Table 3 Results of postoperative SPECT and comparison with preoperative SPECT

Postoperative SPECT	*n*	Comparison with preoperative SPECT Defect area		PE*	DVT*
Nonsegmental	9 (19)	Normal	7	—	—
		<4 small defects	2	—	—
Segmental	9 (14)		7	2	2
		≥ 1 small			
		1 moderate to			
		<2 large defects	0	0	0
		≥ 2 large	2	2	1
Total	18 (33)			4	3

Note. Numbers in parentheses indicate the number of defects among the respective patients. Defect areas were classified according to size of defect, i.e., small defects (<25% of the segment), moderate defects (25%–75% of the segment), and large defects (>75% of the segment)

[a]Confirmed by MDCT

Comparison with baseline images did not contribute to the number of detected segmental defects. Five patients (24%) had segmental defects among 21 patients without defects preoperatively, and 4 patients (36%) had segmental defects among 11 patients with preoperatively nonsegmental defects. MDCT confirmed PE in two of five patients and in two of four patients with normal and nonsegmental defects preoperatively, respectively. We found no tendency toward PE in patients with nonsegmental defects preoperatively.

Risk factors for PE and DVT

Preoperative patient background, D-dimer, and TAT levels were compared between patients with and patient without MDCT-confirmed PE or DVT (Table 4). We found five patients who had PE or DVT, and in those patients the operation time, estimated blood loss during operation, and preoperative D-dimer level were significantly greater than in patients without PE or DVT.

Discussion

In this study, we examined prospectively the usefulness of lung SPECT in screening for PE by performing preoperative and postoperative examinations. Several attempts at effective diagnosis of PE by PIOPED criteria and PISA-PED criteria have been made [8, 11]. However, as these studies employed only plannar images, and were based on correlative findings with pulmonary angiography, which has a low sensitivity [7], different or modified approaches that can effectively diagnose PE are needed, especially for patients with elective surgery. The usefulness of preoperative and postoperative lung scintigraphy has been demonstrated

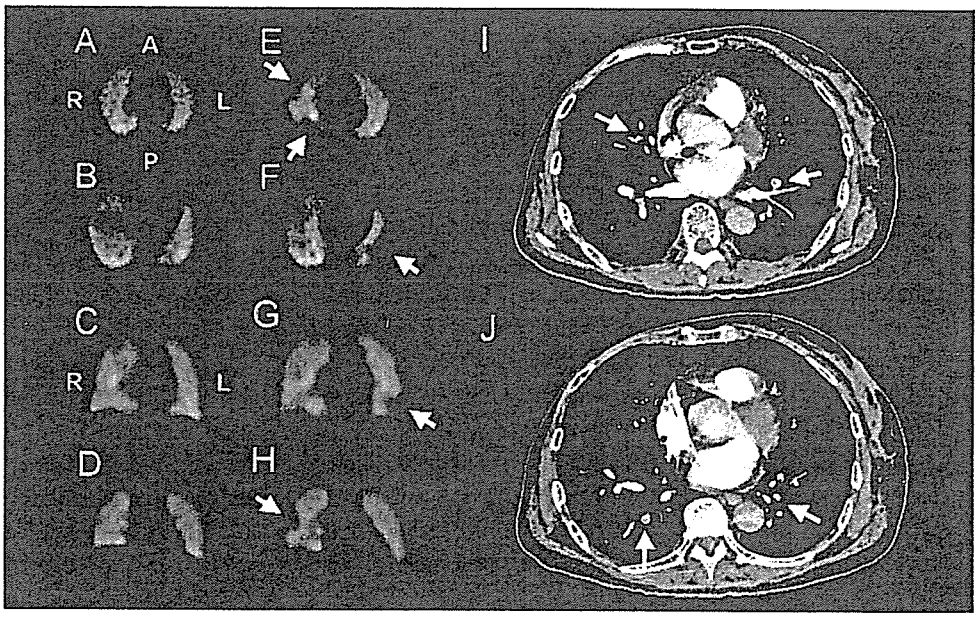

Fig. 3 Baseline SPECT (A–D) and postoperative SPECT (E–H) in a patient with multiple emboli in both lungs. Defects are marked by arrows. I and J: Postoperative MDCT showed thrombosis in branches of the right middle lobe artery and left lower lobe arteries. SPECT, single-photon emission computed tomography; R, right; L, left; A, anterior; P, posterior

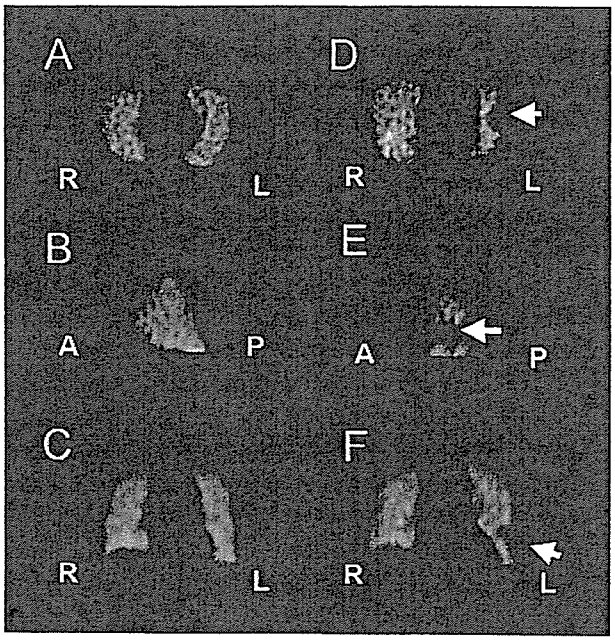

Fig. 4 Baseline SPECT (A–C) and postoperative SPECT (D–F) in a patient with postoperative segmental defect. Defects are marked by arrows. SPECT, single-photon emission computed tomography; R, right; L, left; A, anterior; P, posterior

Table 4 Comparison of patients' background according to SPECT and CT findings

	MDCT-confirmed PE and DVT	Normal	*P* value
N	5	27	
Age (yr)	58.2 ± 2.3	60.7 ± 10.2	0.60
Sex (M:F)	3:2	16:11	0.98
Disease			
Sigmoid colon cancer	2	5	
Rectal cancer	3	15	0.53
Pancreatic cancer	0	6	
Transverse colon cancer	0	1	
Blood loss (g)	2520 ± 2142	992 ± 1352	0.043
Operation time (min)	555 ± 299	311 ± 186	0.021
D-dimer (μg/ml)	1.59 ± 1.11	0.70 ± 0.71	0.025
TAT (μg/L)	4.59 ± 3.56	3.37 ± 4.03	0.57

Note. MDCT, multidetector helical computed tomography; PE, pulmonary embolism; DVT, deep venous thrombosis; TAT, thrombin-antithrombin complexes

in orthopedic surgery [16, 17, 20, 21]. Detection of additional defects postoperatively is a key for the diagnosis of PE, and asymptomatic PE is a common event in postarthroplasty patients. However, the usefulness of serial SPECT has not been demonstrated in patients elected to undergo gastrointestinal malignancy surgery. Since postoperative scan with conventional planar scan has a low specificity [22] and overestimates the frequency of postoperative PE [23], it is useful to compare pre- and postoperative imaging studies. However, our results showed that it is unnecessary to compare pre- and postoperative SPECT images to screen postoperative PE, because all additionally detected segmental defects were found only postoperatively, and preoperative detection of nonsegmental defects did not contribute to the detection of postoperative PE. In fact, preoperative SPECT was useful in the detection of preoperative PE in only one patient.

By performing SPECT serially, we found four (13%) patients with PE, two of whom were symptomatic, and five (16%) patients with highly suspected asymptomatic PE, suggesting a high incidence of postoperative PE (up to 28%) including asymptomotic PE in Asian patients elected for gastrointestinal malignancy surgery.

In this protocol, only perfusion SPECT was performed serially for comparative purposes, because (1) comparison of pre- and postoperative perfusion SPECT images can clearly demonstrate preexisting abnormalities or abnormalities after operation as reported by Bergqvist et al. [16]; (2) a PISA-PED study showed that the diagnosis of PE can be accomplished by perfusion scan alone [11]—although nonsegmental defects representing PE may be missed by PISA-PED criteria, this problem can be overcome by comparison of pre- and post-operative scans; and (3) preoperative ventilation scan was not helpful, and postoperative ventilation scan was needed only when baseline preoperative perfusion scan was not available [21].

