Table 2 Patient characteristics

	D1	D2	Total
No. of patients	76	86	162
Median age (range)	64 (34-81)	61.46 (25-80)	62.01 (29-81)
≥70	22	18	40
Sex (m/f)	39/37	48/38	87/75
Location			
Upper	9	11	20
Medium	18	22	40
Distal	49	52	101
Diffuse	-	1	1
Tumour stage			
pT1	27	27	54
pT2	23	28	51
pT3	26	31	57
Type of resection			
Total gastrectomy	19	22	41
Distal gastrectomy	57	64	121
Splenectomy (S)	3	9	12
Distal pancr. + S	1	3	4

tumour. The mean number of nodes removed was 27.0 during a D1 gastrectomy and 36.6 during a D2.

Post-operative course

Table 3 gives data on post-operative course. Overall, the post-operative hospital morbidity was 13.6%. The rate was higher in the D2 group (16.3%) than in D1 group (10.5%), but this difference was not statistically significant. In both groups there were more complications after total than after distal gastrectomy, but again this difference was not significant.

As regards major abdominal infections, no anastomotic dehiscence occurred and only one case of duodenal stump leakage was registered, while two pancreatic leakages and two cases of acute pancreatitis were observed.

Reoperation was necessary after five major surgical complications (Table 3). The overall hospitality mortality was 1/163. This death occurred after a D1 gastrectomy (1/76) and was due to an intraoperative stroke; obviously no significant difference could be observed between D1 and D2 group as concerns mortality.

Post-operative hospital stay

The data on hospital stay excluded the early death (intraoperative), and consequently were based upon 161 patients. The median time of hospital stay was 12 days for D1 groups (mean 13.75, range 8-78) and 12 days for D2 group (mean 13.15, range 8-27). The effect of splenectomy on duration of hospital stay was not clear: patients having received splenectomy stayed in hospital half-a-day more (12.5 days, mean 13.49, range 9-17) than patients without splenectomy 12 days, (mean 12.87, range 8-78, see Table 4).

Discussion

Despite its recent decline, gastric cancer is still a common lethal disease in western countries. For apparently resectable cancers, surgery offers the best loco regional control; but unfortunately, average 5-year survival rates for treated patients remain low in the western world, ranging from 15 to 30%.[11,13] Over the years, Japanese surgeons have performed radical procedures involving extended lymphadenectomy, and have reported impressive survival figures with extremely low morbidity and mortality.[1,2,14] Two recent European randomised trials, however, failed to demonstrate a significant

Table 3 Post-operative complications and mortality

	D1 (76)	D2 (86)	Global (162)
Non-surgical complications	4 (5.26%) Cardiac 2 Pulmonary 2	7 (8.13%) Pulmonary 4 Pleural 3	11 (6.79%)
Surgical complications	4 (5.26%) Pancreatic leakage 1 Intraperit. haemorrhage 2 Colonic perforation 1*	7 (8.13%) Pancreatic leakage 1 Intraperit. haemorrhage 1* Duodenal leakage 1* Acute pancreatitis 2* Abdominal abscess 2	11 (6.79%)
Total morbidity	8 (10.52%)	14 (16.27%)	22 (13.58%)
Mortality	1 (1.31%)	-	1 (0.61%)

* Requiring reoperation.

Table 4 Lengths of hospital stay

	D1	D2	S0	S+
Days median (range)	12 (8-78)	12 (8-27)	12 (8-78)	12.5 (9-17)
Days mean	13.75	13.15	12.87	13.49

S0, splenectomy not performed; S+, splenectomy performed.

survival benefit of radical D2 gastrectomy over standard D1 resection.[5,6] The benefit of D2 gastrectomy's potential for reducing loco regional recurrence may be nullified by the significant increase of post-operative morbidity and mortality. These unfavourable results have been attributed to many factors, including the lack of technical experience of surgeons dealing with extended gastrectomy, the large number of elderly patients presenting with associated vascular and cardio respiratory diseases, the large number of centres involved in randomised trials with consequent low quality control, and particularly the distal pancreatico-splenectomy routinely performed during total gastrectomy in the D2 arms of randomised trials. Subset analysis of the MRC and Dutch randomised trials has recently indicated that the poorer outcomes in D2 resections are largely due to pancreas and spleen removal.[7,15]

We performed a previous prospective multicentre phase 1-2 study on feasibility and safety of D2 gastrectomy with pancreas preserving technique, involving only a few surgeons. In this study, distal pancreatico-splenectomy was not performed unless the pancreas was suspected of being involved by the tumour. We observed that, when performed in specialized centres, with a strict quality control system, by experienced surgeons, D2 gastrectomy with pancreas preservation could be safe in Western countries. Our morbidity and mortality rates were not only absolutely comparable to those observed after standard resections but also very close to those shown by Japanese surgeons.[8]

Compared to the patients in the Dutch and British trials our patients were younger, and had a higher proportion of early and distal cancers, and these factors may help to partially explain the striking difference between our morbidity and mortality results and those in these trials.

Having reached a good standard of experience in D2 procedures, we planned a new trial, randomising patient to either D1 or D2 gastrectomy.

To maintain a homogenous level of acquired technical experience in D2 procedures, only surgeons already involved in our previous study were allowed to participate in this new trial; this should avoid bias associated with new surgeons who have not yet completed their learning curve. After careful review of the safety results obtained in the first trial, four out of the nine surgical teams did not join this new randomised trial because completion of their learning curve could not be proven (see above).

These preliminary data seem to confirm our previous reports. Overall morbidity is around 14%; although this figure is a slight underestimate due to the fact that the majority of centres have registered in their database major and minor non-surgical but only major surgical complications, it is very low, and comparable to the best results shown by Japanese authors.[14] The overall morbidity is higher in D2 gastrectomy, but the difference between the two groups of patients is not statistically significant. Moreover, the rate of complications after D2 gastrectomy (16.35%) is considerably better than the rates of both arms (D1 and D2) in the English and Dutch trials.[5,6]

The ASA grade is a fairly crude and subjective measure of patient fitness, and it is not possible to make realistic comparisons of comorbid pathology and organ functional reserve between our patients and those in the Dutch and British trials. We cannot exclude the possibility that difference between these populations contributed to the difference in morbidity and mortality results. In support of our belief that proper surgical training and quality control played the leading part in our low morbidity, we observed very few 'technical' complications requiring re-operation, such as anastomotic leakage (seen in only one duodenal stump leak).

The importance of pancreatic complications after extended gastric surgery, was confirmed by our data. Although the pancreas was not removed routinely during D2 total gastrectomies, three out of the seven complications registered after a D2 procedure were related to the pancreas (two acute pancreatitis and one pancreatic leakage), and two of these required a reoperation.

Overall mortality was very low, at 0.6%. This rate is comparable to those shown by eastern authors in series from experienced centres, and is strikingly different from the rates of both arms reported in MRC and Dutch trials. Our study was powered to detect a difference in 5 year survival between D1 and D2 surgery: detecting a morbidity or mortality difference would require a larger number of

patients, and it is therefore, possible that a small difference exists. Our preliminary results are sufficient to indicate that any such difference is likely to be too small to be clinically important.

These preliminary results confirm that the radical technique of extended lymph node removal can be performed in Western centres without an increase in post-operative morbidity and mortality, if some conditions are respected. First, surgeons involved in these procedures should have completed their learning curve under strict quality control, possibly by a Japanese instructor; second, this procedure should be performed only in selected patients, suitable for extended surgery and with a potentially curable cancer; third, a policy of removing the spleen only when oncologically necessary, with preservation of the tail of the pancreas is associated with low morbidity and mortality, and routine pancreatico-splenectomy is absolutely to be avoided during total gastrectomy.

We found that after an adequate learning period, D2 gastrectomy can offer morbidity and mortality results comparable to those reported in Japanese series.

