JCOG 0110　胃がん外科/SPNX

コピーして保管して下さい

a9609000109a

手術所見記録 2

術後14日以内にデータセンターに郵送

施設名　○○○○○がんセンター　　担当医　○× ○×

患者イニシャル　姓 A 名 A　　性別　男　　生年月日　昭和30年10月10日

カルテ番号　12345-6789　　割り付け群 ＊ 群　　登録番号

記入者名：CRC記入可（自署）

西暦　　年　月　日

＜切除所見＞

1. 手術的根治度（胃癌取り扱い規約13版）　1□ 根治度A　2□ 根治度B　3□ 根治度C　99□ 不明

2. 脾臓摘出

A 群　0□ 温存　1□ 摘出 → 理由

B 群　0□ 温存　1□ 摘出 → 理由

3. 膵被膜剥離　0□ なし　1□ 一部　2□ 完全

4. 合併切除臓器　0□ なし　1□ あり → □ 副脾　□ 副腎　□ 結腸　□ 胆嚢　□ 肝　□ 横隔膜　□ その他（　　）

5. 再建法　1□ R-en-Y　4□ 空腸間置　6□ ダブルトラクト　88□ その他（　　）

6. 切除近位断端（口側）　0□ PM（－）　1□ PM（＋）　99□ PMX

7. 切除遠位断端（肛門側）　0□ DM（－）　1□ DM（＋）　99□ DMX

8. 郭清リンパ節総個数　　個　（術当日に新鮮標本から摘出したリンパ節の総個数）

9. 各リンパ節郭清個数

No.10（脾門）　0□ 郭清せず　1□ 郭清 → 郭清個数　　個

No.11p（脾動脈幹近位）　0□ 郭清せず　1□ 郭清 → 郭清個数　　個

No.11d（脾動脈幹遠位）　0□ 郭清せず　1□ 郭清 → 郭清個数　　個

備　考

DC記入

receive1(　)　check1(　)　check2(　)　input1(　)　input2(　)　confirm(　)

query(　)　receive2(　)　check3(　)　input3(　)　confirm(　)　fix(　)

(　)　(　)　(　)　(　)　memo

JCOG 0110　胃がん外科/SPNX

コピーして保管して下さい

9 606001 000110

術後記録（術当日～初回退院）　退院後14日以内にデータセンターに郵送

施設名　○○○○○がんセンター　担当医　○× ○×

患者イニシャル　姓 A 名 A　性別　男　生年月日　昭和30年10月10日

カルテ番号　12345-6789　割り付け群　＊ 群　登録番号

記入者名：CRC記入可（自署）

西暦　年　月　日

1. 術後合併症（手術当日～初回退院）

(1) 肺梗塞　0□ なし　1□ あり

(2) 腹腔内出血　0□ なし　1□ あり

(3) 縫合不全　0□ なし　1□ あり

(4) 膵液瘻　0□ なし　1□ あり

(5) 腹腔内膿瘍　0□ なし　1□ あり

(6) 吻合部狭窄　0□ なし　1□ あり → 内視鏡的ブジー　0□ なし　1□ あり

(7) イレウス　0□ なし　1□ あり → □ 麻痺性　□ 閉塞性

(8) 肺炎　0□ なし　1□ あり

(9) 深部静脈血栓症　0□ なし　1□ あり

(10) 術後4日以降の出血　0□ なし　1□ あり → ドレーンからの出血　0□ なし　1□ あり（出血量　ml）

(11) 術後人工呼吸器使用の有無　0□ なし　1□ あり

(12) その他の合併症　0□ なし　1□ あり

ありの場合

詳細

2. 手術翌日～初回退院の輸血

自己血　0□ なし　1□ あり → □□ 単位

全血　0□ なし　1□ あり → □□ 単位

濃赤　0□ なし　1□ あり → □□ 単位

3. 再手術

0□ なし　1□ あり → 再手術日 □□□□年 □□月 □□日

内容

4. 術後の初回退院日

□□□□年 □□月 □□日

0□ 軽快　2□ 転院による　1□ 死亡 →

詳細

コメント

DC記入　receive1(　) check1(　) check2(　) input1(　) input2(　) confirm(　)
query(　) receive2(　) check3(　) input3(　) confirm(　) fix(　)
(　) (　) (　) (　)　memo

JCOG 0110　胃がん外科/SPNX

コピーして保管して下さい

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病理所見記録 1

手術後病理所見が出たら速やかにデータセンターに郵送

施設名　○○○○○がんセンター　　担当医　○× ○×

患者イニシャル　姓 A 名 A　　性別　男　　生年月日　昭和30年10月10日

カルテ番号　12345-6789　　割り付け群　＊ 群　　登録番号

記入者名：CRC記入可（自署）

西暦　年　月　日

＜病理組織学的所見＞　胃癌取り扱い規約13版による

1. 最深部の組織学的深達度（T因子）　10□ pT1　20□ pT2　30□ pT3　40□ pT4　88□ その他（　）
   → 浸潤臓器（　）
2. U領域の組織学的深達度（T因子）　10□ pT1　20□ pT2　30□ pT3　40□ pT4　88□ その他（　）
   → 浸潤臓器（　）
3. 組織学的リンパ節転移（N因子）　00□ pN0　10□ pN1　20□ pN2　30□ pN3
4. 組織学的切除近位断端（口側）　0□ pPM(－)　1□ pPM(＋)　99□ pPMX
5. 組織学的切除遠位断端（肛門側）　0□ pDM(－)　1□ pDM(＋)　99□ pDMX
6. 原発巣の主な組織型（1つ選択）　10□ 乳頭腺癌(pap)　21□ 管状腺癌－高分化型(tub1)　22□ 管状腺癌－中分化型(tub2)　31□ 低分化腺癌－充実型(por1)　32□ 低分化腺癌－非充実型(por2)　40□ 印環細胞癌(sig)　50□ 粘液癌(muc)　88□ その他（　）
7. 総合的根治度　1□ fA　2□ fB　3□ fC
8. 総合Stage　11□ ⅠA　12□ ⅠB　20□ Ⅱ　31□ ⅢA　32□ ⅢB　40□ Ⅳ

