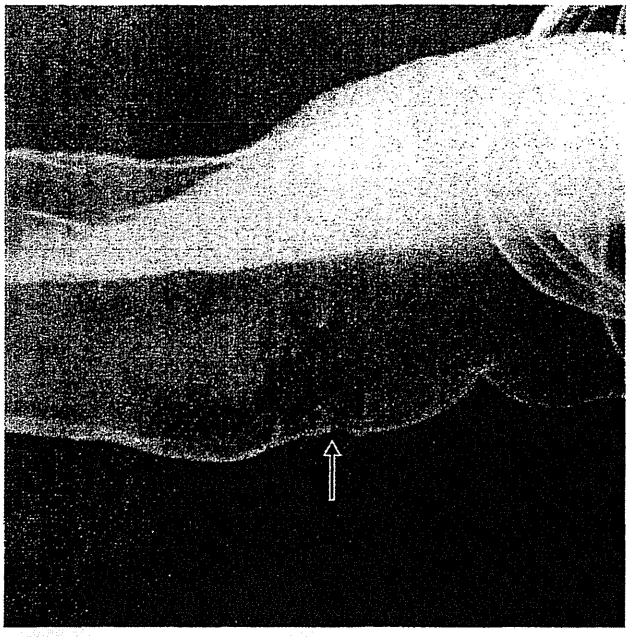
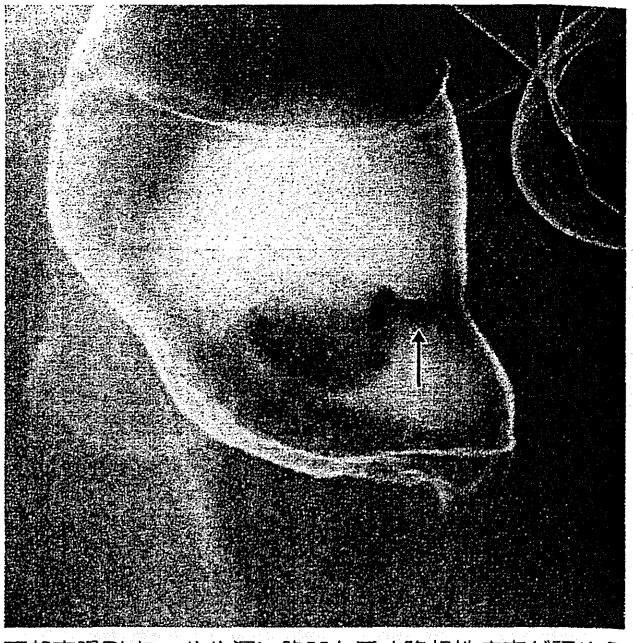
図7　浅い陥凹成分を有する大腸癌(図4と同一症例)



横行結腸のⅡc＋Ⅱa型早期大腸癌(↑)。大きさは13×11mm。深達度はpSM(1,250μm)。病変部にバリウムを移動させるため，腹臥位で撮影した。圧迫することによって正面視でき，病変の辺縁部分にわずかなバリウムのたまりが観察される。また，病変に向かうわずかな粘膜ひだの集中もみられる。

図8　深い中心陥凹を有する大腸癌



下部直腸Rbに，やや深い陥凹を示す隆起性病変が認められる。前壁側より強い粘膜ひだの集中(↑)が認められ，深達度はSM高度浸潤からMPと判断される。術前深達度診断はMPとした。Ⅱa＋Ⅱc型早期大腸癌で，大きさは22×14mm，深達度はpSM(2,300μm)であった。

る。また，中心陥凹が広く浅い場合でも，そのなかに結節状の隆起成分がみられる場合は進行癌である。**図5**に横行結腸の深達度pSM，Ⅱc＋Ⅱa型早期大腸癌を示す。病変の周囲に薄くバリウムを移動させ，隆起性病変の立ち上がり，高さ，辺縁の性状を観察し，隆起の中央部にバリウムを移動させて中心陥凹を観察した写真である。病変は平坦な隆起を主体とする病変で，中央部分にわずかにバリウムのたまりがみられ，浅い陥凹面を伴っていることがわかる。またわずかに病変に向かう粘膜ひだの集中(後述)も認められ，SMに中等度以上浸潤した病変と診断される。

・粘膜ひだの集中の有無(図7～9)

粘膜ひだの集中は，M癌にはみられない。大腸では胃のような消化性潰瘍はみられないので，(深い)生検あるいはポリペクトミーなどの既往がなく，粘膜ひだの集中がみられた場合は，少なくとも中等量程度の癌巣がSM以深に浸潤した癌と判断される。深達度が深くなるにつれて粘膜ひだの集中は強くなり，ひきつれ像を呈するようになってくる(**図9**)。

■ 内視鏡による深達度診断(図10)

内視鏡診断においては，まず遠景からの全体像－病変の広がり，病変部の進展程度などの観察を行い，次いで病変周囲および病変部の詳細な観察を行う。SM癌浸潤距離とリンパ節転移には相関関係がみられ，浸潤距離が1,000μm未満ではリンパ節転移は少ないが，1,000μm以上ではリンパ節転移率は10%強との報告[8,9]が多く，M～SM軽度浸潤とSM中等度浸潤～SM高度浸潤とを鑑別することは，次に述べる内視鏡治療を含めた治療方針の決定に際し重要となる。緊満感，易出血性，表面の不整(粗造・崩れ・白苔付着など)，陥凹の形状と深さ，粘膜ひだの集中などがSM高度浸潤を示唆する所見である[10]。より詳細な深達度診断には，インジゴカルミン散布による色素内視鏡観察や拡大内視鏡観察によるpit pattern診断[11]，観察光の分光特性を狭帯域特性へ変更するnarrow band imaging(NBI) system[12]などが有用である。**図11**にpit pattern分類を示す。色素内視鏡観察やpit pattern診断，NBIは深達度診断ばかりでなく，腫瘍と非腫瘍との鑑別－癌か腺腫かの鑑別に有用で，治療方針決定の際の補助診断として用いられている[11～13]。

図9　粘膜ひだ集中の強い大腸癌

上行結腸前壁に，粘膜ひだの集中が強く，壁のひきつれを伴った低い隆起性病変が認められる(↑)。隆起腫瘤型1型進行癌。大きさは13×12mm。癌巣は広い範囲でSMに高度浸潤しており，中心部ではMPに達していた。

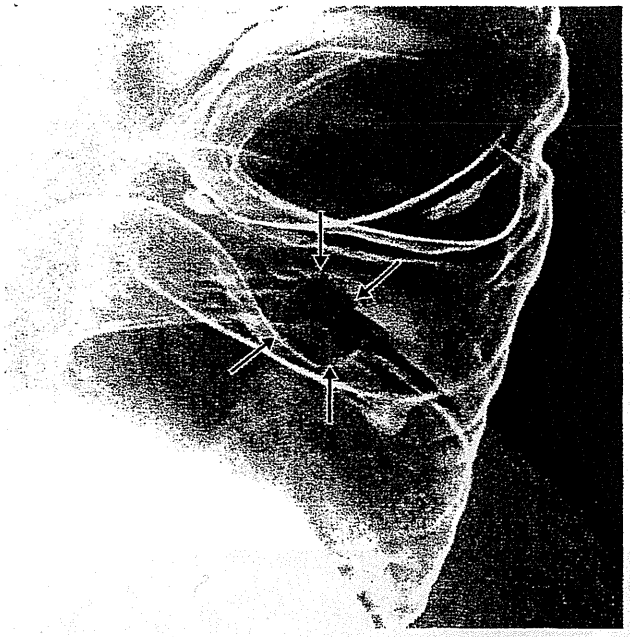
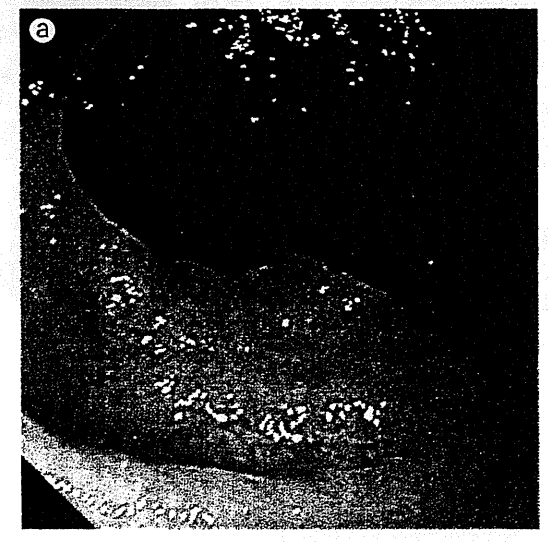
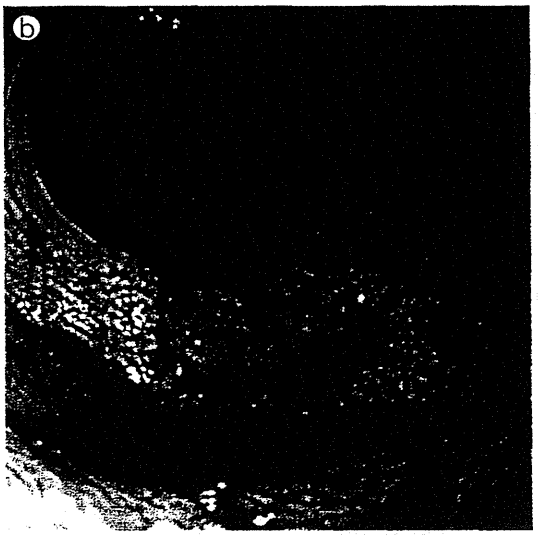


