

が、骨盤内の深い部位での視野展開は容易ではない。また、鉗子による盲目的な操作は損傷を広げるばかりか、修復を困難にするため避けるべきである。

止血操作の基本手技としては図3、表2に示すよう、手指またはツッペルガーゼによる圧迫と側壁縫合、鉗子による“つまみ”や下大静脈や腸骨静脈など口径の大きな血管で損傷部位が大きな場合には、バルーンカテーテルを血管内に挿入してバルーンを拡張させて出血を制御する方法がある²⁾。小さな裂傷では図4aに示すよう直接、縫合修復する³⁾。

しかし、仙骨静脈からの出血は、上記のいずれも適応とはなり得ない。まず圧迫止血を試みるべきであり、シート状の止血剤を用いるのも効果的である。止血に難渋する場合にはテフロン製 pledget を用いた縫合止血(図4b)が有効であり、筆者らは腹直筋筋膜を用いた pledget が効果的であった症例を経験している。

総腸骨動静脈や外腸骨動静脈損傷で全周性に欠損した場合や腫瘍の浸潤のため血管合併切除が必要なときは、血管外科医に依頼し端々吻合や代用血管を用いて血管の再建⁴⁾を施行する。

5. 神経損傷

下腹神経や骨盤神経叢など自律神経の損傷に対する救済処置はない。一方、閉鎖神経を誤って損傷した場

合には縫合接着を行っておくと神経機能回復の可能性はある。

おわりに

直腸癌手術、とくに再発手術は難易度の高い手術であり、術中偶発症の発生頻度も高い。偶発症発生の要因を理解し、良好な視野のもとに正しい手術操作を心がけることが大切である。また、偶発症に対する適切な処置とくに、骨盤内血管損傷に対する止血の基本操作や対処法を習熟することが肝要である。

文 献

- 1) 緒方裕, 大北亮, 赤木由人, 石橋生哉, 森眞二郎, 白水和雄: 大腸癌における自律神経温存のためのNo.253リンパ節郭清; 神経染色法を用いて, 手術, 60:1057~1060, 2006.
- 2) 久保良彦, 笹嶋唯博, 山本浩史, 稲葉雅史, 郷一知, 東信良: 術中血管損傷の処置, 手術, 50:795~800, 1996.
- 3) 多田祐輔, 神谷喜八郎, 進藤俊哉: 汚染術野における血行再建のコツ, 手術, 50:776~784, 1996.
- 4) 緒方裕, 石橋生哉, 田山慶一郎, 的野敬子, 青柳成明, 白水和雄: 外腸骨動・静脈合併切除, 人工血管による同時再建により根治術を施行しえた大腸癌局所再発の1例, 手術, 59:1068~1072, 2005.

直腸癌手術に対する神経温存 D3 郭清手術 手技—開腹アプローチ—

赤木 由人* 白水 和雄*² 緒方 裕*

はじめに

直腸癌における神経温存手術は、内腸骨動脈領域の側方リンパ節、下腸間膜動脈領域や大動脈周囲のリンパ節の郭清により、自律神経が損傷されたために生じた機能障害の反省から、1980年代より提唱されるようになった術式である。直腸癌手術と関連する自律神経系は、下腸間膜動脈起始部で大動脈左右から出る腰内臓神経、それらが動脈前面で交差合流して形成する下腹神経叢、これがさらに岬角近くで左右に分岐し、仙骨より前方に向かう骨盤内臓神経と合流する骨盤神経叢である。詳細は前稿で述べてあるので、本稿では腫瘍が腹膜反転部付近に存在する進行直腸癌を想定して、上記のすべての神経を温存し、主リンパ節および側方リンパ節郭清を伴う手術手技について述べる。

I. 手術手技

手術の操作は、S状結腸と下行結腸の一部を後腹膜からの授動、下腸間膜動脈根部、同静脈の処理、間膜および口側結腸の切離、直腸間膜

* Yoshito AKAGI et al. 久留米大学外科

*² Kazuo SHIROUZU 同外科 教授

key words : 直腸癌, 自律神経温存手術, 低位前方切除術, 側方郭清

の剝離授動、直腸切離、側方郭清、吻合という手順で行っている。

1. 上部自律神経温存（腰内臓神経～下腹神経叢～左右下腹神経）

結腸間膜の剝離は尿管と総腸骨動脈が交差する部位の内側（大動脈分岐部より外側の高さ）から行う。これはS状結腸を牽引することで、仙骨前面の剝離層である結合織と下腹神経が比較的容易に確認できるからである。この層を頭側に向かってホワイトラインまで切開を延ばし、腎筋膜前葉と後腹膜下筋膜を大動脈前面まで進める。この剝離面には血管はないので、ほぼ無血状態で剝離可能である。この場合、助手が十分にカウンタートラクションをかけることが肝要である。また、肥満で脂肪の多い人や剝離層がよくわからない場合は、至適剝離層よりも背側に入ってしまうことがあるので、下行結腸側のホワイトラインから先に切開剝離を始めると、剝離層を間違わずに進めることができ、余計な出血を来すことは少ない。

大動脈近傍まで達すると、上下腹神経が白色調の索状物として確認できることが多い。確認できればこの時点で間膜より十分に鋭的に剝離しておく（慣れないうちはテーピングしておくとうわりやすい）。この神経叢がわからないと、剝離が大動脈前面へ向かってしまい、神経を間膜側に残したまま授動することになる。次にS状結腸を左側に牽引し、下大静脈右側で後腹膜

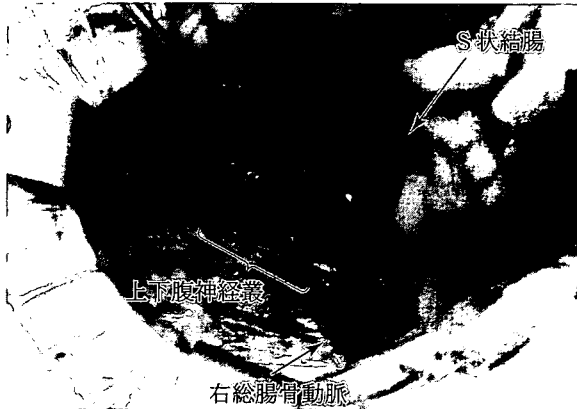


図 1
S状結腸を左側に牽引し、上下腹神経の走行を確認しながら切離できる。(左が頭側)

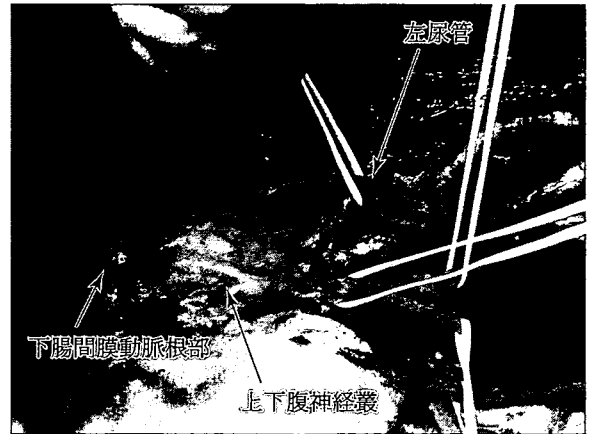


図 2
下腸間膜動脈の根部を結紮・切離した上下腹神経叢が大動脈前面に温存されている。(左が頭側)

を切開する。左側の剥離が十分にできていると、後腹膜を切開、牽引するのみで結腸が授動され、上下腹神経の走行を確認しながら切離できる(図1)。切開は十二指腸水平脚まで、さらに同部位の大動脈前面で逆U字に行い、下腸間膜動脈根部を明らかにする。

大動脈前面には左右の頭背側から走行する数本の腰内臓神経が合流交錯してネットワークを形成している。この確認は肉眼的にはなかなかむずかしいと思われ、メチレンブルーを希釈した液体で染色すると比較的明瞭となり、神経温存には効果的と考えられる¹⁾。したがって、大動脈外膜がむき出しになるような剥離は神経を損傷していると考えられ、脂肪織を残すような剥離が妥当と思われる。下腸間膜動脈の根部を結紮・切離したあとは、すでに剥離した結腸間膜とともに腹側に牽引することで、上下腹神経の走行が確認でき、それを大動脈に残すように剥離すれば損傷なく行える(図2)。

これらの操作で、上下腹神経叢が大動脈前面に温存され、同定ができればこの後の操作が容易となる。

2. 下部自律神経温存(左右下腹神経～骨盤内臓神経～骨盤神経叢)

S状結腸を離断し、直腸側断端を腹腔外尾側へ挙上すると上方側から温存してきた下腹神経の走行がよりはっきりする(図3)。その下腹神経が骨盤側に残るように直腸固有筋膜を尾側に向かって剥離を進める。この直腸間膜背側(直腸後腔)は血管のない白い膜状の結合織であり、この層をWaldeyer筋膜まで剥離を進める(図4)。次に、左右の骨盤腹膜切開線を腹膜反転部まで延長し、直腸と骨盤腹膜にカウンターアクションをかけると良好な視野が展開する。直腸後壁側から側方に左右に回り込むように下腹神経の内側を剥離していくと、骨盤神経叢の内側に至る。

再度、後壁に戻ってWaldeyer筋膜を鋭的に穿破すると肛門挙筋が現れる。さらに索状物として触知される尾骨直腸靭帯を切離すると直腸後壁の固定が解除され、直腸は十分に腹側に挙上され、神経の走行がよりはっきりとする(図5)。この部位における操作のコツは術者、あるいは助手が切離した直腸を牽引しつつ、さらに剥離操作部位を腸ペラなどで先を利かせるように腹側に圧迫し、良好な視野を保持することである。視野が良くなると同時に切離する結合



図3 直腸側断端を腹腔外尾側へ挙上すると下腹神経の走行がよりはっきりする。(手前が頭側)

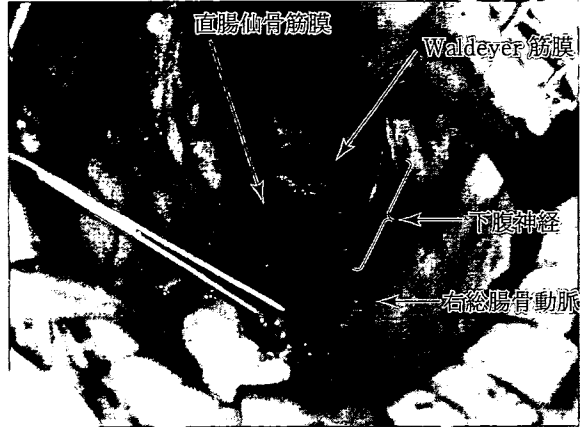


図4 直腸後腔を剥離すると直腸仙骨筋膜に達し、それを切開するとWaldeyer筋膜に達する。(手前が頭側)

