

図1 腫瘍の局在 当センター141例の術前内分泌+前立腺全摘におけるリスク*別の腫瘍mappingデータ

* D' Amicoらによるリスク分類: Int J Radiat Oncol Biol Phys 43: 587-590, 1999

しており、かつてのような大量出血をきたすことはまれである。

ここで問題となるのは前立腺尖部と尿道には明確な境界がないことである。発生学的に前立腺は尿道括約筋の中にあたかも風船がふくらんだ様な発生をしており、尿道括約筋は前立腺腹側にも存在している。前立腺尖部では尿道前面に腺組織が乗り上げていることもあれば、後面で尿道前立腺境界部を超えてさらに末梢に進展している(この形態をクロワッサン型と呼んでいる)こともある。前立腺全摘においては発生学的に境界のない組織をいかにして認識し、確実に処理を行うかという点が問題となる。その点では前立腺尖部の処理ではmm単位の処理が要求される。局所放射線治療においても前立腺尖部に十分な放射線量を確保することが必要と考えられるが、前立腺尖部を正確に認識することは比較的困難と考えられ尿道括約筋にもある程度の放射線が照射されることはありうることではと考えられる。

また前立腺と直腸との間にはいわゆる

Denonvilliers' fasciaがあるとされるが、本邦の症例では前立腺と直腸との間にはほとんど脂肪織がなく、1~2mm程度の索状物(Denonvilliers' fascia)が存在するのみである。前立腺全摘においてはこのことを認識していないと直腸損傷につながる。同様に放射線治療においては直腸線量をコントロールするためにはその境界は1~2mmしかないということである。このことは本邦におけるdose escalationによる放射線治療の直腸への遅延性反応の懸念が米国より高いのではとの想定がある。

4. 局所前立腺癌治療の治療間成績比較の問題

局所前立腺癌は一般的にその予後が良好であり、治療の優劣の比較のためにはPSA failureをsurrogate end pointとして解析されることが多い。NCIのphysicians data query (PDQ[®])によるstrength of endpoint(表1)にも述べられているように、本来なら癌治療の優劣に関してはまずtotal mortalityがどうかという点となるべきであるが、局所前立腺癌に対して根治手術後の

表1 strength of endpoint in NCI physicians data query (PDQ^{R3})

1. total mortality (or overall survival from a defined time)
2. cause-specific mortality (or cause-specific mortality from a defined time)
3. carefully assessed quality of life
4. indirect surrogates
 - 1) disease-free survival
 - 2) progression-free survival
 - 3) tumor response rate

(<http://www.nci.nih.gov/cancertopics/pdq/levels-evidence-adult-treatment/HealthProfessional/page3>)

PSA failureが臨床的再発につながるまで平均8年、その後これが最終的な生存に参与するのは平均5年というデータがある¹⁷⁾ように、survivalによる治療の優劣を判定するためにはかなりの経過観察が必要となる。そのためPSA failureを用いた治療法の比較は理解できるものであるが、局所前立腺癌に対する手術療法と放射線治療におけるPSA failureの定義が全く異なることを留意する必要がある。

根治手術後のPSA failureの定義は測定感度以上とされる。Tandem-R PSAの測定限界が0.1ng/dlのためか0.2ng/dl以上が一般的な基準として採用されることが多い。しかし文献的にはPSAの絶対値とともに連続上昇などの付帯条件を採用しているものも多々認められる。これらの混乱はPSA failureとされる病態が実際の生存率と必ずしも相関していないことによる。たとえば術後PSA値が10年先に0.2ng/dlを超えたからといって、期待余命にもよるがこのような症例が前立腺癌死する危険性はきわめて低いと考えられる。最近では術後の評価のためには腫瘍の増殖するスピードと相関すると考えられるPSA doubling time (PSADT) が大切との主張が見受けられ、より理解可能なsurrogate end pointではないかと考えられる¹⁸⁻²⁰⁾。術後PSAが測定可能となったことと、真に前立腺癌細胞の残存との間にも確証がないことも混乱の原因である。つまり術後PSAが測定可能となった場合にいえることは「前立腺細胞」が体内に存在している可能性が高いということのみであり、本当にそのことが「前立腺癌細胞」が遺残していることと必

ずしも相関しないことである。このような細胞レベルでの変化を画像などで確定できないこともこの大きな要因である。また根治手術後PSAが測定限界に低下しない場合にはPSA failureの起点日は手術日となる(癌なし生存期間0日)となることも治療間の比較では留意が必要である。

放射線治療後のPSAの評価はさらに容易ではない問題をはらんでいると思われる。根治放射線治療後のPSA failureの定義としてはASTRO criteriaによる判定がもっともconventionalであると思われる。この定義では手術療法と異なり癌なし生存期間が0日となることはまずない。放射線治療では手術療法と異なり、正常前立腺細胞が体内から完全に消失するとは考えにくい。そのためPSA failureとして測定限界以下という定義にはできない。しかし正常前立腺細胞のPSA doubling timeは30年ともいわれているように正常の前立腺細胞も増殖し肥大症となっていく。一方、前立腺癌と診断され、watchful waitingを施行された症例において再生検を行ってみるとPSAが安定していても、相当な細胞量が確認されることがある。

これは前立腺正常細胞(前立腺肥大も含む)から分泌されるPSAの割合が多く、このため癌の増殖に伴うPSAの産出の増加がマスクされたことによるのではと思われる。したがってPSA値が上昇していないからといって本当にすべての癌細胞が消滅したという証明にはならない。前立腺生検はこのような状況に対して一定の情報を提供してくれると考えられるが、癌が証明されなかったといって本当に癌なしとなってい

表2 本邦における前立腺全摘のmorbidity
(1991~1998 n=638)

complication	%
intraope	
rectal injury	3.0
major bleeding	0.3
ureteral injury	0.2
early postope	
thrombo-embolic	0.7
wound infection	7.5
anastomotic leak	4.1
prolonged lymph	2.2
gastrointestinal	0.8
lympocele	0.6
vesical bleeding	0.3

BJU Int 85 : 287-294, 2000より

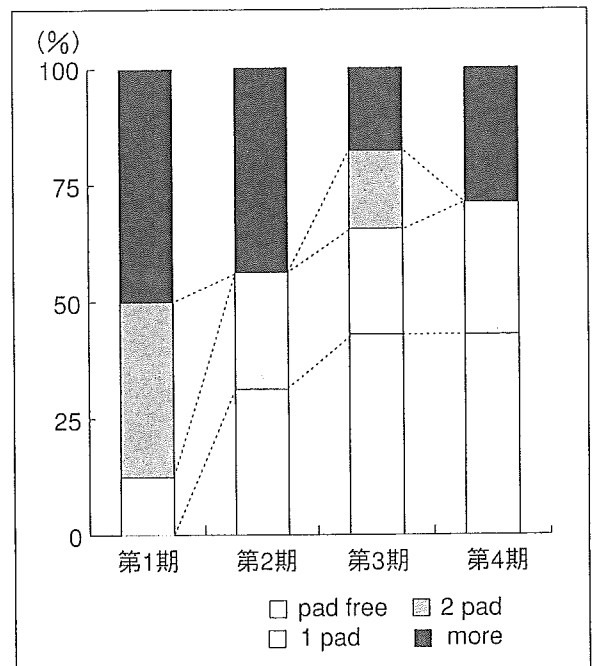


図2 尿道カテーテル抜去直後の尿禁制 pad使用量による評価

るかの証明にはならない。また放射線治療後の再生検では適切な時期に対してはまだ明確なエビデンスはないと思われる。放射線治療の後、たとえばPSA値が高めで安定しているような場合、本当に癌なし生存とするのか、きわめて低い値であるが、PSA値が高感度PSAのように0.001のオーダーまで測定可能である場合、3 point連続上昇したからといって本当に将来、前立腺癌死の可能性があるのか、このような問題は前立腺を体内から完全に摘出することを目指す前立腺全摘以上に混乱がある。

現在、局所前立腺癌に対する治療法比較に最も必要なのは、NCIのプロトコールスタディにおけるendpointの指摘にあるように最終的な生存率の優劣である。したがって治療法の後、症例が癌死する確率を判定することではと思われるが、このためには15年近い経過観察が必要であり、即座に結論できない。症例選択に対するバイアスもあり、単純に治療成績の比較も無意味である。いずれにしても局所前立腺癌に対する治療成績の比較をPSA failureで行うことは不正確であることを認識する必要がある。

5. 前立腺全摘のmorbidityと泌尿器科医からみた放射線治療後の遅発性放射線反応の懸念

根治的前立腺全摘は当然、外科的治療であり、侵襲を伴う治療法であることは疑念がない。1990年代前半ではこの手術はまだかなりの出血と術後morbidityを伴う治療法であった。その後、症例の集積、技術の改良などの結果、high volume center病院では前立腺全摘のmorbidityは格段に向上している。本邦における前立腺全摘のmorbidityをまとめたデータ²¹⁾を表2に示す。当センターにおける前立腺全摘では近年では入院期間は平均10日前後、尿道カテーテル留置期間は5~6日、出血量は5~600cc程度まで改善し、術後尿失禁についてもカテーテル抜去直後でも5割弱はその段階でpad freeとなっている(図2)。詳細は省略するが横軸の“時期”とは手術に関するいろいろな技術の改良を行った期間であり、第4期が最も新しい方法でのデータである。

このような状況を考慮するとき放射線治療であるから低侵襲であるとはいえない側面があると感じている。たとえば3D-CRTでは35日近い通院期間を要し、この治療期間に対する仕事の休

業、通院に要する時間的、金銭的な負担という面も考慮して治療法のmorbidityは語られるべきではと感じている。

放射線治療におけるmorbidityの関心として、直腸障害がよく議論されているが、泌尿器科医として放射線治療の遅発性反応の懸念は少し異なる。実際に放射線治療後に起こる症状のうち泌尿器科医にとって最もつらいのは、頻度はまれではあるが膀胱出血、タンポナーデである。この出血は容易には止血できず、患者は昼夜を問わず相当な苦しみを味わうことになる。残念ながら、この実情を放射線科医は知らないのではと思われる。なぜならこのような障害はかなり時間が経過してから起こることもあり、対応はほとんど泌尿器科医に託されるからである。コントロールが不良の場合には膀胱全摘や尿路変向が適応となるが、このような手術療法の侵襲は、直腸障害のために施行される人工肛門の比ではない。前立腺全摘後、相当な局所再発は別としてこのような副作用が起こることはない。

