A



Recurrence after resection of colorectal hepatic metastasis
- —□— More than 24 months after surgery
- —●— 13-24 months after surgery
- —✕— 7-12 months after surgery
- —○— Within 6 months after surgery

*Time after surgery (years)*

B



Recurrence after resection of colorectal hepatic metastasis
- —□— More than 24 months after surgery
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- —✕— 7-12 months after surgery
- —○— Within 6 months after surgery

*Time after recurrence (years)*

**Figure 3.** (A) Cumulative survival curves after resection of colorectal hepatic metastasis according to the time to recurrence. (B) Cumulative survival curves after recurrence after resection of colorectal hepatic metastasis according to the time to recurrence.

relative risk (RR) = 5.16; 95% confidence interval (CI), 2.10–12.69], bilobar metastases ($P$ = 0.04; RR = 2.73; 95% CI, 1.03–7.27), microscopic positive surgical margin ($P$ = 0.03; RR = 2.25; 95% CI, 1.11–4.59) and CEA level above 15 ng/ml ($P$ = 0.02; RR = 1.96; 95% CI, 1.09–3.55) had a predictive value for decreased recurrence-free survival after CHM resection. Median disease-free survivals and 1-year recurrence rates of patients with the aforementioned factors were 4.6, 5.6, 5.0 and 8.4 months and 100, 70, 79 and 65%, respectively.

Histological type of poorly differentiated signet ring cell or mucinous adenocarcinoma in the primary tumor and CEA level above 15 ng/ml were also the poor prognostic factors for overall survival (data not shown).

## DISCUSSION

The goal of this study was to assess the correlation between time to recurrence after CHM resection and prognosis. Results showed that prognosis of patients with recurrence within 6 months after resection was significantly worse than that of patients with recurrence after more than 6 months. Our findings indicate that short time to recurrence after CHM resection correlates with a poor prognosis.

The main reason 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. Most patients who could not undergo a second resection

Table 2. Correlation between clinicopathological factors and disease-free survival after hepatectomy for colorectal hepatic metastases

| Variable | No. of patients | Median disease-free survival (months) | P-value |
|---|---|---|---|
| **Primary colorectal lesion** | | | |
| Location | | | |
| Colon | 73 | 9.0 | 0.67 |
| Rectum | 28 | 9.5 | |
| TNM Classification | | | |
| I, II | 25 | 6.2 | 0.87 |
| III, IV | 76 | 9.6 | |
| Lymph node metastasis | | | |
| Absent | 35 | 9.0 | 0.79 |
| Present | 66 | 9.5 | |
| Histological type of adenocarcinoma | | | |
| Well- or moderately differentiated | 94 | 11.3 | <0.01 |
| Poorly differentiated signet ring cell or mucinous | 7 | 5.1 | |
| **Hepatic metastases** | | | |
| Number of tumors | | | |
| Solitary | 58 | 13.6 | <0.01 |
| ≥2 | 43 | 5.9 | |
| Maximum size of the tumor (cm) | | | |
| <5 | 77 | 9.0 | 0.58 |
| ≥5 | 24 | 13.4 | |
| Distribution of metastases | | | |
| Unilobar | 67 | 13.5 | <0.01 |
| Bilobar | 34 | 5.7 | |
| Microscopic surgical margin | | | |
| Negative | 87 | 10.3 | 0.03 |
| Positive | 14 | 6.4 | |
| CEA level before treatment (ng/ml) | | | |
| <15 | 47 | 15.4 | 0.04 |
| ≥15 | 54 | 8.4 | |
| Synchronous/metachronous | | | |
| Synchronous | 39 | 9.1 | 0.84 |
| Metachronous | 62 | 9.3 | |
| Interval between colorectal resection and hepatectomy | | | |
| <1 year | 65 | 7.8 | 0.11 |
| ≥1 year | 36 | 13.5 | |

CEA, carcinoembryonic antigen.

had extensive disease such as hepatic or pulmonary recurrence with much tumor burden, recurrence involving multiple organs, or distant metastases outside liver and lung that were not suitable for resection. In this series, re-resection

rates of recurrence in the remnant liver and lung were relatively low (42 and 40%, respectively) when recurrences were observed within 6 months after CHM resection, whereas they were high (76 and 75%, respectively) when recurrences were observed more than 6 months after resection.

Tumor doubling time is correlated with prognosis in various cancers (17–20). In CHM, it has been reported that short tumor doubling time is a poor prognostic factor for both overall and disease-free survival (21). Short time to recurrence represents short tumor doubling time. Those results are in accord with those of the present study.

