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16.7. JCOG 臨床試験審査委員会ならびに効果・安全性評価委員会

本研究実施計画書は参加施設の IRB 審査への提出に先立ち JCOG 臨床試験審査委員会の審査承認を得たものである。

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16.8. データセンター

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17. 研究結果の発表

　本試験終了後、研究代表者は速やかにその結果をまとめ、参加者の了解の後しかるべき英文誌および学会に発表する。全研究協力者は List of authors として論文に掲載する。

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19. 付表

・胃癌取扱い規約リンパ節分類および群分類
・説明文書・同意書
・ヘルシンキ宣言（和訳）
・ケースレポートフォームドラフト

付表 1

胃癌取扱い規約第 13 版におけるリンパ節の番号と名称

No.1	右噴門リンパ節
No.2	左噴門リンパ節
No.3	小弯リンパ節
No.4sa	大弯リンパ節左群（短胃動脈）
No.4sb	大弯リンパ節左群（左胃大網動脈に沿う）
No.4d	大弯リンパ節右群（右胃大網動脈に沿う）
No.5	幽門上リンパ節
No.6	幽門下リンパ節
No.7	左胃動脈幹リンパ節
No.8a	総肝動脈前上部リンパ節
No.8p	総肝動脈後部リンパ節
No.9	腹腔動脈周囲リンパ節
No.10	脾門リンパ節
No.11p	脾動脈幹近位リンパ節
No.11d	脾動脈幹遠位リンパ節
No.12a	肝十二指腸間膜内リンパ節（肝動脈に沿う）
No.12b	肝十二指腸間膜内リンパ節（胆管に沿う）
No.12p	肝十二指腸間膜内リンパ節（門脈に沿う）
No.13	膵頭後部リンパ節
No.14v	上腸間膜静脈に沿うリンパ節
No.14a	上腸間膜動脈に沿うリンパ節
No.15	中結腸動脈周囲リンパ節
No.16a1	腹部大動脈周囲リンパ節 a1
No.16a2	腹部大動脈周囲リンパ節 a2
No.16b1	腹部大動脈周囲リンパ節 b1
No.16b2	腹部大動脈周囲リンパ節 b2
No.17	膵頭前部リンパ節
No.18	下膵リンパ節
No.19	横隔下リンパ節
No.20	食道裂孔部リンパ節
No.110	胸部下部食道リンパ節
No.111	横隔上リンパ節
No.112	後縦隔リンパ節

付表2

原発巣の占居部位によるリンパ節群別一覧表（胃癌取扱い規約第13版）

占居部位 リンパ節 No.	LMU/MUL MLU/UML	LD/L	LM/M/ML	MU/UM	U	E+
1	1	2	1	1	1	
2	1	M	3	1	1	
3	1	1	1	1	1	
4sa	1	M	3	1	1	
4sb	1	3	1	1	1	
4d	1	1	1	1	2	
5	1	1	1	1	3	
6	1	1	1	1	3	
7	2	2	2	2	2	
8a	2	2	2	2	2	
8p	3	3	3	3	3	
9	2	2	2	2	2	
10	2	M	3	2	2	
11p	2	2	2	2	2	
11d	2	M	3	2	2	
12a	2	2	2	2	3	
12b/p	3	3	3	3	3	
13	3	3	3	M	M	
14a	M	M	M	M	M	
14v	2	2	3	3	M	
15	M	M	M	M	M	
16a2/16b1	3	3	3	3	3	
16a1/16b2	M	M	M	M	M	M
17	M	M	M	M	M	M
18	M	M	M	M	M	M
19	3	M	M	3	3	2
20	3	M	M	3	3	1
110	M	M	M	M	M	3
111	M	M	M	M	M	3
112	M	M	M	M	M	3

E+:食道に浸潤する癌　　群分類の「M」は遠隔転

説明同意文書

研究名：JCOG 0110-MF「上部進行胃癌に対する胃全摘術における脾合併切除の意義に関するランダム化比較試験」

1) あなたの病状

担当医から説明がありましたように、あなたの胃にがんができています。あなたの胃がんは進行がんと考えられており、胃の入り口に近い部位に生じていて、完全に切除するためには胃を全部摘出すること（胃全摘）が必要です。ただし肝臓や遠くのリンパ節への転移は見つかっておらず、手術で根治が望める状態であると考えられています。胃がん手術後の予後は、がんの深さ、リンパ節転移の程度、腹膜や肝臓などへの転移の有無によって決まります。胃がんの進行程度を表すステージ（病期）は、ステージ 1A、1B、2、3A、3B、4 の 6 段階ありますが、これまでの検査の結果、あなたの胃がんはステージ 1B から 4 までの範囲にあると考えられ、予想される 5 年生存率も 20%から 90%と幅があります。最終的なステージは手術後の病理検索の結果で決まります。

