

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させていただくとして、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 μ m以上”がある。この根拠は、1,000 μ m以下ではリンパ節転移はほとんどなく1,000 μ m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られる。

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させていただきたい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ユ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

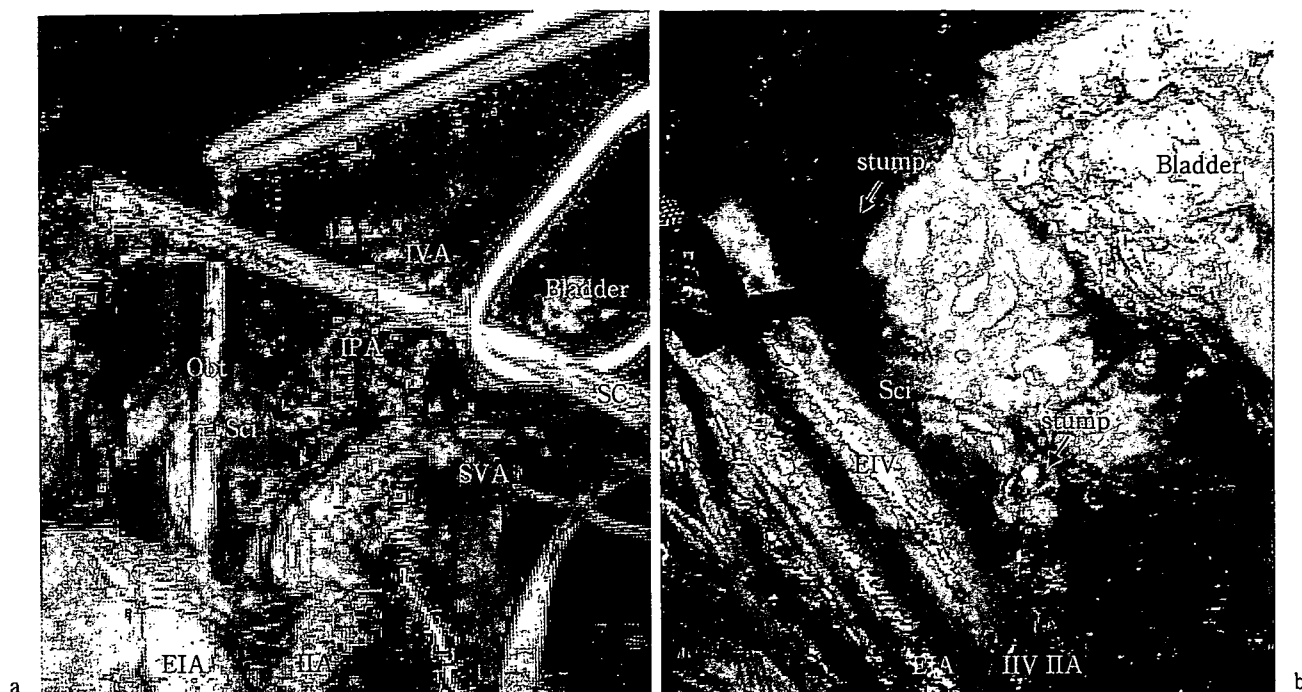


図3 側方郭清の程度

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ユアーでシーリング。骨盤神経叢，閉鎖神経も含めて転移リンパ節を一括摘除した。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

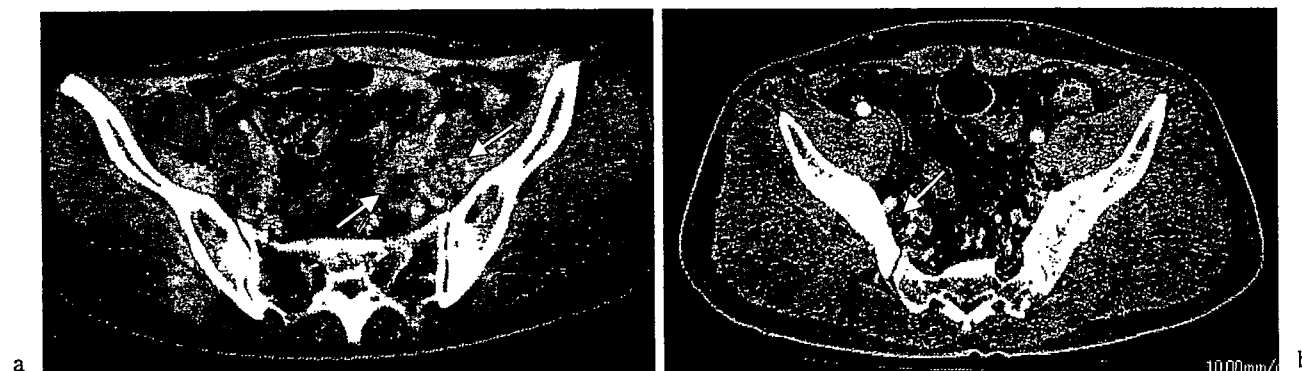


図4 画像診断による側方転移診断

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を導入することによって今後さらに成績が向上するものと期待している⁹⁾。

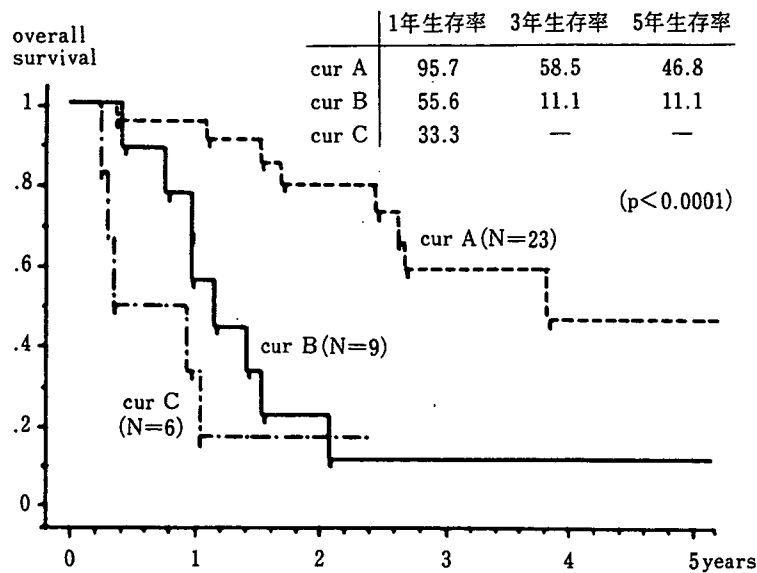


図5 直腸癌側方陽性38例の根治度別生存率

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5mm以下の術前CTまたはMRIでmesorectum外に転移の疑われる短径10mm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-0212¹²⁾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。