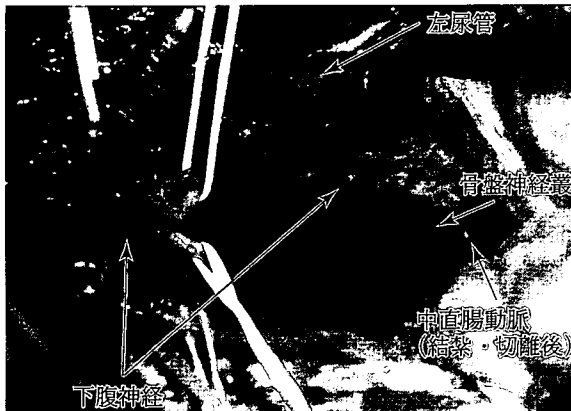


図5 直腸後壁を十分に腹側に挙上すると、神経の走行がよりはっきりとする。(左が頭側)

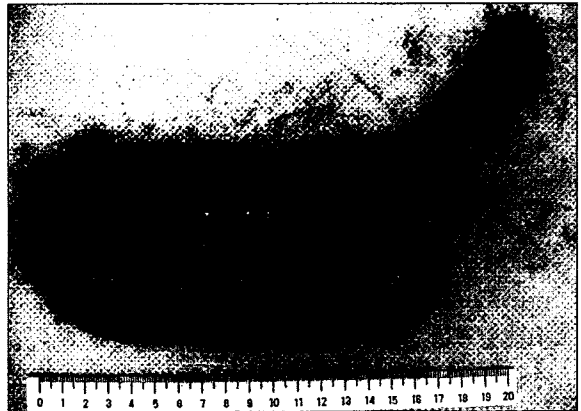


図6 TMEを施行された摘出標本の直腸間膜剥離面。平滑で光沢をもって見える。

織の層がはっきりするので、圧排を少しずつ奥に進めながら行くと剥離層を誤らない。また、この操作においては電気メスやCooperなどで鋭的、鈍的に剥離しても出血はほとんどみないが、とくに下部直腸になると正中部で強い線維組織がみられ、これを背側に入ってしまうと仙骨前の静脈叢から出血を来すので、直腸側に沿って切離するのが肝要である。またここでは、骨盤内臓神経の損傷に注意が必要である。

第2~4仙骨神経は仙骨外側から立ち上がる索状物として認識される。したがって、前述の正中の線維組織を切離して対側に牽引すると、損傷の可能性を減らすことができる。このように直腸固有筋膜が破れないように肛門挙筋が露出するところまで剥離を進めることが重要である〔摘出標本をみると直腸間膜の剥離面が薄い膜に覆われて光沢をもって見え(図6)、いわゆるtotal mesorectal excision : TME²⁾がな

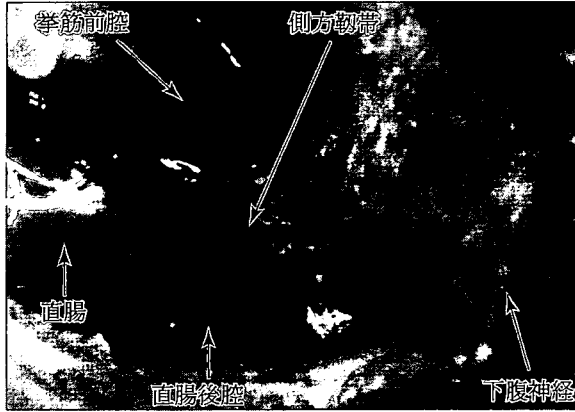


図 7
直腸側腔は直腸後腔、挙筋前腔につながる。直腸を対側に牽引しながら開窓すると直腸と骨盤をつなげている側方靱帯が同定できる。



図 8 左側方郭清
内腸骨動脈外側の閉鎖腔を神経、血管だけにする。(左側が頭側)

れてなければならない]。

次に直腸前方の剥離を行う。腹膜翻転部腹膜を切開し、脂肪織を切離すると直腸の筋線維が確認される。これに沿い Denonvilliers 筋膜を精囊(子宮・腔)から剥離する。癌の浸潤がないかぎり、前立腺(腔)の後壁は容易に剥離可能である。男性の場合、精囊外側の脂肪織を鈍的に剥離し安易に切離していくと、しばしば neurovascular band (神経血管束)を損傷し、出血をみることがあるので注意が必要である。

腹膜翻転部より尾側の直腸外側と内腸骨血管の間には脂肪織が存在するので、鈍的に剥離すると直腸側腔に至る。これは先に剥離した直腸後腔、挙筋前腔につながるの、直腸を対側に牽引しながら開窓すると、直腸と骨盤をつなぎ神経血管束を形成している側方靱帯が同定できる(図7)。ここでは下腹神経や骨盤神経叢を確認しつつ、直腸に向かう血管や神経は切離するが、腹側にある精囊や膀胱に向かう神経の損傷を回避しなければならない。両側の側方靱帯が切離されると、直腸はほぼ遊離されたことになる。

直腸側壁における側方靱帯の切離の際に、骨盤神経叢から膀胱枝などの臓側枝が走行していることを留意しながら、ここの操作を確実に行

うことも自律神経温存術のポイントの一つとなる。

3. 側方リンパ節郭清

側方郭清は腹腔内や腹膜外からのアプローチがあり、内・外腸骨動脈間の閉鎖腔(No.283)や、内腸骨動脈周囲(No.263)の直腸側腔、膀胱側腔の脂肪織を摘出することである。我々は同部位が直視下に見え、視野が良好な外側アプローチで行っている³⁾。この際、内腸骨動脈、上膀胱動脈、下腹神経などにテーピングしておく、郭清が安全で系統的に十分に行える。中直腸動脈根部(内腸骨末梢)リンパ節郭清の際には、骨盤内臓神経が近接しているためその損傷に留意が必要である。

腹膜の剥離は内・外腸骨動脈部位を想定し、そこに向かって正中切開部腹膜の剥離から始める。血管が同定できたらそれを露出するように、外側から内側に向かって閉鎖神経、動・静脈を明らかにしつつ骨盤側壁、後方の坐骨神経が露出するまで行い、閉鎖リンパ節郭清を終了する(図8)。ついで、内腸骨動脈に沿ってその周囲を剥離・露出し、上膀胱動脈を確認する。この内側下方には骨盤神経叢が存在するので、血管にテーピングし外側に牽引すると、神経叢と血

管の間にスペースを作ることができ、神経損傷をより回避できる。さらに末梢では内腸骨動・静脈から分岐する閉鎖動・静脈、下膀胱動・静脈、その内背側の梨状筋から骨盤神経叢に向かう骨盤神経 (S3, S4) があることを考慮し、その温存に努めながら周囲脂肪織を摘出 (閉鎖動・静脈は合併切除することもあるが、とくに問題ないと思われる) して側方郭清を終了する (図9)。

森ら⁴⁾は自律神経温存をする側方郭清術における要点を次のように挙げている。

①閉鎖リンパ節郭清では腹膜外経路で行うのが確実だが、腹膜内経路と併用することで内腸骨動脈末梢部が直視下に操作可能となり、その内側に存在する骨盤神経叢の温存が容易である。

②上膀胱動脈の露出とテーピングによる牽引で、内腸骨動脈末梢部との間が開大する。内腸骨動脈の末梢に梨状筋を確認でき、その内側のS3起始部の温存が容易になる。

③下膀胱動・静脈を確認し、これらを膀胱流入部まで、周囲脂肪織を含めて切除すると、下膀胱動・静脈の裏に存在するS4起始部の確認温存が容易になる。

また、森ら⁴⁾は本術式の手技において、鉏による鋭的操作は神経叢をできるかぎり薄く剥離可能で、神経周囲のリンパ節転移、脂肪浸潤組織の摘出が可能であるが、神経損傷を多くしているという問題点も挙げている。

おわりに

直腸癌に対する自律神経温存術の手技について述べた。本術式の手技は標準的な直腸癌の手術手技に加え、解剖学的知識とリンパ節郭清の基本的な手技が身につけていれば可能なものと思われる。

ポイントは3つ。下腸間膜動脈起始部の処理を行う際の腰内臓神経の温存の場合と、仙骨前



図9 左側方郭清

内腸骨動脈に沿って剥離を進め、神経叢と血管の間にスペースを作る。上膀胱動脈が分岐したあとの内腸骨動脈の末梢では閉鎖動脈、下膀胱動脈がみられる。骨盤神経叢に向かう骨盤神経 (S3, S4) はこの内背側に存在する。(左が頭側)

面における直腸剥離と下腹神経の温存、側方靱帯切離の際の骨盤神経叢の温存に尽きる。

そして何よりも、本術式が患者の術後のQOLに関わるものであり、術者である以上看過できない手技であるということを念頭において励行することである。

文献

- 1) 緒方 裕ほか：大腸癌における自律神経温存のためのNo.253リンパ節郭清—神経染色法を用いて—。手術 60：1057-1060, 2006
- 2) Heald RJ et al：The mesorectum in rectal cancer surgery—the clue to pelvic recurrence? Br J Surg 69：613-616, 1982
- 3) 森田隆幸ほか：下部直腸癌に対する腹膜外からの側方郭清。手術 48：1501-1508, 1994
- 4) 森 武生ほか：骨盤内自律神経温存術の適応と手技及び問題点。外科治療 77：555-560, 1997

Isolated tumor cell in lateral lymph node has no influences on the prognosis of rectal cancer patients

M. Hara · T. Hirai · H. Nakanishi · Y. Kanemitsu ·
K. Komori · M. Tatematsu · T. Kato

Accepted: 23 January 2007 / Published online: 21 February 2007
© Springer-Verlag 2007

Abstract

Background and aims The aim of this study was to determine the incidence of isolated tumor cells (ITC) and micrometastasis in lateral lymph nodes of patients with rectal cancer and its possible correlation with prognosis.

Materials and methods One hundred seventy-seven rectal cancer patients who underwent curative resection with lateral lymph node dissection were enrolled. Dissected lymph nodes were examined using hematoxylin–eosin staining (HE) and immunohistochemistry (IHC) with anti-keratin antibody (AE1/AE3). States of lymph node metastasis were divisible into three groups: detectable with HE (HE+), detectable with only IHC (HE–/IHC+), and undetectable even with IHC (IHC–). Almost all the HE–/IHC+ group was classified as ITC consisting of a few tumor cells according to the UICC criteria (ITC+). Survival rates were compared among HE+, ITC+, and IHC–.

Results ITC+ were detected in 24.1% of patients with HE-negative lateral lymph nodes. No significant difference in overall 5-year survival was observed between ITC+ and IHC– patients (76.1 and 82.9%, respectively, $p=0.25$). Multivariate analysis showed that perirectal HE+ lymph

nodes, but not ITC+ lateral lymph nodes, was an independent prognostic factor.