2) 胃がんとリンパ節転移、リンパ節郭清、予後

胃がんはリンパ節に転移しやすいがんです。リンパ節転移が進むと、全身にがん細胞が広がります。早期胃がんでも約 10%、進行がんでは 50%以上の確率でリンパ節転移が認められます。胃がんのリンパ節転移は、胃のすぐそばのリンパ節（第 1 群リンパ節）に生じて徐々に離れた部位（第 2 群、3 群リンパ節）へと広がりますので、たとえ転移があってもこれを遠くから包み込むようにして十分に切除することにより、治癒する可能性が得られます。リンパ節に転移があるかどうかは手術中には正確に判断できず、摘出したリンパ節を術後に顕微鏡で検査して初めて転移の有無が判明します。リンパ節の切除（郭清といいます）は、胃がんの手術において重要な部分を占めており、通常、第 2 群までのリンパ節が郭清されます。

3) 上部胃がんと脾臓

胃がんでは、がんが胃のどの位置にあるかによって、転移しやすいリンパ節の場所が変わります。「第 2 群リンパ節」といっても、胃の上部のがんと下部のがんでは範囲が異なるのです。胃の左背側には脾臓という握りこぶしくらいの大きさの臓器がありますが、胃上部のがんの場合、この脾臓のすぐそば（脾門部）のリンパ節にも転移することがあり、この脾門リンパ節も第 2 群に含まれています。したがって、胃上部の進行胃がんに対しては、胃と同時に脾臓も合併切除することが行われてきています。

4) 脾臓の役割

脾臓は、古くなった血小板などの血液成分を壊す働きがあります。また、体の免疫の調整に関しても一役を担っています。脾臓を摘出（脾摘）すると、一時的に血液中の血小板の数が増加しますが、やがて骨髄が代役を果たすようになりますので数ヶ月で血小板数は元に戻ります。また、免疫力が低下することがあり、肺炎球菌などの感染が起こりやすく

なるとされています。脾臓はまた、腫瘍に対する生体の免疫に関与するという研究があります。が、脾臓を摘出することが腫瘍の増殖とどう関係するかは、明確にされていません。

5) 胃全摘と脾摘

　胃上部の進行がんでは胃全摘とともに脾摘も行われると述べましたが、実は脾臓を同時に摘出することの意義はきちんと証明されているわけではありません。脾門部のリンパ節に転移があった場合、脾摘を行うとこの転移を切除することができますが、一方で、脾摘操作により術中の出血量が増え、術後の合併症（脾臓のそばにある膵臓からの膵液の漏れや、腹腔内の感染）が生じやすくなったり、脾臓を失うことにより体の免疫力が低下して肺炎球菌という細菌の感染症が増えたりする可能性もあります。西洋諸国では、脾摘により術後の合併症率や手術死亡率が明らかに高くなるため、近年これを極力避けようという考えが支配的になっています。しかしわが国では、術後合併症は増えても手術死亡率が高くなるという事実はなく、むしろ転移リンパ節を切除する意義が注目されています。

　これまでに胃上部進行がんで脾摘を行った記録を検討すると、約 15〜20%の患者さんで脾門リンパ節に転移が見られ、その転移のある患者さんの 20〜25%が 5 年以上生存しています。つまり脾摘をしたから助かった、と考えられる患者さんがいます。ところが一方、脾摘をした患者さん全体としなかった患者さん全体を比べると、脾摘をしなかった患者さんの生存率の方が高いという結果も出ています。ただしこれは、より進行したがんの場合ほど脾摘が行われることが多いため、脾摘患者さんの生存率が低く出てしまうとも解釈されています。

6) この臨床試験について

　このように、胃上部の進行がんに対して胃全摘を行う場合に、同時に脾摘を行うことが生存の可能性を高めるかどうかは分かっていません。これまでにも多くの学会で論じられてきましたが結論は出ていません。

　この問題に科学的な結論を下すためには、きちんと計画された臨床試験が必須となります。本臨床試験は、がんの専門病院を中心に構成される日本臨床腫瘍研究グループ（JCOG）の胃がん外科チームが厚生労働省の研究費を得て計画したもので、同じような病態の多数の患者さんに、脾摘を行うグループと行わないグループに分かれていただき、長期間経過を追って、どちらが優れた術式かを決めようというものです。この臨床試験で得られた結果は、将来、多くの胃がん患者さんが胃全摘を受ける際に、脾摘が行われるかどうかを決定する大変重要な根拠となるはずです。

7) この臨床試験の実際の手順

　あなたがこの臨床試験への参加に同意されたとしましょう。手術が始まり、通常の手順で腹腔内が検索されます。腹膜転移や肝転移がないことが確認され、腹膜洗浄細胞診も行われます。大動脈周囲などの胃から離れた部位のリンパ節に転移がないこと、さらに脾門部にも明らかに腫脹したリンパ節はないことが確認されます。胃全摘を行えばがんは取り切れそうだ、という段階にきました。ここまで確認して初めて、臨床試験に登録するかど