またほとんど問題とされていないが、意外に泌尿器科医が面倒と感じるのは放射線に伴う頻尿、夜尿、膀胱刺激などである。このような症状に致して有効な治療薬が乏しく、症状が改善しにくいことにもよる。

最もミゼラブルなのが、膀胱尿道瘻、直腸瘻である。かつて婦人科領域の放射線治療後、10年20年後にこのような病態をきたしたことがあり、その対応を行っていたのは、治療を施行した放射線科医でも婦人科医でもなく、結局、泌尿器科医が対応しており、その悲惨さを身にしみ感じていた。近年の放射線治療ではこのような事態はおそらく発生しないかもしれないが、

前述したように前立腺と直腸との間にほとんど距離のない本邦での前立腺癌症例において、そのなかでも特に若年者についてdose escalation治療を適応していく場合には注意が必要ではと考えている。

6. 局所前立腺癌に対する手術法による治療成績の相違

一口に前立腺全摘といっても神経温存を含めた米国を中心とする前立腺全摘と我々が実施している広汎前立腺全摘ではカバーできる範囲が全く異なると考えている。たとえば一般的な前立腺全摘ではorgan confined diseaseか否かが重要なPSA failureの規定因子となり、したがって一般的には被膜外浸潤を伴った前立腺癌は手術療法の対象外と認識されていることはすでに述べた。事実T3前立腺癌に対する治療成績では本質的に局所再発の危険が高いとされている²²⁻²⁸⁾。

前立腺癌の術前画像診断などによる予想が困難であることよりPSA, Gleason, T stageから局所の浸潤度やリンパ節転移を予想するPartin table²⁹⁾に代表されるようなノモグラムが一定の役割を持って受け入れられている。ところが本邦の前立腺癌ではリンパ節転移が少ない印象があり、このような米国を中心とするノモグラムを”直輸入”はできない。リンパ節転移の頻度が少ないこと、あるいは本邦では性機能障害が精神的負担と直接関しないことが多々認められること、癌に対する手術療法に過大の期待があることなどを考慮すると、被膜外浸潤を伴う前立腺癌でも条件によっては十分手術で根治が望める症例があると想定される^{27) 28)}。

このような発想からstage C前立腺癌に対して前

表3 対象と方法

- 200年1月～2003年12月まで
- cT3N0M0
- Gleason Score 7～9 (GS10を除く)
- 神経温存を意図しない手術に同意
- 6～9カ月の術前内分泌療法施行
- 術後は結果の如何にかかわらず経過観察

表4 背景

	最小—最大	平均値	中央値
年齢 (歳)	53—74	64.1	65.5
PSA (ng/dl)	2.45—124	20.64	13.24
Gleason score	6—9	7.68	7
観察期間 (日)	112—1,500	581.7	455.5

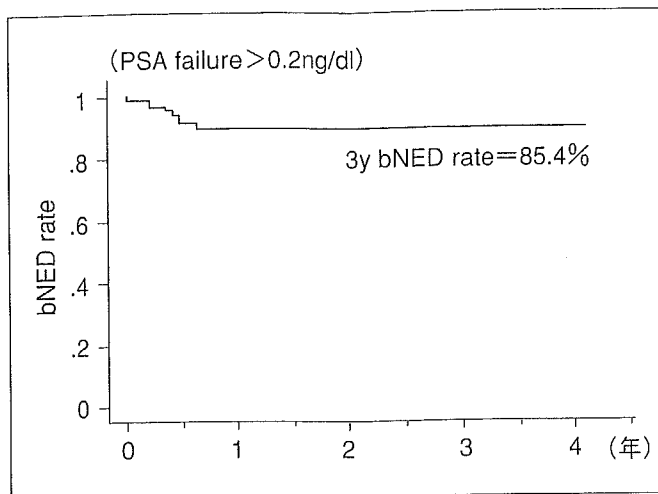


図3 high Gleason score, stage Cに対する広汎前立腺全摘の成績 (n=70)

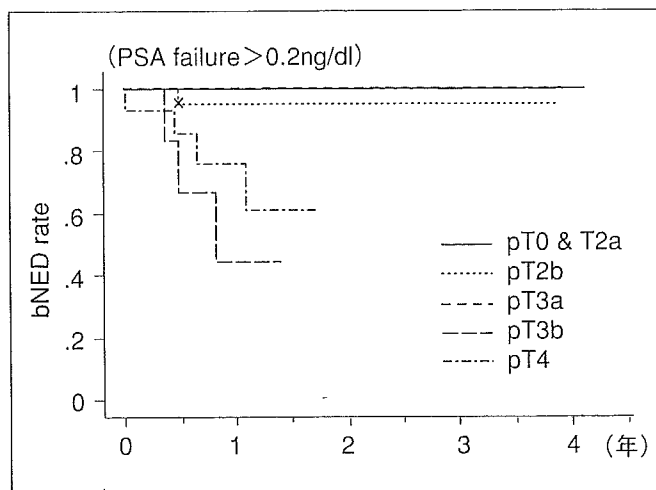


図4 pT分類別bNED rate

立腺周囲を広汎に切除する手術法を開発した³⁰⁾。その後、本手術法cT3N0M0に対して術前内分泌療法の後、prospectiveに適応した。以下にその結果を呈示する。

対象と背景を表3, 4に記載した。平均観察期間はまだ短く、早急な結論はできないがPSA failureを0.2ng/dl以上と定義し、解析を行うと3年bNED率は85.4%となっている(図3)。また摘出標本でのpT分類別のbNED率を図4に示した。pT3b, pT4以外の予後はきわめて良好である。これはstage Cでかつhigh Gleason症例を対象とした前立腺全摘の成績として、これまでの常識を覆すデータではと考えている。

以上のことより、たとえstage Cといえども確実な切除を追求することは明らかに本邦でのcT3N0M0前立腺癌の治療成績を向上させる可能性があると考えている。

おわりに(治療法による“棲み分け”のためになにが重要か)

前立腺癌を取り巻く状況ではPSA eraとなり早期前立腺癌が本邦でも多くなり、そのための治療法として無治療待機療法、手術療法、放射線治療、小線源治療あるいはHIFU療法なども治療の選択として登場してきた。その中で手術療法あるいは放射線治療、そのいずれにも、その治

療法の治療成績に有利な症例のみを選択して治療しようとしているように思えてくる。たとえば前立腺全摘の適応としてlow Gleason, low PSA, low volumeな前立腺癌を選択すべきであるとか、小線源療法のよい適応としてPSA<10, Gleason score 6かそれ以下がよい、などである。確かにこのような症例はその治療法には、より予後が良好であり、格好の「宣伝」材料となるのであるが、このような局所療法に好都合な症例の選択は、果たしてそのようなgood riskの症例を治療する必要があるのかという皮肉にも似たジレンマを生んでいる。実際このようなgood riskの症例ではSwedenの研究³¹⁾にもあるように無治療経過観察でもさほどの予後の差は認められない。

現在、転移性前立腺癌が完治できないことは「やむなし」としても、局所前立腺に対する治療法を考える上で最も重要なのは、治療法の如何にかかわらず予後が良好と考えられる前立腺癌の治療法に対する侵襲の優劣ではなく、局所進行癌をどうやって完治させるか、あるいは完治が不可能でも最もQOLを高く保障できるかということが、癌治療として本邦の臨床腫瘍医が最も取り組まなくてはならない問題ではないのかと思える。