By performing SPECT preoperatively, perfusion defects were detected in 12 patients (36%) and PE was diagnosed in one patient with pancreatic cancer, who was successfully treated with anticoagulant therapy [19]. In the other 11 patients, all detected defects were nonsegmental. The majority of these defects were also detected as nonsegmental defects in the postoperative SPECT, suggesting that these defects were not related to PE. In this regard, Tetalman et al. [24] identified perfusion defects in 22% of healthy volunteers. Furthermore, 27% of orthopedic surgery patients and 19% of general surgery patients had preoperative perfusion defects [16, 25]. The higher incidence in our patients may be due to the high sensitivity of SPECT itself.

We found 33 defects in 18 patients in postoperative SPECT scans. All segmental defects were detected postoperatively and comparison with baseline scan was not needed, demonstrating that postoperative SPECT is sufficient for screening postoperative PE in this study setting. In studies using planar images, detection of differences between pre- and postoperative scans was useful because of its low spatial resolution and low specificity [16, 17, 19]. In

contrast, SPECT imaging has a higher specificity [12], allows segmental localization of the perfusion defect, and reveals additional defects not seen on planar scans [13]. Lesions involving less than 35% of the lung segment or involving the entire segment were detected on SPECT [14]. However, only 77% of these lesions were detected on planar studies [26]. Furthermore, defects in the medial basal segment of the right lower lobe were not identified in planar studies but were easily seen using the SPECT. Thus, SPECT is more suitable for detailed definition of PE, including its location, shape, and size, and PE can only be predicted by postoperative scan.

We found five patients with segmental defects postoperatively in whom the final diagnosis could not be established with MDCT and eight new nonsegmental defects in six patients. Thus, what are those defects that are detected postoperatively? Obstructive airway disease such as airway obstruction after operation should be ruled out [7]. Since previous reports have described cases of isolated PE on a subsegmental level, which was detected as nonsegmental perfusion defects [13], it is possible that the postoperative defects are undetected PE. Especially, as we did not find any cause for these segmental defects in other imaging modalities and the sensitivity of SPECT was very high compared with that of planar scintigraphy [12, 13, 27, 28], it was strongly suggested that these segmental defects were due to asymptomatic PE. In this series, CT did not detect any embolus in patients who had PE preoperatively. The sensitivity of CT is relatively low, ranging from 66% to 93% compared with SPECT [29], and Reinartz et al. [13] reported that PE was confirmed in 64% of patients with low-probability scans diagnosed by SPECT, suggesting that PE is likely to be found in the PIOPED category "low probability" when classified by SPECT. The 4-detector MDCT used in this study is not suitable for detection of isolated subsegmental PE [30]; rather, a 16- or 64-detector MDCT is required for precise diagnosis. In our series, the five patients with segmental defects and six patients with nonsegmental defects were asymptomatic. Thus, it is important that a diagnostic strategy and a detailed treatment plan are established for patients with postoperative inconclusive segmental defects and nonsegmental defects. As a consensus, patients with small PE need anticoagulation when there are additional risk factors, such as DVT, inadequate cardiopulmonary reserve, and recurrent small PE and pulmonary artery hypertension [30]. Further clinical trials are necessary.

It is important to bear in mind in clinical practice the possible existence of a certain proportion of patients with malignancy who have preexisting PE. Since it is practically impossible to perform lung scintigraphy preoperatively and postoperatively for all patients, simple methods to detect high-risk patients for preexisting PE and postoperative PE are needed. The D-dimer level seems to be useful in the detection of PE [28], and one case had an elevated D-dimer level (1.58 μg/ml) [19]. Our evaluation of preoperative risk factors for postoperative PE or DVT showed that patients with PE or DVT had a longer operation time, greater blood loss, and an elevated D-dimer level. These results suggest that patients with an elevated D-dimer level who elect to undergo complicated surgery are at high risk for postoperative PE or DVT. Thus, preoperative D-dimer level can be a useful marker for pre- and postoperative PE.

In conclusion, postoperative SPECT is sensitive for screening of PE and preoperative SPECT is not necessary when PE is screened by visualization of at least two planes of SPECT images. The incidence of PE including asymptomatic PE was at least 12.5% among patients who underwent surgery for gastrointestinal malignancy, and asymptomatic PE is a common event in such patients. Patients with high D-dimer levels preoperatively and scheduled to undergo complex and long gastrointestinal surgical procedures should be placed under surveillance for PE.

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臨床

直腸癌側方リンパ節郭清の現状と今後

Now and future of lateral lymph node dissection for advanced lower rectal cancer

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直腸癌に対する側方リンパ節郭清は，時代の変遷とともに自律神経全温存が標準となり合併症も少なく安全な手技になってきた．一般的な郭清の適応は，腫瘍下縁が腹膜反転部より肛門側にあり，かつ，深達度A以深，直腸間膜内リンパ節転移陽性である．また，大腸癌治療ガイドラインには，郭清により骨盤内再発リスクは50%減少し5年生存率は9%改善すると，その有用性が明記されている．しかしながら，現行の適応は直腸間膜内の側方転移危険因子に基づくものであり，今後の課題として，直接的な側方転移診断精度の向上とそれに伴う郭清の効率化があげられる．さらに，この手術手技を広く標準化するためには，外科的教育システムを構築する必要がある．

はじめに

進行直腸癌に対する側方リンパ節郭清(以下，側方郭清)はわが国独自の手術手技であるが，残念ながら欧米から広い支持を得ているとはいえない．自律神経機能廃絶時代の悪夢を克服できずに現在に至っている感がある．しかしながら，わが国における膨大なリンパ節のマッピングデータから転移のターゲットとなるリンパ節が解剖学的に明らかになり，とくに自律神経については非温存から全温存へと時代の要請とともに変化してきている．また実際の現場では手技の向上や器械の進歩から安全な郭清が可能となっている．

本稿では過去の暗黒時代を原体験していない筆者が若手外科医として側方郭清の現状と今後の課題について検討を加えた．

I. 欧米の拡大郭清とわが国の側方郭清の相違

欧米の拡大郭清とわが国の側方郭清の相違を正しく認識することは，相互理解を深める鍵でもあり現行のTNM分類を正しく理解するうえでも重要である．直腸癌における最初の根治手術は1908年に提唱されたMiles手術である．以降，欧米ではMilesの郭清範囲をもとに局所再発率を下げるべく拡大郭清が行われた．具体的な郭清範囲は，高橋[1]が示しているように1985年のGlass

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Key words：直腸癌／自律神経温存／側方郭清

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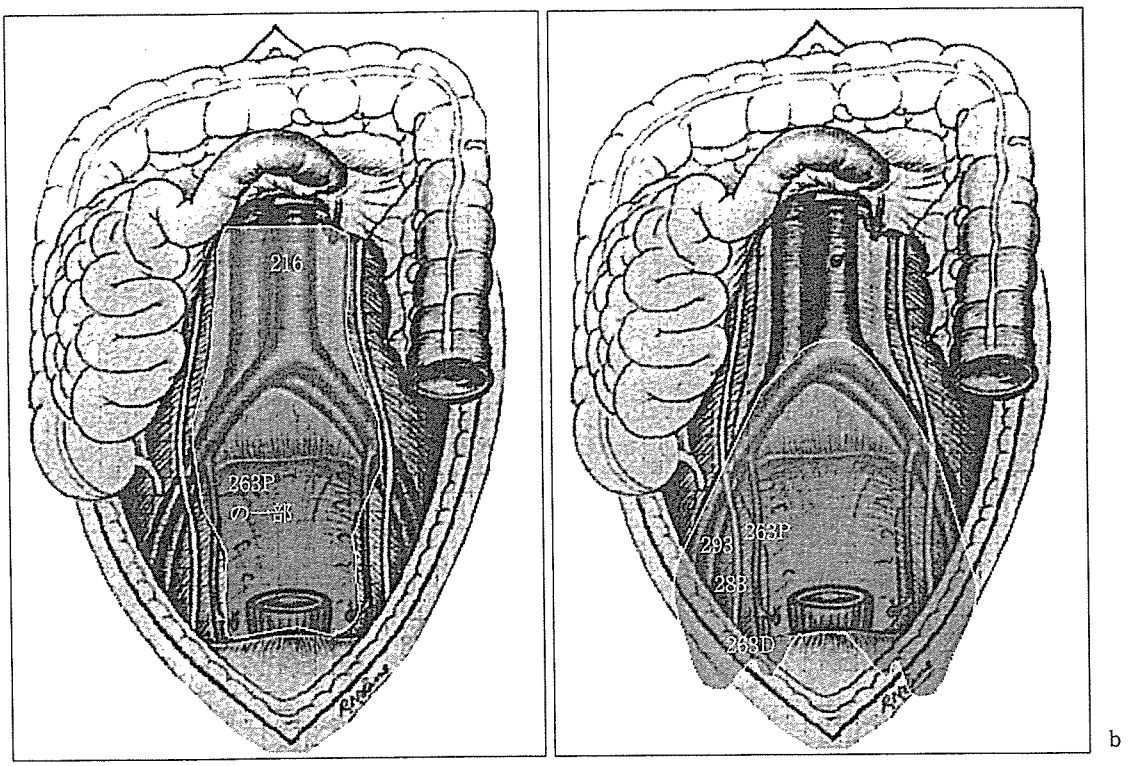


図1 直腸癌に対する欧米の拡大郭清(a)とわが国の側方郭清(b)の郭清範囲の相違（文献2より引用，改変）

表1 TNM分類における直腸癌の所属リンパ節（文献3より抜粋）

	Regional Lymph Nodes
For each anatomic site or subsite the following are regional nodes :	
Rectum	superior, middle, inferior rectal (haemorrhoidal)
	inferior mesenteric
	internal iliac
	mesorectum (paraproctal)
	lateral sacral, presacral, sacral promontory (Gerota)
Metastasis in nodes other than those listed above is classified as distant metastasis.	

