TABLE II. Univariate and Multivariate Prognostic Analysis in (A) 73 Curative YCC (Learning Set) and (B) 144 Curative YCC (Validation Set)

		Univariate analysis		Multivariate analysis		
Variables		DSS (5 years)	*P*-value	HR	95% CI	*P*-value
(A)						
Histology	Differentiated/poorly differentiated	83%/50%	0.0247	71.8	6.372–810.327	0.0005
pN factor	Absence/presence	98%/50%	<0.0001	60.3	5.658–643.017	0.0007
K-ras mutation	Absence/presence	90%/57%	0.0014	5.5	1.192–25.480	0.0289
PreoperativeCA19-9 value	Low/high	83%/62%	NS	1.1	0.210–6.113	NS
Preoperative CEA value	Low/high	83%/76%	NS	0.9	0.244–4.036	NS
Sex	M/F	79%/84%	NS	0.7	0.196–2.646	NS
Vascular permeation	Absence/presence	92%/79%	NS	0.4	0.041–4.431	NS
pT factor	pT0, 1, 2/pT3, 4	100%/75%	NA			
Lymphatic permeation	Absence/presence	100%/77%	NA			
(B)						
pN factor	Absence/presence	96%/69%	<0.0001	4.3	1.090–17.131	0.0373
Preoperative CA19-9 value	Low/high	87%/62%	0.0041	3.9	1.119–13.720	0.0326
Vascular permeation	Absence/presence	97%/80%	0.0144	3.7	0.453–31.022	NS
K-ras mutation	Absence/presence	90%/76%	0.0236	3.6	1.339–9.948	0.0114
Sex	M/F	84%/87%	NS	1.3	0.559–4.291	NS
Preoperative CEA value	Low/high	87%/79%	NS	0.7	0.204–2.409	NS
pT factor	pT0, l, 2/pT3, 4	98%/79%	0.0064	0.3	0.032–3.370	NS
Family history	Absence/presence	87%/86%	NS			
Histology	Differentiated/poorly differentiated	85%/100%	NA			
Lymphatic permeation	Absence/presence	100%/79%	NA			

DSS, disease-specific survival; NS, not significant; NA, not assessible.

and HR = 3.6; $P = 0.0114$, respectively) independently of TNM factors and/or tumor markers, respectively (Table II).

Curatively Resected Stage III YCC Patients With K-*ras* Mutations Included More Patients With Metachronous Distant Metastasis of CRC

Since K-*ras* mutations were identified as a prognostic factor independent of TNM stage-determining factors, sub-analysis was performed by stage. As a result, K-*ras* mutations had prognostic relevance only in stage III in both learning sets (n = 26, $P = 0.011$, Fig. 4C) and validation sets (n = 55, $P = 0.024$, Fig. 4D). In the 81 stage III YCC patients who were curatively operated (learning plus validation sets), the presence of a K-*ras* mutation had significant predictive value in prognosis ($P = 0.002$; Fig. 5B). Even when stage III YCC patients were subdivided into JCCC N1 and N2 cases, patients with no K-*ras* mutation showed ~80% survival rate (Fig. 5C,D), a result much better than expected for ordinary stage III CRC.

In the 81 stage III YCC cases, K-*ras* mutation was not associated with the administration of adjuvant chemotherapy; 75 patients (93%) underwent 5-FU-based adjuvant chemotherapy (concomitant administration of leucovorin/isovorin, n = 16 or CPT-11, n = 1), orally (n = 59), or intravenously (n = 16). Twenty-nine of the 75 patients had a K-*ras* mutation (39%), while six patients who did not undergo adjuvant chemotherapy included four patients with K-*ras* mutation (67%; no statistical difference), and there was no significant difference in prognosis between the patients with adjuvant chemotherapy and without it (the follow-up periods ranged from 2 to 60 months).

K-*ras* mutations did not have any predictive value in stage 0/I/II/IV patients examined in the current study. Among the 66 stage 0/I YCC patients, only one with a K-*ras* mutation died due to recurrence. Of the 70 stage II YCC patients, 3 died due to recurrence, in which 20 (10%) had a K-*ras* mutation, and 1 of 49 (2%) did not (not statistically significant). In the 19 stage IV YCC patients, K-*ras* mutation was not associated with the survival status (data not shown).

DISCUSSION

The current study separated YCC patients without a K-*ras* mutation from other CRC patients from a prognostic viewpoint, and found that they showed the best prognosis among all CRC. This finding was unlikely to have resulted from the different distribution of stages within each group that were separated in terms of age and tumor location, because the prognostic relevance of K-*ras* mutation was proven even after adjusting for stage in multivariate analysis (Table II). In particular, stage III YCC patients without K-*ras* mutations clearly showed the best prognosis (~80%) as compared to other stage III CRC patients (50–60%; Figs. 2 and 3). On the other hand, in stage II YCC, a mutated K-*ras* indicated a poorer prognosis (90%) than wild-type K-ras (98%), with very rare recurrence (only 3 patients) among the 69 cases. For stage II YCC patients, we could not find a significant difference in the prognostic value, putatively due to the small number tested and small number of events included, and this should be confirmed in the future. Prognostic markers of stage II CRC, such as DNA ploidy [34], genomic imbalance [35], and microsatellite instability (MSI) [36], have been recognized as vital indicators in patient selection for post-operative adjuvant chemotherapy.

Stage III YCC patients without K-*ras* mutations had a 5-year survival rate of about 80% after surgery, comparable to that of stage II CRC patients [35]. This finding suggested that stage III YCC without a K-*ras* mutation can be recognized as stage II CRC from a prognostic viewpoint, and treated similarly, including adjuvant chemotherapy. For stage III CRC, oxaliplatin-including regimens (FOLFOX or FLOX) were demonstrated to be more effective than surgery alone in the MOSAIC trial [37] and the NSABP C-07 trial [38]; however, an adjuvant effect was achieved in only 6–7% of stage III patients or possibly in high-risk stage II patients [37]. As FOLFOX is expensive and labor-intensive, and also has serious complications, the selection of patients who truly need potent adjuvant chemotherapy is eagerly anticipated. The present study indicates that K-*ras* mutations could be a biomarker for patient selection in stage III CRC. RASCAL-2 is a larger version of RASCAL [39], the largest survey (at that time) of K-*ras* mutations in primary tumor tissues, which included data collected

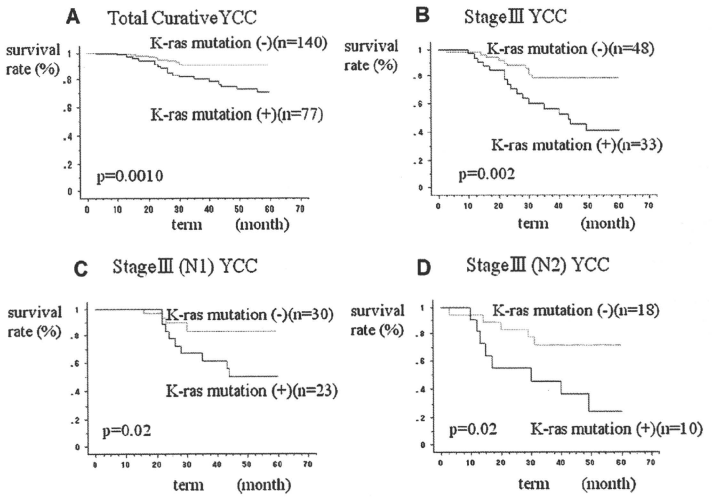

Fig. 5. Prognostic significance of K-*ras* mutation in stage III YCC in curable cases. **A**: Validation of significant difference in survival comparison between presence and absence of K-ras mutation in 217 YCC cases ($P = 0.0010$). **B**: Significant difference in survival according to K-ras mutation in stage III (Dukes C) YCC ($P = 0.002$). **C**: Significant difference in survival according to K-ras mutation in stage IIIA (N1) YCC ($P = 0.02$). Note that stage IIIA (N1) YCC patients without a K-ras mutation had more than an 80% survival rate. **D**: Significant difference in survival according to K-ras mutation in Stage IIIB (N2) YCC ($P = 0.02$). Note that Stage IIIB (N2) YCC patients without K-ras mutation had ~70% survival rate.

