Lymphadenectomy for gastric cancer: still a matter of debate?

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BACKGROUND: *For more than a century the extent of surgical treatment of gastric cancer is a matter of debate. Through experience, evaluation and research, the outcome of gastric cancer has improved. Many aspects are of influence of outcome, but only a radical resection can offer long-term outcomes. In this review, we will discuss the history and current status of the extent of lymph node dissection.*
MATERIALS AND METHODS: Some *issues about the extent of gastric resection seem to have been settled. For survival it is not necessary to perform a total gastrectomy if free resection margins can be obtained with a subtotal gastrectomy. In the context of postoperative morbidity and mortality a subtotal gastrectomy is to be preferred. Microscopic resection line involvement has shown to be of great influence on prognosis.*
DISCUSSION: *At this moment the main discussion centres around the extent of lymph node dissection, locoregional recurrence and to the influence of additional treatment. For many years it has been debated whether an extended lymph node dissection for gastric cancer is beneficial. Theoretically, removal of a wider range of lymph nodes by extended lymph node dissection increases the chances for cure. Such resection, however, may be irrelevant if there are no lymph nodes affected or if the cancer has developed into a systemic disease, or if it increases morbidity and mortality substantially.*
CONCLUSION: *Relapse after curative surgery because of local recurrence or regional lymph node metastasis have been shown in up to 87.5% of patients. The extent of surgery, however, may be of influence on the locoregional recurrence rate.*

KEY WORDS: Gastric Cancer, Lymphadenectomy, Surgery

Extent of lymphadenectomy: Western vs Eastern results

The Japanese Research Society for the Study of Gastric Cancer (JRSGC) has provided guidelines for the standardization of surgical treatment and pathological evaluation [6]. These guidelines are also recommended by the American Joint Committee on Cancer (AJCC) and the International Union Against Cancer (UICC) in their fourth manual for staging of cancer [7,8]. According to these guidelines, 16 different lymph node stations are identified surrounding the stomach (Fig. 1). In general, the perigastric lymph node stations along the lesser (stations 1, 3, and 5) and greater (stations 2, 4, and 6) curvature are grouped N1, whereas the nodes along the left gastric (station 7), common hepatic (station 8), celiac (station 9), and splenic (stations 10 and 11) arteries are grouped N2. Minor modifications from this schedule occur depending on the location of the tumour. Further lymph node dissections of stations 13–16 (N3 and N4) are also described. Lymph node dissection is classified accordingly, D1–D4. A D1 dissection entails removal of the involved part of the stomach (distal or total), includ-

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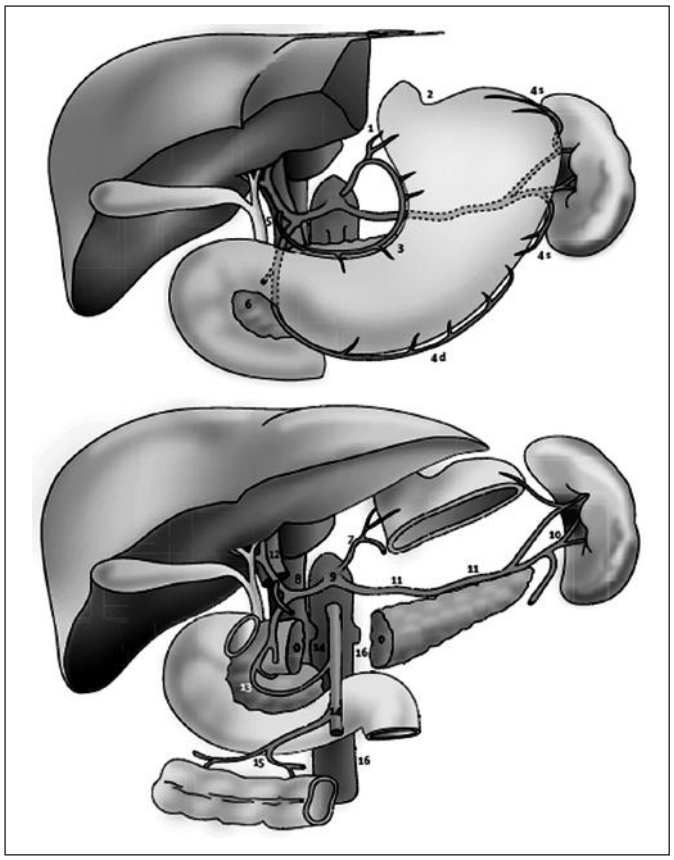