文 献

- 1) Lu-Yao GL et al : Population-based study of long-term survival in patients with clinically localized prostate cancer. *The Lancet* 349 : 906-910, 1997
- 2) Elgamal AA et al : Impalpable invisible stage T1c prostate cancer ; characteristics and clinical relevance in 100 radical prostatectomy specimens ; a different view. *J Urol* 157 : 244-250, 1997
- 3) Graverson PH et al : Radical prostatectomy versus expectant primary treatment in stages I and II prostatic cancer. A fifteen-year follow-up. *Urology* 36 : 493-498, 1990
- 4) Gibbons RP : Total prostatectomy for clinically localized prostate cancer ; long-term surgical results and current morbidity. *NCI Monogr* 7 : 123-126, 1988
- 5) Pound CR et al : Prostate-specific antigen after anatomic radical retropubic prostatectomy. Patterns of recurrence and cancer control. *Urol Clin North Am* 24 : 395-406, 1997
- 6) Ohori M et al : Can radical prostatectomy alter the progression of poorly differentiated prostate cancer?. *J Urol* 152 : 1843-1849, 1994
- 7) Lerner SE et al : Extended experience with radical prostatectomy for clinical stage T3 prostate cancer ; outcome and contemporary morbidity. *J Urol* 154 : 1447-1452, 1995
- 8) Walsh PC et al : Impotence following radical prostatectomy ; insight into etiology and prevention. *J Urol* 128 : 492-497, 1982
- 9) Labrie F et al : Down-staging of early stage prostate cancer before radical prostatectomy ; the first randomized trial of neoadjuvant combination therapy with flutamide and a luteinizing hormone-releasing hormone agonist. *Urology Symposium* 44 (6A) : 29-37, 1994
- 10) Van Poppel H et al : Neoadjuvant hormonal therapy before radical prostatectomy decreases the number of positive surgical margins in stage T2 prostate cancer ; interim results of a prospective randomized trial. The Belgian Uro-Oncological Study Group. *J Urol* 154 : 429-434 : 1995
- 11) Hugosson J et al : The risk of malignancy in the surgical margin at radical prostatectomy reduced almost three-fold in patients given neo-adjuvant hormone treatment. *Eur Urol* 29 : 413-419, 1996
- 12) Soloway MS et al : Randomized prospective study comparing radical prostatectomy alone versus radical prostatectomy preceded by androgen blockade in clinical stage B2 (T2bNxM0) prostate cancer. The Lupron Depot Neoadjuvant Prostate Cancer Study Group. *J Urol* 154 : 424-428, 1995
- 13) Klotz LH et al : CUOG randomized trial of neoadjuvant androgen ablation before radical prostatectomy ; 36-month post-treatment PSA results. *Canadian Urologic Oncology Group. Urology* 53 : 757-763, 1999
- 14) Aus G et al : Three-month neoadjuvant hormonal therapy before radical prostatectomy ; a 7-year follow-up of a randomized controlled trial. *BJU Int* 90 : 561-566, 2002
- 15) D' Amico AV et al : Defining the implant treatment volume for patients with low risk prostate cancer ; does the anterior base need to be treated?. *Int J Radiat Oncol Biol Phys* 43 : 587-590, 1999
- 16) Takashima R et al : Anterior distribution of Stage T1c nonpalpable tumors in radical prostatectomy specimens. *Urology* 59 : 692-697, 2002
- 17) Pound CR et al : Natural history of progression after PSA elevation following radical prostatectomy. *JAMA* 281 : 1591-1597, 1999
- 18) D' Amico AV et al : Surrogate end point for prostate cancer-specific mortality after radical prostatectomy or radiation therapy. *J Natl Cancer Inst* 95 : 1376-1386, 2003
- 19) D' Amico AV : Predicting prostate-specific antigen recurrence established ; now, who will survive? *J Clin Oncol* 20 : 3188-3190, 2002
- 20) Iselin CE, et al : Radical perineal prostatectomy ; oncological outcome during a 20-year period. *J Urol* 161 : 163-168, 1999
- 21) Arai Y et al : Radical retropubic prostatectomy ; time trends, morbidity and mortality in Japan. *BJU Int* 85 : 287-294, 2000
- 22) Van den Ouden D et al : Radical prostatectomy as a monotherapy for locally advanced (stage T3) prostate cancer. *J Urol* 151 : 646-651, 1994
- 23) Lerner SE et al : Extended experience with radical prostatectomy for clinical stage T3 prostate cancer ; outcome and contemporary morbidity. *J Urol* 154 : 1447-1452, 1995
- 24) Di Silverio F et al : DNA ploidy, Gleason score, pathological stage and serum PSA levels as predictors of disease-free survival in C-D1 prostatic cancer patients submitted to radical retropubic prostatectomy. *Eur Urol* 30 : 316-321, 1996
- 25) Gerber GS et al : Results of radical prostatectomy in men with locally advanced prostate cancer ; multi-institutional pooled analysis. *Eur Urol* 32 : 385-390, 1997
- 26) Theiss M et al : Radical prostatectomy as primary monotherapy in capsule penetrating prostatic carcinoma. 15 years outcome. *Urologe A* 36 : 343-347, 1997
- 27) van den Ouden D et al : Progression in and survival of

patients with locally advanced prostate cancer (T3) treated with radical prostatectomy as monotherapy. J Urol 160 : 1392-1397, 1998

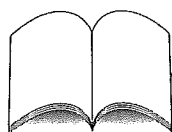
- 28) van Poppel H et al : Radical prostatectomy can provide a cure for well-selected clinical stage T3 prostate cancer. Eur Urol 38 : 372-379, 2000
- 29) Partin AW et al : Combination of prostate-specific antigen, clinical stage, and Gleason score to predict pathological stage of localized prostate cancer. A multi-institutional update. JAMA 277 : 1445-1451, 1997
- 30) 藤元博行 : 神経温存を意図しない広汎前立腺全摘, 新癌の外科 手術手技シリーズ 2 泌尿器癌. p100-107, メディカルビュー, 2001
- 31) Holmberg L et al : Scandinavian Prostatic Cancer Group Study Number 4. ; a randomized trial comparing radical prostatectomy with watchful waiting in early prostate cancer. N Engl J Med 347 : 781-789, 2002

Summary

Curability and disability of radical prostatectomy for localized prostate cancer in Japan

To optimize the favorable therapeutic modality for localized prostate cancer, the overview of controversial issues concerning radical prostatectomy reviewed. In addition, for radiation oncologists, some valuable information included anatomical consideration of the prostate apex and the Denonvilliers' fascia was presented. For T1c-T2b prostate cancer, many urologist has believed radical prostatectomy to be most effective definitive therapy and T3 prostate cancer to be out of indication of radical prostatectomy. In Japanese prostate cancer, node positive disease seem to be less occurrence from the prostate cancer in USA and patients strongly want to cure of disease by surgery. So, extended resection surrounding the prostate for cT3 prostate cancer had been developed from 1998 in our hospital. In 70 cases with cT3 and Gleason score 7-9 prostate cancer, 3y bNED rate revealed to be 85.4% in this extended resection. The result indicates the possibility of cure of disease in even local advanced prostate cancer by extended resection in Japanese prostate cancer.

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外国文献紹介

大腸二重造影検査, CT擬似大腸鏡検査, 大腸鏡検査の前向き調査による比較分析
Rockey DC et al : Analysis of air contrast barium enema, computed tomographic colonography and colonoscopy : prospective comparison. Lancet 365 : 305-311, 2005

大腸検査としては、従来バリウム検査と内視鏡が実施されてきたが、近年CTの三次元構築を利用した擬似大腸鏡検査が行われるようになった。筆者らは、便潜血、下血、鉄欠乏性貧血等があるか大腸癌の家族歴がある614例に対して、大腸ポリープや大腸癌の検索を目的として、バリウム検査、CT、内視鏡を実施し、これらの検査法の病変検出能を比較した。その結果、10mm以上の病変の検出能は、バリウム検査が48%、CT 59%、内視鏡98%であり、6~9mmの病変の検出能は各々、35%、51%、99%であった。そして、大腸ポリープと大腸癌に関しては、これら3つの検査法の中では、大腸鏡が最も病変の検出能において優れていたと述べている。

瀬戸一彦

Treatment of early gastric cancer in the elderly patient: results of EMR and gastrectomy at a national referral center in Japan

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Background: The Japanese population is rapidly aging, and the actual number of elderly patients with gastric cancer, including early cancer, has been increasing, even though the standardized incidence of gastric cancer in the population is decreasing. The optimal treatment for these patients remains a challenge to the surgeon. The aim of this retrospective analysis was to describe the results of gastrectomy and EMR for early gastric cancer in elderly patients (80 years of age and over).

Methods: This is a retrospective review of 93 elderly patients who had undergone gastrectomy or EMR at the National Cancer Center Hospital for early gastric cancer. EMR was performed aiming en bloc local resection with a clear curative margin (R0). The clinicopathologic characteristics, comorbidity, postoperative mortality, and outcome were recorded.

Results: Gastrectomy was performed in 44 patients (surgery group) and EMR in 49 patients (EMR group). There were significant differences in mean tumor size ($p < 0.05$), histologic type ($p < 0.05$), and depth of tumor invasion ($p < 0.05$) between the two groups. There was no significant difference in comorbidity between the two groups. No operative death was reported in either group. In the EMR group, 7 patients were reported to have recurrence of local disease and two patients died of advanced disease. There were no significant differences in the overall 3-year survival rate or the 5-year survival rate between the surgery group and EMR group (73.5% vs. 82.5% and 55.0% vs. 62.5%, respectively).

Conclusions: EMR (R0) resection was performed safely in the elderly, and the overall results were excellent, the same as the results with gastrectomy. Gastrectomy can still be performed if EMR is unsuccessful. (Gastrointest Endosc 2005;62:868-71.)

The actual number of patients with early gastric cancer is increasing in the aging population of Japan.¹ Gastrectomy with nodal dissection has been the standard treatment for patients with early gastric cancer²; however, because early gastric cancer has a low incidence of lymph-node metastasis,^{3,4} surgeons, therefore, are faced with the problem of managing elderly patients (80 years of age and over) with early gastric cancer. The introduction of EMR, however, has provided an alternative curative modality for the treatment of early gastric cancer.

Elderly patients have a limited life expectancy, and operations, such as a total gastrectomy, are often associated with poor postoperative quality of life (QOL).⁵⁻⁷ Significant comorbidity risk factors, such as cardiovascular disease or respiratory disease, may also hamper recovery.⁸

The measure of the QOL, therefore, is much more important in the elderly than in the younger patients.

The aim of this retrospective analysis was to describe the results of gastrectomy and EMR for early gastric cancer in elderly patients.

PATIENTS AND METHODS

Patients

A total of 2519 cases of early gastric cancer were treated in our divisions between July 1985 and June 1999. The majority of the patients had been referred by other hospitals. Gastrectomy was used to treat 1773 of the patients, and EMR was used to treat the other 746 patients; 93 (3.7%) of the 2519 patients were elderly (80 years of age and more). Their cases were reviewed in this analysis. The patients were divided into two groups: a group treated by gastrectomy (surgery group, $n = 44$) and a group treated by EMR (EMR group, $n = 49$). EMR was performed aiming

TABLE 1. Patient characteristics

Characteristic	Surgery group	EMR group	p value
	(n = 44)	(n = 49)	
Mean age, y	82.2	84.2	0.552
Gender ratio, M:F	27:17	31:18	0.430
Preexisting comorbidity, n (%)			
Cardiovascular diseases	19 (35.8)	14 (28.6)	0.142
Respiratory diseases	12 (22.6)	7 (14.3)	0.121
Liver dysfunction	2 (3.8)	0	0.131
Renal dysfunction	4 (7.5)	2 (4.1)	0.326
Anemia and/or hypoproteinemia	10 (22.7)	8 (16.3)	0.435
Diabetes	6 (11.3)	4 (8.2)	0.395
Other malignancy	3 (5.7)	3 (6.1)	0.892
None of the above	19 (35.8)	15 (30.5)	0.283
Eastern Cooperative Group performance status, n (%)			
0 or 1	44 (100)	48 (98)	0.514
2 or more	0	1 (2)	

en bloc local resection with a clear curative margin (R0). Most patients satisfied the Gastric Cancer Treatment Guideline of the Japanese Gastric Cancer Association.⁹ The patients' clinical records were retrieved, and their clinicopathologic characteristics, comorbidity, postoperative mortality, and clinical outcome were reported. All of the patients were treated in the Gastric Surgery Division or the Endoscopic Division of the National Cancer Center Hospital. The gastrectomy and the EMR specimens were classified according to Japanese Classification for Gastric Carcinoma.¹⁰ In the EMR group, follow-up endoscopy was performed at 3 and 6 months of EMR, and then yearly to examine the patients for local recurrence. The patients in the surgery group underwent abdominal US or CT every year to examine for distant recurrence, and follow-up endoscopy has been performed every year.