Our results suggest that recurrence-free survival can be a surrogate endpoint for adjuvant trial in resectable CHM. Moreover, recurrence within 6 months should be a major target for additional chemotherapy because of a great number and the poor prognosis of these patients. Theoretically, if we can determine which patients will have a recurrence with short recurrence-free survival, we could identify which ones would possibly benefit from neoadjuvant chemotherapy. Adam *et al.* (22) showed efficacy of neoadjuvant chemotherapy for CHM patients with four or more tumors regardless of initially resectable or not, as long as objective tumor response or stabilization was achieved by chemotherapy, and demonstrated the possibility of neoadjuvant chemotherapy for resectable CHM. However, neoadjuvant chemotherapy sometimes causes chemotherapy-associated steatohepatitis which may increase operative morbidity (23,24); then, neoadjuvant chemotherapy should be recommended for high-risk patients for recurrence.

In the present study, histological type of poorly differentiated signet ring cell or mucinous adenocarcinoma in the primary tumor, bilobar metastases, microscopic positive surgical margin and CEA above 15 ng/ml were the independent prognostic factors for poor recurrence-free survival. Especially, histological type of poorly differentiated signet ring cell or mucinous adenocarcinoma in the primary tumor exhibited the strongest power for predicting early recurrence because all patients with the factor had recurred within 10 months. Then, histological type of poorly differentiated signet ring cell or mucinous adenocarcinoma in the primary tumor, which was not considered in other large studies (2,5), should be considered as one of the preoperative predictors of early recurrence after CHM resection. Patients with the factor are recommended to receive neoadjuvant chemotherapy. Bilobar metastases and CEA above 15 ng/ml were also prognostic factors for recurrence; however, long-term recurrence-free survival was achieved in some patients with the factors. Neoadjuvant chemotherapy for patients with either of the factors is controversial. In addition, considering the correlation between positive surgical margin and early recurrence, hepatic surgeons should pay much attention to keep negative surgical margin during hepatic dissection in order to prevent early recurrence.

In a retrospective analysis of consecutive 1001 CHM patients by Fong *et al.* (5), poor prognostic factors for recurrence after CHM resection were positive surgical margin, extrahepatic disease, node-positive primary, less than
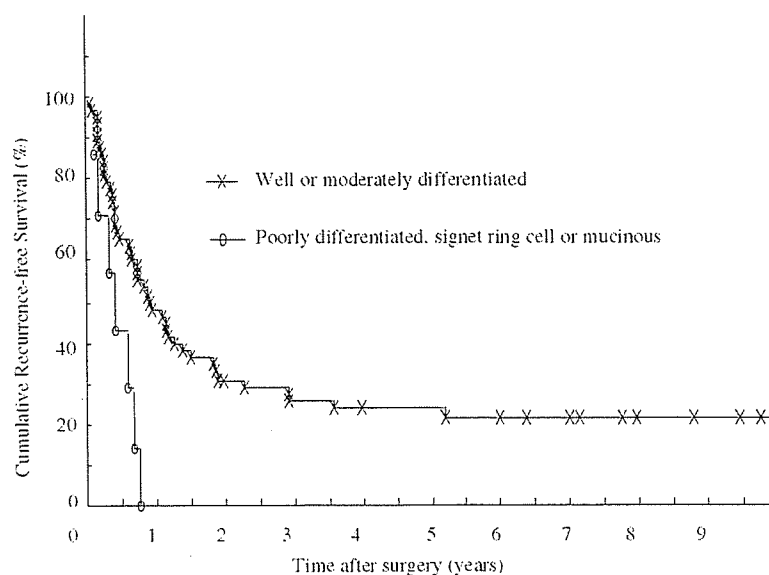
**Figure 4.** Recurrence-free survival curves after resection of colorectal hepatic metastasis according to the histological type of primary tumor.

**Table 3.** Multivariate analyses of factors affecting disease-free survival after hepatectomy for colorectal hepatic metastases

| Variable | Relative risk (95% CI) | $P$-value |
|---|---|---|
| **Primary colorectal lesion** | | |
| Histological type of adenocarcinoma | | |
| Well- or moderately differentiated | – | <0.01 |
| Poorly differentiated signet ring cell or mucinous | 5.16 (2.10–12.69) | |
| **Hepatic metastases** | | |
| Number of tumors | | |
| Solitary | – | 0.60 |
| ≥2 | 1.29 (0.50–3.38) | |
| Distribution of metastases | | |
| Unilobar | – | 0.04 |
| Bilobar | 2.73 (1.03–7.27) | |
| Microscopic surgical margin | | |
| Negative | – | 0.03 |
| Positive | 2.25 (1.11–4.59) | |
| CEA level before treatment (ng/ml) | | |
| <15 | – | 0.02 |
| ≥15 | 1.96 (1.09–3.55) | |

CI, confidence interval; –, reference.