Fig. 1: Right cardial nodes; 2: left cardial nodes; 3: nodes along lesser curvature; 4s and 4d: nodes along greater curvature; 5: suprapyloric nodes; 6: infrapyloric nodes; 7: nodes along left gastric artery; 8: nodes along common hepatic artery; 9: nodes around celiac axis; 10: nodes at splenic hilus; 11: nodes along splenic artery; 12: nodes in hepatoduodenal ligament; 13: nodes at posterior aspect of pancreas head; 14: nodes at root of mesenterium; 15: nodes in mesocolon of transverse colon; 16: paraaortic nodes.

ing greater and lesser omentum. The spleen and pancreas tail are only resected when necessitated by tumour invasion. For a D2 dissection, the omental bursa is removed with the front leave of the transverse mesocolon, and the mentioned vascular pedicles of the stomach are cleared completely. Resection of the spleen and pancreatic tail was initially regarded necessary to achieve adequate removal of D2 lymph node stations 10 and 11 in proximal tumours, but spleen- and pancreas-preserving lymphadenectomies have become standard.

As standard treatment of gastric cancer in the Western world for many years, a total or subtotal gastrectomy was used, with more or less complete removal of omentum and perigastric lymph nodes (D1 dissection). Hospital mortality, most often defined as death within 30 days postoperatively, has decreased over the years. Before the 1970s a median mortality rate of 15% was reported, but in the decade before 1990 this decreased to 4.6% [9]. The 5-year survival in curative resections also improved in these years from 38% before 1970 to 55% in the decade before 1990 [10]. A survey by the American College of Surgeons showed a 77.1% resection rate in 18,365 patients, with a postoperative mortality rate of 7.2% and 5-year survival rate of 19%. Only 4.7% of these were D2 dissections. Stage-related 5-year survival rate was 50% for stage I, 29% for stage II, 13% for stage III and 3% for stage IV [11].

From Japanese centres, 5-year overall survival rates above 50% are reported, and rates above 70% are reported for curative resections, whereas hospital mortality is approximately 2% [10, 12, 13]. In a recent randomised trial between D2 and D4 resection a postoperative mortality rate of 0.8% for both groups is reported [14]. Japanese National stage-related 5-year survival rate is reported 96.6% for stage I, 72% for stage II, 44.8% for stage III, and 7.7% for stage IV [13]. Differences in surgical techniques are in part responsible for these better outcomes. In Japan more often a total gastrectomy in combination with en bloc resection of adjacent organs is performed compared to Western countries as well as a standard extended lymph node dissection. This aggressive approach is believed by the Japanese to be the main explanation for the difference in stage-specific survival [15-18]. Other factors contribute, however, such as a lower age of Japanese patients, less systemic (e.g., cardiovascular) disease, less obesity, earlier diagnosis also due to screening programs, stage migration, and a more aggressive chemotherapy policy in Japan. The extent of surgery will especially be of influence on locoregional control. In Dutch trial locoregional recurrence was registered in 58% of the D1 group and in 45% of the D2 group after 11 years. In a Japanese study with extensive surgery (D2 or more) a local recurrence rate of less than 1% has been reported [19].

In the last decade D2 dissections have become more popular in Western countries as well. Non-randomised gastric cancer studies from Germany, England, Norway, Italy, and the United States have reported postoperative mortality rates between 3% and 8%, morbidity rates between 22% and 38%, and 5-year survival rates between 26.3% and 55% for D2 dissections [20-26].

The variability in outcomes is substantial, likely because of the different definitions of D2 dissections in most series and the abandonment of pancreatico-splenectomy in latter series. Comparison with patients who had a limited (D1) lymph node dissection (usually in historical comparison) all contain a large selection bias. Nevertheless they showed better results for D2, although morbidity rates seemed to be higher. D2 dissection thus appears to improve survival even in Western countries, but results are still not near to those reported by the Japanese.

Randomized trials

Based on these retrospective data, four randomised studies comparing D1 and D2 dissections have been conducted [27-30].