Conclusions ITC in lateral lymph nodes does not contribute to the prognosis of rectal cancer in patients who undergo extended lateral lymph node dissection, unlike HE+ lateral lymph node metastasis.

Keywords Rectal cancer · Lateral lymph node metastasis · Isolated tumor cell · Immunohistochemistry · Lateral lymph node dissection

Introduction

Malignant tumors originating from pelvic urogenital organs such as the uterus and prostate often metastasize to pelvic lymph nodes. The prognostic value and therapeutic significance of pelvic lymph node metastasis in such cancers at certain stages have been determined [1–3]. In rectal cancer, however, pelvic lymph nodes were considered sites of distant metastasis in the studies by Bacon and Sauer [4] and Deddish and Stearns [5] in the 1950s. As a result, total mesorectal excision (TME), in combination with radiotherapy and chemotherapy, had been advocated to improve the therapeutic outcome of rectal cancer [6–11]. In contrast, in Japan, lateral lymph node dissection, which evolved from pelvic node dissection, has developed as an extended requisite procedure for advanced rectal cancer [12–14]. For this reason, pre- or postoperative radiotherapy has not become an established procedure in such cases.

Over the past decade, lymph node micrometastasis from colorectal cancer has been reported as a prognostic factor [15–17], although other studies have claimed the contrary [18–20]. To date, however, only one small-scale study (66 patients) has investigated micrometastasis in lateral lymph

This paper is not based on a previous communication to a society or meeting.

M. Hara · T. Hirai (✉) · Y. Kanemitsu · K. Komori · T. Kato
Department of Gastroenterological Surgery,
Aichi Cancer Center Hospital,
1-1 Kanokoden, Chikusa-ku,
Nagoya, Aichi 464-8681, Japan
e-mail: thirai@aichi-cc.jp

M. Hara · H. Nakanishi · M. Tatematsu
Division of Oncological Pathology,
Aichi Cancer Center Research Institute,
Aichi, Japan

nodes of patients with rectal cancer in Japan [21]. Recently, the UICC have adopted criteria for micrometastasis as isolated tumor cells (ITC) and “micrometastasis” [22–25], but little is known about the correlation between ITC and the prognosis of colorectal cancer. In this paper, we describe a larger scale immunohistochemical study of lymph node micrometastasis in 177 rectal cancer patients who underwent lateral lymph node dissection, aimed at evaluating the incidence and prognostic value of ITC in lateral lymph nodes.

Materials and methods

Lateral lymph node dissection and surgical procedure

According to the Japanese classification of colorectal carcinoma [25], as shown in Fig. 1, lateral lymph node dissection refers to complete dissection of internal iliac lymph nodes (#272), middle rectal root lymph nodes (#262), and obturator lymph nodes (#282). Lymph nodes such as aortic bifurcation (#280), common iliac (#273), and external iliac lymph (#293) nodes are not necessary, but are usually included in lateral lymph node dissection. Lateral lymph node dissection is performed for curative intent in Japan while those lateral lymph nodes are categorized as distant lymph node in TNM classification. Based on our

previous studies of the incidence of lateral lymph node metastases, the pre- or intraoperative indications for lateral lymph node dissection are as follows: the primary cancer located above the peritoneal reflection (upper rectum: Ra) with invasion to the serosa, or non-peritonealized perirectal tissue or deeper, or the primary cancer located below the peritoneal reflection (lower rectum: Rb) or anal canal (P) with invasion to the muscularis propria or deeper. With regard to surgical procedures, mesorectal excision should be performed so that the detached surface is negative for cancer, whereas alignment of the autonomic nerves is confirmed. If infiltration to the nerves is suspected or if lateral lymph node metastasis is macroscopically confirmed, then the ipsilateral autonomic nerves are excised. The upper margin of mesenteric lymph node dissection is the root of the inferior mesenteric artery (#253). The anal margin distance should be 4 cm or more for Ra and 2 cm or more for Rb, and total mesorectal excision is performed for Rb. Lymph nodes located along the bowel axis are classified as lying beneath the tumor (T), on the anal side from the tumor (A), or on the oral side from the tumor (O).

Patient characteristics

Between 1987 and 1999, 581 patients with primary, single rectal cancer underwent initial curative resection at the

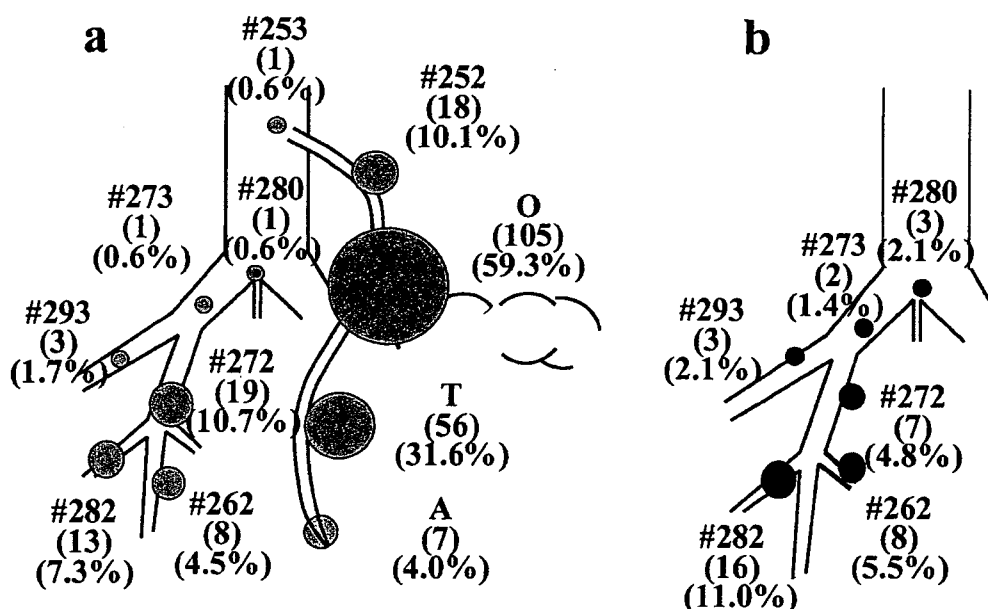


Fig. 1 Numbers of patients with HE+ lateral and perirectal lymph nodes (LN) among all 177 patients (a) and those with ITC+ in lateral LN among 145 HE-negative patients (b). Numbers in upper and lower parentheses mean the number and percentage of node-positive patients, respectively. LNs were classified as common iliac LN (#273), internal iliac LN (#272), middle rectal root LN (#262),

obturator LN (#282), aortic bifurcation LN (#280), external iliac LN (#293), inferior mesenteric trunk LN (#252), and inferior mesenteric root LN (#253). LNs along the bowel axis were classified as lying beneath the tumor (T), on the anal side from the tumor (A), and on the oral side from the tumor (O)

Department of Gastroenterological Surgery, Aichi Cancer Center Hospital. Of these patients, 177 (112 men and 65 women) underwent lateral lymph node dissection, according to our previously described indication, and were enrolled in this study. No patients have lost to follow-up. Mean patient age was 56.0 years (range, 28–78 years). The histological type was well-differentiated adenocarcinoma in 13 cases, moderately differentiated adenocarcinoma in 145, poorly differentiated adenocarcinoma in 11, and mucinous carcinoma in eight. Rectal cancer mainly affected Ra ($n=51$), Rb ($n=119$), and P ($n=7$; Table 1).

The surgical methods comprised abdominoperineal resection (APR, $n=82$), low anterior resection (LAR, $n=91$), and the Hartmann procedure ($n=4$). The mean number of dissected lymph nodes per patient was 17.0 ± 7.9 for perirectal lymph nodes and 28.4 ± 11.3 for lateral lymph nodes. Follow-up rate was 100%, and median duration of follow-up was 2,472 days (range, 97–5,145 days). Preoperative pelvic

irradiation was not performed, and postoperative pelvic irradiation was performed on 23 patients, most of whom had lateral lymph node metastases. Postoperative 5-fluorouracil-based chemotherapy was performed for 70 patients.

Immunohistochemical analysis

A total of 5,024 lateral and 3,012 perirectal harvested lymph nodes from 177 patients were examined by routine hematoxylin–eosin (HE) staining, and 32 patients were identified as having lateral HE metastasis (La HE+). Excluding those 32 patients, immunohistochemical analysis was performed on 4,035 lateral lymph nodes of 145 patients without lateral lymph node HE metastasis (La HE–). Micrometastasis was evaluated by two pathologists. Single cancer cells and small cell clusters scattered in sinusoids were regarded as ITC (La ITC+; Fig. 2), and a metastatic focus measuring between 0.2 and 2 mm in diameter was regarded as a “micrometastasis” based on the UICC criteria [22–25]. Contaminating normal epithelial cells and cancer cells from the primary tumors were carefully eliminated to avoid any false-positive results.

For immunohistochemical analysis (IHC), surgically dissected lymph nodes were fixed in buffered formalin, embedded in paraffin, and consecutive 4- μ m sections were prepared. IHC was performed using the indirect enzyme-labeled antibody technique with a mouse monoclonal antibody against a broad spectrum of cytokeratin (AE1/AE3, Dako, Copenhagen, Denmark) as the primary antibody as follows. After being deparaffinized with xylene and dehydrated in ethanol, sections were heated in a microwave oven at 98°C for 15 min for antigen retrieval. To inactivate endogenous peroxidase activity, these sections were immersed in methanol with 0.3% hydrogen peroxide for 30 min, followed by normal horse serum for 30 min to block nonspecific reactions. The sections were incubated at 4°C overnight with the AE1/AE3 antibody at 1:100 dilution in phosphate buffered saline (PBS; pH 7.2) containing 1% bovine serum albumin. After washing with PBS, the sections were incubated with a biotinylated second antibody for 30 min. The sections were washed again with PBS, and then incubated with streptavidin–peroxidase complex (Vectastain ABC kit; Vector, Burlingame, CA) for 60 min. The chromogen was developed with 0.01% diaminobenzidine, and the sections were counterstained with Meyer’s hematoxylin.

