

SURGICAL APPROACHES IN RESECTABLE OESOPHAGOGASTRIC CANCER

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Abstract

Surgery still offers the best chance of cure for patients with resectable oesophagogastric cancers. Complete tumour resection with clear margin is imperative. The role and extent of lymphadenectomy remains controversial. Operative approach is individualised according to tumour location and stage, the patient's surgical fitness and the surgeon's experience. Technological advances facilitate more accurate tumour staging and the development of minimally invasive surgical techniques. Patients with oesophagogastric cancers should be managed in the multidisciplinary setting and their tumours resected by experienced surgeons with adequate case volume.

Surgery remains the main curative treatment modality for patients with resectable oesophagogastric cancers. Optimal preoperative workup with accurate tumour staging and assessment of surgical fitness improves patient selection for appropriate therapy. Modern imaging with high resolution CT scanning, together with whole body PET scanning for oesophageal cancers and staging laparoscopy and peritoneal cytology for gastric tumours, identify the majority of patients with metastatic disease, avoiding unnecessary laparotomy. Bulky resectable primary oesophagogastric tumours with or without nodal involvement have been shown to benefit from multimodality therapy.¹

Once patients with oesophagogastric cancers have been appropriately worked up, the aims of surgery are to resect the primary tumour and its draining lymph node basins with clear margin (R0 resection) and to perform a suitable reconstruction that minimises operative mortality and morbidity. This paper will concentrate on the surgical principles and the controversies regarding different surgical approaches to the treatment of oesophagogastric cancers.

Oesophageal cancer

An R0 resection, complete removal of the tumour macroscopically and microscopically, is widely accepted as providing the best chance of cure for patients with localised resectable oesophageal cancer. At the site of the primary oesophageal tumour, longitudinal surgical margins are much easier to assess than circumferential resection margin. Meticulous dissection is required to reduce the likelihood of a positive circumferential margin, which has been shown to be a poor prognostic indicator. The median overall survival for patients with involved circumferential margin is significantly less than those with clear margin (9.4 months versus 21.6 months).²

Extent of lymphadenectomy

The presence of lymph node metastasis confers poor prognosis, but the role of radical lymphadenectomy in oesophageal cancer surgery remains controversial. Undoubtedly, extensive lymph node resection provides accurate tumour staging and prognostication, but its impact on patient survival is a topic for debate. Published data from clinical trials are limited and often difficult to

compare due to the variable definitions used for the extent of lymphadenectomy.³

The most radical lymph node resection in oesophagectomy is a 3-field lymphadenectomy. This involves the removal of abdominal nodal stations related to the stomach (a D2 lymphadenectomy) and all draining lymph nodes associated with the oesophagus in the chest including the thoracic duct and the inferior cervical lymph nodes. The term 2-field lymphadenectomy is defined as the removal of all nodal tissues related to the stomach in the abdomen and the oesophagus in the chest, but not the cervical lymph nodes.

To date, there are only three randomised control trials examining the role of lymphadenectomy in oesophageal cancer surgery. In the only prospective randomised trial comparing 3-field lymphadenectomy versus 2-field lymphadenectomy performed by Nishihira et al, extended lymph node resection yielded a non-significant improvement in five-year overall survival rate (66% v 48%), but incurred greater operative morbidity (56% v 30%).⁴ In the study by Hulscher et al, there was no significant difference in overall survival for patients who had transhiatal oesophagectomy with conservative lymphadenectomy compared to those who underwent transthoracic oesophagectomy with a more extensive infracarinal lymph node resection.⁵ Formal 2-field lymphadenectomy has been shown in a small randomised trial by Fang et al to yield better five-year survival rates than selective nodal sampling (36% v 25%) in patients undergoing thoraco-abdominal oesophagectomy.⁶

Conceptually extended lymphadenectomy should confer a survival benefit to patients with limited nodal spread but without distant metastatic disease. However there is no reliable tool to identify these patients pre operatively. The 7th edition of the American Joint Committee on Cancer Staging Manual staging system for oesophageal and gastroesophageal junction cancers recommends extended lymphadenectomy.⁷ Surgeons are required to balance the risk of an aggressive surgical approach with a small potential survival benefit. Superior mediastinal or supracarinal nodal dissection, with or without cervical lymphadenectomy, is technically challenging and has significant morbidity including injury to the recurrent

laryngeal nerves. Many Western oesophageal surgeons perform a more limited lymphadenectomy, involving an infracarinal lymph node resection with or without the removal of the thoracic duct and a modified D2 abdominal lymph node dissection.