The first was by Dent et al. [27], who described a selected group of only 43 patients. In 21 D2 dissections there was no hospital mortality, but morbidity, hospital stay, and blood transfusion requirement was significantly higher in comparison with the D1 dissection group. There was no difference in survival between both groups.

A randomised study by Robertson et al. [28] that included 55 patients was set up to determine the difference in outcomes between a D1 subtotal gastrectomy with omentectomy (n° 25) and a D3 total gastric resection including pancreatico-splenectomy (n° 30) in patients with adenocarcinoma of the gastric antrum. Postoperative death occurred only in one patient in the D3 group due to abdominal sepsis. Morbidity for extended resections increased significantly because half of the patients with D3 dissections developed a subphrenic abscess. Survival was significantly better for patients with a D1 dissection compared with those who had a D3 resection. In both studies there was no benefit from more extended resections.

Recently two large randomised multicentre studies comparing D1 and D2 dissections have been published: the Dutch Gastric Cancer Trial (DGCT) [29] and the British Medical Research Council Gastric Cancer Surgical Trial (MRC) [30].

In the British MRC Gastric Cancer Surgical Trial [29] D1 dissection was compared with D2 dissection in a prospective randomised trial. Central randomisation followed a staging laparotomy. Out of 737 patients with histologically proven gastric adenocarcinoma registered, 337 patients were ineligible by staging laparotomy because of advanced disease and 400 were randomised (200 D1 and 200 D2). Postoperative mortality was significantly higher in the D2 group (13% vs. 6.5% for D1; P = 0.04). Postoperative complications also were significantly higher in the D2 group (46% vs. 28% for D1; P < 0.001). In this study anastomotic leakage (26% vs. 11% for D1), cardiac (8% vs. 2% for D1), and respiratory (8% vs. 5% for D1) complications were most frequent. The 5-year survival rates were 35% for D1 and 33% for D2 dissections. Long-term follow-up results from this study have not yet been reported.

In the Dutch Gastric Cancer Trial [30] 80 hospitals participated to compare morbidity, hospital mortality, survival and cumulative relapse risk after D1 or D2 lymph node dissection for gastric cancer. Between 1989 and 1993, 996 patients were centrally randomised of whom 711 patients (380 D1 and 331 D2) underwent the allocated treatment with curative intent, and 285 patients required palliative treatment. For definition of D1 and D2 dissection the guidelines of the JRSGC were used. Because these guidelines were not regularly used in The Netherlands a Japanese surgeon, experienced in the treatment of gastric cancer was invited to instruct the participating Dutch surgeons. If lymph nodes were harvested from stations that were not supposed to be present according to protocol, this was called contamination. If lymph nodes were not harvested from stations that should have been harvested this was called non-compliance. These differences from the study protocol could occur in both D1 and D2 patients. Especially contamination in the D1 group and non-compliance in the D2 group could lead to decreased distinction between the trial arms. Contamination occurred in 6% of the D1 dissections, whereas non-compliance occurred in 51% of the D2 dissections. The reason for this relative high non-compliance rate is that pathologists at the beginning of the trial were not used to the separation of lymph node stations from the specimen according to the Japanese guidelines. This was adjusted in the course of the trial. This once more indicates that quality control is of utmost importance in surgical trials. After curative resection, D2 patients had higher postoperative mortality (10% vs. 4% for D1; P=0.004). They also had significantly more complications (43% vs. 25% for D1; P<0.001) which led to significant prolonged hospital stay for patients with a D2 dissection. Haemorrhage (5% vs. 2% for D1), anastomotic leakage (9% vs. 4% for D1), and intra-abdominal infection (17% vs. 8% for D1) were the most frequent complications. Five year survival rates were not different: 45% for D1 patients and 47% for D2 patients. In the most recent evaluation the median follow-up for all eligible patients is 11 years (range: 6.8–13.1 years). Four hundred eighty patients (68%) are now deceased, 35% without and 65% with recurrent disease. At 11 years, survival rates are 30% for D1 and 35% for D2 (P= 0.53). The risk of relapse is 70% for D1 and 65% for D2 (P= 0.43). If hospital deaths are excluded, survival rates are 32% for D1 (n° 365) and 39% for D2 (n° 299, P= 0.10). The relapse risk of these patients (n° 664) is in favour of the D2 dissection group (P=0.07). In an univariate analysis of all 711 patients, for none of the subgroups based on the selected prognostic variables was a significant impact found on survival rates between D1 and D2 dissection. Analysis of interaction between covariates and lymph node dissection shows no significance. The only subgroup with a trend to benefit is the N2 disease group. If patients with hospital mortality are excluded, there is a significant survival and relapse advantage for patients with N2 disease who had a D2 dissection (P=0.01). Other stages show no significant difference (N0 P=0.42; N1 P=0.31; N3 P=0.24) in this subset analysis. Furthermore there is no difference in survival after 11 years whether <15 lymphnodes, between 15 and 25 lymph nodes or more than 25 lymph nodes are harvested.

