

Roles of Lymphadenectomy in Gastric Cancer Surgery: Overview

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Abstract: The aim of this study was to investigate the role of extended lymph node dissection in patients with gastric cancer undergoing surgical treatment for GC. The present review was also to evaluate the outcomes of lymphadenectomy in GC patients. We performed comprehensive search including; reviews, RCT, systematic reviews, and case reports using electronic databases such; CENTRAL, MEDLINE and Embase. We restricted our search to only English articles discussing the roles of lymph nodes resection during gastrectomy in case of gastric cancer that published up to April, 2017 with only human subject included. The results of this evaluation showed that D2 as well as D3 lymphadenectomy for gastric cancer could not demonstrate advantages in postoperative survival. Additionally, D3 lymphadenectomy could increase the risk of operative or postoperative problems. Nevertheless, the findings of this research could motivate the clinical area to re-think the inquiry of lymphadenectomy degree and also to perform a brand-new well-designed trial for gastric cancer surgical treatment. Less substantial lymphadenectomies likewise most likely result in increased loco-regional reappearance, and also could impact choices pertaining to adjuvant chemotherapy versus chemoradiation. In regards to overall survival, the impacts of even more considerable lymphadenectomy are tough to determine. In order to improve end results, the choice in between D1 versus D2 lymph node dissection need to be personalized after factor to consider of patient features, tumor phase as well as surgical experience, particularly since tummy cancers cells are now usually thoroughly treated by a multimodal technique consisting of perioperative radiation treatment or chemo-radiation.

Keywords: Lymphadenectomy, gastric cancer, surgical treatment.

1. INTRODUCTION

Gastric cancer (GC) is the fourth cause of death worldwide, Although the incidence of gastric cancer has actually declined over the past 30 years worldwide, especially in Western countries, it continues to be the 2nd leading cause of cancer-related death as well as make up 10.4% of cancer deaths worldwide ⁽¹⁾. There is marked variation in the incidence of gastric cancer with the highest rate of event in Eastern Asia, Eastern Europe, as well as South America, and the lowest incidence in North America and parts of Africa ⁽²⁾. These figures increase 6-fold in Japan, where early detection is ending up being significantly vital. Japanese authors ^(3,4) report survival results significantly better compared to those in Western series, on the basis of the idea of extended lymphadenectomy (EL) ⁽⁴⁾. The incidence of gastric adenocarcinoma differs enormously throughout the world and also country-by-country. Forty-two percent of gastric cancer cases happen in China due to its high incidence and also large populace ⁽⁵⁾. The highest incidence of gastric cancer is found in South Korea at 66.5 - 72.5 per 100,000 men and 19.5 - 30.4 each 100,000 ladies ⁽⁶⁾. There has actually been intense dispute over the level of lymphadenectomy in the therapy of gastric adenocarcinoma for years. Extent of lymphadenectomy includes at least 2 essential problems: (A) adequate staging in terms of number of lymph nodes resected operatively as well as checked out pathologically, and (B) adequate treatment There is little disagreement amongst gastric cancer professionals that the minimum lymphadenectomy that should be done for gastric adenocarcinoma past an early mucosal or submucosal tumor should go to the very least a D1 lymphadenectomy ⁽⁷⁾.

Patients obtaining radical resection will face locally or distally persistent disease, surgery is the only possibly curative treatment for gastric cancer. Regardless of some advancements in perioperative adjuvant treatment for gastric cancer, research studies usually have actually cannot locate any milestone enhancement in overall survival complying with reliable surgical treatment.

Some researchers have actually discovered no distinction between limited lymphadenectomy and also EL, as two big multicenter randomized research studies have shown ^(7,8). Nevertheless, these research studies had issues of procedure offenses (incomplete or a lot more substantial lymph node dissections in the various study groups), a high morbidity/mortality price due to the fact that there were a lot of experiences in various medical facilities, and also, sometimes, an unnecessary degree of body organ resection (that consists of the excision of the tail of the pancreas) ^(8,9).

The aim of this study was to investigate the role of extended lymph node dissection in patients with gastric cancer undergoing surgical treatment for GC. The present review was also to evaluate the outcomes of lymphadenectomy in GC patients.