各リンパ節の転移の有無

			転移個数		郭清個数	
1 右噴門	0□ 郭清せず	1□ 郭清 →	個	99□ 不明	個	99□ 不明
2 左噴門	0□ 郭清せず	1□ 郭清 →	個	99□ 不明	個	99□ 不明
3 小彎	0□ 郭清せず	1□ 郭清 →	個	99□ 不明	個	99□ 不明
4sa 大彎左群(短胃動脈)	0□ 郭清せず	1□ 郭清 →	個	99□ 不明	個	99□ 不明
4sb 大彎左群(左胃大網動脈に沿う)	0□ 郭清せず	1□ 郭清 →	個	99□ 不明	個	99□ 不明
4d 大彎右群(右胃大網動脈に沿う)	0□ 郭清せず	1□ 郭清 →	個	99□ 不明	個	99□ 不明
5 幽門上	0□ 郭清せず	1□ 郭清 →	個	99□ 不明	個	99□ 不明
6 幽門下	0□ 郭清せず	1□ 郭清 →	個	99□ 不明	個	99□ 不明
7 左胃動脈幹	0□ 郭清せず	1□ 郭清 →	個	99□ 不明	個	99□ 不明
8a 総肝動脈幹前上部	0□ 郭清せず	1□ 郭清 →	個	99□ 不明	個	99□ 不明

コメント

DC記入　receive1(　) check1(　) check2(　) input1(　) input2(　) confirm(　)
query(　) receive2(　) check3(　) input3(　) confirm(　) fix(　)
(　) (　) (　) (　)　memo

JCOG 0110　胃がん外科/SPNX

コピーして保管して下さい

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病理所見記録 2

手術後病理所見が出たら速やかにデータセンターに郵送

施設名　○○○○○がんセンター　担当医　○× ○×

患者イニシャル　姓 A 名 A　性別 男　生年月日 昭和30年10月10日

カルテ番号　12345-6789　割り付け群 ＊ 群　登録番号

記入者名：CRC記入可（自署）

西暦　年　月　日

		転移個数		郭清個数	
8p 総肝動脈幹後部	0□ 郭清せず 1□ 郭清 →	個	99□ 不明	個	99□ 不明
9 腹腔動脈周囲	0□ 郭清せず 1□ 郭清 →	個	99□ 不明	個	99□ 不明
10 脾門	0□ 郭清せず 1□ 郭清 →	個	99□ 不明	個	99□ 不明
11p 脾動脈幹近位	0□ 郭清せず 1□ 郭清 →	個	99□ 不明	個	99□ 不明
11d 脾動脈幹遠位	0□ 郭清せず 1□ 郭清 →	個	99□ 不明	個	99□ 不明
12a 肝十二指腸間膜内(肝動脈に沿う)	0□ 郭清せず 1□ 郭清 →	個	99□ 不明	個	99□ 不明
12b 肝十二指腸間膜内(胆管に沿う)	0□ 郭清せず 1□ 郭清 →	個	99□ 不明	個	99□ 不明
12p 肝十二指腸間膜内(門脈に沿う)	0□ 郭清せず 1□ 郭清 →	個	99□ 不明	個	99□ 不明
13 膵頭後部	0□ 郭清せず 1□ 郭清 →	個	99□ 不明	個	99□ 不明
14a 上腸間膜動脈に沿う	0□ 郭清せず 1□ 郭清 →	個	99□ 不明	個	99□ 不明
14v 上腸間膜静脈に沿う	0□ 郭清せず 1□ 郭清 →	個	99□ 不明	個	99□ 不明
15 中結腸動脈周囲	0□ 郭清せず 1□ 郭清 →	個	99□ 不明	個	99□ 不明
16a1 腹部大動脈周囲a1	0□ 郭清せず 1□ 郭清 →	個	99□ 不明	個	99□ 不明
16a2 腹部大動脈周囲a2	0□ 郭清せず 1□ 郭清 →	個	99□ 不明	個	99□ 不明
16b1 腹部大動脈周囲b1	0□ 郭清せず 1□ 郭清 →	個	99□ 不明	個	99□ 不明
16b2 腹部大動脈周囲b2	0□ 郭清せず 1□ 郭清 →	個	99□ 不明	個	99□ 不明
17 膵頭前部	0□ 郭清せず 1□ 郭清 →	個	99□ 不明	個	99□ 不明
18 下膵	0□ 郭清せず 1□ 郭清 →	個	99□ 不明	個	99□ 不明
19 横隔下	0□ 郭清せず 1□ 郭清 →	個	99□ 不明	個	99□ 不明
20 食道裂孔部	0□ 郭清せず 1□ 郭清 →	個	99□ 不明	個	99□ 不明
110 胸部下部傍食道	0□ 郭清せず 1□ 郭清 →	個	99□ 不明	個	99□ 不明
111 横隔上	0□ 郭清せず 1□ 郭清 →	個	99□ 不明	個	99□ 不明
112 後縦隔	0□ 郭清せず 1□ 郭清 →	個	99□ 不明	個	99□ 不明

リンパ節郭清総個数　　個

リンパ節転移個数　　個

コメント

DC記入					
receive1( )	check1( )	check2( )	input1( )	input2( )	confirm( )
query( )	receive2( )	check3( )	input3( )	confirm( )	fix( )
( )	( )	( )	( )	memo	

JCOG 0110　胃がん外科/SPNX　調査

追跡調査用紙

までにデータセンターに郵送

施設名　　担当医

患者イニシャル　姓　名　性別　　生年月日

カルテ番号　　登録番号

記入者名：CRC記入可（自署）

西暦　年　月　日

遅発性合併症
（有害反応）

・「肺炎」「感染」はプロトコール治療との因果関係が否定できないもの（ definit, probable, possible ）で、イベントの回数を記入
（イベントなしは「0」と記入）
・「リンパ球数」と「アルブミン」の検査日は同一日であること

＊38℃以上の発熱を伴うその他の感染

術後 / 項目	3ヶ月	6ヶ月	9ヶ月	1年	1.5年	2年	2.5年	3年	3.5年	4年	4.5年	5年
肺炎	回	回	回	回	回	回	回	回	回	回	回	回
感染＊	回	回	回	回	回	回	回	回	回	回	回	回
体重	kg	kg	kg	kg	kg	kg	kg	kg	kg	kg	kg	kg
リンパ球数	/mm^3 月 日	/mm^3 月 日	/mm^3 月 日	/mm^3 月 日	/mm^3 月 日	/mm^3 月 日	/mm^3 月 日	/mm^3 月 日	/mm^3 月 日	/mm^3 月 日	/mm^3 月 日	/mm^3 月 日
アルブミン	g/dl 月 日	g/dl 月 日	g/dl 月 日	g/dl 月 日	g/dl 月 日	g/dl 月 日	g/dl 月 日	g/dl 月 日	g/dl 月 日	g/dl 月 日	g/dl 月 日	g/dl 月 日

