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Surgical concepts in esophageal cancer

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Summary Despite neoadjuvant treatment being available for esophageal cancer, surgery remains the cornerstone of treatment. The aim of this article is to give a clear and simple overview of current issues in the available surgical strategies relating to locally limited and advanced disease, including the following: clinical staging, preoperative general condition and comorbidities, surgical strategy, surgical approaches, postoperative complications and the role of surgery in advanced disease. Based on a literature search and our personal professional experience to date, enhanced surgical treatment protocols for the treatment of the adenocarcinomas of esophagogastric junction (AEG) and the squamous cell carcinoma of the esophagus are presented and discussed. Eligibility for a surgical resection strongly depends on the stage of the tumor and on the comorbidities. A minimally invasive laparoscopic approach should be preferred in the case of limited disease, regardless of its histology, or limited/advanced intrathoracic squamous cell carcinoma (hybrid technique: laparoscopic approach combined with thoracotomy). The surgical strategy in the case of adenocarcinoma to achieve radical resection depends on the tumor location. Finally, surgery should be performed by a multidisciplinary team that includes medical oncologists, radiation oncologists, gastroenterologists, dieticians and physiotherapists, so as to minimize the postoperative complications rates and improve early postoperative outcomes and overall patient survival. Therefore, we support the centralization of treatment of esophageal cancer to high volume centers.

Keywords Surgery · Esophageal cancer · Multimodal treatment · Adenocarcinoma · Squamous cell carcinoma

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Introduction

Surgery remains as of today the cornerstone treatment to cure esophageal cancer, despite the introduction of neoadjuvant treatment applicable to this type of cancer [1].

This type of treatment however should be designed and implemented by a team of specialists from across the various disciplines, and not just by the surgeon himself, each of them bringing his expertise. In other words a "multidisciplinary" team should be formed involving the engagement of medical oncologists, radiation oncologists, gastroenterologists, dieticians and physiotherapists [2].

The aim of this article is to give an clear and simple overview of current issues in the available surgical strategies relating to locally limited and advanced disease and in doing so we have focused on the following key-considerations in this context: defining clinical staging, preoperative general condition and comorbidity (nutritional and respiratory status), surgical strategy, looking into the different types of surgical approaches (minimally invasive vs open surgery), postoperative complications and focusing on the role of surgery in advanced disease.

Based on the available literature and our personal professional experience to date, we will discuss the introduction of enhanced surgical treatment protocols for the treatment of the adenocarcinomas of esophagogastric junction (AEG) and the squamous cell carcinoma of the esophagus.

Methods

We conducted a review of relevant articles that have been published in "PubMed" since 2014. The search was done using the following keywords on PubMed's website: "esophageal cancer"; "surgery"; "neoadjuvant therapy". Randomized controlled trials, cohort studies, and meta-analyses were also included.

A total of 127 related articles were identified, of which 64 abstracts have been selected and 21 papers have been included in this short review.

Discussion

It has now been widely accepted that AEG and squamous cell carcinomas of the esophagus are not identical diseases and should be treated as two separated diseases.

Despite the different histological entity, whether a patient is eligible for a surgical resection strongly depends on the stage of the tumor and on the comorbidities of the patient [3, 4].

In order to adequately determine and evaluate the staging of the tumor, a thorough clinical screening of the patient and a total body computed tomography (CT) [1, 5] need to be conducted as a bare minimum. Notwithstanding those initial evaluations, in order to determine the local tumor and any lymphatic metastasis, patients who are potential candidates for surgical resection should undergo an endoscopic ultrasound (EUS). The role of 18F-fluorodesoxyglucose positron emission tomography-CT (PET-CT) in preoperative staging is controversial [1, 6, 7].

As soon as these evaluations tests and exams are conducted, a multidisciplinary team is set up to review the results and choose the appropriate treatment of the individual patient. In doing so, the multidisciplinary team would also consider the histological subtype, clinical stage, and the location of the tumor. Patients with cervical squamous cell carcinoma are usually not eligible candidates to undergo surgery for the treatment of the cancer due to the limited successful outcome that may be achieved through the appropriate surgical techniques, such as for example the common difficulty to achieve proximal free resections margins [7, 8].