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Review article

TNM and Japanese staging systems for gastric cancer: how do they coexist?

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Abstract

Two staging systems for gastric cancer, International Union Against Cancer (UICC)/TNM and the Japanese classification, have been used widely for clinical practice and research. The two systems started independently in the 1960s, and underwent several revisions and amendments in order to approach each other, but have become more divergent in the latest editions because of characteristics based on different philosophies. The TNM system adopted a number-based system for N-staging that provides easy and accurate prognostic stratification. Comparative studies have shown that the TNM system has greater prognostic power than the Japanese classification. It contains, however, no treatment guidance and should primarily be used as a guide to prognosis. In contrast, the Japanese classification has been designed as a comprehensive guide to treatment, originally for surgeons and pathologists, and today for oncologists and endoscopists as well. Its anatomical-based N-staging was established based on analysis of lymphadenectomy effectiveness, and naturally provides direct surgical guidance. Clinicians should understand the roles of each system and must not mix the systems or terminology when they report their study results.

Key words Stomach neoplasms · Classification · TNM · Japanese classification · Stage

Introduction

Gastric cancer is the world's second commonest cancer, superseded only by lung cancer in this undesirable world ranking. While the incidence of gastric cancer continues to decline steadily in the West, it is still the commonest malignancy in Japan. However, the chance of cure from the disease remains highest in Japan, where there has been a steady improvement in survival rate over the past three decades. Much of this is due to increased diagnosis of early gastric cancer, which accounts for half of all cases, as well as more radical intervention for advanced disease. By contrast, the majority of the cases in the West present late with advanced disease, and there has not been a significant improvement in the overall survival, despite improvements in surgical technique.

Narrowing the gap between Western and Japanese outcomes will probably require changes at many levels. However, attempts to compare gastric cancer outcomes have been hampered by differences in both the philosophy and practicality of staging the disease in Japan and the West [1].

The two main staging systems for gastric cancer are the TNM staging system of the International Union Against Cancer (UICC), and the Japanese Classification of Gastric Carcinoma by the Japanese Gastric Cancer Association (JGCA). Similarities between these two staging systems exist; namely, that staging is dependent on the extent of the primary tumor, the extent of lymph node involvement, and the presence or absence of distant metastasis. However, there still remain fundamental differences between the two staging systems. The most recognizable difference lies with the classification of regional lymph node spread. The UICC/TNM staging system divides N stage on the basis of the number of metastatic lymph nodes, while the Japanese classification stresses the location of involved nodes.

Staging has a variety of functions, which should be reflected in the staging systems used. In addition to providing an indication of prognosis, staging should ideally be able to provide a framework for treatment decisions, and should allow for evaluation of treatment with meaningful comparisons between different treatments or the same treatment modalities by different groups.

The purpose of this review is to outline the philosophy, background, and major features of the current staging systems and to assess their suitability to serve the above functions.

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Two main classifications

The current main classification systems for gastric cancer are the sixth edition of the UICC/TNM classification (2002) [2] and the thirteenth edition of the *Japanese classification of gastric carcinoma* (second English edition [3] (1998), downloadable from http://www.jgca.jp/PDFfiles/JCGC-2E.PDF), herein referred to as the JGCA classification. Other systems have been proposed, which will be discussed briefly later in the text.

UICC/TNM classification

In 1954, the UICC appointed a Committee on Tumor Nomenclature and Statistics, which subsequently agreed on a technique for classification of cancer according to the anatomical extent of the disease. Gastric cancer was first included in the TNM staging system in 1966. There have been relatively few revisions to the UICC classification, which is now still only in its sixth edition.

The UICC/TNM system was originally a purely clinical classification, so that a disease stage could be decided before any treatment. In gastric cancer, however, surgical findings were indispensable for classification, because the principal prognostic factors were diagnosed only after surgical exploration. The American Joint Committee on Cancer Staging and End Results Reporting (AJCC) was organized in 1959 to develop a staging system acceptable to the American medical profession, basically using the UICC/TNM format. In 1970, the AJCC published a TNM-based staging system, using clinical, surgical, and histological information [4]. The background database was from 1241 patients with gastric cancer, which had been analyzed by a task force from seven American institutions. The system used penetration of stomach wall (T), proximity to the primary cancer of metastatic perigastric lymph nodes (N), and presence or absence of distant metastases (M), including nodes not in the perigastric area, as these criteria had the greatest impact on outcome in the above cohort.

The third edition of the UICC/TNM in 1978 contained a unified classification with the AJCC. The T stage was defined by stomach-wall invasion, but the "clinical T" and "pathological T" had different definitions. The N stage was defined by anatomic location of nodes from N0 to N3. N1 nodes were defined as metastatic perigastric nodes within 3 cm of the primary, and N2 nodes were nodes beyond 3 cm from the primary, or along the celiac, splenic, left gastric, or hepatic arteries. N3 nodes were paraaortic and hepatoduodenal nodes. In the fourth of the TNM classification edition (1987), T stage was unified to the style of the current edition, and the N3 category was dropped and reclassified as M1 (Table 1).

Table 1. TNM classification, 4th edition; 1987

		M0			M1
		N0	N1	N2	
M0	T1	IA	IB	II	
	T2	IB	II	IIIA	
	T3	II	IIIA	IIIB	
	T4	IIIA	IIIB		
M1					IV

N1, perigastric nodes within 3 cm of the primary tumor; N2, nodes beyond 3 cm from the primary, or along the celiac, splenic, left gastric or hepatic arteries

Table 2. TNM classification, 5th edition; 1997

		M0				M1
		N0	N1	N2	N3	
M0	T1	IA	IB	II		
	T2	IB	II	IIIA		
	T3	II	IIIA	IIIB		
	T4	IIIA				IV
M1						

N1, 1–6 involved nodes; N2, 7–15 involved nodes; N3, >15 nodes

The fifth edition (1997) of the TNM classification contains several amendments from the previous edition. The greatest change was that, whereas previously N status was determined by the anatomical site of involved lymph nodes, in the new classification, N stage is determined by the number of metastatic lymph nodes from a minimum yield of 15 lymph nodes in total (N1, 1–6 involved nodes; N2, 7–15 involved nodes; and N3, >15 nodes; Table 2). This had been explored as an option for some time and a proposal to add the number of involved lymph nodes to the anatomical-based N stage was published by the UICC in 1993 [5]. The idea of adopting a number-based N-staging for gastric cancer had also been proposed by some Japanese surgeons [6,7]. Data from a German multicenter gastric cancer study showed the effectiveness of the new proposal in providing better prognostic stratification than previous systems [8].

The new classification was developed, with four N categories (N0 to N3) instead of three as was initially proposed, and was presented in Seoul, Korea, at the 12th International Seminar of the WHO Collaborating Centre for Gastric Cancer in 1996 [9].

In addition to the change in N status, hepatoduodenal nodes are now once again regarded as regional nodal metastases rather than distant metastases, and the stage grouping has been altered, with all N3 patients now classified as stage IV (Table 2). T4N1 disease has also been changed to stage IV, having previously been classified as stage IIIb in 1987.

The latest edition of the TNM classification (sixth edition; 2002) amends pT2 into the subgroups pT2a and pT2b, which represent invasion confined to the muscularis propria and subserosa, respectively. This equates to T2 MP and T2 SS in the JGCA classification.

Japanese classification

The first edition of the General Rules for Gastric Cancer Study was published by the Japanese Research Society for Gastric Cancer in 1962. Stage groups were defined by the extent of serosal involvement (S stage), the location of involved lymph nodes depending on the site of the primary tumor (N stage), and the extent and sites of distant metastases (M, H, and P stages for distant metastasis, and hepatic and peritoneal disease, respectively). In its twelfth edition, the General Rules changed from the S-stage to a T-stage system, which was equivalent to the T-staging of the UICC system.