再発の有無　0□ 再発なし　1□ 再発あり　0□ 不明

無再発または不明の場合　最終無再発生存確認日　西暦　年　月　日

再発の場合　初再発判定日　西暦　年　月　日

前回調査の報告

初再発部位　□リンパ節（部位　）　□肝　□ 腹膜転移
□ 遠隔転移（　）　□その他（　）

再発状況

後治療　0□ なし　1□ 後治療あり
- □ S-1
- □ その他（　）

投与開始日　西暦　年　月　日 ～ 投与終了日　西暦　年　月　日　total　コース

転帰　0□ 生存　最終生存確認日　西暦　年　月　日

前回調査の報告

1□ 死亡　死亡日　西暦　年　月　日

死因　1□ 原病死　2□ 他病死　3□ 治療関連死　8□ その他　9□ 不明

死亡の状況

いずれの死因の場合も
死亡時の状況を記入

コメント

DC記入

receive1(　) check1(　) check2(　) input1(　) input2(　) confirm(　)
query(　) receive2(　) check3(　) input3(　) confirm(　) fix(　)
(　) (　) (　) (　) memo

説明同意文書

研究名：JCOG 0110-MF ver2.1「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（かくせい）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、再発を予防する目的で抗がん剤が使われることがあります。これまでの多くの臨床試験では、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）により再発の危険性を減らすことができるという結論は得られていませんでしたので、本臨床試験でも補助化学療法を行わずに経過を観察することにしていました。しかし 2007 年 1 月に、1000 人以上の進行胃がんの患者さんが参加された大規模な臨床試験において、S-1 という抗がん剤を手術後に服用すると生存期間が延長するという結果が報告されたため、それ以降は進行胃がんの手術後に S-1 を 1 年間服用することが標準治療であると考えられるようになりました。したがって、本臨床試験でも 2007 年 6 月に研究計画を一部改訂し、以降に参加していただく患者さんについては手術後のステージが 2 から 3B までの間に入っていた場合は、原則として S-1 を 1 年間服用していただくことになりました。もちろん不幸にも再発が判明した場合にも、抗がん剤による化学療法を中心に最善の対処をいたします。

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。

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

＿＿＿＿＿＿＿＿＿＿＿＿＿＿病院長　殿

カルテ番号　＿＿＿＿＿＿＿＿

患者氏名　＿＿＿＿＿＿＿＿

臨床研究名：JCOG 0110-MF ver 2.1「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」

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：＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿

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　：＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿＿

説明年月日　：　平成　　年　　月　　日

署名年月日　：　平成　　年　　月　　日

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ORIGINAL ARTICLE – GASTROINTESTINAL ONCOLOGY

The Prognostic Impact of Isolated Tumor Cells in Lymph Nodes of T2N0 Gastric Cancer: Comparison of American and Japanese Gastric Cancer Patients

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ABSTRACT

Background. The clinical significance of immunohistochemically detected isolated tumor cells (ITC) in lymph nodes of gastric cancer patients is controversial. This study examined the prognostic impact of ITC on patients with early-stage gastric cancer in two large volume centers in the United States and Japan.

Methods. Fifty-seven patients with T2N0M0 gastric carcinoma who underwent gastric resection between January 1987 and January 1997 at Memorial Sloan-Kettering Cancer Center (MSKCC) in New York and 107 patients resected at National Cancer Center Hospital (NCCH) in Tokyo between January 1984 and December 1990 were studied. The sections were newly prepared from each lymph node for immunohistochemical staining for cytokeratin. Lymph nodes and original specimens from MSKCC were examined by pathologists in NCCH. The prognostic significance of the presence of ITC in lymph nodes was investigated in patients of both institutions.

Results. ITC were identified in 30 of 57 patients (52.6%) at MSKCC and in 38 of 107 patients (35.5%) at NCCH. In both institutions, there was no significant difference in the prognosis of the studied patients with or without ITC ($P = .22, .86$ respectively).

Conclusions. The presence of ITC detected by immunohistochemistry in the regional lymph nodes did not affect the prognosis of American and Japanese patients with T2N0M0 gastric carcinoma who underwent gastrectomy with D2 lymph node dissection.

The complete removal of tumor is the only potentially curative treatment for patients with gastric cancer. Locally advanced gastric cancer frequently recurs after curative operation and even early gastric cancer relapse.[1] In patients with recurrent disease, there must have been residual tumor cells in the form of occult micrometastases that were left behind at the time of apparently curative surgery.

Recent advances in immunohistochemistry (IHC) and molecular biology allow the identification of discrete and occult tumor cells in the lymph nodes of the patients with malignant disease, which remain undetected by standard hematoxylin and eosin (H&E) staining.[2] After some debate regarding the terminology of occult tumor cells, micrometastases (MM) are defined as deposits of tumor cells of 2 mm or less, but those larger than 0.2 mm and isolated tumor cells (ITC) are defined as single or clusters of tumor cells of 0.2 mm or less.[3,4]

The aim of this study is to analyze whether the presence of ITC in lymph nodes originally considered tumor-negative from curatively resected gastric cancer patients led to worse prognosis in two large-volume centers in the United States and Japan. This comparison would also address the hypothesis that gastric cancer in the West and Japan are different.[5]

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MATERIALS AND METHODS

Patients Source

MSKCC Between January 1987 and December 1997, 1,028 patients underwent gastric resection for gastric carcinoma at Memorial Sloan Kettering Cancer Center (MSKCC) in New York. During this period, 102 consecutive patients were classified with pT2N0M0 disease in the database maintained in the Gastric and Mixed Tumour Department. Two newly prepared sections from each lymph node for H&E staining and IHC and original specimens of resected primary gastric carcinoma were transported to National Cancer Center Hospital (NCCH), Tokyo. Of the 102 cases, 74 were available for pathological evaluation of both lymph nodes and primary tumors by Japanese investigators. In some cases, T stage (depth of tumor invasion) was revised at this review: 11 to T1, 61 to T2, and 2 to T3. In 4 of 61 T2 cases, definite nodal involvement was found by H&E staining at this review. The remaining 57 patients were included in this study.

NCCH Between January 1984 and December 1990, 1,757 patients underwent gastrectomy for gastric carcinoma at the NCCH. During this period, 118 patients were classified with pT2N0M0 disease on the database maintained in the Gastric Surgery Division. Five patients whose paraffin blocks were lost, two patients whose T stage was wrongly recorded, and another two patients who were completely lost to follow-up were excluded from the analysis. In two of 109 patients whose paraffin blocks were available for newly cut, definite nodal involvement was found at this review by H&E. The remaining 107 patients, already analyzed in a previous report,[6] were also evaluated in comparison and combination with the cases of MSKCC.