Statistical procedures

Log-rank test using the Kaplan–Meier method was performed, regarding the endpoint as death, including death related to other diseases. For multivariate survival analysis, the Cox hazard model was used. Chi-squared test was used

Table 1 Characteristics of the 177 rectal cancer patients who underwent curative resection with lateral lymph node dissection

Variables	Values	Percentage
Age (mean years \pm SD)	56.0 \pm 9.9	
Gender		
Male	112	63.3
Female	65	36.7
Tumor location		
Upper rectum (Ra)	51	28.8
Lower rectum (Rb)	119	67.2
Anal canal (P)	7	4.0
pT category		
t2	60	33.9
t3	102	57.6
t4	15	8.5
Stage (TNM)		
1	32	18.1
2	36	20.3
3	109	61.6
Histology		
Well	13	7.3
Moderate	145	81.9
Poor	11	6.2
Mucinous	8	4.5
Perirectal lymph node metastasis		
HE+	79	44.6
HE–	98	55.4
Lateral lymph node metastasis		
HE+	32	18.1
HE–	145	81.9
Harvested lymph node		
Perirectal	17.0 \pm 7.9	
Lateral	28.4 \pm 11.3	

pT depth of tumor invasion according to UICC
Stage 3 included 32 lateral lymph node metastasis

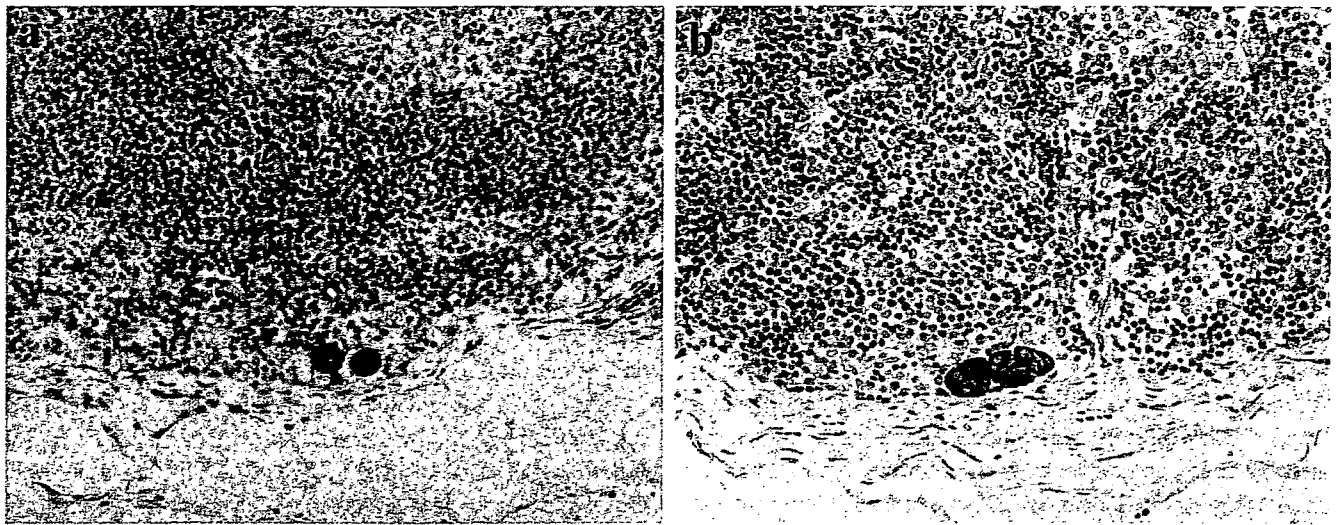


Fig. 2 Micrometastases in lateral lymph nodes stained with anti-cytokeratin antibody. ITC of the single cell type (a) and small cluster type (b) are seen within the marginal sinus of the lymph node (original magnification, $\times 200$)

to assess differences between groups. The level of significance was set at $p < 0.05$.

Results

Incidence of IHC+ lymph nodes

Of 4,035 lateral lymph nodes of 145 La HE⁻ cases, tumor cells were detected in 43 lymph nodes from 36 patients by IHC. Of these 36 patients, one patient (0.7% of La HE⁻) had one lymph node “micrometastasis” as defined by the UICC, and the remaining 35 patients (24.1% of La HE⁻ cases) were proved to have ITC consisting of the single cell type in 27 patients and the small cluster type in eight patients. The mean number of La ITC+ lymph nodes per patient was 1.2 (range, 1–2; Table 2).

Location of lymph node metastases

The location and incidence of HE⁺ perirectal and lateral lymph nodes in all 177 patients and of ITC+ lateral lymph

nodes in the 145 La HE⁻ patients are represented schematically in Fig. 1a and b, respectively. HE⁺ and ITC+ lymph nodes were present among middle rectal root lymph nodes in 4.5 and 5.5% of cases, among internal iliac lymph nodes in 10.7 and 4.8% of cases, and among obturator lymph nodes in 7.3 and 11.0% of cases, respectively. The frequency of both La HE⁺ and La ITC+ was higher around these arteries than in other areas. The total frequency of metastasis (i.e., total of La HE⁺ and La IHC+) was 2–16% for each area. For lateral lymph nodes, the location and relative frequency of ITC+ lymph nodes were quite similar to those of HE⁺ lymph nodes.

Clinicopathological characteristics of lateral lymph node micrometastasis

The correlation between ITC+ lymph nodes and clinicopathological characteristics was examined (Table 3). The frequency of ITC+ lymph nodes was significantly higher in patients with perirectal HE⁺ lymph node (32.5%) than in patients without perirectal HE⁺ lymph node (17.5%, $p = 0.03$), and ITC+ patients were significantly more common among women (38.0%) than among men (17.0%, $p = 0.005$). No significant differences were observed in other variables.

Survival

During more than 5 years of postoperative follow-up, a total of 57 patients died of cancer recurrence ($n = 50$) or other causes ($n = 7$). The 5-year overall survival rate for the 177 patients was 72.9%. When survival of patients with lateral lymph node metastasis-negative (La IHC⁻, $n = 109$), ITC-positive (La ITC+, $n = 35$), and HE metastasis-positive

Table 2 Incidence of micrometastasis in lateral lymph nodes in 177 rectal cancer patients

State of metastasis	No. of patients positive/examined	No. of LN positive/examined
La HE ⁺	32/177 (18.1%)	59/5024 (1.2%)
La HE ⁻ /IHC ⁺		
ITC	35/145 (24.1%)	42/4035 (1.0%)
“micrometastasis”	1/145 (0.69%)	1/4035 (0.02%)
La IHC ⁻	109/177 (61.6%)	3986/4035 (98.8%)

HE⁺ Metastasis detected by HE staining, IHC⁺ metastasis detected by immunohistochemistry, LN lymph node

Table 3 Correlation between ITC of lateral lymph nodes and clinicopathological parameters

Variables	ITC- (n=109)	ITC+ (n=35)	p value
Age			
> or =60	40 (78.4)	11 (21.6)	0.57
<60	69 (74.2)	24 (25.8)	
Gender			
Female	31 (62.0)	19 (38.0)	0.005
Male	78 (83.0)	16 (17.0)	
Tumor size			
> or =5 cm	54 (77.1)	16 (22.9)	0.69
<5 cm	55 (74.3)	19 (25.7)	
Histology			
Poor/mucinous	8 (61.5)	5 (38.5)	0.21
Well/moderately	101 (77.1)	30 (22.9)	
Preoperative serum CEA			
> or =5	34 (68.0)	16 (32.0)	0.11
<5	75 (79.8)	19 (20.2)	
pT category			
t3–t4	65 (71.4)	26 (28.6)	0.12
t2	44 (83.0)	9 (17.0)	
Vessel invasion			
Positive	78 (76.5)	24 (23.5)	0.74
Negative	31 (73.8)	11 (26.2)	
Lymphatic invasion			
Positive	85 (73.9)	30 (26.1)	0.32
Negative	24 (82.8)	5 (17.2)	
Perirectal lymph node			
HE+	52 (67.5)	25 (32.5)	0.03
HE-	47 (82.5)	10 (17.5)	
Adjuvant chemotherapy			
Yes	37 (78.3)	15 (21.7)	0.34
No	72 (71.2)	20 (28.8)	
Postoperative radiation			
Yes	6 (76.3)	3 (23.7)	0.51
No	103 (66.7)	32 (33.3)	

CEA Serum concentration of carcinoembryonic antigen. ITC- One patient with “micrometastasis” is excluded in this group.

(La HE+, n=32) was compared using the Kaplan–Meier method, the 5-year overall survival rates were 82.9, 76.1, and 38.0%, respectively. Apparently, survival of patients with La HE+ was significantly worse than the other two groups (p<0.0001). However, the survival rates of patients with La ITC+ and La IHC- were comparable and showed no significant difference (p=0.25; Fig. 3).

Multivariate analysis (Cox hazard model) of the 144 La HE- patients (excluding one patient with lateral lymph node “micrometastasis”) was performed to ascertain prognostic factors for survival (Table 4). This result showed that perirectal lymph node HE metastasis status was significant prognostic factors (p=0.001 and risk ratio 2.3), but La ITC+ status was not a significant prognostic factor (p=0.25 and risk ratio 1.2).

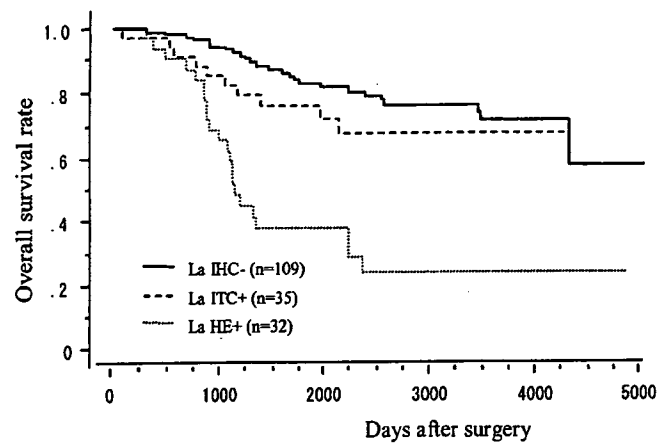


Fig. 3 Survival curves of rectal cancer patients with lateral lymph node dissection stratified according to status of lateral lymph node metastases. Patients with HE+ lateral lymph node is significantly worse than the others (p<0.0001). Survival rate of patients with ITC+ lateral lymph node is not significantly different from those of patients with IHC- lateral lymph nodes (p=0.25)

Discussion

The relationship between lymph node micrometastasis and prognosis in colorectal cancer remains controversial. According to Greenson et al. [15], a difference in the prognosis of Dukes’ B colon cancer exists with respect to IHC+ lymph nodes. Several other studies have documented that IHC+ status is correlated with prognosis and local recurrence [16, 17]. However, Isaka et al. [17] found no significant difference in survival rates between IHC+ and IHC- when sufficient numbers of dissected lymph nodes were examined. Later studies also found no significant difference in survival rates when the number of dissected

Table 4 Multivariate analysis (Cox model of regression) of prognostic factors in 144 rectal cancer patients

	Hazard ratio	95%CI	p value
Gender			
Female/male	1.3	0.9–2.0	0.15
Serum CEA			
<5/> or =5	0.8	0.5–1.2	0.32
Histology			
Well, moderate/poor, mucinous	0.6	0.3–1.2	0.16
Depth of tumor invasion (pT)			
t3, t4/t2	1.4	0.9–2.1	0.13
Adjuvant chemotherapy			
Not done/done	1.3	0.8–1.7	0.44
Postoperative radiation			
Not done/done	1.7	0.8–7.5	0.19
Lateral lymph node			
ITC+/IHC-	1.2	0.8–1.9	0.25
Perirectal lymph node			
HE+ / HE-	2.3	1.5–4.1	0.001

lymph nodes was high [26], and at present, no general consensus has been reached on this issue.