Statistical analysis

The chi-square test and Student *t* test were used to assess statistical significance. Follow-up data for all patients were obtained from the city registry office and from their clinical records. The median follow-up period was 57 months (range, 4-168 months). The 5-year follow-up information was retrieved for all patients. Survival was calculated from the date of treatment. Survival curves were plotted by the Kaplan-Meier method. The difference in survival curves was tested for statistical significance by the

Capsule Summary

What is already known on this topic

- The treatment of early gastric cancer gastrectomy in the elderly is associated with poor postoperative quality of life and significant comorbidity.

What this study adds to our knowledge

- In a retrospective review of 93 elderly Japanese patients at a single institution, EMR was performed safely, with similar results as gastrectomy.

TABLE 2. Histologic findings after EMR and gastrectomy

Characteristic	Surgery group	EMR group	p Value
	(n = 44)	(n = 49)	
Mean (SD) tumor size	2.8 ± 0.5	1.3 ± 0.6	0.003
Histologic type, n (%)			
Well	24 (54.5)	43 (87.8)	0.002
Moderately	16 (36.4)	1 (2.0)	
Poorly	4 (9.1)	5 (10.2)	
Depth of invasion, n (%)			
Mucosa	15 (34.1)	39 (79.6)	0.006
Submucosa	29 (65.9)	10 (20.4)	
Lymph-node metastasis, n (%)			
Positive	6 (13.6)	—	—
Negative	38 (86.4)	—	

log-rank test. All *p* values were two tailed, and *p* < 0.05 was accepted as evidence of statistical significance.

RESULTS

Clinicopathologic features

There was no significant difference in age, gender, or Eastern Cooperative Group performance status between the two groups (Table 1). There were significant differences in mean tumor size (*p* = 0.003), histologic type (*p* < 0.001), and depth of tumor invasion (*p* < 0.001) between the two groups (Table 2). Five patients with poorly differentiated adenocarcinoma underwent EMR because of preoperative morbidity, even though they did not satisfy the criteria for EMR. All patients in the surgery group underwent curative gastric resection (distal gastrectomy in 29, total gastrectomy in 5, proximal gastrectomy in 4, pylorus-preserving gastrectomy in 2, and wedge resection in 4), and 6 (13.6%) of them had group 1 (N1)

TABLE 3. Postoperative morbidity

Characteristic	Surgery group (n = 44)	EMR group (n = 49)
General		
Respiratory	5 (11.3%)	0
Cardiovascular	4 (9.1%)	0
Hepatic	1 (2.3%)	0
Renal	1 (2.3%)	0
Treatment-related morbidity		
Anastomotic leakage	0	—
Stenosis	2	0
Perforation	0	0
Hemorrhage	0	0
Abdominal abscess	0	0
Wound infection	2	—

TABLE 4. Distribution of causes of death

Characteristic	Surgery group (n = 44)	EMR group (n = 49)	p Value
Recurrence	0	2 (4.1%)	0.176
Other malignancy	5 (11.4%)	4 (8.2%)	0.602
Cardiovascular	6 (13.6%)	7 (14.3%)	0.928
Respiratory	4 (9.1%)	6 (12.2%)	0.624
Malnutrition	2 (4.5%)	1 (2%)	0.495
Other diseases	1 (2.3%)	0	0.939
Unknown	3 (6.8%)	1 (2%)	0.257
Alive	23 (52.3%)	28 (57.1%)	0.638

lymph-node metastases. A clear curative margin was not achieved in 11 patients (22.4%) in the EMR group.

Morbidity and mortality

There were no significant differences in the comorbidity rates between the two groups (Table 1). The overall postoperative morbidity rate was 22%, and the most frequent complication was respiratory disease (11.3%; Table 3). The mortality rate was 0% in the surgery group; no morbidity or mortality was reported in the EMR group.

Clinical outcome

A clear surgical margin was not achieved in 11 patients in the EMR group on the first attempt; however, a clear

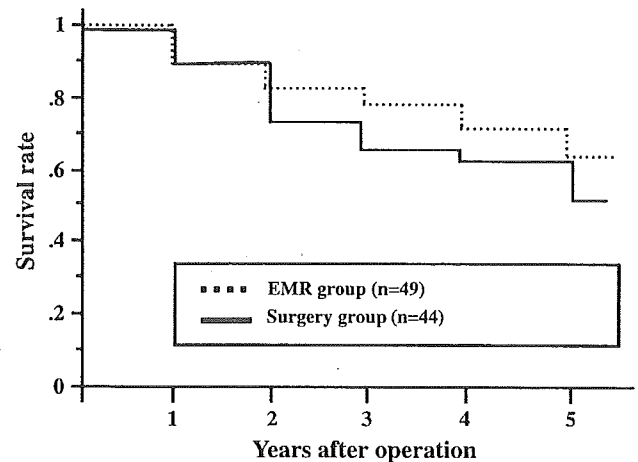


Figure 1. Survival curves of elderly patients with early gastric cancer. The patients were divided into two groups, the surgery group (n = 44) and the EMR group (n = 49). There was no significant difference between the survival curves of the two groups.

margin was achieved in 4 of the patients by additional EMR or gastrectomy. The other 7 patients refused any further treatments. Two of the 7 patients were diagnosed with local recurrence at the original site and died of advanced diseases. None of the patients in the surgery group died of cancer recurrence. The distribution of causes of death in both groups is shown in Table 4. All but two of the patients who died during the follow-up period, died of other causes. The most frequent pattern of failure was cardiovascular disease.

Survival

The overall 3-year survival rate in the surgery group and the EMR group was 73.5% and 82.5%, respectively. The overall 5-year survival rate was 55.0% and 62.5%, respectively. There were not significant differences in survival rates between the groups. The log-rank test showed no significant difference between the survival curves of the two groups (Fig. 1).

DISCUSSION

The choice of treatment of early gastric cancer in elderly patients depends on both the cancer stage and their general fitness. Because of their short life expectancy, it is very difficult to choose gastrectomy for elderly patients. This analysis was intended to elucidate the need for gastrectomy for early gastric cancer in the elderly.

Patients with early gastric cancer are managed according to the Gastric Cancer Treatment Guidelines in Japan. Several recent studies¹¹⁻¹³ report that EMR can be carried out on larger lesions beyond those recommended guidelines, and they were removed, with a high rate of clear margins. The long-term survival results for early gastric cancer after EMR are still being evaluated. Expanding the

criteria for EMR to the treatment of larger tumors may benefit elderly patients with early gastric cancer.

Surgical resection is often recommended to patients in our hospital when curative R0 resection is not achieved by EMR. However, a "watch and see" policy has often been adopted for patients over 80 years of age, instead of performing additional surgery. These patients often have severe comorbidity (as shown by our data) and are often regarded to be at high risk. Several studies have shown that the risks can be minimized by intensive care.^{8,14} Performance status and mental deterioration are not significant prognostic factors in elderly patients with gastric cancer.¹⁴ Our study also showed that surgery could be carried out safely in elderly patients with early gastric cancer.

Gastrectomy has often been reported to significantly impair overall QOL, because of postoperative digestive symptoms, loss of appetite, and malnutrition. Postgastrectomy patients are prone to complications, such as aspiration pneumonia (25%), anastomotic leakage, and wound infection,^{6,7,15} which shorten the overall postoperative survival. In the present study, however, in 3- or 5-year survival rates between the groups, there were no significant differences in our study.

Several studies have reported progression to advanced gastric cancer and death within 2 or 3 years in patients untreated for early gastric cancer.^{2,14} Patients with successfully treated early gastric cancer should have a good outcome.^{16,17} In this study, two of the 7 patients in whom EMR failed to achieve curative resection died of advanced disease. When a clear surgical margin is not achieved, additional surgical resection should be recommended as a curative treatment for early gastric cancer even in elderly patients.

In conclusion, EMR (R0) was performed safely in the elderly. The overall results were excellent, and the procedure can be recommended. Gastrectomy can still be performed if EMR is unsuccessful, because the results of gastrectomy in elderly patients were also excellent. The results reviewed in this study were from a single highly specialized center, with high standards, where endoscopists and surgeons work together. Generalization to nonspecialized centers requires caution.

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REFERENCES

1. Ministry of Health and Welfare. Abridged life table for Japan. 1994. Tokyo: Statistics and Information Department, Minister's Secretariat; 1994.
2. Hashimoto H, Yamashiro M, Nakayama N, et al. Operation for gastric cancer in patients over 80 years [in Japanese with English abstract]. *J Jpn Soc Clin Surg* 1988;493:1347-51.
3. Gotoda T, Yanagisawa A, Sasako M, et al. Incidence of lymph node metastasis from early gastric cancer: estimation with a large number of cases at two large centers. *Gastric Cancer* 2000;3:219-25.
4. Gotoda T, Sasako M, Ono H, et al. Evaluation of the necessity for gastrectomy with lymph node dissection for patients with submucosal invasive gastric cancer. *Br J Surg* 2001;88:444-9.
5. Habu H, Saito N, Sato Y, et al. Quality of postoperative life in gastric cancer patients seventy years of age and over. *Int Surg* 1988;73:82-6.
6. Davies J, Johnston D, Sue-Ling H, et al. Total or subtotal gastrectomy for gastric carcinoma? A study of quality of life. *World J Surg* 1998;22:1048-55.
7. Jentschura D, Winkler M, Strohmeier N, et al. Quality-of-life after curative surgery for gastric cancer: a comparison between total gastrectomy and subtotal gastric resection. *Hepatogastroenterology* 1997;44:1137-42.
8. Katai H, Sasako M, Sano T, et al. The outcome of surgical treatment for gastric carcinoma in the elderly. *Jpn J Clin Oncol* 1998;28:112-5.
9. Nakajima T. Gastric cancer treatment guidelines in Japan. *Gastric Cancer* 2002;5:1-5.
10. Japanese Gastric Cancer Association. Japanese classification of gastric carcinoma. 2nd English edition. *Gastric Cancer* 1998;1:10-24.
11. Hirao M, Masuda K, Asanuma T, et al. Endoscopic resection of early gastric cancer and other tumors with local injection of hypertonic saline-epinephrine. *Gastrointest Endosc* 1988;34:264-9.
12. Inoue H, Tani M, Nagai K, et al. Treatment of esophageal and gastric tumors. *Endoscopy* 1999;31:47-55.
13. Ono H, Kondo H, Gotoda T, et al. Endoscopic mucosal resection for treatment of early gastric cancer. *Gut* 2001;48:225-9.
14. Matsushita I, Hanai H, Kajimura M, et al. Should gastric cancer patients more than 80 years of age undergo surgery? Comparison with patients not treated surgically concerning prognosis and quality of life. *J Clin Gastroenterol* 2002;35:29-34.
15. Roviello F, Marrelli D, De Stefano A, et al. Complications after surgery for gastric cancer in patients aged 80 years and over. *Jpn J Clin Oncol* 1998;28:116-22.
16. Shiraishi N, Inomata M, Osawa N, et al. Early and late recurrence after gastrectomy for gastric carcinoma. Univariate and multivariate analyses. *Cancer* 2000;89:255-61.
17. Sano T, Sasako M, Kinoshita T, et al. Recurrence of early gastric cancer. Follow-up of 1475 patients and review of the Japanese literature. *Cancer* 1993;72:3174-8.