文 献

- 1) 高橋 孝：直腸癌に対する拡大郭清とその意義について。臨床外科 43：1879-1885, 1988.
- 2) Glass RE, Ritchie JK, Thompson HR, et al: The results of surgical treatment of cancer of the rectum by radical resection and extended abdomino-iliac lymphadenectomy. Br J Surg 72: 599-601, 1985.
- 3) Sobin LH, Wittekind C (eds): UICC: TNM Classification of Malignant Tumours. (6th edn), Wiley-Liss, New York, 2002.
- 4) Matsumoto T, Ohue M, Sekimoto M, et al: Feasibility of autonomic nerve-preserving surgery for advanced rectal cancer based on analysis of micrometastases. Br J Surg 92: 1444-1448, 2005.
- 5) Yamakoshi H, Ike H, Oki S, et al: Metastasis of rectal cancer to lymph nodes and tissues around the autonomic nerves spared for urinary and sexual function. Dis Colon Rectum 40: 1079-1084, 1997.
- 6) Ueno H, Mochizuki H, Fujimoto H, et al: Autonomic nerve plexus involvement and prognosis in patients with rectal cancer. Br J Surg 87: 92-96, 2000.
- 7) 森 武生, 高橋慶一, 大植雅之ほか：自律神経温存側方リンパ節郭清術. 手術 55: 457-467, 2001.
- 8) 大植雅之, 関本貢嗣, 池永雅一ほか：骨盤再発手術における止血器具の選択とその使い方. 外科治療 89: 14-21, 2003.
- 9) Grothey A, Sargent D, Goldberg R, et al: Survival of patients with advanced colorectal cancer improves with the availability of fluorouracil-leucovorin, irinotecan, and oxliplatin in the course of treatment. J Clin Oncol 22: 1209-1214, 2004.
- 10) 亀岡信悟, 板橋道朗, 小川真平：直腸癌の周囲リンパ節転移診断. 消化器外科 26: 281-291, 2003.
- 11) Harisinghani MG, Barentsz J, Hahn PF, et al: Noninvasive detection of clinically occult lymph-node metastases in prostate cancer. N Engl J Med 348: 2491-2499, 2003.
- 12) 日本臨床研究グループ(JCOG-0212)：臨床病期 II, III の下部直腸癌に対する神経温存 D3 郭清術の意義に関するランダム化比較臨床実施計画書(ME vs ANP-03), 2005.
- 13) Gray R, Hills R, Stowe R, et al: Adjuvant radiotherapy for rectal cancer: a systemic overview of 8507 patients from 22 randomised trials. Lancet 358: 1291-1304, 2001.
- 14) 棟方昭博：化学療法・放射線療法は大腸癌治療成績の向上に寄与するか. 第65回大腸癌研究会プログラム・抄録集, 2006.
- 15) Martling AL, Holm T, Rutqvist L-E, et al: Effect of a surgical training programme on outcome of rectal cancer in the county of Stockholm. Lancet 356: 93-96, 2000.

特集

機能温存を念頭に置いた直腸癌治療

下部直腸癌における最近の機能温存手術について

齋藤典男*1 鈴木孝憲*1 杉藤正典*1 伊藤雅昭*1
 小林昭広*1 田中俊之*1 角田祥之*1 塩見明生*1
 矢野匡亮*1 皆川のぞみ*1 西澤祐吏*1

Function-Preserving Operation in Patients with Very Low Rectal Cancer: Saito N, Suzuki T, Sugito M, Ito M, Kobayashi A, Tanaka T, Tsunoda Y, Shiomi A, MYano M, Nozomi Minagawa N and Nishizawa Y (Colorectal and Pelvic surgery, National Cancer Center Hospital East)

Intersphincteric resection with or without partial external sphincteric resection represents a safe and oncologically radical procedure allowing preservation of anal function in very low rectal cancer patients. The oncological and functional results seem to be acceptable although short follow-up and functional side effects must be considered.

Bladder-sparing surgery is a viable alternative to total pelvic exenteration in selected patients with locally advanced rectal cancer involving prostate and seminal vesicle. This procedure is simple and provides a better life-style, although it is needed to compare our procedures with neobladder or ileal conduit.

Key words: Very low rectal cancer, Abdominoperineal resection, Intersphincteric resection, Total pelvic exenteration, Bladder-sparing surgery

Jpn J Cancer Clin 52(5): 403~410, 2006

はじめに

下部直腸癌の手術において、近年の手術手技の進歩や手術機器の発達により超低位での吻合が可能となり、肛門温存の症例は増加している。しかし外科的肛門管およびその近傍の超低位直腸癌症例では、腹会陰式直腸切断術 (Abdominoperineal resection: APR) が標準手術法であり、永久人工肛門が必要となり肛門機能は廃絶する。一方最近になり、内肛門括約筋切除 (Intersphincteric resection: ISR) による手術法で APR が回避できる報告が散見されるようになった^{1~7)}。この新しい方法やこれに関連する手術法により、超低位の直腸癌症例でも永久人工肛門から解放され

る可能性が十分にある。このため当施設では ISR を主とした肛門括約筋部分温存手術を積極的に導入し、従来では APR となる多くの症例に対し肛門温存を実施してその腫瘍学および機能的予後を評価している。

また下部直腸進行癌で前立腺・精嚢浸潤が疑われた症例では、従来の標準手術として骨盤内臓器全摘術 (Total pelvic exenteration: TPE) が実施されてきた。結果として排便および排尿経路の変更が必要となりダブルストーマとなることが多く、QOL の低下も否めなかった。しかし根治性を損なわない可能性がある場合、これらの排便・排尿障害を最小限とする無ストーマやストーマ数の減少を目指した手術法の工夫を行う必要がある。当施設では、最近、排便に関しては通常の結腸肛門吻合術や肛門括約筋部分温存術を、排尿に関しては前立腺・精嚢全摘術 (Radical prostatectomy: RP) を積極的に導入し、可能な限り

*1 国立がんセンター東病院大腸骨盤外科

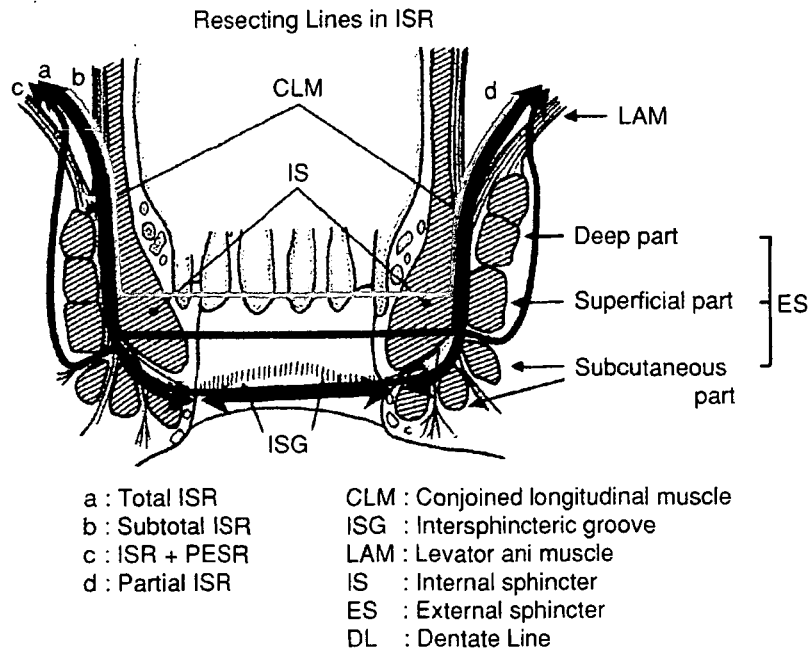


Fig. 1 Resecting lines in ISR

TPE を回避している。つまり排尿に関しては可能な限り膀胱を温存し、膀胱・尿道吻合 (Cystourethral anastomosis: CUA) を行っている。CUA が不可能な場合は、膀胱瘻 (Cystostoma: CS) を造設している。現在、本手術法についてもその腫瘍学および機能的予後を追跡中である。

1. 直腸切断術を回避し得る肛門温存手術

1) 対象

肛門括約筋部分温存手術の対象となる症例は、直腸癌腫の下縁が肛門縁 (Anal verge: AV) より 5 cm 以内に存在し、根治手術の必要な症例である。原則的に肉眼型 Type 3: 4, 組織型が低分化型、および進行度 T4 (TNM 分類) の症例は本手術法の適応から除外している。しかし最近では、T4 症例でも根治性の得られる可能性のある場合に本法を実施している。2005年12月までに、初発下部直腸癌 106 例と再発直腸癌 2 例の 108 例に対して ISR を主とした本手術法を施行した。このうち初発例 106 例中 102 例の curative 症例 (96.2%) を今回の対象とした。

2) 方法

当施設で行っている肛門括約筋部分温存手術の切除線と術式分類を Fig. 1 に示す。腹腔内手術は超低位前方切除と同様である。内肛門括約筋全切除の Total ISR, 齒状線直上で切除する Partial ISR, Partial ISR と Total ISR の間で切除する Subtotal ISR, および内肛門括約筋切除に加え外肛門括約筋の一部を合併切除する ISR + PESR の 4 種類の術式である。結腸・肛門吻合の高さと残存肛門括約筋量は各術式で異なり、術後排便機能と深く関連することになる。

