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PREOPERATIVE DIAGNOSIS OF LYMPH NODE METASTASES AND SENTINEL NODE NAVIGATION SURGERY IN PATIENTS WITH UPPER GASTROINTESTINAL CANCER

Hiroya Takeuchi and Yuko Kitagawa
Department of Surgery, School of Medicine, Keio University, Tokyo, Japan

In spite of recent advances in diagnostic tools such as computed tomography, endoscopic ultrasonography, and positron-emission tomography, preoperative diagnosis of lymph node metastases in patients with upper gastrointestinal (GI) cancer has been problematic because of the low sensitivity and accuracy in the detection of micrometastases. To overcome this issue, the sentinel node (SN) concept has attracted attention in recent years and is anticipated to become a novel diagnostic tool for the identification of clinically undetectable lymph node metastases in patients with early upper GI cancer. For early-stage gastric cancer, in which a better prognosis can generally be achieved using conventional surgical approaches, individualized, minimally invasive gastrectomy based on a combination of laparoscpic surgery with SN navigation surgery should be established as the next surgical milestone. Several issues remain to be resolved in laparoscopic gastrectomy with three-dimensional computed tomography navigation.

胃癌における術前・術中のリンパ節転移診断の方法とその有用性

竹内　裕也　　才川　義朗　　和田　則仁　　須田　康一　　北川　雄光

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胃癌における術前・術中のリンパ節転移診断の方法とその有用性*

慶應義塾大学医学部外科
竹内 裕也　才川 義朗　和田 則仁　須田 康一　北川 雄光

* Pre-and intra-operative diagnosis of lymph node metastasis in patients with gastric cancer

キーワード：胃癌，リンパ節転移，CT，MRI，センチネルリンパ節

要旨：現在，早期胃癌では腫瘍径や肉眼型，組織型などから深達度診断やリンパ節転移頻度予測が可能となっている．しかし，CT，US，EUS，MRI などの術前画像によるリンパ節転移診断はいまだ不完全と言わざるを得ず，実際に郭清範囲を決めるのは術中のリンパ節の視触診や迅速病理診断に委ねられることが多いのが現状である．センチネルリンパ節（SN）生検は，SN に集中した病理学的あるいは分子生物学的転移診断を行うことによって，時間的，経済的に効率よいリンパ節微小転移診断を行うことができる．また SN 転移陰性早期胃癌に対する胃局所切除術や分節切除術は新しい機能温存・個別化縮小手術として注目されている．

はじめに

わが国では先達のたゆまぬ努力により，胃癌の診療においてはつねに世界最高水準の診断・治療が行われてきた．特に胃 X 線造影および胃内視鏡による胃癌診断技術は胃癌の内視鏡治療や外科手術などとともに世界に比類ないレベルに達しているものと言える．早期胃癌では腫瘍径や肉眼型，組織型などから深達度診断やリンパ節転移頻度予測までが可能となっている[1]．「胃癌治療ガイドライン」[1]では，その進行度によって適正なリンパ節郭清範囲が明確に示されており，日常診療の一助となっている．しかし，術前画像によるリンパ節転移診断はいまだ不完全と言わざるを得ず，実際に郭清範囲を決めるのは術中のリンパ節の視触診や迅速病理診断に委ねられることが多いのが現状である．一方で，腹腔鏡下胃癌手術の台頭によって，今後は術前のリンパ節転移診断がより重要になると考えられる．

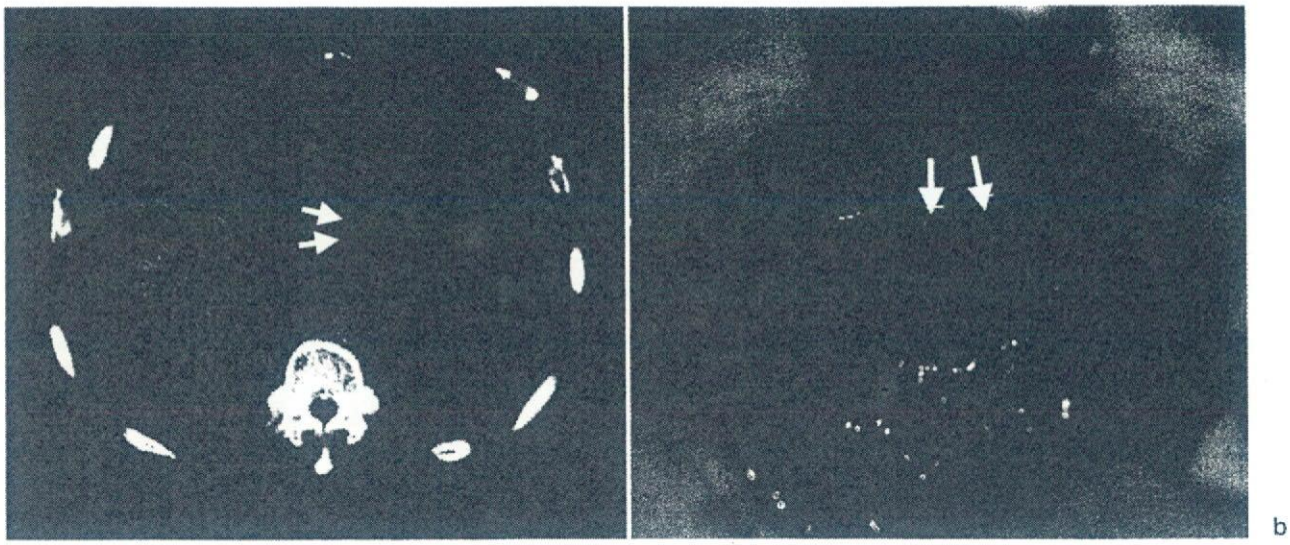
本稿では，胃癌の術前・術中リンパ節転移診断方法とその成績について現状を概説する．

術前リンパ節転移診断

1．CT

これまで，造影 CT を用いた胃癌の所属リンパ節転移診断について数多くの報告がなされてきた（図 1）．様々な診断基準が報告されているが，その正診率は決して高いものではなく，いまだ CT によるリンパ節転移診断能は十分ではない．

安井ら[2]が，胃癌手術時に郭清された 1,949 個のリンパ節の長径を調べたところ，転移陰性リンパ節（1,670 個）は平均 4.5 mm，転移陽性リンパ節（279 個）は 6.7 mm であったと報告した．また，転移陽性リンパ節は陰性リンパ節に比べて CT 上，リンパ節辺縁が整に描出される傾向が高いものの，内部造影像に差はなかったとしている．さらに，CT 画像によるリンパ節転移陽性の診断基準を長径 1 cm 以上かつ辺縁整なリンパ節としたと



a　　b

図1　進行胃癌のリンパ節転移

a：造影 CT．造影効果のある円形の#1，#3，#7 リンパ節（矢印）が複数描出される．
b：術中写真．CT 所見に一致して小彎領域に複数のリンパ節（矢印）が認められる．

ころ，小彎領域リンパ節では描出感度 36%，特異度 94%，正診率 57%，大彎領域では描出感度 0%，特異度 0%，正診率 48%，腹腔動脈領域では描出感度 28%，特異度 63%，正診率 75%であった．

磯崎ら[3]も同様に郭清されたリンパ節と画像で描出されたリンパ節の比較検討を行っている．彼らは，CT のリンパ節描出率は 19%で，CT で描出されるリンパ節の長径が 1.0〜1.5 cm であった場合の実際の転移率は 46%，1.5 cm 以上では 80%であったが，1.0 cm 以下のリンパ節でも 25%に転移を認めたと報告している．

これまでのほかの報告を含めても，長径 1 cm 以上のリンパ節を転移陽性とした場合の正診率はおおむね 40〜80%程度であり，この診断基準には限界があると言える[4]．Fukuya ら[5]は 5 mm ヘリカル CT を用いて長径 5 mm 以上のリンパ節を検討しており，転移陽性検出感度は 75%と報告している．しかし同時に，5 mm ヘリカル CT を用いても長径 5〜9 mm のリンパ節のうちの 45%しか描出されないとしている．その後，2 相造影 CT などの検討でも転移予測率はあまり改善していない．

