# Complete Mesogastric Excision with D2 Lymphadenectomy for Gastric Cancer: Short-Term Results

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## ABSTRACT

**Objective:** To compare the short-term results of complete mesogastric excision with the conventional surgical technique.
**Study Design:** An experimental study.
**Place and Duration of the Study:** Department of Gastroenterological Surgery, Health Sciences University, Basaksehir City Hospital, Istanbul, Turkiye, from April to December 2023.
**Methodology:** Comparison of short-term results of open total gastrectomy + mesogastrectomy with standard total gastrectomy + D2 lymph node dissection at a tertiary centre in terms of peroperative results, histopathological findings, and postoperative short-term outcomes prospectively, with review of the literature.
**Results:** A total of 37 patients were included in the study. The groups involved 26 male and 11 female patients. The study group included 14 patients while the control group involved 23 patients. The mean blood loss (mL) was significantly lower and number of metastatic lymph nodes was significantly higher in the study group.
**Conclusion:** Total mesogastric excision is a safe technique which has advantages over conventional D2 gastrectomy in terms of not only peroperative and short-term outcomes, but also disease-free survival. This is the first study from a different population of the world and initial results can contribute to the literature for universalisation.

**Key Words:** *Complete mesogastrium excision, D2 lymphadenectomy, Gastric cancer, Gastrectomy, Mesogastrectomy.*

**How to cite this article:** Duzkoylu Y, Ozdedeoglu M, Kilavuz H, Demircioglu MK, Karatay H, Nayci AE. Complete Mesogastric Excision with D2 Lymphadenectomy for Gastric Cancer: Short-Term Results. *J Coll Physicians Surg Pak* 2024; **34(08)**:942-947.

## INTRODUCTION

The curative treatment of gastrointestinal tumours is surgery referring to an *en bloc* resection of the primary tumour along with its lymphovascular drainage.[1,2] Similarly, current guidelines from Europe, Japan, and USA for advanced gastric cancer treatment recommend radical gastrectomy with D2 lymph node resection.[3,4] Unfortunately, despite of these radical resections, published literature shows that recurrences occur in up to 38% of patients in 5 years.[5] Moreover, these rates may reach up to 60% in patients with locally advanced tumours following radical surgery.[6]

The possible underlying cause of these adverse results is usually suspected to be free intraperitoneal cancer cells and cancer cells detected in mesogastrium.[7,8]

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*Received: March 05, 2024; Revised: June 03, 2024; Accepted: July 02, 2024*
*DOI: https://doi.org/10.29271/jcpsp.2024.08.942*

Xie *et al.* were among the first surgeons to describe the metastatic route of mesogastrium, showing isolated tumour cells and suggesting it as the underlying cause of loco-regional recurrence.[9,10] Mesogastrium can be accepted as the perigastric envelope-style fascia propria structure.[11] The most optimal way to get rid of these cells is to follow the specific mesenteric layers of the organ as in previous examples of gastrointestinal tumour surgery with lymphatic drainage.[12] Heald *et al.* and Hohenberger *et al.* designed their surgical procedures referring to this concept in colon and rectum tumours, respectively.[13,14] Total mesocolic and mesorectal excisions mainly relied on the resection of the primary tumour with central vascular resection and lymphatic dissection, recommended as standard for colorectal cancers based on excellent recurrence and survival rates.[14,15]

However, this mesentery-based surgery is harder to apply in gastric cancer due to differences in embryological development. A Toldt's-like structure or a single main root vessel is not possible to be defined in gastric anatomy.[15] The difficulties and complexity of dissection of an intact mesogastrium restricted the technique to become standard and to evaluate prospective oncological results.[16] In 2015, Xie *et al.* were again the first researchers to publish their mesogastric excision technique

performing complete mesogastric resection by describing the anatomical mesogastrium, defining and studying in six different anatomical parts with histopathologists.[13-15] Following these advancements in China, Shinohara *et al.* from Japan suggested a complete mesogastrectomy calling their technique 'mesenterisation', emphasising the excison of 'intact fascial package'.[17] Overall, complete mesogastric excision techniques were found to be associated with decreased number of intraperitoneal cancer cells, leading to better survival rates when compared to standard D2 gastrectomy.[18] The objective of this study was to compare the short-term results of this concept of mesogastrectomy.