It is obvious that these only two major randomised trials, the MRC and the DGCT, show the same tendency. Although there was a difference in timing of randomisation, and although there was no quality control in the British trial, the postoperative mortality and morbidity in both trials were significantly higher in the D2 dissection group. Furthermore in both studies there was no 5-year survival advantage for extended (D2) dissections.

From these randomised studies it was concluded that there generally is no support for the standard use of extended (D2) lymph node dissections in Western patients with gastric cancer.
Despite these results, interest in extended lymph node dissections (D2 and greater) has not waned [31]. Investigators have argued that if the complication rate after a D2 dissection could be decreased then there may be a benefit in selected patients. A surgical option that may decrease morbidity and mortality is a modified D2 lymphadenectomy without pancreatectomy and splenectomy (32-35).
In Italy a D1–D2 study is recently completed [36]. The reason to conduct this study was based on one of the main comments on the Dutch and English trials. Namely that too many centres with too little volume and experience in gastric cancer were involved. In a multicentre phase II study, after the experience of the participating centres was optimised, from 1994 to 1996 the efficacy of D2 dissections was evaluated. A main difference from the randomised trials, however, was that a pancreas-preserving D2 dissection was performed. Of 191 participating patients from nine centres (18 surgeons), 20.9% experienced a postoperative complication and 3.1% died postoperatively [36]. From 1998 to 2002 this phase II trial was followed by a randomised D1–D2 trial with five of the previous nine participating centres. An interim analysis was published [37]. Of 162 randomised patients (D1: 76, D2: 86) morbidity was 10.5% and 16.3% respectively (P = 0.29) and mortality 1.3% and 0% respectively. For this study survival results have to be awaited.
In a recently published randomized clinical trial by Degiuli et al. [38], 267 patients with gastric cancer were randomly assigned to either a D1 or a D2 procedure in five specialized centres based on the findings of the phase II trial and published phase III trials, a prespecified non-inferiority boundary at 12 per cent difference between groups was set regarding total morbidity. In the intention-to-treat analysis, the overall morbidity rate after D2 and D1 dissections was 17.9 and 12.0 per cent respectively (P = 0.178), with a 95 per cent confidence interval of the difference of 0 to 13.0 per cent, slightly exceeding the prespecified non-inferiority limit. There was a single duodenal stump leak in the D2 arm (0.7 per cent). The postoperative 30-day mortality rate was 3.0 per cent after D1 and 2.2 per cent after D2 gastrectomy (P = 0.722). Degiuli et al concluded that in specialized centres the rate of complications following D2 dissection is much lower than in published randomized Western trials. D2 dissection, in an appropriate setting, can therefore be considered a safe option for the radical management of gastric cancer in Western patients.
A single-centre randomised trial [41] comparing D1 and D3 dissections was the first to identify a difference (p = 0.041) between overall survival in D1 dissections (53.6%; 95% CI 44.2–63.0) and D3 dissections (59.5%; 95% CI 50.3–68.7). No postoperative deaths occurred and morbidity was 12%. Only 13% of patients in this study had pancreatico-splenectomy compared with 23% in the Dutch gastric cancer trial.
In Japan a recently randomised trial between D2 and D4 dissection (n° 523 patients) was completed .[42] Postoperative mortality in this trial was 0.8% in both arms. The 5-year overall survival rate was 69.2% for the group assigned to D2 lymphadenectomy alone and 70.3% for the group assigned to D2 lymphadenectomy plus PAND; the hazard ratio for death was 1.03 (95% confidence interval [CI], 0.77 to 1.37; P = 0.85). There were no significant differences in recurrence-free survival between the two groups; the hazard ratio for recurrence was 1.08 (95% CI, 0.83 to 1.42; P = 0.56).
Authors concluded that as compared with D2 lymphadenectomy alone, treatment with D2 lymphadenectomy plus PAND does not improve the survival rate in curable gastric cancer.
A meta-analysis of non-randomised and randomised studies could not show any survival benefit from extended lymph node dissections. [41] The risk ratio for survival in the randomised studies was 0.95 (95% confidence interval (CI), 0.83–1.09) and was 0.92 in the nonrandomised studies (95% CI, 0.83–1.02).
In a recent analysis involving patients from the Intergroup 0116 adjuvant chemoradiation trial, Enzinger and colleagues assessed the impact of hospital volume on the outcome of patients who underwent lymphadenectomy [42]. Patients were stratified into two groups: those who underwent D0 dissection (54%) and those who underwent D1 or D2 resection (46%). For patients who underwent D0 dissection, high-volume centers did not have any effect on overall or disease-free survival. However, there was a trend toward improved overall survival among patients who underwent D1 or D2 dissection at moderate to high volume cancer centers.
A recent retrospective analysis has shown that more extensive lymph node dissection influences survival in patients with advanced gastric cancer [43]. This analysis included 1,377 patients diagnosed with advanced gastric cancer in the Surveillance Epidemiology and End Results (SEER) database. Patients who had more than 15 N2 nodes and more than 20 N3 nodes examined had the best long-term survival outcomes.