最近では multi-detector row CT（以下，MDCT）を用いた検討がなされているが，Shinohara ら[6]は長径 8 mm 以上，円形であることなどを転移リンパ節の条件としたところ，リンパ節転移予測正診率は 83%であり，術中の視触診や術中迅速病理診断などによる術中転移診断と遜色ない良好な結果を得たと報告している．しかし，MDCT は再構成画像を用いることなど診断に至るまでの煩雑さが指摘されている[7]．

2．超音波検査（US）と超音波内視鏡（EUS）

超音波検査（以下，US）では一般に胃周囲リンパ節の描出が極めて不良であり，磯崎ら[3]は手術時に郭清された総リンパ節の 5%しか US で描出されなかったとしている．腹腔動脈周囲リンパ節転移の有無を検索するには有効であるという報告もみられるものの，US によるリンパ節の描出は術者の技量や患者の肥満，腸管ガスなどによって左右されることに注意すべきである．

超音波内視鏡（以下，EUS）が胃癌の術前リンパ節転移診断に有用であるか否かは議論の分かれるところである．中村ら[8]は，EUS で胃壁周囲に描出され，境界明瞭で楕円形，低エコーを呈する 5 mm 以上の腫瘤を転移リンパ節と定義したところ，感度 54%，正診率 81%であり，早期胃癌，未分化癌に限るとさらに感度が低下することを報告している．また，リンパ節が腫瘍から離れるにしたがって正診率も低下する傾向がみられた．

これまでの報告では，EUS のほうが CT よりも若干優れているとの報告が多い[9]．しかし，EUS

による転移リンパ節の診断基準が確立していないため，今後も診断基準に関する検討が必要であろう．

3. MRI

先の磯崎ら[3]の報告では，MRIのリンパ節描出率は34%とCT，USに比べて良好で，特にCTに比べ径1 cm以下のリンパ節の描出に優れていた．MRIではT1強調画像で脂肪とリンパ節の区別が比較的容易であること，横断像だけでなく矢状断像，冠状断像からの診断が可能であることなどが小さなリンパ節の描出を可能としている．しかし，MRIは描出されるリンパ節が増える分，実際に転移のあったリンパ節の割合は40%程度にすぎず，むしろUSより劣る結果であった．

4. FDG-PET

胃癌はFDG-PETで描出されにくい疾患であることが知られている．Chenら[10]は，FDG-PETを用いた術前リンパ節転移診断の正診率が47%とCT単独よりも劣っており，CTと併用しても68%であったと報告した．またMukaiら[11]は同様の検討でFDG-PETの感度は35%，特異度97%，正診率68%と報告している．同じ対象でのCTとの比較では感度，正診率では劣るものの，特異度はCTよりも優れていた．彼らは，特に進行胃癌でのFDG-PETとCTの併用がリンパ節転移診断に有用であろうと考察している．今後，PET-CTの普及によって，リンパ節検出感度，正診率の向上が期待されるところである．

術中リンパ節転移診断

1. 肉眼的リンパ節転移と組織学的リンパ節転移との乖離

術前のリンパ節転移診断が必ずしも正確ではないことは前項で概説した通りであるが，術中の肉眼的リンパ節転移と組織学的リンパ節転移との関係はどうであろうか．癌研究所病院外科の大規模な集計では，肉眼的リンパ節転移（N）と組織学的リンパ節転移（n）との一致率はN0（=n0）例で74%，N（+）（=n（+））例で約60%であった[12,13]．一方，たとえばN0と考えられていたのに実際はn（+）例であった症例が25%に認められたように，肉眼的リンパ節転移よりも実際の組織学的リンパ節転移の程度が進んでいることが多かった．この結果は，術前転移診断のみならず，術中のリンパ節視触診でも正確な転移診断は困難であることを示唆するものであり，術中迅速病理診断や予防的リンパ節郭清（D number＞N number）の重要性が認識される．

図2　センチネルリンパ節（#4d）
内視鏡下に原発巣周囲へ色素（isosulfan blue）を注入すると，リンパ管を流出する色素（黒矢印）が腹腔鏡下に視認される．これをたどっていくと，青染する#4dリンパ節（青矢印）が認められる．こののち，#4d領域のSN basin dissectionを施行する．

2. センチネルリンパ節生検

術中のリンパ節転移診断のために，郭清したすべてのリンパ節を迅速病理診断に提出するのはあまり現実的ではない．この問題を解決し，まったく新しい個別化縮小術式を開発する根拠となったのがセンチネルリンパ節理論である．センチネルリンパ節（sentinel node：以下，SN）とは腫瘍から直接リンパ流を受けるリンパ節のことであり，SNは最初のリンパ節微小転移が発生する場所とする考え方をSN理論と呼んでいる（図2）．この理論が正しければ，SNにリンパ節転移がなければそのほかのリンパ節転移は生じていないと判断することができ，SNに集中した病理学的あるいは分子生物学的転移診断を行うことによって，時間的，経済的に効率よいリンパ節微小転移診断を行うことができる．

一方，もしSN理論が成立すれば，SNにリンパ

節転移がなければ SN 以外のリンパ節郭清は不必要と考えることができる．Sentinel node navigation surgery（以下，SNNS）とは，この SN の分布（SN mapping）と生検による転移の有無を指標としてリンパ節郭清を個別的に縮小ないし省略し，それに伴って切除範囲を最小限とすることを目的とした手法である．すでに乳癌では SN 理論の妥当性および臨床的有用性が実証され[14]，SN 転移診断に基づく腋窩郭清の省略など個別化縮小手術が実践されている．早期胃癌は消化器癌のなかでは SN 理論研究が最も進んだ領域であり，SNNS による機能温存・個別化縮小手術への応用が期待されている．

胃癌に対する SN 同定手技に関して，これまでに多数の単施設研究で良好な SN 同定率（90～100%）と転移検出感度（85～100%）が報告されている[15]．当科では 2006 年までに cT1N0 ないし cT2N0 症例の 382 例（うち腹腔鏡下手術は 91 例）に対して RI＋色素併用法による SN 生検を施行した（SN 同定率 96%，転移検出感度 99%）．

最近では腹腔鏡下胃癌手術による低侵襲性の確保と SNNS による機能温存・縮小手術の組み合わせが技術的に可能となっている[16～18]．現在，色素（isosulfan blue）と RI（^{99m}テクネシウムスズコロイド）を内視鏡下に粘膜下注入する併用法（SNNS 研究会/厚生労働省がん研究助成金研究班）の多施設共同研究が進行中であり，今後，SNNS 標準手術手技の確立に向けてその結果が注目されている．登録参加施設は全国 12 施設であり，目標集積症例数は 500 例を予定しているが，2006 年 12 月で 300 例を超え，現在順調に登録集積中である．

3. センチネルリンパ節術中微小転移診断

SN における胃癌微小転移検出のための術中迅速病理診断は，従来は数切片の限られたスライドの顕微鏡下での検索であり，たとえ免疫組織染色を用いたとしてもその検出感度には限界があった．われわれの約 250 例の検討では，HE 染色だけの術中迅速病理診断では永久標本診断と比べ 23%の症例で転移ありの診断ができなかった．これに術中免疫組織染色を加えても 8%の症例がやはり転移を診断できなかった．

近年 RT-PCR 法や OSNA 法などの分子生物学的手法を用いて形態学的には捕捉し得ない癌細胞まで検出することが可能となってきている．これらの手法はリンパ節全体を一度に検索できる利点を有するものの，こうした高感度な手法で検出された「癌細胞」，つまり癌細胞特異的 DNA や癌細胞特異的 mRNA 発現をはたして癌転移と診断してよいのかは意見の分かれるところである．われわれは術中迅速診断法として Roche Diagnostics 社と CK19，CK20，CEA をマーカーとした real time RT-PCR 法を共同開発し，現在，臨床応用に向けて多施設共同研究を計画中である．早期胃癌における癌微小転移や isolated tumor cells（ITC）の臨床的意義については，今後さらなる検証が必要である[19]．