12 months of disease-free interval from the primary resection, 2 or more tumors, tumor size >5 cm and CEA >200 ng/ml. The aforementioned prognostic factors for recurrence were also predictors of poor overall survival, and the fact was consistent with the concept of our results that short time to recurrence

correlated with poor survival. Fong *et al.* proposed a scoring system using five poor prognostic factors and insisted that the scoring system was useful in choosing adjuvant therapy.

The difference between our results and those of Fong's might be partly due to patients' background and the number of patients examined. In the present study, patients with extrahepatic disease were excluded because CHM with extrahepatic disease was totally different from pure CHM considering pathways of metastases. Moreover, none of the patients had received adjuvant chemotherapy after primary colorectal resection or CHM resection. However, the possibility that not all of Fong's predictors could be validated well because of relatively small population of our study cannot be ruled out.

In the present study, patients were followed and examined precisely at least for 5 years in order to elucidate complete profile of recurrence, and then median follow-up of survivors was 87 months. This study has clarified frequencies of the recurrences after CHM resection in liver, lung and other organs respectively according to time to recurrence and also clarified the resection-rates for those recurrences. On the result of the present study, the organ where recurrence had occurred most frequently and the resection-rate for the recurrences differed according to time to recurrence after CHM resection. Frequency of hepatic recurrence decreased rapidly after 2 years of CHM resection; however, that of pulmonary recurrence was not low even more than 2 years after CHM resection. A periodical checkup by chest XP or chest CT adding to abdominal examination is recommended for 5 years at least.

In conclusion, short time to recurrence after CHM resection correlates with a poor prognosis. This result provides grounds for proposal that an effective neoadjuvant chemotherapy and a system using the clinicopathological factors and

pharmacogenetics which identify best candidates for the neoadjuvant chemotherapy are needed in order to reduce early recurrence. Histological type of primary tumor might be a strong predictor for early recurrence after CHM resection.

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## 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

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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 alterative 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, Interssphincteric 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（Interspincteric 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的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
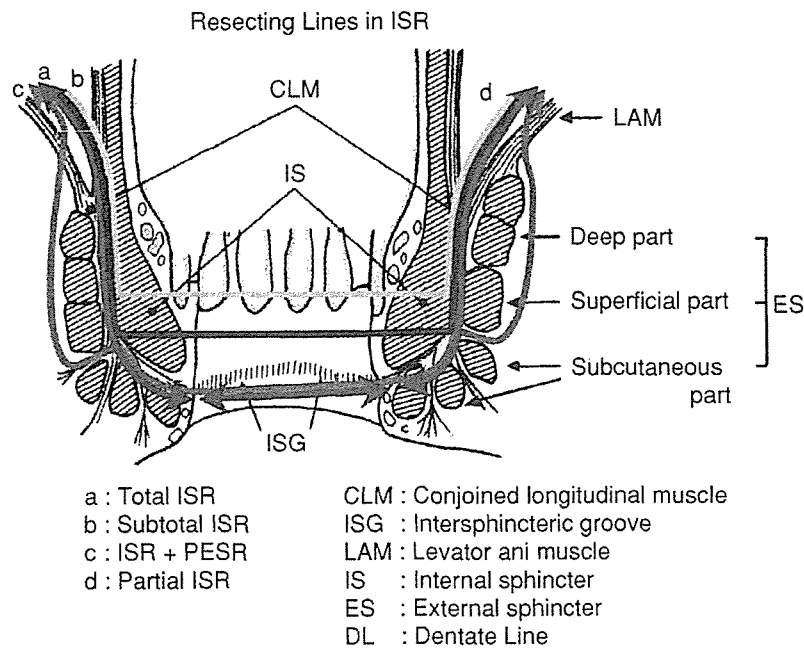
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Resecting Lines in ISR



a : Total ISR　　　　　　CLM : Conjoined longitudinal muscle
b : Subtotal ISR　　　　　ISG　: Intersphincteric groove
c : ISR + PESR　　　　　 LAM : Levator ani muscle
d : Partial ISR　　　　　　IS　 : Internal sphincter
　　　　　　　　　　　　　ES　 : External sphincter
　　　　　　　　　　　　　DL　 : Dentate Line

