D2 vs D2 Plus Para-aortic Lymph Node Dissection for Advanced Gastric Cancer

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ABSTRACT

Objective: Gastric cancer is a common malignancy worldwide. Effective treatment by interdisciplinary cooperation is important and surgery still plays an important role.

Material and Methods: In a ten years period 355 patients were diagnosed to have gastric cancer. 162 patients with median (range) age of 58 (23-83) years were eligible for study. There was 107 patients in D2 and 55 patients in D2 lymphadenectomy plus para-aortic lymph node (PALN) dissection group. Two groups were compared in terms of complications, morbidity, mortality and long-term survival.

Results: The duration of the stay was 12 (8-34) days for D2 and 14 (8-42) days for D2 plus PALN. The total number of operative mortality was 8/162 (5%) and it was not different between the groups. 20 patients (18%) had complications in D2 group and 9 (17%) patients in D2 plus PALN group. Overall survival was also similar between the groups but patients with T3-T4 tumors, patients with stage IIa and IIIB disease and patients with higher ratio of PLN/TLN had better survival with D2 plus PALN dissection. We found that the depth of invasion, PLN, ratio (PLN/TLN), stage and LND were all independent prognostic variables.

Conclusion: This study has shown that D2 plus PALN dissection and for advanced gastric cancer can be performed as safely as a standard D2 dissection by experienced surgeons without increasing postoperative morbidity and mortality. D2 plus PALN dissection should be preferred in an advanced stage of the disease (IIIA-IIIB) as it increases the rate of survival.

Keywords: advanced gastric cancer, d2 lymphadenectomy, d2+paln lymphadenectomy, morbidity, mortality, prognosis

INTRODUCTION

Gastric cancer is a common malignancy worldwide, and the 5-year survival rate in patients with gastric cancer is still poor despite improved survival due to early detection, rational lymphadenectomy and several therapeutic modalities (1). Effective treatment by interdisciplinary cooperation is important and surgery is currently considered the best manner to treat gastric cancer. The extensiveness of lymph node dissection is, however, unclear, and there is no worldwide consensus (2, 3, 4, 5, 6, 7, 8). Extended (D2-3) lymph node dissection has improved survival in Japan (7, 9, 10). However, the results of European studies are somewhat controversial (11, 12, 13, 14, 15, 16, 17, 18).

Japanese surgeons first introduced the extended lymphadenectomy procedure, known today as D2, in the 1960s (19). This technique requires the systematic dissection of lymph nodes in the first tier (perigastric) and the second tier (along the celiac artery and its branches) (20). Superextended lymph node dissection (D3 dissection) has been used in advanced forms gastric cancer in many Japanese centers with the aim of eliminating metastatic lymph nodes, not only in the first and second tiers, but also in the third tier (around the upper abdominal aorta) (21).

D2 dissection for gastric cancer is a standard surgical procedure in Japan and is associated with excellent early and late results (20, 22), whereas it is still controversial in the West (23). All four randomized Western trials failed to show any survival benefit for D2 dissection while finding an association between D2 dissection and increased morbidity and mortality (11, 12, 17, 18, 24), although D2 dissection is already accepted as the standard procedure for resectable gastric cancer in many countries (13, 25, 26).
Success with D2 resection has led to the evolution of a superextended lymphadenectomy and several feasibility studies evaluating dissection of para-aortic lymph nodes have been performed (6, 21, 27, 28, 29). This procedure is performed by selected centers and D3 dissection has been practiced to improve the survival for advanced gastric cancer in this centers (21, 29, 30, 31).

Very few studies from Western centers have compared D2 and D3 dissection in surgical treatment of gastric cancer (32, 33, 34).

In the present study, we aimed to assess the value of radical surgery in gastric cancer by comparing D2 and D2 lymphadenectomy plus para-aortic lymph node (PALN) dissection.

PATIENTS AND METHODS

A prospective trial was designed to compare the two surgical techniques: the extended lymphadenectomy (D2) and the superextended lymphadenectomy (D2 plus PALN) for gastric cancer.

Patients

In a ten years period, 355 patients were admitted to our unit with a diagnosis of gastric adenocarcinoma.

The inclusion criteria for this study included: 1) patients who received curative resection; and 2) patients who underwent extended (D2) lymph node dissection, or superextended (D2 plus PALN) lymph node dissection.