4. センチネルリンパ節生検を応用した早期胃癌に対する機能温存・個別化縮小手術

今後，胃癌における SN 理論の妥当性が証明され，SN 生検の標準手技が確立すれば，SN 転移陰性早期胃癌は郭清の完全省略，胃（原発巣）の局所切除だけで根治術とすることが理論的には可能である．しかし，偽陰性（SN には転移がみられないのに SN 以外のリンパ節に転移を認める）の問題が完全には解決されていない現状では，より安全域のある根治性を損なわない術式が要求される．すなわち，現時点では SN を含むそのリンパ領域（SN basin）を選択的に郭清する術式（SN basin dissection）がよいと考えている．SN 同定の技術的問題や術中迅速診断の見逃しによって偽陰性が生じた場合でも，実際のリンパ節転移は SN basin 内に存在し，また限定される可能性が高い．また，術中の SN だけのサンプリングは原発巣に残存する RI の shine through effect によって同定が容易でないこともあるため，われわれは現在，まず SN basin dissection を行ったのち back table で RI 集積を測定し，術中迅速病理診断と RT-PCR 診断を行っている．

SN に明らかな転移が認められる症例では SN 領域外にも転移が存在する可能性が否定できないため，現時点では標準的な切除郭清術が必要である（**図 3**）．しかし，SN 転移陰性で術中に SN が 1 領

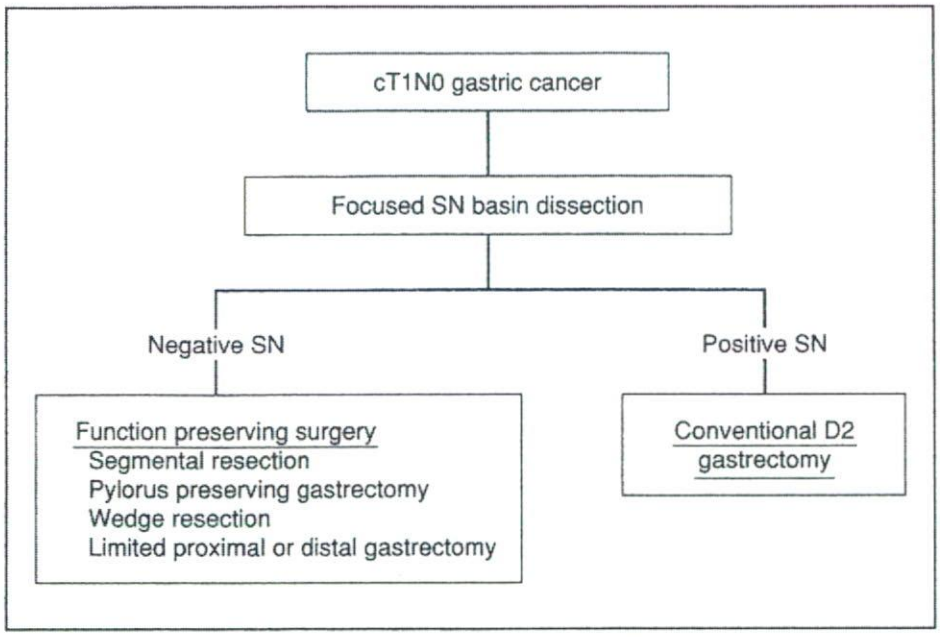


図3　センチネルリンパ節生検を応用した早期胃癌に対する機能温存・個別化縮小手術

域に限定される場合は，その領域の basin dissection と原発巣を含む胃局所切除が可能である．また，SN が 2 領域（小彎，大彎）にわたる場合は，その 2 領域の basin dissection と原発巣を含む胃分節切除が可能と考えられる[20]．われわれはこのような個別化縮小手術を腹腔鏡下に施行することに着手しているが，腹腔鏡下の SN 生検については今後精度の検証を慎重に進める必要があると考えている．

おわりに

胃癌の術前・術中リンパ節転移診断方法について概説した．各種の画像診断技術の進歩にもかかわらず，術前画像による胃癌リンパ節転移診断はいまだ不十分である．現時点では術中リンパ節転移診断が重要であることは明白であり，その意味で SN 生検は新たな break through となることが期待される．しかし，精度の高い SN 生検はどの施設でも容易に可能というわけではないうえ，SN 転移陰性早期胃癌に対する機能温存・個別化縮小手術は画一的な定型手術を行うよりも高度な手術であると言える．一方，安全性，根治性の担保は必要不可欠であり，早期胃癌における SNNS 標準手技の確立と臨床的意義の検証を目的とした多施設共同研究の結果が待たれるところである．

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（TAKEUCHI Hiroya, et al 慶應義塾大学医学部外科：〒160-8582 東京都新宿区信濃町 35）

Role of Salivary Gland Scintigraphy With Tc-99m Pertechnetate in Determining Treatment of Solitary Parotid Gland Tumors: A Retrospective Study

Tadaki Nakahara, MD, Takayuki Suzuki, MD,* Jun Hashimoto, MD,* Naoyuki Shigematsu, MD,* Toshiki Tomita, MD,† Kaoru Ogawa, MD,† and Atsushi Kubo, MD**

Purpose of the Report: Although salivary gland scintigraphy has been useful for the diagnosis of Warthin's tumor (WT), there are no reports concerning the clinical impact of this scintigraphy.

Materials and Methods: We retrospectively investigated 127 patients with solitary parotid tumors who had undergone salivary gland scintigraphy.

Results: For patients who had surgery, the sensitivity, specificity, and accuracy of differentiating WT from non-WTs were 95%, 91%, and 92%, respectively. There was a significant correlation between scintigraphic results and the treatment decisions made for the 127 patients ($\chi^2 = 16.5$, $P = 0.00026$). The proportion of WT patients among those who underwent surgery was 19%, whereas 42% of those who were suspected to have WT from scintigraphy were followed without surgical intervention. The main reasons for clinical observation in these patients were comorbidity, refusal of surgery, and age.

Conclusions: The high percentage of nonsurgical patients suspected to have WT can be explained by the high diagnostic accuracy of salivary gland scintigraphy, which is useful for determining further management when surgery is contraindicated or is refused by the patient.

Key Words: salivary gland scintigraphy, Tc-99m, parotid tumor

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The role of radiologic assessment in the evaluation of a parotid tumor is to localize the mass, identify the extent of its spread, and, ideally, to determine whether the tumor is benign or malignant.[1] For such purposes, ultrasound, computed tomography (CT) and magnetic resonance imaging (MRI) are important noninvasive procedures. In contrast, salivary gland scintigraphy with technetium-99m (Tc-99m) pertechnetate is a unique diagnostic tool that can selectively discriminate Warthin's tumor (WT) from other parotid masses.[2,3] Higher uptake than that of a normal parotid gland even after lemon juice stimulation is a well-known feature of WT in this scintigraphy. Scintigraphy has the potential to contribute to clinical practice because this procedure allows some patients, who are not optimal surgical candidates following a diagnosis of WT, to be adequately followed up.

The current study aimed to determine whether salivary gland scintigraphy can reduce the number of unnecessary operations on patients suspected of having a WT. Specifically, a retrospective study was conducted to investigate the impact of scintigraphic results on treatment decisions for patients with a solitary parotid gland tumor.

MATERIALS AND METHODS

Patients

From May 1999 to March 2004, 196 consecutive patients with either: 1) a surgically confirmed solitary parotid tumor, or 2) a solitary parotid tumor detected with ultrasound, CT or MRI, but not surgically removed, were studied using salivary gland scintigraphy. For the latter, those with short follow-up periods (less than 1 year after radiologic assessment) were excluded. Those with 2 or more tumors or with extraparotid tumors were also excluded. After these exclusions, the eligible patients consisted of 67 men and 60 women with a mean age of 53 ± 17 years (range, 10–92).

Salivary Gland Scintigraphy

Salivary gland scintigraphy was performed 5 minutes after intravenous injection of 370 MBq (10 mCi) Tc-99m pertechnetate. First, the anterior aspect of the bilateral parotid glands and a lateral aspect of a normal gland were scanned. Second, a lateral image of a parotid tumor was obtained. Third, if a parotid tumor was palpable, an additional scan was performed with a round lead marker on the mass to localize the tumor showing a round defect on scintigraphic images. Finally, with lemon juice stimulation, a lateral image of the parotid tumor was obtained (Fig. 1). Each scanning procedure took about 5 minutes.