by groups from 13 countries on the prognostic importance of K-*ras* mutations. RASCAL-2 examined over 4,000 CRC patients and revealed that K-ras mutations had prognostic significance in stage III CRC [40]. RASCAL-2 may be so huge that K-*ras* mutations would have a prognostic impact even if patients were not limited to YCC; however, our results revealed that K-ras mutations did not have any significant impact on prognosis in CRC other than YCC (data not shown). RASCAL-2 showed that only one mutation on codon 12, glycine to valine, found in 8.6% of all patients, had a statistically significant impact on failure-free survival ($P = 0.004$, HR 1.3) and overall survival ($P = 0.008$, HR 1.29), suggesting that this mutation appeared to have a greater impact on outcome in stage III CRC cancers (failure-free survival, $P = 0.008$, HR 1.5; overall survival $P = 0.02$, HR 1.45) than in stage II tumors (failure-free survival, $P = 0.46$, HR 1.12; overall survival $P = 0.36$, HR 1.15). Our SSCP analysis did not reveal the full profile of each mutation, and we would like to elucidate such associations in the near future.

CRC has been recently proposed to originate in two pathways, MSI and chromosomal instability (CIN) [41]. MSI shows a diploid pattern of DNA content, while CIN has an aneuploid pattern. MSI is more characteristic of proximal colon cancer [42] and young CRC [43], which made us speculate that YCC includes more MSI cases than other CRC. Moreover, a K-*ras* mutation was found in only 13% of MSI CRCs [44], indicating that the mutation is more characteristic of CIN than MSI. Hence, we suppose that YCC without a K-*ras* mutation and with a good prognosis largely reflects MSI, consistent with a report that MSI showed a better prognosis than non-MSI [45]. Nevertheless, CRC sometimes harbors both phenotypes (MSI and CIN), and CIN is the dominant phenotype for aneuploidy [46], which is why K-ras mutation, due to its phenotypic dormancy, clearly showed a poor prognosis in YCC in the current study. We are interested in the relationship of both K-ras mutation and the MSI status with patient prognosis in YCC. On the other hand, even in YCC without a K-ras mutation, several patients had a poor prognosis. This may have been caused by B-*raf* mutation, which has a dismal prognosis in microsatellite-stable CRC [47], and such cases can be included in YCC without K-ras mutation. K-ras mutation might be a marker for MSI and not a prognostic indicator itself. Allowing for these findings, we are planning to profile MSI/B-*raf* mutations in combination with the K-*ras* mutational status in order to clearly explain the prognostic status of YCC in stage III.

We interpreted our results to mean that YCC without a K-*ras* mutation represents patients with a normal K-*ras* pathway. K-*ras* pathway activation may be closely associated with prognosis in CRC, and could be a therapeutic target for most CRC cases (except YCC without K-*ras* mutation). Patients with an abnormal K-*ras* pathway through the activation of either upstream or downstream oncogenes, such as EGFR [48], PI3K [49], and B-raf [50], are similar to those with K-*ras* mutations from a biological viewpoint because the K-*ras* pathway is similarly activated. On the other hand, patients with a normal K-*ras* pathway may show biologically different behavior from those with K-*ras* mutations because the K-*ras* pathway is not activated.

As an optimal strategy for solid tumors, attention has recently focused on molecular therapies by identifying genetic alterations that have been of prognostic value [7–10]. On this basis, the authors suggest the K-*ras* pathway as a therapeutic target for CRC. On the other hand, the K-*ras* mutational status was recently demonstrated to

have predictive value for sensitivity against EGFR inhibition, a newly developed CRC molecular target [51–54]. As neutralizing EGFR antibody is effective even against far-advanced CRC without K-*ras* mutation, the development of new treatments, including adjuvant chemotherapy, is eagerly anticipated. On the other hand, CRC with K-*ras* mutation proved ineffective by EGFR inhibition [53]. About 75% CRC cases with K-ras mutation had co-mutated PI3K [49] and, in such cases, downstream inhibition of both B-raf and PI3K may efficiently regulate CRC cells.

None of the rectal patients in the current study underwent radiotherapy either pre- or post-operatively, which may not represent the standard of care of rectal cancer worldwide, and perhaps would effect the outcome of the analysis. In rectal cancer, we would thus examine the K-ras mutation status and prognosis in such patients who undertake the standard therapy in the near future. Actually, we recently adopted neoadjuvant chemoradiotherapy for localized advanced rectal cancer before surgery [55,56]. Even if molecular target therapy such as anti-EGFR MoAb is used, CRC at stage IV has a dismal prognosis [51,52,57] and almost all patients will die of disease progression. That is why improving the prognosis of CRC depends upon improving treatment for curable cases, which includes adjuvant chemotherapy. The most promising treatment strategy for CRC is therefore to develop tailor-made adjuvant chemotherapy using novel indicators on the basis of oncogenic mutational profiles as in the present study.

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特集：Oncologic emergency の診断と治療 II

大腸癌イレウスに対する金属ステント留置術

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要旨：大腸癌イレウスは，oncologic emergency として従来緊急手術の適応であるが，最近では金属ステント（Expandable Metallic Stent：EMS）留置術を含めた経肛門的な減圧術が登場し，情況が変化している。経鼻イレウス管などでは減圧が不良である大腸癌イレウスを経肛門的に減圧し待機的に手術を行う事が可能になり，手術成績の向上，患者の QOL（quality of life）の向上とともに，医師・医療従事者の QOL の向上にも寄与している。挿入率は 9 割以上，臨床的有効率も 9 割程度，挿入時合併症は約 5% と高い有効性と安全性が報告されている。ただし，長期的には逸脱や再狭窄もおのおの約 1 割程度認められる。今後左側大腸癌による狭窄・閉塞に対する第一選択的な手技として普及していくと思われる。

【索引用語】 大腸癌イレウス，大腸狭窄，金属ステント，Self-Expandable Metallic Stent

はじめに

大腸癌イレウス・Malignant colorectal obstruction の頻度は全大腸癌の 3.1～15.8% と報告されており，現在の大腸癌の頻度の増加に伴い，決してまれな病態ではない[1]。診断は，腹部単純 X 線検査での狭窄部位から口側の大腸の拡張像からほぼ診断が可能であり，ガストロ注腸または大腸内視鏡で確定診断を得ることができるため比較的容易である。

治療としては大腸癌における oncologic emergency として，大腸癌穿孔とともに従来緊急手術の適応であり，しかも術後の合併症が多い病態から大腸外科医の悩みの種である。しかし最近では金属ステント（Expandable Metallic Stent：以下，EMS）留置術を含めた経肛門的な減圧術が登場し，情況が変化している。経鼻イレウス管などでは減圧が不良である大腸癌イレウスを経肛門的に減圧し待機的に手術を行う事が可能になり，手術成績の向上，患者の quality of life（以下，QOL）の向上とともに，医師・医療従事者の QOL の向上にも寄与している。大腸癌イレウスの治療方針を考える上で二つの病態が考えられる。狭窄を呈する大腸癌であるが根治的な手術が可能である場合と，多発遠隔転移などで根治的な治療は困難であるが全身状態の改善のためにイレウスの解除が必要な場合である。

I．根治的手術の可能な大腸癌イレウス

イレウスの初期治療としての消化管内減圧は，まず胃管または経鼻イレウス管などの経口的腸管減圧術にて治療されることが多い。しかし大腸狭窄に伴うイレウスでは個々の症例や施設により異なるが，一般的には経鼻的な減圧が困難であり，緊急手術を行わざるを得ない状況が多く，右側では腫瘍から口側の結腸を全切除し回腸と肛門側の吻合を，左側では腫瘍切除と口側結腸の人工肛門を伴う Hartmann 手術が行われる[2]。しかし最近では，内視鏡技術の進歩とともに経肛門的減圧手技が登場し普及してきている[3]（図 1）。