All patients of both institutions underwent partial or total gastrectomy with systematic lymphadenectomy including the complete dissection of perigastric lymph nodes and partial or complete removal of the second-tier lymph nodes along common hepatic, proper hepatic, celiac, and splenic arteries.

Pathology and Immunohistochemistry

All specimens were formalin fixed and paraffin embedded. Lymph nodes were examined by one cross section through the center of each lymph node. Tumors were classified histologically into differentiated and undifferentiated types according to the World Health Organization tumor classification system.[7] The differentiated type includes well or moderately differentiated tubular adenocarcinoma and papillary adenocarcinoma, whereas the undifferentiated type includes poorly differentiated adenocarcinoma, signet ring cell carcinoma, and mucinous adenocarcinoma. Two consecutive sections measuring 4 μm thick were newly cut for H&E staining and IHC.

IHC was performed using AE1/AE3 (Boehringer Mannheim, Indianapolis, IN), a monoclonal antibody that is reactive with a broad spectrum of human cytokeratins. The details of procedures were previously reported.[6] ITC were defined as single or cluster of tumor cells of 0.2 mm or less detected by cytokeratin-specific IHC that could not be detected by ordinary H&E staining.

Statistical Analysis

Statistical analysis was carried out using SPSS software, version 11.5 (SPSS Inc, Chicago, IL). The clinicopathological features of studied cases (United States vs Japan or ITC + vs −) were compared by a chi-square test or a *t*-test. The Kaplan–Meier method was used for making survival curves, and the log-rank test for evaluating the statistical difference between survival curves.

RESULTS

MSKCC

The mean age of studied patients was 67.8 ± SD 12.0 (range, 35–93).

In total, 1,144 lymph nodes of 57 patients were studied (median, 19; range, 1–61).

The patients had 22 and 35 differentiated and undifferentiated type of gastric carcinoma, respectively.

ITC were identified in 30 patients (52.6%) and in 97 lymph nodes (8.48%). The median number of involved lymph nodes with ITC was 3 (range, 1–13) per patient. Seventeen patients had ITC of single-cell type, and 13 had cluster type. The presence of ITC was not correlated with the subtype of gastric carcinoma (10 of 22 patients with differentiated carcinoma vs. 20 of 35 patients with undifferentiated carcinoma. $P = .39$).

The median follow-up for surviving patients was 113 months (range, 8–205). Disease recurrence was observed in 9 of 57 patients; 3 patients had ITC, and 6 patients did not. Twenty patients died of other causes. There were 3 of 30 patients with ITC and 6 of 27 patients without ITC who developed tumor recurrence. The incidence of recurrent disease did not correlate with the presence of ITC ($P = .21$).

The 5-year and 10-year survival rates of patients with or without ITC were 82%, 69% and 64%, 42%, respectively. There was no significant difference between survivals of patients with or without ITC ($P = .22$) (Fig. 1). The type of ITC did not affect survival of patients.

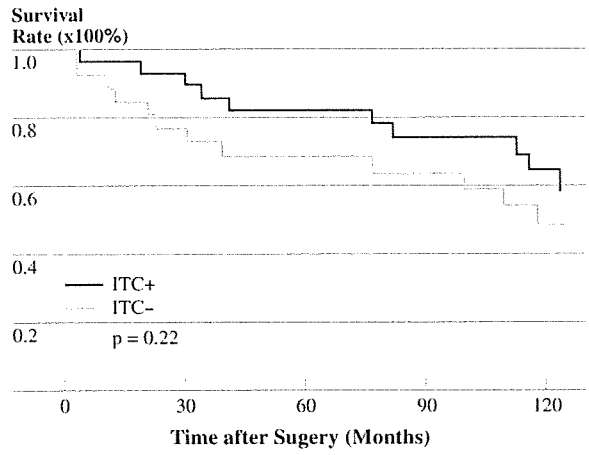

FIG. 1 No significant difference between survivals of patients with or without ITC ($P = .22$) in MSKCC

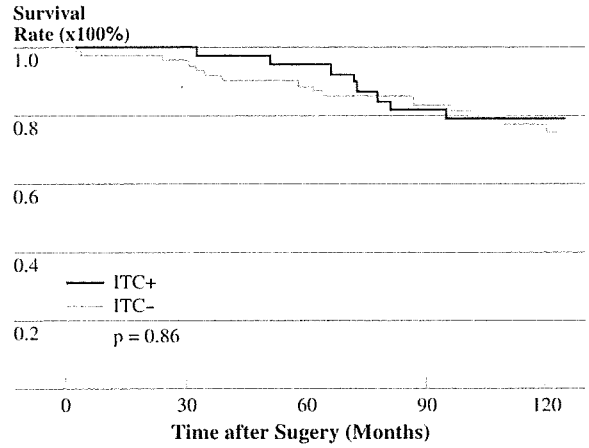

FIG. 2 No significant difference between survivals of patients with or without ITC ($P = .87$) in NCCH

NCCH

The mean age of studied patients was 58.3 ± SD 11.3 (range, 34–88). In total, 4,484 lymph nodes of 107 patients were studied (median, 33; range, 6–173); 55 had differentiated, and 52 had undifferentiated type.

ITC were identified in 38 patients (35.5%) and in 87 lymph nodes (1.94%). The median number of involved lymph nodes with ITC was 1.5 (range, 1–10) per patient. There were 17 patients with ITC of single-cell type and 21 with cluster type. The presence of ITC was not correlated with the subtype of gastric carcinoma (16 of 55 patients with differentiated carcinoma vs. 22 of 52 patients with undifferentiated carcinoma. $P = .15$).

The median follow-up was 120 months (range, 71–185). Disease recurrence was observed in 6 of 107 patients. Two patients had ITC, and four patients did not. Twelve patients died of other causes. There were 2 of 38 patients with ITC and 6 of 69 patients without ITC who developed tumor recurrence. The incidence of recurrent disease did not correlate with the presence of ITC ($P = .91$).

The 5-year and 10-year survival rates of patients with or without ITC were 94%, 89% and 79%, 74%, respectively. There was no significant difference between survivals of patients with or without ITC ($P = .87$) (Fig. 2). The type of ITC did not affect the survival of patients.

DISCUSSION

The current results suggest that the presence of ITC detected by IHC in the lymph nodes of patients with T2N0 gastric carcinoma did not affect their prognosis and that such ITC does not imply systemic disease that is beyond cure with local treatment.