Scintigraphic images of a parotid tumor both before and after lemon juice stimulation were interpreted by 3 specialists in nuclear medicine. The results were classified as persistent

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From the Departments of *Radiology and †Otolaryngology, Keio University School of Medicine, Tokyo, Japan.

Reprints: Tadaki Nakahara, MD, Department of Radiology, Keio University School of Medicine, 35 Shinanomachi, Shinjuku-ku, Tokyo, 160-8582, Japan. E-mail: n-tadaki0909@k6.dion.ne.jp.

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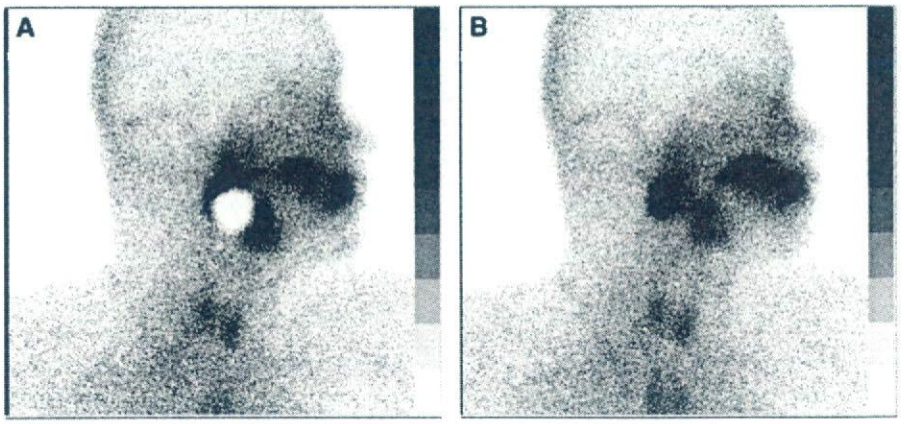

FIGURE 1. A 48-year-old man with a Warthin tumor. (**A**) Right lateral image of the right parotid gland with a round lead marker on the mass. A round defect localizing the tumor is shown. (**B**) The same view after lemon juice stimulation. Persistent uptake was noted in the lower portion of the right parotid gland.

defects, persistent uptake after lemon juice stimulation (when compared with the normal salivary gland), and no abnormalities. The coexistence of a persistent defect with persistent uptake after lemon juice stimulation suggests WT with cystic degeneration. Subjects with these findings were categorized into the persistent uptake group.

Treatment

Treatment policies for parotid tumors were determined in accordance with radiologic assessments, for all patients. Treatment strategies were divided into surgery and clinical follow-up. For clinical follow-up, patients were initially assessed a few months after the treatment decision and every 6 to 12 months thereafter.

Statistical Analysis

First, scintigraphic and surgical results were compared with evaluate the diagnostic accuracy of WT. Second, for all 127 patients who had undergone surgery or had been followed up, the relationship between the treatment decision and scintigraphic results was evaluated. Third, the characteristics of the patients for whom observation was selected were evaluated. Furthermore, the characteristics of the patients who had undergone surgery were compared with those of patients who were scintigraphically suspected to have a WT. A value of $P < 0.05$ was considered to indicate a statistically significant difference.

RESULTS

Pathologic and Scintigraphic Results

Surgical treatment was chosen for 100 patients (80%). There were 60 pleomorphic adenomas (60%), 19 WTs (19%), 9 other benign masses (9%), and 12 malignant tumors (12%).

Among the 100 surgically excised tumors, salivary gland scintigraphy with lemon juice stimulation had shown persistent defects in 68, persistent uptake in 25, and no abnormality in 7 (Table 1). The sizes of the resected tumors in these groups were 28 ± 9 mm (range, 10–52 mm), 27±15 mm (12–90 mm), and 12 ± 2 (10–15 mm), respectively. In the no abnormality group, the masses were significantly smaller than those of the persistent defect ($P < 0.0001$) and persistent uptake ($P < 0.0001$) groups. The sensitivity, specificity and accuracy for differentiating WTs from nonWTs were 95%, 91%, and 92%, respectively.

TABLE 1. Scintigraphic Findings in 100 Surgically Confirmed Tumors

Histology	Pleomorphic Adenoma	Warthin's Tumor	Other Benign Diseases	Malignant Tumors
Scintigraphic results*				
Persistent defect	54	0	7	7
Persistent uptake	3	18	1	3
No abnormality	3	1	1	2

*Lemon juice stimulation.

Seven false-positive results included pleomorphic adenoma (n = 3), mucoepidermoid carcinoma (n = 2), adenoid cystic carcinoma (n = 1), and oncocytoma (n = 1). Contrary to our expectation, 5 of these 7 tumors were relatively large (25–90 mm). False-negative results were obtained in only 1 patient, a 61-year-old woman with a small WT (11 mm).

Relationship Between Treatment Decision and Scintigraphic Results

Table 2 shows the relationship between treatment decision and scintigraphic results. The χ^2 test revealed a significant relationship between treatment decision and scintigraphic results ($\chi^2 = 16.5$, $P = 0.00026$). The main reason for selecting observation, rather than surgery, is shown in Table 3. It is noteworthy that 66% of the patients who were followed up (18/27) were suspected of having a WT on the

TABLE 2. Relationship Between Treatment Decision and Scintigraphic Results

Treatment	Surgery	Clinical Observation
Scintigraphic results*		
Persistent defect	68 (89%)	8 (11%)
Persistent uptake	25 (58%)	18 (42%)
No abnormality	7 (88%)	1 (12%)

*Lemon juice stimulation.

TABLE 3. Main Reasons for Clinical Observation in 27 Patients

Reason	No. Patients with Scintigraphically Suspected Warthin's Tumor
Comorbidity (n = 13)	13/13 (100%)
Angina or other heart diseases (n = 5)	
Cerebral infarction or recent TIA (n = 4)	
Malignancy other than parotid gland (n = 3)	
Severe respiratory dysfunction (n = 2)	
Chronic pyelonephritis (n = 1)	
Severe diabetes (n = 1)	
Refusal of surgery (n = 11)	4/11 (36%)
Age* (n = 3)	1/3 (33%)

TIA, transient ischemic attack.
*Their ages were 78, 79, and 92-year-old.

basis of scintigraphic results. Also, 42% of those with persistent uptake (18/43) were examined regularly without surgical treatment. Tumor growth was confirmed in only one of the 27 patients during a follow-up period of 28 ± 12 months (range, 12–48 months). This patient refused surgery even after tumor growth was recognized.

Patients Undergoing Surgery for WT and Scintigraphically Suspected WT

The characteristics of patients who were operated on or scintigraphically suspected to have WT, but did not receive surgical treatment, are shown in Table 4. Gender, age, and smoking habits were obtained from clinical records, as these factors may be related to this tumor. Tumor size in the followed-up patients was determined on the basis of CT or MRI. Other than age, there were no significant differences in characteristics between the 2 groups. Those under observation were significantly older than the surgical patients ($P < 0.05$).

TABLE 4. Characteristics of Operative Patients and Those Suspected to Have WT

Characteristics	Patients Operated on for WT (n = 19)	Patients with Scintigraphically Suspected WT (n = 18)
Gender		
Male	16*	13
Female	3*	5
Age		
Average ± SD	61 ± 7†	66 ± 10†
Smoking habit		
Yes	15‡	10§
No	2‡	2§
Unknown	3	6

WT, Warthin's tumor.
*‡$P < 0.01$.
†§$P < 0.05$.

Smokers significantly outnumbered nonsmokers among both surgically treated WT patients ($P < 0.01$) and those suspected to have WT ($P < 0.05$). Among those who underwent surgery for WT, male patients significantly outnumbered female patients ($P < 0.01$).