## METHODOLOGY

Ethical approval for this study was granted by the Ethics Committee of Istanbul Basaksehir City Hospital (Dated: 07.04.2023, Approval number: 84/07.04.2023), and the study was registered with the clinical trial number NCT06281379. Following informed consent, gastric cancer patients were enrolled in this single-centric, prospective study comparing short-term results of open total gastrectomy + mesogastrectomy with standard total gastrectomy + D2 lymph node dissection at a tertiary centre. Inclusion criteria were histopathologically confirmed gastric adenocarcinoma without evidence of distal metastasis and resectable tumours which have been treated with open total gastrectomy. Patients with prior upper gastrointestinal system surgery, neoadjuvant therapy, peripheral organ involvement, distant metastasis, and patients who underwent subtotal gastrectomy were excluded from the study. Laparoscopic and robotic operations were also excluded in order to perform better randomisation. The primary endpoint was the peroperative and postoperative short-term results of the surgery.

Total gastrectomy with the similar conceptualisation that had been suggested by pioneer surgeons was performed including a complete resection of mesogastrium tissue.[11-17] *En bloc* resection of the tissue was performed rather than dividing into multiple separated parts as in previous studies and sent for frozen section analysis. A pathologist was invited to the operation room, and the end parts as target layers of mesogastrium were identified macroscopically (shiny and smooth surface of the surgically resected area, including high ligation of the vessels) and frozen section analysis proved the intact fascial package containing a stump-like fascia propria structure histopathologically under haematoxylin and eosin staining (Figure 1 and 2).

Following the surgery, peroperative results were documented, and all the patients underwent a short-term follow-up including postoperative outcomes and complications. Gastrointestinal functions were evaluated twice a day, the nasogastric tube was removed following the first flatus and oral intake was started afterwards as semi-liquid. Later, histopathologically identified tumour features were also evaluated.

Among the variables used in the study, qualitative variables were given as number (percentage) and quantitative variables were given as mean ± standard deviation or median (minimum-maximum) according to whether the data were normally distributed or not. The normal distribution of the data was checked by Shapiro-Wilk's test. Independent samples t-test and Mann-Whitney U test were used in statistical analysis. In the analyses, $p < 0.05$ was considered significant. Analyses were performed using IBM SPSS version 26.0.