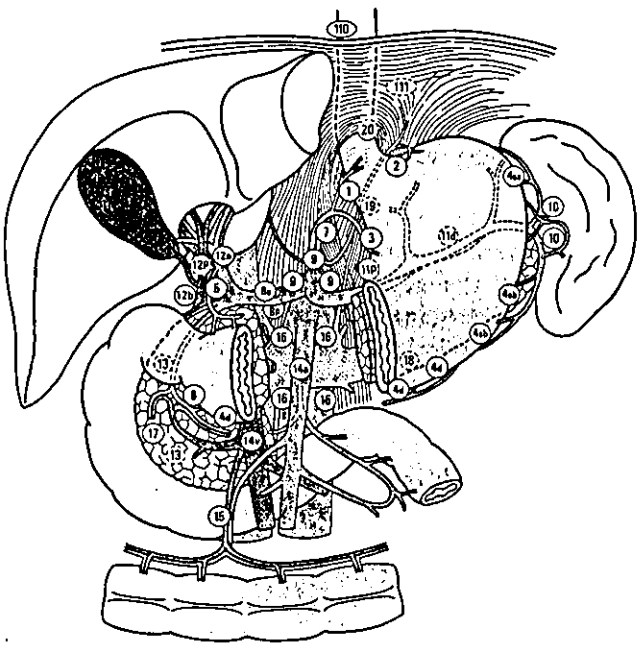

Fig. 1. Lymph node station numbers (*circled*) in the Japanese classification of gastric carcinoma [3]. These stations are further classified into N1/N2/N3 according the location of the primary tumor

The JGCA classification gives a number to all of the regional lymph node stations (Fig. 1), which are classified into three tiers according to the location of the primary tumor. Radical lymphadenectomy in gastric cancer surgery has long been commonplace in Japan and large databases of the incidence and sites of lymph node involvement exist, depending on the site of the tumor and its T stage. The purpose of the meticulous lymph node classification in the General Rules was therefore to guide surgeons to decide the extent and location of lymphadenectomy, so that any potentially involved nodes could be removed according to the site and depth of penetration of the primary gastric cancer.

Lymph node staging was characterized on the basis that gastric cancer metastasizes to groups of lymph nodes arranged radially around the stomach in tiers. The nomination of different lymph node groups to their respective tier was based upon the results of anatomical and physiological studies on lymph flow with different tumor sites.

Various amendments to the original classification followed, and the most recent classification is aimed at surgeons, pathologists, oncologists, and endoscopists who carry out endoscopic mucosal resection (EMR).

English versions were published in the *Japanese Journal of Surgery* in 1973 [10] and 1981 [11] and were referred to in Western studies. However, they were only a digest and could not fully convey the concept or details of the General Rules. The first comprehensive English edition was published in 1995 [12], based on the twelfth Japanese edition, and was named *Japanese classification of gastric carcinoma* (Table 3). The second English edition was based on the thirteenth Japanese edition, and was published in *Gastric Cancer* in 1998 [3].

There were a variety of changes in the most recent edition of the JGCA classification [13], such as rules for EMR and for staging carcinoma of the remnant stomach, and peritoneal cytology has been included in staging.

The most important changes in the current edition from a surgical point of view are the revision of lymph node staging and the consequent limitation of dissection level. Lymph node groups were reallocated from four tiers (N1 to N4) to three tiers (N1 to N3) on the basis of a detailed study of the effectiveness of dissection of different lymph node stations for tumors in the various locations within the stomach. Some lymph node groups, even some perigastric nodes for specific tumor locations, are no longer regarded as regional nodes if involved, but are regarded as sites of distant metastasis (M). This follows because their involvement is rare, and if it occurs, it invariably reflects a very bad prognosis [14]. One example would be the involvement of no. 2

Table 3. Japanese classification, 12th edition; 1993 (1st English edition; 1995 [12])

		P0, H0, M0				P0, H1, N0-2
		N0	N1	N2	N3	
P0 H0 M0	T1	Ia	Ib	II	IIIa	IVa
	T2	Ib	II	IIIa	IIIb	
	T3	II	IIIa	IIIb	IVa	
	T4	IIIa	IIIb	IVa		
P1, H0, T1-3		IVa				IVb (N4, P2,3, H2,3, M1, etc)

Table 4. Japanese classification, 13th edition; 1999 (2nd English edition; 1998 [3])

		M0				M1
		N0	N1	N2	N3	
M0	T1	IA	IB	II		IV
	T2	IB	II	IIIA		
	T3	II	IIIA	IIIB		
	T4	IIIA	IIIB			
H1, P1, CY1, M1						

(left paracardial) nodes in the case of antral tumors. Other node groups, such as 14v (nodes along the superior mesenteric vein) and 12a (along the proper hepatic artery) are common sites of nodal metastasis for lower gastric tumors, and their dissection, even when positive, is often associated with survival. These groups have thus been brought into the N2 tier from the previous N3 tier. As a consequence, the D2 dissection, including all N2 node stations, is more radical than was previously the case, and is better targeted to actual rather than theoretical patterns of spread. D2 dissection can now be applied as standard surgical treatment for advanced gastric cancer. D3 dissection should be regarded as investigational treatment and is not standard. Following the revision of the N staging, there is no longer a category of "D4" dissection. The effect of the changes on stage grouping is that all N3 disease is regarded as stage IV, which is now no longer substratified.

There was a striking resemblance in the staging tables between the second English edition of the JGCA classification (Table 4) and the fifth edition of the TNM classification (Table 2), with the only difference being for the assignment of T4N1 disease, although the definition of N is totally different, as mentioned.

Evaluation and comparison

Similarities and contrasts between staging systems

Unification of staging systems or the concepts of staging is desirable and dialogue between Japanese and Western groups has resulted in alterations in both staging systems to take account of their different approaches.

In 1978, the UICC refined the anatomical-based N grouping into two tiers to reflect radial nodal spread, in keeping with the Japanese principles. N1 involvement was confined to perigastric nodes close to the primary, and N2 nodes referred to those along the hepatic, left gastric, splenic, or celiac arteries, as well as more distant perigastric nodes. This allowed some comparison between Japanese and UICC classifications, as N1 and N2 nodes corresponded to some extent across the two systems, although the anatomical details differed considerably.

The recent change of TNM staging to a number-based node status was a major turnaround that might separate irreversibly the two classifications, which had been converging. However, as far as prognosis is concerned, it has made direct comparison between Western and Japanese patients much easier, as the same data are available for both sets of patients. Now the clinical data recorded by the JGCA system can be exactly translated to the TNM system. The opposite is totally impossible, because the number-based system is a post-hoc pathological staging and bears no relationship to patterns of lymph node spread.

By contrast with the JGCA classification, which provides comprehensive and meticulous guidance to clinicians, the TNM classification is a simple staging system. There is little guidance on management, except that a minimum of 15 lymph nodes is recommended for accurate staging. The stage stratification from the TNM system is simple to apply and gives good prognostic information, but the use of lymph node number alone means that, without supplementary information, stage-dependent management cannot be practiced before final histology is available, as it is impossible to assess the exact number of positive lymph nodes radiologically or even surgically.

Differences in surgical philosophy between Japan and the West

It was Moynihan [15] who said that "Surgery of malignant disease is not the surgery of organs; it is the

anatomy of the lymphatic system". This is undoubtedly a basic principle of Japanese surgical practice. The commonest site of metastasis for gastric cancer is to lymph nodes. Japanese surgeons believe lymph node metastasis is orderly and progresses through the tiers of nodes in a stepwise manner. By defining the lymph node groups in each tier, the surgeon can remove all nodes to the level above that in which positive nodes are apparent or likely, on the basis of preoperative and intraoperative staging.