DISCUSSION

Basically, it is not difficult for experienced head and neck surgeons to perform surgery on parotid gland tumors. The operation can be accomplished in a short time and hemorrhage from the surgical site is minimal. Furthermore, the incidence of postoperative facial nerve dysfunction and Frey's syndrome are low in patients with solitary parotid tumors. For these reasons, the first choice of treatment of a parotid tumor is surgery, irrespective of tumor pathology. On the other hand, there are some parotid tumor patients, particularly those with significant comorbidities or older individuals, for whom the optimal treatment is not necessarily surgery. In addition, one encounters in clinical practice certain patients who are reluctant to undergo any operation. Because the malignant potential of WT is extremely low, its diagnosis in such patients can be among the reasons for choosing careful observation rather than immediately resorting to surgery. Indeed, treatment strategies vary among countries. According to head and neck surgeons in Japan, patients for whom the avoidance of surgery is preferred can be followed up by serial physical examinations once a diagnosis of WT has been made. Similar policies have been described in other reports.[4,5]

Salivary gland scintigraphy with Tc-99m pertechnetate is useful for the diagnosis of WT, especially in combination with lemon juice stimulation. The mechanism of Tc-99m pertechnetate uptake by a WT has been described in other studies.[2,6–8] Indeed, the diagnostic accuracy of the scintigraphy employed herein was 92%, which is consistent with previously reported results.[3,9] Murata et al found the sensitivity, specificity, and accuracy of scintigraphy with lemon juice stimulation to be 78%, 91%, and 87%, respectively,[5] while Miyake et al reported all 3 to be 94%.[9] Salivary gland scintigraphy is a simple, noninvasive test, and the results obtained in the current study, as well as those cited above, confirm its very high diagnostic accuracy and reproducibility.

WT is known to be the second most common benign tumor of the parotid gland, as affirmed in our study. Its incidence varies among countries, ranging from 5% to 30%.[10–13] As there was no pathologic evidence for WT in the patients suspected to have this tumor based on scintigraphy, the prevalence in the current study is surmised to be between 15% (19/129) and 29% (37/129). Gender and smoking habits are major factors influencing WT incidence,[11,14,15] and our current results are consistent with these observations (Table 4). The male-to-female ratios were found to be 5.3:1 for pathologically confirmed WT, and 3.6:1 for those patients with confirmed or suspected WT. According to some large studies, the ratios were reported to range from 10:1 to 2:1.[16–18] Our patient population showed no clear differences from those of other studies.

One possible difference between our results and those of other studies involves tumor size. The false-negative rate for the detection of parotid tumors can change, depending on the proportion of patients with a small tumor, because tumor size may be correlated with the WT detection rate.[9] Our study population did not include patients with multiple parotid gland tumors, which means that incidentally identified tumors, other than the largest and probably those responsible for the patient's symptoms and the treatment decision, are excluded. In this study, the smallest tumor was 10 mm, whereas previous radiologic studies have evaluated smaller parotid tumors.[19,20]

One limitation of this study is that we could not collect sufficient fine needle aspiration (FNA) data to provide meaningful results. Only 15 patients underwent FNA and it was successful in only eight. Although FNA is a relatively safe method of determining tumor pathology, its diagnostic role has not been well established.[21–23] Leverstein et al, describing the surgical results of 88 patients with parotid gland WT,[17] noted that the FNA results correctly represented WT in 47 of 71 patients.

In our study, salivary gland scintigraphy does yield false-positive WT cases. Therefore, this procedure should not be used alone in making treatment decisions. Rather, it is advisable to use scintigraphy in combination with other radiologic findings, FNA results and clinical data whenever possible.

CONCLUSION

In our current patient population, a significant relationship was noted between treatment decisions and scintigraphic results. Forty-two percent of the patients with persistent uptake on salivary gland scintigraphy were followed up without surgery, which may be explained by the high diagnostic accuracy of this modality for the diagnosis of WT. Salivary gland scintigraphy is a useful noninvasive method for deciding on further management strategies for patients with a solitary parotid tumor that may otherwise result in unnecessary surgical procedures.

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Original article

Validity of modified gastrectomy combined with sentinel node navigation surgery for early gastric cancer

Hironori Ohdaira, Hiroshi Nimura, Norio Mitsumori, Naoto Takahashi, Hideyuki Kashiwagi, and Katsuhiko Yanaga

Department of Surgery, The Jikei University School of Medicine, 3-25-8 Nishi-shinbashi, Minato-ku, Tokyo 105-8461, Japan

Abstract

Background. **The present study examined the clinical validity of modified gastrectomy for early gastric cancer, in terms of the results of sentinel node navigation surgery (SNNS), using infrared ray electronic endoscopy (IREE) plus indocyanine green (ICG) staining.**

Methods. **One-hundred and sixty-one patients with fT1N0 gastric cancer were enrolled in the study. ICG (0.5 ml, 5 mg/ml) was injected endoscopically into four quadrants of the submucosa surrounding the cancer. Twenty minutes after the injection, sentinel lymph nodes (SNs) stained with ICG were observed intraperitoneally around the serosa and surrounding fat tissue. IREE was used to illuminate regional lymph nodes from the serosal side.**

Results. **Group 2 lymph nodes were judged as SNs in 52 patients (32%). The most common locations of the SNs were stations No. 7 in each of the upper-, middle-, and lower-thirds of the stomach. In two patients, lymph node metastasis was positive. One of these patients, with cancer in the middle one-third of the stomach, had SNs in stations No. 3, 4sb, 4d, 7, and No. 11p, and had metastatic lymph nodes in No. 3 and No. 7 (all SNs). The other patient, with cancer in the lower one-third of the stomach, had SNs in No. 1, 3, 4d, and 6, and had a metastatic lymph node in No. 4d (SN). Skip metastasis was not observed in this study, and metastatic lymph nodes were judged to have been dissected by the D1+α procedure.**

Conclusion. **For T1N0 gastric cancer, modified gastrectomy (D1+α dissection) combined with SNNS is suitable; however, for those whose Group 2 lymph nodes are judged to be SNs, additional dissection of lymphatic basins detected by SNNS should be performed to confirm the absence of lymph node metastasis.**

Key words Modified gastrectomy · Sentinel node navigation surgery · Group 2 lymph nodes

Offprint requests to: H. Ohdaira
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Introduction

In a study by Bonenkamp et al. [1], patients with gastric cancer treated by extended (D2) lymphadenectomy had a significantly higher rate of complications, a higher postoperative mortality rate and a longer hospital stay than those who had limited (D1) dissection, although 5-year survival rates were similar in the two groups. Unnecessary extended lymphadenectomy should therefore be avoided to reduce the incidence of complications.

Recently, much attention has been paid to the improvement of postoperative function and quality of life after gastrectomy for early gastric cancer without impairing long-term outcome. However, several studies have shown features of skip metastasis in gastric, as well as in other cancers [2–4]. Because minimally invasive surgery has been applied to gastric cancer, the occurrence of skip metastasis is an important issue.

According to the treatment guidelines of the Japanese Gastric Cancer Association (JGCA), endoscopic mucosal resection (EMR) or modified gastrectomy (modified A, D1 + No. 7; modified B, D1 + No. 7, 8a, 9) is indicated for stage IA (T1N0) disease [5].

During the past several years, in patients with cT1N0 or cT2N0 early gastric cancer, we have performed sentinel node navigation surgery (SNNS), using infrared ray electronic endoscopy (IREE) combined with indocyanine green (ICG) injection [6]. With this method, we have encountered patients for whom Group 2 lymph nodes were judged as the sentinel lymph nodes (SNs). For such patients, we should be cautious about the extent of lymph node dissection.

In the present study, we examined the clinical validity of modified gastrectomy for early gastric cancer, in terms of the results of SNNS, using IREE combined with ICG staining.