The exclusion criteria included: 1) patients who received a palliative operation; 2) patients with distant metastasis; 3) patients with intraperitoneal dissemination; 4) patients with previous gastrectomies; and 5) patients with poor performance status.

Based on the inclusion and exclusion criteria, 193 patients were excluded from the study and 162 (107 male) of D2 and 41(12-98) for D2 plus PALN. PLN/TLN ratio was similar in both groups. 20 patients (18%) had complications in D2 group and 9 (17%) patients in D2 plus PALN group. The number of removed lymph nodes were related to dissection and it was 30(10-86) for D2 and 41(12-98) for D2 plus PALN dissection. PLN/TLN ratio was not different between the groups. 20 patients (18%) had complications in D2 group and 9 (17%) patients in D2 plus PALN group.

Evaluating of operative morbidity and mortality

Resected specimens were examined carefully for accurate pathologic staging according to the JGCA rules (35). The following information was included on the case report form for prospective data collection concerning the major groups of operative morbidity: anastomotic leakage, intraabdominal abscess, pancreatic fistula, pneumonia, and others (wound infection, wound dehiscence, pulmonary embolism, MI etc.). Hospital mortality was defined as postoperative death any cause within 30 days, death within the same hospitalization.

A follow-up of patients was performed according to our standard protocol (every 3 months for first 2 years and then every 6 months at least 5 years), which included tumor-marker studies, endoscopic examinations, ultrasonography, computed tomography, and chest radiography.

Two groups were compared in terms of complications, morbidity, mortality and long-term survival. Effect of the type of dissection as well as the diameter of the tumor, T-stage, number of total and positive lymph nodes (TLN and PLN) and survival according to tumor stage were also analysed.

Statistical Analysis

Statistical analysis was performed using SPSS version 17.0 for Windows. Comparisons of clinicopathological differences were made using a Chi-square test for discrete variables. Rate of occurrence of events were evaluated using Fisher’s Exact test. Cumulative survival rate were calculated by using the Kaplan-Meier estimation and examined by the log-rank test. Survival curves compared by Chi-square test. A P-values less than 0.05 was considered to be significant.

RESULTS

Patient demographics, complications and tumor characteristics are presented in Table 1. The two groups were well balanced, as there were no significant differences in their baseline data. The age and sex distribution of the patients were comparable in both groups. The duration of the stay was 12(8-34) days for D2 and 14(10-42) days for D2 plus PALN. The total number of operative mortality was 8/162 (5%) and it was not different between the groups. 20 patients (18%) had complications in D2 group and 9 (17%) patients in D2 plus PALN group. The number of removed lymph nodes were related to dissection and it was 30(10-86) for D2 and 41(12-98) for D2 plus PALN dissection. PLN/TLN ratio was similar in both groups (Table 1).

Table 1. Details of patients.
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| Variable            | D2 (n=107) | D2+PALN (n=55) | p     |
|---------------------|------------|----------------|-------|
| Age                 | 59.3 (23-83) | 58 (32-75)    | ns    |
| Sex (M/F)           | 76/31      | 40/15          | ns    |
| Complications       |            |                |       |
| Wound infection     | 20 (18%)   | 9 (17%)        |       |
| Leakage             | 4          | 2              |       |
| Abscess             | 4          | 2              |       |
| Wound dehiscence    | 2          | 1              |       |
| Pancreatic fistula  | 0          | 1              |       |
| Pneumonia           | 4          | 1              |       |
| Pulmonary embolism  | 1          | 1              |       |
| MI                  | 1          | 0              |       |
| Operative mortality | 5 (5.2%)   | 3 (4.9%)       | ns    |
| Hospital stay (day) | 12 (8-34)  | 14 (10-42)     | ns    |
| Tumor size (cm)     | 7.9 ± 3.4  | 7.1 ± 3.7      | ns    |
| TLN                 | 30 (10-86) | 41 (12-98)     | 0.02  |
| PLN                 | 4 (6)      | 7 (9)          | ns    |
| PLN/TLN             | 0.17 ± 0.3 | 0.17 ± 0.2     | ns    |
| Histologic type     |            |                |       |
| Diffuse             | 45         | 19             | ns    |
| Intestinal          | 53         | 29             |       |
| Unclassified        | 9          | 7              |       |
| Depth of invasion   |            |                |       |
| T1                  | 0          | 0              |       |
| T2                  | 28         | 14             | ns    |
| T3                  | 60         | 32             |       |
| T4                  | 19         | 9              |       |
| Stage grouping      |            |                |       |
| I                   | 0          | 0              |       |
| II                  | 29         | 14             |       |
| IIIA                | 38         | 18             |       |
| IIIB                | 35         | 18             |       |
| IVA                 | 5          | 5              |       |