On the other hand, the status of micrometastasis in lateral lymph nodes of rectal cancer patients remains largely unknown because of the restricted usage of this radical dissection method in countries other than Japan. Shimoyama et al. [21] previously reported that micrometastasis in lateral lymph nodes is a prognostic factor and that the survival rate of patients with micrometastasis is similar to that of patients with overt nodal metastasis. In the present study, however, we found that ITC+ micrometastasis in lateral lymph nodes of rectal cancer patients had no prognostic significance. There are several possible explanations for this discrepancy between the two studies. One likely reason is the difference in the number of dissected lymph nodes and the number of patients. In Shimoyama's study, the number of dissected lateral lymph nodes was 13.6 per case, whereas in our study, 28.4 and 17.0 nodes per cases were dissected in lateral and perirectal lymph nodes. Tepper et al. [27] and Wong et al. [28] reported a significant difference in survival rates between patients with more than, and less than, 14 dissected lymph nodes, which was comparable to that for patients with HE+ overt lymph node metastasis. The good survival rate we found for patients with numerous dissected lateral lymph nodes is consistent with those previous reports [29, 30]. This suggests that when lymph node dissection is insufficient, which means incomplete histological examination of lymph node, the risk for overlooking HE+ lymph nodes increases. The second possible reason is the classification of micrometastasis. In the present study, almost all the minute metastases in lateral lymph nodes (97%) were identified as ITC by the surgical pathologists. In previous studies, no distinction was made between ITC and "micrometastasis" based on the UICC criteria, suggesting a difference in the extent of micrometastasis between the two studies.

Lateral lymph node metastasis is often regarded as a systemic disease, not a regional one [31, 32]. Indeed, hematogenous recurrent metastasis was common along with local recurrence in La HE+ patients. However, the 5-year survival rate in the present study was approximately 40% for La HE+ patients, as compared with 76.1% for La ITC+ patients and 82.9% for patients with IHC-, indicating relatively good survival of La HE+ patients. Lateral lymph node dissection was originally aimed at improving survival of locally advanced rectal cancer patients by decreasing local recurrence. In fact, the survival efficacy of lateral lymph node dissection due to locoregional control has been demonstrated by retrospective clinical studies in comparison with historical controls [12, 13]. Meanwhile, TME does not take into account lateral lymph node metastasis and would leave residual tumor cells in the pelvic cavity in a considerable number of cases (18.1% for La HE+ and 24.8% for La HE-

IHC+ metastasis). Several trials of TME, in combination with preoperative radiotherapy or adjuvant chemotherapy, proved to eliminate successfully those residual cells and improve locoregional control [9–11]. We therefore consider lateral lymph node dissection as an alternative for preoperative radiotherapy. However, the efficacy of lateral lymph node dissection as a therapeutic option could only be shown by prospective randomized clinical study. Adjuvant postoperative chemotherapy with 5-FU and leucovorin as key drugs for stage III colon cancer [33, 34] has been developing since the 1990s, but in Japan, the survival benefit of adjuvant chemotherapy has not yet been proved for rectal cancer. To evaluate the efficacy of systemic chemotherapy aimed at reducing both hematogenous and local recurrence, further randomized clinical trials of fluorouracil leucovorin-based postoperative adjuvant chemotherapy with and without lateral lymph node dissection are now ongoing in Japan.

In conclusion, the results of the present study have demonstrated a high incidence of ITC in HE- lateral lymph nodes of rectal cancer patients. However, the survival of patients with ITC+ lateral lymph nodes in whom a sufficient number of perirectal and lateral lymph nodes were dissected was comparable to that of patients with IHC- lymph nodes. These results suggest that ITC in lateral lymph nodes, if excised by sufficient dissection, does not affect the prognosis, unlike the case for HE+ metastases.

Acknowledgment The authors thank Mrs. H. Ban for expert technical assistance.

References

1. Creasman WT, DeGeest K, DiSaia PJ, Zaino RJ (1999) Significance of true surgical pathologic staging: a Gynecologic Oncology Group Study. *Am J Obstet Gynecol* 181:31–34
2. Bochner BH, Herr HW, Reuter VE (2001) Impact of separate versus en bloc pelvic lymph node dissection on the number of lymph nodes retrieved in cystectomy specimens. *J Urol* 166:2295–2296
3. Heidenreich A, Varga Z, Von Knobloch R (2002) Extended pelvic lymphadenectomy in patients undergoing radical prostatectomy: high incidence of lymph node metastasis. *J Urol* 167:1681–1686
4. Bacon HE, Sauer I (1950) Surgical treatment of cancer of the lower bowel. *Cancer* 3:773–778
5. Stearns MW Jr, Deddish MR (1959) Five-year results of abdominopelvic lymph node dissection for carcinoma of the rectum. *Dis Colon Rectum* 2:169–172
6. Havenga K, Enker WE, Norstein J, Moriya Y, Heald RJ, van Houwelingen HC, van de Velde CJ (1999) Improved survival and local control after total mesorectal excision or D3 lymphadenectomy in the treatment of primary rectal cancer: an international analysis of 1411 patients. *Eur J Surg Oncol* 25:368–374
7. Carlsen E, Schlichting E, Guldvog I, Johnson E, Heald RJ (1998) Effect of the introduction of total mesorectal excision for the treatment of rectal cancer. *Br J Surg* 85:526–529
8. MacFarlane JK, Ryall RD, Heald RJ (1993) Mesorectal excision for rectal cancer. *Lancet* 341:457–460

9. Delaney CP, Lavery IC, Brenner A, Hammel J, Senagore AJ, Noone RB, Fazio VW (2002) Preoperative radiotherapy improves survival for patients undergoing total mesorectal excision for stage T3 low rectal cancers. *Ann Surg* 236:203–207
10. Kapiteijn E, Marijnen CA, Nagtegaal ID, Putter H, Steup WH, Wiggers T, Rutten HJ, Pahlman L, Glimelius B, van Krieken JH, Leer JW, van de Velde CJ (2001) Preoperative radiotherapy combined with total mesorectal excision for resectable rectal cancer. *N Engl J Med* 345:638–646
11. Bonnel C, Parc YR, Pocard M, Dehni N, Caplin S, Parc R, Tiret E (2002) Effects of preoperative radiotherapy for primary resectable rectal adenocarcinoma on male sexual and urinary function. *Dis Colon Rectum* 45:934–939
12. Koyama Y, Moriya Y, Hojo K (1984) Effects of extended systematic lymphadenectomy for adenocarcinoma of the rectum—significant improvement of survival rate and decrease of local recurrence. *Jpn J Clin Oncol* 14:623–632
13. Sugihara K, Moriya Y, Akasu T, Fujita S (1996) Pelvic autonomic nerve preservation for patients with rectal carcinoma. Oncologic and functional outcome. *Cancer* 78:1871–1880
14. Mori T, Takahashi K, Yasuno M (1998) Radical resection with autonomic nerve preservation and lymph node dissection techniques in lower rectal cancer surgery and its results: the impact of lateral lymph node dissection. *Langenbecks Arch Surg* 383:409–415
15. Greenson JK, Isenhardt CE, Rice R, Mojzizik C, Houchens D, Martin EW Jr (1994) Identification of occult micrometastases in pericolic lymph nodes of Duke's B colorectal cancer patients using monoclonal antibodies against cytokeratin and CC49. Correlation with long-term survival. *Cancer* 73:563–569
16. Broll R, Schauer V, Schimmelpenning H, Strik M, Woltmann A, Best R, Bruch HP, Duchrow M (1997) Prognostic relevance of occult tumor cells in lymph nodes of colorectal carcinomas: an immunohistochemical study. *Dis Colon Rectum* 40:1465–1471
17. Isaka N, Nozue M, Doy M, Fukao K (1999) Prognostic significance of perirectal lymph node micrometastases in Dukes' B rectal carcinoma: an immunohistochemical study by CAM5.2. *Clin Cancer Res* 5:2065–2068
18. Jeffers MD, O'Dowd GM, Mulcahy H, Staggs M, O'Donoghue DP, Toner M (1994) The prognostic significance of immunohistochemically detected lymph node micrometastases in colorectal carcinoma. *J Pathol* 172:183–187
19. Adell G, Boeryd B, Franlund B, Sjobahl R, Hakansson L (1996) Occurrence and prognostic importance of micrometastases in regional lymph nodes in Dukes' B colorectal carcinoma: an immunohistochemical study. *Eur J Surg* 162:637–642
20. Cutait R, Alves VA, Lopes LC, Cutait DE, Borges JL, Singer J, da Silva JH, Goffi FS (1991) Restaging of colorectal cancer based on the identification of lymph node micrometastases through immunoperoxidase staining of CEA and cytokeratins. *Dis Colon Rectum* 34:917–920
21. Shimoyama M, Yamazaki T, Suda T, Hatakeyama K (2003) Prognostic significance of lateral lymph node micrometastases in lower rectal cancer: an immunohistochemical study with CAM5.2. *Dis Colon Rectum* 46:333–339
22. Sobin LH (2003) TNM: evolution and relation to other prognostic factors. *Sem Surg Oncol* 21:3–7
23. Sobin LH (2003) TNM, sixth edition: new developments in general concepts and rules. *Sem Surg Oncol* 21:19–22
24. Hermanek P, Hutter RV, Sobin LH, Wittekind C (1999) International Union Against Cancer. Classification of isolated tumor cells and micrometastasis. *Cancer* 86:2668–2673
25. Sobin LH, Wittekind C (2002) TNM classification of malignant tumors, 6th edn. Wiley, New York
26. Yasuda K, Adachi Y, Shiraiishi N, Yamaguchi K, Hirabayashi Y, Kitano S (2001) Pattern of lymph node micrometastasis and prognosis of patients with colorectal cancer. *Ann Surg Oncol* 8:300–304
27. Tepper JE, O'Connell MJ, Niedzwiecki D, Hollis D, Compton C, Benson AB 3rd, Cummings B, Gunderson L, Macdonald JS, Mayer RJ (2001) Impact of number of nodes retrieved on outcome in patients with rectal cancer. *J Clin Oncol* 19:157–163
28. Wong JH, Severino R, Honnebiel MB, Tom P, Namiki TS (1999) Number of nodes examined and staging accuracy in colorectal carcinoma. *J Clin Oncol* 17:2896–2900
29. Moriya Y, Hojo K, Sawada T, Koyama Y (1989) Significance of lateral node dissection for advanced rectal carcinoma at or below the peritoneal reflection. *Dis Colon Rectum* 32:307–315
30. Fujita S, Yamamoto S, Akasu T, Moriya Y (2003) Lateral pelvic lymph node dissection for advanced lower rectal cancer. *Br J Surg* 90:1580–1585
31. Greene FL, Page D, Fleming ID (2002) AJCC Cancer staging manual, 6th edn. Springer, Berlin Heidelberg New York
32. Enker WE, Thaler HT, Cranor ML, Polyak T (1995) Total mesorectal excision in the operative treatment of carcinoma of the rectum. *J Am Coll Surg* 181:335–346
33. (1995) Efficacy of adjuvant fluorouracil and folinic acid in colon cancer. International Multicentre Pooled Analysis of Colon Cancer Trials (IMPACT) Investigators. *Lancet* 345:939–944
34. Wolmark N, Rockette H, Fisher B, Wickerham DL, Redmond C, Fisher ER, Jones J, Mamounas EP, Ore L, Petrelli NJ et al (1993) The benefit of leucovorin-modulated fluorouracil as postoperative adjuvant therapy for primary colon cancer: results from National Surgical Adjuvant Breast and Bowel Project protocol C-03. *J Clin Oncol* 11:1879–1887