大腸癌イレウスの場合は，イレウスの解除とともに大腸癌手術の根治性と手術の安全性の向上を考えなければいけない。大腸癌イレウスの状態で手術をすると汚染手術となり，一期的に吻合した場合は縫合不全などの術後の合併症が多いため，できるだけ保存的にイレウスを解除し緊急手術を回避して，全身状態の改善を待ってから待機的手術をするのが理想である。

経肛門的なアプローチによる術前イレウス解除術としてわれわれが行っている EMS 留置術[4]と経肛門的減圧チューブ[5]がある。

1．術前金属ステント留置術

狭窄型大腸癌の術前処置としての金属ステント留置法は，従来術前処置に難渋し，汚染手術の危険性が高く，二期的手術を選択せざるを得ない左側の狭窄型大腸癌に対して，短期的に EMS を挿入し内瘻化し，狭窄解除する手技である。われわれが 1993 年 11 月に，Stent Endoprosthesis for Colorectal Cancer（以下，SECC）として開発[4]し，それ以降イレウスを含めた通過障害を伴う全周性狭窄型左側大腸癌に対して施行しており，日本消化器内視鏡学会のガイドライン[6]にも記載されている。

2．使用している EMS

現在，本邦で大腸専用の EMS は入手できない。入手可能な消化管用の EMS は Ultraflex™ esophageal

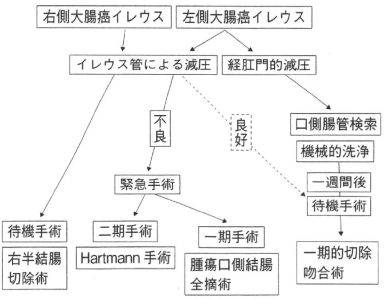
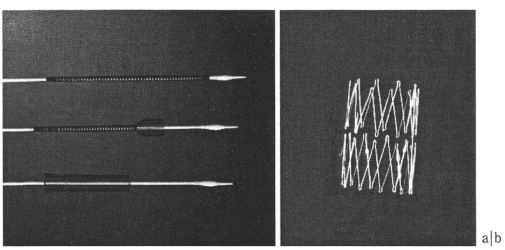


図1 大腸癌イレウスの治療法



a|b

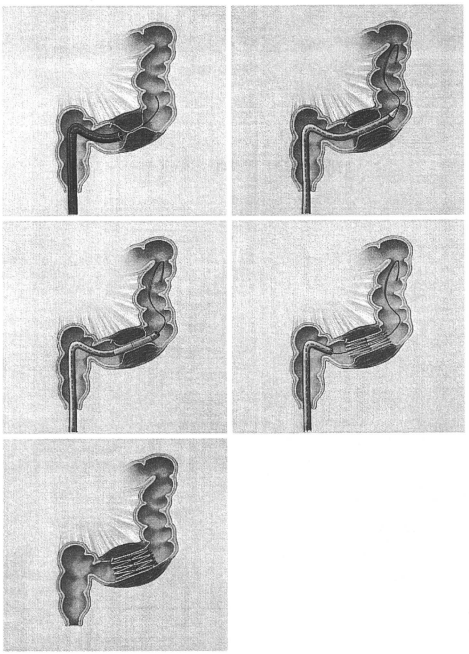
図2 本邦で市販されている消化管用金属ステント EMS
a：Ultraflex™ Boston Scientific 社製 内径 18mm，長さ 100 or 150mm。
b：Z-stent™ Cook 社製 内径 30mm，長さ 50 or 75mm。

stent（Boston 社製）と Z-stent™（Cook 社製）である（図2）。いずれも self-expandable metallic stent 自己拡張型金属ステントである。サイズは狭窄の長さによって異なるが，一般的に口径 18～22mm，長さ 70～150mm のものが使用される。なお，欧米では大腸に対しては鉗子孔を通過する Trough the scope（TTS type）の EMS が一般的である。現時点では個人輸入でのみ購入が可能で，使用は困難である。現在各メーカーと PMDA（独立行政法人医薬品医療機器総合機構）などが早期導入に向けて活動している。2009 年に胃十二指腸への EMS が認められたので大腸用 EMS も数年以内には国内で使用可能になると思われる。

3. EMS 留置法（図3）

前処置はとくに不要であるが，残便や狭窄の部位により適切な浣腸を施行する。基本的に sedation は行っていない。まず大腸内視鏡を挿入し狭窄部を確認する。透視下でも狭窄部位が明確になるように，狭窄部肛門側を金属クリップにてマーキングする。その後内視鏡よりガイドワイヤーを挿入し狭窄部より充分口側に進める。ガイドワイヤーは先端の柔軟なものを使用し，シースを用いて狭窄部に誘導する（図3a）。次にガイドワイヤーを残したまま，内視鏡を抜去しイントロデューサーをガイドワイヤーに沿い挿入する（図3b）。Ultraflex™ の場合はあらかじめ EMS がイントロデューサーに組み込まれており，マーカーで EMS の位置を確認後固定糸を牽引することで self expanding する（図3c）。EMS が狭窄部を拡張するとともに EMS は固定される（図3d）。引き続き，ガストログラフィン®（アミノトリゾ酸ナトリウムメグミン meglumine sodium amidotrizoate）による造影と大腸内視鏡観察にて内腔を確認し，EMS の位置，出血・穿孔等の合併症のないことを確認し手技は終了する。

本法施行後は運動制限はなく，施行直後より頻回の泥状便が排出されることが多い。腹部単純 X 線検査にて内腔が十分に確保されたことを確認した上で，数日後にバリウムにて注腸検査を施行し，口側腸管の情報を得る。可能であれば経口摂取も開始する。約1週間後に通常と同様に十分な機械的前処置を行い手術を行う（図4）。



a | b
c | d
e |

図3 EMS留置法
a：狭窄部肛門側マーキング後ガイドワイヤーを挿入。
b：内視鏡抜去，イントロデューサーをガイドワイヤーに沿い挿入。
c：マーカーでEMSの位置を確認後リリース。
d：EMSが拡張固定。

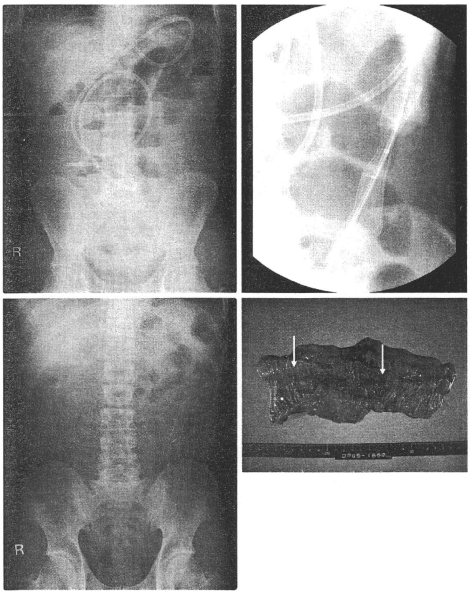
4. SECC：EMS留置術の適応と成績

SECCの適応は，狭窄部位が左側大腸である症例で，イレウスを含めた全周性狭窄による通過障害の症状が強いものである。右側の大腸癌イレウス症例では，経鼻イレウス管で小腸減圧を行えば，腫瘍の口側を切除可能であり経肛門的減圧の必要性はない。

下部直腸癌ではEMSが切除線にかかると縫合不全の原因となるために適応外であり，経肛門的減圧チューブか二期的手術の適応である。

本法では厚生労働省の認可や保険適用がないために，使用する場合は十分なインフォームドコンセントのもとに，購入費は各施設の負担となる。可能な限り院内の倫理委員会にかけた方がよい。