Moreover, the eligibility of the patient to undergo surgery must be assessed on its preoperative general conditions. Cardiovascular, metabolic and respiratory comorbidities are risk factors that can give rise to several postoperative complications, including anastomotic leakage and respiratory failure. In addition diabetes mellitus, congestive heart failure and hypertension can be associated with an increased rate of anastomotic complications [4, 9].

The patient's age also plays a significant role in selecting the appropriate treatment and its ongoing evaluation and management in cancer patients although age itself might not influence postoperative outcomes as it is often assumed. In other words an older patient should not be precluded from undergoing surgical treatment based solely on age as surgery might indeed extend that patient's life expectancy [10]. Therefore treatment decisions should be made on an individual basis and with enhanced levels of caution in older patients.

Other factors such as the nutritional deficiencies and preoperative pulmonary function are also strictly connected with a high risk for early postoperative anastomotic leak and pneumonia [11]. Many studies, in the context of patients after a perioperative or neoadjuvant treatment, showed a significant reduction of early major surgical complications where preoperative nutritional and cardiorespiratory conditions had been improved as a result of physiotherapy (such as inspiratory muscle training) and high calorie and protein diet [12]. Therefore, preoperative optimization of nutritional and respiratory status is mandatory to avoid potential postoperative anastomotic leak and pneumonia.

Adenocarcinoma

The selection of optimal neoadjuvant or perioperative treatment is based on tumor location. The preferred treatment of AEG I tumors in most cancer treatment centers according to the CROSS trial [13] is radiochemotherapy. Treatment of AEG II tumors is controversial between radio-chemotherapy and perioperative treatment with systemic chemotherapy such as the FLOT regimen. In most cancer treatment centers in Europe, patients with AEG III tumors will be treated with perioperative treatment according to the FLOT-4 trial [14].

As regards the choice of surgical approach and strategy, localization of the tumor and its histology is fundamental to the appropriate surgical decision. Multimodal therapeutic strategy, based on evidence-based medicine and ESMO guidelines, is showed in Fig. 1 [7]. In the case of locally limited adenocarcinoma (staging Ia–Ib), primary resection is recommended and should be performed with a minimally invasive approach, according to the surgeon's experience.

The type of the procedure should be chosen based on the endoscopic revaluation aimed at defining the tumor localization, according to Siewert's classification.

We suggested, as other centers did, in case of AEG I tumor, to perform a subtotal esophagectomy (2 fields lymphadenectomy: abdominal and intrathoracic), with intrathoracic anastomosis. Gastrectomy with extended intra-abdominal lymphadenectomy and transhiatal anastomosis is mandatory in the case of AEG III adenocarcinoma. AEG II tumor has controversial surgical indications due to difficulties to achieve an adequate radical intra-abdominal/intrathoracic lymphadenectomy and free resections