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Original article

Pancreaticoduodenectomy for advanced gastric cancer

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Abstract

Background. Although pancreaticoduodenectomy has been rarely performed for gastric cancer because of frequent morbidity and mortality, some favorable results after this procedure have been reported recently. Our objective was to present our data that might aid in the selection of patients to undergo this procedure.

Methods. Between 1970 and 2001, 23 patients who had pancreaticoduodenectomy for gastric cancer with tumor invading the pancreatic head were identified, and they were the subjects of this study. Clinical, operative, and pathological data, and morbidity and mortality rates were collected and analyzed. Survival outcome was also calculated and analyzed.

Results. Five patients underwent this procedure for disease in the gastric remnant, 18 undergoing the procedure for primary tumors. Median operating time was 8 h (range, 6–13 h), and median blood loss was 1600 ml (range, 700–16000 ml). Regarding extent of gastrectomy, all patients with primary cancer ($n = 18$) underwent a distal gastrectomy and patients with disease in the gastric remnant ($n = 5$) underwent a completion gastrectomy. Incurable factors, including paraaortic lymph node metastasis, positive lavage cytology, or peritoneal dissemination were found in 8 patients. The postoperative morbidity rate was 73.9%; however, operation-related death was zero. The overall 5-year survival rate was 34.3%. The 5-year survival rate of the 8 patients with incurable factors was 0%, while that of the 15 patients without incurable factors was 47.4%.

Conclusion. If an R0 resection can be achieved by pancreaticoduodenectomy, this procedure should be performed for patients with tumor invading the pancreatic head. Patients with incurable factors should not be considered for pancreaticoduodenectomy.

Key words Gastric cancer · Pancreaticoduodenectomy · Combined resection of adjacent organs

Introduction

Complete removal of all evaluable disease, i.e., R0 resection, is vital to a successful outcome in gastric cancer treatment. Extended surgery is occasionally required for advanced gastric cancer with infiltration of adjacent organs to achieve complete tumor clearance. For locally advanced gastric cancer with infiltration of the pancreatic head or duodenum, pancreaticoduodenectomy (PD) is required. However, this procedure has been rarely performed because of substantial morbidity and mortality [1]. Prior to the 1990s, few reports regarding PD for gastric cancer had been published [2]. Only Kishimoto et al. [3] and Scott et al. [4] referred to a long survivor after this procedure in their reports about gastrectomy with combined resection. Recently, with current advances in operative techniques and in nutritional support, some favorable results of the patients undergoing this procedure have been reported [5–7]. However, only a few reports with a large number of cases have been published so far. In the current study, we present our data that might aid in the selection of patients to consider who should undergo this procedure.

Subjects and methods

A retrospective review of our prospective database, spanning from 1970 to 2001 and containing 9349 patients, identified 195 (2.1%) who had locally advanced cancer with macroscopically suspected infiltration of the pancreatic head. We included patients with pancreatic head invasion from metastatic lymph nodes, and excluded type 4, linitis plastica cancer. Of the 195 patients identified, 23 underwent PD with presumed curative intent, and they were the subjects of this study.

In these 23 patients, clinical data, including age, sex, symptoms, and primary tumor or tumor in the gastric remnant, were collected and analyzed, using the appro-

Table 1. Patients undergoing pancreaticoduodenectomy

		Disease	Stage	pT	pN	P	CY	Adjuvant Chemo.	Combined resection	Recurrence	FUT (months)	Status
1	63/F	Primary	IV	4	1	0	0	—	Liver	N	13	DOD
2	42/M	Primary	IIIB	3	1	0	ND	—		—	157	DOC
3	64/M	Primary	IIIB	2	2	0	0	—		—	182	NED
4	67/M	Primary	IV	3	2	0	ND	—		—	87	DOC
5	76/M	Primary	IV	4	3	0	0	—	Colon	Unclear	4	DOD
6	67/M	Primary	IIIB	4	0	0	0	+		—	26	DOC
7	65/M	Primary	IV	4	3	0	1	+		N	6	DOD
8	74/F	Primary	IV	2	3	0	0	—	Colon	H	34	AWD
9	70/M	Primary	IV	4	2	0	0	—	Colon	N, H	14	DOD
10	62/M	Primary	II	2	0	0	0	—	Colon	—	52	NED
11	65/M	Primary	IV	4	2	0	0	—		N	36	AWD
12	65/F	Primary	IV	4	2	0	0	—		N, H, spleen	12	DOD
13	58/M	Primary	IV	4	3	0	0	—	Colon	N	6	DOD
14	60/M	Primary	IIIB	2	2	0	0	—	Colon	—	12	NED
15	64/M	Primary	IV	4	2	1	1	—	Colon	Unclear	19	DOD
16	51/F	Primary	IIIB	2	2	0	0	—		H	11	DOD
17	61/M	Primary	IV	4	1	0	ND	—		H	4	DOD
18	70/M	Primary	IV	4	3	0	1	—		N, lung	4	DOD
19	60/M	Remnant	IV	4	2	1	1	—		N	13	DOD
20	57/M	Remnant	IV	4	1	0	0	—	Liver, colon	N, H	26	DOD
21	64/F	Remnant	IIIB	4	0	0	0	—		N	64	DOD
22	47/M	Remnant	IV	4	3	0	0	—		N	17	DOD
23	60/M	Remnant	IIIB	4	0	0	0	—	Colon	P	4	AWD

Primary, Primary tumor; remnant, tumor of the gastric remnant; P, peritoneal dissemination; CY, lavage cytology; ND, not done; N, lymph node; H, liver; FUT, follow-up time; NED, no evidence of disease; AWD, alive with disease; DOC, dead of other cause; DOD, dead of disease; unclear, site of recurrence unclear

appropriate nonparametric tests. Operative data, including operating time, blood loss, hospital stay, extent of gastrectomy, extent of lymphadenectomy, and combined resection with PD, were also evaluated. Pathological data, including pT, pN stage, site of tumor, and incurable factors, such as paraaortic lymph node metastasis (pN3), peritoneal dissemination, and positive lavage cytology, were analyzed according to the Japanese classification. Perioperative morbidity and mortality were also investigated.

The survival data of the 195 patients with tumors invading the pancreatic head, including the 23 PD patients, were calculated by the Kaplan-Meier method and analyzed by the log-rank method.

Results

Demographics

Of the 195 patients with tumors invading the pancreatic head, 151 (77%) underwent resection, and the remaining 44 underwent only an exploration or a bypass surgery. In 68 patients, an R0 resection was carried out. In 45 patients with R0 resections, a lesser pancreatic resection (not PD) was performed because of a slight degree of tumor infiltration. The remaining 23 patients (12%) underwent PD (Fig. 1).

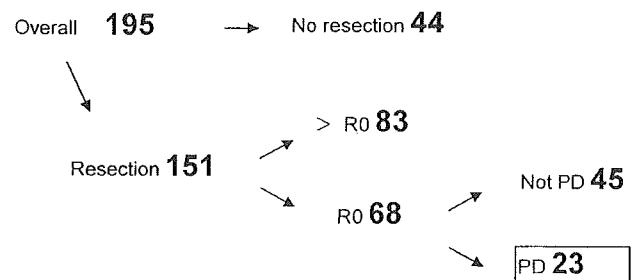


Fig. 1. Patients with tumors invading the pancreatic head. *No resection*, patients undergoing only exploration or bypass operation. *Not PD*, patients undergoing R0 resection, but with a lesser pancreatic resection than pancreaticoduodenectomy (PD)

In the 23 patients undergoing PD, the median age at the time of resection was 64 years (range, 42–76 years), with a male-to-female ratio of 18:5 (Table 1). Twenty-one patients (91.3%) were symptomatic, most commonly with abdominal pain ($n = 13$) and symptoms due to obstruction, including fullness and vomiting ($n = 11$).

Eighteen patients underwent the PD procedure for primary cancer and 5 for gastric remnant cancer following previous Billroth I gastrectomy. Of the 5 patients with gastric remnant cancer, 4 had undergone distal partial gastrectomy for gastric cancer. Two of these

patients had early cancers, and the other 2 had advanced disease. The disease-free intervals were 1.5 and 6 years for those with advanced cancers and 8 and 10 years in those with early cancers. The fifth patient had had a partial gastrectomy for a benign gastric ulcer 30 years previously.