の論文[2]が理解しやすい．Glass は St Mark's 病院で30年以上にわたって行われた拡大術式を radical resection and extended abdomino-iliac lymphadenectomy として紹介している．郭清範囲を大腸癌取扱い規約(第7版)に準じて検討してみると，わが国の側方郭清との相違は図1aのように，①その名の通り大動脈と下大静脈リンパ節216の郭清が中心である．②内腸骨リンパ節の中枢側263P は郭清範囲に含まれているが一部であり，末梢側263D は含まれていない．③閉鎖リンパ節283と外腸骨リンパ節293は含まれていない．

一方，わが国の側方郭清は図1bのように，263P，263D，283，293のリンパ節郭清はほぼ必須であり，216の郭清は不要である．このような歴史的な背景を考慮して現行の TNM 分類[3]における直腸癌の所属リンパ節を見てみると，そこには閉鎖リンパ節283や外腸骨リンパ節293は当然含まれず，表1の internal iliac(内腸骨リンパ節)とは Glass の論文から推測すると263P(内腸骨リンパ節中枢)の一部に相当する領域であり263D(内腸骨リンパ節末梢)は含まれていないと考えるのが妥当である．また，TNM 分類に示されているように所属リンパ節以外のリンパ節転移を遠隔転移と定義すると，263D，283，293へのリンパ

節転移は遠隔転移となり，その領域に生じた再発は局所再発と定義されないことになる．つまり欧米の拡大郭清とわが国の側方郭清とでは郭清範囲は明らかに異なり，そこから導きだされる局所再発率，生存率などの臨床データを一律に比較検討することは困難であり，論文を読む際には注意を要する．

表2　直腸癌骨盤神経叢周囲の微小転移

進行度	症例数	上方 LN (HE)	骨盤神経叢周囲微小転移	側方 LN (HE)
I	4	0	0(0/16)*	0
II	7	0	0(0/28)	0
III	6	6	0(0/24)	2
IV	3	3	2(2/10)	3
	20	9	2(2/78)	5

*微小転移陽性数/検体数

II. 進行直腸癌における自律神経全温存術の妥当性

直腸癌手術における自律神経の取扱いは非温存，部分温存から全温存へと次第に推移してきている．これは外科医が術後の QOL 向上を目指したためであろうが，神経温存の有無と局所再発の関係を厳密に比較検討した報告はなく，実際には温存しても局所再発率は上がらなかった，あるいは画像的に温存した神経周囲の局所再発は少なかったなどという報告が多い．そこで，すでに神経全温存を標準術式として取り入れていたわれわれは進行直腸癌20例を対象に骨盤神経叢周囲の結合織を1症例に4検体(計78検体)採取して，神経叢周囲の微小転移の有無を HE 染色よりも鋭敏な RT-PCR 法を用いて検討した[4]．表2に結果を示す．20例中9例に上方転移を，5例に側方転移を認め，側方転移例はすべて上方転移を伴っていた．Stage IV の遠隔転移部位は肝2例，大動脈リンパ節転移1例の3例であり，すべての症例で根治 B 以上の手術が可能であった．われわれの予想に反して，微小転移は78検体中2検体(3％)と低率であった．また微小転移は遠隔転移を伴う Stage IV の2例にのみ存在した．リンパ節転移との関係では，上方リンパ節転移のみの Stage III の4例に微小転移はなく，上方転移と側方転移を伴った Stage III の2例と Stage IV の3例の計5例中2例にのみ微小転移が存在した．上方および側方転移を伴ったその他の3例に骨盤神経叢周囲の微小転移が存在しなかったという事実は，図2に示すように，下部直腸癌の側方リンパ節転移の成

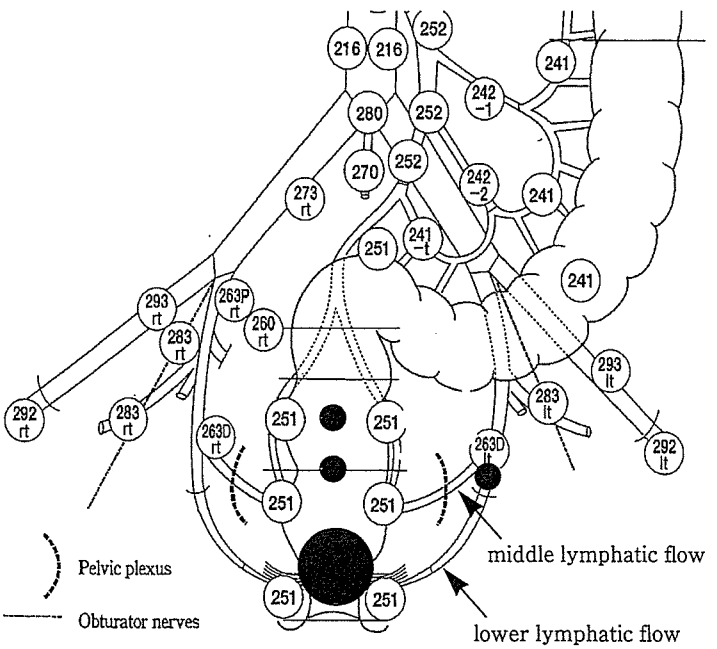


図2　側方領域への転移経路としてのリンパ流
上方および側方転移を伴い骨盤神経叢周囲の微小転移が存在しなかった3症例では，側方転移経路として直腸の lower lymphatic flow の重要性が示唆された．大きい●は主腫瘍，小さい●は転移リンパ節．

立にはリンパ流として骨盤神経叢を貫くと考えられている middle lymphatic flow だけでなく，lower lymphatic flow も関与していることをあらためて示唆するものである．また，微小転移を伴っていた2例はともに1年生存が得られずきわめて予後不良であった．

比較的最近わが国から報じられた自律神経非温存術後の切除標本における詳細な病理学的検討によると[5)6)]，Stage III，IV の直腸癌の中には自律神経浸潤が認められる症例が存在するため神経温存は慎重にすべきであると注意を促している．しかしながら彼らの報告でもこのような神経浸潤例に長期生存はなく[6)]，われわれの微小転移例と同程度の予後であった．予防的側方郭清例の神経全温存は妥当であろうが，神経浸潤例における浸潤部以外の予防的神経切除は妥当であるのか？われわれはこのような予後不良例では逆に術後の QOL 向上に配慮する必要があるという立場から，自律神経は全温存を大原則とし，神経浸潤が見られた際にはその部位を切除し他は可及的に温存するという立場で臨んでいる．