現在までの当科の成績は97例にSECC施行を試み，89例92%に挿入可能で，狭窄解除率98%と良好な成績であった。留置不可だった症例の腫瘍占居部位は主に下行S状結腸曲（SD junction）周囲で，横行結腸，直腸は全例留置可能であった。留置例のEMS留置から手術までの期間は，最長16日間平均6.3日であった。いずれも偶発症なくポリエチレングリコール液による機械的洗浄を行う事ができた。SECCの偶発症として，97例中，挿入時穿孔3例（3.1%，部位はいずれもS状結腸），挿入時逸脱3例（3.1%，部位は下行結腸，S状結腸，上部直腸）であった。それ以外に，術中微少穿孔1例（S状結腸），術中逸脱1例（上部直腸）も経験したが，これらはいずれも臨床的にはとくに問題とはならなかった。穿孔・逸脱症例のうち緊急手術となったのは4例4.1%であったが，元来が緊急手術の必要なイレウス症例であり，手技導入による予後の悪化はないと判断している。世界の大腸EMS留置報告集計での術前EMS留置の成績は，留置成功率が92%，臨床的有効率が85%で，そのうち95%に一期的手術が行われ，偶発症として，留置時穿孔5%，留置時逸脱3%が認められる[7]。出血は全例留置直後に



a | b
c | d

図 4 術前 EMS 留置術が有効であった症例
40 歳代，男性．下行結腸癌イレウス。
a：腹部単純 X 線像立位：土曜日イレウスにて来院し即日イレウス管挿入するも改善せず。
b：EMS 留置透視像：月曜日に EMS 留置施行，イレウス管抜去。
c：腹部単純 X 線像臥位：火曜日にイレウス解除を確認後飲水開始，木曜日食事開始。
d：手術検体（中央に EMS）：挿入後 8 日目にポリエチレングリコール液で機械的前処置を行い 9 日目に開腹で手術を施行，手術検体で多少口側の浮腫を認めるが，腸管の拡張はなかった。

少量認めるが一過性であり全身状態に対する影響はない。約半数の患者が留置部の軽度の疼痛・不快感を訴えるが，鎮痛剤を必要とする例はなく，日数の経過とともに漸減してくる。

大腸癌イレウスに対して SECC の後に手術を待機的に行うと緊急手術を施行した群と比較して明らかに短期的な手術成績を向上させる事ができる。特に感染症の減少は著明である[8]。

5. SECC：EMS 留置術と経肛門的減圧チューブとの比較（表 1）

経肛門的減圧チューブは，経肛門イレウス管として市販されている。挿入成功率が 60 ～ 100%，挿入可能例のイレウスの解除率は 80 ～ 100%と良好な成績が報告されている[9]。しかしガイドワイヤーによる穿孔（0 ～ 6%）やイレウス管先端部による潰瘍形成，穿孔や穿通も報告されており，とくに穿孔率が約 10%と高いのが問題である[10]。EMS 留置と比較するとチューブの内腔が狭いため閉塞が比較的起きやすく，イレウス解除に時間がかかり，経口摂取開始も困難である。また連日の持続した微温湯などによる洗浄が必要であり，医療サイドの管理の困難さも指摘されている。また，減圧チューブの使用により吻合部再発をきたしたとの報告も認められる[11]。

本邦では，市販されている経肛門的減圧チューブが一般的であるが，欧米では EMS 留置が経肛門的減圧術の主流である。EMS 留置は，口側病変の情報獲得の点と，食事開始や管理の容易さから患者の QOL の点で優位である。経肛門的減圧チューブは，現在セットとして市販されている点，また腫瘍に対する愛護性の点で優位といえる。

表1 経肛門的減圧術の比較

	金属ステント EMS	減圧チューブ
挿入成功率，減圧率	良好	良好
挿入の容易さ	同等	同等
減圧の早さ	早い	遅い
挿入後の管理	容易	やや煩雑
挿入後の食事摂取	可能	困難
挿入時の QOL	良好	やや不良
腫瘍に対する影響	やや侵襲的？	吻合部再発の可能性？
腫瘍口側の潰瘍・穿孔	ない	約 10%？
長期留置	可能	やや不安
市販化	開発中	3社より市販

Ⅱ．根治的手術の不可な大腸癌イレウス（姑息的 EMS 留置）

1. 適応

基本的に腫瘍の切除による生命予後の改善は認められないが，イレウス解除による全身状態の改善が必要である。従来，根治手術が困難な場合や他の癌，悪性腫瘍による大腸狭窄に対しては一般的に姑息的な人工肛門造設術や腫瘍切除術が行われていた。しかし人工肛門の造設を含めた姑息的な手術は予後の不良な患者にとっても家族にとってもできれば避けたい治療法である。そこで手術に代わる方法として EMS 留置が海外でも本邦でも導入されている[12)13)]。

留置法は術前の方法とまったく同じである。経肛門的減圧チューブは，長期の留置はできないために適応とはならない。または一度経肛門的減圧チューブを挿入してから EMS の留置をしている報告も多い。

2. 成績

現在までの当科の成績は 29 症例 35 例に EMS 留置を試み，33 例 94%に挿入可能であった。狭窄原因は，原発性大腸癌 20 例（根治術不能 13 例　高齢 7 例）69%，大腸癌局所再発 6 例 21%，前立腺癌 S 状結腸浸潤 1 例，卵巣癌 S 状結腸浸潤 1 例，胃癌腹膜播種横行結腸浸潤 1 例であった。狭窄部位は盲腸から直腸まで全大腸で，盲腸の 1 例は屈曲が強くガイドワイヤーができなかったために，S 状結腸の 1 例は多発する狭窄のために留置できなかった。挿入留置時における偶発症や死亡例はなかった。留置期間は 1～576 日，中間値は 170 日であった。留置後長期における偶発症は，再狭窄が腫瘍の EMS 内腔への増殖による狭窄（ingrowth）：3 例 8.5%，固い便塊による閉塞：1 例 3%，直腸腟瘻＋腫瘍の EMS 端から内腔への増殖による狭窄（overgrowth）：1 例 3%の合計 5 例 14%で，stent in stent や heart probe，内視鏡的洗浄にて対処した。また Migration（EMS の位置変位）が 4 例 11%認められ，前立腺癌による S 状結腸狭窄例では Hartmann 手術を施行，2 例は EMS の再挿入を，1 例は経過観察を行った。また，1 例で高度の便秘による狭窄部より口側での穿孔が発生し死亡した。文献的には，姑息的治療目的の有効率は 90%，穿孔率は 4%，migration（逸脱）率は 10%，再閉塞率は 10%で，死亡率は 0.5%で比較的安全で有効な手技であると報告されている[7)]。

3. 予後と経過観察など

姑息的 EMS 留置後の長期予後に関しては EMS 留置群と手術群で差がないとの報告[12)]があり，EMS による予後への影響もないと考えられる。Xinopoulos ら[14)]の EMS と人工肛門造設とのランダム化比較試験では，効果や安全性で差はなく，EMS は患者の QOL の向上と共に cost-effective であると報告されている。ただし，出血は予防できないので，出血による貧血を呈する患者には適応とはならない。寝たきりの高齢者など，全身状態から根治的手術を避けたい患者にも良い適応である。留置後の逸脱や穿孔，再閉塞，腫瘍の増大にともなう他臓器（膀胱や十二指腸など）への浸潤の早期発見のためにも留置後は定期的な腹部単純 X 線検査や注腸，CT 検査などが必要である。

おわりに

大腸狭窄に対して過大侵襲手術や緊急手術を回避するために，内視鏡下の EMS 留置術や経肛門イレウス管は今後一層普及すべき手技である。安全で一般的な手技として確立するためには，特に大腸専用の EMS 器具およびキットの認可・保険収載が待たれる。それにより，大腸癌イレウスに対する第一選択的な手技となり，oncologic emergency が emergency でなく純粋に oncology に従った治療に集中できるようになると思われる。

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Stenting for Malignant Colorectal Obsruction

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Colorectal cancer obstruction is an oncologic emergency that had been treated with emergency surgery. However, decompression through the anus including a colonic stent (Expandable Metallic Stent：EMS) changed the conventional practice. Instead of a conventional ileus tube, through nose with poor effectiveness, the transanal decompression method (colonic EMS) has improved the treatment approach by avoiding emergency operations. It has given better operative results, improved the patients' QOL (quality of life) as well as allowing a higher QOL for the doctors and co-medical staff. It has been reported that colonic EMS has obtained a high clinical success rate of approximately 90% and minimal complication rate of approximately 5%. On the other hand we should note that there has been approximately 10% of migration and 10% of re-obstruction in the long term follow up. In the future, colonic EMS is considered to be the first choice in the treatment of obstructive colorectal cancer in Japan.