Operative data

The median operating time for PD was 8h (range, 6–13h), with a blood loss of 1600ml (700–16000ml). The median length of postoperative hospital stay was 37 days (range, 25–92 days). Regarding extent of gastrectomy, patients with primary cancer ($n = 18$) underwent a distal gastrectomy and those with gastric remnant cancer ($n = 5$) underwent a completion gastrectomy. As to extent of lymph node dissection, 14 patients underwent D2 lymphadenectomy and 9 underwent D3. In 9 patients, a combined resection of the colon was performed because of direct infiltration of the mesocolon (Table 1). Two patients underwent a partial hepatectomy because of a direct invasion of the liver. Modified Child's method was selected for a reconstruction for all patients. Two patients received postoperative adjuvant chemotherapy of 5-fluoruracil (5-FU) after surgery.

Pathology

Resection specimens from all patients revealed adenocarcinoma of gastric origin. In 7 patients, infiltration of the pancreatic head could not be confirmed histopathologically. Regarding site of tumor, 18 primary tumors involved the antrum, and 11 of these tumors extended into the duodenum.

Incurable factors, including pN3, peritoneal dissemination, and positive lavage cytology were found in eight patients (Table 1). No patient in this series had a visceral metastasis. In 6 patients, pN3 was found. These patients had been considered as negative for pN3 intraoperatively, but the finding was changed to positive by pathological examination postoperatively. Of these 6 patients, 2 also had positive lavage cytology. Two patients had positive lavage cytology and peritoneal dissemination synchronously; the peritoneal dissemination was a single nodule that was removed easily at operation.

Seventeen patients developed recurrences. The most common recurrence sites were nodal, in 11 patients, followed by liver, in 6; peritoneum in 1; lung in 1, spleen in 1, and unclear, in 2.

Morbidity and mortality

Postoperative complications were seen in 17 patients (73.9%; Table 2). Pancreatic fistula was the most

Table 2. Postoperative morbidity

	<i>n</i>
Postoperative morbidity	17 (73.9%)
Pancreatic fistula	10 (43.5%)
Abdominal abscess	3 (13.0%)
Anastomotic or jejunal stenosis	3 (13.0%)
Cholangitic infection	3 (13.0%)
Anastomotic leakage	2 (8.7%)

Table 3. Survival of patients with tumor invading the pancreatic head

	<i>n</i>	Median survival (months)	5-Year survival rate (%)
Overall	195	10	13.6
No resection	44	7	0
Resection	151	12	17.7
>R0	83	8	7.9
R0	68	21	29.3
Not PD	45	22	28.1
PD	23	17	34.3

No resection, Patients who underwent only exploration or bypass operation; not PD, patients who underwent R0 resection but received a lesser pancreatic resection than PD

common. All patients who developed this complication recovered, after receiving drainage and continuous irrigation, using double-lumen drainage tubes. No operation-related death occurred in this series.

Regarding the long-term postoperative morbidity, body weight at 12 months was maintained within 10% of the preoperative weight in all patients who lived for more than 1 year. Serum albumin levels were not decreased. However, two patients who underwent PD with completion gastrectomy required total parenteral nutrition (TPN) at home, for 1 and 3 years, respectively, after discharge from hospital, because of malnutrition. Postoperative pancreatic endocrine function was adequate in all patients, but three patients required pancreatic exocrine enzyme support postoperatively.

Survival

In the 195 patients with tumors invading the pancreatic head, the 5-year survival rate was 13.6%. Of these 195 patients, the 68 patients who underwent an R0 resection showed a better survival outcome, with a 5-year survival of 29.3%. In patients who had R0 resections, there was no significant difference in survival between patients who underwent PD and those not receiving PD (Table 3).

In the 23 PD patients, the median follow-up time was 13 months (range, 4–182 months). The status of the

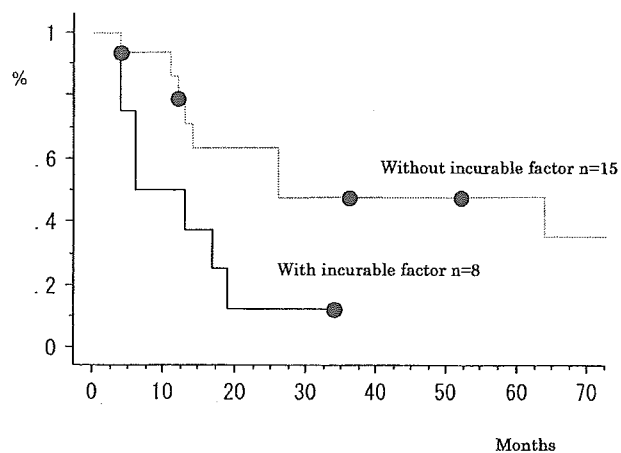


Fig. 2. Survival curves of patients undergoing pancreaticoduodenectomy (PD). The overall 5-year survival rate and the median survival of the 8 patients with incurable factors were 0% and 6 months, respectively, and these values in the 15 patients without incurable factors were 47.4% and 26 months ($P = 0.035$)

patients was as follows: no evidence of disease, 3; alive with disease, 3; dead of other causes, 3; and dead of disease, 14. The overall 5-year survival rate was 34.3%. The 5-year survival rate and the median survival of the 8 patients with incurable factors (pN3, positive lavage cytology, and peritoneal dissemination) were 0% and 6 months respectively, while these values in the 15 patients without incurable factors were 47.4% and 26 months (Fig. 2). Four patients have survived for more than 5 years.

Discussion

In our data, of 195 patients with tumors invading the pancreatic head, 23 (12%) underwent PD. This procedure has been rarely performed because of high morbidity and mortality rates. Prior to the 1990s, there had been only a few reports about this procedure [2–4]. Recently, with current advances in operative techniques, nutritional support, and antibiotics, some favorable results have been reported [5–11]. Ohashi [9] reported a large number of patients (145) undergoing this procedure. The 5-year survival rate of patients undergoing PD in that study was 6%, and it was approximately equal to the result for patients undergoing more than R0 resection in our data. Thus, it is inferred that Ohashi's subjects included patients with far-advanced tumors that could not be removed by this procedure. With proper indications, PD could account for 10% of surgeries for tumors invading the pancreatic head, and the number of patients who would have this procedure would be around 30, even at a large institution.

In our study, tumor infiltration of the pancreatic head could not be confirmed in 7 patients (30%) histopathologically. Such patients, theoretically, could have avoided this procedure; however, inconsistency between macroscopic and microscopic findings of infiltration has been reported to be 30%–50%, often because of inflammatory reactions surrounding the tumor [8,12]. Even if the latest diagnostic modalities, such as computed tomography (CT), magnetic resonance imaging (MRI), and endoscopic ultrasound (EUS) are used, it is very difficult to distinguish between inflammatory reactions and tumor infiltration before operation. Intraoperative ultrasound could be more helpful than these modalities, but it was not used in any patients in the present series. It seems that inconsistency at a level of around 30% is unavoidable at present.

Morbidity after PD was in Ohashi's study [9] 51.6% and 37.8% in that of Shchepotin et al. [11]. Regarding mortality, these authors reported rates of 6.3%, and 10.8%, respectively. Buchholtz et al. [1] recommended that PD should not be performed for gastric cancer because of an unacceptable risk, with no greater degree of palliation. The morbidity rate in our series (73.9%) was higher than the rates in these previous reports [9,11], to be sure. However, the operative mortality rate was 0% and all surviving patients could resume a regular life. Pancreatic fistula was the most common complication in this series. This is critical, as it may lead to intraabdominal abscess and rupture of arterial aneurysm. This complication was diagnosed by the detection of infectious drain discharge with a high concentration of amylase (>10000 IU/l). For the early detection of pancreatic fistula, the concentration of amylase in the drain discharge is checked routinely after PD. When pancreatic fistula has developed, continuous drainage is performed, initially. If there is infection, continuous irrigation, using double-lumen drainage tubes, is done. To achieve better control of this complication, the medical staff including not only the surgeon but also nursing staff, have to be skilled at careful drain management. Therefore, this procedure should be performed only at institutions where PD for pancreatic cancer is frequently performed.

No patient in our series developed diabetes mellitus after PD, and only three required pancreatic exocrine enzyme support postoperatively. However, after PD with completion gastrectomy, two patients required TPN at home for a long period because of malnutrition. Total gastrectomy combined with PD should be considered very carefully, as nutritional problems may be severe.

The overall prognosis of patients with tumors invading the pancreatic head was poor; however the 5-year survival rate of patients undergoing R0 resection was about 30% in this series. In the patients with R0 resec-

tions, there was no significant difference in survival between those requiring PD and those not requiring PD. Thus, to achieve R0 resection is an important objective, irrespective of whether or not PD is performed.

Ajisaka et al. [5] and Shchepotin et al. [11] reported that the 5-year survival rates of patients undergoing PD were 35% and 17%, respectively. In a study of 26 patients undergoing PD combined with right hemicolectomy, Yonemura et al. [10] reported that the 5-year survival rate of 13 patients with tumors infiltrating the pancreatic head was 55%. In our series, the 5-year survival rate for such patients was 34.3%. In PD patients without incurable factors, the 5-year survival rate was higher, at 47%, and 4 patients have survived for more than 5 years. Careful application of the PD procedure can achieve improved survival outcome. Kodama et al. [13] and Habu et al. [14] mentioned that a small amount of peritoneal dissemination and limited liver metastasis, respectively, were not contraindications for PD. However, most patients in the present series who had incurable factors died of the disease soon after operation. Incurable factors, such as pN3, positive lavage cytology, peritoneal dissemination, and visceral metastasis, should be regarded as a contraindication for PD.

In summary, the results after PD for patients with advanced gastric cancer with tumors invading the pancreatic head were acceptable from the aspects of morbidity, mortality, and survival benefit. If an R0 resection can be achieved by PD in such patients, this procedure should be performed. Patients with incurable factors should not be considered for PD. The combination of PD and total gastrectomy should be considered with caution.