2. METHODOLOGY

We performed comprehensive search including; reviews, RCT, systematic reviews, and case reports using electronic databases such; CENTRAL, MEDLINE and Embase. We restricted our search to only English articles discussing the roles of lymph nodes resection during gastrectomy in case of gastric cancer that published up to April, 2017 with only human subject included.

3. RESULTS

○ Classification of lymph node stations and types of lymphadenectomy:

The lymph nodes terminals of the stomach are classified anatomically as well as identified numerically by the Japanese Gastric Cancer Association (JGCA) as published in the Japanese classification of gastric carcinoma: 3rd version in 2011 ⁽¹⁰⁾ (**Figure1**). **Table 1** displays the different lymph nodes stations and their anatomical definitions. Formerly, in its description of 2nd version of Japanese classification of gastric carcinoma, JGCA classified regional lymph nodes right into 3 teams based on the place of primary gastric tumor ⁽¹²⁾. These three groups of lymph node containers were utilized to describe the extent of lymph nodes breakdown in a gastrectomy: D0 breakdown - no dissection or incomplete breakdown of the team 1 nodes; D1 - breakdown of all the group 1 nodes; D2 - dissection of all the team 1 and group 2 nodes; and D3 - dissection of all the team 1, 2 and also 3 nodes. This needs to be understood that each lymph nodal terminal would lug a various meaning for a certain primary tumor location - suprapyloric (terminal 5) falls under group 1 for an antral primary tumor while it would certainly come under group 3 for proximal third gastric cancer. As anticipated, this category was viewed to be fairly made complex in the surgical society, specifically among western specialists; and also rightly so, it cannot amass widespread approval ⁽¹³⁾. In order to bring uniformity in the extent of lymphadenectomy, JGCA incredibly streamlined the interpretation of lymphadenectomy in its recent category ⁽¹⁴⁾. The lymph node terminals 1-12 and 14v have been categorized as regional gastric lymph nodes while metastasis to any other node terminal classified as M1 ⁽¹⁴⁾.

Table 1: Anatomical definition of lymph node stations

Lymph node station	Label	Anatomical description
1	Right paracardial	Right paracardial LNs, including those along the first branch of the ascending limb of the left gastric artery
2	Left paracardial	Left paracardial LNs including those along the esophagocardiac branch of the left subphrenic artery
3	Lesser curvature	3a: Along the branches of the left gastric artery 3b: Along the 2 nd branch and distal part of the right gastric artery
4	Left gastric curvature	4sa: Left greater curvature LNs along the short gastric arteries (perigastric area) 4sb: Left greater curvature LNs along the left gastroepiploic artery (perigastric area)
	Right greater curvature	4d: Rt. greater curvature LNs along the 2 nd branch and distal part of the right gastroepiploic artery
5	Suprapyloric	Along the 1 st branch and proximal part of the right gastric artery
6	Infrapyloric	Along the first branch and proximal part of the right gastroepiploic artery down to the confluence of the right gastroepiploic vein and the

Lymph node station	Label	Anatomical description
		anterior superior pancreaticoduodenal vein
7	Left gastric artery	Along the trunk of left gastric artery between its root and the origin of its ascending branch
8	Common hepatic artery	8a: Anterosuperior LNs along the common hepatic artery 8p: Posterior LNs along the common hepatic artery
9	Celiac	Along the coeliac artery
10	Splenic hilum	Lymph nodes in the splenic hilum including those adjacent to the splenic artery distal to the pancreatic tail, and those on the roots of the short gastric arteries and those along the left gastroepiploic artery proximal to its 1 st gastric branch
11	Splenic artery	11p: Proximal splenic artery LNs from its origin to halfway between its origin and the pancreatic tail end 11d: Distal splenic artery LNs from halfway between its origin and the pancreatic tail end to the end of the pancreatic tail
12	Hepatoduodenal ligament	12a: Hepatoduodenal ligament LNs along the proper hepatic artery, in the caudal half between the confluence of the right and left hepatic ducts and the upper border of the pancreas 12b: Hepatoduodenal ligament LNs along the bile duct, in the caudal half between the confluence of the right and left hepatic ducts and the upper border of the pancreas 12p: Hepatoduodenal ligament LNs along the portal vein in the caudal half between the confluence of the right and left hepatic ducts and the upper border of the pancreas
13	Posterior pancreatic head	On the posterior surface of the pancreatic head cranial to the duodenal papilla
14v	Superior mesenteric vein	Along the superior mesenteric vein
15	Middle colic vessels	Along the middle colic vessels
16	Para-aortic	16a1: Paraaortic lymph nodes in the diaphragmatic aortic hiatus 16a2: Paraaortic lymph nodes between the upper margin of the origin of the celiac artery and the lower border of the left renal vein 16b1: Paraaortic lymph nodes between the lower border of the left renal vein and the upper border of the origin of the inferior mesenteric artery 16b2: Paraaortic lymph nodes between the upper border of the origin of the inferior mesenteric artery and the aortic bifurcation
17	Anterior surface of pancreatic head	On the anterior surface of the pancreatic head beneath the pancreatic sheath
18	Inferior border of the pancreatic body	Along the inferior border of the pancreatic body
19	Infradiaphragmatic	Infradiaphragmatic, predominantly along the subphrenic artery
20	Paraesophageal, esophageal hiatus	In the diaphragmatic esophageal hiatus
110	Paraesophageal, lower thoracic	In the lower thorax
111	Supradiaphragmatic	Supradiaphragmatic lymph nodes separate from the esophagus
112	Posterior mediastinal	Posterior mediastinal lymph nodes separate from the esophagus and the esophageal hiatus