3) 成績

(1) 肛門温存率

Fig. 2 に最近 10 年間の Rb-P 癌の治癒切除症例における肛門温存率の推移を示すが、肛門括約筋部分温存手術を積極的に導入した 2000 年以降では極めて高い肛門温存率 (88.4%) を示した。

(2) 施行術式

Table 1 に対象 102 例の術式を示す。対象例の腫瘍下縁から AV までの距離は、中央値で 3.8 cm であった。Total ISR 20 例, Total ISR + PESR 8 例, Subtotal ISR 50 例, Partial ISR 24 例であった。このうち 46 例は、Neoadjuvant therapy (45 Gy, 5-Fu) を施行した症例である。102 例中 3 例は、合併症のため追加手術 (APR,

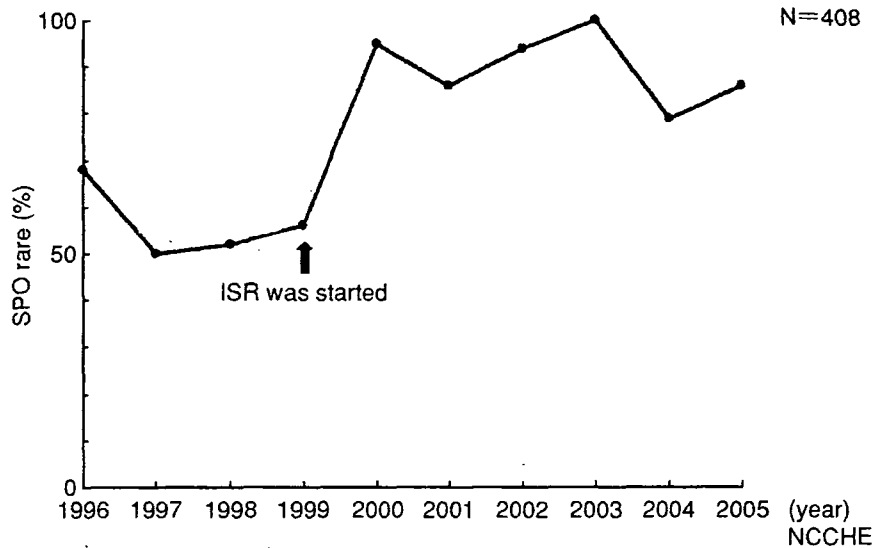


Fig. 2 Sphincter preserving operation (SPO) in very low rectal cancer (Rb-P)

Table 1 Patients Undergoing Curative ISR

Nov. 1999~Dec. 2005

No. of Patients	: 102
Gender	: Male 78, Female 24
Age, median (range; yr)	: 57 (27~73)
Distance to AV, median (range; cm)	: 3.8(1.5~5.0)
Surgical procedure	: Total ISR: 20 Total ISR with PESR: 8 Subtotal ISR: 50 Partial ISR: 24
Neoadjuvant therapy (45 Gy, 5-Fu)	: 46
Tumor stage (p)	T0; 8, T1; 10, T2; 22, T3; 59, T4; 3
Surgical margins	Radial margin: 3.5±2.6 mm Distal margin: 12.4±10.1 mm (Partial ISR: 16 mm, Subtotal ISR: 17 mm, Total ISR: 12 mm)

28 → APR: 1
28 → Hartmann: 2

Follow-up period: 36 months, median (range: 3~74 months)

ハルトマン)を受けている。組織学的な腫瘍進行度はT0: 8例 (Neoadjuvant therapyで腫瘍消失), T1: 10例, T2: 22例, T3: 59例, T4: 3例であった。平均のRadial marginは3.5±2.6 mm, 平均のDistal marginは12.4±10.1 mmであり, Safety marginが得られている。

(3) 周術期合併症

手術に関連する合併症は32例(31.4%)に認められ, 主なものは骨盤内膿瘍と縫合不全に関連するものであった。重篤例は5例(4.9%)に認められ, このうち3例は追加手術による術式変更が必要となった。手術関連死亡例は, 現在のところ

認められていない。

(4) 予後

Fig. 3にDisease-free survival (DFS) curve, Overall survival (OS) curveを示す。観察期間中央値は36カ月であるが, 4年OSは76%, 3年DFSは70%であった。再発は102例中19例に認められ, 再発部位は肺が13例と最も多く, 局所(骨盤内リンパ節が多い)は6例, 肝が5例, 鼠径リンパ節も4例あった(重複を含む)。局所再発率は, 現在のところ5.9%である。

(5) 術後排便機能

一時的人工肛門の閉鎖が終了して6カ月以上

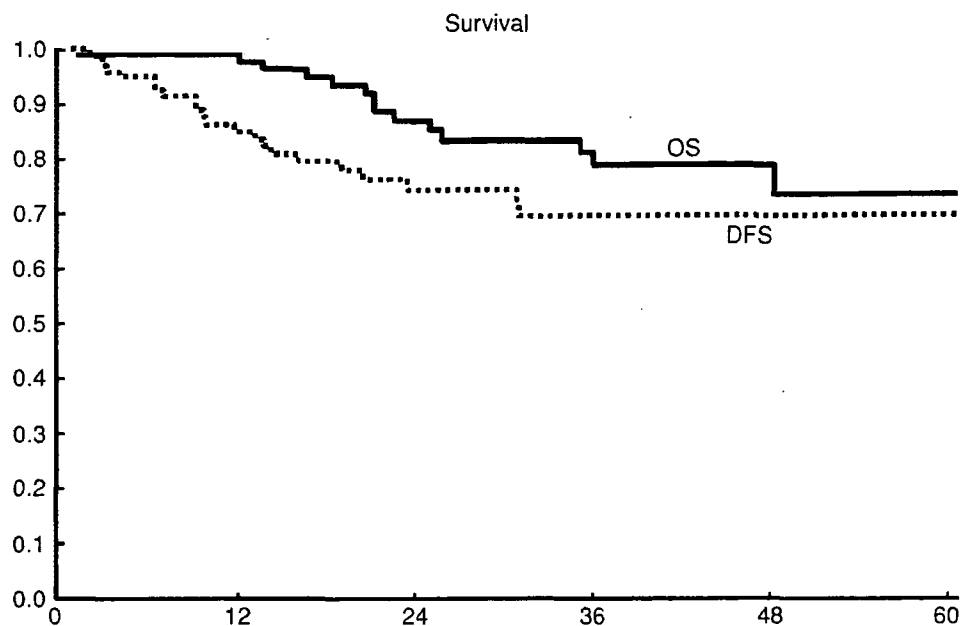


Fig. 3 Survival

Table 2 Functional Results After ISR

(N=63, 24M \leq)

Worse functional status	After stoma closure			
	3Mo	6Mo	12Mo	24Mo
Stool frequency: 10/day \leq	46	29	21	9
Urgency: (+)	51	34	21	13
Feces-flatus discrimination: (-)	32	16	12	9
Day-soiling: 1/week \leq	63	53	29	26
Night-soiling: 1/week \leq	67	52	44	30
				(%)
Continance status	6Mo	12Mo	24Mo	
Wexner Score*	11.2 \pm 4.0	8.4 \pm 4.5	7.8 \pm 4.2	
Kirwan classification	Grade I	0	23	36
	Grade II	9	17	14
	Grade III	70	48	43
	Grade IV	19	12	7
	Grade V	2	0	0
				(%)

* Mean \pm SD

を経過し、十分な調査結果が得られた63症例の排便状況をTable 2に示す。上段の表は、排便機能の悪い項目の出現頻度を経時的に検討したものである。下段の表は、Continanceの状況をWexner Score⁸⁾、およびKirwan分類⁹⁾で評価したものである。平均排便回数10回/日以上、Urgency (+)、便・ガス識別不可、日中のSoiling