うか決定されます。以上のうちどれか一つでも当てはまらない場合は、臨床試験には入らずに、担当医が最良と考える治療が行われます。

　臨床試験に登録されると、胃全摘に加えて脾摘を行うかどうかが決定されることになります。二つのグループで患者さんの特徴に偏りが生じないよう、病院とは独立した JCOG のデータセンターが、ランダム割付けと呼ばれる方法で決定します。この結果にしたがって手術が行われます。あなたは手術後に、担当医から脾摘が行われたかどうかを知らされますが、その後の治療や経過観察は脾摘の有無にかかわらずまったく同じように行われます。この臨床試験には、合計 500 人の患者さんの登録を予定しています。

　進行胃がんの手術後に、再発を予防したいという考えから抗がん剤が使われることがあります。しかしこれまでの多くの臨床試験でも、手術でがんが取りきれたと考えられる場合に抗がん剤を使うこと（補助化学療法といいます）で再発が予防されるという結論は得られていません。本臨床試験では、補助化学療法を行わずに経過を観察することになります。不幸にも再発が判明した時は、抗がん剤をはじめとするあらゆる手段で対処します。もしあなたが初めから補助化学療法を希望される場合はこの臨床試験には参加できませんので、担当医にお知らせください。

8)　その他の治療法について

　あなたの胃がんを治療するには、内視鏡的切除では不十分で、手術が必要です。また、抗がん剤や放射線療法だけでは治癒は望めません。手術方法としては、ご説明しました胃全摘術の他に、胃の下部を残す噴門側胃切除術という方法があります。ただし、あなたの胃がんでは十分な範囲の胃とリンパ節を切除する必要があるため、たとえ胃の下部を残しても十分な機能は望めず、むしろ食べ物の流れが悪くなる場合もありますので、胃全摘が望ましいと考えられています。リンパ節の郭清範囲では、ご説明しました第 2 群までの郭清が現在標準的に行われていますが、さらに遠くの第 3 群までの郭清も技術的には可能です。ただし第 3 群までの郭清が胃がんの治癒に貢献するかどうかは分かっておらず、現在臨床試験が進められています。

9)　この臨床試験に参加することの利益と不利益

　この臨床試験に参加することで、医療費の免除などの直接的な利益は得られません。もちろん従来から行われている手術ですので、経済的負担が増えるということもありません。

　臨床試験に登録されるかどうかは、手術中に腹腔内を十分検索してから決定されますので、この試験に同意したからといって無理やり無用な手術が行われるということもありません。脾摘を行うことも行わないことも、外科医には十分に慣れた手順ですから、新しい種類の合併症が生じるということもありません。

　この臨床試験では術後 5 年間にわたる経過追跡の内容が詳細に規定されていますので、試験に参加しない場合よりも細かいフォローアップが行われることになるでしょう（そのために若干医療費が増える可能性があります）。

10)　この臨床試験への参加に同意されなかった場合、および同意の撤回

この臨床試験への参加に同意されなかった場合でも、あなたはいかなる不利益も受けることはありません。また一旦同意しても、いつでもこれを撤回することができます。

11）　人権およびプライバシーの保護、データの二次利用

　この臨床試験に参加した場合、あなたのお名前や個人情報は厳重に保護されます。データセンターのデータベースにも、あなたのお名前は登録されません。

　この試験が適正かつ安全に実施され、患者さんの人権が守られており、かつ検査や診断の結果が正しく報告されていることを確認する目的で、JCOG 委員会の指名する他の医療機関や研究機関の研究者（医師など）が、あなたのカルテや検査記録を直接見にくる調査を行うことがあります。この場合もあなたの個人的情報は厳重に守られ、外部に漏れることはありません。

　また、JCOG 委員会が承認した場合に限り、あなたの個人識別情報とリンクしない形でデータを二次利用する可能性があります（本臨床試験と同様の目的で行われた他の試験と、総合的に解析する場合、など）。この場合もあなたの個人的情報は厳重に守られます。