Seminars in
Colon & Rectal
Surgery

Topology of the Fascial Structures in Rectal Surgery: Complete Cancer Resection and the Importance of Avoiding Autonomic Nerve Injury

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To decrease local recurrence and avoid autonomic nerve injury, mobilization of the rectum is performed by anatomical dissection along the fascial planes. Anterior to the rectum, Denonvilliers' fascia divides into several laminae at both sides and separates the mesorectum from the autonomic nerves. This fascia is better preserved when the tumor is not located on the anterior wall of the rectum. Posterior to the rectum, the prehypogastric nerve fascia covering the hypogastric nerves is evident between the fascia propria of the rectum and the parietal pelvic fascia. The prehypogastric nerve fascia connects to 1 of the lateral laminae of Denonvilliers' fascia. The dissection plane posterior to the rectum is between the fascia propria of the rectum and the prehypogastric nerve fascia. After dissection both anterior and posterior to the rectum, the medial part of the lateral ligament becomes clearly identifiable. The parietal pelvic fascia is located dorsal to the hypogastric nerves and ventral to the pelvic splanchnic nerves. Appropriate selection of dissection planes ensures the complete capture of the mesorectal package and simultaneously reduces the risk of nerve injury.

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Previous Understandings of Fasciae Around the Rectum

Anterior to the Rectum

Origin of Denonvilliers' Fascia

In 1836, Denonvilliers[1] reported this fascia as a prostatoperitoneal membranous layer between the rectum and seminal vesicles. Two theories have been advanced regarding the development of Denonvilliers' fascia. In 1899, Cunéo and Veau[2] suggested that Denonvilliers' fascia developed from fusion of the embryonic peritoneum of the rectovesical culde-sac. Elliot Smith[3] supported the peritoneum fusion theory in studies of fetal dissections. In 1945, Tobin and Benjamin[4] concluded that the fascia was derived from the peritoneum based on a histologic study. In 1948, Uhlenhuth et al[5] also presented macroscopic anatomical evidence strongly supporting the peritoneal fusion theory. Recently, van Ophoven and Roth[6] concluded that Denonvilliers' fascia develops from fusion of 2 walls of the embryologic peritoneal cul-de-sac.

However, a different hypothesis exists regarding the development of Denonvilliers' fascia. In 1922 and 1923, Wesson,[7,8] who had provided the first histologic evidence supporting the peritoneal fusion theory, stated the septum was formed by the condensation of loose areolar tissue. In 1956, Silver[9] noted that the septum appears to form simply as a condensation of loose areolar tissue based on histologic examination of 52 embryos and fetuses.

Anatomy of Denonvilliers' Fascia

Milley and Nichols[10] disclosed that Denonvilliers' fascia histologically consisted of dense collagen, smooth muscle fibers, and coarse elastic fibers. In 1993, Richardson[11] demonstrated a dense double layer of elastin in the recto-genital septum under electron micrography. Although Denonvilliers' fascia has been suggested to consist of 2 fasciae, van Ophoven and Roth[6] and Bisset et al[12] concluded that the posterior layer of Denonvilliers' fascia actually corresponds to the fascia propria of the rectum. Kourambas et al[13] stated that this fascia had no definite layers and no definable lateral edge that widened and connected with the fascia running lateral to the rectum (pararectal fascia) posteriorly or with the fascia be-

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tween the levator ani and prostate (lateral pelvic fascia) anteriorly.

In the caudal border of Denonvilliers' fascia, Milley and Nichols[10] stated that this fascia attaches to the rectourethralis muscle, and Silver[9] described Denonvilliers' fascia as continuing to the external longitudinal muscle coat of the rectum. In 1993, Sato[14] demonstrated that the caudal end of Denonvilliers' fascia attached to the perineal body.

In 1980, Goligher[15] described Denonvilliers' fascia as more strongly adherent to the rectum than to the prostate, but Tobin[6] stated that this membrane was located between the loose connective tissue around the rectum and the more dense fibromuscular connective tissue around the prostate and seminal vesicles. Kiyoshima et al[16] also reported that Denonvilliers' fascia adhered tightly to the center of the posterior aspect of the prostatic capsule in 97% of cases. Huland and Noldus[17] described easy separation of Denonvilliers' fascia from the rectum during prostatectomy.

Posterior to the Rectum

Reliable surgical dissection planes for dissection of posterior and lateral sides of the rectum have been proposed by many surgeons. These may arise from multilaminar fascial structures around the rectum. Surgeons and anatomists commonly recognize a fascia surrounding the mesorectum, but this is variously named the fascia propria of rectum,[12,18,19] the perirectal fascia,[20] the rectal fascia,[21] or the visceral layer of the pelvic fascia.[22-25]

Understandings also differ regarding the fascial constitution between the rectal fascia and sacrum. One interpretation is that no fascia is present between the rectal fascia and the hypogastric nerves (Fig. 1A),[18,22,26] while the other is that a fascia exists ventral to the hypogastric nerves (Fig. 1B).[12,19,20,25] Takahashi et al[23] described the hypogastric nerves as wrapped with the visceral endopelvic fascia (Fig. 1C). While agreeing, in part, Havenga et al[24] and Mutean[21] described the fascial constitution as differing between the upper and lower pelvis (Fig. 1D and E).

In 1974, Crapp and Cuthbertson[27] reported the rectos acral fascia as a constantly situated sheet of fascia running from the periosteum overlying the body of the fourth sacral vertebra to the rectal fascia, 3-5 cm above the anorectal junction. Based on detailed dissections of 45 cadavers, Sato and Sato[28] reported that the rectos acral fascia originated between

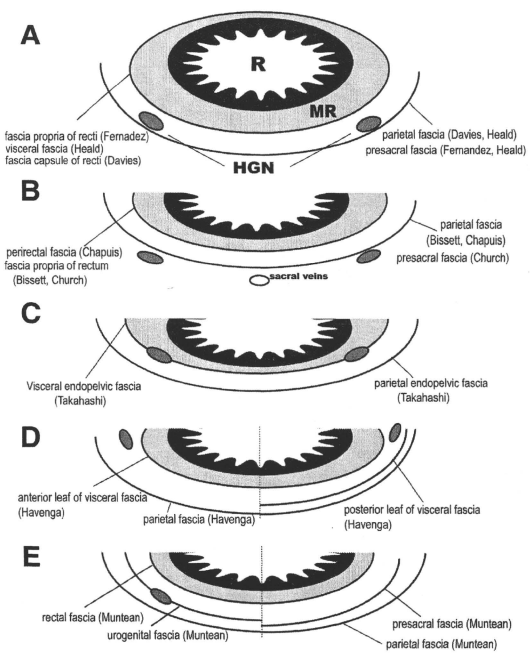

Figure 1 Previous interpretations of retrorectal fascial structures. (A-E) represent schematic views of previous interpretations of retrorectal fascial structures. (D and E) The right half of the panel represents the superior level, and the left half is the inferior level. R, rectum; MR, mesorectum; HGN, hypogastric nerves.