や夜間のsoilingが1回/週以上あり、などの排便状況の悪い項目の出現は経時的に減少するが、soilingは2年経過しても30%前後の症例に認められた。Wxner scoreも、経時的に変化し、排便状況の改善が認められた。またKirwan分類でも、Grade IVのmajor soilingを認める症例は経時的に減少し、2年経過した時点では7%のみの

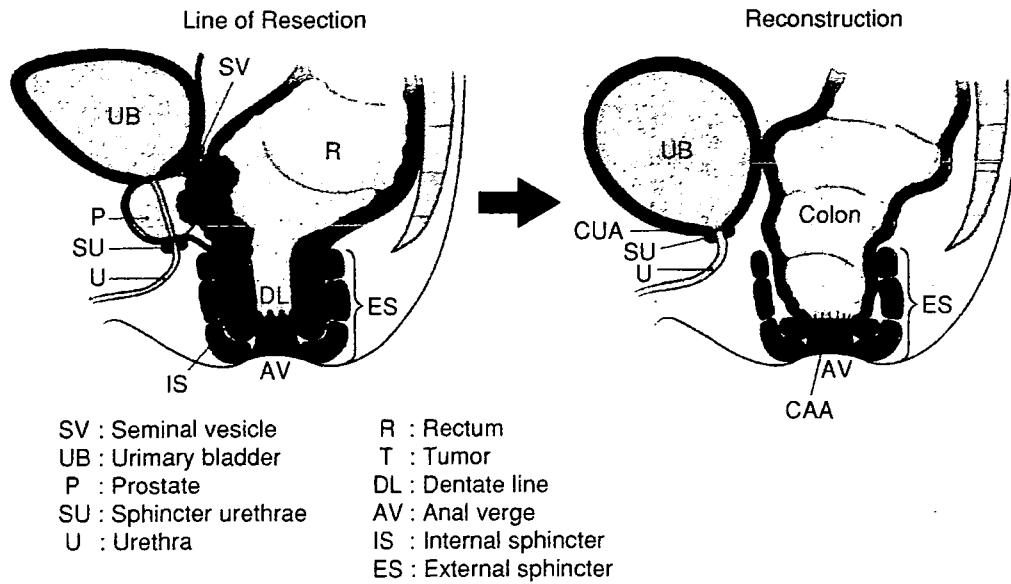


Fig. 4 Surgical Procedure

症例であり、全くの失禁例 (Grade V) は認められなかった。このように排便機能障害はある程度認められるものの、日常生活に大きな障害をきたさない症例が大半であった。

2. TPE を回避し得る Bladder-Sparing surgery

1) 対象

本手術法の対象例は、下部直腸進行癌で臨床的に前立腺・精嚢浸潤があると判断される症例であり、広範な膀胱浸潤と顕著な骨盤内リンパ節転移を伴わない症例である。従来このような症例ではTPEを実施していたが、本術式を導入した2000年以後ではTPE症例は大幅に減少している。2005年12月までに、従来ではTPEの適応である11症例にBladder-Sparing surgeryを施行した。内訳は原発例8症例と直腸癌術後骨盤内再発例3症例である。各症例ともに、術前診断および術中所見で前立腺または前立腺および精嚢に浸潤が疑われた症例である。

2) 方法

本手術法をFig. 4に示す。通常の下部直腸癌の手術にRadical postatectomyを併用し、可能な限り膀胱・尿道吻合および肛門括約筋部分温存手術を施行する術式である。尿道括約筋が温存不

可能の場合は、残存膀胱を用いた膀胱瘻を造設した。また肛門括約筋の温存不能の場合、APRを施行しstomaを造設した。本術式は、可能な限りstoma数を減らす方法である。

3) 成績

(1) 施行術式

Bladder-sparing surgeryを行った11症例の術式をTable 3に示す。肛門温存 (ISR, UltraLAR) 例が4例、膀胱・尿道吻合 (CUA) 例は7例、膀胱瘻は4例であった。膀胱瘻を含めたdouble stoma例は4例であるが、各症例ともに通常では回腸導管が必要となる症例 (尿道括約筋温存不能) であった。

(2) 病理組織学的所見

病理組織学的な前立腺・精嚢浸潤例は11例中8例であった。全症例において組織学的surgical marginsは陰性であり、cancer-freeのmarginが得られている (Table 4)。

(3) 予後

観察期間の中央値は25カ月であるが、11例中10例が生存中である。再発手術例の1例は、術後約4カ月で再々発のため癌死している。この症例のみに局所再発を認めたが、他の10例には局所再発は認められず、本法による局所制御は許容範囲内であった。再発例3例における再発部位は肝2例、肺1例であり、肝転移再発の2例

Table 3 Patients Undergoing Bladder-Sparing Surgery

Patient No.	Age (years)	Clinical invaded organ	Surgical procedure	Reconstruction	
				Urinary	Fecal
Primary					
1	60	P·SV	ISR+RP	CUA	CAA
2	60	P·SV	APR+RP	CUA	Stoma
3	72	P	APR+RP	CUA	Stoma
4	66	P	ISR+RP	CUA	CAA
5	57	P	APR+RP	CS	Stoma
6	43	P	APR+RP	CS	Stoma
7	52	P	APR+RP	CS	Stoma
8	68	P	ISR+RP	CUA	CAA
Recurrent					
9 (Post LAR)	52	P	APR+RP	CS	Stoma
10 (Post APR)	54	P·SV	APTR+RP	CUA	Stoma
11 (Post AR)	26	P·SV	Ultra LAR+RP	CUA	CACA

P: Prostate

SV: Seminal vesicle

ISR: Intersphincteric resection

APR: Abdominoperineal resection

LAR: Low anterior resection

AR: Anterior resection

RP: Radical prostatectomy

APTR: Abdominoperineal tumor resection

CUA: Cysto-urethral anastomosis

CS: Cystostomy

CAA: Colo-anal anastomosis

CACA: Colo-anal canal anastomosis

Table 4 Histopathology and Prognosis

Patient No.	Tumor stage	Invaded organ	Surgical margins	Recurrence site	Survival
1	T3 N0 M0	(-)	Negative	Liver→Resection	60Mo ANED
2	T3 N0 M0	(-)	Negative		41Mo ANED
3	T4 N0 M0	P	Negative		31Mo ANED
4	T3 N2 M0	(-)	Negative	Liver→Resection	30Mo ANED
5	T4 N0 M0	P	Negative	Lung (multiple)	27Mo AWD
6	T4 N0 M0	P	Negative		25Mo ANED
7	T4 N2 M0	P	Negative		22Mo ANED
8	T4 N0 M0	P	Negative		13Mo ANED
9	Recurrence	P	Negative		22Mo ANED
10	Recurrence	SV	Negative		12Mo ANED
11	Recurrence	P·SV	Negative	Pelvis, Skim, Lung	4Mo DOD

P: Prostate

ANED: Alive with no evidence of disease

Mo: Months

AWD: Alive with disease

DOD: Dead of disease

は肝切除により disease-free で生存中である。

(4) 術後機能

術後1年以上の経過した膀胱・尿道吻合症例5例の排尿機能は、全例で腹圧排尿パターンによる自排尿が可能であった。一回尿量は250 (range: 150~350) ml で、残尿量は10 (range: 0~20) ml

とほとんど認めなかった。昼間の尿失禁は認めず、夜間の尿失禁は1回/月の程度に存在するかしないかの程度であり、満足度の高い状況であった。

また肛門を使用して(一時的人工肛門閉鎖後)1年以上経過した肛門温存症例3例の排便状況は

前述したISR症例の排便機能と同様であり、continenceは保たれていた。排便回数は平均5回/日であり、便とガスの区別および夜間のsoilingなどに軽度の障害を認める程度であった。排便機能に関しても、比較的良好な状況であった。

