variables. Peritoneal recurrence-free survival curves and cancer-specific survival curves were estimated using the Kaplan-Meier technique and were compared using the log-rank test. For cancer-specific survival, only cancer-related deaths were considered; data on patients who had died from other causes or who were still alive at the end of the study were censored. A Cox proportional hazards model was used to assess risk (expressed as hazard ratio [HR]) under simultaneous contributions from several covariates. *P* values of <0.05 were considered statistically significant.

RESULTS

Postoperative Mortality and Morbidity

None of the patients died postoperatively, nor were any deaths related to the use of IPC with MMC. Grade 3–4 complications for surgery did not occur in any of the patients. Only 1 patient (1.9%) had an IPC-related event, which was grade 3 skin ulceration at the drain insertion site. Other grade 3–4 complications for IPC related did not occur.

Relationship Between Intraperitoneal Chemotherapy and Clinicopathologic Factors

The mean follow-up period was 83.1 months (range, 16–189 months). Overall, 31 of the 52 patients (59.6%) were administered IPC with MMC. In Table 1, comparison of the CRC patients shows no significant differences between the 2 groups regarding age, gender, tumor size, tumor site, depth of invasion, regional lymph nodes, TNM stage, lymphatic invasion, or adjuvant chemotherapy. Positive peritoneal lavage cytology was found only in patients with T3 and T4 tumors. A significant correlation was found between IPC with MMC and the histologic grade or venous invasion ($P = 0.0138$ and 0.0361, respectively).

Univariate Analyses of Factors Affecting Peritoneal Recurrence-Free and Cancer-Specific Survival

IPC with MMC and various clinicopathologic factors were evaluated for their impact on prognosis in univariate analyses of the data from all 52 patients (Table 2). In univariate analysis, the histological grade and IPC were significantly associated with peritoneal recurrence-free survival ($P = 0.0257$ and 0.0003, respectively). The histological grade, depth of invasion, lymphatic invasion, venous invasion, distant metastasis, and IPC were significantly associated with cancer-specific survival ($P = 0.0152$, 0.0181, 0.0066, 0.0135, 0.0006, and 0.0001, respectively). However, adjuvant chemotherapy and regional lymph node status were not associated with peritoneal recurrence-free and cancer-specific survival.

Kaplan-Meier curves for peritoneal recurrence-free survival and cancer-specific survival in the 52 patients with

TABLE 1 Characteristics of the patients with colorectal cancer according to intraperitoneal chemotherapy with mitomycin C ($N = 52$)

	Intraperitoneal chemotherapy (+) ($N = 31$)	Intraperitoneal chemotherapy (−) ($N = 21$)	*P* value
Age (mean ± SD, years)	60.7 ± 9.6	60.7 ± 11.6	0.9926
Gender			
Male	13	12	0.2815
Female	18	9	
Tumor size (mean ± SD, cm)	5.2 ± 2.1	4.9 ± 1.7	0.6415
Tumor site			
Colon	18	14	0.5316
Rectum	13	7	
Histologic grade			
Well	13	2	0.0138
Others	18	19	
Depth of invasion			
T3	17	6	0.0613
T4	14	15	
Regional lymph nodes			
N (−)	7	1	0.1225
N (+)	24	20	
TNM stage			
II	5	1	0.1972
III	19	11	
IV	7	9	
Lymphatic invasion			
No	7	1	0.1225
Yes	24	20	
Venous invasion			
No	9	1	0.0361
Yes	22	20	
Adjuvant chemotherapy			
No	8	2	0.1739
Yes	23	19	

Well well-differentiated adenocarcinoma, *Others* moderately differentiated adenocarcinoma, poorly differentiated adenocarcinoma, mucinous adenocarcinoma, *SD* standard deviation

TABLE 2 Univariate analysis of the clinicopathologic factors for peritoneal recurrence-free and cancer-specific survival in all patients ($N = 52$).