The JGCA classification is much more than a simple staging system, as it outlines a whole approach to gastric cancer. Rules are defined for diagnosis, surgical procedures, histology, and staging, as well as details of how to prepare the surgical specimen and lymph nodes. The JGCA classification details which node groups to remove depending on the site of the tumor and the level of dissection required. Stage grouping for prognosis naturally uses the same nodal tier basis for N-stage stratification, as it reflects both the spread of the disease and its treatment strategy.

On the other hand, the focus in Western surgical philosophy has been that prognosis is determined to a great extent by the biology of the primary tumor, and that lymph node metastasis is a marker of tumor dissemination [16]. Extended clearance of lymph nodes, unless obviously involved, is perceived to incur excessive morbidity with doubtful survival advantage. Thus, the TNM system places emphasis on prognostic staging and provides little treatment guidance.

Nevertheless, some European surgical groups consider the extended lymphadenectomy as an effective local tumor control and continue to employ D2 dissection and Japanese style N-staging [17].

Prognostic value

Japanese versus TNM classification. Since the introduction of number-based nodal staging in the UICC/TNM system, several Japanese authors have been able to compare prognosis by Japanese and TNM staging in the same patients.

In a study by Fujii et al. [18], 1489 patients were classified retrospectively according to the two classifications. They found that the survival curves in relation to the nodal staging of the two classifications were more or less similar, in that a decrease in survival was associated with an increase in the nodal classification. However, there was more homogeneity in the TNM stage groups than with the JGCA: when the patients with "n1" metastasis by the JGCA system were subdivided according to the TNM number-based system, there were significant differences in survival between "n1/pN1" and "n1/pN2". The same was true for JGCA "n2" patients classified as pN1 or pN2 by TNM stage. However, there was no difference in survival when each of TNM pN1 and pN2 groupings was subdivided into JGCA "n1" and "n2", i.e., patients with "pN1/n1" or "pN1/n2" shared similar survival curves, as did those with "pN2/n1" and "pN2/n2". This suggests that the prognostic impact of TNM pN stage is superior to that of JGCA "n" staging.

Ichikura et al. [19], Hayashi et al. [20] and Ichikawa et al. [21] also published their results from patients who underwent clinically curative gastric resection, using the JGCA and the fifth TNM classifications. All three groups of authors concluded that the TNM classification for lymph node involvement was superior to the JGCA classification in terms of homogeneity and prognostic value.

Similar conclusions were drawn by Kodera et al. [22], and they found that, even when lymphadenectomy was limited to perigastric lymph nodes, as in a standard Western style D1 resection, there was a difference in survival between pN1 and pN2, which supports the use of the new TNM classification.

In summary, therefore, the number-based N staging has greater prognostic power than the anatomical-based system.

Old TNM (1987) versus new TNM (1997) classification. Direct comparisons of the old and new TNM systems have been published by a variety of authors. Katai et al. [23] analyzed the results of 4362 patients who underwent resection for gastric cancer and found that the new system provided better prognostic stratification than the old system. However, patients classified as "pT4N1" in the new system fared better than other patients in stage IV and would have been better classified as stage IIIB.

Karpeh et al. [24] looked at the old and new AJCC/TNM classifications in 1038 patients, the majority of whom had undergone extended lymph node dissection; they also concluded that node numbers provided more homogeneous survival curves and better prediction of outcome than sites of metastases as defined by the 1987 AJCC/TNM criteria. These authors also strongly countenanced the minimum requirement of 15 nodes to limit stage migration.

Kranenbarg et al. [25] evaluated the old and new TNM classifications for their practicality and prognostic value, using the data of 1078 patients from the Dutch Gastric Cancer Trial. They found that the new (1997) TNM classification gave better prognostic stratification than the old (1987) classification.

The above studies differed from the conclusion reached by Mendes-de-Almeida et al. [26], who found the new TNM classification not very effective in improving the prognostic stratification of lymph node involvement when compared with the old TNM classification. A similar conclusion was drawn by de Manzoni et al.

[27], who concluded that both the site and the number of positive lymph nodes were independent prognostic factors in gastric cancer. Lee et al. [28] did not find superiority of the new classification, and questioned the validity of the current cutoff point for N-staging.

Practicalities of the classifications

Pre- and intraoperative staging. The TNM staging system was originally designed to help plan management before any treatment, and it is often applied in a preintervention setting, but offers little descriptive information on gastric cancer. Treatment planning often relies on supplementary information, in addition to the TNM or stage descriptor.

The recent change in TNM nodal staging further limits the ability to accurately stage patients before treatment. It is true that, in any case, the preoperative assessment of regional lymph nodes in gastric cancer using radiological imaging methods has a low accuracy rate, but counting involved lymph nodes radiologically is impossible, whereas identification of the sites of abnormal nodes is included within standard radiological reporting. Because neoadjuvant chemotherapy is attracting increasing interest today, the importance of pretreatment staging inevitably increases. The N-staging of the current TNM system does not function in this regard, and some modification might be required in the future.

The intraoperative findings during surgery may include macroscopic laparotomy findings, frozen section examination, cytology results, and the macroscopic findings of the resected specimen. Within the JGCA classification, there is clear guidance on the relevance of metastatic disease in the peritoneal cavity or any of the relevant lymph node groups, enabling surgical strategy to be decided on the basis of knowledge of the likely oncological outcome of the patient. While all the same information is available to the Western surgeon, TNM staging has little to offer in regard to strategy, unless frank, previously unrecognized metastases are found.

One example is positive peritoneal cytology, which represents stage IV disease by the current JGCA classification and is equivalent to distant metastasis in terms of prognosis. A positive finding will render a procedure palliative [29,30], and should restrict the need to pursue a radical resection.

Peritoneal cytology is not represented in the current TNM classification, and requires additional annotation if it is to be included in trials or treatment protocols.

Lymph node retrieval. The processing of lymph nodes is detailed and time-consuming with the Japanese system [31], and has been criticized for being complicated and unnecessarily labor-intensive, as it is performed by the surgical team. By contrast, in the West, the pathologist is in charge of the resected specimen, is often unaware of the precise location of the relevant lymph nodes, and is unlikely to be able to allocate each lymph node to its corresponding site and tier following an en-bloc resection. Now the number-based system can be easily applied in the West.

The TNM classification stated, in the fifth edition that, for pN0, "histological examination of a regional lymphadenectomy specimen will ordinarily include 15 or more lymph nodes". While many authors have supported the validity of the minimal number of 15 for staging [32,33], some surgeons have suggested that it could be reduced without influencing the prognostic analysis, thereby considerably reducing "unclassified (pNX)" cases. Kranenbarg et al. [25] suggested that a minimum of 5 consecutive negative nodes would suffice to stage gastric cancer as pN0, based on the data from the Dutch D1/D2 trial. Ichikura et al. [34] found that the survival rate for patients with 10 to 14 negative nodes was as good as the rate for those with 15 or more negative nodes, and suggested that the minimum number to be examined for pN0 could be reduced to 10.

In the latest edition of the TNM classification, the following sentence has been added to the pN0 definition: "If the lymph nodes are negative, but the number ordinarily examined is not met, classify as pN0". This appears to mean that the figure of 15 is a recommendation, but no longer a requirement, for pN0 staging.

In node-positive patients, the current TNM classification may cause serious problems of underestimation. For example, if 6 lymph nodes only were retrieved, and all were positive for cancer cells, the staging would be assigned as pN1 in this system. It is highly likely that such a patient would have had further positive nodes that had been dissected, but not retrieved, and thus could have been staged as pN2 or pN3 if 16 or more nodes had been retrieved. This is not an unlikely situation in Western general hospitals; Mullaney et al. [35] assessed the number of lymph nodes documented for surgically managed patient in the West Midlands, United Kingdom, and found that only 31% of surgically resected patients could be staged with at least 15 nodes.