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References

1. Buchholtz TW, Welch CE, Malt RA. Clinical correlates of resectability and survival in gastric carcinoma. *Ann Surg* 1978;188:711-5.
2. O'Brien PH, Mincey KH. Analysis of pancreaticoduodenectomy. *J Surg Oncol* 1985;28:50-8.
3. Kishimoto H, Koga S. Evaluation of gastrectomy combined with the resection of other organs in the treatment of gastric cancer. *Jpn J Surg* 1979;9:173-9.
4. Scott HW Jr, Adkins RB Jr, Sawyers JL. Results of an aggressive surgical approach to gastric carcinoma during a 23-year period. *Surgery* 1985;97:55-9.
5. Ajisaka H, Fujita H, Kaji M, Maeda K, Yabushita K, Konishi K, et al. Treatment of patients with gastric cancer and duodenal invasion. *Int Surg* 2001;86:9-13.
6. Menjo M, Nimura Y, Hayakawa N, Kamiya J, Kondo S, Nagino M, et al. Ten-year survival after pancreaticoduodenectomy for advanced gastric cancer — report of two cases. *Hepatogastroenterology* 1999;46:1253-6.
7. Hirose K, Onchi H, Iida A, Katayama K, Yamaguchi A, Nakagawara G. Surgical results of pancreaticoduodenectomy for carcinoma of the distal third of the stomach. *Int Surg* 1999;84:18-24.
8. Piso P, Bellin T, Aselmann H, Bektas H, Schlitt HJ, Klempnauer J. Results of combined gastrectomy and pancreatic resection in patients with advanced primary gastric carcinoma. *Dig Surg* 2002;19:281-5.
9. Ohashi I. Combined resection of adjacent organs for advanced cancer of the stomach: pancreaticoduodenectomy and left upper abdominal evisceration (in Japanese). *Surg Ther* 1985;52:173-80.
10. Yonemura Y, Ooyama S, Matumoto H, Kamata T, Kimura H, Takegawa S, et al. Pancreaticoduodenectomy in combination with right hemicolectomy for surgical treatment of advanced gastric carcinoma located in the lower half of the stomach. *Int Surg* 1991;76:226-9.
11. Shchepotin IB, Chorny VA, Nauta RJ, Shabahang M, Buras RR, Evans SR. Extended surgical resection in T4 gastric cancer. *Am J Surg* 1998;175:123-6.
12. Maehara Y, Oiwa H, Tomisaki S, Sakaguchi Y, Watanabe A, Anai H, et al. Prognosis and surgical treatment of gastric cancer invading the pancreas. *Oncology* 2000;59:1-6.
13. Kodama I, Takamiya H, Mizutani K, Ohta J, Aoyagi K, Kofuji K, et al. Gastrectomy with combined resection of other organs for carcinoma of the stomach with invasion to adjacent organs: clinical efficacy in a retrospective study. *J Am Coll Surg* 1997;184:16-22.
14. Habu H, Saito N, Sato Y, Takeshita K, Sunagawa M, Endo M. Results of surgery in patients with gastric cancer extending to the adjacent organs. *Hepatogastroenterology* 1990;37:417-20.

進展様式に基づいた消化器癌手術のこつと工夫

7. 進展様式に基づく直腸癌術式の選択と手術のコツ

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キーワード 直腸癌術式, 臨床試験, intersphincteric resection, 術前病期診断

I. 内容要旨

術前病期診断, sentinel node navigation surgery, single tumor cell 及び病理組織学的知見に関する最近の内外の研究成果をレビューした. 術前病期診断においては MRI 検査が重要でかなりの精度で診断可能となってきた. 欧米で重要視されている circumferential resection margin の検索はリンパ節転移検索とは相容れずそれぞれ短所長所がある. intersphincteric resection は肛門直腸接合部に発生した癌腫に対する直腸切断術に代わる選択術式であるが適応基準を今後検討する必要がある. sentinel node navigation surgery や single tumor cell に関する知見は蓄積されてきたが術式選択のための方法論には至っていない. 提示した諸課題に解答を与えるためには多施設共同による補助放射線化学療法と手術療法に関する臨床試験が不可欠であることを強調した.

II. はじめに

過去 30 年間の直腸癌術式の変遷を概観すると 1970 年代半ばからの 10 年間は拡大郭清時代, その後 10 年間は画像診断の進歩と骨盤内自律神経の解剖と機能の理解を基盤とした自律神経温存術時代, そして今日までの 10 年間は自然肛門温存術の適応拡大, 補助療法導入, 側方郭清功罪の再検証の時代と言える. 第 105 回外科学会では“側方郭清は必要か”と言うシンポジウムも開かれる. 本稿では直腸癌進展様式に関する研究成果を文献的に検証し手術療法における諸課題に考察

を加える.

III. 術前病期診断

欧米では T3 以深直腸癌に対し術前放射線治療が標準的となり MRI を用い局所再発高危険群の絞込みが積極的に行われている¹⁾²⁾. mesorectum は直腸, リンパ節, 血管, 神経を含む周囲の脂肪結合組織からなり mesorectal fascia が周囲を取り囲む. 病理組織像と錯覚するかのような精度で mesorectum を描出することができ空間分解能に優れた MRI は他の画像診断に勝ることは論をまたない. 1) T stage : EUS は 69%—97% の正診率で早期癌や mp 癌の T stage 評価は可能であるがこれ以深では正診率が劣る. また術者の技量に影響を受け mesorectal fascia や側方リンパ節は描出できないなどの制約がある. しかし, spiculation が繊維化なのか癌細胞を含む繊維化なのか, T2 と borderline T3 との鑑別など MRI を用いても不可能である. T3 と診断されても mesorectal fascia までに 5mm 以上の距離があるのか fascia 近くに進展が及んでいるのかの区別も必要である. 欧米では MRI 所見に基づく新たな T staging の必要性が術前補助放射線化学療法の適応面より議論されている. 2) circumferential resection margin (CRM) : 大腸癌研究会は規約の初版より外科的剝離面 (EW) の重要性に留意していた. しかし, リンパ節転移程度の評価に重点が置かれ EW の組織学的判定は犠牲となってきた. そのため EW の長さ別の局所再発率や生存率のデータは少ない. 一方, 欧米では Quirke 報告³⁾以来切除材料の輪切り標本で CRM 検索が行われている. Nagtegaal

SELECTION AND TECHNIQUES OF SURGICAL PROCEDURES BASED ON THE MODE OF CANCER SPREAD OF RECTAL CANCER

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らは Dutch TME trial で集積した 656 例を検討し CRM 2mm 以下では局所再発率が有意に高く CRM は TNM とは独立した因子であると報告した⁴⁾。この臨床試験では 17% に CRM 陽性が見られ recto-sacral fascia 尾側において直腸剝離が浅くなり直腸固有筋膜ぎりぎりの層で行われていた可能性が高い。このように手術内容の差(欧米は TME あるいはそれ以下, 日本は TME あるいはそれ以上の切除範囲)を考慮すると相互に正しく標本整理が行われてきたと言える。直腸後腔は正中仙骨血管を直視する層で, 側方は内腸骨血管に沿う層で, 前方は Denonvilliers 筋膜を摘除側に付ける層で直腸を剝離すると隣接臓器浸潤例を除き EW 陽性になるような症例はまずない。一方, T4 disease は欧米では術前放射線化学療法の対象に位置づけられている。日本では単施設からの報告のみで多数例の成績はないが手術万能主義の傾向が見られる。T4 の 86% は骨盤内臓器への浸潤, 残りは骨盤壁へ浸潤で尿路系浸潤例には bladder-sparing surgery と骨盤内臓全摘術が同頻度に採用されたと Moriya らは報告した⁵⁾。術前放射線化学療法がどの程度の downstaging をもたらし bladder-sparing surgery の採用がどれぐらい増加するのか T4 を対象とした多施設共同研究が必要である。3) N stage: 大きなリンパ節が描出されても炎症か転移かを鑑別できないし直腸癌では正常径リンパ節内の微少転移発見率が高いなどで正診率に大きな差 (62%—83%) が報告されている。転移特異的診断法がない現状では大きさを基準とせざるを得ない。MRI では網内系に取り込まれる造影剤を用いリンパ節性状から転移の有無を鑑別しようとする試みもある⁶⁾。予防的側方郭清効果を検証している JCOG0212 (TME vs 自律神経温存 D3) ではリンパ節径 1cm 未満を側方転移陰性として eligible criteria を設けている。一方明らかな側方リンパ節転移例には側方郭清を行うべきである。しかし複数個の側方転移例や両側転移例では 1 個や 2 個の側方転移例に比較して側方郭清後の治療成績は不良である。従って近い将来, 日本において臨床的側方陽性例を対象に自律神経温存 D3 vs TME + 術前放射線化学療法の臨床試験を行うべきである。FDG-PET によるリンパ節転移描出の報告もあるが 28% と sensitivity は低い。PET は遠隔転移診断には有効であるが膀胱と重なりリンパ節転移の診断には無力である。

IV. 術前病理診断

画像診断の進歩は著しく術前病期診断の精度は改善

したが十分とは言えない。Ueno らは大きな粘膜下層生検により外科切除材料と同等の 'budding' '低分化度' '脈管侵襲' の 3 つの悪性度に関する情報が得られ, リンパ節転移個数, リンパ節外転移, CRM, 側方転移と有意に相関し, 3 因子が無い群の局所再発率は 5%, 1 因子で 13%, 複数の因子で 36% と報告した⁶⁾。局所再発率はこうした生物学的悪性度のみでなく患者側 (性差, 肥満度など) や術者側要因 (手術例数, リンパ節郭清内容など) にも影響を受ける。Meyerhardt らは男性直腸癌患者において肥満群は低位前方切除術より直腸切断術の採用頻度が高く局所再発率も非肥満群に比較し高率であったが, 女性患者では術式の選択も局所再発率も肥満の影響を認めなかったと報告した⁷⁾。解剖学的制約 (狭骨盤と内臓脂肪) に加え, 肥満患者のインスリン分泌過多が insulin-like growth factor I などを用進させ癌細胞増殖に有利に働く腫瘍学的メカニズムの関与も指摘されている。生物学的諸因子以外の要因がどの程度治療成績に影響を与えるか検討が必要である。