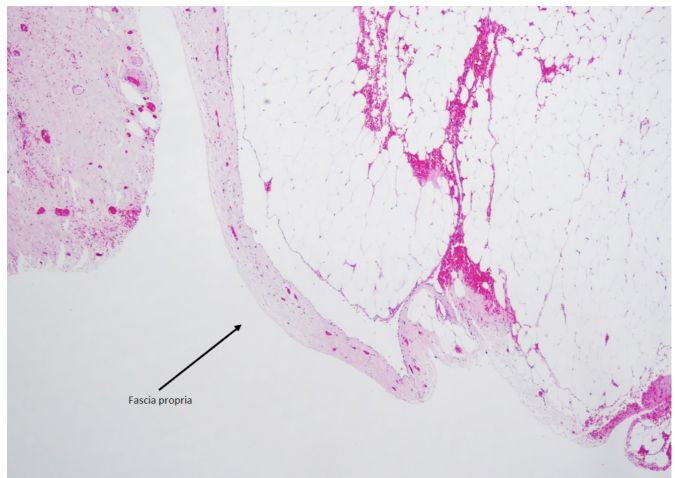


**Figure 1: Fascia propria, haematoxylin eosin staining, 100x.**

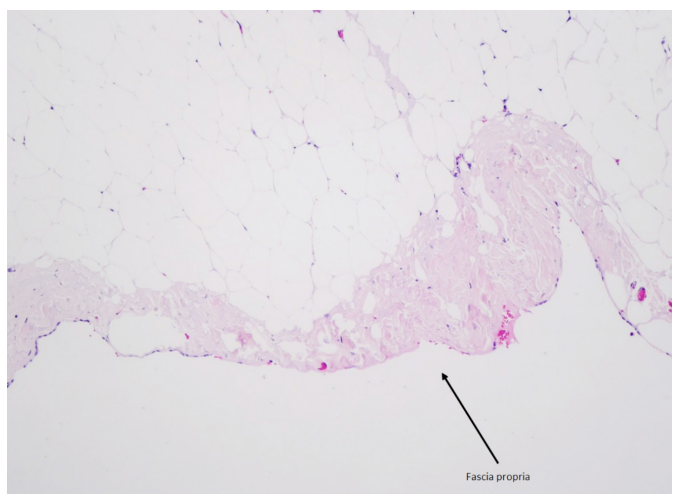


**Figure 2: Fascia propria, haematoxylin eosin staining, 200x.**

## RESULTS

Thirty-seven patients who underwent total gastrectomy for primary gastric cancer at the tertiary centre between April and December 2023 were enrolled in the study. The groups involved 26 (70.2%) males and 11 (29.7%) female patients with a mean age of 66.027 ± 8.6 years (Table I). The study group (Group B) involved 14 mesogastrectomy patients while the control group (Group A) included 23 patients who had undergone total gastrectomy with conventional D2 lymph node dissection. The authors did not encounter any operation-related deaths preoperatively.

Among both groups, the most common T stage was found to be 4a. N stage was found to be as 3b and 3a in most of the patients in the study and control groups, respectively. In terms of TNM classification, stage 3b was the most common (Table II). Median tumour size was similar between the groups, 7.4 and 7 cm, respectively (Table I).

**Table I: Distribution of parameters the groups.**

| Variables | Group A | | Group B | | p-value |
|---|---|---|---|---|---|
| | Mean ± Standard deviation | Median (95.0% lower CL for median-95.0% upper CL for median) | Mean ± Standard deviation | Median (95.0% lower CL for median-95.0% upper CL for median) | |
| Age (years) | 68.429 ± 7.871 | 69.5 (65-73) | 64.565 ± 8.867 | 66 (64-73) | 0.189* |
| BMI | 23.929 ± 2.645 | 23.5 (22-25) | 23.696 ± 3.267 | 24 (24-26) | 0.823* |
| OT (m) | 267.857 ± 62.779 | 285 (210-330) | 280.435 ± 60.489 | 270 (240-300) | 0.865** |
| Blood loss (mL) | 95.357 ± 12.929 | 92.5 (85-110) | 127.174 ± 19.876 | 125 (125-135) | <0.001** |
| HS | 9.214 ± 6.554 | 6.5 (6-8) | 8.783 ± 5.248 | 8 (6-10) | 0.988** |
| OI | 2.286 ± 0.469 | 2 (0-0) | 3.478 ± 0.994 | 3 (3-5) | <0.001** |
| Tumour size | 7.421 ± 2.55 | 7.4 (5-9.5) | 6.543 ± 3.79 | 7 (4-9) | 0.449* |
| T.Lap | 45.286 ± 17.238 | 41 (32-57) | 37.783 ± 12.944 | 34 (31-46) | 0.141* |
| Met.Lap | 15.714 ± 16.184 | 12 (6-21) | 7.435 ± 7.083 | 8 (1-13) | 0.039** |

** Independent samples t-test; ** Mann-Whitney U test.*
*BMI: Body mass index; OT (m): Operation time in minutes; HS: Hospital stay; OI: Oral intake start; T.Lap: Total number of dissected lymph nodes; MetLap: Number of metastatic lymph nodes.*