III. 側方郭清の適応—10% rule—

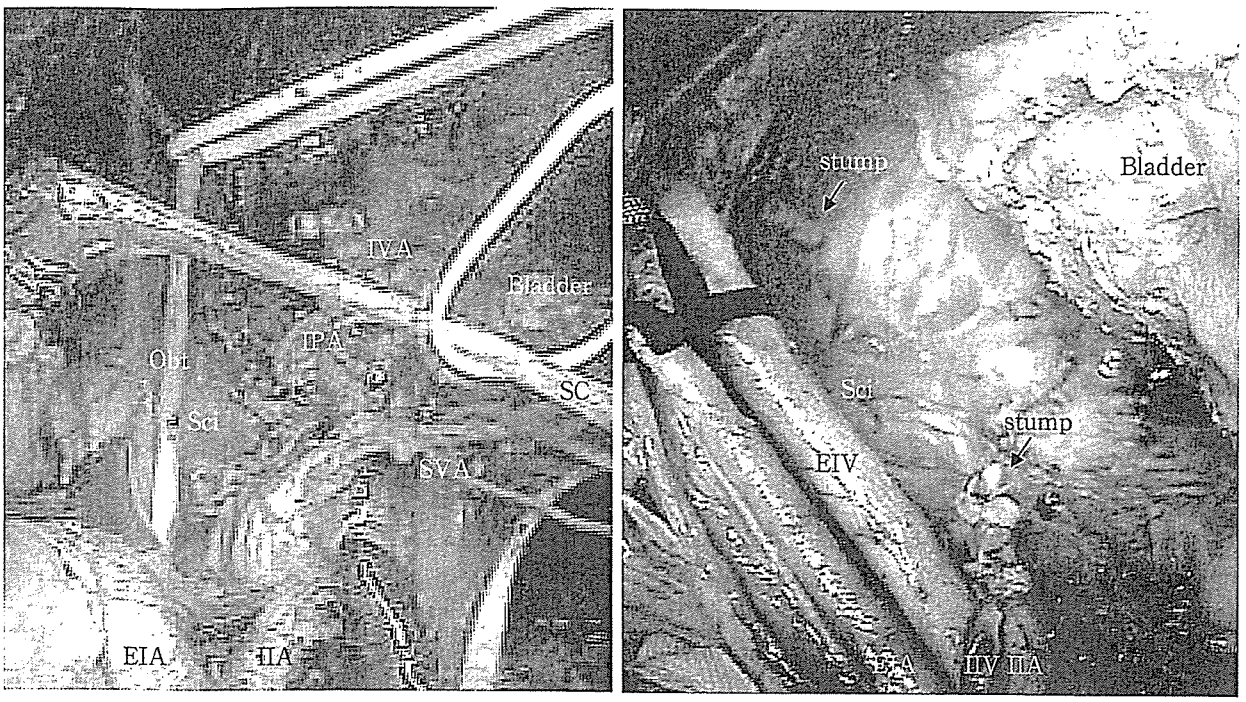
2005年に出版された大腸癌治療ガイドライン(医師用)によると，大腸癌研究会の多施設プロジェクト研究における直腸癌2,916例の分析で，腫瘍下縁が腹膜反転部より肛門側にあり，かつ，直腸壁を貫通している癌の側方リンパ節転移率は20.1%(側方郭清例のみ)であった．さらにこの適応に基づき側方郭清を行うと，骨盤内再発リスクは50%減少し，5年生存率は9%改善することが明記されている．側方郭清の骨盤内再発回避率と5生寄与度の計算式は他稿を参考にしていただくとして，現在の一般的な中下部直腸癌における側方郭清の適応は，腫瘍下縁が腹膜反転部より肛門側にあり，かつ深達度 A 以深，直腸間膜内リンパ節転移陽性である．ガイドライン(括弧内は当施設)における側方転移率は，深達度 SM 0.9%(0%)，MP 5.4%(3.6%)，SS/A1 7.7%(8.9%)，SE/A2 18.0%(23.0%)，Si/Ai 28.8%(11.1%)，直腸間膜内リンパ節転移陽性27%(25%)である．つまり側方郭清適応の根拠は，側方転移率が10%以上の症例となる．側方郭清はすべての施設で行われている手技ではない．しかしながらたとえば，通常の大腸 SM 癌の内視鏡摘除後の外科的追加腸切除はほぼ全施設で行われていて，その適応の1つに“sm 浸潤度1,000 μm 以上”がある．この根拠は，1,000 μm 以下ではリンパ節転移はほとんどなく1,000 μm 以上では転移率が10%以上になるということである．これは側方郭清の適応とほぼ同様である．これからみても予防的リンパ節郭清の適応として，いわゆる“10% rule”は存在し，現行の側方郭清の適応は妥当であると考える．

IV. 側方リンパ節郭清手技

自律神経温存側方リンパ節郭清の基本手技についてはすでに文献が数々あるので参考にしていただきたい[7)]．側方郭清の短所とも言われる出血量と手術時間の問題については，クーパーをバイポーラシザーズに持ち変えて出血量を軽減し，側方腹膜切開を省略して時間短縮をするなどの試みがなされている．図3に予防的側方郭清例と内腸骨血管を合併切除した側方郭清例(CT は図4a)における郭清後の側方領域を示した．予防的郭清は比較的手技が容易であるが，内腸骨血管合併切除でもリガシュアーを用いて血管を一括してシーリングするなどの工夫で出血も少なくなっている．昨今の手術器械の進歩も側方郭清手技の安全性に貢献している[8)]．

V. 側方陽性例の成績

図5に当施設で手術を行い2年以上経過観察した側方陽性例の根治度別生存率を示す．根治度 A の5年生存率は46.8%と良好であるが，根治度 B，C では長期生存が困難である．また腫瘍側の因子では，組織型 well/mod vs por/sig/muc，側方



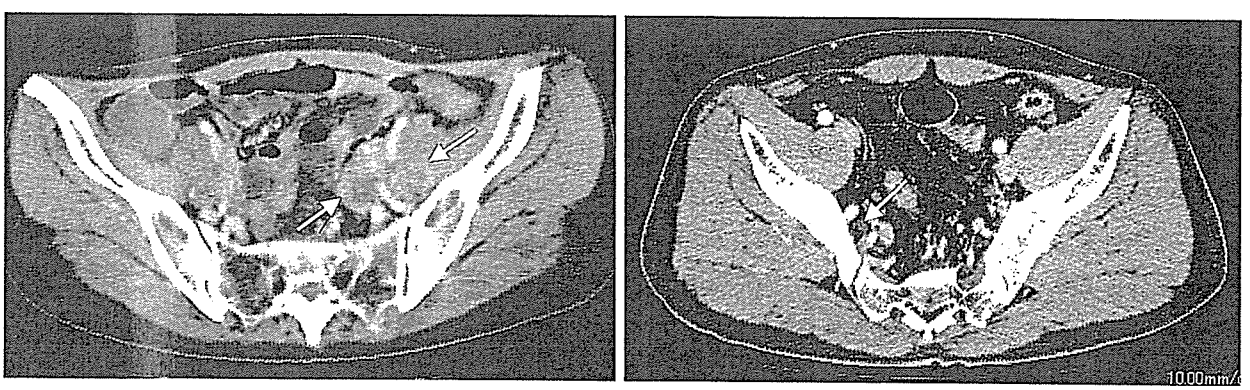
a　b

図3　側方郭清の程度

a：予防的側方郭清．閉鎖神経，精索をベッセルループで確保している．総出血量550 ml.

b：内腸骨血管を合併切除した側方郭清(図4 a症例)．転移リンパ節は内腸骨動静脈，骨盤神経叢，閉鎖神経と剝離不可能であった．内腸骨動静脈を中枢側で刺通結紮した後，末梢側を上膀胱動脈を含めてリガシュアーでシーリング．骨盤神経叢，閉鎖神経も含めて転移リンパ節を一括摘徐した．総出血量840 ml.

EIA：外腸骨動脈　IIV：外腸骨静脈　IIA：内腸骨動脈　IIV：内腸骨静脈　SVA：上膀胱動脈　IVA：下膀胱動脈　Sci：坐骨神経　Obt：閉鎖神経　SC：精索



a　b

図4　画像診断による側方転移診断

a：術前から明らかだった側方転移例．左内腸骨血管を挟み込むように2 cm 大の転移リンパ節が累々と腫大していた．

b：術中に診断した側方転移例．MP，N0 で側方郭清の適応はなく画像診断も転移陰性であったが，術中に硬い径3 mm のリンパ節をサンプリングし転移と診断した．

リンパ節転移個数2個以下 vs 3個以上，総リンパ節転移個数8個以下 vs 9個以上，などで生存に有意差を認めた．根治 A の初再発部位は，肺，肝，局所が1/4ずつを占め，以下，遠隔リンパ節，骨，腹膜と続いている．

現在われわれは根治 B 以上が望める側方陽性例を積極的な手術適応としているが，側方陽性例の術後 adjuvant として CPT11や Oxaliplatin を導入することにで今後さらに成績が向上するものと期待している[9]．