12）　質問の自由

　この臨床試験の内容や治療の内容について、ご不明な点がありましたらご質問ください。

　この臨床試験の当院における研究責任者、担当医は、

　　　　＊＊＊＊　です。（各施設で記入）

　この臨床試験の研究代表者および研究事務局は以下の通りです。

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同　意　書

<u>　　　　　　　　　　　　　　　　</u>病院長　殿

カルテ番号　<u>　　　　　　　　　　　</u>

患者氏名　　<u>　　　　　　　　　　　</u>

臨床研究名：<u>JCOG 0110-MF「上部進行胃癌に対する胃全摘術における脾合併切除の意義</u>
<u>に関するランダム化比較試験」</u>

説明内容：

- ☐　病名、病状、予後
- ☐　本研究が臨床試験であること。厚生省研究助成金に基づく公的研究で
     あること。
- ☐　試験の背景、目的、意義
- ☐　治療の内容
- ☐　治療法がランダム割付されること
- ☐　治療により期待される効果と予測される副作用
- ☐　費用が保険制度に従った自己負担であること
- ☐　本試験に参加しなかった場合に受けられる他の治療法
- ☐　試験参加に伴って生じる利益と不利益
- ☐　試験に参加しない場合でも不利益を受けないこと
- ☐　試験への参加に同意した後でも随時これを撤回できること
- ☐　第三者による病歴の直接閲覧の可能性、データ二次利用の可能性
- ☐　プライバシーは守られること
- ☐　現状に応じた変更の可能性（緊急の場合等の医学的処置）
- ☐　質問の自由

上記の臨床試験について、担当医から説明を受けよく理解しましたので、試験に参加します。

患者本人署名：<u>　　　　　　　　　　　　　　　　　　　　　　　</u>

署名年月日　：　　平成　　　　　　年　　　　　月　　　　　日

私は、今回の試験について上記の項目を説明し、同意が得られたことを認めます。

担当医署名　：<u>　　　　　　　　　　　　　　　　　　　　　　　</u>

説明年月日　：　　平成　　　　　　年　　　　　月　　　　　日

署名年月日　：　　平成　　　　　　年　　　　　月　　　　　日

Original article

Risk factors for pancreas-related abscess after total gastrectomy

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Abstract
Background. European clinical trials of gastrectomy have shown that pancreas-related complications are the major cause of mortality. The aim of this study was to determine the risk factors for pancreas-related abscess after gastrectomy and to evaluate the effects of the abscess on postoperative mortality.
Methods. Between 1992 and 1999, 663 consecutive patients with gastric carcinoma underwent total gastrectomy. Data from these patients were analyzed, to identify the predictors of pancreas-related abscess caused by pancreatic juice leakage, by a multiple logistic regression model.
Results. On multivariate analysis, increasing age ($P = 0.018$) and body mass index ($P = 0.006$) were independent preoperative risk factors. Dissection along the distal splenic artery was an intraoperative risk factor. The hazard ratios were increased 9.13-fold ($P = 0.000$) with a pancreas-preserving operation and 16.72-fold ($P = 0.000$) by distal pancreatectomy. Patients with the abscess had a higher postoperative mortality rate ($P = 0.008$), and a higher re-operation rate ($P < 0.001$) than patients without the abscess.
Conclusion. Pancreas-related abscess is more likely to occur in older, obese patients undergoing node dissection along the distal splenic artery. Abscess formation is associated with a higher mortality and re-operation rate. Spleen preservation should be evaluated in Japan.

Key words Gastric cancer · Morbidity

Introduction

The most frequent major complication after gastrectomy with extended dissection is pancreatic juice leakage [1], because recently, the incidence of anastomotic leakage has decreased remarkably [2]. Pancreatic juice leakage is often followed by contamination, resulting in a peripancreatic abscess. Secondary hemorrhage from major arteries damaged by contamination can be fatal. European clinical trials of gastrectomy have shown that pancreas-related complications are a major cause of mortality [3,4].

The prediction and early detection of pancreas-related complications may be helpful. The aim of this study was to determine risk factors for pancreas-related abscess after gastrectomy, caused by pancreatic juice leakage, and to evaluate the effects of the abscess on postoperative mortality.

Patients and methods

Six hundred and sixty-three consecutive patients with gastric carcinoma underwent total gastrectomy, between 1992 and 1999, at the National Cancer Center Hospital, Tokyo. Data for these patients were analyzed to identify the predictors of pancreas-related abscess caused by pancreatic juice leakage, using a multivariate logistic regression model.

The diagnosis of a pancreas-related abscess was made when purulent fluid containing turbid necrotic debris drained from the peripancreatic area for more than 7 days. The abscess cavity was assessed by computed tomography (CT) scan and contrast study through drains. We recorded an abscess regardless of its cavity size. When we found anastomotic leakage radiologically on initial diagnosis of the abscess, we excluded these patients from the pancreas-related abscess group.

The preoperative and perioperative data were collected from the patients' records and stored on our gastric surgical database.

Operative techniques

Total gastrectomy with Roux-en-Y esophagojejunostomy was performed in 623 patients (94.0%), as the standard operation. Forty patients (6.0%) underwent jejunal interposition. Pouch formations were added in 7 patients (1.1%). The extent of nodal dissection along the distal splenic artery and splenic hilum varied, including no dissection of these nodes. Distal pancreatectomy or the Maruyama pancreas-preserving method [5] was usually performed for advanced tumor (T2, T3, and T4). The splenic arteries were sacrificed distally to the dorsal pancreatic arteries, in all patients, when we performed pancreas-preserving total gastrectomy. At least one drainage tube was applied in the left subphrenic space in all patients. In most cases, the amylase level of the drainage fluid was determined on the first postoperative day. All patients received antibiotic prophylaxis for the same period.