症例報告

前立腺浸潤下部直腸癌に対し直腸切断術および 前立腺全摘術を施行した1例

愛知県がんセンター中央病院消化器外科, 同 泌尿器科*

武藤 俊博 平井 孝 林 宣男* 金光 幸秀
小森 康司 安藤 公隆 加藤 知行

症例は58歳の男性で、血便を主訴とし近医で下部直腸腺癌と診断され当院紹介となった。腫瘍は直腸前壁の1/2周2型病変で、腫瘍下縁までの距離は歯状線より2cmであった。CT, MRI, 超音波内視鏡検査にて前立腺左側への浸潤が疑われた。術前全身検査にて遠隔転移なく、2005年5月、直腸切断術、前立腺全摘術および側方郭清を施行し治癒切除を得た。病理組織学的検査にて前立腺浸潤と、とくに左骨盤壁方向の剥離断端で癌の露出がないことが確認された。膀胱尿道吻合部の縫合不全があったが保存的に軽快した。左側の骨盤神経叢は切離したものの十分な膀胱機能が温存された。本術式は、浸潤が前立腺に限局した局所進行直腸癌に対して、surgical margin を確実に確保でき、かつ骨盤内臓全摘術を避けうる有用な方法であると考え報告した。

はじめに

前立腺のみに浸潤した局所進行下部直腸癌に対する前立腺全摘術は、報告例は少ないが骨盤内臓全摘術 (total pelvic exenteration; 以下, TPE と略記) を回避できる術式である。最近経験した1症例を報告し、本術式の適応と手技について考察した。なお、本文中の表記は大腸癌取り扱い規約第6版¹⁾に従った。

症 例

症例：58歳，男性

主訴：血便

現病歴：2004年4月血便に気づいたが、放置していた。2005年3月近医を受診し直腸癌と診断され当院紹介となった。

直腸指診：前～左壁に可動性不良の2型腫瘍を触知。腫瘍下縁まで肛門縁より4cmであった。

入院時血液検査所見：腫瘍マーカーはCEA 3.9 ng/ml, CA19-9 35.0U/mlと基準値以内であった。

注腸造影 X線検査所見：下部直腸（以下，Rb）前壁に2型腫瘍を認めた。

大腸内視鏡検査所見：歯状線より2cm口側に前壁1/2周，2型腫瘍を認め生検にて中分化腺癌と診断された。

CT所見：腫瘍は直腸間膜を越え，前立腺左側に浸潤が疑われた（Fig. 1）。

超音波内視鏡検査所見：直腸腫瘍の前立腺左側への浸潤が示唆された。

MRI所見：前立腺左側への明らかな浸潤を認め，腫瘍左側は膀胱下腹筋膜まで達していると考えられた（Fig. 2）。

遠隔転移を認めず前立腺への限局した浸潤を来した直腸癌と診断し，2005年5月，直腸切断術，前立腺全摘術および両側側方郭清を施行した。

手術所見：Rb, 2型, 1/2周, ant (35×60mm) 2型, P₀, H₀, N₁ (1群傍直腸リンパ節), Ai (prostate) であった。

手術手技：①下腸間膜動脈は根部で切離し，S状結腸を離断した。②直腸背側の剥離を進め，仙骨直腸靭帯を切開し挙筋上腔を展開した（Fig. 3 a）。③前方は直腸膀胱窩の腹膜を切開後精嚢と膀

<2006年11月22日受理>別刷請求先：武藤 俊博
〒464-8681 名古屋市千種区鹿子殿1-1 愛知県がんセンター消化器外科

Fig. 1 CT suggested the tumor infiltrating into the left side of the prostate (arrow heads).

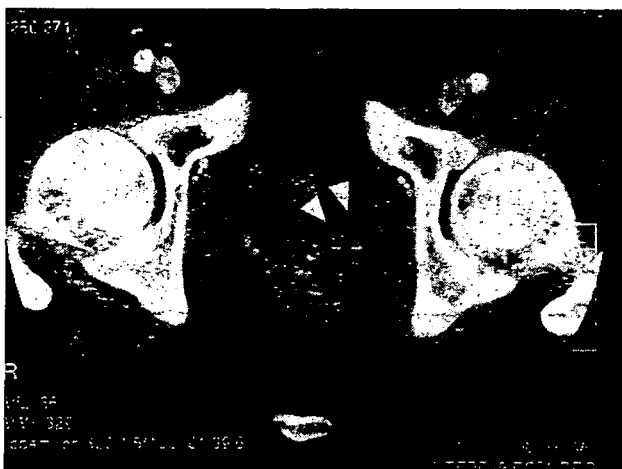
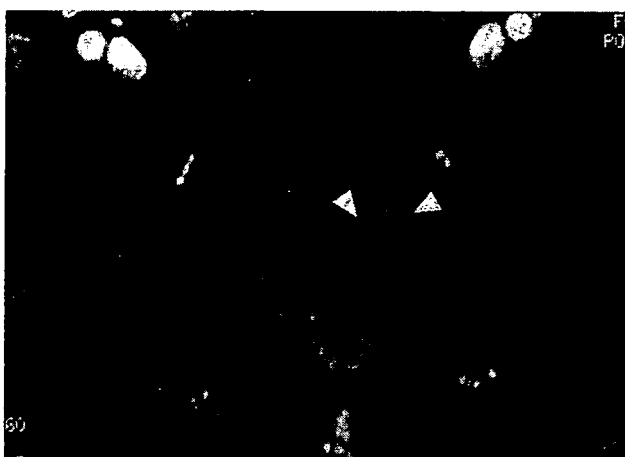
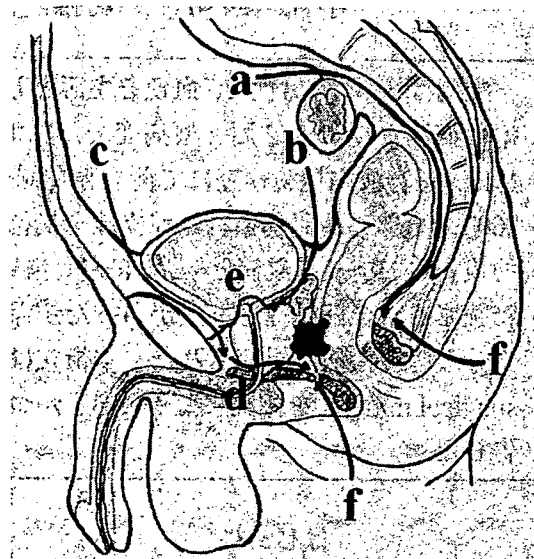


Fig. 2 MRI clearly indicated the tumor extension (arrow heads).



膀胱の間の剥離を前立腺まで進めた(Fig. 3b)。④右側は骨盤神経叢を温存し側方靭帯を切離した。⑤左側は直腸間膜を超えた浸潤と前立腺浸潤があるため、膀胱側腔を開放し内腸骨血管の外側に入った。左側下腹神経は上下腹神経叢下端で切離した。上膀胱動脈を温存しその末梢の内腸骨動脈は、骨盤神経叢とともに切除した。⑥ついで、泌尿器科医の協力のもと、前立腺周囲の処理に入る。右側も膀胱側腔を開放し dorsal venous complex を結紮切離後(Fig. 3c)、前立腺の遠位で外尿道括約筋を温存し尿道を切離した(Fig. 3d)。左側は下膀胱静脈(lateral venous complex)を内腸骨静脈からの分岐で切離した。右側は下膀胱動静脈および骨盤神経叢の、前立腺精嚢枝のみを切離し膀胱頸部

Fig. 3 Sagittal shema indicates the summarized procedure. a ; Opening of retrorectal space. b ; Dissection between seminal vesicle and bladder. c ; Opening of anterior and lateral space of the bladder and bunching of dorsal vein complex. d; Transection of urethra preserving external sphincter muscle. e ; Resection at the upper edge of prostate preserving internal sphincter muscle. f ; Perineal approach.



右側の neurovascular bundle は温存した(Fig. 4)。膀胱頸部にて内尿道括約筋を温存し尿道を切離した(Fig. 3e)。⑦会陰操作を加えて直腸と精嚢前立腺を一塊に摘出した(Fig. 3f)。⑧両側側方リンパ節郭清を完成させた。右側は静脈還流温存のため#262 郭清の際も、下膀胱静脈は温存した(Fig. 4)。最後に膀胱尿道吻合を施行した。出血1,300ml, 手術時間490分で無輸血であった。

病理組織学的検査所見：中分化腺癌が前立腺被膜に浸潤している(Fig. 5)。Ai (prostate), ly3, v2, n1 (1群 2/4, 2群 傍直腸リンパ節 0/7, #252 0/5, #253 0/0, #262R 0/1, #272R 0/5, #282R 0/9, #262L 0/1, #282L 6/0, #293L 0/1, #280 0/6), ow (-), aw (-), ew (-)であった。腫瘍は3時方向で直腸間膜を超えた浸潤があり、同部位の剥離面でewは1mmとなった。その外側は閉鎖腔の遊離空間であり surgical margin は確保されたと判断した。

術後経過：術後膀胱尿道吻合の縫合不全を来し骨盤膿瘍を形成したが、CTガイド下経仙骨的膿

Fig. 4 At the right side, pelvic nerve plexus and inferior vesical veins were preserved. r-CIA ; right common iliac artery. r-CIV ; right common iliac vein. r-IPA ; right internal pudendal artery. r-SVA ; right superior vesical artery. r-ON, A, V ; left obturator nerve, artery, vein. r-HN ; right hypogastric nerve. r-PN ; right pelvic nerve plexus.