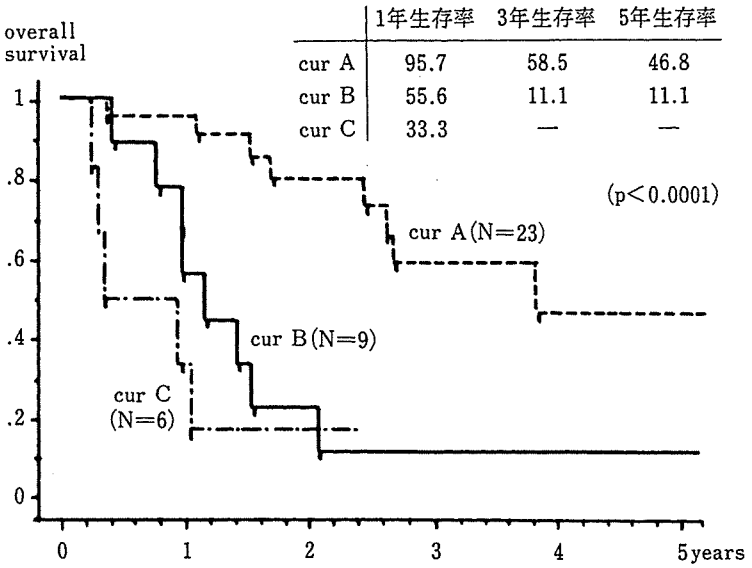


図5 直腸癌側方陽性38例の根治度別生存率

VI. 側方転移診断の課題

III. では，側方郭清の適応を深達度 A 以深，直腸間膜内リンパ節転移陽性と記載したが，実際にはこれらの危険因子は直腸間膜内(inside)の因子であり，側方転移と相関があるものの，対象となる側方領域(outside the boundaries of TME)とは解剖学的に離れた領域にある．これが現行の適応基準に至った経緯としてはおそらく側方領域に対する術前画像診断精度の低さがあげられる．しかしながら近年の画像診断の進歩は目覚しく[10]，側方診断精度を高めることは郭清効率を高めるためにも重要な課題である．最近開催された学会・研究会の抄録集から術前側方転移精度に関する多施設のデータをまとめて表3に示した．これらは多施設の heterogeneous なデータであり用いた診断装置もリンパ節転移診断基準も多少の異なりがあるため解釈には慎重を要す．少なくとも以下の注意が必要である．

① CT の進歩はとくにめざましく MDCT (=MSCT，マルチスライス CT)で，何列の検出器であるか，slice 厚はどれだけか，また，あらゆる部位で高い分解能をもつ任意方向の多断面表示(MPR, multi planar reconstruction/reformation)を用いているか，

② MRI ではルーティンに diffusion MRI を撮影しリンパ節のあたりをつけているか，矢状断で側方転移を診断しているか，

③リンパ節の造影効果を診断に取り入れているか，

④診断は放射線診断医のみか，どれくらい診断時間をかけているか，バイアスは入らないのか，

⑤個々のリンパ節転移診断が，術後の病理診断と 1 対 1 対応で比較可能か，病理診断だけを Golden standard とせずに術後の側方再発の有無を考慮に入れているか，

などである．残念ながら，当施設の側方転移診断精度は，感度60%(12/30) 特異度75.6%(59/78)，陽性反応的中率48.6%(18/37)，陰性反応的中率83.1%(59/71)であり，画像診断が偽陰性で側方転移があった症例が12例も存在していたため現状では満足できる診断レベルとは言えない．この術前画像診断と病理診断の乖離を埋める手立てとして，われわれは MP 以深であれば全例に直腸を摘出後に膀胱側腔を展開して内腸骨動脈周囲を両側から挟みこむようにリンパ節転移の有無を検索する側方リンパ節触診を行っている．この結果，

表3　術前側方リンパ節転移診断精度の比較

施設／報告者	当施設	国立がんセンター中央病院 藤田ら		東京女子医大 小川ら			国際医療センター 竹下ら	防衛医大 石黒ら	国立がんセンター中央病院 赤須ら
期間	2000～	～1997	1998～	NA			1995～	1998～	NA
側方陽性数／郭清数	30/108	18/112	18/83	NA			16/29	23/188	NA/52
器機	CT/MRI	通常CT	thin slice CT	CT	MRI	MRI 矢状断	thin slice CT	MRI	TSMRI
転移 LN	≧5 mm	≧6 mm		NA	NA	NA	NA	≧5 mm	NA
感　度	60.0	22	50	60.0	72.7	100	88.2	60.9	88
特異度	75.6	91	94	95.2	93.8	94.6	82.1	95.8	89
陽性反応的中率	48.6	33	69	NA	NA	NA	NA	66.7	NA
陰性反応的中率	83.1	86	87	NA	NA	NA	NA	94.6	NA
正診率	71.3	NA	NA	93.5	92.2	95.0	NA	91.5	89
年度／抄録*	2006 消外	2005 大肛		2006 大研			2006 大研	2006 大研	2006 大研

*消外：第61回消化器外科学会　大肛：第60回大腸肛門病学会　大研：第64回大腸癌研究会

2005年1月以降に根治B以上の手術を行った下部直腸癌のうち10例に側方陽性を経験しているが，5例は図4bのように術中にはじめて転移リンパ節と診断されている．

しかしながら，表3のようにかなり精度の高い側方転移診断がなされている施設も存在している．また最近，いわゆるナノテクを使った新しいUSPIO(ultrasmall particles of iron oxide)を用いたMRIでは，臨床的にoccultであったリンパ節転移が高率に検出可能になったという報告がなされた[11]．画像診断の向上は日進月歩であり，将来的にはこれらを積極的に取り入れることで，現行の直腸間膜内の危険因子に基づく側方郭清の適応から脱皮し，直接的な側方転移診断に基づく郭清が可能になるものと期待している．最終的には，さらなる効率的な側方郭清(表3の側方陽性数／郭清数＝側方郭清陽性率)を行い，なおかつ側方再発率を減らすことが目標である．

おわりに

側方陽性根治A症例における良好な成績から術前側方陽性例に対して郭清を行うことについて異論はないと思われる．問題は術前診断と病理学的診断との乖離であり，欧米に側方郭清の有用性を示すためにも郭清効率を高める努力は必要である．現在われわれはこの手立てとして側方リンパ節触診を行っているが，やはりより汎用性のある画像に基づく側方転移診断の向上が果たす役割は大きい．また，“slice幅5 mm以下の術前CTまたはMRIでmesorectum外に転移の疑われる短径10 mm以上の腫大結節がない”臨床病期II，IIIの下部直腸癌症例を対象とした側方郭清の意義については，現行のJCOG-0212[12]臨床比較試験の結果を待ちたい．

今年の第65回大腸癌研究会では，海外で直腸癌の局所制御あるいは生存延長目的に手術と併用されている放射線療法[13]が，テーマとして取り上げられた[14]．わが国では側方郭清が行われているせいか全体的にはnegativeな報告が多かった印象である．しかしながら放射線療法と新しい化学療法の併用により，あるいは局所再発高危険群を選別することで，今後わが国でも有用性が証明される可能性がある．

最後に，側方郭清はわが国独自の手術手技であるがより広く標準化するためには，ストックホルムにおけるTME projectのような[15]，surgical training programが必要である．

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Original Paper

Colonic J-Pouch Decreases Bowel Frequency by Improving the Evacuation Ratio

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KEY WORDS:
Colonic J-pouch; Defecography; Transit study; Evacuation ratio; Contraction ratio

ABSTRACT

Background/Aims: To compare the functional outcome of ultra-low anterior resection for rectal cancer with colonic J-pouch reconstruction with that of straight reconstruction.

Methodology: Twenty-three patients who underwent ultra-low anterior resection with or without J-pouch reconstruction underwent bowel transit study, videodefecography, and answered a questionnaire survey 4 months and 1 year after surgery. Eleven healthy subjects underwent similar testing as controls.

Results: Patients with a J-pouch had less frequent stools than patients with straight reconstruction 4 months after surgery ($p<0.05$), but the two groups were similar at 1 year. Bowel transit time was similar at both study points. The evacuation ratio was higher after J-pouch than straight reconstruction 4 months after surgery ($p<0.05$). However, the ratio improved in the straight group, and no difference existed at 1 year. Colonic contraction was seen only near the anastomosis 4 months after surgery, but the contraction proximal to the anastomosis improved over the next 8 months.

Conclusions: J-pouch reconstruction facilitates evacuation by improving the evacuation ratio. Although straight anastomosis caused excessive stool frequency 4 months after surgery, colonic function continued to improve and was comparable with J-pouch and straight reconstruction 1 year after surgery because the contraction ratio proximal to the anastomosis improved.

INTRODUCTION

Generally, ultra-low anterior resection for rectal cancer avoids the need to create a permanent colostomy, but it often results in excessive stool frequency which decreases the quality of life. It has been reported that functional outcome after low anterior resection for rectal cancer can be improved by the construction of a colonic J-pouch. However the reasons for this improvement are poorly understood. Therefore construction of a colonic J-pouch is a controversial procedure, and its use varies from institution to institution.

This study compared the functional outcome of ultra-low anterior resection with and without colonic J-pouch reconstruction using new indicators of bowel function termed the evacuation ratio and the contraction ratio.

METHODOLOGY

Between April 1999 and March 2001, ultra-low anterior resection with the primary anastomosis (<4cm above the dentate line) was performed in 23 rectal cancer patients. Patients were assigned randomly to the J-pouch with a 5-cm limb (n=13) or to the straight anastomosis (n=10) by a computer-generated table of random numbers. Informed consent was obtained from all patients.