Statistical methods

Univariate analyses were performed in order to predict those preoperative and perioperative variables that were associated with a pancreas-related abscess. Fischer's exact test and the Mann-Whitney test were used as appropriate.

To develop a model for predicting postoperative pancreas-related abscess in terms of pre- and perioperative variables, three preoperative and six perioperative variables were entered in multiple logistic regression analysis. All the statistical procedures were performed with the SPSS 11.5 statistical package (SPSS Japan, Tokyo, Japan). The limit for statistical significance was $P < 0.05$.

Results

The overall incidence of pancreas-related abscess was 11.5%. The median amylase level of the drainage fluid on the first postoperative day was 1942 I/l (range, 22–387000) U/l overall, and it was 1682 (22–303800) U/l in patients without abscess and 6590 (96–387000) U/l in patients with abscess.

The male-to-female ratio was 2.5:1, and the mean age was 59.9 ± 11.6 years. The proportion of patients with early gastric cancer (T1) was 21.1%. Operation with curative intent was performed in 82.5% of the patients. Nodal dissection along the distal splenic artery was performed in 68.0% of the patients and D2 dissection or more was carried out in 67.6 % of the patients. The median operation time was 263 min (90–580 min). Median blood loss was 567 ml (250–4457 ml).

Univariate analysis identified several preoperative patient-related factors as having a high association with pancreas-related abscess. The preoperative demographic data are shown in Table 1, for patients with and without the abscess. Increasing age ($P = 0.004$) and increasing body mass index ($P = 0.008$) had a strong association with postoperative pancreas-related abscess.

Perioperative data are also presented in Table 1. Univariate analysis showed that depth of tumor invasion ($P = 0.007$), operation time ($P = 0.024$), extent of dissection ($P = 0.000$), and dissection along the distal splenic artery ($P = 0.000$) were all associated with a greater incidence of abscess formation. The method of dissection along the distal splenic artery was categorized into one of five variations.

Multivariate analysis identified three independent factors as predictors of postoperative pancreas-related abscess formation (Table 2). Increasing age and increasing body mass index increased the risk of the abscess by 1.4- and 1.1-fold, respectively.

Dissection of nodes along the distal splenic artery and in the splenic hilum was an intraoperative risk factor. If the relative risk for the abscess was set at 1 for patients with neither splenectomy nor pancreatectomy, the hazard ratios were 9.1 for pancreas-preserving operation and 16.7 for distal pancreatectomy.

The postoperative outcomes of the patients with and without pancreas-related abscess were compared (Table 3). The patients with the abscess had a higher postoperative mortality rate. Patients with pancreas-related abscess had 7.6-fold increased mortality compared to patients without the abscess. The re-operation rate for patients with pancreas-related abscess was 32-fold greater than that for patients without the abscess.

Discussion

Increasing body mass index increases the risks of pancreas-related abscess. The literature also reports fat volume as being a risk factor in increasing postoperative complications [6,7]. Nodal dissection along the distal pancreas and in the splenic hilum in obese patients is a difficult task, even in the hands of experienced surgeons specializing in the treatment of gastric carcinoma.

Patients in the West usually have a higher body mass index than those in Japan [8]. The observed high morbidity rates in Western randomized trials for D2 dissection may be related to the greater obesity of these patients.

Increasing age also increases the risk of abscess formation. Patients in the West receiving gastrectomies are usually older than those in Japan, as well as having a

Table 1. Univariate analysis of variables associated with pancreas-related abscess

	No abscess ($n = 587$)	Abscess ($n = 76$)	P value; patients with vs without abscess
Preoperative variables			
Sex			
Male	413 (87.1%)	61 (12.9%)	0.080
Female	174 (92.1%)	15 (7.9%)	
Age (years)	59.5 (22–91)[a]	62.8 (44–84)[a]	0.004
Body mass index (kg/m²)	21.7 (12.2–37.7)[a]	22.6 (15.0–31.5)[a]	0.008
Perioperative variables			
Depth of tumor invasion			
Early (T1)	133 (95.0%)	7 (5.0%)	0.007
Advanced (T2, T3, T4)	454 (86.8%)	69 (13.2%)	
Curability of operation			
Curative (R0)	480 (87.8%)	67 (12.2%)	0.200
Noncurative (R ≧ 1)	107 (92.2%)	9 (7.8%)	
Operation time (min)	260 (90–580)[a]	286 (140–540)[a]	0.024
Blood loss (ml)	565 (25–3776)[a]	587.5 (70–4457)[a]	0.123
Extent of dissection			
D0, D1	207 (96.3%)	8 (3.7%)	0.000
D2, D3	380 (84.8%)	68 (15.2%)	