Patients were followed up for a period of 75(22-130) months. We observed that better overall survival with D2 plus PALN than D2 (Figure 2). Patients with T3-T4 tumors (Figure 3-4) had better survival with D2 plus PALN dissection than D2 alone. Patients with Stage IIIA also had better survival with D2 plus PALN than D2.
We found that depth of invasion (T) (T small number 1,2 is better than 3,4), positive lymph node (LN(-) is better), lymph node ratio (PLN/TLN <0.2 is better than >0.3), stage (lower the stage better than 3,4), positive lymph node (LN(-) vs D2 plus PALN dssection for advanced gasrctc cancer)

**Figure 6.** Survival curves in patients with stage IIIB.

DISCUSSION

Gastric cancer still remains a major health problem, numerous aspects of surgical treatment still remain unresolved. Despite improvements in local control and empirical chemotherapy, prognosis particularly for advance stage patients remains poor worldwide. New therapeutic strategies are needed.

Treatment of advanced gastric cancer has become much more sophisticated and complicated than ever. New directions in cancer biology research and new randomized trials promise to reach the goal of an individualized approach (37, 38). Recently, the decision was reached that the only possibility for curative treatment of gastric cancer remains surgical resection. 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 (17, 39). Such resection, however, may be irrelevant if there are no lymph nodes affected, if the cancer has developed into a systemic disease, or if resection increases morbidity and mortality substantially (17, 39, 40). From this point of view, several studies have compared generally D1 dissection with D2 dissection (11, 12, 13, 24). However, only a few study have compared D2 dissection with D3 dissection (20, 27, 32, 33, 34, 36, 41, 42, 43). Therefore, in this study, we prospectively compared D2 dissection morbidity, mortality and outcome with those of D2 plus PALN dissection.

There is a wide variation in operative morbidity and mortality following gastric cancer surgery among countries and institutions (20). The presence of comorbid disease that affects patient fitness for surgery, surgical experience of the operator, and the workload volume seem to be important factors (20).

D2 dissection is a safe procedure in specialized centers, where it is associated with a low risk of postoperative complications and mortality (13, 25, 26, 44). The risk of complications can be reduced by avoiding resection of the pancreatic tail and spleen (14, 27). These associated procedures were strongest factors influencing morbidity and mortality in the two European randomized trials, without any offering any potential improvement in long-term survival (17, 18, 45). Recently, based on the results of British (12) and Dutch (11) trials, D1 gastrectomy has been routinely used for the treatment of gastric cancer in Western countries (43). These trials suggested that a high incidence of postoperative complications after D2 gastrectomy offset the more beneficial surgical results obtained with D2 surgery. However, in Japan, D2 gastrectomy is a accepted as the gold standard on the basis of abundant data (43). For gastric cancer, only potentially curative resection (R0) achieves good outcomes, and, in view of the distribution of lymph node metastases, D1 gastrectomy is insufficient for advanced gastric cancer (41). On the other hand, safety outcomes after more extended lymph node dissection (ie, D1 vs. D3, or D2 vs. D3) were analyzed in a few study (20, 27, 32, 33, 34, 36, 41, 42, 43, 46).

In JCOG9501 study (36) a total of 523 patients were assigned to compare the treatment of D2 versus D3 (D2 + PAN ) lymph node dissection. The results showed that the surgical mortality rate was very low in both groups (0.8%). No significant difference was found between the two treatment groups in terms of 5-year recurrence-free survival (62.6% vs. 61.7%, respectively), but the overall perioperative complication rate in the D3 group was higher than that in the D2 group (28.1% vs. 20.9%, respectively) (36). These trials showed that there were no significant survival rate benefit for performing PAN dissection in curable gastric cancer patients and simultaneously revealed its association to a higher surgical morbidity. They reported that gastrectomy with D2...
lymphadenectomy has been considered as the standard routine lymphadenectomy for locally advanced gastric cancer (36).