Lymph Node ratio

The ratio between metastatic and examined lymph nodes (N ratio) has been recently proposed [44-46] as a novel prognostic factor that can identify prognostic subgroups among patients with N1 and N2 disease, and reduce the phenomenon of stage migration. The ratio between positive and examined lymph nodes has been proposed as a simple, convenient and reproducible system that can

be used to better identify subgroup of gastric, breast, and colon cancer patients with similar prognosis, thus minimizing the stage migration phenomenon that can be observed using the current TNM staging system.

The actual TNM staging system edited by the AJCC and UICC states that "the complete pathologic assessment of the regional lymph nodes (pN) ideally entails removal of a sufficient number of lymph nodes to evaluate the highest pN category"; hence, the minimum number of assessed regional nodes after gastric cancer resection should be equal or greater than 15. The TNM staging system also suggests that "if pathologic assessment of lymph nodes reveals negative nodes but the number of examined lymphnodes is smaller than the suggested number for lymph node dissection, classify the N category as pN0" [47].

Limited lymphadenectomy frequently leads to the retrieval of a number of lymph nodes that is well below the minimum requirement according to the AJCC/UICC proposal [12] and it frequently happens in community hospitals of Western countries [48-50].

During the last decade several studies evaluated the prognostic impact of the ratio between the number of positive nodes and analyzed nodes (N ratio) in gastric cancer and up to now all supported the simplicity, reproducibility, and value of this staging system [44, 45, 51]. The main advantages of the N ratio are that it is much less influenced by the extent of lymphadenectomy and that the "stage migration" phenomenon is rarely observed when this classification is adopted [52-53]. This was stated to occur also when the number of retrieved lymph nodes was fewer than 15 [44, 46, 53]. Nonetheless, the vast majority of these studies were carried out in specialized centers where an extended lymphadenectomy was usually performed. As a consequence, high numbers of retrieved lymph nodes were normally reported and cases with fewer than 15 nodes examined were frequently excluded [46-53].

The Italian Research Group for Gastric Cancer (IRGGC) reported the results of a multicenter study on 1853 patients, among which 432 patients had fewer than 15 nodes analyzed. In that study, the N ratio was confirmed to be a simple and reproducible prognostic tool that allows stratification of gastric cancer patients who underwent limited lymph node dissections. Even in this experience, D2 lymphadenectomy was performed in more than 40% of the patients and the median number of retrieved nodes was 11 [51].