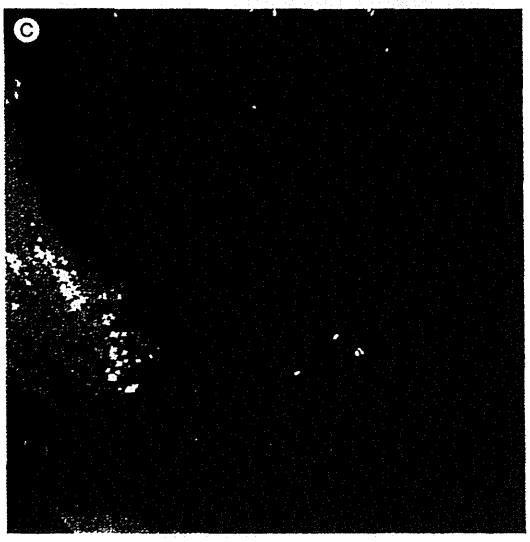
図10　Ⅱa＋Ⅱc型早期大腸癌[9×8mm，pSM(650μm)]

a：通常内視鏡像
盲腸に浅い中心陥凹を有する平坦隆起性病変が認められる。



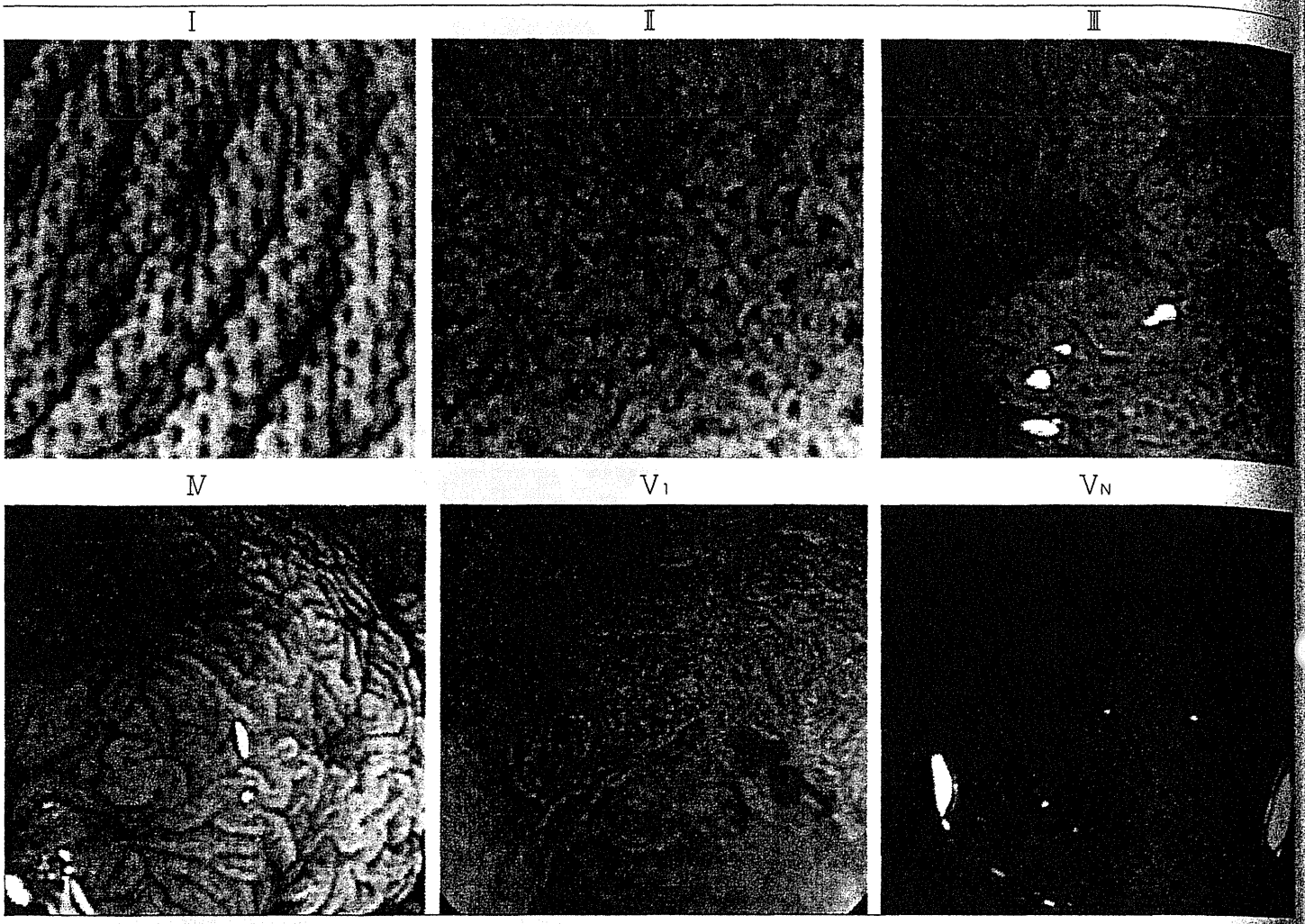


b：インジゴカルミン散布による色素内視鏡像
病変の表面性状および境界の明瞭化がみられる。



c：narrow band imaging(NBI)
病変はbrownish areaとして認められ，視認性は向上し，表面の微細構造観察も優れている。

図11　拡大内視鏡観察によpit pattern分類



非腫瘍性pit：円形から類円形のpitは正常腺管や炎症性腺管にみられⅠ型に，星芒状または乳頭状のpitは過形成ポリープにみられⅡ型に分類される。
粘膜内腫瘍pit：管状または類円形の密在するpitは腺腫にみられⅢ型に，樹枝状や脳回様のpitは管状絨毛腺腫にみられⅣ型に分類される。
Ⅴ型pit：pit patternの不整を呈するV_I型，pit patternが消失し無構造な表面構造を呈するV_N型に分類される。SMに中等度以上浸潤している指標とされる。
（佐野病院　佐野　寧先生のご厚意による）

内視鏡治療の適応基準

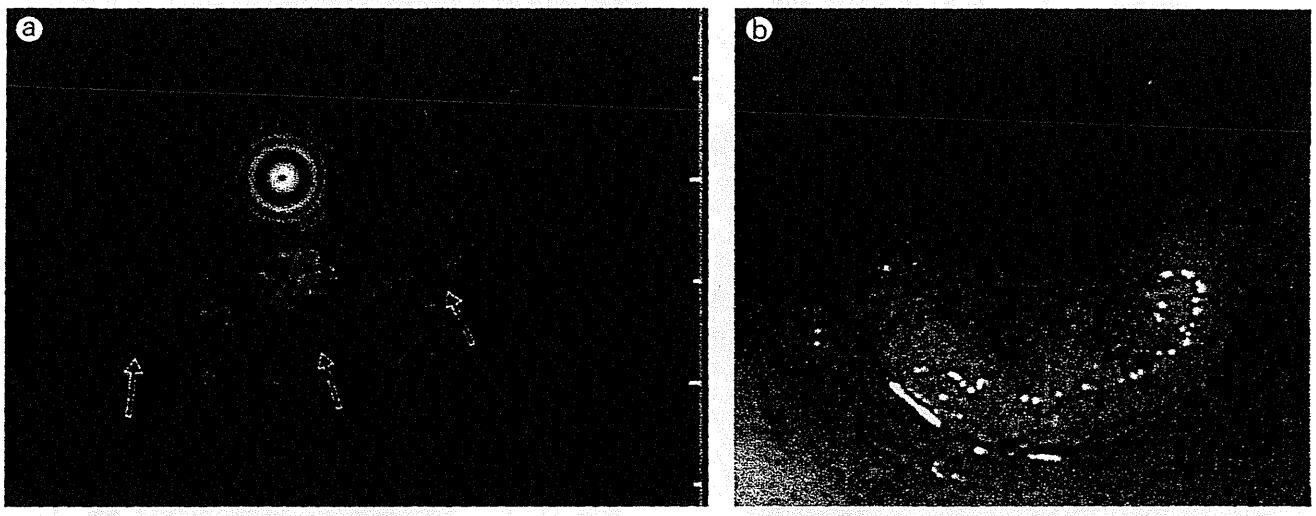
大腸内視鏡検査の普及とともに，内視鏡的に大腸の病変部を切除し治療する内視鏡的摘除術が広く行われるようになってきている。内視鏡治療にはスネアを用いて病変を茎部から焼灼切除するポリペクトミー，EMR，専用のナイフを用い粘膜下層の剥離を行う内視鏡的粘膜下層剥離術（endoscopic submucosal dissection；ESD）などがある。

内視鏡的摘除術はリンパ節転移の可能性がほとんどなく，腫瘍が一括切除できる大きさと部位にある病変を対象とすることが原則で，具体的には，

①粘膜内癌または粘膜下層への軽度浸潤癌
②最大径2cm以下
③肉眼型は問わないこと

の3点が適応基準とされている[13]。ESDを用いれば2cmを超える病変も一括切除が可能であるが，本手技は難易度が高く，穿孔などの偶発症の可能性も高いことから，一般化するまでには至ってはいない。内視鏡的摘除術は摘除生検であり，切除標本の組織学的検索によって治療の根治性と外科的追加切除の妥当性を判断する。垂直断端が陽性の場合は外科的切除が望ましく，摘除標本の組織学的検索で，①SM浸潤度1,000 μm以上，②脈管侵襲陽性，③低分化癌，印環細胞癌，粘液癌，④浸潤先進部の簇出（癌の浸潤先進部における単個の癌細胞あるいは腺管構造をつくらない小塊状～索状の癌胞巣の存在）などの所見が1つでも認められた場合は，リンパ節郭清を含めた外科的切除を考慮する[13]。前述したように，術前内視鏡診断に

図12　Ⅱa＋Ⅱc型早期大腸癌



a：EUS像
腫瘍は低エコーを呈し，粘膜下層に高度浸潤するが，固有筋層（↑）は保たれており，深達度SMと診断される。大きさは22×14mm。

b：内視鏡像

おけるSM深部浸潤の診断指標として，「緊満感，びらん，潰瘍，ひだ集中，変形，硬化像」などがあげられる[10]。

超音波内視鏡による深達度診断

大腸壁の超音波内視鏡（endoscopic ultrasonography；EUS）による層構造は，食道・胃と同様に5層構造として一般に描出され，癌巣は低エコーの壁肥厚像として描出される（**図12**）。EUSは癌の浸潤像を直接捉えて診断することができることから，より正確な壁深達度診断ができるものと期待される。しかし大腸の解剖学的特徴から必ずしも病変全体をくまなく観察できるわけではなく，内視鏡診断で深達度診断に迷わないような症例における有用性は低いとの報告[14]もあり，壁深達度の補助診断として用いられているにとどまっている。

●壁外進展診断，リンパ節転移および遠隔転移診断

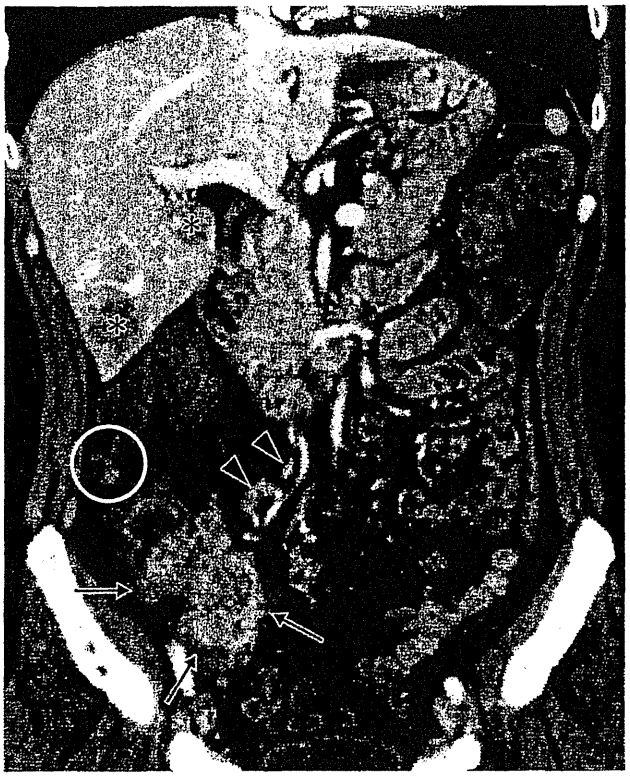
壁外進展診断やリンパ節転移および遠隔転移診断は，CTやMRI，超音波などの病変部の断層面を捉えることのできる断層影像法が有用である。近年，これら画像診断装置の進歩はめざましく，時間分解能，空間分解能ともに飛躍的に向上し，さまざまな画像処理法や新たな造影剤も開発され，より詳細な検討が可能となってきている。

multidetector-row CT（MDCT）の登場は，生体情報をボリュームデータとして得ることを可能とし，多断面再構成法（multiplanar reformation；MPR）や三次元画像処理によるCT colonoscopyなど，従来の画像表示法とは異なる視点からの表示法を可能とし，CT診断の新たな方向性を示している[15]。また，組織分解能に優れるMRIは，直腸などの骨盤領域の描出に優れている。