Dissection methods for nodes along the distal splenic artery

	Splenectomy	Distal pancreatectomy	Dissection along distal splenic artery			
1.	No	No	No	155 (98.1%)	3 (1.9%)	0.000
2.	Yes	No	No	49 (90.7%)	5 (9.3%)	
3.	No	No	Yes	10 (83.3%)	2 (16.7%)	
4.	Yes	No	Yes	309 (86.3%)	49 (13.7%)	
5.	Yes	Yes	Yes	64 (79.0%)	17 (21.0%)	

Splenectomy (yes), pancreatectomy (no), dissection along distal splenic artery (yes) indicates pancreas-preserving total gastrectomy method
[a] Median values, with ranges in parentheses

Table 2. Multivariate predictors of pancreas-related abscess

Variables	P value	Odds ratio	95% Confidence interval of odds ratio
Preoperative variables			
Age (continuous)	0.018	1.414	1.060–1.886
Body mass index (continuous)	0.006	1.126	1.035–1.225
Perioperative variables			

Dissection methods for nodes along the distal splenic artery

	Splenectomy	Distal pancreatectomy	Dissection along distal splenic artery			
1.	No	No	No		1	
2.	Yes	No	No	0.012	6.601	1.505–28.953
3.	No	No	Yes	0.011	11.973	1.760–81.468
4.	Yes	No	Yes	0.000	9.130	2.791–29.864
5.	Yes	Yes	Yes	0.000	16.724	4.675–59.823

Table 3. Relationship of postoperative events to pancreas-related abscess

Variables	No abscess ($n = 587$)	Abscess ($n = 76$)	P value
Re-operation	4 (0.7%)	17 (22.4%)	< 0.001
Operation-related death	4 (0.7%)	4 (5.3%)	0.008

higher body mass index [9,10]. The observed high morbidity rates in Western trials were related to the age distribution [11], similar to our findings here.

Our study shows that the dissection of nodes alongside the distal splenic artery and nodes in the splenic hilum is an intraoperative risk factor. Distal pancreatectomy with splenectomy had the highest odds ratio. However, even when we performed pancreas-preserving total gastrectomy to avoid pancreas-related complications, there was still a considerably higher odds ratio of abscess formation. Pancreas-preserving splenectomy is part of the standard operation in specialized centers in Japan. Splenectomy without dissection along the distal splenic artery also had a high risk of abscess formation.

Japanese retrospective studies have shown that 20%–30% of patients with advanced cancer in the proximal stomach have nodal metastasis in the splenic hilum, and that gastrectomy with resection of these nodes can yield a 5-year survival of 20%–25% [12]. Consequently, in Japan, dissection of nodes in these areas is performed routinely.

Although mortality rates from gastrectomy complicated by pancreas-related abscess are lower in Japan than those reported in Western series [3,4], pancreas-related abscess formation remains a strong factor in the mortality and morbidity rates in both Japanese and Western centers.

Evaluation of the role of splenectomy for proximal gastric cancer is important. Spleen preservation, avoiding thorough nodal dissection in the splenic hilum as well as in the distal splenic artery, as described by groups in the United Kingdom [13,14], should be evaluated in Japan. The Japan Clinical Oncology Group have recently started a randomized controlled trial to evaluate the effect of splenectomy on postoperative morbidity and longterm cancer-free survival [15].

Conclusions

Pancreas-related abscess after gastrectomy is more likely to occur in older, obese patients undergoing node dissection along the distal splenic artery. Because the abscesses are associated with high mortality and re-operation rates, the role and oncologic value of splenec-

tomy has to be considered more carefully. This now forms the basis of a nationwide trial.

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From a new Editor-in-Chief

An international forum for discussion of gastric cancer is needed, particularly now

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Gastric cancer may or may not be changing. According to the estimate by the International Agency for Research on Cancer, the worldwide incidence of gastric cancer in 2002 was 933,937, of which no less than 56% of cases were from East Asia (China, Japan, and Korea) alone. Interestingly, gastric cancer in this high-incidence area is not, or only very slowly, undergoing the phenomenon of "proximal shift" of tumors, which today is a definite trend in gastric cancer in the West. The difference between East and West in terms of tumor biology as well as treatment modality seems to be becoming greater over the years. Now many physicians and researchers in both hemispheres are wondering if they are fighting against the same disease that the other side is.

In such a situation, the role of the International Gastric Cancer Association (IGCA) is particularly important. It provides opportunities for worldwide specialists to meet and discuss the disease. Our journal, *Gastric Cancer*, should also be a forum for global discussion as the only international journal specialized in this malignancy.