Patients in the two groups were similar with respect to age, gender, distance between the anastomosis and the dentate line, nerve preservation, and Dukes stage **(Table 1)**.

Bowel function was evaluated by a bowel transit study, a videodefecography, and a questionnaire administered before surgery, 4 months and 1 year after surgery.

Bowel Transit Study

Twenty radiopaque markers within a gelatin capsule (Sitzmarks: Konsyl Pharmaceuticals, U.S.A.) were ingested, and a plain film of the abdomen was taken 8, 24, 32, 48, and 96 h after ingestion. The half-dose transit method was used, and segment transit time for each segment of the colon was calculated before surgery and 4 months after surgery. Each segment was defined as follows; Ascending colon: A, Transverse colon: T, Descending colon: D, Sigmoid colon and (neo) Rectum: SR.

Videodefecography

Thick barium sulfate of standardized consistency and viscosity was introduced into the (neo) rectum using a caulking gun injector until the contrast reached the sacral promontory (approximately 120g). Evacuation was videotaped fluoroscopically with the

patient in the sitting position.

The weight of infused contrast (W1) and evacuated contrast in 1 minute (W2) were recorded. The evacuation ratio was given by calculating W2/W1 x 100(%). The contraction ratio (CR) was the post-evacuation diameter of the colon divided by the pre-evacuation diameter (x 100(%)) which were calculated by lateral view of pelvic X-ray. The CR was calculated 5, 10, and 15cm above the anastomosis (CR5, CR10, and CR15, respectively).

Videodefecography was taken only postoperation (4 months and 1 year after surgery) because the examination was prevented by the existence of the tumor preoperation, so eleven healthy volunteers underwent the same examination and served as normal controls.

Questionnaire Survey

A questionnaire was administered 4 months and 1 year after surgery inquiring as to the number of bowel movements per day, fecal soiling, and urgency.

Student's *t* test was used for intergroup comparisons. *P* values less than 0.05 were considered significant.

RESULTS

1. Relationship between Bowel Frequency and Results of the Examination

The patients were divided into two groups to evaluate a relationship between bowel transit time and bowel frequency: high frequency (>5 bowel movements per day) and low frequency. The left colonic transit time was longer in patients in the high bowel frequency group than those in the low **(Figure 1)**.

There was a tendency towards an inverse correlation between the evacuation ratio by videodefecography and the number of bowel movements per day. The patients with a low evacuation ratio tended to have more frequent stools **(Figure 2)**.

2. Comparison of Colonic Function between J-Pouch and Straight Reconstruction

Patients who underwent J-pouch reconstruction had fewer stools per day than patients who received straight reconstruction 4 months after surgery, but the two groups were similar at 1 year. Soiling and urgency were similar at both sampling points **(Table 2)**.

The bowel transit time was longer postoperatively than it was preoperatively, especially in the left colon (D, SR), and that was similar in the two groups postoperatively **(Figure 3)**.

Patients with a J-pouch had a higher evacuation ratio (71%) than patients with a straight reconstruction (48%) 4 months after surgery. At 1 year, however, the two groups were similar **(Table 3)**.

The contraction ratio at different distances proximal to the anastomosis shows that powerful contractions occurred only near the anastomosis (CR5). The CR5 in J-pouch patients was higher than it was in patients with a straight reconstruction. One year after surgery, CR5, CR10 and CR15 in straight reconstruction patients both were higher than they were 4 months after surgery **(Table 3)**.

TABLE 1 Patients' Characteristics

	Type of reconstruction		
	J-pouch (n=13)	Straight (n=10)	
Age (yr)	55±10	64±9	(ns)
Gender ratio (M:F)	7:6	6:4	(ns)
Distance from dentate line (cm)			
anterior wall	2.6±1.2	2.4±1.2	(ns)
posterior wall	2.0±1.5	2.3±1.2	(ns)
Nerve preservation			
hypogastric nerve	complete : 4, partial : 0	complete : 4, partial : 0	(ns)
pelvic plexus	complete : 5, partial : 7	complete : 6, partial : 3	(ns)
Dukes stage (A:B:C:D)	6:1:5:1	3:1:6:0	(ns)

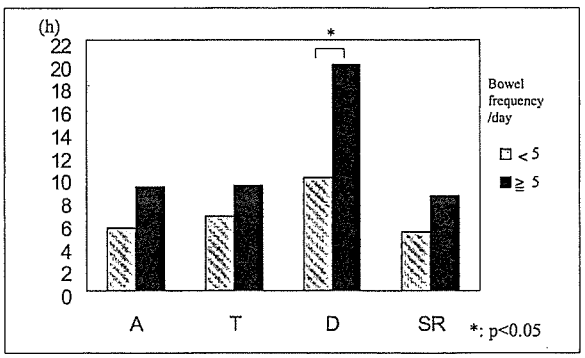

FIGURE 1 Segmental transit time between high and low bowel frequency group. Each segment was defined as follows; Ascending colon: A, Transverse colon: T, Descending colon: D, Sigmoid colon and (neo) Rectum: SR. The left colonic transit time was longer in patients in the high bowel frequency group (>5 bowel movements per day) than in patients in the low.

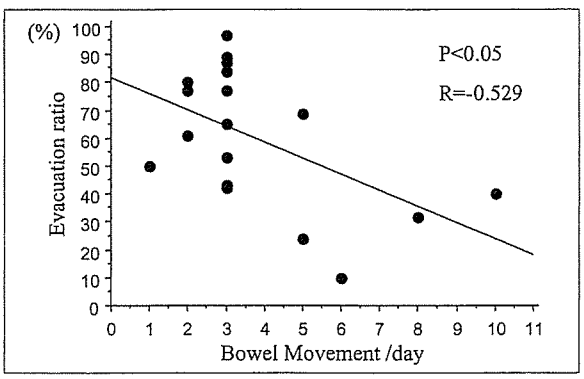

FIGURE 2 Relationship between evacuation ratio and bowel frequency. There was a tendency towards an inverse correlation between the evacuation ratio and the number of bowel movements per day. The patients with a low evacuation ratio tended to have more frequent stools.

DISCUSSION

The introduction of stapling devices has improved the safety of ultra-low anterior resection for rectal cancer. However, the ability of the rectum to function as a stool reservoir decreases in proportion to the amount of rectum removed, and conventional low anterior resection can result in dyschezia. Lazorthes

TABLE 2 Postoperative Functional Results

	Stool frequency (/day)		Soiling (%)		Urgency (%)	
	J-pouch	Straight	J-pouch	Straight	J-pouch	Straight
4M	3.0*	6.2*	31	20	0	20
8M	3.2**	6.2**	15	0	0	0
1Y	2.7	2.5	0	0	0	0

*, **: $p<0.05$.
J-pouch (n=13), Straight (n=10).

TABLE 3 Evacuation Ratio and Contraction Ratio

	Period	ER (%)	CR5 (%)	CR10 (%)	CR15 (%)
Control		89±12*1	50±16*2	31±15*3*4*5	33±5*6*7
J-pouch	4M	71±19	52±24	16±10*3	4±4*6
	1Y	77±19	50±15	5±2*4	14±4
Straight	4M	48±21*1	31±10*2	7±4*5	3±3*7
	1Y	70±24	47±21	21±3	12±10

*1-6 $p<0.05$.
ER: Evacuation ratio, CRx: contraction ratio x cm above the anastomosis.
Control values were derived from 11 healthy volunteers.

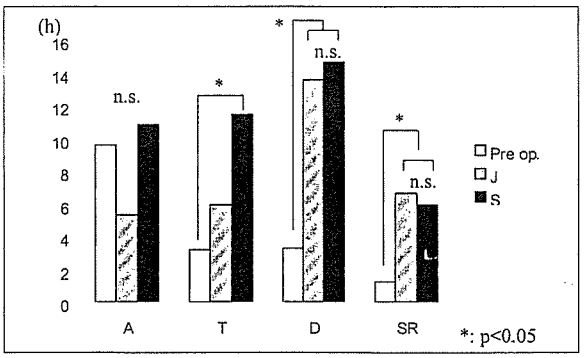

FIGURE 3 Segment transit time between J-pouch and straight reconstruction. The bowel transit time was longer postoperatively than it was preoperatively, especially in the left colon (D, SR). Bowel transit time was similar in patients with J-pouch and straight reconstruction.