大腸癌の癌巣から壁外周囲脂肪織へ伸びる毛羽立ち像や索状影は，癌巣が筋層または漿膜を越えて周囲脂肪織への浸潤を示している可能性が高く，このような所見が明らかな場合は壁外に進展している場合が多い（**図13**）。また癌巣と隣接臓器とが接し，その境界が平滑でなく凹凸不整がみられる場合また不明瞭な場合には，隣接臓器に直接浸潤している可能性が高い（**図14**）。

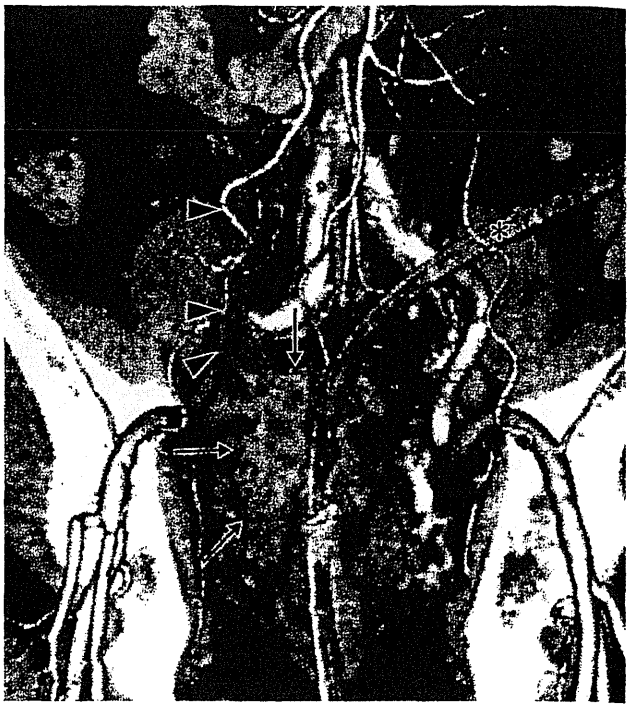
転移リンパ節は領域リンパ節－腸管周囲の腸管傍リンパ節，その腸管へ分布する脈管周囲の中間リンパ節，大動脈周囲の主リンパ節また側方リンパ節の腫大として同定される（**図13**）。一般にリンパ節転移の診断は形状と大きさから判断され，類円形で1cm以上に腫大したものは，転移リンパ節の可能性が高い。しかし，1cm以下のリンパ節でも転移しているものがあり，現時点においてもリンパ節転移の有無を正確に画像から診断できるまでには至ってはおらず，術前に指摘するにとどまっている。

図13　壁外進展とリンパ節転移および遠隔転移



進行盲腸癌のCT冠状断像
盲腸部の壁肥厚と壁外周囲脂肪織へ伸びる毛羽立ち像や索状影(↑)がみられ，深達度SEと診断。癌巣に分布する回結腸動脈近傍には結節影(▲)がみられ，中間リンパ節(#202)への転移と診断。上行結腸近傍には不整形軟部影(○)がみられ腹膜播種が疑われる。肝転移(＊)もみられる。

図14　S状結腸癌：尿管浸潤像



CT三次元像処理冠状断像
S状結腸の壁肥厚と右側骨盤腔に進展する不整形軟部腫瘤影(↑)が認められる。この腫瘤影に右尿管(▲)は巻き込まれ，中枢側尿管の拡張がみられる。
＊はイレウス管。動脈を三次元表示している。(ZIO soft使用)

大腸癌の遠隔他臓器転移は肝臓，次いで肺に多く認められる。肺転移検索は胸部X線，CTなどにより，肝転移検索は超音波，CT，MRIなどにより行われている。肝転移巣検索は，MRIでは癌組織の拡散の低下を利用した拡散強調像(diffusion weighted imaging；DWI)[16]，および肝細胞特異性造影剤Gd-EOB・Primovistを用いたGd-EOB MRIが[17]，超音波では持続性の高い肝造影効果を示すソナゾイド®を用いた造影超音波が[18]，より精度の高い診断情報を提供するものとして利用されている(**図15**)。

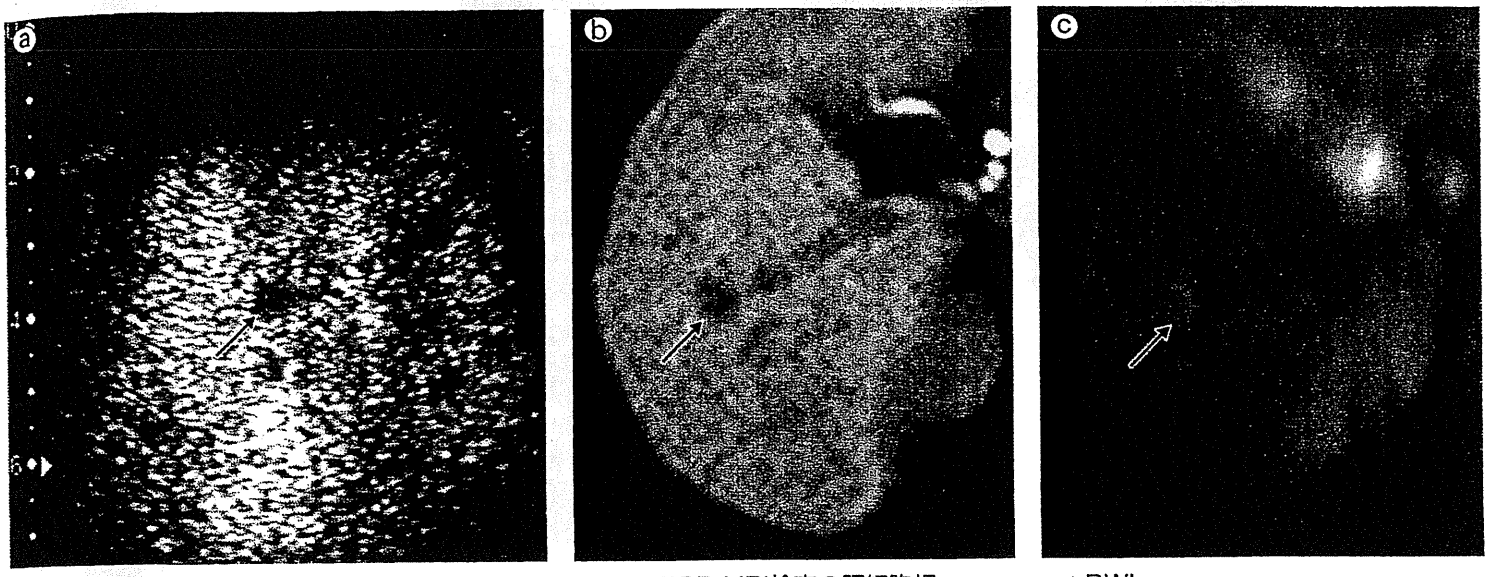
直腸癌－肛門温存について

大腸癌，特に直腸癌においては，過去には根治性を追求した徹底的リンパ節郭清と病変と周囲臓器とを*en bloc*に切除する拡大手術が数多く施行されてきたが，術後の生活の質(quality of life；QOL)の低下に目が向けられるようになり，臓器温存を考慮した治療法が考慮されるようになってきた。肛門温存の適応を決める際，病変と恥骨直腸筋の上縁にあたる外科的肛門縁－Herrmann lineとの距離が重要となる。癌腫下縁から肛門側断端までの距離(DW)を少なくとも2cm以上確保し，さらに術後肛門機能を十分維持するためにはHerrmann lineまでの直腸を残すことが望ましい。したがって，癌腫下縁が歯状線から最低でも3～4cm以上離れているものが一般に適応とされている。ここでは，下部直腸～肛門管の解剖およびこの部の画像診断について解説する。

○下部直腸・肛門管の解剖(図16)

発生学的には直腸と肛門管との境界は歯状線と定義され，肛門縁から歯状線までの管腔を解剖学的肛門管とよぶ。しかし臨床的な取り扱いにおいては不便なため，実際に狭くなっている部分－肛門縁から恥骨直腸筋付着部上縁までを外科的肛門管とよび，広く用いられている。肛門管の狭い管状部を通過すると，ちょうど終末直腸粘膜の直腸柱を越えたあたりでドーム状の広い部分となる。