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的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いている．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，歯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,
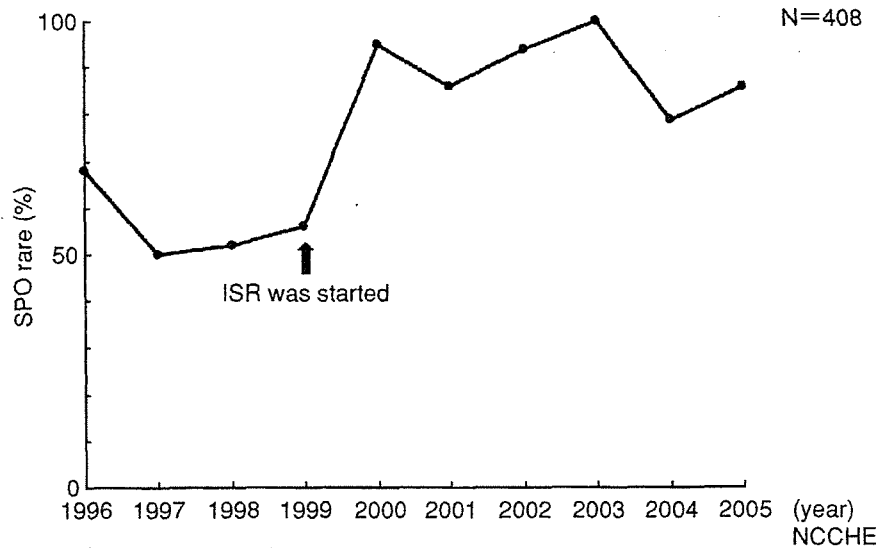
Fig. 2　Sphincter preserving operation (SPO) in very low rectal cancer (Rb-P)

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　　　28 ＜ APR: 1 |
| | Partial ISR: 24　　　　　　　 Hartmann: 2 |
| 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) |

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

200
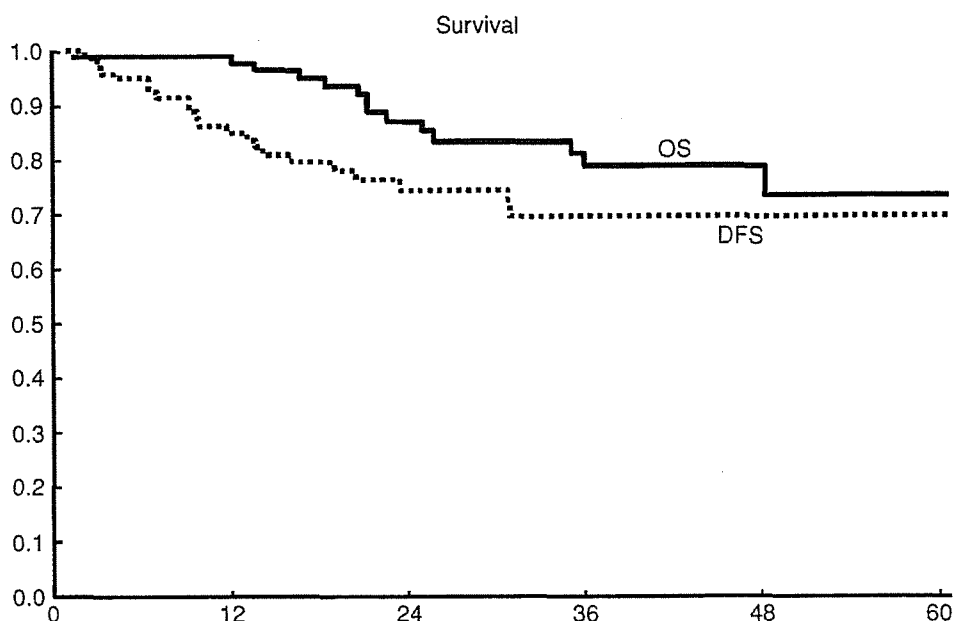
Survival



Fig. 3　Survival

Table 2　Functional Results After ISR

(N＝63, 24M≦)

| Worse functional status | After stoma closure | | | |
|---|---|---|---|---|
| | 3Mo | 6Mo | 12Mo | 24Mo |
| Stool frequency: 10/day≦ | 46 | 29 | 21 | 9 |
| Urgency: (＋) | 51 | 34 | 21 | 13 |
| Feces–flatus discrimination: (−) | 32 | 16 | 12 | 9 |
| Day–soiling: 1/week≦ | 63 | 53 | 29 | 26 |
| Night–soiling: 1/week≦ | 67 | 52 | 44 | 30 |