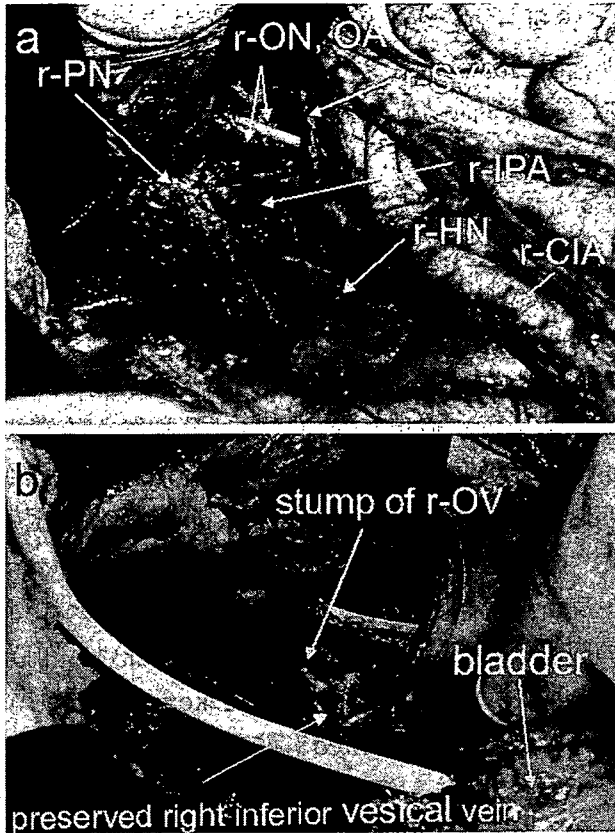
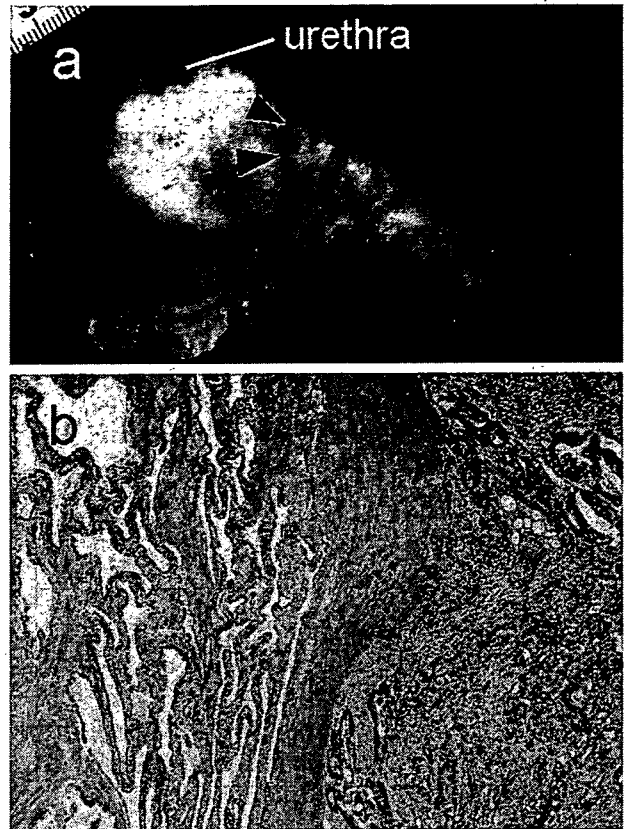


Fig. 5 Fixed transectional specimen correspond to axial CT showed infiltration into the left side of the prostate (A). Cancer cells microscopically infiltrated into the capsule of the prostate (B).



瘍ドレナージと膀胱カテーテル留置による持続導尿にて保存的に軽快した。術後2か月の時点で残尿もみられず自排尿に問題なく膀胱機能は温存された。尿失禁などの排尿障害も認めていない。UFT 500mg/日内服による術後補助化学療法を外来にて6か月間施行し、術後12か月の時点で腫瘍マーカー、画像診断上再発は認めていない。

考 察

直腸癌が精囊腺、前立腺、膀胱壁、子宮、膣など単一隣接臓器のみに浸潤している場合や、浸潤が疑わしい場合、TPEではなく surgical margin を確保できれば当該臓器のみを合併切除する術式は、TPE とは異なり不要な侵襲と重大合併症の回避および quality of life の向上につながる。膀胱温存手術の有用性は、1999年 Balbay ら²⁾がまとまっ

た症例数をもとに報告している。術前 TPE が必要と評価された局所進行直腸癌手術例 35 例(うち術前放射線療法施行は 27 例)において術中所見により、膀胱部分切除、前立腺全摘または部分切除、精囊切除、女性に対する子宮・膣合併切除などの膀胱温存手術を施行し、95% の高い病理組織学的治癒切除率を得た。そして、局所再発率 14%、3 年生存率 39% で、同時期に TPE を施行した 46 例と有意差はなかったとし、膀胱温存の有用性を主張した。

一方、最近では局所進行直腸癌に対する術前放射線化学療法による、56%³⁾、58%⁴⁾の down staging と、6~33%^{3)~5)}の病理学的完全消失が報告されている。これらの文献では Ai 症例の down staging と術式縮小の関連は不明であったが、合併切除を避けるうる方法として今後期待される補助療法である。しかし、down staging が得られず本術式を適用した場合膀胱尿管吻合部縫合不全の

Table 1 Reported cases that required combined en bloc prostatectomy for rectal cancer (1985-2005)

Case	Author	Year	Preoperative radiotherapy	Procedure	Lateral dissection	Curativity	Pathology	Leakage of urinary anastomosis	Dysuria	Local recurrence	Prognosis
1	our case 1	1994	(+)	APR	R, L	curA	squamous cell carcinoma, ai-prostate n3 (# 282L)	(+)	(+) severe, RU : 50ml	(+) 8M	8M, relapsed 12M, dead
2	Whig, J.N ⁹⁾	2003	(+)	LAR	NA	curA	NA	(-)	(±) mild, RU : NA	(-)	37M, lung metastasis resected
3	Whig, J.N ⁹⁾	2003	(+)	APR	NA	curA	NA	(+)	(±) mild, RU : NA	(-)	50M, disease free
4	Whig, J.N ⁹⁾	2003	(+)	APR	NA	curA	NA	(+)	(-) mild, RU : NA	(-)	15M, disease free
5	Nakao ¹⁰⁾	2002	(-)	APR	L	curA	adenocarcinoma a2 n1 (# 251)	(+)	(±) incontinence at night, RU : 0ml	(-)	14M, disease free
6	our case2 (current case)		(-)	APR	R, L	curA	adenocarcinoma, ai-prostate n1 (# 251)	(+)	(-) RU : 0ml	(-)	36M, disease free

APR : abdominoperineal resection. LAR : low anterior resection. SCC : squamous cell carcinoma. RU : residual urine. NA : not available.

リスクがさらに高まることが予測される。照射後の深達度評価の問題もあり、現段階では明らかなAi症例は腫瘍学的に必要な浸潤臓器切除がまず考慮されるべきと考える。

なお、1965年から1999年における当院での浸潤他臓器合併切除直腸癌は140例で⁶⁾、うちTPEは16例、治癒切除96例、遠隔転移症例を除いた非治癒切除13例であった。5年生存率は治癒切除かつ組織学的浸潤陽性で54%、治癒切除かつ組織学的浸潤陰性73%、局所再発率はそれぞれ19%、9%と至適合併切除であったと考えられる。しかし、前立腺全摘術の適用は本症例を含めて2例にとどまる。

Ike⁷⁾らはCT、超音波内視鏡検査にて腫瘍と前立腺の距離が2mm以内のT3⁸⁾直腸癌に対し超音波切開装置を使用した前立腺部分切除が有効であったと報告しているが、本症例のように浸潤が明らかな症例では、surgical marginの確保が困難で、その適応はないと考えられる。

局所進行直腸癌に対する前立腺全摘術についての報告は少ない。「直腸癌 (rectal cancer)」, 「前立腺全摘 (術) (prostatectomy)」をkey wordとして医学中央雑誌, PubMedによる1985年~2005年までの検索において、合併症、術後排尿機能、転帰に言及しているものに限ると2件4例のみ⁹⁾¹⁰⁾であった。根治性を確保しつつ排尿機能を温存する場合は神経を温存する必要があり手技が複雑となることと、前立腺浸潤は部分切除ですませたり、TPEを適応としていたため、これまでは本術式は外科医の選択肢に入れられていなかったと考えられる。ここでは、検索症例に当院で経験した2例を合わせた6例を検討した (Table 1)。

前立腺全摘術は直腸切断術と同時に施行されていることが多いが、低位前方切除も可能でありCampbellら¹¹⁾も本術式の概要を報告している。

全例病理組織学的に治癒切除が得られていた。側方リンパ節転移陽性の症例1以外は局所再発を認めていない。

合併症では膀胱尿道吻合部縫合不全が6例中5例と高頻度に発生しているが、すべて持続導尿などにて保存的に軽快している。術前放射線照射、

直腸切除による膀胱尿道吻合部の後方支持組織の喪失⁹⁾,膀胱血流の低下・うっ滞が原因と考えられている。

5例で自排尿可能であり,記述のあった2例では残尿もみられず膀胱機能は温存された。排尿障害は許容範囲内と考えられる。片側骨盤神経叢温存にもかかわらず腹圧排尿となった症例1のように,膀胱機能の十分な温存ができない場合もある。

今回,検索しえた文献では側方郭清,合理的な血行処理,膀胱機能温存のための工夫についての言及はなかったが,当院で経験した2症例より以下の点が手技的に重要と考えられた。

A₂以深の下部直腸癌では約20%の側方転移があり¹²⁾,我々は両側側方郭清が予防的に必要であると考えている。効果的な郭清と膀胱血行(特に静脈還流)の温存を両立させなければならない。動脈系の上膀胱動脈は腫瘍から距離があるので通常温存できる。一方,静脈系はdorsal venous complexが切断されるため側方リンパ節262番の郭清野に入る下膀胱静脈(lateral vein complex)を少なくとも片側は温存し膀胱の静脈還流を保つことが必要である。また,262番は腫瘍に近く最も転移率の高い側方リンパ節のため,この領域の徹底した郭清が両側において必要な場合,骨盤神経叢や膀胱静脈の温存は困難となり膀胱機能温存を前提とした本術式は適応外と考える。また,膀胱機能の十分な温存のためには尿道括約筋と骨盤神経膀胱枝の温存も必要となるため泌尿器科医の協力が欠かせない。

郭清と膀胱静脈還流温存はcontraversialな面もあり,どの程度の側方郭清が至適かは,今後明らかになるであろう側方郭清臨床試験(JCOG 0212)¹³⁾の結果を踏まえて検討する必要がある。

前立腺浸潤直腸癌に対する前立腺全摘術併施は,解決すべき課題は残るが,侵襲が大きくquality of lifeを損なう拡大手術を避け,根治性を落とすことなく浸潤範囲を合併切除しうる術式の一つと考えられる。