Patients and methods

The study protocol was approved by the Ethics Committee for Biomedical Research of the Jikei Institutional Review Board, and all patients provided informed consent. Patients admitted to Jikei University Hospital with gastric cancer with no obvious metastasis were enrolled prospectively in the study, and cT1N0 or cT2N0 gastric cancer patients who gave informed consent underwent SNNS. In this study, 161 patients with fT1N0 (pT1pN0) disease were evaluated. Patients who had lymph node metastasis diagnosed by preoperative abdominal computed tomography or ultrasonography; and those with T2 subserosal or T3 lesions (according to the tumor node metastasis [TNM] classification system), confirmed by endoscopic ultrasonography, were excluded. SNNS was performed according to the methods of Nimura et al. [6]. Briefly, 0.5 ml ICG (5 mg/ml; Diagnogreen; Daiichi Pharmaceutical, Tokyo, Japan) was injected endoscopically in four quadrants of the submucosa surrounding the gastric cancer, using an endoscopic puncture needle during open or laparoscopic surgery. Twenty minutes after the injection, SNs stained with ICG were observed intraperitoneally around the serosa and surrounding fat tissue. IREE (Olympus Optical, Tokyo, Japan) was used to illuminate regional lymph nodes from the serosal side. Positive staining was confirmed by at least four surgeons and an endoscopist during surgery (Fig. 1). If possible, suspected SNs were examined by frozen section, with hematoxylin-and-eosin staining, to determine the pathological diagnosis. Lymph node dissection and gastrectomy were performed according to the criteria of the gastric cancer treatment guidelines of the JGCA, followed by a definitive pathological examination that included hematoxylin-and-eosin staining, and immunohistochemical staining with anticytokeratin antibody (CAM 5.2; Becton Dickinson, San Jose, CA, USA).

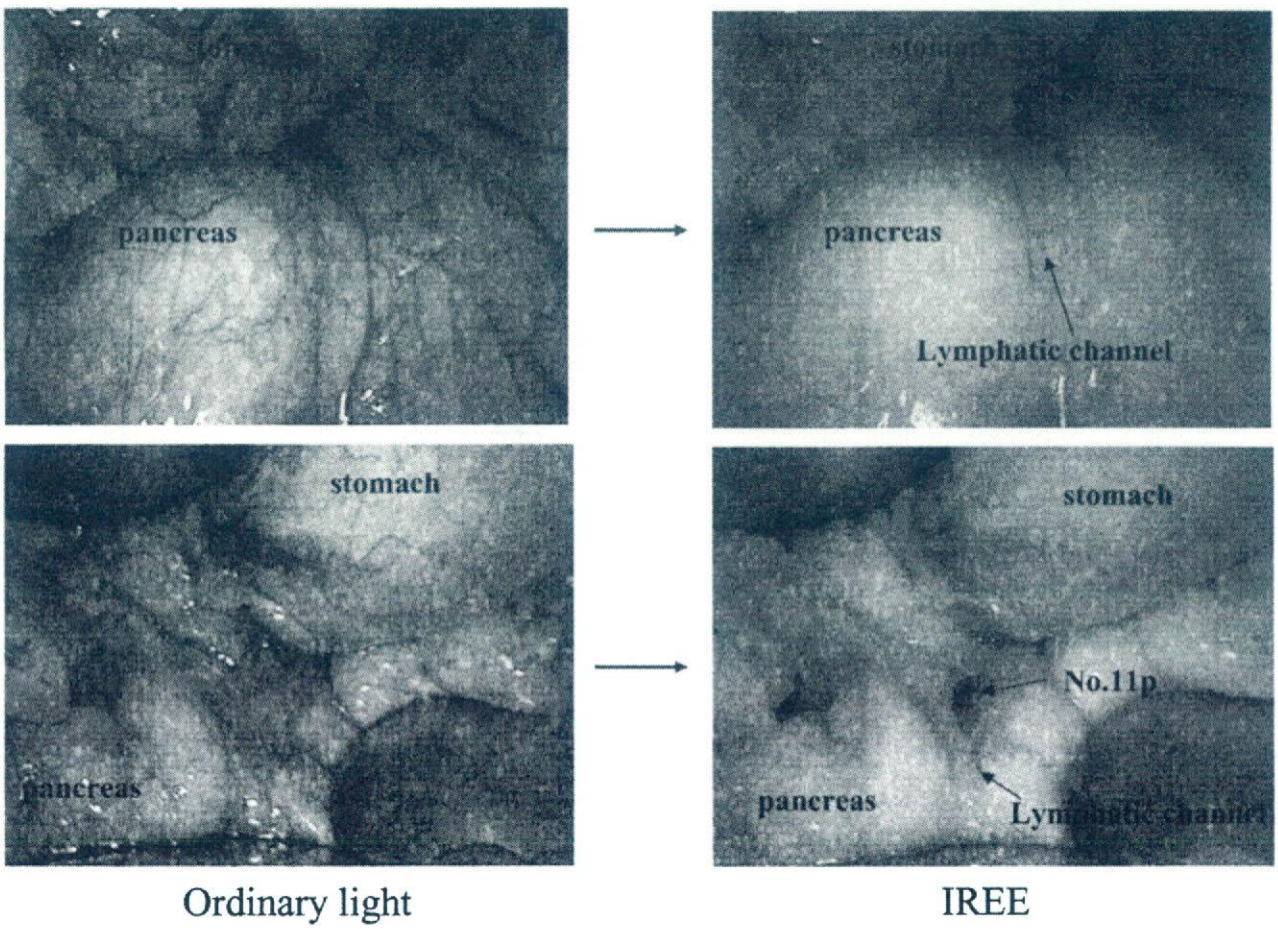

Fig. 1. Lymphatics stemming from the carcinoma. Lymphatic channels from the tumor follow a path crossing the anterior surface of the pancreas, revealing green-stained sentinel nodes (station No. 11p). *IREE*, infrared ray electronic endoscopy

Results

Group 2 lymph nodes were judged as SNs in 52 patients (32%; Table 1). Distal gastrectomy was performed in almost two-thirds of the 52 patients and the extent of lymph node dissection was D1+α in 58% of these patients.

The most common lymphatic basin of the cancer in the upper one-third of the stomach was the left gastric artery area (eight patients), while the most common location of SNs in cancer in the upper one-third of the stomach was station No. 7 (seven patients; Table 2). However, one patient had an SN in No. 4d.

For cancer in the middle one-third of the stomach, mainly the lymphatic compartments around both the left gastric artery and the right gastric artery were stained. Thirty-one of these patients had SNs in the No. 7 area, but in 7 patients, staining with ICG was seen in No. 9, 11p, 12a, or 14v.

Gastric cancers in the lower one-third of the stomach predominantly drained to the right side, around the right gastroepiploic artery and the right gastric artery. Common locations of SNs were stations No. 7 and No. 8a (11 patients). However, SNs were also observed in the areas of No. 1, 11p, and 14v.

Lymphatic basins positive for ICG, in relation to the cancer location, are shown in Table 2. Only two patients had no drainage to the left gastric artery area. For cancers in the middle and lower one-thirds of the stomach, the most common drainage in the lymphatic basins was to the left gastric artery and the right gastroepiploic artery areas.

Two patients had lymph node metastasis (Fig. 2). Case 1 had a 45 × 23-mm submucosal signet ring cell carcinoma in the greater curvature of the middle one-third of the stomach, which had three lymphatic basins (left gastric artery, right gastric artery, and right gastroepiploic artery areas) and SNs in No. 3, 4sb, 4d, 7, and 11p. Metastatic lymph nodes were located in No. 3 and No. 7, which were all SNs. Group 2 lymph nodes, No. 8a and No. 11p, were dissected. Case 2 had a 23 × 12-mm submucosal signet ring cell carcinoma in the anterior wall of the lower one-third of the stomach, which had two lymphatic basins (left gastric artery and right gastroepiploic artery areas) and SNs in No. 1, 3, 4d, and 6. A metastatic lymph node was located in No. 4d, and this was an SN. D1+α resection was performed.