Furthermore, some authors have even suggested that 15 nodes may not be sufficient for accurate staging of metastatic nodes. Lee et al. [36] reported a retrospective analysis of 4789 patients with gastric cancer and suggested that, for advanced disease and in particular for stage IIIB, more than 15 nodes may be required for optimal staging. They indicated that, with a smaller number of nodes examined, there is a high possibility of underestimation and stage migration.

Ichikura et al. [34] emphasized that, though the mini-

mum number for pN0 could be reduced from 15 to 10, accurate staging of pN1 and pN2 requires the examination of 20 or more nodes, because the number of metastatic nodes was significantly correlated with the number of examined nodes.

Stage migration. The issue of stage migration, or the "Will Rogers phenomenon" [37], is frequently cited as a potential cause of differences in outcome between Japanese and Western patients [1]. Japanese patients undergo D2 dissection as the standard treatment, and, because more nodes are harvested, they are more likely to have positive nodes picked up compared to D0/D1 gastrectomy. The same patients in an extended lymphadenectomy series will thus be allocated a worse prognostic stage than their counterparts who had a D0/D1 gastrectomy. This will improve the survival data for all stages, purely by reallocation of patients with lymph node metastases into higher stages [38].

The introduction of the number-based N-staging may reduce stage migration among the groups with different extents of lymphadenectomy [39], if the resected nodes are fully retrieved. However, enthusiasm for nodal retrieval rather than extent of lymphadenectomy may directly influence the N-staging in this system.

Japanese surgeons usually retrieve as many lymph nodes as possible, because the nodes are literally their "harvest" of cancer surgery, while Western pathologists would be reluctant to retrieve more than the minimum requisite. The only means to prevent or minimize stage migration in the number-based system is to keep nodal retrieval at a high level (e.g., at least 15). Now that the minimum requisite of 15 is practically abolished in the sixth TNM edition, underestimation and consequent stage migration may further enlarge the apparent differences in treatment results between Japan and the West.

Other Classifications

Numerous classifications have been proposed by individual groups after sub-analysis of their own data. Most are adaptations of either anatomical or numerical systems of N-staging, as in the two major classifications.

Adachi et al. [40] and Whiting et al. [41] both employ anatomical nodal staging, with junctional nodes between conventional N1 and N2 tiers. Whiting et al. [41] suggested that junctional nodes could be assessed during surgery to decide whether or not to proceed to D2 dissection, if these nodes were involved. The rationale is based on the apparently high morbidity of D2 dissection in Western series, and they suggested that D2 dissection should be avoided if possible.

Kato et al. [42] address the issue of limited nodal dissection and describe the predictive value of the number of metastatic nodes in the Japanese (old and new classifications) "n1" perigastric stations. They found their system to have higher sensitivity, specificity, and accuracy than the TNM system or the Japanese system.

Finally, Yu et al. [43] have proposed a frequency system, based on the ratio of metastatic to dissected regional lymph nodes (more or less than 25% involved). Such a system weights against limited nodal dissection, and is a relevant approach, assuming extended lymphadenectomy has an independent survival impact.

Conclusion

Despite repeated comparisons between Japanese and Western staging systems, the systems do not, and were not designed to, fulfill the same role. The JGCA classification is a comprehensive guide to the anatomical-based treatment of gastric cancer and its regional metastases. The staging system within the JGCA classification is highly detailed and anatomically based, and it is inseparable from the guidance on surgical treatment, which is its primary focus.

The TNM system is primarily used as a guide to prognosis. It contains no treatment guidance and has recently changed to a number-based N stage, which most accurately reflects metastatic burden and, hence, prognosis. It provides a simple and reliable means of comparison of outcome between series. In Western practice, importance is placed on both surgeon and pathologist to ensure a nodal yield of at least 15 nodes. The value of the number-based nodal system for comparison will be lost if node yields are low, as a consequence of stage migration, and comparison between patients classified by the TNM and Japanese systems will remain inadequate, as the Japanese approach of D2 dissection and specimen preparation invariably results in greater node yields.

As the two systems are different in principle, it is important that clinicians involved in the treatment of gastric cancer understand the roles of each system. Surgeons using the Japanese system are able to report results by both the Japanese and the TNM staging, which will help comparisons of outcome. However, the two systems are not interchangeable, and the systems and their terminology should not be mixed if clarity is to be maintained.

Alternative staging systems continue to be proposed. Most adapt either anatomical or number-based systems, confirming the independent value of each approach.

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FROM THE ASCO-JSCO JOINT SYMPOSIUM

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Role of surgery in multidisciplinary treatment for solid cancers

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Abstract In the evolution of solid cancer, there are four steps: noninvasive tumor, local invasive cancer without metastasis, local invasive cancer with lymph node metastasis, and eventually systemic disease. For the first three phases, local treatment, including lymph node dissection, may cure the disease. The choice of local treatment depends on the tumor characteristics, but surgery remains important in many of these cancers. Gastric cancer is one of the typical tumors which remain locally invasive, with or without nodal metastasis, but without systemic metastasis for a rather long period. Metastasis to lymph nodes occurs, frequently even in T1 tumors, but seldom to other sites until the late stage. Thus, the target of local control is the regional lymph nodes. The Intergroup study IT-0116 proved the effect of chemoradiotherapy (CRT) for curable gastric cancer, and thus proved the insufficiency of limited surgery (D0/1). The conventional method of local control for gastric cancer is surgery, including regional lymph node dissection (D2). However, the superiority of D2 has not been proven by randomized controlled trials (RCTs). But all RCTs so far have a crucial problem in the quality of treatment given in the D2 arm. D2 is not a dangerous procedure if done by specialists in large-volume hospitals. D0/1 plus CRT is better than D0/1 alone, but it may be worse than D2 alone. The survival benefit of CRT after D2 is an open question. Establishing standard adjuvant chemotherapy after D2 is a more urgent clinical issue, and there is no reason to abandon D2 gastrectomy for curable gastric cancer in Japan.

Key words Role of surgery · Gastric cancer · Chemoradiotherapy · Local control

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The role of surgery in multidisciplinary treatment for cancer

We believe that solid cancers evolve as follows: lesions without invasion, then locally invasive cancer, which will soon metastasize to regional lymph nodes and then to other organs as systemic disease. The initial lesion of cancer is sometimes noninvasive, and is therefore called dysplasia, in spite of cellular or structural atypia, in the West. There are many arguments about dysplasia and early noninvasive cancer between the West and Japan, including, recently, lung cancer. Due to the development of helical computed tomography (CT), very early cancers, i.e., possible noninvasive cancers, are now being diagnosed in many countries, including the United States and Japan. For a long time, in Japan, we have diagnosed these lesions (which are called dysplasia in the West) in the stomach or in the colon, as cancer. It is well known that many of these dysplastic lesions will invade in a rather short time, at which time they are locally invasive cancers (at this point, a diagnosis of cancer is made in the West). The lesions then start to show metastasis to the regional lymph nodes, and then finally, become systemic disease, with metastases in many distant organs. For noninvasive cancer or dysplasia, just observation or limited resection, such as endoscopic mucosal resection (EMR), is the best way to manage them. For locally invasive cancer, just a wide excision could be sufficient. However, as it is impossible to discriminate exactly between locally invasive lesions with and without regional lymph node metastasis, these lesions are often treated by a wide excision plus lymph node dissection. Recently, sentinel-node biopsy has been used to discriminate those lesions with or without nodal metastasis and to minimize the level of aggressive surgery for these tumors. If the tumor becomes systemic disease, local control plus systemic treatment is mandatory if we aim to cure the disease. As the weapon for local treatment, surgery is most frequently used, but radiation can also be used, depending on the tumor characteristics. Different cancers have different patterns of tumor development or evolution. For example, small-cell

lung cancer has a very short span of limited disease, and most of the lesions of this cancer are already local regional disease plus systemic metastasis when diagnosed. At the opposite extreme is gastric cancer. In Japan, more than half of newly diagnosed lesions are T1, early gastric cancers. Advanced lesions of gastric cancer still have only local invasion and regional lymph node metastasis, which can often be cured by surgery alone. Squamous cell cancer of the esophagus would be situated between these two extremes.