(%)

| Continence status | | 6Mo | 12Mo | 24Mo |
|---|---|---|---|---|
| Wexner Score* | | 11.2±4.0 | 8.4±4.5 | 7.8±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±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，Continence の状況を Wexner Score[8]，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

Line of Resection　　　　　　　　　　Reconstruction



SV : Seminal vesicle　　　R ： Rectum
UB : Urimary bladder　　　T ： Tumor
P ： Prostate　　　　　　　DL : Dentate line
SU : Sphincter urethrae　　AV : Anal verge
U ： Urethra　　　　　　　IS ： Internal sphincter
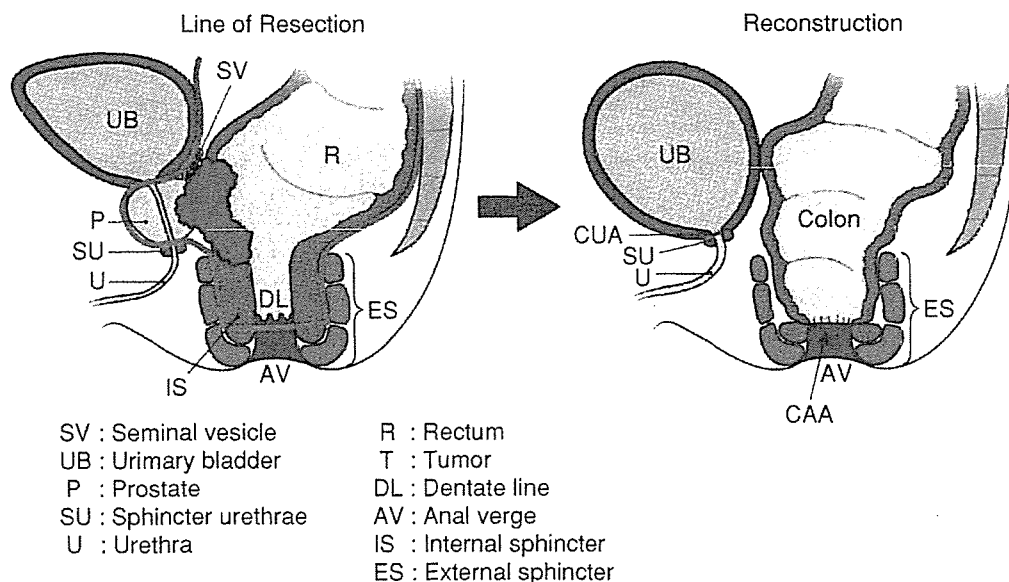　　　　　　　　　　　　　ES : External sphincter

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

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, Ultra
LAR）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 | Reconstruction 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
AWD: Alive with disease
DOD: Dead of disease

Mo: Months

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soil-ing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．

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

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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]

L ocal 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) standards[17] 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.
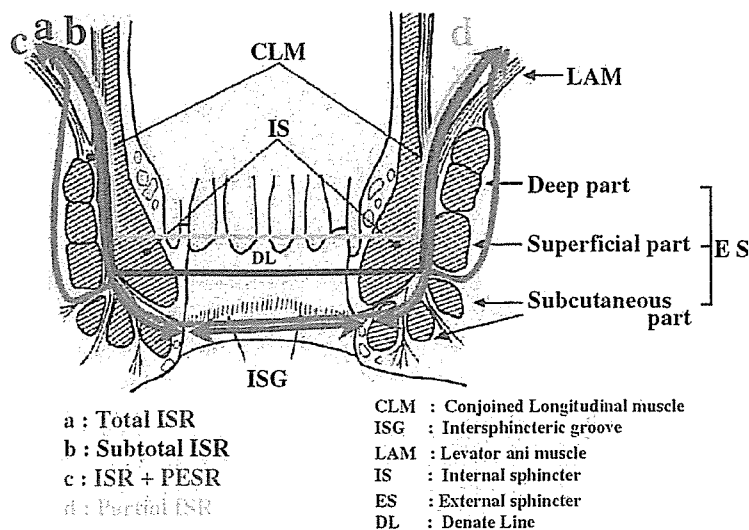
### Surgical Technique and Classification

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 ischiorectal 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 $\geq 2$ 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.