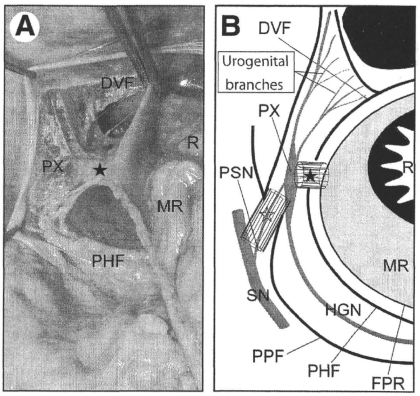

Figure 2 Lateral ligament of the rectum. (A) is an operative photograph of the left lateral ligament. (B) is a schematic view of the left lateral ligament. The lateral part of the ligament (open star) is beside the pelvic splanchnic nerves, and the medial part (black star) is near the rectal branches of the pelvic plexus. DVF, Denonvilliers' fascia; HGN, hypogastric nerves; MR, mesorectum; PHF, prehypogastric nerve fascia; PPF, parietal pelvic fascia; PSN, pelvic splanchnic nerves; PX, pelvic plexus; R, rectum; SN, sacral nerve.

the third and fourth sacral vertebrae in most cases, but in some cases from any part between the second sacral vertebra and the first coccygeal vertebra. However, Church et al,[19] Havenga et al,[24] and Diop et al[25] described the rectos acral fascia as an adhesion of 2 fasciae existing posterior to the rectum.

Lateral to the Rectum

In 1949, Goligher[29] described the lateral ligament as an important structure during rectal surgery, and Michels et al[30] confirmed this structure from anatomical dissections in 1963. Sato and Sato[28] described the lateral ligament as a structure between the pelvic side wall and rectum and consisting of 2 segments: a lateral segment of the ligament composed of the pelvic splanchnic nerves and a medial segment constituting the rectal branches of the pelvic plexus and lymphatic vessels.[28] The visceral branches of the pelvic plexus were first reported by Kimmel and McCwea[31] in 1959 (Fig. 2).

Various reports have described relationships of the middle rectal artery to the lateral ligaments. Boxall et al[32] reported that the middle rectal artery does not run in the lateral ligament, while sometimes the accessory middle rectal arteries run in this ligament. Nano et al[33] recently reported that the ligament contains fat tissue, vessels, and nerve filaments, and that the middle rectal artery courses anteriorly and inferiorly in respect to the lateral ligament. In 1997, Rutegard et al[34] reported the lateral ligament as histologically consisting of clear nerves, fat, and fibrous tissue in all 13 specimens they examined, with small blood vessels included in only 2 specimens. Heald et al[35] described none of the lateral ligaments in his paper regarding the surgical procedure for total mesorectal excision, although Moriya et al[36] and Enker[37] stressed the lateral ligament as an important structure during rectal surgery with nerve preservation, the medial segment to be divided during rectal mobilization, while the lateral segment is to be preserved.

Fascial Structures Around the Rectum

Fascia Propria of the Rectum

The fascia propria of the rectum is a thin visceral fascia covering the rectum and mesorectum. The mesorectum is a distinct compartment that contains the superior rectal arteries and veins, mesorectal fat, lymphatic vessels, and nodes. This fascia is also called the peri-rectal fascia, rectal fascia, and visceral fascia (Figs. 3 and 4).

Denonvilliers' Fascia

Denonvilliers' fascia is clearly identifiable between the fascia propria of the rectum and the seminal vesicles or prostate. The recto-vaginal septum in women corresponds to Denonvilliers' fascia. The consistency of Denonvilliers' fascia varies between individuals, from a fragile translucent layer to a tough leathery membrane.[10] The recto-vaginal septum is less prominent in women than Denonvilliers' fascia is in men. The fascia is thicker in younger individuals and thins out

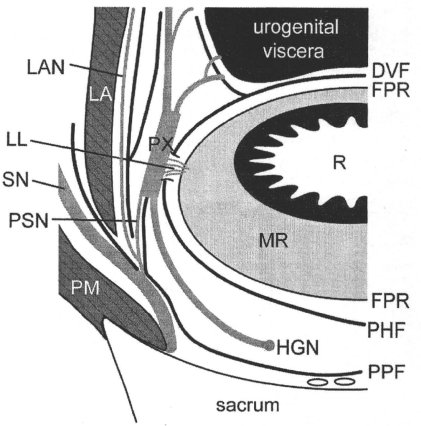

Figure 3 Schematic representation of fasciae around the rectum (horizontal). DVF, Denonvilliers' fascia; FPR, fascia propria of rectum; HGN, hypogastric nerves; LA, levator ani muscle; LAN, levator ani nerve; LL, lateral ligament; MR, mesorectum; PHF, prehypogastric nerve fascia; PM, piriformis muscle; PPF, parietal pelvic fascia; PSN, pelvic splanchnic nerves; PX, pelvic plexus; R, rectum; SN, sacral nerve.

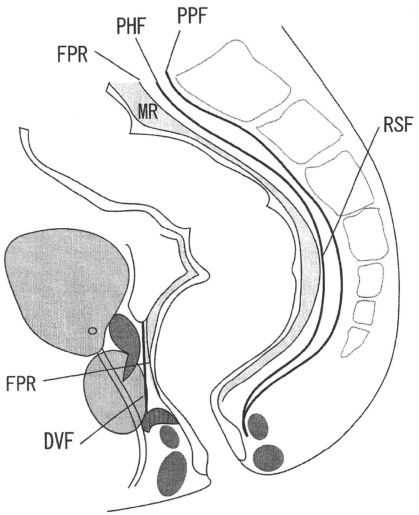

Figure 4 Schematic representation of fasciae around the rectum (sagittal). DVF, Denonvilliers' fascia; FPR, fascia propria of rectum; MR, mesorectum; PHF, prehypogastric nerve fascia; PPF, parietal pelvic fascia; RSF, rectosacral fascia.

with age and may be more obvious in patients with preoperative radiotherapy to the pelvis or with transmural inflammation of the rectum (ie, Crohn's disease).[19]

Laterally, Denonvilliers' fascia divides into several thin laminae, and 1 of the lateral continuations extends dorsolaterally and separates the mesorectum from the pelvic plexus and urogenital neurovascular bundle.[38] The caudal part of the Denonvilliers' fascia joins the prostate or recto-urethral muscle, and for that reason, is more easily separated from the rectum than from the prostate.

Prehypogastric Nerve Fascia

The prehypogastric nerve fascia is variously known as the urogenital fascia,[21] hypogastric nerve sheath,[39] or uretero-hypogastric fascia.[40] This fascia is located immediately behind the fascia propria of the rectum, covering the right and left hypogastric nerves[41] and the pelvic plexus, and connecting with the lateral continuations of Denonvilliers' fascia at the level of the pelvic plexus (Fig. 2). The left ureter runs dorsal to the prehypogastric fascia, while the right ureter runs ventral to the fascia.[42]

Parietal Pelvic Fascia

The parietal layer of the pelvic fascia is located dorsal to the hypogastric nerves and ventral to the sacral veins and iliac vessels and divides into several laminae extending ventrolaterally: (1) the fasciae lining or enclosing the pelvic plexus; (2) the fasciae providing a posterior attachment for the levator ani muscle and lining the medial or superior surface of the muscle sheet; and (3) the fasciae enclosing the pudendal nerve and associated inferior gluteal and internal pudendal vessels.[41] The most medial fascia covers the pelvic splanchnic nerves and fuses with the prehypogastric nerve fascia at the pelvic plexus.

Rectosacral Fascia

The rectosacral fascia is not a true fascial structure[41] but represents part of any thickened pelvic fascia[19] or adhesion or of connections between the layers of fasciae existing posterior to the rectum: the fascia propria of the rectum; the prehypogastric nerve fascia; or the parietal pelvic fascia.[25] Clinically, however, a band is apparent between the posterior wall of the rectum and the sacrum at 3-5 cm above the anorectal junction, or higher, as described by Havenga et al.[24] One reasons for this finding is that fascia-like structures easily develop or become thickened during dissection or surgery, as noted by Range and Woodburne.[43] This fascia should not be confused with Waldeyer's fascia, which only refers to the most distal portion of the presacral fascia joining the anorectal junction.[19,27]

Autonomic Nerves

Sympathetic supply to the rectum and upper anal canal originates in the first and second lumbar spinal segments. The fibers are distributed through the inferior mesenteric plexuses via the lumbar splanchnic nerves and through the pelvic plexus via the sacral splanchnic nerves. Parasympathetic nerves are supplied to the rectum through the pelvic plexus via the pelvic splanchnic nerves.[44]

The pelvic urogenital autonomic nerve system is present immediately outside the rectum. Nerve-sparing surgery aims to preserve several major nerve structures in the pelvis, including peripheral nerve bundles, such as the hypogastric nerves, pelvic splanchnic nerves, and cavernous nerves (Fig. 5).