Open surgical techniques for oesophagectomy

There are several open surgical approaches in oesophageal cancer surgery. Combined left thoracotomy through a single thoracoabdominal incision is often practiced in Asian countries. The three common techniques for oesophageal cancer resection in Western countries are the Ivor Lewis transthoracic oesophagectomy (right thoracotomy and laparotomy), the transhiatal oesophagectomy (laparotomy, blunt mediastinal dissection and left neck incision with cervical anastomosis) and the McKeown 3-phase oesophagectomy (right thoracotomy, laparotomy and left neck incision with cervical anastomosis). Although the site of the primary tumour and the degree of local invasion, and the patients' cardiorespiratory reserve can contribute to decision making, the choice of surgical techniques is often related to the surgeon's experience and preference.

There has been considerable controversy among oesophageal surgeons regarding which of the two commonly performed surgical approaches, the transthoracic or the transhiatal, yields the best short-term and long-term outcomes. The transthoracic approach allows a more thorough inspection and dissection of the oesophagus and draining lymphatic tissue under direct vision. Theoretically, this will optimise R0 resection by improving circumferential margins and the extent of lymphadenectomy, leading to an improved oncological outcome. However, a combined thoracotomy and laparotomy can adversely impact patients' recovery, many of whom may already have compromised cardiorespiratory reserve. Another disadvantage of the transthoracic approach is that a leak from an intrathoracic anastomosis can cause life threatening mediastinitis and sepsis. Proponents of the transhiatal approach emphasise that avoidance of a thoracotomy would minimise pulmonary complications and post-operative pain, and a leak from the cervical anastomosis is much easier to manage and poses less of a threat to the patient.

There are four randomised control trials,^{5,8-10} and two meta-analyses comparing the transthoracic versus the transhiatal approaches for oesophageal cancer resection.^{11,12} Overall, there is no significant difference in oncological outcome between these two types of oesophagectomy. However, the transthoracic technique is associated with higher intra-operative blood loss, post-operative mortality and pulmonary complication, while the transhiatal approach had a higher incidence of anastomotic leakage and recurrent laryngeal nerve injury.

Minimally invasive oesophagectomy

Advances in instrumentation together with increased experience in laparoscopic and thoracoscopic surgery have led to the development of minimally invasive oesophagectomy. The advantage of this approach is to allow surgeons to perform an optimal tumour resection under direct vision, while minimising the potential adverse impact on patients' recovery by avoiding thoracotomy and/or laparotomy

incisions. The term minimally invasive oesophagectomy has been used to describe totally minimally invasive operations or hybrid procedures, where either the thoracic or abdominal component is performed endoscopically.

Since Cuschieri et al described on their initial experience in thoracoscopic mobilisation of the oesophagus in 1992,¹³ many case control series of minimally invasive oesophagectomy have been published. In the largest known comparative study of 446 cases, Smithers et al reported longer operating time, less blood loss, shorter hospital stay and greater stricture rate for the minimally invasive surgical approach, but no significant difference in mortality or survival when compared with open transthoracic oesophagectomy.¹⁴ Luketich et al showed in their series of 220 patients that a totally minimally invasive Ivor Lewis oesophagectomy can be performed successfully in 92.8% of cases with low mortality rate (1.4%) and anastomotic leak rate (11.7%), and a short hospital stay of seven days.¹⁵

There are three published meta-analyses comparing open oesophagectomy to either a totally minimally invasive oesophagectomy or to the hybrid operation.¹⁶⁻¹⁸ These concluded that minimally invasive oesophagectomy has an equivalent oncological outcome to the open procedure, but with less operative blood loss, reduced respiratory complications, and shorter ICU and hospital length of stay. To date there is no published randomized control trial comparing minimally invasive to open oesophageal cancer resection. Thus the results of the proposed TIME trial,¹⁹ randomising patients to either open transthoracic oesophagectomy or minimally invasive oesophagectomy, will be most welcome.

Gastroesophageal junction cancers

There are divided opinions in the literature regarding the aetiology, classification and treatment of gastroesophageal junction cancers. Should gastroesophageal junction tumours be managed as oesophageal or gastric cancers, or as their own entity? This is an important clinical question since there are differences in tumour biology, multimodality therapy and surgical approaches for oesophageal and gastric cancers.