Table 1. Characteristics of patients with Group 2 lymph nodes judged to be SNs

Age (years)	59.7 ± 10.0 (35–76)
Sex ratio (M:F)	37:15
Tumor location	
Upper one-third	7
Middle one-third	33
Lower one-third	12
Extent of resection	
Proximal gastrectomy	2
Distal gastrectomy	33
Total gastrectomy	4
Pylorus-preserving gastrectomy	5
Segmental gastrectomy	5
Wedge resection	3
Extent of dissection	
D1+α	30
D1+β	6
D2	9
LBD	7

LBD, Lymphatic basin dissection; SN, sentinel lymph node

Table 2. Lymphatic basins positive for ICG, in relation to the cancer location

Location of tumor	Lymphatic basin		Location of SNs	
Upper one-third	LGA alone	4	No. 7	7
	LGA and PGA	2	No. 4d	1
	LGA, LGEA, and PGA	1		
	LGA, LGEA, and RGEA	1		
Middle one-third	LGA alone	11	No. 7	31
	LGA and RGEA	16	No. 8a	4
	LGA and RGA	2	No. 9	1
	LGA, LGEA, and RGEA	1	No. 11p	4
	LGA, RGEA, and RGA	1	No. 12a	1
	LGA, LGEA, RGEA, and RGA	1	No. 14v	1
Lower one-third	LGA alone	1	No. 7	6
	RGE alone	2	No. 8a	5
	LGA and RGEA	2	No. 1	2
	LGA and RGA	1	No. 11p	1
	RGA and RGEA	2	No. 14v	3
	LGA, RGA, and RGEA	4		

LGA, Left gastric artery; RGA, right gastric artery; PGA, posterior gastric artery; LGEA, left gastroepiploic artery; RGEA, right gastroepiploic artery

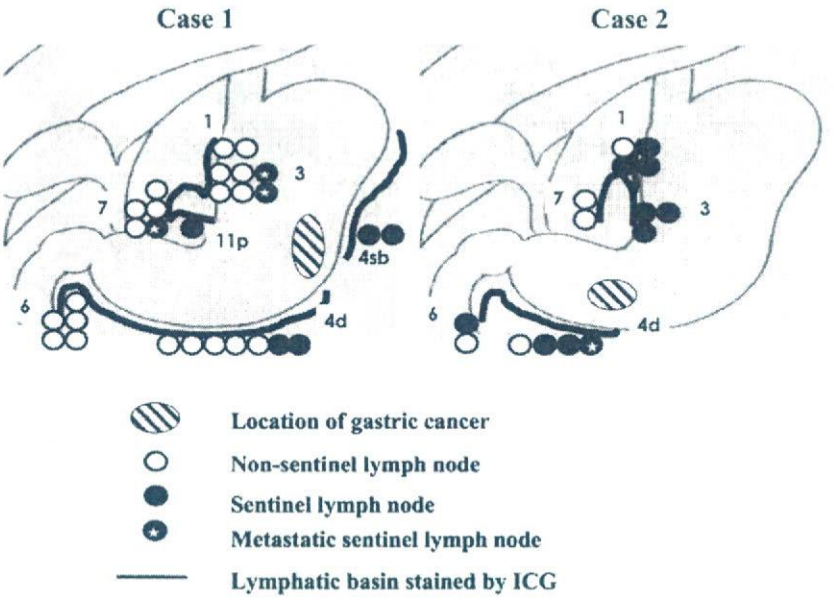

Fig. 2. Details of the two patients who had metastatic lymph nodes. Case 1 had a 45 × 23-mm submucosal signet ring cell carcinoma in the greater curvature of the middle one-third of the stomach, which had three lymphatic basins, in the left gastric artery (LGA), right gastric artery (RGA), and right gastroepiploic artery (RGEA) areas, and sentinel lymph nodes (SNs) in stations No. 3, 4sb, 4d, 7, and 11p. Metastatic lymph nodes were located in No. 3 and No. 7; these were all SNs (n2 [3/29] No. 1, 0/2; No. 3, 2/6; No. 4sb, 0/2; No. 4d,. 0/7; No. 5, 0/1; No. 6, 0/5; No. 7, 1/5; No. 11p, 0/1). Case 2 had a 23 × 12-mm submucosal signet ring cell carcinoma in the anterior wall of the lower one-third of the stomach, which had two lymphatic basins (LGA and RGEA) and SNs in No. 1, 3, 4d, and 6. A metastatic lymph node was located in No. 4d, and this was an SN (n1 [1/16] No. 1, 0/4; No. 3, 0/3; No. 4d, 1/4; No. 6, 0/2; No. 7, 0/2; No. 8a, 0/1). *IGC*, indocyanine green

All the SNs in Group 2 lymph nodes were detected with IREE plus ICG. Skip metastasis was not observed, and metastatic lymph nodes were judged to have been dissected by the D1 + α procedure. There were no cases of postoperative metastasis or recurrence.

Discussion

According to the treatment guidelines of the JGCA, endoscopic mucosal resection (EMR) or modified gastrectomy is indicated for stage IA (T1N0) disease as the routine practice [5]. In addition, local resection and segmental resection are proposed for clinical trials [5]. These recommendations are based on the large amounts of data obtained from patients who have undergone gastrectomy in Japan. Although the guidelines were developed based on as much evidence as possible, the guideline-developing committee did face difficulties because of the lack of evidence for various aspects of treatments [7].

During SNNS using ICG, we sometimes encountered SNs in the Group 2 lymph node area. These findings suggest that even early gastric cancer may be associated with metastasis to the Group 2 lymph node area, or skip metastasis. Therefore, we were faced with the following question: "Is D1+α lymph node dissection really enough for T1N0 gastric cancer?"

As to the skip metastasis of gastric cancer, Park et al. [8] analyzed findings in 14 patients with such metastasis among 266 patients who had undergone more than D2 lymph node dissection . The incidence of skip metastasis was 5.3%, and only 1 patient with early gastric cancer had such metastasis. The lymph node stations of the skip metastasis were No. 7, 8a, 9, 11p, and No. 1. The survival rate did not show any statistically significant difference between those with and those without skip metastasis. Park et al. [8] concluded that D2 lymph node dissection should be performed until sentinel lymph node (SN) detection became feasible and reliable, and that the potential risk from skip metastasis was not great, and therefore skip metastasis itself should not be a major consideration in therapeutic decisions.

Kikuchi et al. [9] analyzed the topographical pattern of lymph node metastasis for pN1 patients with curative resection. Skip metastasis occurred in 5%, and the common stations for such a metastasis were No. 7 and No. 8a. This pattern of metastasis was found in 14% of the patients with single positive nodes. Kikuchi et al. [9] noted that although perigastric nodes were important first sites of drainage, the distribution of positive nodes depended on the tumor location.

Accordingly, in view of both the complexity of the lymphatic circulation and skip metastasis, previous studies have recommended the routine use of systemic D2 dissection [9–11]. However, the feasibility and reliability of SNNS is a prerequisite for limited gastric resection [9–11].

In western countries, Roviello et al. [12], in their multicenter retrospective study, confirmed nodal involvement to be a significant prognostic factor for early gastric cancer. In view of the trend to a lower risk of recurrence when more than 15 nodes were retrieved and the better staging achieved, they concluded that D2

lymphadenectomy was the treatment of choice. However, Degiuli et al. [13], in their retrospective analysis, reported that the survival benefit of D2 gastrectomy for early gastric cancer was not documented either in the overall population or in subset analyses of patients with increased risk of nodal metastasis.

Recently, reports on SNNS for gastric cancer have increased, in which technical improvements have been documented [14–20]. Using infrared ray electronic endoscopy (IREE), we previously reported a sensitivity of 100%, specificity of 67%, positive predictive value of 29%, and negative predictive value of 100% for the detection of SNs [6].

In the present study, common locations of SNs were stations No. 7 and No. 8a. During the SNNS, if these lymph nodes were stained green, we were afraid that they may have been the stations of skip metastasis, as reported by others [9,10]. Interestingly, in the middle- and lower-thirds of the stomach, stations No. 11p and No. 14v (which are necessary to include for more than D2 dissection) were included as SNs. However, metastatic lymph nodes were located in stations No. 3 and No. 7 in one patient, and in No. 4d in another patient. They were all SNs. Furthermore, skip metastasis were not observed and metastatic lymph nodes were considered to have been dissected by the D1+α procedure.

In T1N0 stage disease, the first sites of metastasis are the perigastric nodes, and skip metastasis seems to occur rarely. In previous studies, almost all patients with skip metastasis had advanced cancer [8,9,10,11]. As mentioned previously, in the study by Park et al. [8], only one patient with early gastric cancer had skip metastasis.