**Table II: Staging and postoperative complications.**

| Variables | Categories | Group | | p-value |
|---|---|---|---|---|
| | | A | B | |
| | | Count (percent) | Count (percent) | |
| Wound infection | - | 12 (85.71%) | 19 (82.61%) | 0.999** |
| | + | 2 (14.29%) | 4 (17.39%) | |
| Pulmonary infection | - | 9 (64.29%) | 20 (86.96%) | 0.215** |
| | + | 5 (35.71%) | 3 (13.04%) | |
| Pancreatic fistula | - | 12 (85.71%) | 21 (91.30%) | 0.625** |
| | + | 2 (14.29%) | 2 (8.70%) | |
| Ileus | - | 14 (100.00%) | 20 (86.96%) | 0.275** |
| | + | 0 (0.00%) | 3 (13.04%) | |
| Differentiation | Low | 8 (57.14%) | 12 (52.17%) | 0.483* |
| | Medium | 5 (35.71%) | 6 (26.09%) | |
| | Well | 1 (7.14%) | 5 (21.74%) | |
| Tumour localisation | Cardia | 8 (57.14%) | 5 (21.74%) | 0.058* |
| | Corpus | 6 (42.86%) | 15 (65.22%) | |
| | Antrum | 0 (0.00%) | 3 (13.04%) | |
| L | - | 1 (7.14%) | 5 (21.74%) | 0.376** |
| | + | 13 (92.86%) | 18 (78.26%) | |
| V | - | 3 (21.43%) | 7 (30.43%) | 0.710** |
| | + | 11 (78.57%) | 16 (69.57%) | |
| PN | - | 1 (7.14%) | 9 (39.13%) | 0.056** |
| | + | 13 (92.86%) | 14 (60.87%) | |
| T | 1a | 0 (0.00%) | 2 (8.70%) | 0.287* |
| | 1b | 1 (7.14%) | 4 (17.39%) | |
| | 2 | 0 (0.00%) | 2 (8.70%) | |
| | 3 | 3 (21.43%) | 6 (26.09%) | |
| | 4a | 10 (71.43%) | 8 (34.78%) | |
| | 4b | 0 (0.00%) | 1 (4.35%) | |
| N | 0 | 1 (7.14%) | 7 (30.43%) | 0.336* |
| | 1 | 1 (7.14%) | 2 (8.70%) | |
| | 2 | 3 (21.43%) | 2 (8.70%) | |
| | 3a | 4 (28.57%) | 8 (34.78%) | |
| | 3b | 5 (35.71%) | 4 (17.39%) | |
| M | 0 | 12 (85.71%) | 22 (95.65%) | 0.544** |
| | 1 | 2 (14.29%) | 1 (4.35%) | |
| Stage (TNM) | 1A | 1 (7.14%) | 5 (21.74%) | 0.515* |
| | 1B | 0 (0.00%) | 2 (8.70%) | |
| | 2A | 0 (0.00%) | 1 (4.35%) | |
| | 2B | 0 (0.00%) | 0 (0.00%) | |
| | 3A | 3 (21.43%) | 4 (17.39%) | |
| | 3B | 4 (28.57%) | 7 (30.43%) | |
| | 3C | 4 (28.57%) | 3 (13.04%) | |
| | 4 | 2 (14.29%) | 1 (4.35%) | |

** Independent samples t-test; ** Mann-Whitney U test.*
*L: Lymphoid invasion; V: Vascular invasion; PN: Perineural invasion; T: Tumour size stage; N: Lymph node stage; M: Distant metastasis.*

The mean operative time for the patients in mesogastrectomy group was 267.857 ± 62 minutes while the same duration was found to be 280.435 ± 60 minutes in the control group. The difference was not statistically significant. The mean blood loss (mL) was 95.357 ± 12 in the study group and 127.174 ± 19 in the control group (p <0.001, Table I).

A median number of 45.286 ± 17.23 lymph nodes were harvested from gastrectomy specimens in mesogastrectomy group including 15.714 ± 16.18 metastatic lymph nodes. The same findings were 37.783 ± 12.94 and 7.435 ± 7.08 in the control group, respectively. Number of metastatic lymph nodes in the study group was found to be statistically increased when compared to the control group (p <0.05, Table I).

The postoperative follow-up data revealed that the postoperative hospital stay (days) was similar in both groups without statistical significance. Postoperative flatus was earlier in the study group and the incidence of paralytic ileus was 0% while the same ratio was 13% in the control group but the difference was not significant. The start of oral intake (semi-liquid diet) was earlier in mesogastrectomy group. The incidence of postoperative wound infection was lower in the peresent study group without statistical significance (Table II). The rate of overall complications was found to be slightly decreased in the study group.

## DISCUSSION

Gastric cancer is the second most common cause of cancer-related deaths worldwide and surgery is accepted as the gold standard curative treatment.[19] Unfortunately, despite total resection of the tumour with extended lymph node dissection, loco-regional recurrences may be encountered up to 38% in 5 years and these recurrences are known to be the main cause of poor survival rates following surgery.[5,20] Xie *et al.* suggested that standard resection plus D2 lymph node dissection was not enough to eliminate the adjacent tissues, so they described a new possible metastatic pathway and the anatomic structure of the mesogastric tissue.[9] Similar to mesocolic and mesorectal tissues, mesogastrium should contain mesenteric vessels and wrap the stomach as an envelope which may prevent the spillage of free cancer cells resulting from broken lymphovascular vessels during dissection.[21,22] The advancements in understanding the concept of mesogastrium led the researchers to show the importance of resecting the primary tumour with its mesentery as intact as possible to avoid possible recurrences.[15,17] Following the Chinese researchers, Kumamoto *et al.* followed the concept of the total excision of mesogastric tissue with their *en bloc* technique.[23] Similarly, Qui *et al.* introduced the dissection of the perigastric space called 'enjoyable space'.[16] However, a standardised mesogastric resection has not been determined yet.