Since its first publication in 1998, *Gastric Cancer* has maintained some unique features as the joint official journal of IGCA and the Japanese Gastric Cancer Association (JGCA). The editorial board consists of the same number of members from both associations, and any submitted manuscript is reviewed by a team composed of referees from both associations. Even the position of Editor-in-Chief has been shared; Professor J. Rüdiger Siewert from IGCA and Dr. Oichiro Kobori from JGCA formed a good partnership to develop a high-quality peer-review system.

Now I have succeeded Dr. Kobori to undertake the JGCA's part as an Editor-in-Chief. My task is clear: to further expand the journal's scope as a forum for global discussion and to enhance the journal's status in the field of oncology.

Both Professor Siewert and I are surgeons. Approximately 80% of the JGCA and IGCA members are also surgeons. However, our journal is not a surgical journal. Our editorial board has prominent medical oncologists and scientists to welcome any category of papers related to gastric cancer. Our goal is comprehensive understanding and consequent conquest of gastric cancer.

In 2004, a total of 1,450 English papers having the keyword "stomach neoplasms" were published, according to the PubMed database. Of these, 513 papers (35.4%) were from Japanese institutions or had at least one Japanese author. Considering the high incidence of

the disease in Japan, this high proportion is understandable. *Gastric Cancer* is a quarterly journal, and we published 41 papers in 2004. This accounted only for 2.8% of the above-mentioned 1,450, and I would aim at doubling this within 3 years. Of all 268 papers published in volumes 1 to 7 of *Gastric Cancer*, 207 (77.2%) were from Japanese institutions. Although this high proportion is due largely to the fact that the membership ratio of JGCA to IGCA is 6 to 1, I hope we will receive more papers from outside Japan to make our journal a truly international forum.

As a gastric surgeon, I have visited 22 countries either for giving lectures or live demonstrations of surgery. As a host at the National Cancer Center Hospital, Tokyo, I have received visitors from an additional 21 countries and had intensive discussions with all of them. I believe I am part of a global network of gastric cancer specialists, on a personal level, and I intend to make full use of that network to increase the value of the journal.

Dear colleagues: Please do not hesitate. You have good reasons to write papers for *Gastric Cancer*:

1. Your paper will be sent directly to 6,000 worldwide specialists of gastric cancer.
2. The abstract of your paper is immediately listed in Medline and PubMed.
3. The PDF file of your paper is uploaded on the Springer website and can be downloaded through their 4,500 worldwide access sites in addition to downloading by our 6,000 subscribers.
4. Your paper may be selected for the Nishi Award of the JGCA (the best three papers each year) and you will be awarded US$2,000.

I am looking forward to your participation in this international forum for gastric cancer.

Takeshi Sano
Editor-in-Chief

Identification of risk factors for the development of complications following extended and superextended lymphadenectomies for gastric cancer

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Background: Extended lymphadenectomy for gastric carcinoma has been associated with high mortality and morbidity rates in several multicentre randomized trials.

Methods: Using data from 523 patients registered for a prospective randomized trial comparing extended (D2) and superextended (D3) lymphadenectomies, risk factors for overall complications and major surgical complications (anastomotic leakage, intra-abdominal abscess and pancreatic fistula) were identified by multivariate logistic regression analysis.

Results: Mortality and morbidity rates were 0·8 per cent (four of 523) and 24·5 per cent (128 of 523) respectively. Pancreatectomy (relative risk 5·62 (95 per cent confidence interval (c.i.) 1·94 to 16·27)) and prolonged operating time (relative risk 2·65 (95 per cent confidence interval 1·34 to 5·23)) were the most important risk factors for overall complications. A body mass index of 25 kg/m^2 or above, pancreatectomy and age greater than 65 years were significant predictors of major surgical complications.

Conclusion: Pancreatectomy should be reserved for patients with stage T4 disease. Age and obesity should be considered when planning surgery.

Introduction

Despite a declining incidence in Western Europe[1] and the USA[2], gastric carcinoma remains the second commonest cause of cancer death worldwide, with over 600 000 deaths per year[3]. Given the poor outcome of irresectable disease treated by other therapeutic modalities in phase II and III trials[4,5], the curative treatment of gastric carcinoma remains primarily surgical. Although the presence of distant metastases usually precludes curative surgery, this does not necessarily apply to disease in the regional lymph nodes, which can be dissected *en bloc* with the primary lesion[6,7]. This type of resection may allow cure, provided that metastases are within the margins of dissection. Removal of a wider range of lymph nodes by extended lymph node dissection might increase the

chance of cure, but is inappropriate if the cancer has spread systemically.