As to the lymphatic basins that were positive for ICG, we found that the left gastric artery compartment was the most common area, regardless of the location of the cancer. Furthermore, as many as 61.5% of the patients in our study had more than one lymphatic basin positive for ICG, including the left gastric artery area (mainly the left gastric artery and right gastroepiploic artery areas).

Miwa et al. [20] advocated the concept of lymphatic basin dissection with SNNS, using patent blue as a tracer. The sensitivity and accuracy of their method were 85% and 98%, respectively. They reported that T1 gastric cancer involved a single lymphatic basin in 42% of their patients with gastric cancer, two lymphatic basins in 47%, and three in 12%. Similar to findings in our study, they found that the most common drainage lymphatic basins were the left gastric artery and right gastroepiploic artery areas, especially for cancers in the middle and lower one-thirds of the stomach. In their series, patients with one or two basins were treated with limited gastric resection with en-bloc dissection of the blue lymphatic basins, and none developed recurrence or died of cancer.

If SNs are detected in Group 2 lymph nodes during modified gastrectomy (such as local resection, segmental gastrectomy, pylorus-preserving gastrectomy, or distal as well as proximal gastrectomy), dissection of the lymphatic basin positive for ICG would identify metastatic lymph nodes. In patients in whom the lymphatic basin positive for ICG includes the left gastric artery area, No. 7 is the most important lymph node station.

Therefore, for patients with T1N0 gastric cancer, modified gastrectomy (D1+α dissection), combined with SNNS, is suitable; however, for those whose Group 2 lymph nodes have been judged as SNs, additional dissection of the ICG-positive lymphatic basin, detected by SNNS, should be performed to confirm the absence of lymph node metastasis.

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特集 センチネルリンパ節理論の消化器癌への応用

2 センチネルリンパ節の同定
(3) 赤外光の応用

二村 浩史* 成宮 徳親** 小山 友己*
三森 教雄* 柏木 秀幸* 矢永 勝彦*

Key words：早期胃癌，インドシアニングリーン，赤外線腹腔鏡システム，腹腔鏡下手術，センチネルリンパ節ナビゲーション手術

要 旨

赤外観察下でのSNNS(センチネルリンパ節ナビゲーション手術)は従来の色素法に比べて明瞭にセンチネルリンパ節(SN)の同定ができた．とくに腹腔鏡下では他の方法に比べて有用かつ実用的である．今後，endoscopic submucosal dissection(ESD)と腹腔鏡手術のコラボレーションに際しての有用性が期待される．

はじめに

本稿では，センチネルリンパ節(SN)の同定法の一つである赤外光観察について述べる．とくに，われわれの胃癌における赤外法の成績をもとに，従来の色素やアイソトープ法との比較，腹腔鏡下胃癌手術への応用，endoscopic mucosal resection(EMR)やendoscopic submucosal dissection(ESD)とのコラボレーションの可能性について考察した．

*東京慈恵会医科大学外科
(〒105-8461 東京都港区西新橋3-25-8)
**柏健診クリニック

Ⅰ．SNNSの臨床研究の現状

この項のポイント
- ICGはわが国でもっとも使いやすく安価で安全な色素である．
- ICGを用いたSNNSは実際には視認しづらいが，赤外線観察で明瞭に観察できる．

消化器癌，とりわけ胃癌におけるセンチネルリンパ節ナビゲーション手術(以下，SNNS)の臨床研究は，現在わが国を中心にトレーサーとして色素やアイソトープを用いたり，それぞれの弱点を補うべく併用で行われ，良好な成績が報告されてきた[1)~3)]．また，色素のなかでもっともわが国で手に入りやすく，安価かつ安全であるindocyanine green(ジアグノグリーン，第一製薬，東京；以下，ICG)を用いたSNNSにおいてもその有用性が報告された[4),5)]．そこでわれわれは，2000年5月から経内視鏡的にICGを局注しSNNSを行った．SN同定率は6例中3例，50%で，6例中2例にリンパ節転移を認めたが，いずれも偽陰性であった．ラーニングカーブは20例ほどとされているが，green nodeが薄い場合の視認は困難であった．

ICGの吸収波長は805 nmと，赤外光の波長

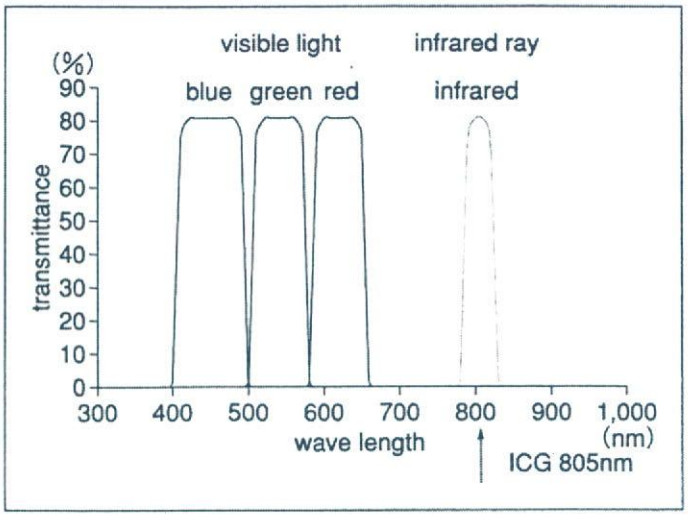

図1　赤外線観察の原理
〔二村浩史，他：消化器内視鏡　17；738-741，2005[7]より引用〕

と一致している[6),7)](図1)．その性質を利用して，赤外線内視鏡を用いてSNNSを行ったところ，不可視のICG陽性リンパ管やリンパ節が観察できた[8)]．そこでわれわれ独自の方法である赤外法，すなわちICGをトレーサーとして赤外光観察下でのSNNSの臨床研究を始めた．

Ⅱ．赤外法の実際

この項のポイント
- 術中内視鏡の前に空腸をクランプすることが，腹腔鏡下のSNNSのやりやすさや安全性につながる．
- 赤外線観察でのSN同定にはリンパ流域切除が必要である．

まず術中に，トライツ靭帯の近傍の空腸を鉗子でクランプし小腸に送気されないようにし，上部消化管内視鏡を施行する．術前に内視鏡下で，癌の辺縁に4個クリップをした部位の粘膜下に5 mg/m*l*のICGを0.5 m*l*ずつ計2 m*l*を23もしくは25ゲージの穿刺針で局注する．その後20分間，赤外線腹腔鏡システム(infrared ray laparoscopy system，オリンパスメディカルシステムズ，東京；以下，IRLS)(図2)を用いて通常光と赤外光で胃壁周囲を観察する(**図3a，b**)．20分間でもっとも遠くに流れたICG陽性リンパ管およびICG陽性リンパ節を遠位端とし，その部分までの脂肪組織を一括で切除するリンパ流域切除（lymphatic basin dissection；LBD)[9)]を施行するか，クリップや針糸でマーキングをしておき，胃切後にサイドテーブルでその脂肪組織内のリンパ節を取り出し，再度，赤外線で観察しICG陽性リンパ

文献紹介

6) 成宮徳親，二村浩史，藤崎順子，他：赤外線内視鏡システムによるsentinel lymph node観察．Gastroenterol. Endosc. 45；2338-2345，2003

赤外線内視鏡の原理やなぜICGを用いると赤外線でよく見えるのかを説明している．また，どのくらいの深さまで観察できるかを実験しており，3 mmの深さの脂肪織まで観察できるとしている．

8) Nimura, H., Narimiya, N., Mitsumori, N., et al.：Infrared ray electronic endoscopy combined with indocyanine green injection for detection of sentinel nodes of patients with gastric cancer. Br. J. Surg. 91；575-579，2004

実際に開腹手術と腹腔鏡下手術で赤外線観察SNNSを行い，赤外光観察では肉眼観察に比べて偽陰性がなく，SN同定率，感度ともに有意に優れており，赤外線観察は胃癌SNNSに有用であるとしている．