Summary
Treatment of Esophageal Cancer: Systematic Review on Surgical Techniques

The incidence of esophageal cancer in Canada is low. This disease affects mainly men and has a rapid progression. Its dire prognosis is due primarily to the rich blood and lymph supply to the esophagus and to patients' poor clinical condition often associated with weight loss and comorbidities. Tumour extent and lymph node involvement are the two most important prognostic factors for esophageal cancer. The therapeutic strategy consists of assessment of the patient's clinical condition, tumour staging and different treatment modalities, including surgical resection with neoadjuvant or adjuvant chemotherapy or radiation therapy. The two most common histological types are squamous cell carcinoma and adenocarcinoma. The incidence of adenocarcinoma is increasing in Canada and in many Western countries, and some authors have proposed treating these two histological types as distinct entities. Obesity, tobacco use and alcohol consumption are the primary risk factors for esophageal cancer.

The surgical treatment of esophageal cancer is complex. It aims to achieve complete tumour resection (R0) with a subsequent improvement in survival and to decrease the risk of postoperative mortality and complications. This risk is high, however, and overall five-year survival rates are low, approximately 25% after surgery alone.

Recommendations in the different clinical practice guidelines available worldwide diverge as to the choice of type of resection. On the basis of the outcomes of a large randomized controlled trial, the Belgian Health Care Knowledge Centre (KCE) recommends the en-bloc resection technique with two-field lymph node dissection. The U.S. guidelines published by the National Comprehensive Cancer Network (NCCN) indicate that the choice of type of resection is based on surgeon experience and preference and on patient preference. The Scottish Intercollegiate Guidelines Network (SIGN) makes no recommendation on the choice of technique. The Société française de chirurgie digestive (SFCD) and the Association de chirurgie hépatobiliaire et de transplantation hépatique (ACHBT) recommend the transthoracic approach, or transhiatal esophagectomy in the event of contraindications to thoracotomy or of a high operative risk. Two-field lymph node dissection is then indicated. Three-field lymph node dissection is recommended only for tumours in the upper third of the esophagus.

This document was produced at the request of the Direction de la lutte contre le cancer, on the recommendation of the Comité de l'évolution des pratiques en oncologie (CEPO), and is a systematic review of studies comparing the efficacy of different surgical techniques, including invasive procedures, minimally invasive techniques, and lymph node dissection, for the curative treatment of esophageal cancer.

Methodology

This assessment includes the analysis of health-technology assessment reports, clinical practice guidelines, systematic reviews with or without meta-analyses, randomized controlled trials (RCTs) and non-randomized controlled studies of the surgical treatment of esophageal cancer, published until December 2009. Regular updates were performed until the time of publication.

The selected studies were designed to assess the comparative efficacy of :

- invasive transthoracic vs transhiatal surgical techniques;
- minimally invasive vs invasive surgical techniques;
- two-field vs three-field lymph node dissection.

Primary efficacy endpoints were mortality during initial hospital stay or 30 days post surgery, overall and disease-free survival, and adverse effects associated with the surgical procedure. Secondary endpoints were operative data, oncological results, and quality of life.

Results

The specific characteristics of esophageal cancer (low incidence and rapid progression) make it difficult to recruit study patients. The selected studies did not have sufficient statistical power to detect a difference between the two surgical treatment groups in terms of primary and secondary endpoints. A non-significant result may indicate that the studies were unable to show a difference, and not that the procedures are equivalent.

The heterogeneity of tumour characteristics (histological type, location, stage) and of patient clinical characteristics, the different surgical techniques proposed and the lack of standardization of these techniques do not make it possible to conduct controlled studies of high methodological quality. Few RCTs have been published on the topic, and most of the studies are non-randomized and retrospective, and compare patient groups that are generally non-equivalent. As a result, studies of poor and average methodological quality were selected, and their results must be interpreted with caution.