Focus on gastric cancer

Table 1 shows the pattern and incidence of metastasis from gastric cancer, according to the tumor depth.[1] Lymph nodes, liver, and peritoneum are the three frequently involved sites. Other sites in the body, such as lung, bone, brain or skin, may have metastasis from gastric cancer, but only at the end of the disease development, at the terminal stage in these patients.

Table 1. Biological behavior of gastric cancer: incidence of metastasis and 5-year survival

Depth	*n*	LN	Liver	Peritoneum	5-Year survival
pT1					
M	1063	3.3	0.0	0.0	93.3
SM	881	17.4	0.1	0.0	88.9
pT2					
MP	436	46.4	1.1	0.5	81.3
SS	325	63.7	3.4	2.2	65.8
pT3					
SE	1232	78.9	6.3	17.8	35.5
pT4					
SI	724	89.8	15.5	41.6	10.1
Overall	4683	47.8	4.5	11.5	60.3

Patients operated on between 1972 and 1991, at the National Cancer Center Hospital (NCCH), including those with exploratory laparotomy: there were 22 non-resected patients, in whom T was unknown

As shown in Table 1, metastasis occurs almost exclusively to lymph nodes until the primary tumor becomes T3. Liver metastasis occurs in just 6% of the patients with T3 tumor, and in 15.5% of those with T4 tumor. Peritoneal metastasis occurs only after the tumor has reached the serosa, becoming a T3 tumor; the incidence remains at less than 20% in T3 tumors. On the other hand, the incidence of lymph node metastasis is rather high, even in the early stage of disease evolution. Even T1 submucosal invasive tumors have nodal metastasis in nearly 20% of cases. If the tumor becomes T2, over 50% of patients have regional lymph node metastasis. If these nodal metastases were to be left behind after surgery, they would metastasize and eventually become systemic disease.

So, if the patients are treated by D2 or more extensive surgery, which is the standard treatment in Japan, local regional recurrence is not common, as shown in Table 2.[1] This means that D2 dissection can provide rather good local control. By far the commonest site of recurrence is the peritoneum, and systemic and hematogenous metastases are rare (just 7% of all treated patients). Therefore, in patients with gastric cancer, local control can lead to a fairly high success rate for cure. Only 28% of patients developed recurrence; thus, over 70% of patients survived without recurrence. If these tumors are treated by very limited surgery, local regional recurrence could be a big problem.

Dr. Gunderson[2] reported the pattern of failure after limited surgery with curative intent at his institute. Fifty-four percent of recurrences occurred only in the gastric bed, and recurrences reached nearly 90% if all those with local regional failure were included regardless of other type of recurrence. This shows the importance of local control for gastric cancer.

In gastric cancer, the lymph nodes are the most important metastatic site. Table 3 shows the topographical pN stage according to the tumor depth.[1] The deeper the tumor, the more frequently lymph nodes are metastatic and the more frequently distant regional nodes become metastatic. If the tumor becomes T3, three-fourths of patients have nodal metastasis. If the tumor remains as T1 or T2, we do not see distant regional lymph node metastasis very often.

Table 2. Primary site of recurrence after ≥D2

Depth	*n*	Recurrence	LN + RF	Peritoneum	Hematogenous (%)
pT1					
M	1063	2	0	0	2 (0.2)
SM	881	18	6	3	9 (1.0)
pT2					
MP	436	45	10	9	26 (5.9)
SS	325	74	15	28	31 (9.5)
pT3					
SE	1232	625	146	330	149 (12.1)
pT4					
SI	724	562	173	283	106 (14.6)
Overall	4683	1326 (28.3%)	330 (7.0%)	635 (13.6%)	323 (6.9%)

Patients operated on between 1972 and 1991, at the NCCH, including those with exploratory laparotomy

A large proportion of patients have N2 disease; even in T2 tumor, over 20% of patients have N2 disease, and in the T3 tumors, over 40% of patients have N2 disease. This means that main target of local control in gastric cancer is lymph node metastasis. There are several grounds for saying that good local control is essential to cure this cancer. First, Professor Siewert reported that R0 resection is by far the most important prognostic factor after curative operation.[3] Second, the results of the Intergroup study (IT-0116) showed that adding irradiation to adjuvant chemotherapy could improve the results of limited surgery alone, which could not be achieved by adjuvant chemotherapy alone.[4] Good local control by radiation, together with chemotherapy, could improve the results of treatment remarkably. The researchers of the Intergroup study also carefully analyzed the prognostic factors in the patients treated in that trial, and found that surgical under-treatment was an independent prognostic factor. This theory can be applied to some other solid cancers as well.

The preferred method of local control depends on the efficacy of treatment other than surgery. If we see a non-Hodgkin's lymphoma in the stomach, we do not operate on the patients now, and chemotherapy alone can often control both the primary site and the metastasis. Of course, chemoradiotherapy does work, too. Regarding squamous cell carcinoma of the esophagus, chemoradiotherapy can often control the primary tumor and the nodal metastasis, although the local recurrence rate is as high as 20%–30% after chemoradiotherapy. For gastric cancer, even chemoradiotherapy can seldom control an advanced primary tumor, but it may well control nodal disease. Based on the results of the IT-0116 study, if gastric cancer is treated by limited surgery plus chemoradiation (CRT), the primary lesion is controlled by the surgery, and micrometastases in lymph nodes are controlled by the chemoradiation. If gastric cancer is treated by D2 surgery, both the primary and these metastases are controlled by surgery.

Table 4 shows a comparison of two studies, the IT-0116 study, and the Japan Clinical Oncology Group (JCOG) 9501 study.[5] The JCOG 9501 study is a trial organized by the Gastric Surgery Division of JCOG to evaluate the role of paraaortic lymph node dissection, which is quite extensive surgery. There are remarkable differences between these two trials: in the IT-0116, surgery was rather limited (D0; very limited resection) in 54% of patients, and D1 surgery was done in 36%, while so-called Japanese-type surgery was done in only 10%. But in the JCOG 9501 study, half of the patients underwent D2 dissection, the standard surgery in Japan. The other half underwent much more extensive surgery (D3 dissection). Regarding adjuvant treatment, those allocated to the test arm in the IT-0116 study underwent 45-Gray radiotherapy together with chemotherapy (5-fluorouracil [5-FU] and leucovorin). In the JCOG 9501 trial, none of the patients underwent adjuvant treatment until they developed recurrence. There was no difference in tumor locations between these two trials, although researchers in the United States always say that they have more proximal tumors than antral tumors. Unlike the pattern of tumor location in the general population, a much larger proportion of patients in this American trial had antral tumors, while more tumors of the body were seen in the Japanese trial. Tumor depth is shown in Table 4: 14 T1, 74 T2, 175 T3, and 18 T4 in the IT-0116 study; and 23 T1, 257

Table 3. Lymph node metastasis according to the depth of tumor invasion

Depth	No.	pN+ (%)	pN0	pN1	pN2 (%)	pN3	pN4
T1							
M	619	14 (2)	605	9	5 (0.8)	0	0
SM	499	89 (18)	410	60	29 (5.8)	0	0
T2							
MP	276	126 (46)	150	74	47 (17)	5	0
SS	207	130 (63)	77	65	57 (28)	3	5
T3							
SE	646	484 (75)	162	171	266 (41)	28	19
T4							
SI	152	121 (80)	31	31	65 (43)	12	13
Total	2399	964 (40)	1435	410	469 (20)	48	37