Superior Hypogastric Plexus

The superior hypogastric plexus is a network of sympathetic pre- and postganglionic fibers emerging from the second to fourth lumbar splanchnic nerves and located 3-7 cm caudal to the origin of the inferior mesenteric artery and just caudal to the bifurcation of the aorta.[45] The plexus extends down about 4 cm with fine nerve-fibers to the rectum and divides into right and left hypogastric nerves.

Hypogastric Nerves

The hypogastric nerves represent extensions of the sympathetic nerves dividing from the superior hypogastric plexus, and extending down along the pelvic wall under the prehypogastric nerve fascia to connect the pelvic plexuses, while sending small rectal branches around the superior rectal artery penetrating through 2 fasciae: the prehypogastric nerve fascia; and the fascia propria of the rectum. The hypogastric nerves play a role in ejaculatory function, causing closure of

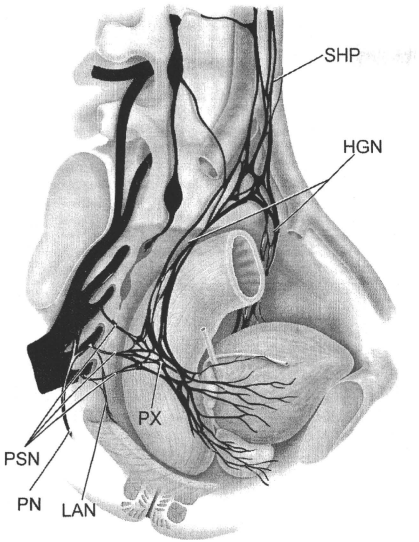

Figure 5 Topographic anatomy of the pelvic autonomic nerves. HGN, hypogastric nerves; LAN, levator ani nerve; PN, pudendal nerve; PSN, pelvic splanchnic nerves; PX, pelvic plexus; SHP, superior hypogastric plexus.

the internal ostium of the urethra and constriction of the internal sphincter muscles. According to the severity of damage to the hypogastric nerves, various disturbances of ejaculatory function may develop, including retrograde ejaculation.

Pelvic Splanchnic Nerves

The pelvic splanchnic nerves, which are parasympathetic nerves, form as branches of the second, third, and fourth (mainly the third and fourth) sacral nerves emerging from the anterior sacral foraminae on either side. The pelvic splanchnic nerves, which often form a common trunk with the levator ani nerves at their origin, run to the target pelvic organs via the pelvic plexus and to the sigmoid and descending colon as far as the splenic flexure and distal transverse colon along to the inferior mesenteric artery and left colic artery. These nerves activate the smooth muscle of the rectum, anus, and bladder wall and inhibit the vesical sphincter.

The cavernous nerves (nervi erigentes) supplying vasodilator fibers to the erectile tissue of the penis and clitoris, and arise mainly from the fourth pelvic splanchnic nerve, run in the neurovascular bundles posterolateral to the prostate[46] and penetrate the rectourethralis muscle posterior to the anorectal junction in about half of cases.[47]

Pelvic Plexus

The pelvic plexus, also known as the inferior hypogastric plexus, appears as a meshlike triangle located under the prehypogastric nerve fascia on the pelvic side walls anterolateral to the rectum and posterolateral to the seminal vesicles, prostate, and urinary bladder in men, and lateral to the uterine cervix, vaginal fornix, and bladder and often extending into the broad ligaments of the uterus in women. This plexus is mainly formed by the hypogastric nerves and pelvic splanchnic nerves and sends nerve branches arising at the anteroinferior corner of the plexus to the genitourinary organs, running with the blood vessels (neurovascular bundles).

Levator Ani Nerves

The levator ani nerves represent 1 of the components of the pudendal plexus. The origins of the nerves often form a common trunk with the pelvic splanchnic nerves and extend down along the levator ani under the thick parietal pelvic fascia (levator ani fascia), sending branches to the muscles. Injury to the levator ani nerves means that the dissection has deviated from the recommended plane, within the distal pelvis, and may present as urinary or fecal incontinence.[48]

Pudendal Nerves

The pudendal nerves, which are mainly sensory nerves for the perineum, arise from the sacral plexus (second to fourth sacral nerves), leave the pelvic cavity through the greater sciatic foramen, enter the gluteal region, cross the sacrospinous ligament close to the ischial spine, and run through the pudendal canal (Alcock's canal) toward the ischio-anal fossa. These nerves then divide into the inferior rectal, perineal, and dorsal nerves of the penis or clitoris.

Surgical Dissection Planes

Total mesorectal excision (TME)[35] or tumor-specific mesorectal excision[48] are the standardized procedures for rectal cancer surgery. The purpose of TME is removal of the rectum and mesorectum enveloped by the visceral layer of the pelvic fascia as a package, including lymphatic channels draining from the area harboring the cancer, and, together with sphincter-preservation, to preserve the autonomic nerves distributing to the urogenital organs. However, even in recent reports using TME, complicated urinary and sexual dysfunctions are common.[49-54]

Various discussions about the surgical plane of TME have been presented.[38,55] Many surgeons have recommended surgical planes outside the intact Denonvilliers' fascia. However, Lindsey et al[56] and Kinugasa et al[38] claimed that removing Denonvilliers' fascia with the mesorectum is not always necessary. The most dangerous points of nerve injury during surgical dissection are the anterolateral sites of the rectum, where laminated leaves of the lateral parts of Denonvilliers' fascia and nerve branches from the pelvic plexus cross[38] (Fig. 2). Denonvilliers' fascia can be preserved when the tumor is not located on the anterior wall of the rectum.

Two surgical dissection planes are possible posterior and lateral to the rectum: between the fascia propria of the rectum and the prehypogastric nerve fascia; and between the prehypogastric nerve fascia and the parietal pelvic fascia. The first dissection plane is better to avoid nerve damage. A dissection plane behind the parietal pelvic fascia risks injury not only to the pelvic plexus, but also to the levator ani nerves.[49,57] The risk of nerve injury varies with surgical dissection plane selected.[58,59] The surgical dissection plane selected should thus be considered along with the location and depth of the tumor.

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ORIGINAL ARTICLE

Diverting stoma in rectal cancer surgery. A retrospective study of 329 patients from Japanese cancer centers

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Abstract
Background A diverting stoma (DS) has been constructed for many patients with low anterior resection (LAR), but it is still controversial whether DS can prevent anastomotic leakages. The aim of this study was to investigate the risk factors of anastomotic leakage including DS construction, and to evaluate the clinical course affected by DS according to the necessity of urgent abdominal reoperation for anastomotic leakage.

Patients and methods This was a retrospective analysis of 329 middle or lower rectal cancer patients who underwent LAR with mechanical reconstruction using circular staplers. Clinical data were collected from five cancer centers in Japan.

Results The overall anastomotic leakage rate was 10.0% (33 of 329). We experienced one mortality in this series (0.3%; 1/329). Clinical factors associated with DS construction included tumor location, operation time, intraoperative bleeding, lateral lymph node dissection, simultaneous resection of other organs, and the level of anastomosis, respectively.

On univariate analysis, high ligation of the inferior mesenteric artery had a significantly high leakage rate, but not on multivariate analysis. DS construction had no connection with the overall leakage rate. Concerning the clinical course affected by DS, the frequency of urgent reoperation was significantly increased in patients without DS compared with those with DS, 11.1% and 54.2%, respectively ($p=0.04$).