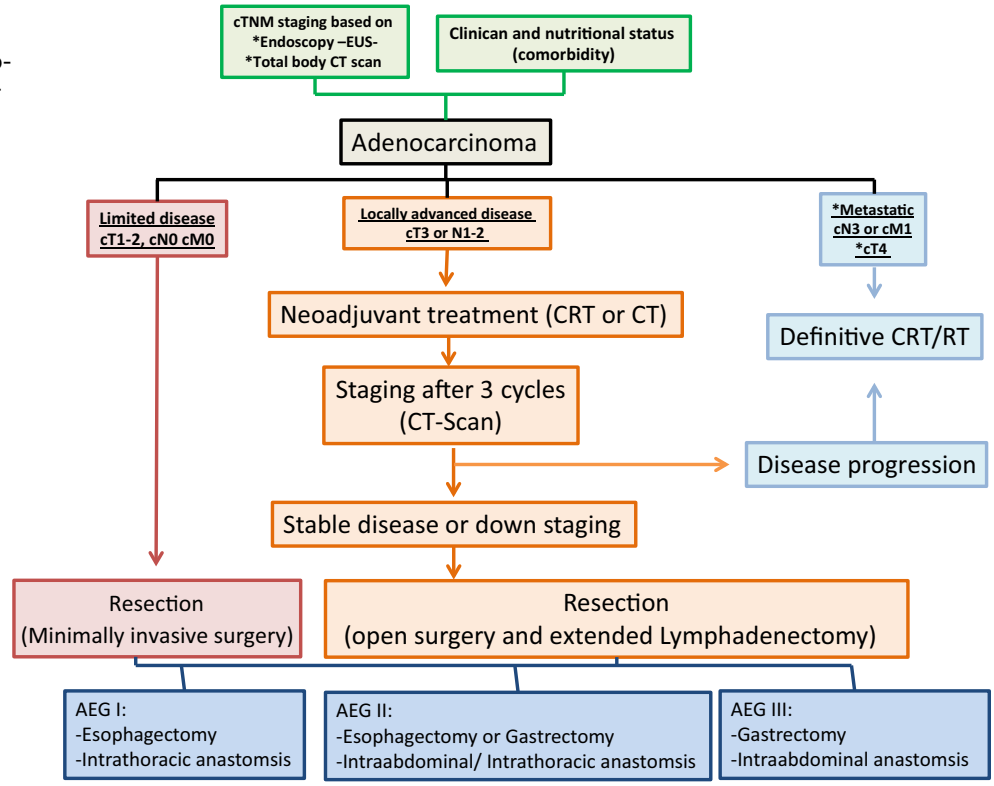

Fig. 1 Algorithm for the treatment of esophageal adenocarcinoma. *CRT* chemo-radiotherapy, *CRT/RT* chemo-radiotherapy/radiotherapy, *CT* chemotherapy, *EUS* endoscopic ultrasound

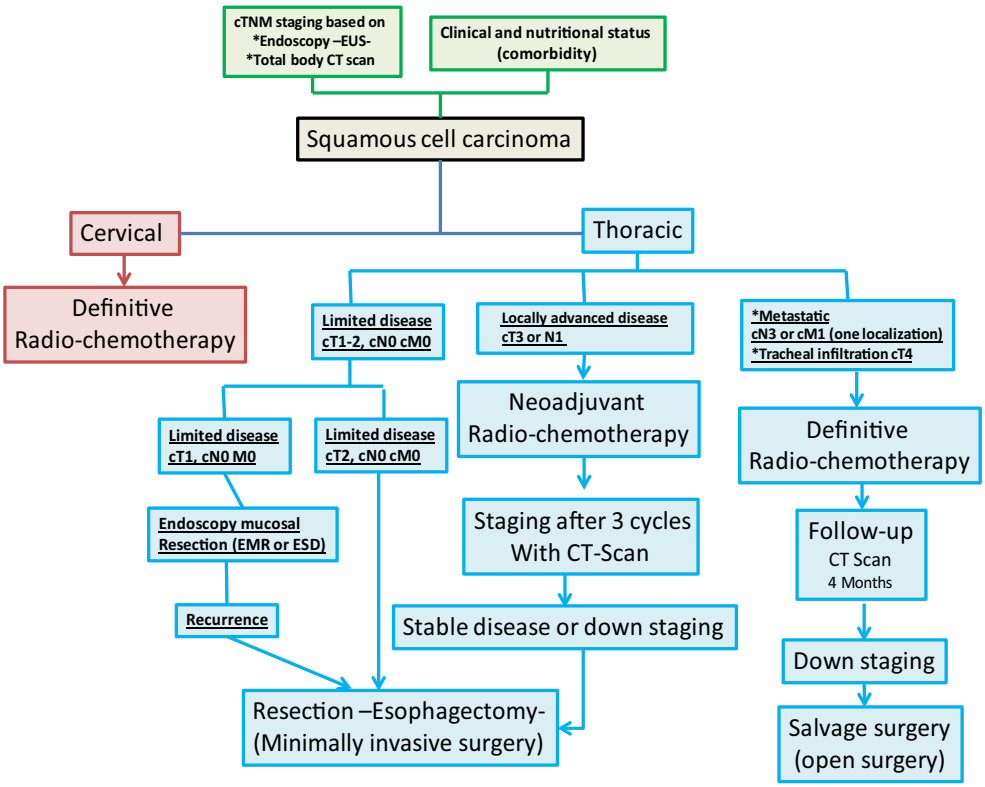

Fig. 2 Algorithm for the treatment of squamous cell carcinoma

esophageal margins. Based on intraoperative conditions, an expert surgeon would opt either for intra-abdominal anastomosis (gastrectomy) or for a subtotal esophagectomy with intrathoracic anastomosis.