However, the effect of the D3 dissection on gastric cancer patients with PAN metastasis is still debatable (47). D3 lymphadenectomy may be beneficial in some patients with PAN metastasis, but more research is needed for appropriate patient selection.

Some studies have shown that incidence of metastasis to paraortic lymph node could be around 20% (48), and the 5-year survival rate for patients with para-aortic node metastasis who had undergone para-aortic node dissection could be up to about 20%. Therefore, the rationale of therapeutic para-aortic lymphadenectomy for advanced gastric cancer is suggested for further evaluations (48). D2 plus para-aortic lymphadenectomy after neo-adjuvant or conversion chemotherapy could be considered as a promising treatment for patients with para-aortic lymph nodes involved (48).

Bencivenga et al. (49) reported that, the debate concerning the role of “prophylactic” super-extended lymphadenectomy apparently came to an end after the publication of the JCOG 9501 trial that found no survival advantage when D2 lymphadenectomy was extended to PANs in patients with T2b, T3, and T4 gastric cancer (36). Consequently, prophylactic D2 plus PAN dissection is no longer recommended as a first-choice treatment for patients with curable gastric cancer in the Japanese guidelines. However, it should be remembered that the baseline prevalence of 16 metastases in that trial was rather low (8.5%), probably because it only enrolled patients without macroscopic metastases to PANs, and the control group underwent D2 lymphadenectomy extended to the posterior nodal stations (12p, 13, and 14v), which are not usually resected in the case of a conventional D2 (19).

Liang and Deng reported that (50), the following are indications for D2+PAND candidates: 1) patients in good condition with no serious organ dysfunction; 2) patients without peritoneal dissemination or liver metastases; 3) patients with pathologic N2, N3a and N3b stage disease or positive No.9 LN; 4) patients with Bormann type III/IV disease; and 5) patients with upper-middle third or occupied more than one-third. However, they recommend that D2+PAND should be carried out only in cancer centers equipped with surgeons with extensive experience for extended LN dissection, because there are some complications in rare situations, such as complications like formation of chylous fistula. In addition, multiple methods should be used in selecting the suitable cases for further study.

Dong and Deng also reported that (51), prophylactic D2 + PAND has not shown a survival benefit, but improved survival with therapeutic PAND may benefit from related clinicopathological factors. Then, based on the survival benefit of PAND, given that many clinicopathological factors were reported to be highly related to PAN involvement, it is necessary to verify the lymphatic flow to PANs in gastric cancer and define accurate predictors for PAN metastasis and then explore indications for PAND. To date, CS chemotherapy combined with surgery plus extensive lymphadenectomy is considered the standard treatment for advanced gastric cancer in Japan. Therefore, neo-adjuvant and adjuvant chemotherapy must not be ignored in the treatment of PAN metastasis. In the future, multimodal therapy including PAND combined with appropriate chemotherapy and with other therapies, such as conversion surgery or radiotherapy, remains to be evaluated in the form of a clinical trial to obtain improved prognosis and as few complications as possible (51).

A recent studies clearly showed that standard D2 and extended D3 dissection can be performed safely without any increase in postoperative morbidity and mortality (20, 41). Both the morbidity and mortality rates and the percentage of individual complications in our trial have shown no significant differences between the D2 and D2 plus PALN groups. Hospital stay was also similar both groups in our study. In the light of these results, we confirm that D2 plus PALN dissection may be performed in specialized centers with an acceptable operative risk.

In this study, we observed a positive linear correlation between removed lymph node and more extensive lymph node dissection (Table 1). Some authors have suggest that better disease control could be achieved through ‘inducing a reduction of metastatic nodes ratio’ just by extending the number of dissected nodes (13, 52, 53, 54). Schwarz et al. (55) believe that their results for a therapeutic benefit as a result of extended lymph node dissection, even in patients with more advanced yet resectable gastric cancer. They showed that stage-based survival prediction of advanced gastric cancer without distant metastases depends on total lymph node number and number of negative lymph nodes (55). Kunisaki et al. (43) also showed that the incidence of lymph node recurrence in the surgically dissected area was significantly lower in D3 patients. They suggest that D3 gastrectomy might be effective for metastatic lymph nodes in the para-aortic regions (43).