In gastric cancer, the main target of local control is lymph node metastasis

Table 4. Comparison of the results of IT-0116 and JCOG 9501

	IT-0116	JCOG 9501
Surgery	D0/D1/D2-54%:36%:10%	D2/D3-50%:50%
Adjuvant	Radiation 45 Gy Chemotherapy 5-FU + LV	None
No of patients	281 (Test arm)	523
Tumor location	Antrum, 53%; corpus, 24%; cardia, 21%; multiple, 2%	Lower third, 41%; middle third 39%; upper third, 19%
pT stage (1:2:3:4)	14:74:175:18	23:257:230:13
Treatment-related deaths	3 (1.1%) + Postop.	4 (0.8%)
Survival	3-Year: 50% 5-Year: 42%	5-Year: 71.4 (66.5%–76.3%)

Table 5. Estimated 5-year survival of the IT-0116 patients if they would have undergone D2-3 surgery

IT-0116 patients	NCCH[a] 5-Year survival	Calculated survival proportion	CIH[b] 5-Year survival	Calculated survival proportion
T1, 14	92.2	12.9	96.6	13.5
T2, 74	77.5	57.4	80.6	59.6
T3, 175	47.1	82.4	40.2	70.4
T4, 18	29.9	5.4	17.4	3.1
42%		56.3%		52.2%

[a]Results of National Cancer Center Hospital[6]
[b]Results of Cancer Institute Hospital[7]

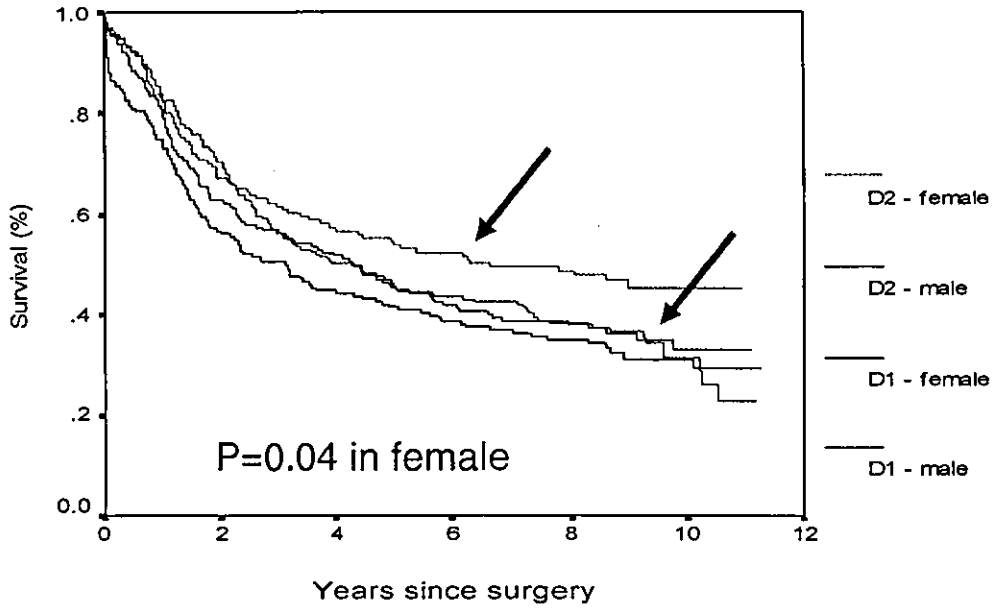

Fig. 1. D1 vs D2 for males and females. High postoperative mortality did not confound comparison in female patients

T2, 230 T3, and 13 T4 in the JCOG 9501. As to the treatment-related death rate (TRD), 1.1% was reported in IT-0116, and 0.8% in JCOG 9501. However, if the total population that could be candidates in this trial is considered, the TRD should be higher in IT-0116, because some postoperative deaths that occurred before enrolment in this trial were not counted. The survival results of IT-0116 are 50% at 3 years and 42% at 5 years, while the overall survival rate at 5 years is 71.4% in the JCOG 9501 study, although the observation time is not sufficient. As there is a non-inegligible difference of T-stage distribution between the two trials, this survival comparison is not fair. It is possible, however, to calculate the survival proportion by applying the survival rates of Japanese institutes by pT stage. The hypothetically estimated survival rates are then over 52%, which is about 10% better than the actual survival rate of the patients in the IT-0116 study (Table 5).

The results of the IT-0116 trial are interpreted as follows: (1) D0/1 surgery is proven to be inadequate treatment in terms of local control, (2) the results achieved are worse than the standard level of those treated by D2 surgery, (3) surgical under-treatment clearly undermined survival, (4) whether D0/1 + CRT can be as good as D2 alone should be tested by a RCT, (5) whether CRT after D2 can improve the results of this type of surgery alone is another question. At the same time, another question arose. Why was D2 not better than D1 in the western RCTs?

In fact, the Dutch and Medical Research Council (MRC) trials did not prove the effect of D2 dissection.[8,9] However, the quality of D2 dissection in these trials was questionable, with quite high postoperative mortality with extremely small hospital volume. The TRD rate of D2 was as high as 10% and the quality of postoperative care to avoid operative deaths was very poor, due to the small hospital volume. Not only in these trials but also in several other RCTs in surgery, a high TRD rate offsets the long-term effect of treatment. In the two trials on squamous cell carcinoma of the esophagus reported at the 39[th] annual meeting of the American Society of Clinical Oncology (ASCO), i.e., the German[10] and French[11] trials, a benefit of surgery after CRT was not seen in long-term survival, with a remarkable difference of the TRD rates between CRT alone versus CRT plus surgery. Based on the experience in these RCTs, we may say that proper D2 dissection is technically demanding surgery, requiring experience and specific postoperative care, and it should be carried out at specialist centers in the west.

In the Dutch trial, D2 started with a handicap of about 6%, within 3 months, but caught up with the curve of D1,

Table 6. Morbidity and mortality after D2 dissection for gastric cancer

Trial	Type	Number of patients	Number of D2 dissections per hospital/year	Mortality	Morbidity	Reference
Hong Kong[12]	RCT	30	7.5	3%	57%	Ann Surg
MRC[7]	RCT	200	1.5	13%	46%	Lancet
Dutch[6]	RCT	331	1.0	10%	43%	Lancet
Italian[13]	Phase II	191	8.0	3%	21%	JCO
Sue-Ling[14]	Retrospective	142	14.2	5%	17%	BMJ
Pacelli[15]	Retrospective	157	15.7	4%	22%	Br J Surg

Table 7. Mortality after major postoperative complications

Complications	Dutch trial (n = 711)		NCCH (1980s) (n = 1197)		P Value
Leakage	19/46	41.3%	12/84	14.3%	0.0005
Distal	9/22	40.1%	2/23	8.7%	0.012
Total	10/24	41.7%	10/60	16.7%	0.0047
Abscess/pancreatic fistula	19/91	20.9%	2/75	2.7%	0.0004

Experience is needed to manage major adverse effects to avoid treatment-related deaths TRD, which occur slightly more often in surgery than in chemotherapy. Hospital volume is a concern

although the difference never reached statistical significance. The hospital mortality for D2 and D1 showed a large difference, at nearly 10% for D2, and 4% for D1. But this difference was seen only in male patients, in whom hospital mortality was 4.2% for D1 versus 14% for D2. There was no difference in mortality between D1 and D2 in female patients. Accordingly, the hazard ratio between D1 and D2 by time for each sex is completely different. In female patients, the hazard ratio is almost constant. The survival curves by procedure by sex are shown in Fig. 1. As we would expect, the survival curves of the female patients do not cross, as typical model curves of survival showing a constant hazard, and the P value is 0.04. We can confirm that high immediate mortality easily offsets the long-term effect of any cancer treatment.

Table 6 shows the relation between the hospital volume and the TRD rates in many trials or consecutive series of D2 dissection for gastric cancer. The Dutch and MRC trials show extremely low numbers of patients treated per year, per hospital, and show extremely high hospital mortality, compared with other reports.