Squamous cell carcinoma

In the case of squamous cell cT1 tumor, patients should undergo a primary endoscopic resection: endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) are both regarded as effective endoscopic resection techniques [15]. Primary esophagectomy is suggested in the case of locally limited disease (cT2) and thoracic localization (staging Ia–Ib). A minimally invasive laparoscopic approach should be preferred because an intra-abdominal lymphadenectomy is not required.

Some authors suggest, regardless of clinical staging, an hybrid technique (laparoscopic approach with thoracotomy) which combines the advantages of laparoscopic technique and, at the same time, permits a radical extended intrathoracic lymphadenectomy [16, 17].

In the case of squamous cancer staging IIa–b and IIIa–b, neoadjuvant radio-chemotherapy is mandatory [13]. Even many experienced centers prefer definitive CRT for esophageal tumors with a very proximal/cervical location. Definitive chemo-radiotherapy or radiotherapy alone, should be also preferred for patients not willing to undergo esophageal surgery or who are medically unfit for major surgery, regardless of the histology.

Multimodal therapeutic strategy, in the case of squamous cell carcinoma, is showed in Fig. 2.

Until now, in the case of locally limited adenocarcinoma or squamous cell carcinoma, no data showed a significant oncological advantage in terms of overall survival between minimally invasive and open surgery. In the literature, the postoperative advantages, in terms of reduction of complications after minimally invasive procedures, is still not clear. All authors agree observing a significant reduction of postoperative pain and blood transfusion with a collateral earlier mobilization of the patient after a robotic or laparoscopic procedure [18, 19]. However the regular review comparing minimally invasive technique to open surgery showed that perioperative mortality and major early morbidity (anastomotic leak, chyle leak, vocal cord damage, and pulmonary complications) of the two surgery techniques are similar [16–19].

If we focused on local advanced tumor, not primary resectable, surgery alone would not be a standard treatment since a complete (R0) tumor resection can be achieved only in 30% of T4 cases and the long-term survival of the patient is statistically low (less than 20%). Meta-analysis demonstrate that patients with locally advanced squamous cell carcinoma benefit from preoperative radio-chemotherapy, with higher rates of complete tumor resection and better local tumor control and survival [13].

In case of T4 adenocarcinoma, no data showed a better overall survival after definitive medical treatment and following salvage surgery, if CT scan detected a tumor down staging, as compare with surveillance alone.

In case of squamous cell carcinoma, there are currently no randomized studies comparing neoadjuvant radio-chemotherapy with planned surgery or definitive radio-chemotherapy with close surveillance and salvage surgery on demand for local tumor persistence or progression [20].

Since esophageal cancer varies widely in tumor size, location, lymph node metastasis, and the patient's general health status, choosing the appropriate type of resection for each patient is still a difficult decision. Of note, the results of large, multicenter studies in different health systems provide sufficient evidence to support the centralization of esophagectomy to high volume centers, with a lower rate of morbidity and better infrastructure to deal with complications following major surgery, thereby preventing further mortality [7, 21].

Conclusion

- As of today several elements of surgical strategy, such as the surgical approach and the role of surgery in case of advanced and metastatic disease, in the case of esophageal cancer, regardless of its histology, remain a topic of debate.
- Esophageal surgery should be carried out by experienced surgeons, so as to minimize the postoperative complications rates, improve the early postoperative outcomes and the overall patient survival. Therefore we support the need of centralization of esophageal cancer to high volume centers.
- A minimally invasive laparoscopic approach should be preferred in the case of limited disease, regardless of histology, or limited/advanced intrathoracic squamous cell carcinoma (hybrid technique: laparoscopic approach combined with thoracotomy).
- Surgical strategy in the case of adenocarcinoma is dependent on the tumor location to achieve radical resection.

Conflict of interest P.N.C. Girotti and I. Königsrainer declare that they have no competing interests.

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