



Two Field versus three Field Lymphadenectomy in Carcinoma Esophagus: Current Perspectives

Saravanan MN*

Department of GI Surgery & Liver Transplant, GB Pant Institute of PGMER, India

Abstract

The extent of lymphadenectomy in curative resection for esophageal cancer can be a standard 2-field, extended 2-field or a 3-field lymphadenectomy. Japanese surgeons base their adoption of the 3-field lymphadenectomy (3FL) on the superior survival with comparable mortality even though morbidity is higher compared to the 2-field lymphadenectomy (2FL). Selective performance of 3FL based on sentinel node sampling and other imaging strategies has been described. Thoraco-laparoscopic approach has been increasingly utilised in the performance of systematic lymphadenectomy. There is still no clear consensus on the choice between 2FL and 3FL.

Keywords: Lymphadenectomy; Thoraco-laparoscopic approach; Esophageal cancer

Introduction

The 3-field lymphadenectomy has been practised since 1980s in Japan as a part of radical resection in esophageal cancer. It is unclear whether the cited superior survival benefits due to stage migration and improved staging, rather than actual therapeutic benefit. Compared to the 2-field lymphadenectomy and its modifications, the 3-field dissection has higher morbidity. This along with the paucity of data from randomized trials has led most western centres to adopt the 2-field lymphadenectomy, even as Japanese surgeons continue to practice 3-field lymphadenectomy as their experience precludes them from conducting randomized trials out of ethical concerns. Predominant adenocarcinomas in the west and varied tumour biology have been cited for differences in outcomes. This review describes the current terminology, the outcomes in short term and long term and factors that can possibly help choosing between the 2 techniques.

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*Correspondence:

Saravanan MN, Department of GI Surgery & Liver Transplant GB Pant Institute of PGMER, New Delhi, 110002, India, Tel: 919999871310; 919718599581;

E-mail: mnsaravanan@rediffmail.com

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Terminology and Components

In 1994, the Consensus Conference of the International Society for Diseases of the Esophagus (ISDE) held at Munich defined the extent of lymphadenectomy as standard, extended, total mediastinal and three-field lymphadenectomy. Accordingly, the term 2-field lymphadenectomy (2FL) is used for abdominal and mediastinal lymph node dissection while the term 3-field lymphadenectomy (3FL) is used for removal of abdominal, mediastinal and cervical lymph nodes [1].

Currently used terminology includes standard 2-field, extended 2-field and 3-field lymphadenectomy. The area of dissection for lymphadenectomy includes the bilateral lower cervical lymph nodes (including cervical paraesophageal and bilateral supraclavicular lymph nodes), the mediastinal lymph nodes (including the paraesophageal lymph nodes and the lymph nodes along bilateral recurrent nerves) and the upper abdominal lymph nodes (D2 lymphadenectomy). The 3FL involves dissection in all of these 3 anatomical compartments, while the extended 2FL includes dissection of all the compartments except the bilateral cervical lymph nodes. The standard 2FL does not include the systematic nodal dissection of the upper mediastinal lymph nodes and is also sometimes referred to as a modified “infracarinal 2-field lymphadenectomy” [2,3].

Rationale for Extended Lymphadenectomy

The seminal paper by Akiyama and colleagues has been the premise for the proponents of the 3-field approach. The cited reasons behind performing a 3-field lymphadenectomy include:

1. Incidence of cervical lymph nodal involvement to the tune of 30% in lower and mid esophageal cancer.
2. It enables complete tumour (N) staging by way of systematic dissection.

3. Reduced risk of loco-regional recurrence with better overall survival.

Akiyama and colleagues cited a 5-year survival of 55% for the 3-field approach as compared to 38% for the 2-field approach from a single institute series of 913 esophagectomies [4].

Outcomes of 2FL v/s 3FL

Operative

Duration of surgery and intraoperative blood loss is expectedly more with 3FL dissection compared to 2FL.

Postoperative morbidity

3FL had more complications than 2FL in terms of anastomotic leak and recurrent nerve palsy, while the incidences of chylothorax and pulmonary complications were not significantly different in a meta-analysis [5]. While the range of overall morbidity after 3FL and 2FL is 54-64% and 42-56% respectively, mortality is comparable in high volume centres [6,7]. Risk of recurrent laryngeal nerve palsy is about 20-28% after 3FL compared to 10-14% following 2FL [6-8]. Western series describing their experience with 3F dissection have reported lower rates of nerve injury between 3-9% [9,10]. Incidence of neck leak (anastomotic) ranges from 33-36% in 3F dissection and 11-23% in 2F dissection [7,11]. Again western experience with 3F dissection reported a lower leak rate between 4-11% [9,10].