In our study, we also observed a positive relation between more lymph node positivity and T-stage. Shen et al. (56) showed that greater numbers of dissected lymph nodes could lead to a better prognosis in patients with pT3N2 disease and even in patients with pT3N3 disease. This findings indicates the important impact of thorough lymph node dissection on survival, even in patients with pT3N3 gastric cancer, who many believed had incurable disease (56).

Several papers have reported a correlation between survival benefits and D3 lymph node dissection (20, 32, 41, 43, 57, 58). Kunisaki et al. (43) suggest that D3 dissection may confer a survival advantage with respect to D2 dissection in patients with tumor diameters measuring 50-100 mm and pN2 disease.

In our survival analyses, we observed four three results: First, better overall survival with D2 plus PALN than D2. Second, better survival with D2 plus PALN in T3-T4 tumors. Third, better mean survival and 5-year survival in stage IIA – IIIB. This might imply that D2 plus PALN dissection does contribute to improved survival at advanced stage of gastric cancer.

In early stages of the disease D2 is safer and better, D2 plus PALN dissection be preferred in an advanced stage of the disease as it increases the rate of survival. Although D2 plus PALN patients had slightly longer hospital stay, extended lymph node dissection performed without any increase on morbidity and mortality.

We observed that depth of invasion (T), positive lymph nodes (PLN), lymph node ratio (PLN/TLN), stage and lymph node dissection are prognostic variables. From the all prognostic variables, only lymph node dissection influenced by the surgeon. Our results were in agreement with those of Japanese and support the efficacy of extended lymph node dissection in surgical management of gastric cancer for the Western patients as well.

In conclusion, this study has shown that D2 plus PALN dissection and for advanced gastric cancer can be performed as safely as a standard D2 dissection by experienced surgeons without increasing postoperative morbidity and mortality. D2 plus PALN dissection should be preferred in an advanced stage of the disease (IIIA-IIIB) as it increases the rate of survival.
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REFERENCES

1. Takagane A, Terashima M, Abe K, Araya M, Irimoda T, Yonezawa H, Nakaya T, Inaba T, Oyama K, Fujiwara H, Saito K. Evaluation of the ratio of lymph node metastasis as a prognostic factor in patients with gastric cancer. Gastric Cancer 1999; 2: 122-128.

2. Shimoyama S, Kaminishi M, Joujima Y, Oohara T, Harnada C, Teshigawara W. Lymph node involvement correlation with survival in advanced gastric carcinoma: univariate and multivariate analyses. J Surg Oncol 1994; 57: 164-170.

3. Kunisaki C, Shimada H, Yamaoka H, Wagauchi J, Takahashi M, Akyma H, Nomura M, Moriwaki Y. Significance of para-aortic lymph node dissection in advanced gastric cancer. Hepatogastroenterology 1999; 46: 2635-2642.

4. Mishima Y, Hirayama R. The role of lymph node surgery in gastric cancer. World J Surg 1987; 11: 406-411.

5. Maruyama K, Okabayashi K, Kinoshita T. Progress in gastric cancer surgery in Japan and its limits of radicality. World J Surg 1987; 11: 418-425.

6. Maeta M, Yamashio H, Saito H, Kato K, Kondo A, Tsujitani S, Ikeguchi M, Kaibara N. A prospective pilot study of extended (D3) and superextended para-aortic lymphadenectomy (D4) in patients with T3 or T4 gastric cancer managed by total gastrectomy. Surgery 1999; 125: 325-331.

7. Maehara Y, Kakeji Y, Koga T, Emi Y, Baba H, Akazawa K, Sugimachi K. Therapeutic value of lymph node dissection and the clinical outcome for patients with gastric cancer. Surgery 2002; 131: 85-91.

8. McCulloch P, Nitta ME, Kaza H. Gama-Rodriguez J. Gastroctomy with extended lymphadenectomy for primary treatment of gastric cancer. Br J Surg 2005; 92: 5-13.

9. Kasakura Y, Moroi F, Kakabayashi K, Kishi C, Fujii M, Takayama T. An evaluation of the effectiveness of extended lymph node dissection in patients with advanced gastric cancer: a retrospective study of 1403 cases at a single institution. J Surg Res 2002; 103: 252-259.