a : Total ISR
b : Subtotal ISR
c : ISR + PESR
d : Partial ISR

CLM : Conjoined Longitudinal muscle
ISG : Intersphincteric groove
LAM : Levator ani muscle
IS  : Internal sphincter
ES  : External sphincter
DL  : Denate Line

| 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-flurouracil (250 $mg/m^2/day$) was administered to these patients during radiotherapy to increase radiotherapeutic efficacy. Although revaluation 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 tegaful 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 ischiorecal 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
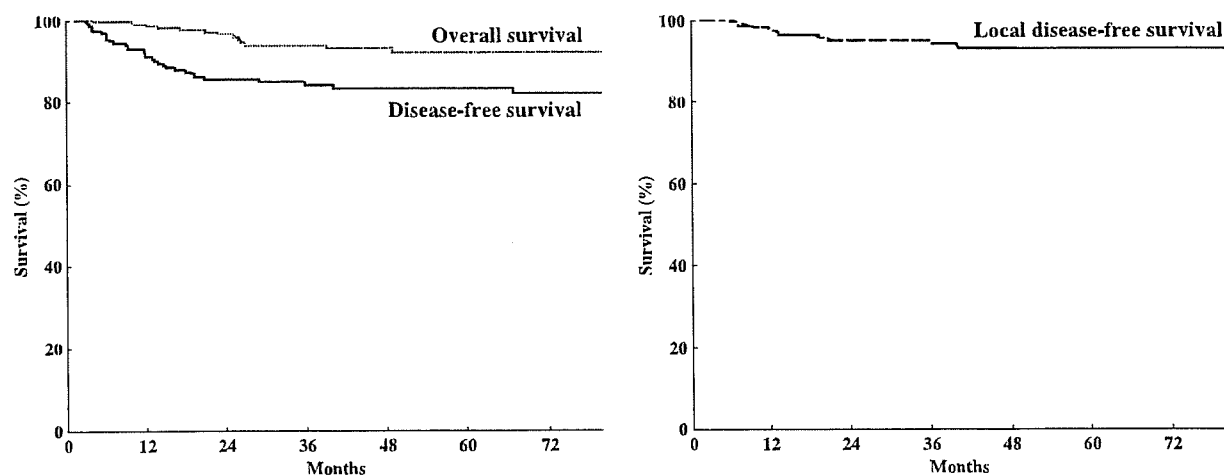


**Figure 2.** Overall survival was 91.9 percent and disease-free survival was 83.2 percent at five years. Acceptable local control also was obtained.

**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 nodes[18–22] 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

syndrome.[33–37] Most authors believe preservation of the whole anal sphincter and mucosa is crucial for maintenance of good continence. APR thus represents a standard surgery when distance between the lower edge of the tumor and the anal ring is <2 cm.[38] However, in this study, 93 percent of patients showed good or relatively good continence (Kirwan's Grade 1–111) at 24 months after stoma closure. Mean Wexner score was 7.8 at 24 months after stoma closure. Bretagnol *et al.*[14] and others have reported similar results.[7,10–12] However, seven patients displayed worsened continence. In addition, three patients could not undergo closure of the diverting stoma because of anal dysfunction. Furthermore, patients who underwent total ISR with or without PESR displayed significantly worsened continence compared with partial and subtotal ISR groups in our experience. Information on the potential functional adverse effects after total ISR should be provided to patients preoperatively.

Fecal incontinence after ISR is primarily caused by anal-sphincter insufficiency. Physiologic studies have shown that removal of the internal anal sphincter is associated with a significant decrease in resting pressure.[7,10,12] Anal sphincter insufficiency also may be caused by injury of the external anal sphincter during ISR. Furthermore, neorectal insufficiency may facilitate fecal incontinence, as demonstrated by randomized studies comparing straight and J-pouch coloanal anastomoses.[14,39,40] Anal functions in ISR procedures need to be investigated to compare straight, J-pouch, and transverse coloplasty coloanal anastomoses. More careful intraoperative management, additional surgery, such as colonic pouch, biofeedback treatment, and careful patient selection may facilitate improved outcomes in terms of anal function.

## CONCLUSIONS

Curability with ISR procedures was verified histologically in patients with very low rectal cancer. Acceptable oncologic and functional results were obtained by using ISR procedures in patients with very low rectal cancer <5 cm from the anal verge. These procedures can be recommended for APR candidate patients; however, information on potential functional adverse effects after ISR should be provided to patients preoperatively.

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