To guide clinical management and facilitate comparison of data across different institutions, Siewert et al proposed a morphologically and anatomically based classification of gastroesophageal junction cancers.²⁰ Type I tumours are adenocarcinomas located within two centimetres proximal to gastroesophageal junction. Type II tumours are true cardia carcinomas or "junctional cancers" ranging two centimetres above to one centimetre below gastroesophageal junction. Type III tumours are subcardial adenocarcinomas within five centimetres of gastroesophageal junction. Epidemiological data has shown type I gastroesophageal junction tumours to resemble oesophageal adenocarcinomas, with high prevalence of Barrett's intestinal metaplasia (81%) and gastroesophageal reflux disease (84%), and lymphatic spread occurring in both cephalad and caudal direction. Type II tumours have both gastric and oesophageal malignant features. Like gastric adenocarcinomas,

intestinal metaplasia is rare in type III tumours and almost all nodal metastases are located in the abdomen.²⁰ The ability to achieve R0 resection with adequate nodal clearance is the main determinant in choice of operation for gastroesophageal junction tumours. As advocated by the Siewert's group, most surgeons would perform oesophagectomy for type I cancers and extended total gastrectomy or proximal partial gastrectomy with radical nodal dissection for type III tumours.

The treatment of Type II gastroesophageal junction cancers, especially the bulky primaries and/or those with nodal involvement, has yet to be standardised. Apart from surgeons' preference and experience, the extent of tumour invasion of the oesophagus and/or the presence of mediastinal nodal metastases dictates the operative approach. An extended total or proximal partial gastrectomy, with transhiatal resection of the distal oesophagus, can be performed in type II tumours with minimal or no oesophageal extension and no obvious involved mediastinal node. Oesophagectomy with proximal resection of stomach and formal mediastinal nodal dissection is recommended for patients with bulky gastroesophageal junction cancers to achieve a clear proximal surgical margin.

Gastric cancer

The surgical approach and outcome of patients undergoing gastric cancer surgery differ significantly between Western and Asian countries. With the second highest incidence of gastric adenocarcinomas globally, Japan has a nationwide public education and screening program resulting in almost 50% of patients presenting with early stage gastric cancers.²¹ Japanese surgeons have been advocating R0 tumour resection with radical extensive lymphadenectomy, as standard treatment because they have shown that very good long-term survival can still be achieved in gastric cancer patients with nodal metastases. In contrast, the majority of Western patients present with advanced gastric cancers and have a poor prognosis even when treated with multimodality therapy. There is considerable variation in surgical approaches among surgeons in Western countries, as many believe nodal involvement to be a marker for systemic disease; if so extended lymph node resection would not impact on patient outcome. Given the low case volume of gastrectomy coupled with high prevalence of obese patients, many Western surgeons find radical gastrectomy with extended lymphadenectomy technically challenging, resulting in higher operative morbidity and mortality.

There are three important components to considering gastric cancer surgery. Firstly, the oncologic component of removing the cancer and its draining lymph nodes. Secondly, the extent of lymphadenectomy required to achieving a long-term disease free and overall survival. Finally, the method of reconstruction.

Extent of lymphadenectomy

Gastric cancers spread predominately by direct extension, lymphatic, haematogenous and peritoneal spread.²² The Japanese have extensively investigated the pattern of lymphatic spread and incorporated this into their approach

to radical gastric surgery. They introduced the concept of lymphatic nodal stations, numbering the stomach's named regional lymph nodes from 1-16, and then grouping these into four nodal tiers N1-4. N1 nodes are located along the lesser and greater curve, while left gastric, common hepatic, coeliac and splenic arteries nodes are N2, with N3 and N4 being more distant nodes.²³

These tiers lead to the modern classification of gastric surgery into a D1 resection, encompassing the N1 tier, and the more radical D2 resection, encompassing an N1 and N2 nodal resection. Initially this included the removal of the omental bursa with spleen and distal pancreas to facilitate complete lymphadenectomy. A D2 resection is considered in Japan to be the standard of care for a patient with resectable gastric cancer.²⁴

Controversy still exists as to what operation is appropriate in the Western setting. There have been a number of studies investigating the D1 versus D2 resection, the largest being the British Medical Research Council and the Dutch gastric cancer trials.^{25, 26} Neither trial used neoadjuvant or adjuvant therapies. The British Medical Research Council trial found no statistical difference in the five-year survival rates (35% D1 v 33%D2) but an increased complication rate (28% D1 v 46% D2) and mortality rate (6.5% D1 v 13% D2) in patients who had more extensive lymphadenectomy.²⁶ The Dutch trial initially also found no significant difference in disease-free or overall survival between the D1 and D2 groups.²⁵ Subsequent 11 year follow-up data showed improved survival for a subgroup of patients with stage II and IIIa disease who had a D2 resection.²⁷ In their 15 year follow up paper, these Dutch investigators reported the D2 patient cohort had better overall survival (21% D1 v 29% D2), and less gastric cancer related death (48% D1 v 37% D2 p=0.01) and local relapse (22% D1 v 12% D2).²⁸ The higher postoperative mortality, morbidity and reoperation rates in the D2 group in both the British Medical Research Council and Dutch trials have been attributed to splenectomy and distal pancreatectomy. Many surgeons have now abandoned this part of a D2 gastrectomy as the high perioperative complication rate appears to outweigh any potential survival benefit.²⁹