図15　Gd-EOB MRIと造影超音波
50歳代，女性。直腸癌肝転移。

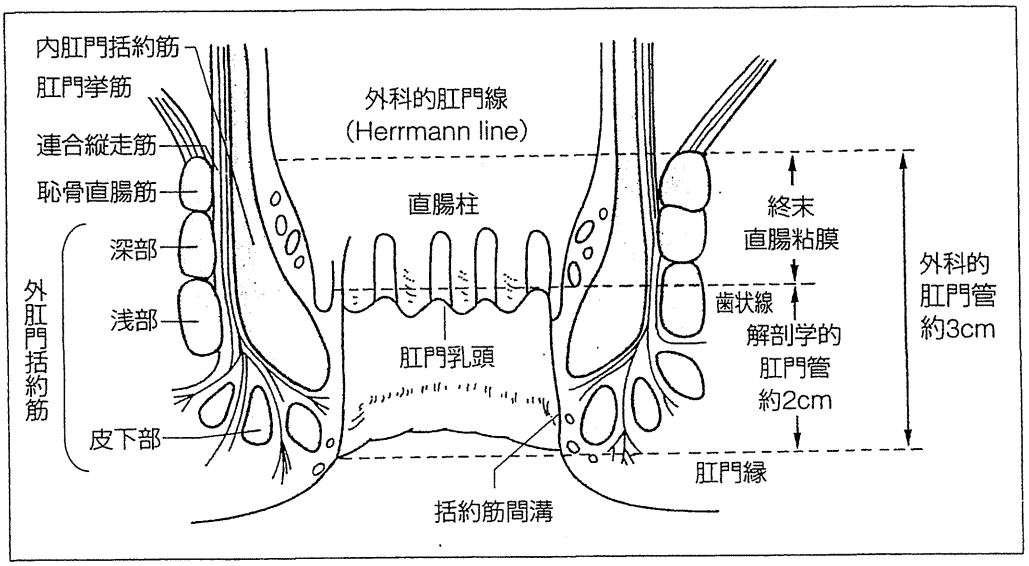


a：造影超音波検査
肝S6にφ7mmの内部血流を伴うSOL(↑)を認め転移と診断。

b：Gd-EOB MRI検査の肝細胞相
同部に低信号域(↑)をみる。

c：DWI
淡い高信号域(↑)として描出され転移疑いと診断した。

図16　下部直腸・肛門管の解剖図

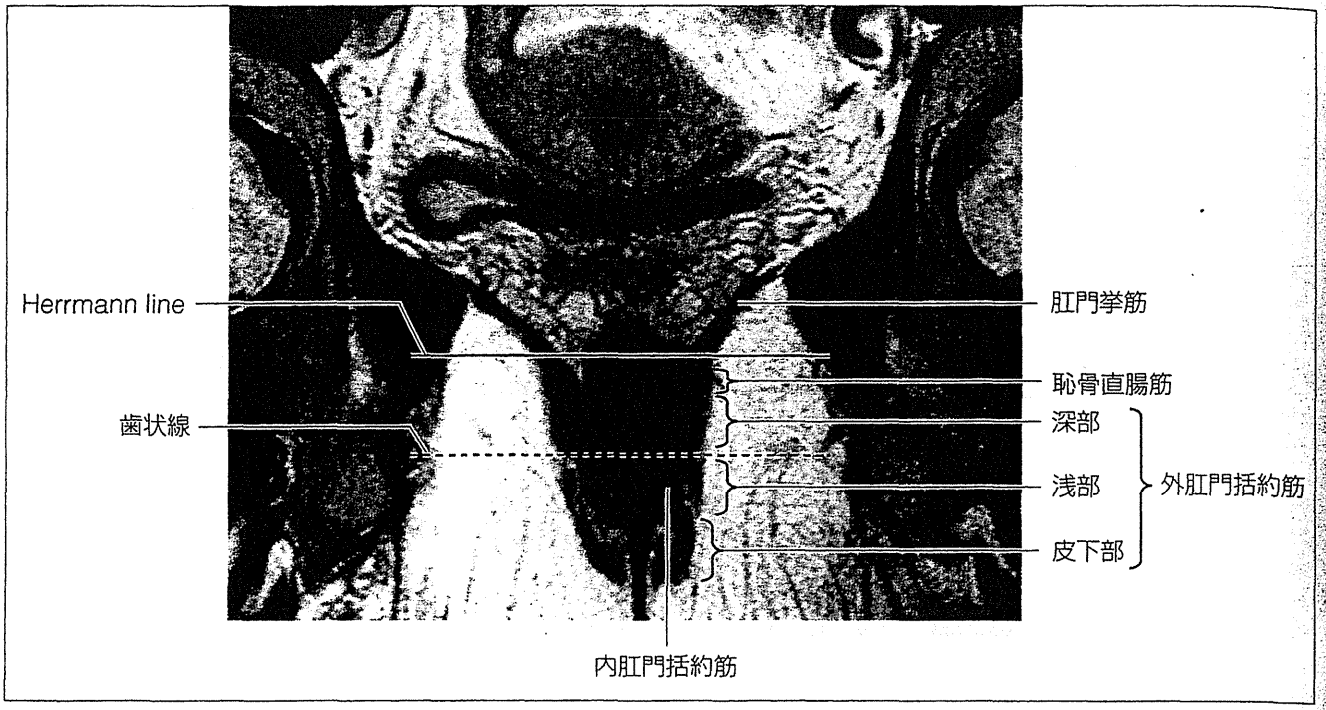


ここが恥骨直腸筋付着部上縁にあたり，直腸柱上端のHerrmann lineとほぼ一致する。したがって外科的肛門管周囲は，直腸の輪状筋より連続する内肛門括約筋とその外側を取り巻く外肛門括約筋によって包まれている。

●下部直腸癌の診断

下部直腸癌の壁深達度診断は，肛門挙筋および肛門管に沿って内・外肛門括約筋が良好に描出される骨盤底に垂直なMRI冠状断像が有用である(**図17**)[19]。下部直腸癌の診断にあたっては，①癌巣と歯状線との距離，②癌の壁深達度，の2点が治療方針決定のうえで重要となる。病変部と歯状線またはHerrmann lineとの距離の長・短により術式が大きく異なってくることより，正確な距離の診断が非常に重要である。最近では十分なDMや外科的剥離ライン(RM)が確保できない下部進行直腸癌に対し，肛門機能温存術－内肛門括約筋合併切除術が考案され，従来直腸切断術の適応であったこのような症例の大多数において，直腸切断術が回避されるようになってきている[20]。

図17　下部直腸・肛門管のMRI解剖



骨盤底に垂直なMRI冠状断像。図16と対比していただきたい。

おわりに：これだけは覚えておいてほしいこと

大腸癌の病期診断を行うにあたり大切なことは，まず癌の壁深達度を推定すること，次いでリンパ節転移，そして肝臓や肺などへの遠隔臓器転移の有無をチェックすることである。「大腸癌取扱い規約（第7版）」に比べ「TNM分類（第6版）」はstage分類が細かく規定されているが，必ずしも予後を的確に反映した分類とはなっていない[21]。**表1**に示した大腸癌取扱い規約の進行度分類を参考にして，リンパ節転移および遠隔転移がなく，癌の深達度が筋層まではStage Ⅰ，それ以深はStage Ⅱ，リンパ節転移があればStage Ⅲ，遠隔転移があればStage Ⅳと覚えておいていただきたい。UICCの今回の改訂（第7版）ではさらにstageが細分化されているが，この意義については現時点では明らかではなく，今後の報告でその有用性が明らかにされると思われる。

謝辞

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雑誌「胆と膵」連載

ちょっと気になる胆・膵画像―ティーチングファイルから―＜第４回＞

脂肪を内包する後腹膜腫瘤の１例

関口　隆三・黒木　嘉典・菱沼　正一

医学図書出版株式会社

連載

胆と膵 Vol. 31 (7) p.634～635, 2010

ちょっと気になる胆・膵画像―ティーチングファイルから―（第４回）

脂肪を内包する後腹膜腫瘤の１例

関口　隆三[1)]・黒木　嘉典[1)]・菱沼　正一[2)]

1）栃木県立がんセンター画像診断部
2）同　消化器外科

Ⅰ．症　例

68歳，女性。5年前，近医検診精査のCTにて膵頭部背側に径20mmの腫瘤を指摘。積極的に悪性を示唆する所見なく，経過観察となった。4年5ヵ月後のCTにて腫瘤は40×20mmと増大。悪性腫瘍の可能性が示唆され，手術を勧められた。本人，セカンドオピニオンを希望され，当院受診となった。腫瘤に伴う自覚症状は特に認めていない。

Ⅱ．画像所見

当院受診時の単純CTでは，膵頭部背側に45×25mmの低吸収値を呈する境界明瞭な類円形腫瘤を認める（図1）。腫瘤は脂肪濃度を呈し，内部右側寄りに網状～線状の軟部陰影がわずかに認められるが，結節成分はみられない。MRIでは，腫瘤はT1強調画像およびT2強調画像で不均一な高信号（図2a, b），脂肪抑制T2強調画像では低信号（図2c）を示し，脂肪成分が主体の腫瘤であると判断される。腫瘤の右側には信号強度のやや異なる領域を認め，CTでわずかにみられた軟部陰影部分と一致している。患者は前医初回CT検査時，造影剤アレルギーを認め，その後は単純CTにて経過観察されており，当院では単純検査のみ施行した。