Transthoracic vs transhiatal technique

In general, the studies yielded similar postoperative mortality rates among the patients with esophageal cancer who underwent transthoracic or transhiatal esophagectomies. Furthermore, for patient subgroups, the results of a few studies showed the following:

- a gain in overall median or five-year survival and in disease-free survival in favour of the en-bloc transthoracic procedure in patients with adenocarcinoma of the esophagus who had had one to eight involved lymph nodes in the resection specimen;
- with respect to squamous cell carcinoma, complete resection, no lymph node involvement (N0) and dissection of more than 16 involved lymph nodes, rather than the type of surgical procedure, were factors associated with better short-term and long-term (five-year) survival.

A single RCT reported more frequent pulmonary complications and chylothorax in patients who underwent en-bloc transthoracic procedures.

Cervical anastomosis promotes the formation of anastomotic leaks. The transhiatal approach requires a cervical anastomosis in all cases and therefore leads to a high risk of cervical anastomotic leaks. Furthermore, the thoracic and mediastinal leaks that may occur after transthoracic surgery are associated with a greater risk of complications.

The en-bloc transthoracic technique permits dissection of a greater number of lymph nodes. However, it increases the risk of pulmonary complications liable to prolong hospital and intensive care stays.

Available results on complete resection rates and tumour recurrence rates are not sufficient to conclude on the superiority of one technique over the other.

There were no differences in quality of life among patients who underwent either of the two surgical techniques.

Minimally invasive esophagectomy (MIE) vs invasive techniques

The systematic reviews concluded on the feasibility of MIE, which leads to lower postoperative morbidity and mortality and shorter hospital stays. However, these reviews stressed the need for better controlled studies, especially randomized ones.

The results of two poor-quality retrospective studies indicate that invasive and minimally invasive esophagectomy are equivalent in terms of postoperative morbidity and mortality and overall five-year survival. The procedure is longer with MIE. These data are not sufficient to conclude on the efficacy of MIE.

Two-field lymph node dissection vs three-field lymph node dissection

Three-field lymph node dissection differs from two-field dissection as follows:

- significantly lower rates in postoperative mortality and anastomotic leaks (one RCT);
- greater incidence of recurrent laryngeal nerve paralysis (one RCT);
- longer procedure (two RCTs);

- greater total number of dissected lymph nodes (two RCTs).

Nevertheless, tumour recurrence rates do not differ, regardless of the extent of lymph node dissection. A subgroup analysis of patients who had complete resections (R0) in relation to the presence (N1) or absence (N0) of lymph node involvement showed that three-field lymph node dissection achieved better median and overall five-year survival rates.

However, it is impossible to ensure that these outcomes were due to the extent of lymph node dissection rather than to other differences in the surgical techniques.

Conclusions

In light of the analysis of the selected studies on the surgical treatment of esophageal cancer, and given that the studies were limited in number, had low statistical power owing to small samples and were of poor methodological quality, AETMIS has reached the following conclusions:

No difference was shown between the transthoracic and transhiatal techniques in terms of:

- postoperative mortality, regardless of histological tumour type;
- cardiac or infectious complications.

Transthoracic en-bloc esophagectomy (according to the results of one RCT):

- increases the risk of pulmonary complications and chylothorax in patients with adenocarcinoma of the esophagus or of the gastro-esophageal junction;
- permits dissection of a greater number of lymph nodes;
- improves long-term overall survival (five-year) and disease-free survival when the number of involved lymph nodes (N1) is less than eight in the case of adenocarcinoma of the distal esophagus or of the gastro-esophageal junction; and when tumour resection is complete, there is no lymph node involvement (N0) and the resection specimen has more than 16 involved lymph nodes in the case of squamous cell carcinoma of the esophagus.

Transhiatal esophagectomy:

- increases the risk of recurrent laryngeal nerve lesions.

Cervical anastomosis:

- is associated to anastomotic leaks; these leaks are frequent but have less severe consequences than thoracic or mediastinal leaks. Note that the transhiatal technique is always associated with a cervical anastomosis.

Minimally invasive esophagectomy:

- The weakness of the available evidence on the efficacy of the different invasive and non-invasive techniques, on the one hand, and on that of the multiple combinations of these techniques, on the other hand, does not make it possible to conclude on the superiority of MIE in terms of short-term and oncological outcomes. Minimally invasive esophagectomy remains under development.

Three-field lymph node dissection:

- Available data are insufficient to conclude on the clinical benefit of extending lymph node dissection to the cervical region.