まとめ

標準治療では永久stomaを伴う直腸切断術の適応となる超低位直腸癌症例において、その大半はISRを主とした肛門括約筋部分温存術による肛門温存が可能となった。この新しい機能温存手術の腫瘍学的妥当性が認められつつあり、術後の排便機能も許容範囲内と考えられる。しかし種々の排便機能障害が存在するのも事実であり、これらに関する対策と術前からの詳細な説明が必要である。

また前立腺浸潤を伴う下部直腸進行癌症例の標準手術では、骨盤内臓全摘術(TPE)が一般的でありdouble stomaとなる場合も多い。排便および排尿経路の変更により、QOLの低下が認められる。今回呈示したBladder-sparing surgeryではTPEの回避が可能となり、QOLの向上、許容される局所制御、および根治性の得られることが示唆された。また本法では本来の残存膀胱を使用するため、小腸による代用膀胱に比べて優位な点もあると考えられる¹⁰⁾。本手術法の報告は少ないものの、報告例では予後とQOLが比較的良好である^{11~15)}。しかし肛門括約筋部分温存手術と本法併用の報告は、現在のところ認められない。このため、今後の長期的観察による評価が必要である。

おわりに

下部直腸癌の治療では、常に根治性と機能保持の点で問題となることが多い。この両方を満足するための治療法の開発が要望され、最近では少しずつその効果も認められつつある。

新しい手術法の開発はもちろん重要であるが、従来の定型的手術法にこだわることなく総合的な立場より手術方針を決定することが必要である。

新しい術式と従来の標準手術の良さを適正にcombinationし、根治性と機能温存に関して過不足のない治療の提供が望まれる。「温故知新」とは、誠に有難い言葉である。

文献

- 1) Schiessel R, Karner-Hanusch J, Herbst F, et al: Intersphincteric resection for low rectal tumours. *Br J Surg* 81: 1376-1378, 1994
- 2) Rullier E, Zerbib F, Laurent C, et al: Intersphincteric resection with excision of internal anal sphincter for conservative treatment of very low rectal cancer. *Dis Colon Rectum* 42: 1168-1175, 1999
- 3) Renner K, Rosen HR, Novi G, et al: Quality of life after surgery for rectal cancer: do we still need a permanent colostomy?. *Dis Colon Rectum* 42: 1160-1167, 1999
- 4) Shirouzu K, Ogata Y, Araki Y, et al: A new ultimate anus-preserving operation for extremely low rectal cancer and for anal canal cancer. *Tech Coloproctol* 7: 203-206, 2003
- 5) Saito N, Ono M, Sugito M, et al: Early results of intersphincteric resection for patients with very low rectal cancer: an active approach to avoid a permanent colostomy. *Dis Colon Rectum* 47: 459-466, 2004
- 6) Rullier E, Laurent C, Bretagnol F, et al: Sphincter-saving resection for all rectal carcinomas: the end of the 2-cm distal rule. *Ann Surg* 241: 465-469, 2005
- 7) Schiessel R, Novi G, Holzer B, et al: Technique and long-term results of intersphincteric resection for low rectal cancer. *Dis Colon Rectum* 48: 1858-1865, 2005
- 8) Jorge JM, Wexner SD: Etiology and management of fecal incontinence. *Dis Colon Rectum* 36: 77-97, 1993
- 9) Kirwan WO, Turnbull RB Jr, Fazio VW, et al: Pullthrough operation with delayed anastomosis for rectal cancer. *Br J Surg* 65: 695-698, 1978
- 10) Fujisawa M, Ueno K, Kamidono S: Novel bladder sparing surgery for select patients with advanced rectal carcinoma. *J Urol* 167: 643-644, 2002
- 11) Campbell SC, Church JM, Fazio VW, et al: Combined radical retropubic prostatectomy and proctosigmoidectomy for en bloc removal of locally invasive carcinoma of the rectum. *Surg Gynecol Obstet* 176: 605-608, 1993
- 12) Balbay MD, Slaton JW, Trane N, et al: Rationale for bladder-sparing surgery in patients with locally advanced colorectal carcinoma. *Cancer* 86: 2212-

- 2216, 1999
- 13) Wiig JN, Waehre H, Larsen SG, et al: Radical prostatectomy for locally advanced primary or recurrent rectal cancer. *Eur J Surg Oncol* **29**: 455-458, 2003
- 14) 齋藤典男, 鈴木孝憲, 杉藤正典: 骨盤外科の発展に向けて. *京府医大誌* **111** (10): 683-691, 2004
- 15) 箕畑順也, 平井 孝, 小森康司・他: 前立腺・精嚢全摘をともなう直腸切断術を施行した肛門管扁平上皮癌の1例. *日本大腸肛門病学会誌* **59**: 265-269, 2006

Intersphincteric Resection in Patients with Very Low Rectal Cancer: A Review of the Japanese Experience

Norio Saito, M.D.,¹ Yoshihiro Moriya, M.D.,² Kazuo Shirouzu, M.D.,³ Koutarou Maeda, M.D.,⁴ Hidetaka Mochizuki, M.D.,⁵ Keiji Koda, M.D.,⁶ Takashi Hirai, M.D.,⁷ Masanori Sugito, M.D.,¹ Masaaki Ito, M.D.,¹ Akihiro Kobayashi, M.D.¹

¹ Department of Surgical Oncology, National Cancer Center Hospital East, Kashiwa, Japan

² Department of Surgery, National Cancer Center Hospital, Tokyo, Japan

³ Department of Surgery, Faculty of Medicine, Kurume University, Kurume, Japan

⁴ Department of Surgery, Fujita Health University, Toyoake, Japan

⁵ Department of Surgery 1, National Defense Medical College, Tokorozawa, Japan

⁶ Department of Gastroenterological Surgery, Graduate School of Medicine, Chiba University, Chiba, Japan

⁷ Department of Gastroenterological Surgery, Aichi Cancer Center, Nagoya, Japan

PURPOSE: This study was designed to evaluate the feasibility and oncologic and functional outcomes of intersphincteric resection for very low rectal cancer. **METHODS:** A feasibility study was performed using 213 specimens from abdominoperineal resections of rectal cancer. Oncologic and functional outcomes were investigated in 228 patients with rectal cancer located <5 cm from the anal verge who underwent intersphincteric resection at seven institutions in Japan between 1995 and 2004. **RESULTS:** Curative operations were accomplished by intersphincteric resection in 86 percent of patients who underwent abdominoperineal resection. Complete microscopic curative surgery was achieved by intersphincteric resection in 225 of 228 patients. Morbidity was 24 percent, and mortality was 0.4 percent. During the median observation time of 41 months, rate of local recurrence was 5.8

percent at three years, and five-year overall and disease-free survival rates were 91.9 percent and 83.2 percent, respectively. In 181 patients who received stoma closure, 68 percent displayed good continence, and only 7 percent showed worsened continence at 24 months after stoma closure. Patients with total intersphincteric resection displayed significantly worse continence than patients with partial or subtotal resection. **CONCLUSIONS:** Curability with intersphincteric resection was verified histologically, and acceptable oncologic and functional outcomes were obtained by using these procedures in patients with very low rectal cancer. However, information on potential functional adverse effects after intersphincteric resection should be provided to patients preoperatively. [Key words: Very low rectal cancer; Intersphincteric resection; Abdominoperineal resection; Coloanal anastomosis; Anal function]

Sponsored by a Grant-in-Aid (14-10) for Cancer Research from the Ministry of Health, Welfare and Labor of Japan.

Reprints are not available.