In 2017, Shinohara *et al.* showed in their study aiming for the universalisation of total mesogastric excision, the number of resected lymph nodes was higher than the control group.[17] Similarly in this study, an increased number of dissected lymph nodes in the study group was detected without statistical significance. However, the results revealed significantly increased number of metastatic nodes ($p < 0.05$) which may be important for disease-free survival rates.[20] One year later, Shen *et al.* published a distal gastric cancer model study in which they did not find any statistical differences in means of the number of lymph nodes, but they showed a significantly lower amount of blood loss in total mesogastrectomy patients when compared to standard surgery.[15] Similarly, in this study blood loss was significantly reduced in mesogastrectomy group ($p < 0.001$). As pioneers of mesogastric excision concept, Xie *et al.* reported in their first randomised controlled trial in 2021 that patients receiving complete mesogastrectomy showed decreased blood loss, increased number of harvested lymph nodes, and earlier postoperative flatus when compared to conventional surgery.[24] In this study, postoperative paralytic ileus was reduced in the study group and a semi-liquid diet was started right after the first flatus which was earlier than the control group but not statistically significant. Following these researchers, Qui *et al.* compared the mesogastrectomy patients with conventional surgery in upper gastric cancers and showed lower mean operative time, decreased blood loss, and reduced hospital stay with similar rates of postoperative short-term complications, suggesting the concept of total mesogastric excision is a safe and feasible method.[16] The results were similar in terms of blood loss but the mean operative time was slightly reduced in the study group without statistical significance. This may be due to the fact that the study group consisted of the study's initial cases. The hospital stay was not reduced but a decreased total number of postoperative complications was detected, especially in terms of wound infection and postoperative ileus, which were found to be decreased in the study group.

In the largest meta-analysis comparing D2 lymphadenectomy with complete mesogastrium excision *versus* conventional D2 gastrectomy for advanced gastric cancer, researchers showed shorter operative time, lower blood loss, higher number of mean harvested lymph nodes, shorter time to first flatus, reduced hospital stay, decreased incidence of postoperative complications, and significantly better 3-year disease-free survival rates, suggesting that radical gastrectomy with complete mesogastric excision is a reliable and safe procedure with faster postoperative recovery, lower risk of complications and improved survival rates when compared to conventional D2 gastrectomy.[25] Due to the short term results of this study, similar advantages of total mesogastric excision may be suggested in terms of blood loss, harvested malignant lymph nodes, and better postoperative comfort.

The limitation of the study is the absence of long-term oncological results, which can be obtained during follow-up with addition of new cases. Although multi-centre studies with long-term results are needed, this work is the first study from a different population of the world and the initial results can contribute to the literature for the optimisation and universalisation of total mesogastric excision in the future.

## CONCLUSION

The mesogastric excision technique is safe and has advantages over conventional D2 gastrectomy in terms of not only peroperative and short-term outcomes, but also disease-free survival.

**ETHICAL APPROVAL:**

Ethical approval for this study was granted by the Istanbul Basaksehir City Hospital's Ethics Committee (Dated:

07.04.2023, Approval number: 84/07.04.2023), and the study was registered in clinicalTrials.gov under the number NCT06281379.

**PATIENTS' CONSENT:**
Written informed consent was provided by the patients.

**COMPETING INTEREST:**
The authors declared no conflict of interest.

**AUTHORS' CONTRIBUTION:**
YD, MO: Literature review, designing, and drafting of the manuscript.
HK, HK: Drafting, analysing, and revising the manuscript for important intellectual content.
MKD, AEN: Drafting and revising the manuscript.
YD, AEN: Conceptualisation and data curation.
MO, AEN: Revising the manuscript.
All authors approved the final version of the manuscript to be published.

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