(1) and Parc (2) reported in 1986 that colonic J-pouch improves postoperative rectal function. Hida *et al.* (3) recommended that a J-pouch be constructed when the anastomosis is <8cm from the anal verge because a satisfactory functional outcome can be obtained with straight reconstruction when the distance is >9cm. In recent years, a small J-pouch, with a 5 or 6-cm limb, has been recommended because it is difficult to evacuate a large pouch (4-7). Based on these recommendations, we used a J-pouch reconstruction with a 5-cm limb when the anastomosis was <4cm above the dentate line in this study.

It has been reported that J-pouch reconstruction improves rectal compliance (8), reduces the frequency of strong contractions (9), and increases the anorectal pressure gradient (9,10), all of which improve function.

We used a colonic transit study with radiopaque markers to evaluate motor activity of the colon. The reproducibility of this method has been validated (11). The postoperative bowel transit time was longer than in healthy controls, especially in the left colon, and corresponded to excessive stool frequency. These results suggest that the bowel frequency is related to the transit time of the left side colon.

In videodefecography, evacuation ratio and contraction ratio were obtained to evaluate the evacuation function of the colonic segment above the anastomosis. Also patients with a low evacuation ratio tended to have more frequent stools (12). Decreased motor activity of the colon proximal to the anastomosis prolongs the transit time and decreases the evacuation ratio (13). Denervation (14), poor blood supply (15), and the appearance of strong contractions (15,16) are thought to be causes of decreased motor activity after low anterior resection, and contribute to dyschezia.

The motor activity proximal to the anastomosis was decreased at 4 months regardless of whether a J-pouch was constructed. Contraction of the colon occurred only near the anastomosis. However the evacuation ratio was higher when a J-pouch was constructed. These results show that the J-pouch does not improve colonic transit time, but decreases stool frequency by facilitating fuller evacuation during each bowel movement.

It has been reported that the advantages of J-pouch over straight reconstruction are short-term and that the functional results are similar after 1 or 2 years (17,18). Our study reproduced this finding. Interestingly, the CR10 and CR15 were both higher at 1 year than they were 4 months after surgery in both groups. Improvement has been attributed to recovery of the nerve function (18) and reduction in the frequency of strong contraction (15), but further study is needed to clarify the cause of dyschezia after ultra-low anterior resection.

CONCLUSIONS

Decreased motor activity of the colon proximal to the anastomosis increases stool frequency after ultra-low anterior resection. Colonic J-pouch reconstruction did not improve colonic transit time, but did decrease stool frequency secondary to an improvement in the evacuation ratio. Stool frequency in patients with a straight reconstruction decreased during the first year after surgery because the contraction ratio proximal to the anastomosis improved.

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Short Time to Recurrence After Hepatic Resection Correlates with Poor Prognosis in Colorectal Hepatic Metastasis

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Background: Early recurrence is a major problem after hepatic resection of colorectal hepatic metastasis (CHM). Our aim was to investigate the relationship between time to recurrence after CHM resection and overall survival.
Methods: A retrospective analysis was performed for 101 consecutive patients who underwent hepatic resection for CHM and have been followed more than 5 years.
Results: Among 101 patients, 82 (81%) had a recurrence. Overall survival of patients with recurrence within 6 months after CHM resection was significantly worse than that of patients with recurrence after more than 6 months ($P < 0.01$). Overall survival was poorer when time to recurrence was shorter. One of the reasons for poor prognosis of patients with recurrence within 6 months was that only a few patients could undergo a second resection for recurrence after CHM resection. Histological type, including poorly differentiated signet ring cell or mucinous adenocarcinoma in the primary tumor, bilobar metastases, microscopic positive surgical margin and carcinoembryonic antigen (CEA) above 15 ng/ml had predictive value for decreased recurrence-free survival after CHM resection.
Conclusion: Short time to recurrence after CHM resection correlates with a poor prognosis. Histological type of poorly differentiated signet ring cell or mucinous adenocarcinoma in the primary tumor might be a predictor for early recurrence after CHM resection.

Key words: colorectal cancer – hepatic metastasis – resection – recurrence

INTRODUCTION

Hepatic resection is currently the only potentially curative treatment for colorectal hepatic metastasis (CHM) (1–6). However, frequent recurrence is a major problem after surgery, with 80–85% of patients experiencing a recurrence (2,3,6). Thus, reduction of recurrence is necessary to improve prognosis after CHM resection.

A correlation between a short time to recurrence after resection of the primary tumor and poor prognosis after resection of recurrence has been demonstrated in colorectal cancer (2,5), breast cancer (7), hepatocellular carcinoma (8) and renal cell carcinoma (9). In CHM, however, the correlation between time to recurrence after resection for CHM and prognosis is still obscure. The relation between time to recurrence after resection and prognosis is complicated in CHM because many recurrences after CHM resection can be resected, and resection sometimes contributes to long-term survival (10–12).

This study was conducted to determine the correlation between time to recurrence after CHM resection and prognosis by scrutinizing recurrence after CHM resection, which may suggest the best timing for adjuvant chemotherapy and elucidate whether time to recurrence can be a surrogate endpoint for adjuvant study in resectable CHM. We also compared clinicopathological factors and time to recurrence to find out preoperative predictive factors for early recurrence.

PATIENTS AND METHODS

PATIENT POPULATION

A total of 101 patients who had undergone hepatic resection for CHM at the National Cancer Center Hospital East between September 1992 and January 2000 and have been followed precisely for more than 5 years were examined retrospectively. The patients consisted of 56 (55%) men and 45 (45%) women, ranging in age from 23 to 78 years (mean, 60 years). None of the patients had received adjuvant chemotherapy after primary colorectal resection.

The criteria for hepatectomy were as follows: metastatic lesions were confined to the liver and all lesions could be

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resected using oncologic principles while preserving liver function. Extended lobectomy plus partial resections were considered as the upper limit of hepatectomy that could be performed safely, and trisegmentectomy was applied only when the volume of the residual liver was deemed to be abundant. Neither the number of metastatic tumors nor tumor size, in themselves, excluded patients from hepatectomy.

No patient received adjuvant therapy after CHM resection.

Surgical Procedure

After laparotomy, a careful search was performed for local recurrences, extrahepatic metastases and peritoneal dissemination in the abdominal cavity. Any suspicious lesions were examined by biopsy. If the regional lymph nodes (hepatoduodenal or peripancreatic lymph nodes) were positive, dissection of the regional lymph nodes was performed. Intraoperative bimanual liver palpation and ultrasonography were performed to confirm tumor location and size of the lesions in all patients; all resections were ultrasound-guided procedures. Hepatic resection was performed with tumor-free resection margins using the forceps fracture method under inflow occlusion (Pringle's maneuver).

Clinical Follow-up

After hepatic resection, patients were closely followed up with diagnostic imaging (chest X-ray and abdominal CT every 3 months, measurement of serum carcinoembryonic antigen (CEA) levels every month and annual colonoscopy to detect tumor recurrence) up to 5years. After 5 years patients were followed up every 6 months or annually.

Morphologic Investigations

The resected colorectal specimens and hepatic specimens were fixed in 10% phosphate-buffered formalin and cut at intervals of 5 mm and 10 mm, respectively, and then embedded in paraffin. Serial sections of 3 μm thickness were stained with hematoxylin and eosin for morphologic examination. Histological diagnosis was performed according to the World Health Organization intestinal tumor classification (13).

Statistical Analysis

The chi-square test and student *t*-test were used to compare data (Dukes' stage, primary location, positive regional lymph node, size of tumor, number of tumors, synchronous/metachronous, tumor distribution and ratio of recurrence) between subgroups based on time to recurrence. Mann–Whitney's *U*-test was used to compare preoperative serum CEA level between subgroups. Analyses of survival were performed using the Kaplan–Meier method (14), and differences between the curves were tested using the log-rank test. The log-rank test was also used to examine the significance of associations between survival curves and CEA cutoff values of 10, 15, 20, 25, 30, 35, 40, 45, 50, 60, 70, 80, 90, 100 and 200 ng/ml.

Factors related to survival were analyzed with the Cox proportional hazards regression model (15). A P-value of <0.05 was considered statistically significant.

RESULTS

Surgical Resections

Partial resection was performed on 47 patients, subsegmentectomy on 9, segmentectomy on 25, lobectomy on 11, extended lobectomy on 6 and trisegmentectomy on 3 according to Couinaud's anatomical classification (16). A microscopic positive surgical margin was observed in 14 patients. There was no perioperative mortality. Twenty-one complications were observed: 7 cases of biliary leak; 6 cases of intra-abdominal abscess; 4 cases of wound infection; and 1 case each of liver failure, ileus, lung abscess and urinary tract infection.