10. Adachi Y, Kitano S, Sugimachi K. Surgery for gastric cancer: 10-year experience worldwide. Gastric Cancer 2001; 4: 166-174.

11. Bonenkamp JJ, Songun I, Hermans J, Sasako M, Velwkaart K, Plukker JT, van Elk P, Obertop H, Gouma DJ, van Lanschot J, Taat CW, van Meyenfeldt MF, Tilanus H, Dutch Gastric Cancer Group. Extended lymph node dissection for gastric cancer: morbidity and mortality results from a prospective randomized controlled trial comparing D2 and extended para-aortic lymphadenectomy – Japan Clinical Oncology Group Study 9501. J Clin Oncol 2004; 22: 2767-2773.

12. Baba H, Yokita S, Natsugoe S, Miyazono T, Shimada M, Nakano S. Para-aortic lymphadenectomy in patients with advanced gastric carcinoma of the upper-third of the stomach. Hepatogastroenterology 2000; 47: 893-896.

13. Maruyama K, Sasako M, Kinoshita T, Sano T, Kato K. Surgical treatment for gastric cancer: the Japanese approach. Semin Oncol 1996; 23: 360-368.

14. Saegawa T, Solano H, Vega W, Mena F. The effectiveness of extended lymph node dissection for gastric cancer performed in Costa Rica under supervision of a Japanese surgeon: a comparison with surgical results in Japan. Ann J Surg 2008; 195: 53-60.

15. Dent DM, Madden M, Price SK. Randomized comparison of R1 and R2 gastrectomy for gastric carcinoma. Br J Surg 1988; 75: 110-112.

16. Roukos DH, Lorenz M, Karakostas K, Paraschos PF, Batis C, Kapnas AM. Pathological serosa and node-based classification accurately predicts gastric cancer recurrence risk and outcome, and determines potential and limitation of a Japanese-style extensive surgery for Western patients: a prospective with quality control 10-year follow-up study. Br J Cancer 2001; 84: 1602-1609.

17. Roviello F, Marelly D, Morgagni P, on behalf of the Italian Research Group for Gastric Cancer. Survival benefit of extended D2 lymphadenectomy in gastric cancer with involvement of second level lymph nodes: a longitudinal multicenter study. Ann Surg Oncol 2002; 9: 894-900.

18. Kodera Y, Sasako M, Yamamoto S, Sano T, Hashimoto A, Kunita A, on behalf of the Gastric Cancer Study Group of Japan Clinical Oncology Group. Identification of risk factors for the development of complications following extended and superextended lymphadenectomies for gastric cancers. Br J Surg 2005; 92: 1103-1109.

19. Kunisaki C, Shimada H, Yamaoka H, Takahashi M, Oookubo K, Akijama H. Indications for paraaortic lymph node dissection in gastric cancer patients with paraaortic lymph node involvement. Hepatogastroenterology 2000; 47: 586-589.

20. Isozaki H, Kajitani T, Arai K, Nomura E, Izumi M, Mabuchi H. Effectiveness of paraaortic lymph node dissection for advanced gastric cancer. Hepatogastroenterology 1999; 46: 549-554.

21. Yokemura Y, Katayama K, Kamata T, Fushida S, Segawa M, Oyama S. Surgical treatment of advanced gastric cancer with metastasis in para-aortic lymph node. Int J Surg 1991; 76: 222-225.

22. Kitamura M, Arai K, Iwasaki Y. Clinico-pathological studies on paraaortic lymph node metastasis and postoperative quality of life in gastric cancer patients. Jpn J Gastroenterol Surg 1995; 28: 923-926.

23. Marrelli D, Pedrazzani C, Neri A, Corso G, DeFeo A, Pinto E, Roviello F. Complications after extended and superextended lymphadenectomy in patients with advanced gastric cancer. J Clin Oncol 2007; 25: 25-33.
postoperative mortality and complications. Surg Today 2000; 30: 700-705.

34. Bostanci EB, Kayaalp C, Ozgul Y, Aydin C, Atalay F, Akgolu M. Comparison of complications after D2 and D3 dissection for gastric cancer. Eur J Surg Oncol 2004; 30: 20-25.