V. 自然肛門温存術はどこまで可能か?

切除断端下縁までの距離 (distal clearance margin, DCM) に関し多くの報告がある。集約すると "two-centimeter rule of distal margin" が妥当と思われる。しかし治癒切除直腸癌で肛門側壁内進展が 2cm にも達する例は稀である。肛門側間膜内進展 (リンパ節転移や節外進展) も 2cm を超えることは少ない。実際には直腸間膜が確実に 2cm 以上切除されていることが重要である。Rb 進行癌に対する括約筋温存手術には Double stapling techniques が汎用される。この高さでは間膜は無く直腸間膜の処理は不要な高さである。一方, Ra や Rs 直腸癌に対して total mesorectal excision ではなく tumor-specific mesorectal excision が行われる。後者すなわち間膜容積の大きい腹膜翻転部レベルでの処理では意外な pitfall がある。つまり DCM は 2cm で十分と言う認識で間膜切除デザインを行うと骨盤深部ではそのような精度での切除は困難で予定線より口側にずれ短い DCM となり易い。特に狭骨盤や肥満男性患者では pitfall となり surgeon-related な局所再発を招く。この種の局所再発は実地臨床では意外に多いのではないかと。そこで Rs や Ra の進行癌では 4cm 以上の DCM 確保するよう心がけることを薦めたい。そうすることによって壁内や間膜内進展に対する対策も担保されることになる。この意味では TME は側方転移を考慮しなくてよい Ra に対する合理的手術と言える。

VI. Intersphincteric resection (ISR) について

従来、直腸切断術の適応と考えられていた肛門縁5 cm 以内の癌腫に対しても超低位前方切除術やISRが積極的に採用されるようになった。ISRは永久的人工肛門を回避する術式で1994年のSchiesselらの報告にみられるように術後排便機能もほぼ満足できる⁹⁹⁾。直腸切断術で得られた病理標本を用い壁内進展に関する検討がなされ、budding, 4分の3以上の環周率, 肉眼3型が壁内進展の頻度と相関する。この3因子は術前評価可能で、いずれの因子もなければ歯状線上や近傍の癌腫に対してone-centimeter ruleを適応してもよいと報告しISR適応拡大に根拠を与えた¹⁰⁾。またMRIを用い可及的に内外肛門括約筋, 肛門拳筋への浸潤の有無を描出しISR適応の根拠とする研究もある。ISRは直腸切断術の適応であった下部直腸癌に対する選択術式となったが次のような不安要素が内在する術式である。

1. 癌根治性低下 2. 術後低排便機能 3. 術中implantation この術式の適応検討は大きな研究課題と言える。ISR遂行上の留意点について言及しておきたい。1. 内外括約筋間の剝離を指ないし長い鋏で腹腔側より可及的に行い肛門側からの指標とする 2. DCRは少なくとも1cm以上を確保する 3. Implantation 防止目的で肛門側剝離がある程度進んだ段階でwater-tightに閉鎖後生理食塩水とインジン液で徹底的に洗浄を行う。以上3点が重要であるがISRの難易度は患者の体型に依存することを知るべきである。筋肉が発達した大柄男性や内臓肥満患者では経肛門的操作は深く狭い術野となり難度は高い。ISRでは切除再建は経肛門的に行われるため会陰部が最大限に展開できる砕石位を取りローンスタースタ社hook retractorを使用し肛門開大を計る。Bittorfらは¹¹⁾pouch再建が良好な排便機能を齎すと報告しているがどの再建術式が排便機能にとって最適かわが国独自の検討が必要である。なぜなら食生活の差により便性状は異なるからである。

VII. Sentinel nodes (SLNs) navigation surgery (SLNNS) は直腸癌で有効か?

SLNsとは原発巣から最も転移しやすいリンパ節で、SLNNSはそれが存在するとの仮説で成り立っている概念である。色素や放射性物質を用い術中に取り出し転移の有無を検索し転移がなければ郭清せず転移があれば郭清を行う。つまり縮小手術を裏付ける術中検査法

である。乳癌やメラノーマはSLNsは原発巣から離れたところにあり有効であるがリンパ流が豊富かつ原発巣の直下から始まる臓器では腫瘍近傍に注射するため注射部位と重なり背景との区別が困難で有効性が劣る。消化管癌への検証の試みはあるがSensitivityは70—100%と開き0—40%のfalse negativeもあり郭清度選択の指標としての意義は少なく、SLNs検索の意義は効率的リンパ節転移検出にあると言える。stage I/IIをstage IIIにupstageし、補助療法の対象を広げることにより患者に利益をもたらすとの考え方で、欧米ではこの目的で大腸癌に応用されている¹²⁾¹³⁾。

VIII. 遊離癌細胞と微小転移

UICCのTNM分類第6版では潜在癌細胞はIsolated Tumor Cells (ITC, 遊離癌細胞)と定義され、2mm以下の通常の病理検査で認識できる小さな転移を微小転移(micrometastasis)として区別している。リンパ節を連続切片で検索すると33%の症例に微小転移が見られるとの報告もありThe World Congress of Gastroenterologyで12個の検索が最低必要との提案がされ最新のTNM分類にも反映されている。免疫組織学的検索では10%—76%の著しい幅でITCが認められている。予後への影響ありとなしとする報告が相半ばしている。Nakanishiらはcytokeratineとp53を用いた無再発群と再発群の摘出リンパ節に関する症例対象研究でITCは興味ある現象であるが適切なリンパ節郭清下では予後への影響はないと報告した¹⁴⁾。RT-PCRによる検索でもITC陽性率には28%—82%と幅がある。最近、骨髄中のITCとrelapse-free survivalとの間に相関を認めたとする報告がある。ITC検索の今日的意義はSLNNSと同様にupstageすることにより化学療法の適応を正当化することにある。

IX. おわりに

側方郭清の意義は1970年代後半に世界に発信したメッセージであった。しかし欧米はもとよりアジアにおいても現時点では普及していない。第一は側方転移頻度が高くなく側方転移郭清後の5生率も高くないことである。第二は欧米患者は肥満と高度な動脈硬化が高率に認められ側方郭清は難しい手術に位置づけられ、難度に見合うだけの郭清効果が証明されていないことである。欧米では放射線化学療法が進歩し側方転移に対する効果を補助療法に求めている。本稿で取り上げた臨床的諸課題は倫理性が担保された臨床試験を通じて

初めて科学的解答がえられることを知るべきである。アンケート調査や後ろ向き研究からは世界に発信できるメッセージは生まれない。日本の基幹病院の規模は諸外国特に東アジア諸国と比較しても極めて小さい。世界や東アジアに発信できる成果を挙げるためには多施設共同で前向き研究ができる体制を構築することが急務である。

文 献

- 1) Brown G, Richard CJ, Newcombe RG, et al. : Rectal carcinoma : thin-section MR imaging for staging in 28 patients. *Radiology*, 211 : 215—222, 1999.
- 2) Beets-Tan RG, Beets GL : Rectal cancer : review with emphasis on MR imaging. *Radiology*, 232 : 335—346, 2004.
- 3) Quirke P, Durdey P, Dixon MF, et al. : Local recurrence of rectal adenocarcinoma due to inadequate surgical resection. Histopathological study of lateral tumor spread and surgical excision. *Lancet*, 8514 : 996—999, 1986.
- 4) Nagtegaal IID, Marijnen CA, Kranenburg EK, et al. : Circumferential margin involvement is still an important predictor of local recurrence in rectal carcinoma : not one millimeter but two millimeters is the limit. *Am J Surg Pathol*, 26 : 350—357, 2002.
- 5) Moriya Y, Akasu T, Fujita S, et al. : Aggressive surgical treatment for patients with T4 rectal cancer. *Colorectal Dis*, 5 : 427—431, 2003.
- 6) Ueno H, Mochizuki H, Shinto E, et al. : Histologic indices in biopsy specimens for estimating the probability of extended local spread in patients with rectal carcinoma. *Cancer*, 94 : 2882—2891, 2002.
- 7) Meyerhardt JA, Tepper JE, Niedzwiecki D, et al. : Impact of body mass index on outcomes and treatment-related toxicity in patients with stage II and III rectal cancer. Findings from Intergroup Trial 0114. *J Clin Oncol*, 22 : 648—657, 2004.
- 8) Schiessel R, Karner-Hanusch J, Herbst F, et al. : Intersphincteric resection for low rectal tumors. *Brit J Surg*, 81 : 1376—1378, 1994.
- 9) Saito N, Ono M, Sugito M, et al. : Early results of intersphincteric resection for patients with very low rectal cancer. An active approach to avoid a permanent colostomy. *Dis Colon Rectum*, 47:459—466, 2004.
- 10) Ueno H, Mochizuki H, Hashiguchi Y, et al. : Preoperative parameters expanding the indication of sphincter preserving surgery in patients with advanced low rectal cancer. *Ann Surg*, 239:34—42, 2004.
- 11) Bittorf B, Stadelmaier U, Gohl J, et al. : Functional outcome after intersphincteric resection of the rectum with coloanal anastomosis in low rectal cancer. *Eur J Surg Oncol*, 30 : 260—265, 2004.
- 12) Saha, S, Wiese D, Badin J, et al. : Technical details of sentinel lymph node mapping in colorectal cancer and its impact on staging. *Ann Surg Oncol*, 7 : 120—124, 2000.
- 13) Bertoglio S, Sandrucci S, Percivale P, et al. : Prognostic value of sentinel lymph node biopsy in the pathologic staging of colorectal cancer patients. *J Surg Oncol*, 85 : 166—170, 2004.
- 14) Nakanishi Y, Ochiai A, Yamauchi Y, et al. : Clinical implications of lymph node micrometastasis in patients with colorectal cancer. A case control study. *Oncology*, 57 : 276—280, 1999.

SELECTION AND TECHNIQUES OF SURGICAL PROCEDURES BASED ON THE MODE OF CANCER SPREAD OF RECTAL CANCER

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The author reviewed recent results of Japanese and international studies on preoperative staging, pathology of bisected specimens, sentinel node navigation surgery, and single tumor cells in rectal cancer. Preoperative staging with high accuracy is possible using high spatial MRI imaging. Examination of circumferential resection margins is incompatible with that of lymph nodes. Intersphincteric resection can be an alternative to abdominoperineal resection for selected rectal tumors located at the anorectal junction without compromising the chance for cure. Although information on sentinel node navigation surgery and isolated single cells has accumulated, the selection of surgical procedures should not be based on these investigations. We emphasize that multi-institutional clinical trials of adjuvant chemoradiotherapy and surgical treatment are indispensable for developing treatments for rectal cancer in Japan.