In Japan, gastrectomy plus extended systematic lymphadenectomy (D2 resection) has long been the standard treatment, even for superficial cancers[8]. Success with D2 resection has led to the evolution of a superextended lymphadenectomy (D3 resection) and several feasibility studies evaluating dissection of para-aortic lymph nodes have been performed[9–12]. A randomized trial (Japan Clinical Oncology Group (JCOG) 9501) was launched in 1995, primarily to explore the potential survival benefit of D3 over D2 dissection[13]. This trial has provided the opportunity to evaluate prospectively collected data on gastric cancer surgery in Japan. The present study represents a detailed analysis of risk factors for overall and surgical complications following D2 and D3 resections.

Patients and methods

Between June 1995 and April 2001, 523 patients registered in the JCOG 9501 study were allocated randomly to either D2 (263 patients) or D3 (D2 plus para-aortic lymph node dissection; 260 patients) resection. Eligibility criteria and the method of randomization have already been reported in detail[13]. In brief, patients aged less than 75 years of age with histologically proven and resectable primary gastric carcinoma with an estimated depth of SS (penetrating the muscle layer), SE (penetrating the serosa) or SI (invasion to an adjacent organ) were recruited after giving informed consent. Patients found positive for free cancer cells by cytological examination of peritoneal washes and those with Borrmann type 4 tumours (linitis plastica type) were excluded. Twelve institutions participated in the trial initially and 12 other institutions were added to increase patient recruitment.

After laparotomy, cytological examination of peritoneal washes was performed, followed by gross examination of the abdominal cavity and the primary lesion. Only patients who were negative for free cancer cells in the abdominal cavity and without evidence of gross para-aortic lymph node spread, peritoneal carcinomatosis or other distant metastasis were eligible to participate. The patients were allocated randomly to either D2 or D3 resection by the minimization method of balancing the groups according to T stage (T2 versus T3/T4), gross appearance (Borrmann types 1 and 2 versus Borrmann types 3 and 5) and institution. The surgeons were notified immediately of the allocation results and completed the operation accordingly.

Patients underwent appropriate gastrectomy with systematic lymphadenectomy as allocated. Perigastric lymph nodes (nodal stations 1, 3, 4, 5 and 6 according to the Japanese Classification of Gastric Cancer[14]) and nodes at the base of the left gastric artery (7), along the common hepatic artery (8) and at the base of the splenic artery (11) were resected routinely. Lymph nodes along the hepatoduodenal ligament and behind the pancreatic head (12 and 13) were resected when the primary lesion was located in the lower third of the stomach. Lymph nodes along the left side of the cardia (2), within the splenogastric ligament (4sa) and at the splenic hilum (10) were resected with the spleen when total or proximal gastrectomy was performed. Concurrent resection of the pancreatic tail was not routine during either D2 or D3 resection and was reserved for patients with direct invasion to the pancreas. In patients randomized to superextended lymphadenectomy, para-aortic lymph nodes from the level of the coeliac trunk down to the root of the inferior mesenteric artery (16a2 and 16b1) were dissected. The mode of reconstruction following resection was not specified.

All information on complications was extracted from the case-report forms for the trial. Anastomotic leakage, intra-abdominal abscess and pancreatic fistula were considered to be major surgical complications. Anastomotic leakage was defined as dehiscence confirmed by radiographic examination using contrast medium. Pancreatic fistula was diagnosed if there was prolonged purulent discharge containing pancreatic juice from the drainage tube.

Factors that might affect the risk of overall and major surgical complications were evaluated by univariate analysis using cross-tabulations. Variables analysed included extent of lymphadenectomy, splenectomy, pancreatectomy, type of gastrectomy, pathological (p) T category (pT2 and pT3 versus pT4), sex, age, body mass index (BMI), operating time, amount of blood loss and need for autologous blood transfusion. Operating time and blood loss were divided into tertiles for analysis. Two factors associated with surgical experience were also evaluated: institutions that enrolled over 20 patients versus those with fewer patients and first and second halves of the trial (1995–1998 versus 1999–2001). The χ^2 test was used to assess differences in proportions. The independent contribution of various factors was assessed by multivariate logistic regression analysis, with mutual adjustment of potential risk factors for complications. All factors analysed in the univariate analysis were included as variables in the multivariate analysis. Two-sided P values are presented. Statistical analysis was performed using SAS® version 8.12 (SAS Institute, Tokyo, Japan).

Results

Total gastrectomy was performed in 199 (38·0 per cent) of 523 patients and proximal gastrectomy in four;

Table 1 Complications

Severe abdominal complications	
Pancreatic fistula	30
Abdominal abscess	29
Anastomotic leakage	11
Other complications	
Pneumonia	16
Anastomotic stenosis	14
Bowel obstruction/ileus	16
Lymphorrhoea	10
Thoracic effusion requiring thoracic drainage	7
Severe feeding problem requiring prolonged hyperalimentation	6
Wound abscess	5
Postoperative bleeding	3
Severe diarrhoea	3
Urinary tract infection	3
Catheter-induced sepsis	3
Pulmonary embolism	2
Cardiac failure	1
Cholecystitis requiring percutaneous drainage	1