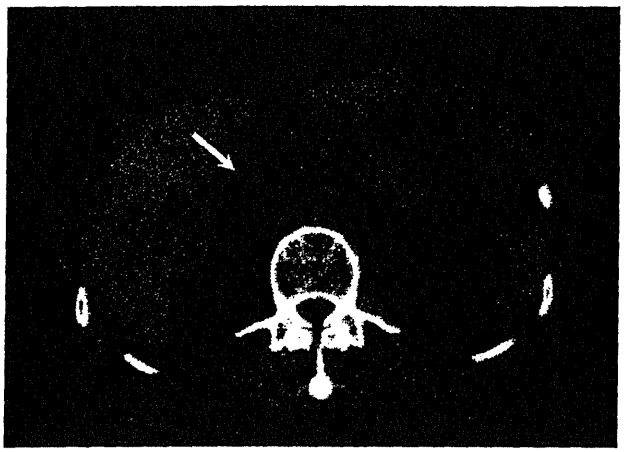


図１　単純CT画像

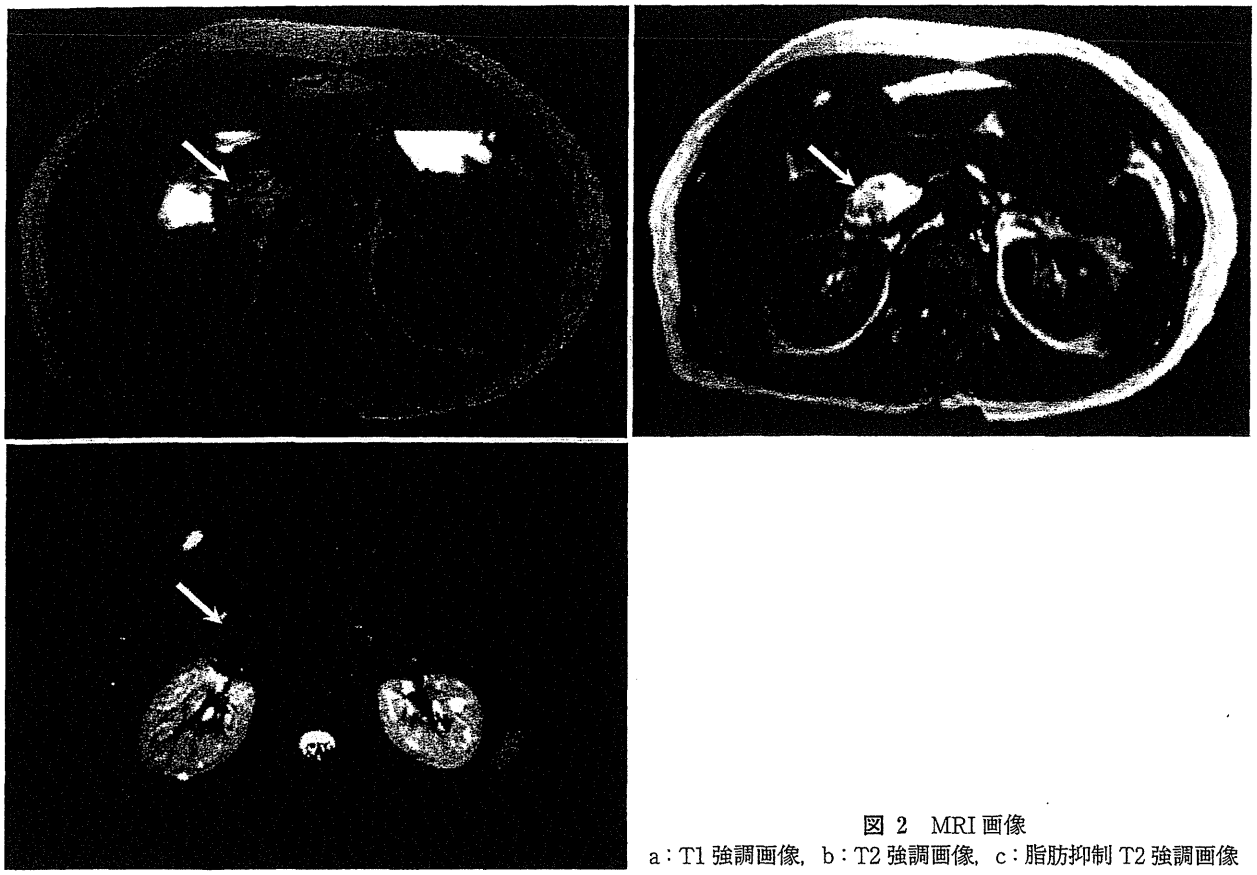
Ⅲ．術前診断・病理組織所見

画像所見からは，腫瘤の原発巣確定―膵内か膵外か―には至らず，膵頭鉤部または膵頭部背側の後腹膜原発の脂肪腫または高分化型脂肪肉腫と術前診断し，手術が施行された。腫瘤は薄い被膜を伴う大部分が成熟した脂肪織より構成され，膵との連続性はなく，腫瘤内部および辺縁部に膵組織を認め，後腹膜の脂肪腫様病変を伴う異所性膵と診断された。

Ⅳ．考　察

脂肪肉腫の多くは境界不明瞭で脂肪組織を内包する大きな腫瘤として認められる。しかし高分化型脂肪肉腫は，脂肪成分を主体とする腫瘤内部にわずかに軟部陰影を有し，脂肪腫と画像所見からは鑑別できない症例があることが知られている。本症例では腫瘤の増大傾向もみられたことから，高分化型脂肪肉腫の可能性は否定できないと判断し，手術が施行された。

異所性膵の大半は十二指腸や胃，空腸など上部消化管に4cm以下の粘膜下腫瘍として認められ，本症例の様に後腹膜腫瘍として認めることは稀である[1)]。本症例のように，腫瘤の大部分を成熟した脂肪織より構成される後腹膜の異所性膵の報告は著者の文献検索した範囲ではみあたらず，本症例は初回報告例と思われる。



a|b
c

図 2　MRI 画像
a：T1 強調画像，b：T2 強調画像，c：脂肪抑制 T2 強調画像

膵脂肪腫は稀な疾患であり，本症例と非常に類似した画像を呈する。境界明瞭でほとんどが脂肪成分で構成される腫瘤像を呈し，わずかに隔壁や脈管成分を有することがあり，大きさは 4mm～5.3cm と報告されている[2,3]。膵脂肪腫の報告は組織学的な裏付けなく，画像所見のみからなされているものがほとんどである。これまで報告された症例の中に，本症例と同様に後腹膜の脂肪腫様病変を伴う異所性膵症例が含まれていた可能性が考慮された。今後類似画像症例を経験した際の鑑別診断の一つに加えて頂ければ幸いである。

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The Laryngoscope

Diagnosis of the Extent of Advanced Oropharyngeal and Hypopharyngeal Cancers by Narrow Band Imaging With Magnifying Endoscopy

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Objectives/Hypothesis: Narrow band imaging combined with magnifying endoscopy (NBI-ME) is useful for the detection of superficial cancer in the oropharynx, hypopharynx, and esophagus. We used NBI-ME to evaluate the frequency of superficial cancer spread (SCS) contiguous with advanced oropharyngeal and hypopharyngeal cancers and esophageal cancers.

Study Design: Retrospective.

Methods: We retrospectively studied 45 patients with oropharyngeal and hypopharyngeal cancer and 44 with esophageal cancer who underwent NBI-ME from October 2006 through April 2009. The following variables were evaluated: 1) the frequency of SCS contiguous with advanced oropharyngeal and hypopharyngeal cancer and esophageal cancer, and 2) the influence of SCS contiguous with advanced oropharyngeal and hypopharyngeal cancer on clinical T category and clinical stage.

Results: SCS contiguous with the primary tumor was found in 49% (22/45) of the patients with advanced oropharyngeal and hypopharyngeal cancer and in 52% (23/44) of those with advanced esophageal cancer. When SCS contiguous with the primary tumor was included in the evaluation of tumor size in advanced oropharyngeal and hypopharyngeal cancer, the clinical T category and clinical stage were revised in 20% (9/45) and 4% (2/45) of patients, respectively; SCS was $\leq$2 cm in 64% of cases (14/22) and between >2 cm and $\leq$4 cm in 36% (8/22).

Conclusions: NBI-ME should be included in the pretreatment diagnostic work-up to evaluate lesion extent and decide optimal surgical margins and radiation fields in patients with advanced oropharyngeal and hypopharyngeal cancer.

Key Words: Narrow band imaging, magnifying endoscopy, lesion extent, head and neck cancer.

Level of Evidence: 3b

***Laryngoscope,* 121:753–759, 2011**

INTRODUCTION

The advent of narrow band imaging (NBI) and high-resolution magnifying endoscopy (ME) has facilitated the detection of superficial cancer in the oropharynx, hypopharynx, and esophagus.[1–6] These techniques have also enabled the lateral spread of superficial cancer contiguous with advanced oropharyngeal, hypopharyngeal, and esophageal tumors to be visualized, allowing an accurate evaluation of lesion extent, which is essential for setting surgical margins and radiation fields. We used NBI combined with ME (NBI-ME) to examine the frequency of superficial cancer spread (SCS) contiguous with advanced oropharyngeal and hypopharyngeal cancers and esophageal cancers.

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MATERIALS AND METHODS

We retrospectively studied 45 patients with oropharyngeal and hypopharyngeal cancer and 44 with esophageal cancer who underwent NBI-ME at Kitasato University Hospital from October 2006 through April 2009. All patients met all of the following criteria: 1) no previous treatment for head and neck cancer or esophageal cancer, 2) a histopathological diagnosis of squamous-cell carcinoma, 3) advanced cancer, 4) computed tomography (CT) had been performed, and 5) chromoendoscopy with Lugol's iodine solution had been performed (only for patients with advanced esophageal cancer).

The following variables were evaluated: 1) the frequency of SCS contiguous with advanced oropharyngeal and hypopharyngeal cancer and esophageal cancer, and 2) the influence of SCS contiguous with advanced oropharyngeal and hypopharyngeal cancer on clinical T category and clinical stage. In this study, we performed NBI with a high-definition videoendoscopy system (with a CV-260SL processor and a CLV-260SL light source; Olympus Optical Co., Ltd., Tokyo, Japan) and an optical magnifying endoscope with a system that could magnify objects up to 80 times (GIF type H260Z videoendoscope; Olympus). A 1.5% solution of Lugol dye was used to perform chromoendoscopy according to the Lugol dye-staining method (Lugol

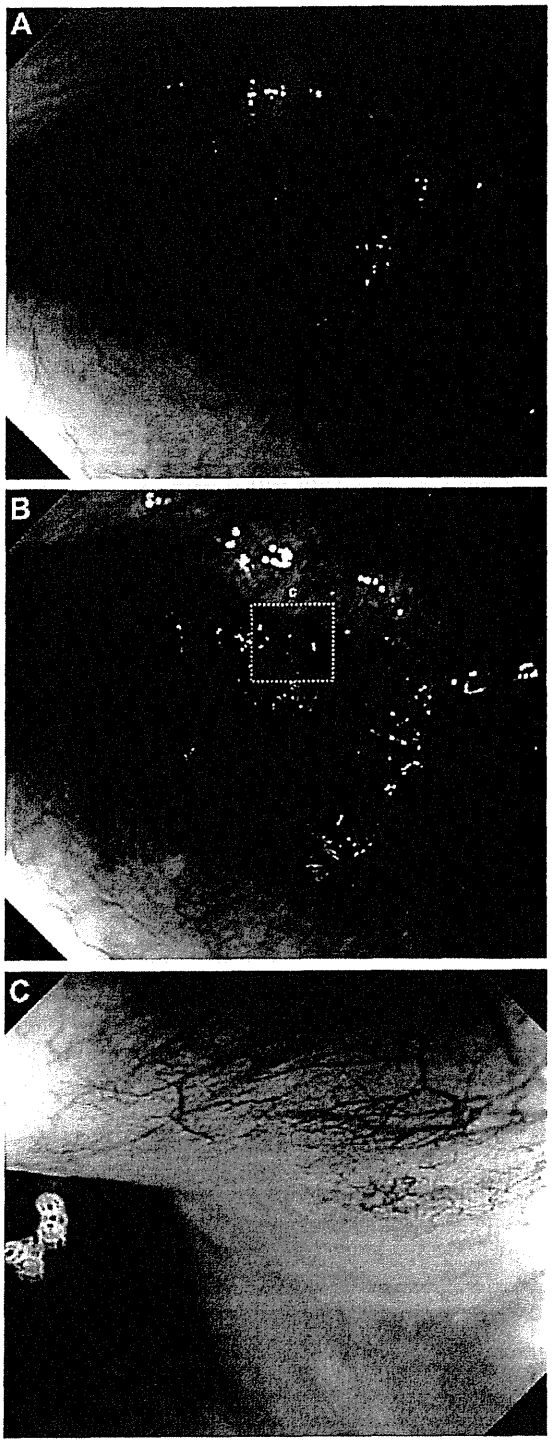

Fig. 1. Normal mucosa in the left postcricoid area. (A) White light endoscopy. (B) Narrow band imaging. (C) Narrow band imaging-magnifying endoscopy, showing a regular microvascular pattern beneath the epithelium.

chromoendoscopy)[7] in all patients with esophageal cancer. Examinations in patients with advanced oropharyngeal and hypopharyngeal cancer were performed in the following order: white light endoscopy, NBI endoscopy, and NBI-ME. In patients with advanced esophageal cancer, examinations were done in the following order: white light endoscopy, NBI endoscopy, NBI-ME, and Lugol chromoendoscopy. Superficial cancer was defined as a lesion with high-grade intraepithelial neoplasia or microinvasive cancer as diagnosed endoscopically according to the World Health Organization classification of tumors.[8] Advanced cancer was defined as a lesion with deeper invasion. Superficial cancer contiguous with the primary tumor was diagnosed endoscopically on the basis of 1) a well-demarcated area and 2) an irregular microvascular pattern.[2–6] Endoscopic images were reviewed by an otolaryngological endoscopist (h.m.) and a gastrointestinal endoscopist (c.k.). Clinical T category and clinical stage were assessed according to the 7th edition of the International Union Against Cancer (UICC) tumor-node-metastasis (TNM) staging system.[9] At the time of endoscopy, we estimated the size of the lesion by placing biopsy forceps (FB-25K-1; Olympus) alongside the lesion; the fully opened cup of the forceps was 6 mm in diameter.