35. Japanese Gastric Cancer Association. Japanese gastric cancer treatment guidelines 2018 (5th edition). Gastric Cancer. 2020;10.1007/s10120-020-01042-y. doi:10.1007/s10120-020-01042-y.

36. Sasako M, Sano T, Yamamoto S, Kurokawa Y, Nashimoto A, Kuriata T, Hiratsuka M, Tsujinaka T, Kinoshita T, Arau K, Yamamura Y, Okajima K, & Japan Clinical Oncology Group (2008). D2 lymphadenectomy alone or with para-aortic nodal dissection for gastric cancer. The New England Journal of Medicine, 359(5), 453-462. https://doi.org/10.1056/NEJMoa0707035.

37. Briassoulis E, Liakakos T, Dova L, Fatouros M, Tsekens P, Roukos DH, Kappas AM. Selecting a specific pre- or postoperative adjuvant therapy for individual patients with operable gastric cancer. Expert Rev Anticancer Ther 2006; 6: 931-939.

38. Liakakos T, Roukos DH. More controversy than ever: challenges and promises towards personalized treatment of gastric cancer. Ann Surg Oncol 2008; 15(4): 956-960.

39. Ozmen MM, Zulfikaroglu B, Kucuk NO, Ozalp N, Aras G, Koseoglu T, Koç M. Lymphoscintigraphy in detection of the regional lymph node involvement in gastric cancer. Ann R Coll Surg Engl. 2006;88(7):632-8.

40. Ozmen MM, Ozmen F, Zulfikaroglu B. Lymph nodes in gastric cancer. J Surg Oncol. 2008;98(6):476-81.

41. Kulig J, Popiela T, Kolodziejczyk P, Siezega M, Szczepanik A, on behalf of the Polish Gastric Cancer Study Group. Standard D2 versus extended D2 (D2+) lymphadenectomy for gastric cancer: an interim safety analysis of a multicenter, randomized, clinical trial. Am J Surg 2007; 193: 10-15.

42. Danielson H, Kokkiola A, Kiviluoto T, Siren J, Louhimpo J, Kivilaakso E, Puolakkainen P. Clinical outcome after D1 vs D2-3 gastrectomy for treatment of gastric cancer. Scand J Surg 2007; 96: 35-40.

43. Kunisaki A, Akymama H, Nomura M, Matsuda G, Otsuka Y, Ono H, Nagahori Y, Hosoi H, Takahashi M, Kito F, Shimada H. Comparison of surgical results of D2 vs D3 gastrectomy (para-aortic lymph node dissection) for advanced gastric carcinoma: a multi-institutional study. Ann Surg Oncol; 2006; 13(5): 659-667.

44. Roukos DH, Kappas AM. Perspectives in the treatment of gastric cancer. Nat Clin Pract Oncol 2005; 2: 98-107.

45. Cuschieri A, Weedon S, Fielding J, Bancewicz J, Craven J, Joycepal V, Sydes M, Fayers P. Patient survival after D1 and D2 resections for gastric cancer: long-term results of the MRC randomized surgical trial. Surgical Co-operative Group. Br J Cancer 1999; 79: 1522-1530.

46. Wu CW, Hsiung CA, Lo SS, Hsieh MC, Shia LT, Whang-Peng J. Randomized clinical trial of morbidity after D1 and D3 surgery for gastric cancer. Br J Surg 2004; 91: 283-287.

47. Kyokawa T, Fukagawa T. Recent trends from the results of clinical trials on gastric cancer surgery. Cancer Communications 2019; 39(1), 11.

48. Zhang YK, Yang K. Significance of nodal dissection and nodal positivity in gastric cancer. Translational Gastroenterology and Hepatology 2020; 5.

49. Bencivenga M, Verlato G, Mengardo V, Scorsone L, Sacco M, Turrioni L, Giacopuzzi S, de Manzoni G. Is There Any Role for Super-Extended Lymphadenectomy in Advanced Gastric Cancer? Results of an Observational Study from a Western High Volume Center. Journal of clinical medicine 2019; 8(11), 1799.

50. Liang H, Deng J. Evaluation of rational extent lymphadenectomy for local advanced gastric cancer. Chinese Journal of Cancer Research 2016; 28(4), 397.