Sentinel Lymph Node (SLN) identification for gastric cancer

SLN identification may have a select role for gastric cancer patients. The overall premise is that using the injection of a dye or radioactive tracer, the first possible site of metastasis from the primary tumor is identified, thereby allowing more detailed inspection of the LN most likely to be involved with cancer. There is no standardized approach, with groups reporting the cancer is injected, endoscopically [54] or intra-operatively [55], in either the sub-mucosa [54] or subserosa [55], with 2% patent blue dye [55], 1% isosulfan blue [55], technetium-99m Sn colloid [54], or combination of dye and radio-labeled tracers[57], identified either by direct visualization or a hand-held gamma probe, depending upon the tracer used. These groups have reported an average of 1.5-4.1 SLN detected with a sensitivity of 72.7-93%, a specificity of 75% and an accuracy of 74-100% [54-57], but a negative predictive value of 50% [55]. The stage of the cancer may influence the sensitivity and specificity of the technique because of the pre-test probability of having a positive LN to be identified. As well, in cases of patients with clinically positive LN there may be false negative SLN, as the cancer has completely obstructed the lymphatics, causing the tracer to flow to second level (negative) nodes [57].

The utility of the SLN in influencing patient care has not yet been established. In areas with advanced presentation of gastric cancer, the high rate of nodal involvement may negate any usefulness for this technique. However, within more advanced gastric cancer cases, SLN identification may allow the pathologist to more closely inspect select LNs, resulting in more patients being accurately staged. Additionally, one report stated that in 38 patients, 1,251 LNs were identified by palpation alone, with an additional 1,004 detected based on staining with methylene blue dye [58]. On the other hand, in regions with a screening program and presentation of the disease at early stages, identification, and examination of sentinel nodes may allow for selection of node negative patients for less invasive and less aggressive surgical resections, such as laparoscopic wedge resections for T1N0 cases, which may have fewer complications and better quality of life [55]. In early gastric cancers, recurrence was 1.8% in node negative patients and 9.5% in node positive patients [59]. Thus, more thorough examination of SLN may allow detection of node positive patients, influencing decisions for adjuvant therapy.

Importance of lymph nodes on treatment decisions for gastric cancer

Within the past 7 years, multi-disciplinary care has become more complex. In 2000, the first RCT evidence of benefit of treatment of gastric cancer using a combination of chemotherapy and radiation following surgery was released from the INT-0116 trial [49]. Following surgery, patients were randomized to no further treatment versus 5-FU and 4,500 cGy of radiation. The median survival was 27 months for the surgery group and 36 months for the chemoradiation group. There was a 1% death rate in the chemoradiation group [49]. The protocol was open to Stage Ib through IVM0 patients,

excluding T1N0. Given this requirement, up to 11% of patients may be incorrectly denied adjuvant chemoradiation since the vast majority of patients in the US have inadequate LN staging [60]. Furthermore, many experts have argued against the wide-spread adoption of the INT-0116 adjuvant chemoradiation protocol [61], because at least 54% of the patients were treated with a D0 lymphadenectomy, while 36% received a D1 and only 10% a D2 lymphadenectomy [49]. Critics of adoption of the INT-0116 protocol suggest that the addition of adjuvant chemoradiation confers the same survival benefit as an adequate LN dissection, by compensating for the lack of clearance of nodal basins [61]. The rate of local, regional, and distant recurrence were 29%, 72%, and 18% for the surgery only group, and 19%, 65%, and 33% for the surgery and chemoradiotherapy group for the INT-0116. It is hypothesized that the increased rate of distant relapses is perhaps due to a longer survival time in the treatment arm of the INT-0116 trial [61]. However, these arguments against the INT-0116 protocol are not supported by a large non-randomized trial conducted in Korea, following a D2 resection, in which adjuvant chemoradiation also appeared to improve survival [62].

In 2003, results from another RCT (the Medical Research Council Adjuvant Gastric Infusional Chemotherapy or MAGIC Trial) showed survival benefit for patients receiving chemotherapy prior to and after surgery [63]. Patients were randomized to either surgery alone or three cycles of pre-operative epirubin, cisplatin, and infused fluorouracil (ECF), then surgery, followed by three more cycles of ECF chemotherapy. The MAGIC trial showed a significant survival benefit (P = 0.009) despite the fact that only 41.6% of patients in the treatment arm were able to complete the chemotherapy regimen. The trial also showed significant shrinkage of the tumor for the chemotherapy arm (3 cm vs. 5 cm, P<0.001) and a trend for less advanced nodal disease (84.4% vs. 70.5%, P = 0.01) [63]. A more recent trial also demonstrated improvement in overall survival for patients treated with adjuvant chemotherapy (S-1) versus surgery alone [64]. Importantly, these two trials show that there does appear to be a significant benefit to adjunct chemotherapy, even within cohorts of patients who have had a D2 LN dissection. The MAGIC [63] and the S-1 [64] trials had 68% and 100% of patients with a D2 resection, respectively. Therefore, there is increasing support for adjuvant therapy, even in patients with aggressive surgical control [63].