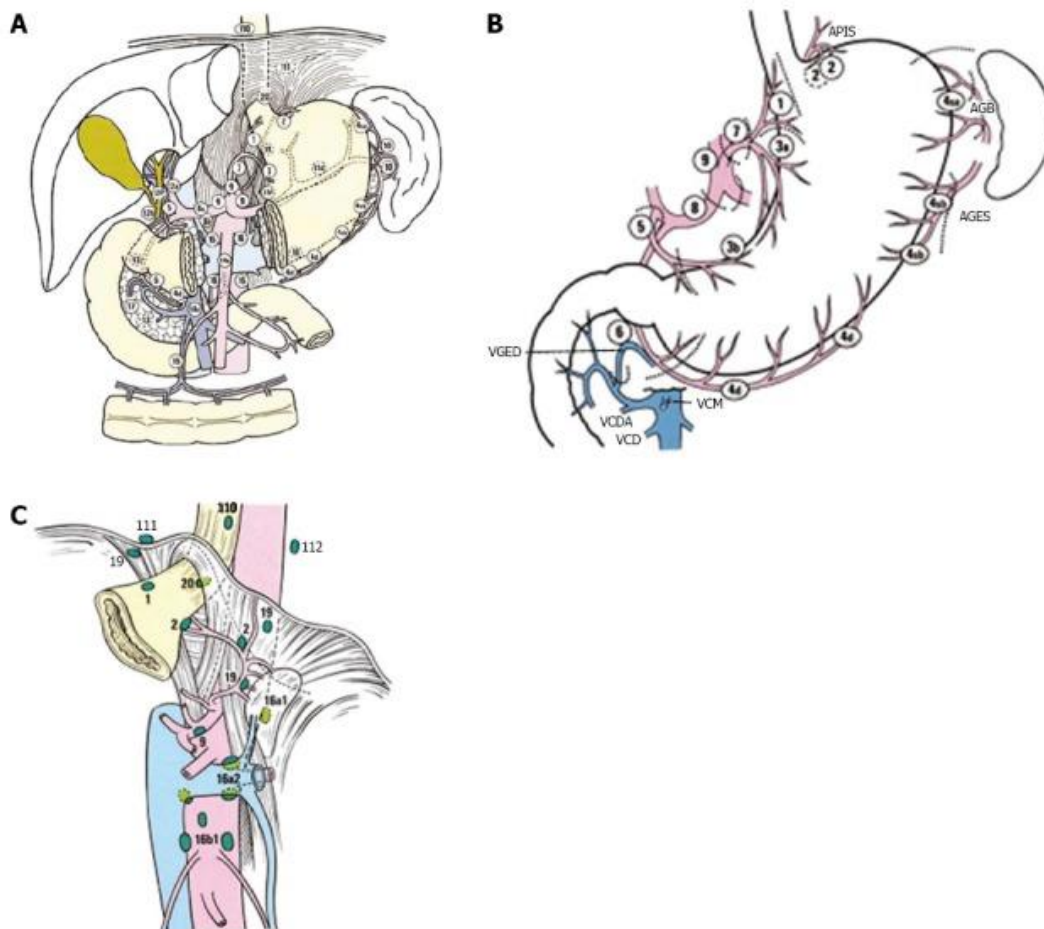


Figure 1: Locations of lymph node station. A: Numbering and locations of lymph node station; B: Location of lymph node stations in the posterior area; C: Location of lymph node stations in subphrenic region.