Correspondence to: Norio Saito, M.D., Colorectal and Pelvic Surgery Division, National Cancer Center Hospital East, 6-5-1 Kashiwanoha, Kashiwa, Chiba 277-8577, Japan, e-mail: norsaito@east.ncc.go.jp

Dis Colon Rectum 2006; 49: S13-S22

DOI: 10.1007/s10350-006-0598-y

© The American Society of Colon and Rectal Surgeons

Local control and survival for patients with rectal cancer have been improving with the development of surgical techniques and combined adjuvant therapies.^{1,2} The advent of mechanical low-stapling and double-stapling techniques and sutured coloanal anastomosis has facilitated easier anastomosis at the distal rectum. These methods have increased the frequency of sphincter salvage. Nevertheless, permanent colostomy is still performed in approximately 20 percent of patients with low rectal cancer. Abdomi-

noperineal resection (APR) is a standard surgery for low rectal cancers located <5 cm from the anal verge or <2 cm from the dentate line (DL). These cancers may be associated with lymph node metastasis along the levator ani muscle or in the fatty tissue of the ischiorectal fossa,³ and also may have the potential for microscopic involvement of the rectal wall below the tumor.⁴ APR has been established as a standard procedure in patients with lower rectal cancer. Patients undergoing APR can experience some problems with quality of life, because permanent colostomy results in psychologic and social limitations.^{5,6}

In recent years, intersphincteric resection (ISR) with coloanal anastomosis has been proposed to avoid permanent colostomy for rectal cancers located <5 cm from the anal verge, although these tumors are not generally considered for sphincter-saving procedures.⁷⁻¹³ Several studies have reported that local control and functional results after ISR are satisfactory.^{7,10-14} Experiences with ISR, including partial external sphincteric resection (PESR), also have been reported in recent studies^{12,15}; however, data remain scarce. The rationale for ISR in patients with very low rectal cancer is described in this review article by using data from Japanese experiences and Western reports, and our theoretic background is provided based on the histologic evidence.

PATIENTS AND METHODS

Pathologic and Theoretic Background

The pathologic study was performed by a surgical pathologist (KS) at Kurume University. In this pathologic study of 213 surgical specimens from APR for lower rectal cancer or anal canal cancer excluding anal cancer, the external sphincter muscle, puborectalis muscle, and fatty tissue of ischiorectal fossa were investigated for direct invasion and skip metastasis. The entire tumor mass was sectioned at 5-mm intervals, including oral and anal parts up to 5 cm from the tumor. The same surgical pathologist (KS) made all final pathologic diagnoses.^{15,16}

Patient Population

A total of 228 consecutive patients (168 males) who underwent ISR between 1995 and 2004 were identified from the hospital databases, and medical charts were retrospectively reviewed. These 228 patients received ISR at seven institutions in Japan

that participated in the "Studies on preservation of anal function for very low rectal cancer patients," sponsored by Grant-in-Aid 14-10 for Cancer Research from the Ministry of Health, Welfare and Labor of Japan. Median age was 58 (range, 27-77) years. All 228 patients displayed adenocarcinoma located <5 cm from the anal verge.

The anal verge was defined as the terminal part of the surgical and anatomic anal canal. The intersphincteric groove (ISG) exists between the terminal part of the internal sphincter (IS) and the subcutaneous part of the external sphincter (ES). Exact level of the lower edge of the tumor from the anal verge was assessed and measured by digital examination and endoscopy. All tumors found infiltrating the rectal wall on digital examination, computed tomography (CT), magnetic resonance imaging (MRI), or endorectal ultrasonography (US) were eliminated from consideration for local excision. Patients were classified according to International Union Against Cancer (UICC) standards¹⁷ after preoperative diagnosis using CT, MRI, US, colonoscopy, chest radiography, and biopsy.

An exception to selection of ISR was made if malignant infiltration of other organs or of the striated muscles of the pelvic floor (such as levator ani muscle or external sphincter) was suspected, if tumors displayed low differentiation on histopathology, or if preoperative anal function demonstrated marked insufficiency. Patients with synchronous metastases also were excluded from ISR. These patients were treated by using conventional APR. In the present study, ISR was performed mainly in very low rectal cancer patients with T3, T2, or T1 (massive invasion of the submucosa) disease lying <5 cm from the anal verge. All resected specimens were examined to determine macroscopic and microscopic surgical margins (distal and radial). Postoperative mortality and morbidity, local control, and survival also were investigated.

Surgical Technique and Classification

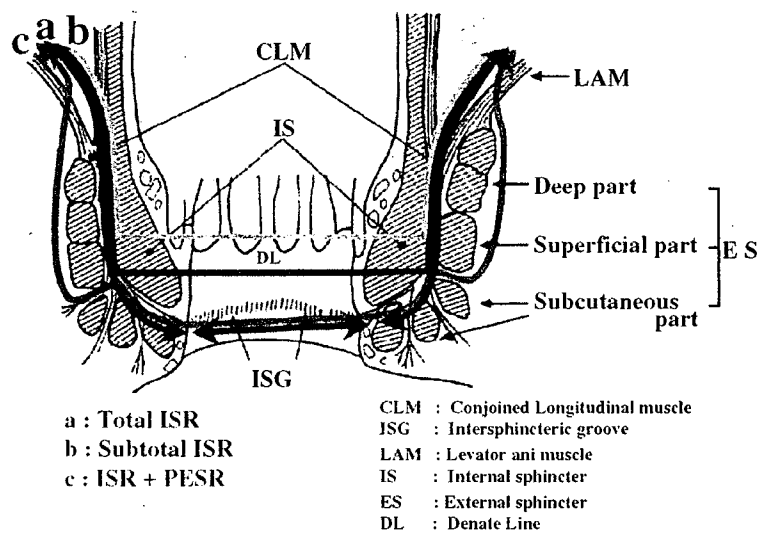
ISR was performed according to the methods previously reported by Schiessel *et al.*⁷ and others.^{10,12,15} The surgical technique included both abdominal and perianal approaches. Abdominal dissection was performed first. Total mesorectal excision (TME) with lateral node dissection was undertaken. During the abdominal approach, the autonomic nerve system was preserved to the fullest

extent possible, using Japanese methods previously described.¹⁸⁻²² The rectum was mobilized carefully as low as possible to the pelvic floor to facilitate the perianal approach. The IS was then exposed and circumferentially divided from the puborectalis muscle and ES. During these procedures, the tumor was evaluated through gentle palpation by the surgeon. If tumor had invaded beyond the rectum into the puborectalis muscle or ES at the anorectal junction or anal canal, the puborectalis muscle was resected and fatty tissue of the ischioanal fossa was visualized. ISR plus PESR was performed in those patients.

After the abdominal approach, perianal resection was performed. Circumferential incision of the mucosa and IS was initiated 1 to 2 cm distal to the tumor. The anal orifice was closed by pursestring suture to avoid spread of tumor cells during perianal operation.¹² Once the intersphincteric space was entered, careful dissection continued upward between the smooth and striated sphincters under constant guidance by the abdominal surgeon.

Total ISR involved complete excision of the IS for tumors spreading to or beyond the DL. The distal cut-end line was at the ISG. Total ISR was unnecessary in patients with tumor located ≥ 2 cm from the DL. Those patients underwent subtotal ISR. The distal cut-end line was between the DL and ISG, and the DL was included in the resected specimen. In patients with tumor located from >2 to 3 cm from the DL, the distal cut-end line was just on or above the DL. This procedure, partial ISR, sometimes includes conventional coloanal anastomosis procedures. When patients displayed tumor invading the ES, ISR plus PESR was performed. At least the subcutaneous part of the ES was preserved in these patients. ISR was classified into four types: total ISR; subtotal ISR; partial ISR; and ISR + PESR (Fig. 1).

After specimen removal and generous irrigation of the pelvic cavity, the sigmoid colon was pulled down and coloanal anastomosis with or without colonic pouch was made according to the method described by Parks.²³ Anastomoses were performed by using perianal manual suturing in all patients.



Type of ISR	Anastomotic line	Sacrificed sphincter
Partial	Just on DL or within 1cm oral side from DL	Partial IS
Subtotal	Between DL and ISG	Almost all of IS
Total	Just on ISG	Total IS without or with partial ES

Figure 1. Resecting lines in intersphincteric resection (ISR) are illustrated. PESR=partial external sphincteric resection.