The clinical significance of occult tumor cells in the lymph nodes of gastric cancer patients has been controversial. A negative impact on prognosis was reported by some authors,[8–11] but not by others.[6,12–15] In general, the studies including a majority of early gastric cancer patients have a problem of less disease specific death for prognostic evaluation. If many cases of locally advanced gastric cancer that invades to the serosal surface of the stomach are included, the prognostic significance of occult tumor cells in lymph nodes is easily confounded by frequent peritoneal dissemination.[16] For this reason, patients with early-stage disease staged as T2N0 by postoperative examination were analyzed. Analysis of a large group of uniform tumors allows more definitive conclusions to be drawn regarding the prognostic impact.

Occult tumor cells have recently been classified into ITC, which are single cells or a small cluster that is no larger than 0.2 mm, and MM, which are tumor cells of 2 mm or less but larger than 0.2 mm according to UICC. ITC do not show morphological evidence of metastatic activity such as penetration of a vascular or lymph sinus wall, tumor cell growth, and stromal reaction.[17,18] In some reports, ITC do not become metastatic and will be presumably erased by host immune response.[19] In others, tumorigenicity of a single tumor cell is reported.[20] Does ITC have malignant metastatic potential?[21]

'We cannot answer whether a lymph node including ITC should be dissected, because all of the studied patients underwent standard lymph node dissection.[22] Our adequate lymph node dissection could have caused the outcomes to be the same for patients with or without ITC, but on the other hand ITC in the lymph nodes could be ignored without dissection. If ITC in the lymph nodes has malignant metastatic potential, our data suggest they did not travel beyond the surgical field. In our previous report,

most of ITC were found in perigastric nodes.[6] This may be caused by the good prognosis of T2N0. In more advanced-stage gastric cancer, it is possible ITC can reach further stations or distant organs and lead to poor prognosis. The previous reports[11,23] including advanced-stage gastric cancer patients show the negative prognostic impact of occult tumor cells, but the importance of ITC in clinical outcome is an area of debate.[24–26]

Doekhie et al. reported a similar result to this study, that the presence of occult tumor cells in the lymph nodes in gastric cancer patients did not predict disease recurrence.[14] Patients with fewer than five lymph nodes examined or with many lymph nodes involved by occult tumor cells did not have a worse prognosis if those patients had undergone a D2 dissection in the Dutch trial.[27] Presumably, ITC include both malignant cells that have metastatic potential, and those that do not.

Whether the additional information of ITC can be adopted for clinical practice is an important issue. The strategies of adjuvant therapy for gastric cancer patients have been recently standardized. In the United States, node-positive patients are the indication of adjuvant chemoradiotherapy based on the result of INT0116.[28] In Japan, pt2n0 patients are not the indication of adjuvant chemotherapy, but pt2n1 or pt3 patients are the indication of adjuvant chemotherapy based on a randomized control clinical study.[29] The studied group of pt2n0 patients may be applicants for adjuvant therapy in the United States where complete D2 dissection is not popular except for large-volume centers such as MSKCC. The biological malignant potential of ITC cannot be evaluated from this study, so the clinical application of ITC must be argued carefully.

Our study has the additional value of comparing gastric cancer patients in the United States and Japan from the view of prevalence of ITC. Geographic difference of gastric carcinoma in the West and Japan has been argued.[30–34] The similarity of expression of some oncogenes and the discrepancy of microsatellite instability were previously reported.[35,36] In this study, American patients were significantly more likely to have ITC (30 of 57, 52.6% vs. 38 of 107, 35.5%; $P = .03$), and the incidence of undifferentiated gastric carcinoma was more frequent in American patients, but not significant (35 of 57, 61.4% vs. 52 of 107, 48.6%; $P = .12$). American patients were older than Japanese patients ($P < .0001$). These findings may be accounted for by the biological difference of gastric cancer in the two regions, but they are not connected to the relative worse prognosis of American patients. It may well be that the greater number of lymph nodes resected and examined in Japan makes the diagnosis of T2N0 more accurate in Japan prior to examining for ITC.

In conclusion, the presence of ITC in the lymph nodes of patients with T2N0 gastric carcinoma did not have any prognostic impact, and ITC did not imply the systemic disease in the United States as in Japan.

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ORIGINAL ARTICLE – HEPATOBILIARY AND PANCREATIC TUMORS

Therapeutic Value of Lymph Node Dissection in Advanced Gastric Cancer with Macroscopic Duodenum Invasion: Is the Posterior Pancreatic Head Lymph Node Dissection Beneficial?

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ABSTRACT

Background. In advanced gastric cancer (AGC) with duodenum invasion, the posterior pancreatic lymph nodes are susceptible to metastasis because of their proximity to the duodenum. The therapeutic value of lymph node dissection in this area for AGC with macroscopic duodenum invasion remains unclear.

Methods. Patients who had undergone curative gastrectomy for lower-third AGC from 1970 to 2004 at the Cancer Institute Hospital were recruited for this study. Clinicopathological data were collected retrospectively, and compared between cases of AGC with duodenum invasion (AGC-DI group) and AGC without duodenum invasion (AGC-nDI group). In the AGC-DI group, the therapeutic value of lymph node dissection was evaluated using a therapeutic index (multiplication of the frequency of metastasis to the station by the 5-year survival rate of patients with metastasis to that station).

Results. The AGC-DI group generally had tumors of higher pathological stage, which might account for the poorer 5-year survival rate compared with that of the AGC-nDI group (50.1% versus 68.5%; $P = 0.0002$). The incidence of lymph node metastasis was higher in the AGC-DI group than that in the AGC-nDI group, including nodes in the posterior pancreatic head (23.9% versus 7.0%, $P < 0.0001$). In the AGC-DI group, posterior pancreatic head lymph node dissection was of therapeutic value (4.19) equivalent to dissection of second-tier lymph nodes.

Conclusions. The dissection of posterior pancreatic head lymph nodes might be effective in AGC with macroscopic duodenum invasion since this has therapeutic value equivalent to that of second-tier lymph node dissection and might improve patients' long-term outcomes.