Japanese surgeons have assessed an even more extended resection of D2 with removal of the para-aortic nodes (D3 gastrectomy), but found no improvement over a D2 resection.³⁰ Therefore a spleen/pancreas preserving D2 resection is currently considered the operation of choice for resectable gastric cancer.

Types of gastrectomy

The type of operation has changed little in recent years, but the method of performing it has. A distal gastric cancer that can be removed with more than a five centimetre proximal margin and leaving enough functional proximal stomach can be treated with a radical distal gastrectomy.³¹ Otherwise, a total gastrectomy is preferred as gastric cancers can be multifocal and have submucosal spread.³² For a proximal tumour, a total gastrectomy allows wider surgical margins and a more extensive lymph node dissection when compared with a proximal partial gastrectomy. However hospital morbidity,

mortality and survival do not seem different.³³ Regarding the functional outcome, total gastrectomy is associated with less acid/bile reflux and anastomotic leak but more dumping syndrome, lipid malabsorption, anaemia and impaired bone metabolism compared to a proximal gastrectomy. Preservation of the pyloric branch of the vagal nerve may prevent much of the reflux symptoms.³³ Reconstruction in all cases is with the jejunum, classically via a Billroth II or a Roux-en-Y anastomosis. Various designs of jejunal pouch reconstruction have been attempted, however large trials comparing it to a traditional Roux-en-Y anastomosis are few. It appears that the major benefit of a pouch is in the early post-operative period where better food intake and increase in weight are noted. However, with prolonged follow-up these advantages seem less pronounced.³⁴

More recently there has been a major push to perform these operations using a minimally invasive approach initially with laparoscopic surgery and more recently using a robot. Additionally endoscopic mucosal resection has been offered as an alternative to radical surgery for intramucosal early gastric cancer, as approximately 96% of early gastric cancers do not have lymph node metastases.³⁵ The procedure should be performed in a high volume centre with considerable experience in this technique, which will involve close surveillance and long term follow-up.³⁶ There are currently no randomised control trials comparing endoscopic mucosal resection to standard open surgery.³⁷

When comparing laparoscopic with open gastrectomies, most of the studies have originated in Japan, with many of the early series utilising laparoscopic gastrectomy for early and/or distal gastric cancers.³⁸ With the advancement in laparoscopic technology and improved experience with laparoscopic surgery, more extensive surgeries, including laparoscopic assisted total gastrectomy, laparoscopic assisted D2 dissections, laparoscopic assisted proximal gastrectomy and pylorus-preserving gastrectomy, are becoming more common. The range of patients for whom laparoscopic surgery is considered appropriate has been expanded to include overweight patients with increased co-morbidities.³⁹ When comparing laparoscopic with open gastrectomy, there is a longer operating time for laparoscopic gastrectomy in most studies, however with experience this difference is shrinking. Laparoscopic gastrectomy has a lower blood loss, a faster return of gastrointestinal function, quicker ambulation and a shorter post-operative stay. There was no significant difference in cancer related mortality and the number of dissected lymph nodes was similar between the two groups.⁴⁰

As with other areas of surgery, there has been a recent push towards the use of a robot when performing a gastrectomy. A recent review of the published literature showed 10 original articles reporting 199 robotically assisted gastrectomies. It is thought that the surgery is safe, with low mortality (1.5%) and morbidity (15%).⁴¹ However, due to the limited number of studies and relatively short follow-up it is too early to make conclusions regarding this new technology.

Conclusion

Surgical approaches in resectable oesophageal and gastric cancers have evolved, with more accurate preoperative assessment of tumour stage and the development of better operative instrumentations. Operative procedure for each patient needs to be planned and individually tailored according to tumour characteristics, surgical fitness and the need for pre-operative therapy. Controversies regarding the extent of lymphadenectomy and various surgical techniques remain with more trials needed to evaluate both oncological and functional outcomes. Given the low incidence of oesophagogastric cancers in Western countries, these operations should be performed in tertiary centres with adequate case volumes and surgical experience to optimise patient outcome.

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