Table 7 shows the mortality after major complications, comparing the results of the Dutch trial and those of the National Cancer Center Hospital (NCCH) in the 1980s.[1] Even in a high-volume hospital, major complications, such as anastomotic leakage or intraabdominal abscess, were not rare. However, in the Dutch trial, over 40% of patients died when they developed anastomotic leak, while only 14% of such patients died in the NCCH. As to mortality after abdominal abscess, a difference of nearly ten times was observed. Experience is needed to manage major adverse effects to avoid TRD, which occurs slightly more often in surgery than in chemotherapy or CRT. In this regard, hospital volume is a concern.

The Japanese perspective of the role of D2 dissection in multidisciplinary treatment for advanced gastric carcinoma can be summarized as follows. The superiority of D2 has not been proven by RCTs. But all RCTs so far have a crucial problem in regard to the quality of treatment given in the D2 arm. D2 is not a dangerous procedure if it is done by specialists in large-volume hospitals. D0/1 plus CRT is better than D0/1 alone, but it may be worse than D2 alone. The survival benefit of CRT after D2 is an open question. Establishing standard adjuvant chemotherapy after D2 is a more urgent clinical issue. There is no reason to abandon D2 gastrectomy for curable gastric cancer in Japan.

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Gastric cancer surgery in the elderly without operative mortality

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Abstract

Background: Surgeons are increasingly being faced with the problem of treating elder gastric carcinoma patients. Recent improvements in the techniques for preoperative diagnosis and perioperative management have been made. The purpose of this study was to elucidate whether these improvements have produced a decrease in postoperative complications and mortality and resulted in a better clinical outcome.

Methods: Between 1993 and 2003, 141 elderly patients (aged 80 years or above) with gastric cancer underwent operation under the care of dedicated staff surgeons. The results of treatment were analysed.

Results: 52 (36.9%) patients had a diagnosis of gastric cancer during a health-check. Only 19 patients (13.5%) had no preoperative risk factors. The ASA score was II in 80%. Approximately 35% of the patients had early gastric cancer. Nodal metastasis was observed in 56% of the patients. The proportion of stage I patients was 40%.

Resection rate was 95.7%. Reduced nodal dissection (<D2) was common (47%). The surgery-related complication rate was as low as 8% and the number of operation-related deaths was zero. The 3 (5) year survival rates were 59.0 (48.2–69.8), 48.8 (36.0–61.6) % overall, and 70.0 (58.3–81.7), 56.6 (41.4–71.8) % after curative resection. The 3 (5) year survival rate was 80.3 (63.9–96.7), 73.6 (54.0–93.2) % for early gastric cancer.

Conclusions: Gastrectomy for elder patients can be carried out very safely by specialists with an excellent patient prognosis.

Keywords: Gastric carcinoma; The elderly

1. Introduction

The Japanese population is ageing. Life-expectancy is currently 78.36 years for men and 85.33 years for women [1]. Despite a decrease in the incidence of gastric carcinoma, the number of patients aged 80 years and older (elder patients) with this disease is increasing. We previously reported the outcome of 112 elderly gastric cancer patients treated between 1971 and 1990 and showed gastric cancer surgery in elderly patients without co-morbidities was safe [2]. Since then, improvements have been made with regard to socioeconomic conditions, medical progress for perioperative care and operative apparatus, and preventive medicine. The purpose of this study was to elucidate whether these improvements have produced a decrease in postoperative complications and mortality, and resulted in a better clinical outcome.

2. Patients and methods

Out of 4395 patients with gastric adenocarcinoma who underwent laparotomy under our care (5 dedicated staffs, specialists in gastric cancer) between 1993 and 2003, 141 patients (3.2%) were 80 years of age and older. Since 2001, we have recorded every patient with gastric carcinoma who has visited our hospital. One hundred and seventy-two elderly patients with gastric carcinoma visited our hospital between 2001 and 2003. Sixty patients (35%) were operated upon by us and other 112 patients (65%) were treated either by

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endoscopic mucosal resection for early gastric cancer or best-supportive care for advanced tumours.

Curative operations were our aim, even in the elderly patients. However, we did try to perform limited dissection and to avoid total gastrectomy as long as curability was preserved [2].

Surgical specimens were examined and scored according to the Japanese Classification of Gastric Carcinoma [3]. Medical records were reviewed for preoperative medical conditions, further histological, and follow-up data. The latest follow-up was July 24, 2004. The conclusive physical status of patients and their surgical risks were classified according to the American Society of Anesthesiology classification of physical status (ASA class I–V). Survival rate was calculated using the Kaplan-Meier method with 95% Confidence Limits (CL).

3. Results

3.1. Patients' characteristics

The median age was 83 years (80–94 years). There were 95 male and 46 female patients. Eighty-nine patients (63.1%) visited hospital with symptoms. However, 52 (36.9%) patients had a diagnosis of gastric cancer during a health-check. Twenty patients (14.2%) were treated for other cancers before the diagnosis of gastric cancer. Median Body Mass Index (BMI) was 21.4 (11.7–32.5) Kg/m^2: BMI$<$20 ($n=50$), 20$\leq$BMI $<$24 ($n=62$), BMI$\geq$24 ($n=29$).

3.2. Preoperative morbidity (Table 1)

Table 1 Nineteen patients (13.5%) had no preoperative risk factors. Over 20% of the elderly patients had hypoalbuminaemia ($<$35g/l), and 16% had anaemia (haemoglobin $<$100 g/l). Electrocardiogram (ECG) abnormalities were detected in 55 patients (39.0%). Master's two-step exercise test was positive in 18 patients (12.8%). Abnormalities detected by echocardiography were mild in all cases. More than 35% of patients had abnormal respiratory function test. Fifty-seven patients (40.4%) had chronic diseases such as hypertension (22.7%), ischaemic heart disease (3.5%), and diabetes mellitus (9.9%). The ASA score was either II or III. in every patient.

3.3. Extent of tumour spread (Table 2)

Table 2 Approximately 35% of the patients had early gastric cancer. Nodal metastasis was observed in 56% of the patients. Distant metastasis was observed in liver up and peritoneum. We did not operate upon patients with

Table 1
Preoperative co-morbidities

	No. of patients	(%)
Hypoalbuminaemia Alb $<$35g/l	30	(21.3)
Anaemia Hgb $<$100 g/l	22	(15.6)
Abnormal heart evaluation		
ECG abnormalities	55	(39.0)
Master's two-step test-positive	18	(12.8)
Echocardiography		
Valve diseases	22	(15.6)
Low ejection fraction	3	(2.1)
Respiratory function test abnormal	53	(37.6)
Liver dysfunction	0	(0)
Creatinine clearance $<$ 0.83 ml/s	21	(14.9)
Hypertension	32	(22.7)
Ischaemic heart disease	5	(3.5)
Abdominal aorta aneurysm	3	(2.1)
Diabetes Mellitus	14	(9.9)
ASA score = III	28	(19.9)

ASA, see text for definition.

Table 2
Extent of tumour spread

	No. of patients	(%)
Depth of tumour invasion		
T1	50	(35.5)
T2	28	(19.9)
T3	49	(34.8)
T4	14	(9.9)
Nodal involvement		
N0	62	(44.0)
N1	34	(24.1)
N2	33	(23.4)
N3	12	(8.5)
Peritoneal seeding		
P0	134	(95.0)
P1	7	(5.0)
Liver metastasis		
H0	137	(97.2)
H1	4	(2.8)
Other distant metastasis		
M0	141	(100)
M1	0	(0)
Lavage cytology		
CY0	125	(88.7)
CY1	16	(11.3)
Stages		
IA	44	(31.2)
IB	13	(9.2)
II	21	(14.9)
IIIA	20	(14.2)
IIIB	13	(9.2)
IV	30	(21.3)