○ **Removal of lymph node in case of early GC:**

The extent of lymphadenectomy in early gastric cancer (EGC) is highly dependent from lymph nodal spread of very early forms. It is popular that the likelihood of lymph node metastasis in EGC is a lot less than in innovative kinds. The risk ranges notably according to pathological qualities of EGC. Invasion of submucosa, tumor grading, dimension, macroscopic look, and also lympho-vascular invasion have actually been recognized as strong risk factors for lymph node metastases in EGC⁽¹⁴⁾. Consequently, these factors are taken into account for developing the indicators to endoscopic resection procedures (endoscopic mucosal resection, EMR, or endoscopic submucosal breakdown, ESD) in the JGCA standards^(13,14,15). Inning accordance with these predictive factors, subgroups of patients with virtual no risk of lymph node metastases have actually been recognized. The resection is judged as alleviative when all the following conditions are fulfilled: en-bloc resection, tumor dimension not higher than 2 centimeters, histology of intestinal-differentiated-type, pT1a, adverse horizontal (lateral) margin, adverse vertical margin, and also no lymphovascular intrusion. The JGCA "increased" requirements tend to consist of bigger tumor dimension, ulcerated or submucosal invading kinds, and also chosen undifferentiated tumors in the indicators to endoscopic treatment^(16,17).

In very early kinds not ideal for endoscopic treatment, the JGCA guidelines guidance a D1 or D1 plus lymphadenectomy in cases with scientifically adverse nodes⁽¹³⁾. The D1 lymphadenectomy involves the elimination of perigastric lymph nodes and also terminal number 7, whereas in the D1 plus the lymph node stations 8a and also 9 for subtotal gastrectomy, with the enhancement of station 11p for overall gastrectomy, should be studied. When lymph nodes are clinically favorable, JGCA treatment guidelines guidance a D2 dissection, which entails the removal of terminals 12a as well as 11p in subtotal gastrectomy, as well as stations 12a, 11d and 10 in overall gastrectomy⁽¹³⁾.

In South Korea the therapy method to very early forms is similar⁽¹⁸⁾. In a current research study from Seoul National University Hospital (SNUH) the appropriate level of lymph node (LN) dissection in lower third was evaluated analysing LN transition patterns from a prospective topographic database, using the Maruyama Index of unresected disease⁽¹⁹⁾. The

evaluated risk of lymph node metastasis in stations 8-12 led the Authors in conclusion that the D1 dissection plus stations 7 and also 8a for mucosal cancer, and also a broadened dissection to the D2 level for submucosal cancer need to be taken into consideration to ensure total elimination of metastatic LNs.

In the West, the clinical setting is instead various from East Asia. In a big series of resected EGC from the Italian Research Group for Gastric Cancer (GIRCG) database, submucosal intrusion, Lauren diffuse/mixed kind, Kodama Pen A type and tumor dimension were discovered to be associated with a raised risk of lymph node metastases⁽²⁰⁾. The risk of favorable nodes is particularly high in diffuse-mixed kind, an aggressive type of gastric cancer with special propensity to lymph node transition as well as peritoneal dissemination in sophisticated types⁽²¹⁾. In the West, the reducing occurrence of gastric cancer is mostly due to the lowering number of intestinal kind tumors of the distal 3rd; thus, proximal tumors and diffuse-mixed kind reveal a relative rise, and also doctors will extra regularly face with this aggressive type of gastric cancer^(22,23). Moreover, endoscopic resections, which are therapy yet additionally staging procedures, are much less taken on in the West, even if their execution in scientific method is boosting, most importantly in specialized centers⁽²⁴⁾; therefore, the medical diagnosis of EGC is clinically-based most of the times. In spite of the current improvement of hosting treatments (CT scan, endoscopic US), the risk of a medical understaging is still considerable, as well as this might be associated with a potentially fatal undertreatment, as the chance of sophisticated nodal standing in non-early forms of gastric cancer in Western patients is remarkable^(25,26). For these reasons, the GIRCG guidelines advice a D2 lymphadenectomy in clinically early kinds not suitable for endoscopic treatment⁽²⁷⁾. Special focus needs to be provided to the removal of infra-pyloric nodes (number 6), which are one of the most typically associated with EGC of the distal belly, most importantly in the diffuse-mixed type, and also to terminal 1 (in subtotal gastrectomy) along with to lymph node terminals from 7 to 12 (station 10 is optional).