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Advanced gastric cancer (AGC) carries a high postoperative morbidity and mortality rate. Although a number of large randomized trials in Europe have failed to prove the efficacy of D2 lymph node dissection for AGC, gastrectomy with this lymph node dissection is performed widely and safely in Japan.[1–7] Therefore, the Gastric cancer treatment guideline established by Japanese Gastric Cancer Association (JGCA) recommends dissection of all second-tier lymph nodes with gastrectomy as standard therapy for AGC in Japan.[8,9]

The JGCA guidelines generally classify perigastric lymph nodes as first-tier lymph nodes, while extraperigastric lymph nodes are classified as second- or third-tier nodes, depending on the tumor location. In lower-third gastric cancer, stations 7, 8a, 9, 11p, 12a, and 14v (located along the left gastric artery, common hepatic artery, celiac axis, proximal half of the splenic artery, proper hepatic artery, and superior mesenteric vein at the lower border of pancreas, respectively) are classified as second-tier lymph nodes and therefore should be dissected during surgery for AGC.[8,9]

Advanced gastric cancers in the lower third of the stomach occasionally invade into the duodenum and are associated with poor prognosis.[10,11] This may be due to different clinicopathological features, including additional sites susceptible to lymph node metastasis such as the posterior pancreatic head (station 13 lymph node). This aspect of AGC remains unclear, as does the therapeutic

value of lymph node dissection at each station in cases with duodenum invasion. Currently the JGCA designates station 13 lymph nodes as third tier and thus does not recommend dissection of these nodes during standard D2 lymph node dissection despite of this station's proximity to the duodenum and possible susceptibility for metastases with duodenal invasion.[8,9]

The present study sought to clarify the distinct clinicopathological characteristics of lower-third AGC with macroscopic duodenum invasion. Site susceptibility for lymph node metastasis and the therapeutic value of dissection at each lymph node station, especially those in the posterior pancreatic head, were also investigated.

PATIENTS AND METHODS

Patients with lower-third AGC with and without duodenum invasion who were treated by gastrectomy at the Cancer Institute Hospital from 1970 to 2004 were recruited in this study. Only patients who underwent curative resection were included. Cases with invasion involving the middle or upper third of the stomach and those with multiple gastric cancer were also excluded from the present study.

Clinicopathological features collected retrospectively from the institute database were as follows: gender, age, surgical procedure, histological type, macroscopic type, size, tumor depth, degree and number of lymph nodes metastases, and pathological stage.

Definition of Duodenum Invasion

Resected specimens were cut at the greater curvature side for inspection by the surgeon immediately after surgery. Tumor invasion directly into the duodenal wall was assigned as AGC with duodenum invasion. The border between gastric wall and duodenum wall was taken as the top of the pyloric ring, according to the Japanese Classification of Gastric Carcinoma (JCGC) 12th edition.

Lymph Node Station Number

Lymph node station number was classified according to the JCGC.[9] In cases of lower-third gastric cancer, stations 3, 4d, 5, and 6 lymph nodes were first-tier lymph nodes, with all located in the perigastric area. Station 1 (right paracardial) was classified as a second-tier lymph node, despite also being in the perigastric area. Stations 7, 8a, 9, 11p, and 12a lymph nodes were second-tier lymph nodes located along the left gastric artery, the common hepatic artery, the celiac axis, the proximal half of the splenic artery, and the proper hepatic artery, respectively. Station 14v lymph nodes were also classified as second-tier nodes and were located along the superior mesenteric vein at the lower border of the pancreas (Fig. 1).

Comparison of Clinicopathological Features and Incidence of Lymph Node Metastasis

Clinicopathological features were compared between AGC with duodenum invasion (AGC-DI group) and AGC without duodenum invasion (AGC-nDI group) to clarify the characteristics of AGC with duodenum invasion.

The incidence of lymph node metastasis for each station was also investigated and compared between the two groups. This parameter was calculated by dividing the number of patients with metastasis at the given station by the number of patients in whom that station was dissected.

Therapeutic Value of Lymph Node Dissection in AGC with Duodenum Invasion

The therapeutic value of lymph node dissection in the AGC-DI group was evaluated by multiplying the frequency

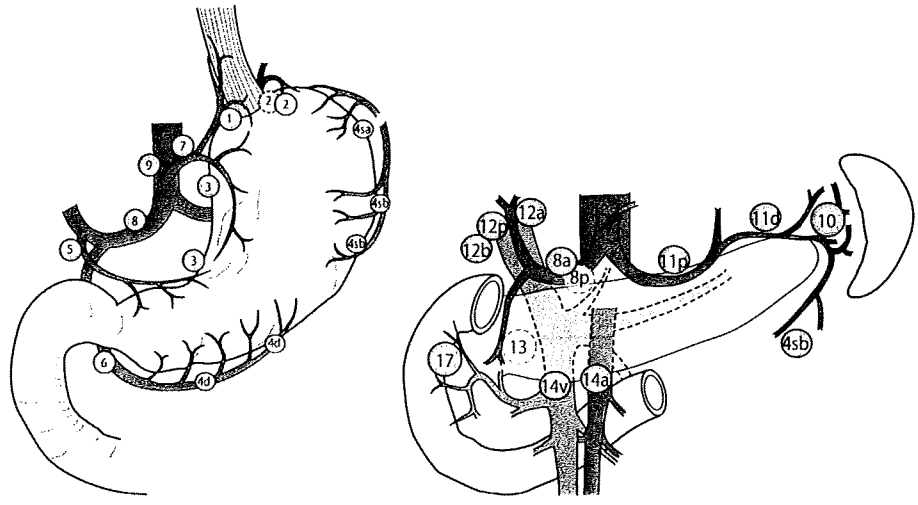

FIG. 1 Number of lymph node station according to the JGCA classification (lower-third gastric cancer). First-tier lymph node stations 3,.4d, 5, 6; second-tier lymph node stations 1, 7, 8a, 9, 11p, 12a, and 14v; third-tier lymph node stations 4sb, 8p, 12p/b, and 13. Paraaortic lymph node (station 16) was also classified as third-tier lymph node (not illustrated)

of metastasis to the station by the 5-year survival rate of patients with metastasis to that station, as proposed by Sasako et al.[12] The cumulative 5-year survival rate for patients with lymph node metastasis was calculated for each nodal station, irrespective of metastasis to other lymph node stations. All postoperative deaths were included in the survival analysis, including from the surgery and due to causes other than cancer.

Statistical Analysis

All continuous data are presented as mean ± standard error. Statistical analysis was conducted using the chi-square and Student's *t*-test. Five-year survival rates were calculated using the life-table method and statistically analyzed using the log-rank test. All statistical analysis was performed using the SAS program system version 9.1.3. Statistical significance was defined as $P < 0.05$.