Oncological

While the incidence of cervical nodal disease with a 3FL varies from 23-33%; based on the tumour location in the upper, mid and lower thoracic esophagus, it corresponds to about 45%, 30% and 20% respectively [9,10,12,13]. Lerut and colleagues noted upstaging to stage IV in 12% of patients with 3FL, with a 8% incidence of skip metastasis to cervical lymph nodes. An average yield of 6-7 positive nodes per patients was observed in western series of 3FL [9,10]. Proponents of 2FL argue that the incidence of isolated recurrence in the neck is low ranging between 6-8.5%. However, cervical recurrence accounts for about 20% of all nodal recurrence [14,15]. Survival advantage observed with 3FL (5 year survival: 40-66%) as compared to 2FL (5 year survival: 26-48%), has been mainly from Japanese data [6,13,16,17]. Statistically significant improvement in 5-year survival was noted in a meta-analysis with a pooled RR of 1.37 (95%CI: 1.18-1.59; P=0.0002) [5].

Evidence from Randomised Data

Kato series

Morbidity was equivalent between 2F and 3F dissection. Locoregional recurrence was higher in 2F (38%) compared to 3F (17%), while distant metastasis occurred in 16% and 17% patients of 2F and 3F group respectively. 3FL group (49%) was found to offer a 5-year survival advantage over the 2FL group (34%) [17].

Nishihara series

No difference was observed between 2FL (30 patients) and 3FL (32 patients) in terms of morbidity and mortality. While recurrence was 24% with 2F and 20% with 3F, 5-year survival was 66% and 48% respectively in 3FL and 2FL arms [18].

Criticism of Literature

Selection bias with poorly matched groups. Randomisation protocol in Kato series has been criticized. Adjuvant/ neoadjuvant therapy is not controlled. Comparison to historic controls in studies

without a comparative arm. Stage migration may explain the improved survival observed with 3FL.

Selective Approach

The risk of over-treating esophageal cancer with a 3FL with a formidably higher risk of recurrent nerve injury which can translate into higher pulmonary complications has been a significant concern. Selective performance of a 3FL with consideration of following factors may therefore be an alternative approach.

Site and number of lymph nodes involved

While 3FL appears to be beneficial in upper and mid-thoracic tumours, there is no consensus on the routine application to lower third tumours. Possible use of sentinel lymph node or imaging guided assessment of the neck may help identifying a high risk group that needs a 3FL. Nakagawa and colleagues concluded that cervical node dissection is only beneficial for patients with cancer of the upper and mid-thoracic esophagus and with less than five positive nodes [19]. Tabira and colleagues suggested that 3FL is beneficial only in patients with metastasis in one to four lymph nodes [20].

Depth

While there is no role in early superficial esophageal cancer, it has a role in tumours beyond T1b upto T3. The incidence of cervical nodal involvement even when the tumour invades up to the submucosa has been over 15% [21].

Imaging based

Selective neck dissection based on a fairly accurate and sensitive cervical ultrasonography to detect cervical lymphadenopathy has been advocated [22].

Sentinel lymph node based

When mediastinal recurrent laryngeal nerve lymph node is positive for malignancy, the incidence of cervical lymph node involvement is between 41-52% as compared to between 10-12% when the recurrent laryngeal nerve node is free of tumour [23-25]. This formed the basis of sentinel nodal sampling from the recurrent laryngeal nerve node and selective neck dissection in one of the following ways: Two staged manner: Based on histopathology (conventional Hematoxylin and Eosin paraffin section). This may be cumbersome when anastomosis has already been performed in the neck [26]. Single staged surgery based on frozen section analysis or reverse transcriptase-polymerase chain reaction for detection of micrometastasis [27].

Other Approaches

Thoracoscopic approach with patient in a prone position with a systematic lymphadenectomy of all lymphnodes below the level of the carina, essentially a modified infra-carinal 2FL, with a laparoscopic upper abdominal D2 lymphadenectomy later in supine position is the author's current practice without a sentinel node sampling. 3FL is selectively considered in the presence of overtly palpable neck nodes. Emerging techniques include endobronchial ultrasound (EBUS) (32%) which is superior in its sensitivity to detect the recurrent laryngeal lymph node metastasis compared to endoscopic ultrasound (EUS) (32%) and CT (29%). A combination of EBUS and EUS has been suggested in sentinel node sampling [28].

Conclusion

The practice of lymphadenectomy reflects the underlying philosophy behind the radicality of the surgical procedure in

esophageal cancer. It seeks to strike a balance between patient safety on one hand and the perceived actual benefit in terms of long term survival in the light of the stage migration seen with extended lymphadenectomy. If patients at high risk of cervical lymphadenopathy are identified preoperatively, selective application of extended lymphadenectomy can help avoid morbidity in the low risk patients.

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