Normal mucosa in the left postcricoid area is shown in Figure 1. On white light endoscopy (Fig. 1A) and NBI (Fig. 1B), a regular microvascular pattern beneath the epithelium was difficult to identify. However, NBI-ME (Fig. 1C) clearly showed a regular microvascular pattern beneath the epithelium. Advanced hypopharyngeal cancers arising in the left postcricoid area are shown in Figure 2 and Figure 3.

In the first case, the tumor was nonulcerative and was situated mainly in the submucosa. SCS extended from the surface of the lesion to its distal border. The greatest tumor dimension was 15 mm in the transverse plane (Fig. 2A) and 22 mm in the coronal plane (Fig. 2B) on CT, and about 25 mm on white light endoscopy (Fig. 2C). Therefore, the lesion was classified as a clinical T2 tumor. NBI showed a well-demarcated, brownish area on the surface of the lesion (Fig. 2D). NBI-ME revealed an irregular microvascular pattern (Fig. 2E). SCS about 10 mm in diameter was contiguous with the anal side of the primary tumor (Fig. 2F), but there was no upgrade of the clinical T category.

In the next case, the tumor was ulcerative and accompanied by SCS only at the border of the lesion. The greatest tumor dimension was 11 mm in the transverse plane (Fig. 3A) and 24 mm in the coronal plane (Fig. 3B) on CT, and about 25 mm on white light endoscopy (Fig. 3C). The lesion was classified as a clinical T2 tumor. NBI showed a well-demarcated, brownish area in the lateral wall (Fig. 3D). NBI-ME revealed an irregular microvascular pattern. SCS extended for about 30 mm from the postcricoid area to the lateral wall via the pyriform sinus and was contiguous with the primary tumor (Fig. 3E). When this spread was included in the evaluation, the clinical T category was upgraded from T2 to T3.

A case of advanced esophageal cancer is shown in Figure 4. White light endoscopy revealed advanced esophageal cancer, occupying half of the circumference of the esophagus (Fig. 4A). NBI showed a well-demarcated, brownish area at the border of the primary tumor (Fig. 4B). NBI-ME revealed an irregular microvascular pattern (Fig. 4C). SCS as an unstained area at the border of the primary tumor was seen on Lugol chromoendoscopy (Fig. 4D). Because the clinical T category of esophageal cancer is based on the depth of tumor invasion, the presence of SCS contiguous to the primary tumor does not alter the classification of clinical T category.

RESULTS

Table I shows the demographic characteristics of the patients. The study group comprised 78 men (88%) and 11 women (12%), with a mean age (±standard

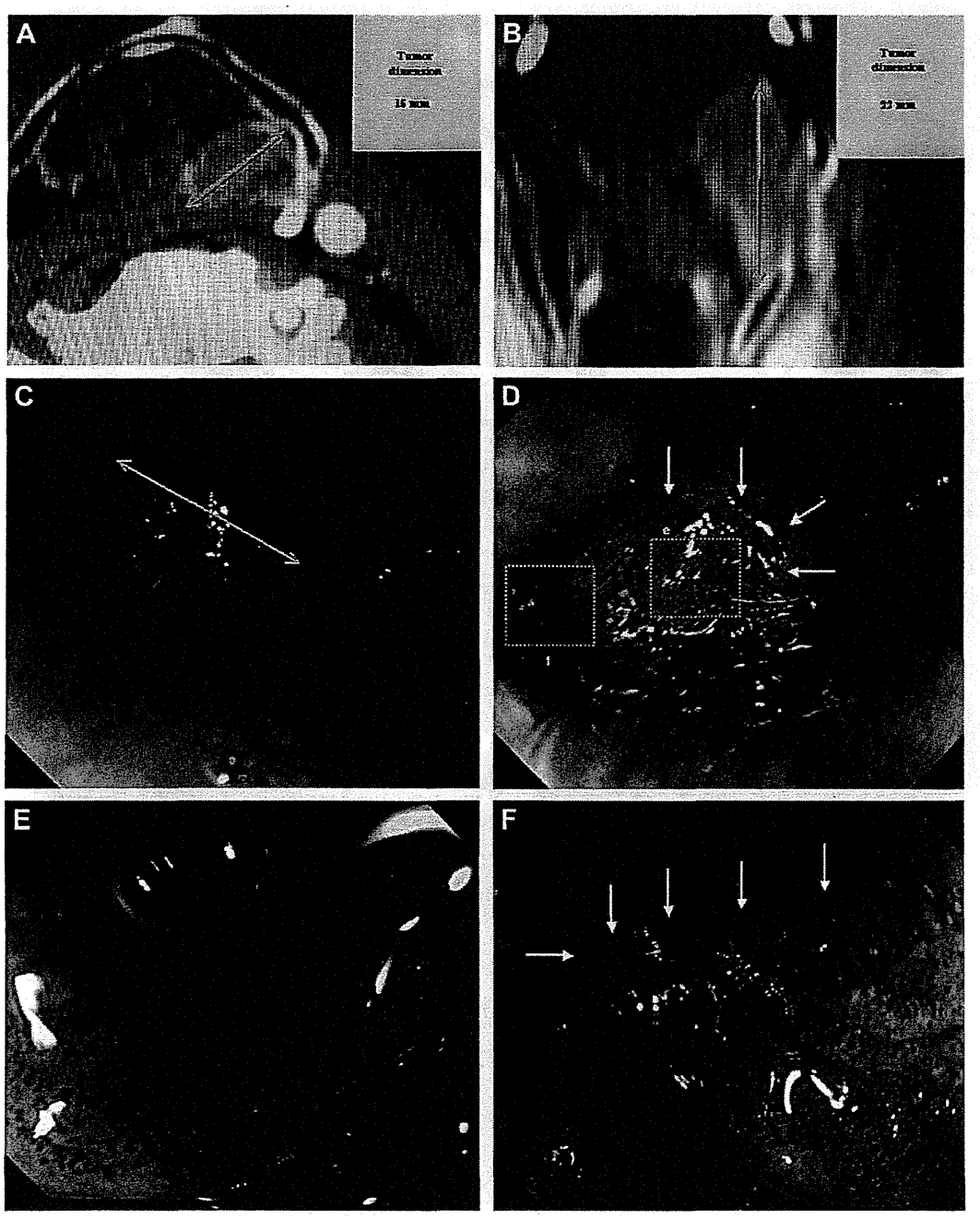

Fig. 2. Advanced hypopharyngeal cancer arising in the left postcricoid area. The tumor was nonulcerative and situated mainly in the submucosa. Superficial cancer spread extended from the surface of the lesion to its distal border. (A) The greatest tumor dimension was 15 mm in the transverse plane on computed tomography (CT). (B) The greatest tumor dimension was 22 mm in the coronal plane on CT. (C) The greatest tumor dimension was about 25 mm on white light endoscopy. (D) Narrow band imaging showed a well-demarcated, brownish area (arrows). (E) Narrow band imaging-magnifying endoscopy revealed an irregular microvascular pattern. (F) Superficial cancer spread about 10 mm in diameter was contiguous with the anal side of the primary tumor (arrows).

deviation) of 66 ± 8.7 years. Among six patients (7%) with oropharyngeal cancer, the primary tumor was located in the anterior wall in four patients (5%), the lateral wall in one patient (1%), and the posterior wall in one patient (1%). Among 39 patients (44%) with hypopharyngeal cancer, the primary tumor was located in the pyriform sinus in 22 patients (25%), the postcricoid area in nine patients (10%), and the posterior wall in eight patients (9%). A total of 44 patients (49%) had primary esophageal cancer.

SCS contiguous with the primary tumor was found in 49% (22/45) of the patients with advanced oropharyngeal and hypopharyngeal cancer and in 52% (23/44) of those with advanced esophageal cancer. In patients with