文 献

- 1) 大腸癌研究会:大腸癌取り扱い規約第6版. 金原出版,東京,1998
- 2) Balbay MD, Slaton JW, Torane N et al: Rationale for bladder sparing surgery in patients with locally advanced colorectal carcinoma. *Cancer* 86: 2212—2216, 1999
- 3) Schaffer M, Thoma M, Wilkowski R et al: Radiochemotherapy as a preoperative treatment for advanced rectal cancer. Evaluation of down staging and morbidity. *Onkologie* 25: 352—358, 2002
- 4) Kurt M, Ozkan L, Erçan I et al: Preoperative chemoradiotherapy in patients with locally advanced rectal cancer. *Hepatogastroenterology* 52: 1095—1100, 2005
- 5) Mehha VK, Poen J, Ford J et al: Radiotherapy, concomitant protracted-venous-infusion 5-fluorouracil, and surgery for ultrasound-staged T3 or T4 rectal cancer. *Dis Colon Rectum* 44: 52—58, 2001
- 6) 加藤知行, 平井 孝, 金光幸秀: 原発性直腸癌における隣接臓器合併切除. *消外* 26: 335—342, 2005
- 7) Ike H, Simada H, Fujii S et al: Extended abdominopeneal resection with partial prostatectomy for T3 rectal cancer. *Hepatogastroenterology* 50: 376—379, 2003
- 8) International union against cancer: TNM classification of malignant tumors. Sixth edition. Wiley-Liss, New York, 2002, p72—80
- 9) Wiig JN, Waehre H, Larsen SG et al: Radical prostatectomy for locally advanced primary or recurrent rectal tumor. *Eur J Surg Oncol* 29: 455—458, 2003
- 10) 中尾照逸, 内田寿博, 塚本義貴: 前立腺・精囊浸潤が疑われた進行直腸癌に対し膀胱温存手術を行った1例. *日臨外会誌* 66: 1125—1129, 2005
- 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) 平井 孝, 加藤知行: 直腸癌に対する側方郭清. 幕内雅敏, 杉原健一編. 大腸肛門外科の要点と盲点2. 文光堂, 東京, 2004, p126—130
- 13) 大腸がん外科グループ: 臨床病期II, IIIの下部直腸癌に対する神経温存D3郭清術に関するランダム化比較試験. 日本臨床腫瘍研究グループ. http://www.jcog.jp/study/12_ccsg/0212.htm

Laparoscopic Mesorectal Excision with Preservation of the Pelvic Autonomic Nerves for Rectal Cancer

Yosuke Fukunaga MD¹, Masayuki Higashino MD¹, Shinnya Tanimura MD¹, Satoru Kishida¹
Yushi Fujiwara¹, Akihito Ogata¹, H Osugi MD²

¹Division of Gastroenterological Surgery, Osaka City General Hospital, and

²Second Department of Surgery, Osaka City University, School of Medicine, Osaka, Japan

Corresponding Author: Dr. Yosuke Fukunaga, Department of Gastroenterological Surgery, Osaka City General Hospital, 2-13-22, Miyakojima-Hondoori, Miyakojima-ku, Osaka, 5340021, Japan

Tel: +81 6 6929 1221, Fax: +81 6 6929 1091, E-mail: YosukeF@aol.com

ABSTRACT

Background/Aims: Laparoscopic mesorectal excision with preservation of the autonomic pelvic nerves for rectal cancer including selected advanced lower rectal cancer is now challenging. The aims of the study were to assess the surgical results and short-term outcomes of this procedure prospectively.

Methodology: Seventy-four of 281 rectal cancer patients, since the introduction of laparoscopic colorectal surgery in our hospital, have undergone laparoscopic rectal surgery. The location of the tumor distributed in upper rectum, 33, middle, 22, and lower 19. The mesorectal excision with preservation of the autonomic pelvic nerves was performed for all the patients. The laparoscopic mesorectal excision was performed under 8 to 10 cmH₂O CO₂ pneumoperitoneum and lymph node dissection was performed along the feeding artery depend on individuals. Ipsilateral lateral lymph node dissection was added for

5 cases of advanced lower rectal cancer.

Results: Open conversion occurred in 4 cases, 2 of those were due to locally advanced tumors and 2 technical difficulties in transaction of the distal rectum. There were 15 postoperative complications, 7 anastomotic leakage (10.6%), 3 transient urinary retention (4.1%), 4 wound infection (5.3%), and 1 small bowel obstruction (1.4%). No mortality was recorded in this series. Time of operation was 203±54 min in mesorectal excision cases and 270±42 min mesorectal excision with lateral lymph node dissection cases. Blood loss was 92±90g and 276±66g respectively. The hospital length-of-stay was 11.7 days in average.

Conclusions: Laparoscopic mesorectal excision with preservation of autonomic pelvic nerves for rectal cancer patients including selected advanced lower rectal cancer is favorable.

KEY WORDS:

Laparoscopic surgery; Preservation of autonomic nerves; Mesorectal excision; Rectal cancer; Lateral Lymph-node dissection

INTRODUCTION

Recent advances in laparoscopic surgery have led to its use for various colorectal diseases and laparoscopic surgery is now routinely used to treat malignant disease. Initially, several reports of port site metastases were published. These were thought to represent exfoliation of cancer cells during the production of pneumoperitoneum and by handling of the tissues due to inexperience with the procedure (1-4). Similar findings have been documented experimentally (5). However, the number of reports of port site metastases has decreased. By minimizing or avoiding tumor manipulation, the use of laparoscopic surgery has now been extended to advanced cancers.

Acceptance of laparoscopic surgery for rectal cancer has met resistance, even though conventional rectal surgery is associated with a high rate of the local recurrence unless complete total mesorectal excision is performed (6). We have found that a magnified view of the deep pelvis via the laparoscopy allows total

mesorectal excision with less blood loss than open procedure. Some of the latest papers, even not randomized controlled trials, have supported the laparoscopic total mesorectal excision in terms of short-term outcomes (7,8). Even for the patients with lower rectal cancer, the laparoscopic view seems to give more benefits than conventional open surgery although some controversies exist concerning the lateral lymph node dissection (9-12).

This paper focused on the mesorectal excision for rectal cancer patients with preserving autonomic nerves under laparoscopic view including some selected advanced lower rectal cancer patients with lateral lymph node dissection. The operative variables and the short-term outcomes after this surgery were assessed.

METHODOLOGY

Three hundred and twenty-eight nonrandomized consecutive patients with a colorectal neoplasm have

undergone laparoscopic colorectal surgery in our hospital since the introduction of this procedure in 1998. During this period, of 281 rectal cancer patients, 74 (26.3%) were treated by laparoscopic anterior resection. The site of rectal neoplasm was defined according to the International Guidelines for Cancer Registrars (13). The protocol, which was changed about the indication in August 2002, was approved by the ethical committee of our hospital and patients gave informed consent. In the first edition of protocol, indication of laparoscopic surgery for rectal cancer was limited to all cases of upper and middle site and early cancers of lower site, but in the new edition that was extended to selected advanced cancers of lower site. The selected cases were identified as tumor confined to the proper muscle layer, occupying within half of the circumference, and without preoperative lymph node metastasis in the lateral region under thin-slice pelvic contrast-enhanced CT exam or MRI. In the absence of specific contraindications to laparoscopy, patients were selected for laparoscopic surgery based on the following criteria: elective surgery, absence of occlusion. Neither morbid obesity, prior major lower abdominal surgery, nor tumor occupying the pelvic space was considered a contraindication to laparoscopic surgery. Partial mesorectal excision was performed for the patients with upper rectal cancer, and a total excision for those with middle and lower. We attempted to preserve the hypogastric nerve and pelvic nerve plexus in all cases. No lymph node dissection of the lateral region was performed for the upper and middle rectal cancers. Ipsilateral lateral lymph node dissection preserving the autonomic nerves was performed in selected lower rectal cancer cases. The bowel reconstruction was basically performed primarily by the double stapling technique. For the middle and lower rectal cancer patients with a satisfactory length of sigmoid colon, J-pouch formation was performed for reconstruction. No bowel restoration of discontinuity was performed for selected lower rectal cancer patients.

Clinical parameters analyzed included patients' characteristics, operative variables, and short-term outcomes. Operative variables included type of operation, blood loss, time of operation, and conversion rate. Conversion to laparotomy was defined as unplanned incision. Short-term outcomes included days needed to regain bowel function, hospital length-of-stay, postoperative morbidity, and 30-days mortality.

Operative Technique

Laparoscopic anterior resection was performed using 5 ports with 8 to 10 cmH₂O of CO₂ pneumoperitoneum. The medial aspect of the rectosigmoid mesocolon was incised to mobilize the retroperitoneal space, preserving both hypogastric nerves. As lymphadenectomy in the mesenteric arterial direction was individualized on a case-by-case basis, the pelvis was approached following the division of the main artery. The rectosigmoid colon was pulled cranially after continuing the dissection laterally, providing excel-

lent exposure of the pelvic space (**Figure 1a**). The reflection of the peritoneum was incised on the anterior wall of the rectum, resecting Denonvillier's fascia to expose the seminal vesicle in men or the vaginal wall in women, and the rectum was mobilized distally so that levator ani was exposed circumferentially (**Figure 1b**).

For the selected lower rectal cancer cases, ipsilateral lateral lymph node dissection on the predominant side of the tumor was added. The lateral lymph node dissection was developed, exposing the internal and external iliac arteries. The internal iliac artery was dissected peripherally, ensuring the superior gluteal artery, obturator artery, inferior vesical artery, and middle rectal artery (**Figure 2a**). Lateral dissection was continued to resect all adipose tissue, including lymph nodes, exposing the obturator nerve to the obturator foramen (**Figure 2b**).

RESULTS

Demographics (Table 1)

74 patients divided into 49 males and 25 females according to gender and of whom median age was 66 ranging from 42 to 94, were recruited. The location of the tumor distributed as 33 upper rectum (44.6%),

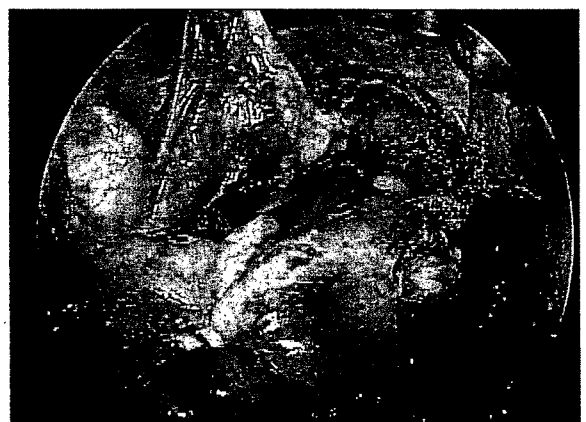


FIGURE 1a The rectosigmoid colon is pulled cranially by using a monofilament ligature.



FIGURE 1b The rectum is entirely mobilized and the levator ani is exposed; total mesorectal excision.