o Regional Lymphadenectomy in case of GC:

Gastric cancer has a high tendency to lymph nodes involvement and also neighborhood spread: the further is the extension of the tumour the even more they are attack⁽²⁸⁾. Nodal dispersing slowly takes place emitting from the primary site^(29,30). and also nodal involvement is just one of one of the most vital prognostic factors. It is as a result clear the reason doctors have always offered a lot relevance to lymphadenectomy as well as its expansion

In fact, lymph node dissection has been discussed for numerous years by cosmetic surgeons: as a result, two various institutions have established^(31,32). In Eastern nations D2 lymphadenectomy has been taken into consideration the guideline since the 60's^(33,34) particularly in Japan^(35,36), where the high incidence of this tumour has actually constantly increased excellent interest. In Asian nations extended lymphadenectomy appears to give superior cause terms of survival and also reoccurrence^(37,38,39), this could be clarified by the Asian larger surgical experience with this sort of dissection^(38,39), and also by the younger age of Asian patients, who therefore have less comorbidities as well as less abdominal fat with a following much easier usefulness of the treatment⁽³⁶⁾. An objection that Western cosmetic surgeons have advocated is that Japanese- as well as Asian in general-results were often offered by non-randomized researches and retrospective surveys⁽³⁷⁾.

On the contrary in Western countries D2 lymphadenectomy was ruled out a standard operating procedure in the professional technique⁽³⁴⁾, the lower occurrence of this tumor and also the ensuing much less confidence of western surgeons in this treatment is surely among the reasons. D2 is a complex and difficult surgical method and an appropriate training is compulsory. Furthermore, inning accordance with former research studies [generally Western randomized professional trials (RCTs)^(37, 40,41) and also succeeding testimonials^(42,43) D2 appeared connected with greater price of medical issues and also higher peri-operative death, without a genuine survival advantage. Driven by these results, Western doctors have always chosen the restricted dissection.

Current data have threatened this historic choice and began to transform Western point of view on D2 lymphadenectomy. As a matter of fact, it has actually been shown^(40,41) that the greater price of death as well as surgical problems with D2 treatment were primarily pertaining to distal pancreatectomy and/or splenectomy, which formerly were included in the basic D2 lymphadenectomy as well as thought about needed for an ample nodal dissection. Older research studies^(35,44) consisted of in the D2 group all patients treated with distal pancreatectomy and splenectomy: these patients had a higher mortality price and also a higher incidence of medical complications (such as fistulas, re-intervention, anastomotic leakage etc.) which influenced their result. The bottom line of debate related to the extent of lymphadenectomy has actually been to balance the oncological advantage vis-à-vis postoperative morbidity and also death^(45,46). The oncological circumstances where survival is believed to be enhanced by the prolonged lymphadenectomy are couple of; in addition, there is paucity of degree I proof verifying the survival advantage⁽⁴⁶⁾. There is a widely held view amongst the western cosmetic surgeons that malignant lymph nodes are signs as well as not guvs of survival^(47,48).

4. CONCLUSION

The results of this evaluation showed that D2 as well as D3 lymphadenectomy for gastric cancer could not demonstrate advantages in postoperative survival. Additionally, D3 lymphadenectomy could increase the risk of operative or postoperative problems. Nevertheless, the findings of this research could motivate the clinical area to re-think the inquiry of lymphadenectomy degree and also to perform a brand-new well-designed trial for gastric cancer surgical treatment. Less substantial lymphadenectomies likewise most likely result in increased loco-regional reappearance, and also could impact choices pertaining to adjuvant chemotherapy versus chemoradiation. In regards to overall survival, the impacts of even more considerable lymphadenectomy are tough to determine. In order to improve end results, the choice in between D1 versus D2 lymph node dissection need to be personalized after factor to consider of patient features, tumor phase as well as surgical experience, particularly since tummy cancers cells are now usually thoroughly treated by a multimodal technique consisting of perioperative radiation treatment or chemo-radiation.

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