RESULTS

From 1970 to 2004, 9,133 patients underwent gastrectomy for gastric cancer at the Cancer Institute Hospital. Of these, 1,369 patients had gastric cancer restricted to the lower third of the stomach and duodenum. Patients not able to undergo curative resection (100 patients), those with early gastric cancer (834 patients), and those with synchronous multiple gastric cancer (40 patients) were excluded from the study. The remaining 395 patients were recruited for analysis: 131 patients had AGC with duodenum invasion (AGC-DI group; $n = 131$) and the remainder had AGC without duodenum invasion (AGC-nDI group; $n = 264$) (Fig. 2).

Table 1 illustrates patient background and operative procedure for both groups. There was no difference in gender or age between groups. Pancreaticoduodenectomy was performed as a curative surgery in 5% of patients from the AGC-DI group (six cases) and in 2% of the AGC-nDI group (five cases).

Table 2 describes the patients' pathological profile. There was no difference in histological type between the groups. Tumors were generally larger and deeper in the AGC-DI group, which also showed a higher N-stage according to both the JCGC and International Union against Cancer (UICC) classifications. Thus, the AGC-DI group comprised patients with more advanced-stage cancer compared with the AGC-nDI group.

The 5-year survival rates were 50.1% for the AGC-DI group and 68.5% for the AGC-nDI group (Fig. 3; $P = 0.0002$).

The frequency of lymph node metastasis for each station is described in Fig. 4. In general, each lymph node station showed a significantly higher incidence of metastasis in the AGC-DI group compared with the AGC-nDI group. There was statistically significant difference in station 5 (19.2% versus 11.5%, $P = 0.0482$), station 6 (72.7% versus 57.4%, $P = 0.0035$), station 7 (20.2% versus 1.8%, $P = 0.0278$), station 8a (40.6% versus 27.5%, $P = 0.0090$), station 13 (23.9% versus 7.0%, $P < 0.0001$), and station14v (22.7% versus 4.0%, $P < 0.0001$).

Table 3 details the therapeutic value of lymph node dissection in the AGC-DI group, based on the calculated therapeutic index. This concept of the therapeutic value of lymph node dissection proposed by Sasako et al. was cited in

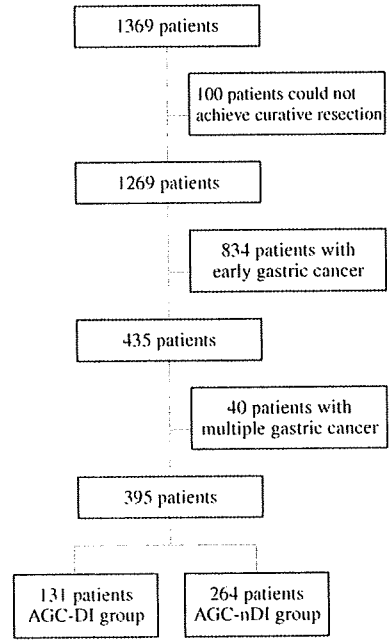

FIG. 2 Patient allocation in the present study. Patients with noncurative resection ($n = 100$), early gastric cancer ($n = 834$) or multiple gastric cancer ($n = 40$) were excluded

TABLE 1 Patient characteristics and operative procedure

	AGC-DI group	AGC-nDI group	*P*-value
Number (*n*)	131	264	
Gender			
Male/female	95/36	203/61	0.3416
Age (years)			
Mean	60.2 ± 1.0	60.8 ± 0.7	
Range	31–85	29–85	0.6575
Performed operation			
Distal gastrectomy	110 (84)	254 (96)	
Total gastrectomy	15 (11)	5 (2)	
Pancreaticoduodenectomy	6 (5)	5 (2)	<0.0001
Mean observation period (months)	74.1 ± 6.6	80.7 ± 4.7	0.4120

TABLE 2 Pathological characteristics of patients

	AGC-DI group (n = 131)	AGC-nDI group (n = 264)	P-value
Histologic type, n (%)			
Differentiated	95 (73)	203 (77)	
Undifferentiated	36 (27)	61 (23)	0.3416
Macroscopic type, n (%)			
0	5 (4)	27 (10)	
1	1 (1)	7 (3)	
2	42 (32)	72 (27)	
3	74 (56)	132 (50)	
4	4 (3)	8 (3)	
5	5 (4)	18 (7)	0.1199
Tumor size (mm), n (%)			
–39	23 (18)	100 (38)	
40–79	93 (71)	143 (54)	
80–	15 (11)	21 (8)	0.0002
Tumor depth, n (%)			
MP	33 (25)	106 (40)	
SS	30 (23)	81 (31)	
SE	59 (45)	76 (29)	
SI	9 (7)	1 (0)	<0.0001
Number of metastasized lymph nodes, n (%)			
0	27 (21)	74 (28)	
1–6	64 (49)	131 (50)	
7–15	25 (19)	48 (18)	
16+	15 (11)	11 (4)	0.0290
Degree of lymph nodes metastasis, n (%)			
N0	27 (21)	74 (28)	
N1	32 (24)	85 (32)	
N2	35 (27)	79 (30)	
N3	37 (28)	26 (10)	<0.0001
Pathological stage (UICC), n (%)			
IB	16 (12)	68 (26)	
II	47 (36)	100 (38)	
IIIA	27 (21)	52 (20)	
IIIB	14 (11)	25 (9)	
IV	27 (21)	19 (7)	0.0003
Pathological stage (JGCA), n (%)			
IB	16 (12)	68 (26)	
II	26 (20)	67 (25)	
IIIA	29 (22)	65 (25)	
IIIB	16 (12)	29 (11)	
IV	44 (34)	35 (13)	<0.0001

the latest edition of JCGC and has been widely accepted among specialists inside and outside Japan.[9,12–14] Lymph node on the posterior surface of the pancreatic head was dissected in 110 of 131 patients (84.0%), and 25 of these were found to have metastasis (23.9%). Five-year survival rate of these 25 patients was 17.5%. From these data, the

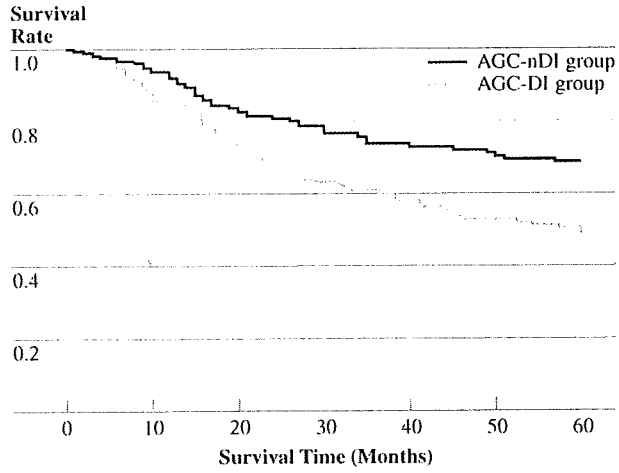

FIG. 3 Five-year survival rates of patients in both groups: AGC-DI group and AGC-nDI group

therapeutic index of station 13 lymph node was 4.19, being of greater therapeutic value than dissection of station 7 (1.01), 9 (3.70), 11p (3.65) or 12a (0) lymph nodes, but of lower value than dissection of station 8a (12.59) or 14v (5.39).