Finally, a diverting stoma using terminal ileum or transverse colon was established. This stoma was closed at three to six months postoperatively.

Adjuvant Therapy

Preoperative radiochemotherapy was performed in 57 patients with T3 tumors who agreed to preoperative adjuvant therapy at the National Cancer Center Hospital East (NCCHE), National Defense Medical College, or Chiba University. Other patients underwent surgery alone, because preoperative radiochemotherapy for resectable rectal cancer is not standard in Japan. The 44 patients from the NCCHE received 45 Gy during a five-week period, followed by operation two weeks later. In addition, continuous infusion of 5-fluorouracil (250 mg/m²/day) was administered to these patients during radiotherapy to increase radiotherapeutic efficacy. Although reevaluation using CT, MRI, US, and colonoscopy was performed in these patients after completion of preoperative radiochemotherapy, all patients underwent ISR. Most patients with Stage III tumor (pTNM pathologic classification) received postoperative chemotherapy with 5-fluorouracil and folinic acid, or tegafur uracil, or others for six months or more.

Follow-Up and Functional Assessment

Follow-up examinations were performed every three months for two years postoperatively, and subsequently every six months. Examinations included clinical, laboratory (including tumor markers, such as carcinoembryonic antigen and carbohydrate antigen 19-9), and radiologic (abdominal and pelvic CT and chest radiography) investigations.

Functional outcomes also were assessed at the same time by using our functional questionnaire. This functional questionnaire asked about stool frequency (number of bowel movements per 24 hours), feces and flatus discrimination, urgency (ability to defer stool evacuation for >15 minutes), fragmentation (≥ 2 evacuations in 1 hour), soiling during the day and night, use of pads, use of medications, and alimentary restriction. Incontinence was assessed by using the continence scores of both the Jorge and Wexner,²⁴ and classification by Kirwan *et al.*²⁵

Median follow-up was 41 (range, 10–84) months. No patients were lost to follow-up, and 57 percent of patients were observed for ≥ 36 months.

Statistical Analysis

Overall survival (OS) and disease-free survival (DFS) were calculated by using Kaplan-Meier methods. Duration to final follow-up evaluation, treatment failure, or death was measured from the date of rectal resection. Assessment of local recurrence was evaluated by using a cumulative local disease-free survival curve. Assessment of recurrence and survival was performed in patients with microscopically curative surgery.

RESULTS

Pathologic Validity

Pathologic study of the 213 surgical specimens from APR for lower rectal cancer or anal canal cancer (excluding anal cancer) revealed neither direct invasion nor skip metastasis in subcutaneous external sphincter muscle or fatty tissue of the ischioanal fossa; however, spread of cancer to the deep and superficial ES muscles or puborectalis muscle was observed in 14 percent. Curative operation was thus accomplished by using ISR in 86 percent of patients undergoing APR. When tumor invasion exceeds the IS at the surgical anal canal, safe surgical margins can be obtained using ISR with combined resection of the deep and superficial ESs. Complete radical surgery can theoretically be accomplished even if subcutaneous ES muscle is not resected.

Population

The study was comprised of 228 patients with very low rectal cancer (including surgical anal canal cancer) who underwent ISR between 1995 to October 2004. Tumor characteristics and surgical procedures are shown in Table 1. Median lower edge of the tumor was 3.4 (range, 2–5) cm from the anal verge. Tumor staging was T3 tumor (n = 103), T2 tumor (n = 78), or T1 (n = 46). Surgical procedure was subtotal ISR in 124 patients, total ISR with or without PESR in 69 patients with tumor located ≤ 2 cm from the anal verge, and partial ISR in 35 patients. These procedures were decided according to tumor localization. All patients underwent coloanal anastomosis by manual suturing. Anastomosis involved a colonic J-pouch (n = 51), coloplasty (n = 25), side-to-end anastomosis (n = 5), or straight anastomosis (n = 147).

Table 1.
Patients Undergoing ISR

	(n = 228)
Age (yr)	58 (27-77)
Male/female ratio	168/60
Tumor	
Distance from anal verge (cm)	3.4 (2-5)
Clinical stage	
T1	46
T2	78
T3	103
T4	1
Procedure	
Partial ISR	35
Subtotal ISR	124
Total ISR (with or without PESR)	69
Morbidity rate	24 percent (55/228)
Mortality rate	0.4 percent (1/228)

ISR = intersphincteric resection; PESR = partial external sphincteric resection.

Data are medians with ranges in parentheses or numbers of patients.

Fifty-seven patients received preoperative radiochemotherapy.

Morbidity and Mortality

Postoperative complications occurred in 55 patients (24 percent), including anastomotic leakage (n = 23), pelvic infection and abscess (n = 10), anastomotic stenosis (n = 7), colonic ischemia and necrosis (n = 4), anovaginal fistula (n = 3), postoperative bleeding (n = 3), mucosal prolapse (n = 3), and postoperative ileus (n = 2). In 9 of these 55

patients (4 percent), additional surgery, such as APR or Hartmann's operation, was required because of postoperative massive hemorrhage, colon necrosis, or anastomotic insufficiency. Surgery-related death occurred in one patient (0.4 percent) who experienced a breakdown of colonic J-pouch and died of sepsis. No differences in morbidity were identified between the radiochemotherapy and surgery-alone groups.

Pathologic Findings

Radical resection of the tumor was achieved in all 228 patients. Surgery was judged as microscopically curative in 225 patients (98.7 percent) who displayed adequate cancer-free margins (distal and radial). Unclear surgical margins were noted in three patients with Type 3 tumor, because microscopic vessel involvements were observed very near to the surgical margins. These three patients were excluded from assessments for recurrence and survival, although none of these patients received additional surgery, such as APR, because obvious positive margins were not identified. Follow-up was performed as usual.

Recurrences

During the median observation time of 41 months, 30 of 225 patients developed recurrence. These recurrences comprised lung metastasis (n = 11), liver metastasis (n = 11), local recurrence including regional lymph node metastasis (n = 8), inguinal lymph node metastasis (n = 4), bone metastasis

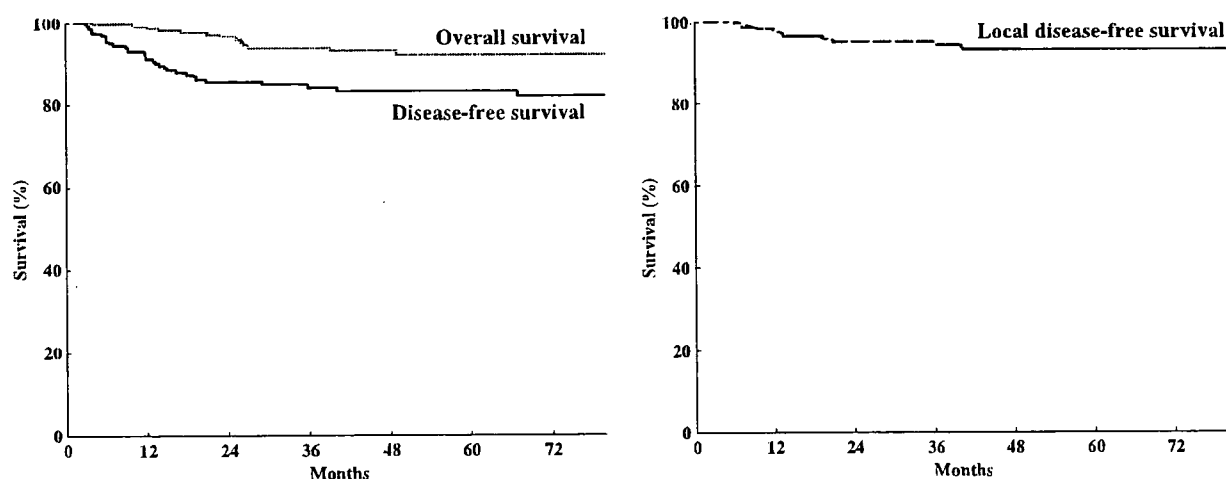


Figure 2. Overall survival was 91.9 percent and disease-free survival was 83.2 percent at five years. Acceptable local control also was obtained.