Conclusions LAR was the safe and preferred option for rectal cancer patients with very low mortality and an acceptable leakage rate. DS did not have a relationship with overall anastomotic leakage, but did seem to mitigate its consequences and reduce the requirement for urgent abdominal reoperation.

Keywords Rectal cancer · Anastomotic leakage · Diverting stoma · Defunctioning stoma · Low anterior resection

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Introduction

Anastomotic leakage is a major problem in rectal cancer surgery, because a sphincter-preserving operation has become standard for many rectal cancer patients. A

temporary diverting stoma (DS) has been constructed for many patients in low anterior resection (LAR). But the indication of DS construction for patients without intraoperative adverse events has not been clarified for a long time. Theoretically, DS was constructed to divert the fecal stream from anastomotic sites, and to protect fragile anastomotic sites. But it remains unproven whether diverting the fecal stream in itself directly prevents leakage. Several retrospective studies showed that the absence of DS was a risk factor for leakage in LAR, whereas others did not. Therefore, it is controversial whether DS can prevent anastomotic leakage. Although recent randomized studies [1, 2] and meta-analyses [3, 4] have shown that DS reduced the incidence of symptomatic leakage in LAR for rectal cancer, there is still limited evidence as to the impact of DS on leakage. Moreover, there have been few analyses about this issue in multicenter studies with a large number of patients from Japan.

The aim of this study was to investigate the risk factors of anastomotic leakage including DS construction, and to evaluate the clinical course affected by DS according to the necessity of urgent abdominal reoperation for such leakage using data collected from five cancer centers in Japan.

Patients and method

Patients

We reviewed the clinical data from five cancer centers in Japan which participated in the "Studies on the standardization for diagnosis, treatment, and follow-up of colorectal cancer patients", sponsored by Grant-in-Aid 18-2 for Cancer Research from the Ministry of Health, Welfare and Labor of Japan. All data on patient demographics, comorbidities, and the histological results were investigated retrospectively from the clinical records of each hospital.

From 2002 to 2004, a total of 329 consecutive patients with primary rectal cancer underwent LAR, and were investigated in this series. LAR was performed on patients with middle or lower rectal cancer, and reconstructions were done using circular staplers. Coloanal anastomosis using the hand-sewn technique was excluded from this study. Patients with subtotal colectomy, total proctocolectomy, abdominoperineal resection, Hartmann's procedure, or with pull-through procedures were also excluded.

Surgical procedure

The inferior mesenteric artery (IMA) was divided either at its origin or below the origin of the left colic artery (LCA). High ligation of IMA was defined as dividing IMA at its origin, while low ligation was defined as dividing IMA below the origin of LCA. For oncological lymph node dissection, we classify regional lymph nodes into three groups: perirectal, intermediate, and main lymph nodes. Perirectal nodes are lymph nodes in the mesorectum along the superior rectal artery. Intermediate nodes are lymph nodes along IMA between the origin of the left colic artery and the origin of the terminal sigmoid artery. Main nodes mean the lymph nodes along the IMA proximal to the origin of the LCA [5]. Lymph node dissection for UICC stage I is complete dissection of perirectal and intermediate lymph nodes, that is, low ligation without lymph node dissection around the root of IMA. Lymph node dissection for stage II, III, and IV is complete dissection of all regional lymph nodes, that is, high or low ligation with lymph node dissection around the root of IMA [6].

After total mesorectal excision or tumor-specific mesorectal excision [7], we performed rectal irrigation, while clamping the anal side of the tumor. The rectum was then divided transversely or vertically [8]. After that, we usually added lateral lymph node dissection for patients diagnosed with stage II, III, and IV [9]. Although the extent of lymphadenectomy for stage IV is still debatable, in the case that every distant metastasis (stage IV) was resectable, we perform full lymph node dissection.

Reconstruction was done using a circular stapler. Most anastomoses were straight, and colonic J pouch or transverse coloplasty pouch was sometimes used at the discretion of the operating surgeon. Intraoperative leakage test by transanal instillation of fluid or air was performed depending on the surgeon. Pelvic drain was used routinely.

Indication of DS construction

No clear applicable criteria for DS construction were stipulated in the present study. The DS construction decision was made by the individual surgeon in each case.

Definition of anastomotic leakage

Anastomotic leakage was defined clinically by the presence of the following: discharge of gas, pus, or feces from the drain or wound; discharge of pus per rectum; or rectovaginal fistula. All clinically suspicious anastomotic leakages were confirmed by one or more of the following image diagnoses: contrast study; CT scan; rectoscopy. If these cases were proven not to show anastomotic insufficiency by these imaging studies, they were defined as pelvic abscess

and not as anastomotic leakage. We did not perform routine diagnostic imaging after LAR to detect anastomotic dehiscence in clinically stable patients.

Variables analyzed

Variables included in this analysis were age, gender, body mass index (BMI), bowel obstruction, tumor location, tumor invasion, adjuvant therapy, level of IMA ligation, lateral lymph node dissection, type of anastomosis (single stapling technique, SST; or double stapling technique, DST), pouch surgery, intraoperative blood loss, operating time, DS construction, synchronous resections of other organs (hepatectomies for simultaneous liver metastasis or extended surgery to adherent organs, or additional cancer resections for double cancers), tumor size, and distal resection margin of specimen.

Bowel obstruction was defined as stenosis preventing the passage of a colon fiberscope. Tumor location was classified into middle or lower rectum according to the main part of the tumor. Tumors in the lower rectum were defined as those in which the main part was located below the peritoneal reflection. Tumor location in relation to the anal verge was preoperatively measured using rigid scope or digital examination. Tumor invasion was classified according to the UICC-TNM classification (6th edition [10]) preoperatively. Tumor size and distal resection margin were measured on the specimen before fixation with formalin. The level of anastomosis from the anal verge was measured with a digital examination. But due to the retrospective nature of this study, when the data were not available, the distance was calculated from the tumor location and distal resection margin.

Statistical analysis

In the univariate analysis, the chi-squared test and Mann–Whitney test were used. After univariate analysis, variables with a p value$\leq$0.1 were selected for multivariate analysis. A multivariate analysis was performed using a binary logistic regression model. All p values $<$0.05 were considered statistically significant.

Table 1 Patient characteristics

Gender	
Male	215
Female	114
Age(years)	59.0±10.5 (23–87)
Tumor location (cm)	6.1±1.7 (4.0–12.0)
Bowel obstruction	
No	305
Yes	18
Missing	6
Tumor invasion	
T1,T2	108
T3,T4	215
Missing	6
Neoadjuvant chemo Tx	
No	324
Yes	5
Anastomosis	
SST	15
DST	314
High ligation	
No	142
Yes	183
Missing	4
LLND	
No	197
Yes	132
Level of anastomosis (cm)	4.1±1.4 (1.0–9.5)
Intraoperative bleeding (ml)	598±590 (10–3723)
Operating time (min)	240±104.1 (90–620)
BMI (k/m^2)	22.6±3.1 (14.1–31.2)
Tumor size (cm)	4.4±2.3 (0–12.0)
Simultaneous resection	
No	292
Yes	37
DS construction	
No	209
Yes	120

Values are number or mean±standard deviation (ranges)

DS diverting stoma, *BMI* body mass index, *SST* single stapling technique, *DST* double stapling technique, *LLND* lateral lymph node dissection

Results

Patient characteristics

From 2002 to 2004, a total of 329 consecutive patients underwent LAR. Patient characteristics were shown in Table 1. One hundred and eighteen middle rectal cancer patients and 211 low rectal cancer patients were investigated in this series. Average distance from the lower edge of the tumor to the anal verge was 6.1 cm (4.0–12.0 cm). Average distance from anastomosis to the anal verge was 4.1 cm (1.0–9.5 cm).

Neoadjuvant chemotherapy was performed for five patients, but others were treated by surgery alone. Neo-