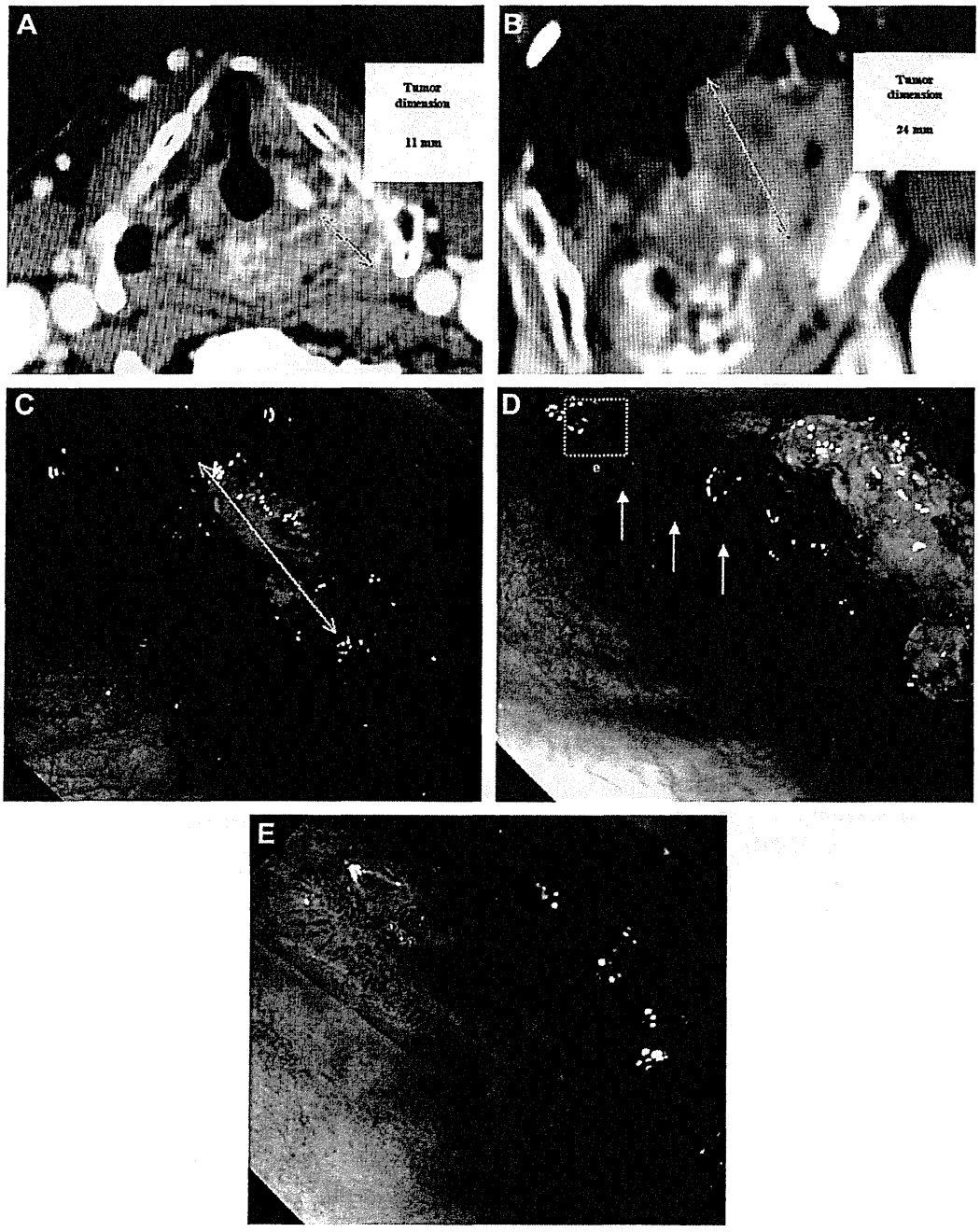

Fig. 3. Advanced hypopharyngeal cancer arising in the left postcricoid area. The tumor was ulcerative, and superficial cancer spread was present only at its border. (A) The greatest tumor dimension was 11 mm in the transverse plane on computed tomography (CT). (B) The greatest tumor dimension was 24 mm in the coronal plane on CT. (C) The greatest tumor dimension was about 25 mm on white light endoscopy. (D) Narrow band imaging showed a well-demarcated, brownish area (arrows). (E) Narrow band imaging-magnifying endoscopy revealed an irregular microvascular pattern. Superficial cancer spread extended for about 30 mm from the postcricoid area to the lateral wall via the pyriform sinus and was contiguous with the primary tumor.

advanced esophageal cancer, the ability to detect SCS was similar for Lugol chromoendoscopy and NBI-ME. The clinical T category was revised in nine patients (20%) who had advanced oropharyngeal and hypopharyngeal cancer; it was upgraded from T1 to T2 in two patients (4%) and from T2 to T3 in seven patients (16%). The clinical stage was revised in two patients (4%); one patient (2%) was upgraded from stage I to II, and one patient (2%) was upgraded from stage II to III. In patients with advanced esophageal cancer, there was no change in clinical T category or in clinical stage (Table II).

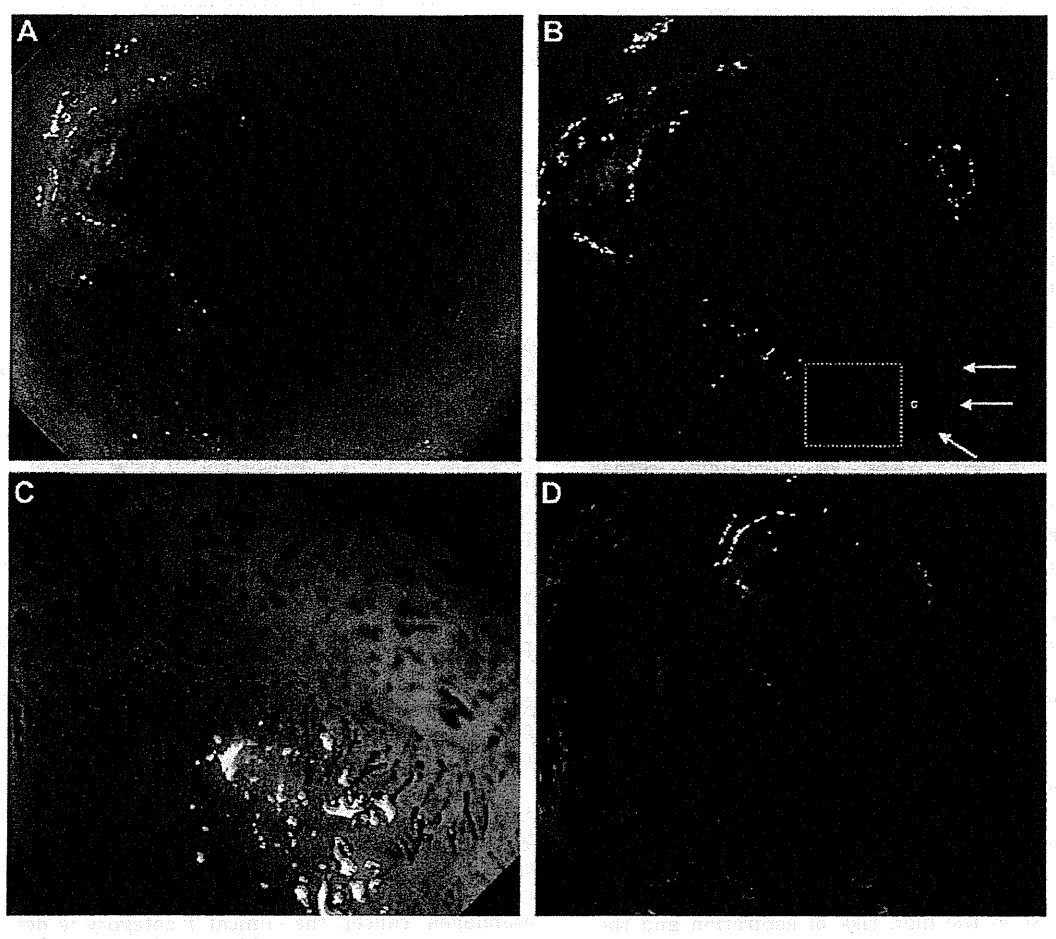

Fig. 4. Advanced esophageal cancer. (A) White light endoscopy revealed advanced esophageal cancer. (B) Narrow band imaging showed a well-demarcated, brownish area at the border of the primary tumor (arrows). (C) Narrow band imaging-magnifying endoscopy revealed an irregular microvascular pattern. (D) Superficial cancer spread appeared as an unstained area at the border of the primary tumor on Lugol chromoendoscopy.

TABLE I.
Patient and Lesion Demographics (n = 89).

Gender, no. (%)	
Male	78 (88)
Female	11 (12)
Age, mean ± SD, yr	66 ± 8.7
Range, yr	45–89
Site of primary cancer, no. (%)	
Oropharynx	6 (7)
Anterior wall	4 (5)
Lateral wall	1 (1)
Posterior wall	1 (1)
Hypopharynx	39 (44)
Pyriform sinus	22 (25)
Postcricoid area	9 (10)
Posterior wall	8 (9)
Esophagus	44 (49)

SD = standard deviation.

The dimensions of SCS contiguous with the primary tumor are summarized in Table III. In advanced oropharyngeal and hypopharyngeal cancer, SCS was ≤2 cm in 64% of cases (14/22), between >2 cm and ≤4 cm in 36% (8/22), and >4 cm in 0% (0/22). In advanced esophageal cancer, SCS was ≤2 cm in 52% (12/23) of cases, between >2 cm and ≤4 cm in 30% (7/23), and >4 cm in 17% (4/23). The size of SCS did not differ between patients with advanced oropharyngeal and hypopharyngeal cancer and those with advanced esophageal cancer (P =.237).

DISCUSSION

A nationwide survey conducted by the Japan Society for Head and Neck Cancer in 2005 reported that no patient with oropharyngeal and hypopharyngeal cancer had carcinoma in situ at initial presentation, suggesting that is it very difficult to visually confirm superficial cancer in the oropharynx and hypopharynx.[10] Laryngoscopy was conventionally used to detect oropharyngeal and hypopharyngeal cancer. However, the advent of NBI-ME has markedly improved the ability to visualize superficial cancer,[2–6] facilitating the diagnosis of SCS

contiguous with advanced cancer. In the present study of SCS contiguous with advanced oropharyngeal cancer and hypopharyngeal cancer, the rates of clearly visualizing "well-demarcated areas" and "irregular microvascular patterns," considered endoscopic characteristics of superficial cancer, on white light endoscopy, NBI, and NBI-ME were 23% (5/22), 82% (18/22), and 100% (22/22) for the former, respectively; and 14% (3/22), 77% (17/22), and 100% (22/22) for the latter, respectively. Therefore, well-demarcated areas and irregular microvascular patterns of SCS were better visualized by NBI and NBI-ME than by white light endoscopy. Furthermore, NBI-ME allowed definitive visualization of both of these characteristics. Muto et al. reported that the sensitivities and accuracies for the diagnosis of superficial cancer in the oropharynx and hypopharynx were 7.7% and 62.9% for white light endoscopy, respectively, as compared with 100% and 86.7% for NBI-ME, respectively. For the diagnosis of superficial esophageal cancer, the sensitivities and accuracies were 55.2% and 56.5% for white light endoscopy, respectively, and 97.2% and 88.9% for NBI-ME, respectively.[5] In the present study, a histopathological diagnosis could be made in 29 (64%) of 45 cases of SCS that were diagnosed endoscopically (14 cases of oropharyngeal cancer and hypopharyngeal cancer and 15 cases of esophageal cancer). However, superficial cancer was histologically confirmed in all cases. These findings indicate that the diagnostic accuracy of NBI-ME for SCS is extremely high.

Lugol chromoendoscopy has been used to diagnose lesion extent in patients with esophageal cancer,[7] but cannot be used to examine the oropharynx and hypopharynx because of the high risk of aspiration and the strong local irritation caused by iodine. In our study, all cases of SCS contiguous with advanced esophageal cancer detected on Lugol chromoendoscopy were also visualized on NBI. This finding suggested that NBI is also likely to be useful for the confirmation of SCS contiguous with advanced oropharyngeal and hypopharyngeal cancer, which cannot be evaluated on Lugol chromoendoscopy. In our study, SCS was associated with 49% of advanced oropharyngeal and hypopharyngeal cancers and 52% of advanced esophageal cancers (i.e., about one half of the patients with each type of cancer). To our knowledge, this is the first time similar frequencies of SCS contiguous with the primary tumor in patients with advanced oropharyngeal and hypopharyngeal cancer, and those with advanced esophageal cancer were reported. Therefore, we believe that our results are very important. Moreover, in 18% (8/45) of patients with advanced oropharyngeal and hypopharyngeal cancer, SCS contiguous with the primary tumor exceeded 2 cm. We therefore consider NBI-ME to be essential for the determination of appropriate surgical margins and radiation fields.

TABLE II.
Frequency of Superficial Cancer Spread Contiguous With Primary Tumor and Effects on Clinical T Category and Clinical Stage.