In the AGC-DI group, 5-year survival rate was better in patients who underwent lymph node dissection of the posterior pancreatic head (52.7%) than in those who did not (47.5%), although the difference was not statistically significant (P = 0.605).

DISCUSSION

In Japan, gastrectomy with D2 lymph node dissection is often performed as a safe and standard surgery for advanced gastric cancer, despite reports of high postoperative morbidity and mortality rates in large European trials.[1–7] According to JGCA guidelines, all first- and second-tier lymph nodes should be dissected during a D2 lymph node dissection.[8,9] For lower-third gastric cancer, second-tier lymph nodes include stations 1, 7, 8a, 9, 11p, 12a, and 14v lymph nodes irrespective of duodenum invasion, and these lymph nodes should be dissected.

The reported incidence of duodenum invasion is 11–25% in surgically resected specimen and 68.5% in autopsy cases.[10,11,15–17] Kekeji et al. reported that AGC with duodenum invasion is often infiltrative and advanced, with invasion into the serosa, and lymph node metastasis was frequently observed compared with AGC without duodenum invasion.[10,11] They also reported poorer 5-year survival rates in AGC with duodenum invasion. Perng et al. also reported that higher stage and larger tumors were frequently observed in AGC with duodenum invasion compared with AGC without duodenum invasion, while macroscopic type 3 and 4 gastric cancer frequently infiltrated the duodenum directly.[18]

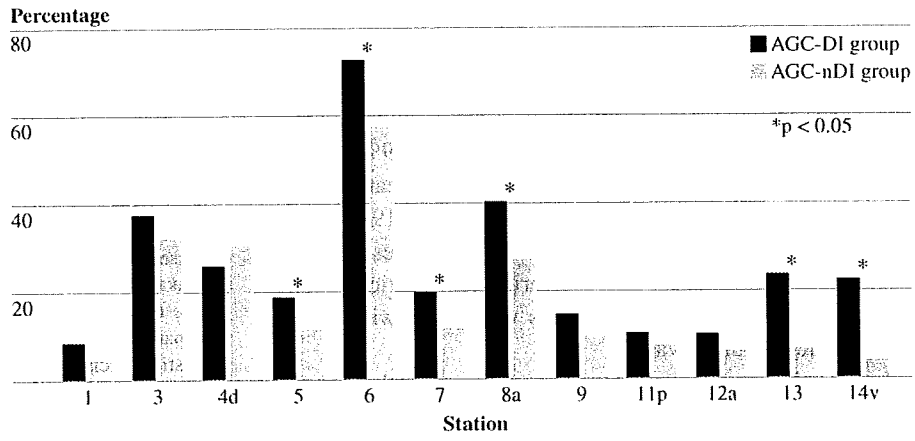

FIG. 4 Frequency of lymph nodes metastasis for each station: AGC-DI group and AGC-nDI group; * $P < 0.05$

TABLE 3 Therapeutic index (multiplication of frequency of lymph nodes metastasis by 5-year survival rate) of each lymph node station

Lymph node station	AGC-DI group		
	Frequency of LN meta (%)	5-Year survival rate (%)	Therapeutic index
1**	8.7	9.1	0.79
3*	37.7	34.2	12.89
4d*	26.4	32.5	8.58
5*	19.2	30.9	5.93
6*	72.7	42.5	30.90
7**	20.2	5.0	1.01
8a**	40.6	31.0	12.59
9**	14.8	24.9	3.70
11p**	10.7	34.2	3.65
12a**	10.5	0	0
13***	23.9	17.5	4.19
14v**	22.7	23.7	5.39

* First-tier lymph node

** Second-tier lymph node

*** Third-tier lymph node

Although the efficacy of systemic lymph node dissection was occasionally evaluated in previous studies, the therapeutic efficacy of lymph node dissection of each station was rarely investigated.[19,20] Sasako et al. proposed a simple index to determine the actual benefit of node dissection, which could circumvent the stage migration phenomenon by calculating the therapeutic efficacy of each station irrespective of other nodal status.[12] Theoretically, the ideal lymph node dissection includes stations with a higher predicted incidence of metastasis. Moreover, lymph node dissection of positive nodes should improve the patient's long-term survival. Therefore, a therapeutic index in their study was calculated by multiplying the frequency of metastasis to the station by the 5-year survival rate of patients with metastasis to that station.

The latest edition of JCGC, which adopts anatomical-based N-staging, was released subsequent to Sasako's report.[12] The JCGC cites the therapeutic index as an effective mean of categorizing each nodal station (N0, N1, N2, N3).[13,14] This latest edition of JCGC and the concept of the therapeutic index are now widely accepted among specialists inside and outside of Japan. We thus adopted this therapeutic index for use in the current study to evaluate the therapeutic efficacy of lymph node dissection of each station.

In the present study, 5-year survival rates were significantly lower in the AGC-DI group than that in the AGC-nDI group. As previously reported, the higher incidence of advanced-stage tumors in the AGC-DI group might account for these lower rates.[11,12,16] The results therefore suggested that an appropriate treatment strategy for AGC with duodenum invasion should be initiated, including effective lymph node dissection, to improve this poor 5-year survival rate. Understanding the relative susceptibility of a nodal area for metastasis might also improve long-term outcomes for these patients.

Different incidences of lymph node metastasis were observed in this study for stations 5, 6, 7, 8a, 13, and 14v between the AGC-DI and AGC-nDI groups. Although this might be due to the higher stage observed in the AGC-DI group, the differences in tumor location between groups might be associated with the difference. Except station 7, all stations in which the incidence of lymph node metastasis was different between the groups were close to the duodenum wall. On the other hand, the incidence of lymph node metastasis did not differ significantly among other lymph nodes (stations 1, 3, 4d, 9, and 11p), which were distant from the duodenum. Therefore, duodenum invasion itself might be associated with the higher incidence of some lymph node metastasis in the AGC-DI group.

Sasako et al. reported a 5-year survival rate of 0% for cases of lower-third AGC with posterior pancreatic head lymph node metastasis. They therefore discounted any