Table 2.
Functional Results After Stoma Closure

	(n = 181)			
	3 Months	6 Months	12 Months	24 Months
Continence				
Wexner score (n = 110)	17 ± 1.7	11.2 ± 4	8.4 ± 4.5	7.8 ± 4.2 ^a
Kirwan classification				
I Perfect	17	19	36	36
II Incontinence of flatus	11	12	16	32
III Occasional minor soiling	45	51	36	25
IV Frequent major soiling	19	16	12	7
V Incontinent (required colostomy)	8	2	0	0

ISR = intersphincteric resection.

Data are means ± standard deviations or percentages.

^a Partial ISR (mean, 6); subtotal ISR (mean, 7.8); total ISR with or without partial external sphincteric resection (mean, 11.1).

(n = 1), and abdominal wall metastasis (n = 1). In seven of eight patients with local recurrence, recurrence occurred in lateral nodes¹⁸⁻²² located between the pelvic plexus and lateral pelvic wall, or in the tissue surrounding the external iliac artery. Local recurrence in one patient occurred in the prostate with multiple lung metastases. Patients with liver or lung metastasis alone received curative partial hepatic or lung resection (n = 9). Patients with regional or inguinal lymph node metastasis also received lymphadenectomy (n = 4). Cumulative local recurrence rate was 5.8 percent at three years and 6.7 percent at five years (Fig. 2). No patients displayed anastomotic recurrence. No differences in recurrence rate or site were noted between preoperative radiochemotherapy and surgery-alone groups, although median observation time was shorter in the preoperative radiochemotherapy group (26 months) compared with the surgery-alone group.

Survival

A total of 18 patients died, with 16 deaths from distant metastasis. OS was 91.9 percent at five years, and DFS was 83.2 percent at five years (Fig. 2). No significant differences in OS or DFS were identified between preoperative radiochemotherapy and surgery-alone groups at three years (DFS: 75.1 vs. 85.8 percent).

Functional Outcome

Of 219 patients excluding patients with additional surgery, such as APR or Hartmann's operation, 181 received diverting stoma closure at a median of five

(range, 3-24) months postoperatively. Stoma closure is planned for 30 patients. Conversely, no plan for stoma closure was made in eight patients because of anal dysfunction (n = 3), early-phase recurrence (n = 3), or anovaginal fistula (n = 2). Continence status is shown in Table 2. Although only 30 percent of patients displayed good continence (Kirwan's Grade 1-11) at six months after stoma closure, 68 percent of patients showed good continence at 24 months after stoma closure. Worsened continence was observed in only 7 percent of patients.

Wexner score was investigated sufficiently in 110 patients, with scores of 11.2 ± 4 at six months after stoma closure, 8.4 ± 4.5 at 12 months, and 7.8 ± 4.2 at 24 months. Anal function improved monthly until 24 months after stoma closure. However, day or night soilings were sometimes observed at 24 months after stoma closure in patients with total ISR. Mean Wexner score at 24 months after stoma closure was 6 in the partial ISR group, 7.8 in the subtotal ISR group, and 11.1 in the group that underwent total ISR with or without PESR. Although no significant differences in Wexner score were apparent between partial and subtotal ISR groups, patients who underwent total ISR with or without PESR exhibited significantly worse continence than those with partial or subtotal ISR (Wexner score, 11.1 vs. 6 and 7.8, respectively; *P* < 0.05).

DISCUSSION

The general consensus is that most rectal cancers <5 cm from the anal verge or <2 cm from the dentate line are treated by using APR. In recent years,

however, the need for a margin of ≥ 2 cm margin has been challenged, and a distal margin of 1 to 2 cm is now considered sufficient in most instances. Sphincter-saving operations, such as ultralow and conventional coloanal anastomosis for cancer of the lower third of the rectum, have been reported by specialized teams, with local recurrence rates of 4 to 13 percent.²⁶⁻³¹ Although ultralow and coloanal anastomosis have been associated with some controversial functional results, patients without permanent stoma have been widely accepted as displaying better quality of life. However, most tumors in these studies have been located ≥ 5 cm from the anal verge. In more recent years, ISR with coloanal anastomosis has been reported for rectal cancer located < 5 cm from the anal verge by a few specialized teams.⁷⁻¹³ However, some fears of oncologic results and poor anal functions have been noted, as patients display reduced surgical margins compared with APR and the internal sphincter is removed.

This study was designed to investigate the pathologic evidence and oncologic and functional results of ISR. In the present series, tumors were located ≤ 5 cm from the anal verge. All these patients would have required APR if treated using standard procedures. According to pathologic examination using resected specimens from APR in this study, curative operation can be accomplished by ISR in almost all patients undergoing APR. In fact, 225 of 228 patients (98 percent) who underwent ISR were considered to display histologically curative results. These results demonstrate the pathologic appropriateness of ISR and the possibility of preserving anal function during the surgical treatment of very low rectal cancers.

Rullier *et al.*¹³ reported 92 rectal carcinomas at 3 cm from the anal verge, finding that the distal resection margin was 2 cm and negative in 98 percent of cases. They also reported that median circumferential margin was 5 (range, 0-15) mm and positive (≤ 1 mm) in ten cases (11 percent). These results show that radical tumor resection can be achieved by ISR procedures in almost all patients with very low rectal cancer.

Morbidity in our study was relatively high, with 55 of 228 patients (24 percent) experiencing complications, although the rate of serious complications was low. Our findings do not differ from those of other reports. Rullier *et al.*¹³ reported similar results, with a morbidity rate of 27 percent, whereas Schiessel *et al.*⁷ described a rate of 18.4 percent (7/38 patients). Unfortunately, one procedure-related

death occurred in the present study. Morbidity rate was particularly high in the first half of our study, although no changes in surgical technique were enacted during this period. Careful treatment and skillfulness in this procedure are needed for these patients if surgery-related complications are to be kept at a minimum.

Although an increase in local recurrence was feared in ISR because of reduced surgical margins compared with APR, cumulative five-year local recurrence rate was 6.7 percent in this series. All local recurrences in this study were outside the normal TME planes. These recurrences would not have been prevented using standard APR and seemed to result from inadequate lateral node dissection. Rullier *et al.*¹³ reported that 1 of 58 patients (2 percent) developed local recurrence during a median observation of 40 months. Schiessel *et al.*⁷ reported that 4 of 38 patients (10.5 percent) exhibited local recurrence during a median follow-up of three years. Local control in this study does not differ substantially from rates in these other reports. These results demonstrate that acceptable local control can be obtained by using ISR procedures. However, two of three patients with unclear surgical margins in this study developed local recurrence with distant metastases during a median observation of 28 months. Achievement of complete microscopic resection seems important for local control. The five-year overall survival rate in our series was 91.9 percent, whereas the five-year disease-free survival rate was 83.2 percent. Rullier *et al.*¹³ reported similar results, with an 81 percent five-year survival rate. Conversely, data for APR patients who underwent surgery in our seven institutions during the same time period showed that APR patients displayed tumors with the same background compared with patients who received ISR, with a median five-year DFS of 65.1 (range, 63.6-70) percent, and median five-year local recurrence rate was 10 (range, 3-19) percent. These data led us to consider the oncologic results of ISR obtained in this study as acceptable. The limit for ISR procedures seems to be circumferential clearance, rather than distal.

Some fears were held for functional outcomes after ISR procedures, because loss of the rectum and IS may induce anal dysfunctions, such as stool frequency, urgency, fragmentation, soiling, and fecal incontinence.^{14,32} Approximately 30 to 60 percent of low colorectal or coloanal anastomoses induce functional disturbances collectively termed anterior resection