	Advanced Oropharyngeal/ Hypopharyngeal Cancer (n = 45)	Advanced Esophageal Cancer (n = 44)
Frequency of superficial cancer spread, no. (%)		
NBI-ME	22 (49)	23 (52)
Lugol chromoendoscopy	NE	23 (52)
Frequency of changes in clinical T category, no. (%)	9 (20)	0 (0)
From clinical T1 to T2	2 (4)	
From clinical T2 to T3	7 (16)	
Frequency of changes in clinical stage, no. (%)	2 (4)	0 (0)
From clinical stage I to II	1 (2)	
From clinical stage II to III	1 (2)	

NBI = narrow band imaging; ME = magnifying endoscopy; NE = not evaluated.

TABLE III.
Dimensions of Superficial Cancer Spread.

	Advanced Oropharyngeal/ Hypopharyngeal Cancer (n = 22)	Advanced Esophageal Cancer (n = 23)	*P* Value*
0 cm to ≤2 cm	14 (64%)	12 (52%)	
>2 cm to ≤4 cm	8 (36%)	7 (30%)	
>4 cm	0 (0%)	4 (17%)	.237

*Calculated using Mann-Whitney *U* test.

Because the 7th edition of the UICC TNM staging system does not include contiguous SCS as a staging factor,[9] we examined whether clinical T category and clinical stage were altered by including contiguous SCS in the greatest dimension of the primary tumor. In esophageal cancer, the clinical T category is determined by the depth of primary tumor invasion.[9] Consequently, the presence of SCS contiguous with the primary tumor does not change the clinical T category. In contrast, the clinical T category of oropharyngeal and hypopharyngeal cancer depends on the greatest dimension of the primary tumor.[9] The inclusion of SCS contiguous with the primary tumor in the evaluation of tumor size may thus alter the clinical T category, potentially affecting the clinical stage grouping. When we included SCS contiguous with the primary tumor in the calculation of the greatest tumor dimension in patients with oropharyngeal and hypopharyngeal cancer, the clinical T category was upgraded in 20% of cases. However, the effect on clinical stage was minimal. Clinical T categories were decided before it was possible to clinically evaluate SCS contiguous with the primary tumor. With improved diagnostic techniques, contiguous SCS can now be evaluated. Therefore, a discussion of whether to include contiguous SCS in the evaluation of clinical T category now appears to be warranted.

CONCLUSION

In this study, advanced oropharyngeal and hypopharyngeal cancer is frequently associated with contiguous SCS. NBI-ME should be included in the pretreatment diagnostic work-up to evaluate lesion extent

and decide optimal surgical margins and radiation fields.

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Efficacy of Preventive Endoscopic Balloon Dilation for Esophageal Stricture After Endoscopic Resection

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Background and Aim: We earlier reported that mucosal defect involving over three-fourths of the circumference of the esophagus after endoscopic mucosal resection (EMR) is a risk factor for the development of the stricture. Although endoscopic balloon dilation (EBD) is a useful procedure to relieve the stricture, there is no standard strategy for preventing development of the stricture. The aim of this study was to evaluate the efficacy and the safety of preventive EBD.

Methods: From 1993 to 2008, 41 consecutive patients with extensive mucosal defect involving over three-fourths of the esophageal circumference after EMR or endoscopic submucosal dissection (ESD) were investigated. Preventive EBD was carried out for 29 cases within 1 week just after EMR/ESD and was repeated once a week until the mucosal defect was completely healed. The remaining 12 cases were not underwent preventive EBD and used as a historic control. If postEMR/ESD stricture developed regardless of preventive EBD, conventional EBD was given repeatedly until the stricture was completely relieved.

Results: Preventive EBD decreased the incidence of stricture (59% vs. 92%, $P = 0.04$), reduced the severity of stricture [(≤ 2 mm; > 2 mm and ≤ 5 mm; > 5 mm) = (1; 2; 14) vs. (4; 4; 3), $P = 0.01$] and shortened the duration required for resolving the stricture (29 d vs. 78 d, $P = 0.04$) even when stricture developed. There was no complication associated with preventive EBD procedure.

Conclusions: Preventive EBD is an effective procedure to prevent postEMR/ESD stricture. Preventive EBD should be considered when EMR/ESD results in a mucosal defect with a circumference greater than three-fourths of the esophageal lumen.

Key Words: endoscopic mucosal resection, endoscopic submucosal dissection, esophageal stricture, endoscopic balloon dilation, prevention

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Endoscopic mucosal resection (EMR) is being increasingly accepted as one of the standard treatment for superficial esophageal cancer because of its minimal invasiveness and excellent survival rate.[1,2] Furthermore, the endoscopic submucosal dissection (ESD) technique has made it possible to carry out *en-bloc* resection of widespread neoplasia, such as a superficial spreading-type of esophageal squamous cell carcinoma and Barrett esophageal cancer.[3–7] However, extended removal of the esophageal mucosa frequently causes severe stricture.[8,9]

Esophageal stricture may markedly interfere with the oral intake of food and fluids, and thus affect the patients' quality of life adversely. In addition, once severe esophageal stricture has developed, it is difficult to resolve the condition. Although endoscopic balloon dilation (EBD) is usually indicated for benign stricture including the cicatricial stricture caused by EMR/ESD, the effect of EBD is sometimes only temporary and the stricture would reappear.[10,11]

Before 2002, we carried out EBD only when the patients complained of dysphagea by postEMR/ESD stricture, and EBD was repeated until the dysphagea was completely resolved. In 2003, we reported that mucosal defects greater than three-fourths of the circumference of the esophagus after EMR are at high risk of developing esophageal stricture.[12] Since then, we started preventive EBD not to develop stricture, before postEMR/ESD mucosal defects develop scarring.

In this study, we evaluated the effectiveness of preventive EBD for the patients with superficial widespread esophageal cancer who developed mucosal defect extending more than three-fourths of the circumference of the esophagus by EMR/ESD.

PATIENTS AND METHODS

Patients

From February 1993 to June 2008, we experienced 64 consecutive patients with widespread mucosal defects greater than three-fourths of the esophageal circumference as a result of EMR/ESD for esophageal cancer. Written informed consent was obtained from all patients before carrying out EMR/ESD and EBD.

Endoscopic Resection Technique

To remove the lesions endoscopically, EMR[13,14] or ESD[5–7] were carried out.

EBD Technique

All patients received administration of 17.5 to 35 mg of pethidine hydrochloride to reduce the suffering from EBD

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procedure. All EBD procedures were carried out using direct visualization and fluoroscopic monitoring. The balloon was positioned across the stenotic site, and then it was inflated carefully with double-diluted contrast agent. During the procedure, patients were closely observed with pulse, blood pressure, and oxygen saturation. When a patient experienced pain during the dilation or when a notch of the balloon placed on the stricture was gradually disappeared, dilation was stopped, and then the balloon was maintained in its inflated state and held close to the tip of the endoscope, and was pushed through the stenotic site as a bougie technique. If the notch of the balloon was rapidly expanded, suggesting a tear at the stenotic site, dilation is immediately stopped and the balloon was deflated, and then the endoscope and deflated balloon were removed.

Four CRE balloon dilators (Boston Scientific Corp. Natick, MA, USA) of different sizes (10 to 12 mm, 12 to 15 mm, 15 to 18 mm, and 18 to 20 mm) were used according to the severity of the stricture. A single balloon was used in each EBD session. When the endoscope could be passed through the site of the mucosal defect, a balloon of 18 to 20 mm was used. When the stricture was less than 10 mm in diameter and larger than 5 mm, a 15 to 18 mm balloon was used. When the stricture was less than 5 mm in diameter and larger than 2 to 3 mm, a 12 to 15 mm balloon was used. When the stricture was a pinhole stricture, a 10 to 12 mm balloon was used. We did not carry out preventive EBD when the luminal diameter was estimated to be greater than 20 mm because the diameter of the lumen would have been greater than that of the fully expanded balloon.

In this study, we defined the EBD procedure carried out immediately after EMR/ESD as "preventive EBD" and that after the development of postEMR/ESD cicatricial stricture as "conventional EBD."

Protocol of the Preventive EBD and Conventional EBD

Preventive EBD was commenced within 1 week after the EMR/ESD and repeated weekly until the complete healing of mucosal defect was observed (Fig. 1). Patients consumed a regular diet during the period of mucosal healing and weekly preventive EBD.

If the postEMR/ESD mucosal defects became scarred with stricture despite repeated preventive EBD, conventional EBD was given repeatedly until the stricture was completely resolved. The time interval of conventional EBD depended on patients' symptom such as dysphagea (usually 2 to 4 wk). The strategy of conventional EBD has not been changed throughout this study period, therefore, the time interval of conventional EBD is not different between 2 groups.

Definition of the Stricture

"Stricture" was defined when a standard 11-mm-diameter endoscope (Q240, 1T240; Olympus Optical Co. Ltd., Tokyo, Japan) could not be passed through the site, or when the patients complaint of dysphagea. Whereas, "complete resolution of the stricture" was defined when a standard diameter endoscope could be passed through the site, and patients' symptoms of dysphagia were completely relieved.

In each EBD sessions in all cases, diameter of stricture was measured by comparing with the diameter of inflated balloon under the fluoroscopic monitoring, and it was classed into 3 groups: more than equal to 2 mm; more than 2 mm and, more than equal to 5 mm; more than 5 mm. The duration required for resolving the stricture was defined as the time interval between the day when the stricture was first observed and the day of complete resolution.

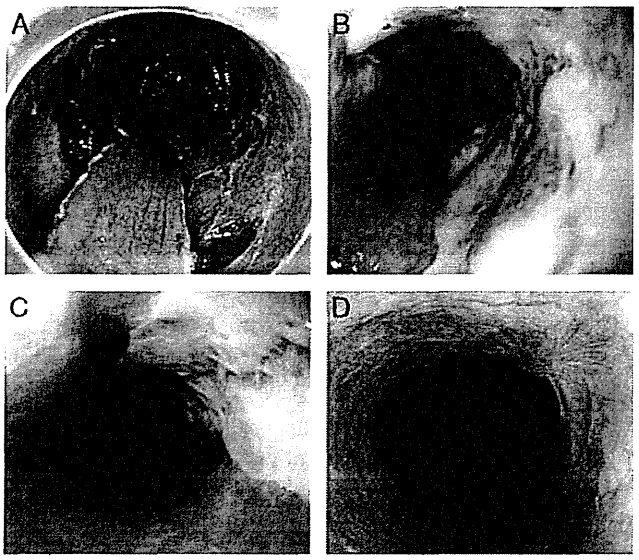

FIGURE 1. A representative case who received preventive endoscopic balloon dilation after a semicircumferential endoscopic submucosal dissection(ESD). A, Semicircumferential mucosal defect immediately after the ESD. B, Mucosal defect 1 week after the ESD. The site gradually developed scarring with mild stricture. C, Mucosal defect 1 month after the ESD. The site developed scarring furthermore, but the stricture was mild. D, PostESD site 2 months after the ESD. The complete healing of the postESD mucosal defect was observed without stricture. The endoscope could be passed through the site and the patient did not complain of any symptom with esophageal stricture.