	No. of patients ($N = 52$)	Peritoneal recurrence-free 5-year survival	*P* value	Cancer-specific 5-year survival	*P* value
Age (years)					
<60	22	70.9	0.5206	31.8	0.3292
≥60	30	73.6		38.6	
Gender					
Male	25	75.4	0.4920	37.3	0.5460
Female	27	69.5		34.1	
Tumor size (cm)					
<5	22	73.7	0.6214	35.0	0.6308
≥5	30	70.6		35.6	
Tumor site					
Colon	32	72.8	0.6258	30.9	0.3632
Rectum	20	70.6		43.6	
Histologic grade					
Well	15	92.9	0.0257	60.0	0.0152
Others	37	59.6		25.1	
Depth of invasion					
T3	23	80.1	0.4984	53.3	0.0181
T4	29	61.7		21.7	
Regional lymph nodes					
N (−)	8	83.3	0.6823	54.7	0.0969
N (+)	44	69.8		31.6	
Lymphatic invasion					
No	8	83.3	0.6823	85.7	0.0066
Yes	44	69.8		26.7	
Venous invasion					
No	10	90.0	0.1884	71.4	0.0135
Yes	42	66.3		28.4	
Distant metastasis					
No	36	71.7	0.8667	45.4	0.0006
Yes	16	80.8		7.7	
Adjuvant chemotherapy					
No	10	71.1	0.7399	45.1	0.2482
Yes	42	72.4		31.6	
Intraperitoneal chemotherapy					
No	21	40.1	0.0003	9.5	0.0001
Yes	31	88.0		54.3	

Well well-differentiated adenocarcinoma, *Others* moderately differentiated adenocarcinoma, poorly differentiated adenocarcinoma, mucinous adenocarcinoma

and without IPC are shown in Fig. 1a and b. The 5-year peritoneal recurrence-free survival rate was 88.0% in patients with IPC versus 40.1% in those without IPC (Fig. 1a). The 5-year cancer-specific survival rate was 54.3% versus 9.5% (Fig. 1b). A significant difference was found in both survival curves ($P = 0.0003$ and 0.0001 respectively).

In addition, separate univariate analyses of the clinical and pathologic factors were performed in patients with stage II or III tumors (Table 3). In this univariate analysis, histological grade and IPC were significantly associated with peritoneal recurrence-free survival ($P = 0.0258$ and 0.0047, respectively). The histological grade, depth of invasion, and IPC were significantly associated with cancer-specific survival ($P = 0.0045$, 0.0341, and 0.0037, respectively). Adjuvant chemotherapy and regional lymph nodes status were not associated with peritoneal recurrence-free or cancer-specific survival.

Figure 1c and d show the Kaplan-Meier curves in patients with stage II or III tumors ($N = 36$). In these patients, the 5-year peritoneal recurrence-free survival rate was 85.6% for patients with IPC versus 45.5% for those without IPC (Fig. 1c), and the cancer specific-survival rate was 67.5% versus 16.7% (Fig. 1d). A significant difference was found in both survival curves ($P = 0.0047$ and 0.0037, respectively).

Multivariate Analysis of Prognostic Factors

Multivariate Cox regression analyses of data from all patients demonstrated that only IPC was an independent risk factor for peritoneal recurrence-free survival [HR, 5.32-fold ($P = 0.0274$)] (Table 4). For cancer-specific survival, distant metastasis was an independent risk factor [HR, 5.24-fold ($P < 0.0001$)]. IPC was not a significant risk factor; however, it showed a tendency for patients to have a poorer survival [HR, 2.16-fold ($P = 0.0938$)]. Regional lymph nodes status was not significant risk factor for recurrence.

Patterns of Recurrence

The patterns of recurrence between the 2 groups in patients with stage II or III tumors were compared (with some overlap, Table 5). The overall peritoneal recurrence rate was 25.0% (9 of 36 patients). The overall peritoneal recurrence rate was 12.5% (3 of 24) in the IPC (+) group and 50.0% (6 of 12) in IPC (−) group. The incidence of peritoneal recurrence in the IPC (+) group was significantly lower than that of the IPC (−) group ($P = 0.0362$). As for the other recurrent sites, no significant difference was observed between the 2 groups.

DISCUSSION

Peritoneal carcinomatosis from CRC is generally considered a terminal stage. However, recently, aggressive