Survival After CHM Resection

The overall 5-year Kaplan–Meier survival rate after hepatic resection for CHM was 42%, with a median survival of

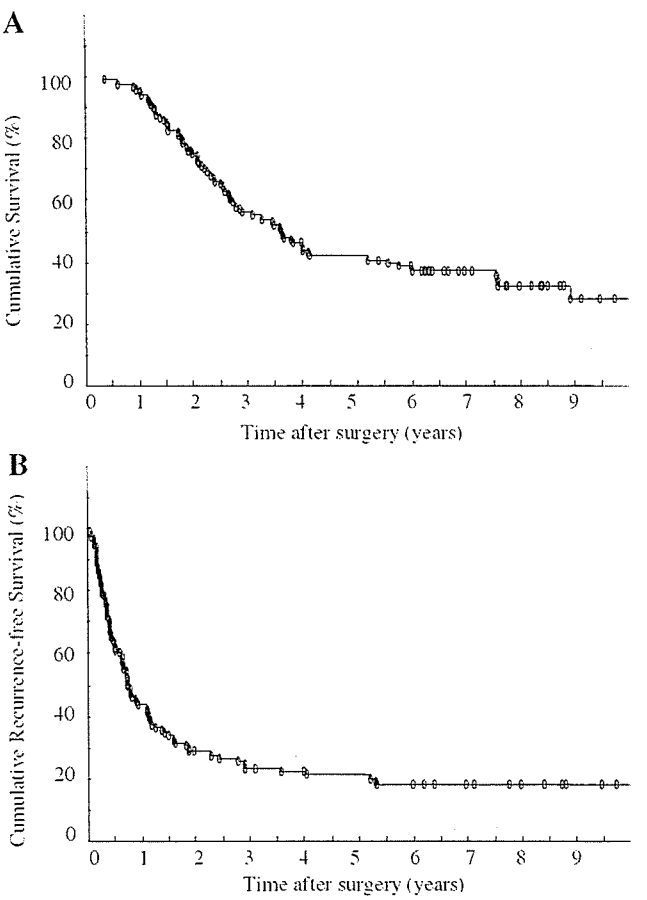

Figure 1. Cumulative survival (A) and recurrence-free survival curves (B) for 101 patients with resected colorectal hepatic metastasis.

34 months (Fig. 1A). Recurrence-free 1-, 3- and 5-year survival rates were 43, 23 and 21%, with a median recurrence-free survival of 9 months (Fig. 1B). The median follow-up duration of survivors was 87 months.

Recurrences After CHM Resection (Fig.2)

Among the 101 patients who underwent CHM resection, 82 (81%) developed recurrences. Locations of recurrences were as follows: liver in 36 patients, lung in 17, both liver and lung in 9, lymph node in 6, peritoneum and local recurrence in 4 each, brain and adrenal gland in 2 each, and ovary and bone in 1 each. Thirty-seven recurrences (45%) occurred within 6 months after hepatic resection and 72 recurrences (88%) occurred within 2 years. The ratio of hepatic recurrences to total recurrences was significantly higher in 1st–12th month than that after 12th month from CHM resection ($P = 0.01$). The ratio of pulmonary recurrence and that of recurrence in organs other than the liver and lung were significantly higher after 24th month ($P < 0.05$) and in 13th–24th month ($P < 0.05$) from CHM resection, respectively, than those in the other period. Of the 82 patients with recurrence after hepatic resection 36 received re-resection. Re-resection could be performed in only 10 of 24 patients (42%) whose recurrence occurred in the liver or lung within 6 months after hepatic resection, whereas re-resection could be performed in 22 of 29 patients (76%) whose recurrence occurred in the liver or lung more than 6 months later ($P = 0.01$). Of the remaining 46 patients, 33 received systemic chemotherapy, 7 received hepatic arterial infusion, 2 received radiation therapy and 4 received best supportive care.

Clinicopathological Features According to Time to Recurrence

Table 1 summarizes the primary and metastatic tumor characteristics. Patients were classified into three subgroups according to time to recurrence after hepatic resection as follows: no recurrence, recurrence within 6 months and recurrence after more than 6 months. There were no significant differences in primary tumor characteristics between the three subgroups. All patients in the no recurrence group had a primary tumor that was classified as a well- or moderately differentiated carcinoma.

In terms of characteristics of the metastatic tumor, the number of tumors was significantly less ($P < 0.01$) and unilobar distribution was seen significantly more frequently ($P < 0.01$) in the no recurrence group compared with the other subgroups.

Survival According to Time to Recurrence

Kaplan–Meier curves for overall survival after CHM resection according to time to recurrence in patients who developed recurrences are shown in Fig. 3A. Patients were divided into four subgroups according to time to recurrence after hepatic resection as follows: within 6 months, 7th–12th month, 13th–24th month and after 24th month. Overall survival of

Resection n=101

Recurrence n=82

Time to recurrence	n	%	Location			
			Liver (resected case)	Lung	Liver + Lung	Others
–6 months	37	45.1	19 (8)	5 (2)	6 (0)	7 (1)
7–12 months	20	24.4	11 (7)	3 (2)	2 (1)	4 (1)
13–24 months	15	18.3	3 (3)	3 (2)	1 (0)	8 (1)
25– months	10	12.2	3 (3)	6 (5)		1 (0)

Figure 2. Locations of recurrence according to time to recurrence after resection of colorectal hepatic metastasis. The number of resected cases for the recurrence is shown in parentheses.

Table 1. Clinicopathological findings of 101 patients with colorectal hepatic metastases according to time to recurrence

Variable	No recurrence (19)	Recurrence within 6 months (37)	Recurrence after more than 6 months (45)	*P*-value*
Primary colorectal tumor				
TNM Classification				0.63
I	1	1	2	
II	4	11	6	
III	10	12	21	
IV	4	13	16	
Location				0.85
Rectum	4	7	17	
Colon	15	30	28	
Number of positive lymph nodes (mean ± SD)	1.3 ± 2.1	2.3 ± 3.8	1.4 ± 1.7	0.29
Histological type of adenocarcinoma				
Well- or moderately differentiated	19	33	42	
Poorly differentiated signet ring cell or mucinous	0	4	3	
Hepatic metastases				
Maximum size of tumor (mean ± SD, cm)	4.5 ± 3.1	3.6 ± 2.1	4.3 ± 3.3	0.26.
Number of tumors (mean ± SD)	1.3 ± 0.6	2.5 ± 1.6	1.9 ± 1.4	<0.01
Preoperative CEA level (mean ± SD, ng/ml)	264.0 ± 818.0	41.3 ± 53.8	220.7 ± 879.7	0.25
Synchronous/metachronous				0.94
Synchronous	7	14	18	
Metachronous	12	23	27	
Distribution of metastases				<0.01
Unilobar	18	20	29	
Bilobar	1	17	16	

SD, standard deviation; CEA, carcinoembryonic antigen.
*Difference between patients with no recurrence and those with recurrence within 6 months.

patients with recurrence within 6 months after resection was significantly worse than that of patients with recurrence in 7th–12th month ($P = 0.04$), that of patients with recurrence in 13th–24th month ($P < 0.01$) and that of patients with recurrence after 24th month ($P < 0.01$). Overall 5-year survival rate in patients who developed recurrence within 6 months after hepatic resection was only 10% with a median survival of 26 months. Overall survival was poorer when time to recurrence was shorter.

Figure 3B shows overall survival after recurrence according to time to recurrence. Overall survival after recurrence of patients with recurrence within 6 months after resection was still worse than that of patients with recurrence in 13th–24th month ($P < 0.04$) and that of patients with recurrence after 24th month ($P < 0.03$). Overall survival after recurrence of patients with recurrence in 7th–12th month after resection seemed to be better than that of patients with recurrence within 6 months, but the difference was not significant ($P = 0.14$). Survival after recurrence tended to be poorer when time to recurrence was shorter. Overall survival after recurrence of patients with recurrence within 6 months after resection was significantly worse than that of patients with recurrence in more than 6 months ($P < 0.01$).

Correlation Between Clinicopathological Factors and Recurrence-free Survival

To find prognostic factors for recurrence-free survival after CHM resection, correlations between clinicopathological factors and recurrence-free survival were analyzed (Table 2). Histological type of tumor, including poorly differentiated signet ring cell or mucinous adenocarcinoma in the primary tumor ($P < 0.01$) (Fig. 4), two or more hepatic tumors ($P < 0.01$), bilobar distribution ($P < 0.01$), microscopic positive surgical margin ($P = 0.03$) and CEA level before hepatic resection above 15 ng/ml ($P = 0.04$) were significantly associated with poor recurrence-free survival.

We examined the independent predictive value of the aforementioned factors in recurrence-free survival. Data were analyzed using a Cox regression model (Table 3). Histological type of poorly differentiated signet ring cell or mucinous adenocarcinoma in the primary tumor [$P < 0.01$;