51. Dong Y P, Deng J Y. Advances in para-aortic nodal dissection in gastric cancer surgery: A review of research progress over the last decade. World Journal of Clinical Cases 2020; 8(13), 2703.

52. Persiani R, Rausei S, Biondi A, Bocci S, Cananzi F, D’Ugo D. Ratio of metastatic lymph nodes: impact on staging and survival of gastric cancer. Eur J Surg Oncol 2008; 34(5): 519-524.

53. Bouvier AM, Haas Q, Pard F, Roignot P, Bonithon-Kopp C, Faivre J. How many nodes must be examined to accurately stage gastric carcinomas? Results from a population based study. Cancer 2002; 1(94): 2862-2866.

54. Inoue K, Kanaye Y, Iijyama H, Sat0 M, Kanbara T, Nakai K, Okumura S, Yamamichi K, Hioki K. The superiority of ratio-based lymph node staging in gastric carcinoma. Ann Surg Oncol 2002; 9: 27-34.

55. Schwarz RE, Smith DD. Clinical impact of lymphadenectomy extent in resectable gastric cancer of advanced stage. Ann Surg Oncol 2007; 14(2): 317-328.

56. Shen J, Kim S, Cheong JH, Kim Y, Hyung WJ, Choi WH, Choi SH, Wang LB, Noh SH. The impact of total retrieved lymph nodes on staging and survival of patients with pT3 gastric cancer. Cancer 2007; 110(4): 745-751.

57. Verlato G, Marrelli D, Accordini S, Bencivenga M, Di Leo A, Marchet A, Petrioli R, Zoppini G, Muggeo M, Roviello F, de Manzoni G. Short-term and long-term risk factors in gastric cancer. World J Gastroenterol 2015; 21(21): 6434-43.

58. de Manzoni G, Verlato G, Bencivenga M, Marrelli D, Di Leo A, Giacopuzzi S, Cipollari C, Roviello F. Impact of super-extended lymphadenectomy on relapse in advanced gastric cancer. Eur J Surg Oncol 2015; 41(4): 534-40.
İleri Evre Mide Kanserlerinde D2 ve D2+ Para-aortik Lenf Nodu Dıseksiyonu Sonuçlarının Karşılaştırılması

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ÖZET

Amaç: Mide kanseri dünya çapında yaygın bir malignitedir. Disiplinler arası işbirliği ile etkili tedavi önemlidir ve cerrahi hala önemli bir rol oynamaktadır.

Gereç ve Yöntemler: Klinikimize on yıl içinde 355 hastaya mide kanser teşhis kondu. Medyan yaş 58 (23-83) olan 162 hasta çalışmaya uygundu. D2'de 107 hasta ve D2 lenfadenektomi artı para-aortik nod (PALN) diseksyon grubunda 55 hasta vardı. İki grup komplikasyon, mortalite, morbidite ve uzun süreli sağkalım açısından karşılaştırıldı.

Bulgular: Hastane kalış süresi D2 için 12(8-34) gün ve D2+ PALN için 14(8-42) gündü. Toplam operatif mortalite sayısı 8/162 (%5) idi ve gruplar arasında farklı değildi. 20 hastada (%18) D2 grubunda komplikasyon, 9 hastada (%17) D2+ PALN grubunda komplikasyon vardı. Genel sağkalım gruplar arasında da benzerdi, ancak T3-T4 tümörler olan hastalar, evre II A ve II B hastalığı olan hastalar ve daha yüksek PLN/TLN oranı olan hastalar D2+ PALN diseksyonu ile daha iyi sağkalım gösterdi. Invazyon derinliği, PLN, PLN/TLN orani, evre ve LND'nun bağımsız prognostik değişkenler olduğunu bulduk.

Sonuç: Bu çalışma, D2+ PALN diseksyonunun ileri evre mide kanseri için, postoperatif morbidite ve mortaliteyi artırmadan deneyimli cerrahlar tarafından standart bir D2 diseksyonu kadar güvenli bir şekilde yapılabileceğini göstermiştir. D2+ PALN diseksyonu, sağkalım oranını artırdığı için hastalığın ileri evresinde (II A-II B) tercih edilmelidir.

Anahtar Kelimeler: ileri evre mide kanseri, d2 lenf nodu diseksiyonu, d2+paln lenf nodu diseksiyonu, prognoz

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