In any case, investment in more adequate surgery is better and more cost effective than adjuvant treatment to compensate inadequate surgery. If, however, inadequate surgery has been performed adjuvant chemoradiotherapy may be of value.

In complex cases that may require multi-visceral resection, or extension of resection due to positive margins, LN status may be useful for determining the best surgical options. In analysis of 2,740 resected cases from Korea, 49 had a positive margin on final histology; survival time was similar (P=0.259) for positive (33 months median survival) and negative (37 months median survival) margin patients with node positive disease. In node negative patients, however, median survival was 174 months for negative margin resections and 37 months for patients with positive margins (P<0.0001), prompting the authors to conclude that more aggressive treatment, including reoperation, should be offered only to node negative patients with positive microscopic margins [63]. Kim et al. [66] published similar findings: of D2/D3 dissection patients who had fewer than 6 LN involved with tumor, survival was significantly worsened by a microscopically positive margin. Furthermore, in patients with an intra-operative reexcision based on an involved margin on frozen section, survival was improved for patients with five or fewer LN involved, but not for patients with more than five LN involved with tumor [66]. Regarding multi-visceral resections to obtain R0 resections, Martin et al. [67] found that the number of organs resected en bloc with the gastrectomy
was the major predictor for severe complications. Significant predictors of survival were T-stage, N-stage, and female sex, with a non-significant trend toward worse survival in patients with more
organs resected [68]. Thus, nodal status may be a more important determinant of survival than R0 resection, especially if patients have $\geq$ 5 LN involved with tumor, and this factor should be considered prior to re-excision, or more aggressive resection in order to obtain negative margins.

Conclusion

Nodal status is one of the most important independent predictors of gastric cancer patient survival. Ongoing RCT studies may further clarify the benefits of an aggressive LN dissection and any long-term benefits. Further investigation is needed to determine if the benefit is conferred by removing more LNs, or by having surgery within a system that performs appropriate staging, and perhaps other parts of patient care. Regardless, given the higher rate of complications associated with a more aggressive resections, it should be advocated that the procedure be performed by experienced surgeons.

Furthermore, adequate training for surgeons performing aggressive lymphadenectomies should be standardized.

Riassunto

L'entità della linfadenectomia nel trattamento chirurgico del cancro dello stomaco è una questione di dibattito da oltre un secolo. Attraverso l'esperienza clinica, i trattamenti integrati e la ricerca traslazionale, la prognosi del cancro gastrico è notevolmente migliorata.

Alcune questioni circa l'estensione della resezione gastrica sembrano essere state risolte. È stato dimostrato che ai fini della sopravvivenza non è necessario eseguire una gastrectomia totale, se i margini di resezione liberi possono essere garantiti attraverso una gastrectomia subtotale [1-3], inoltre per quanto riguarda la morbilità e la mortalità postoperatoria una gastrectomia subtotale è sempre da preferire [1].
È stato inoltre ampiamente dimostrato che l'interessamento microscopico del margine di sezione riveste un ruolo prognosticamente sfavorevole [4].
Attualmente la discussione principale ruota attorno l'entità della dissezione linfonodale, la recidiva loco-regionale e l'influenza dei trattamenti supplementari.
Per molti anni si è discusso se una estesa linfoadenectomia per il cancro gastrico sia vantaggiosa.
Teoricamente, la rimozione di un numero maggiore di linfonodi aumenta le probabilità di guarigione [5]. Una dissezione importante, tuttavia, può essere irrilevante se non ci sono linfonodi interessati o se il tumore risulti già in una fase sistemica, o se aumenta la morbilità e la mortalità in modo sostanziale.
L'estensione della chirurgia, tuttavia, può rivestire un ruolo prognosticamente favorevole in termini di minor tasso di recidiva loco-regionale.

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