

Esophagogastric junction gastrointestinal stromal tumor: Resection vs enucleation

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Abstract

Esophageal gastrointestinal stromal tumors (GISTs) are extremely uncommon, representing approximately 5% of GISTs with the majority of esophageal GISTs occurring at the esophagogastric junction (EGJ). The treatment options available for these GISTs are fairly controversial. Many different options are nowadays at our disposal. From surgery to the target therapies we have the possibility to treat the majority of GISTs, including those which are defined as unresectable. The EGJ GISTs represent a stimulating challenge for the surgeon. The anatomical location increases the possibility of post-operative complications. As the role of negative margins in GIST surgery is still controversial and the efficacy of target therapy has been demonstrated, why not treat EGJ GISTs with enucleation and, where indicated, adjuvant target therapy?

What is an esophagogastric junction (EGJ) gastrointestinal stromal tumor (GIST) and, more importantly, how do you effectively treat it? These questions have no definitive answers. In the available literature on the subject, GISTs of the EGJ are often classified among gastric or esophageal lesions, without specifying the precise anatomical site. The aim of this article is not to establish the anatomical parameters for classifying EGJ GISTs, but rather to consider the available treatment options.

The treatment options available for EGJ GISTs are fairly controversial^[1]. Esophageal GISTs are extremely uncommon, representing approximately 5% of all GISTs with the majority of esophageal GISTs occurring at the EGJ^[2,3]. Relevant literature reports only a few cases of these kinds of tumors, some treated with esophageal resection and others treated with enucleation. We all know how difficult it is to accurately assess the aggressive behavior of a GIST using the official classification criteria of 2002^[4]. This classification considers two parameters: tumor size and mitotic index. Tumors are classified using a ranking system, grouping tumors into very low-, low-, intermediate-, and high-risk categories based on size (< 2 cm, 2-5 cm, 5-10 cm, and > 10 cm) and on number of mitoses within 50 high-power fields (HPFs); such

measurements typically being reported as less than 5, 5 to 10, or greater than 10^[5]. For patients who suffer from a localized and resectable condition, surgery should be the initial stage of treatment. The goal of surgical intervention should be complete resection, leaving a negative margin and an intact pseudocapsule. Anatomical positioning should be considered so as to avoid inadvertently increasing intra- and post-operative morbidity and mortality rates. GISTs typically have promising survival prognoses given the many therapeutic options at our disposal. The use of inhibitors of KIT, PDGFR- α , ARG, c-FMS, ABL and BCR-ABL such as imatinib mesylate^[6,7] during surgery has dramatically improved the prognosis of both operable and inoperable GISTs^[8]. For patients who develop a resistance to imatinib, it is also possible to begin therapy using a multi-target tyrosine kinase inhibitor (sunitinib)^[9].

The main obstacle preventing a comprehensive understanding of EGJ GISTs and their various methods of treatment is the condition's rarity and the subsequent shortage of literature on the subject. The need for more in-depth clinical studies from experienced treatment centers is of utmost importance.

The original approach to surgically treating general GISTs, particularly EGJ GISTs, was initially influenced by distinctly "oncological-oriented" surgical techniques. Such methods included extended resections with complete lymphadenectomies. However, after taking note of the surprisingly low local and lymphatic diffusion rates of these tumors, the current approach has gradually become less aggressive. Nowadays one of the "hot topics" for EGJ GISTs is the ongoing debate between resection and enucleation, both treatments having been incorporated within target therapy. The significance of microscopically negative margins remains a very controversial topic^[10]. In 2004, the GIST Consensus Conference defined such margin negativity as being the primary goal of surgical management of GISTs, agreeing that positive margins had not been conclusively proven to affect the patient's survival^[11]. In the same year, National Comprehensive Cancer Network (NCCN) guidelines stated that the objective of surgical treatment should be the macroscopic resection of the tumor^[12]. Later, in 2007, the NCCN further ratified these guidelines, introducing a set of criteria which ultimately established negative microscopic margins as being the key objective in surgical treatment^[13]. The topic remains highly controversial with many notable authors having yet to come to a general consensus. Some authors, such as Langer *et al*^[14], maintain that the negative microscopic margins serve as a reliable prognostic indicator of tumor recurrence while others, such as DeMatteo *et al*^[15], suggest that recurrences are due more to the biological behavior of the tumor itself than to the microscopic margins. Finally, several authors agree that negative macroscopic margins often require too invasive a procedure, especially if extended surgery could potentially damage neighboring viscera thereby increasing the intra- and post-operative morbidity and mortality rates^[16,17]. Another issue that should be considered is the fact that tumors located

in the stomach often have more favorable recovery outcomes after undergoing such treatment^[8].

Regardless of the technical expertise of the surgeon, esophageal surgery remains a very difficult and precarious procedure. Various studies have been conducted regarding the complication rates of esophageal surgery. For benign pathologies that do not require radical resections or lymphadenectomies, distinct complication rates have been reported. Morbidity and mortality rates for both laparoscopic and open surgery procedures range from 6.4% to 24% and from 0% to 1.3%, respectively^[18-21].

In conclusion, no definitive treatment recommendation can be made due to the fact that the literature supporting each approach has been derived from small case studies from which reliable conclusions cannot be drawn. The inherent risks of aggressive gastroesophageal surgery, a relatively invasive procedure to address a pathology that has demonstrated an increasingly positive response to pharmacological treatments, have to be considered. Moreover, the lack of substantial evidence supporting the claim that extensive resections are correlated with better survival rates has to be kept in mind. Why not consider the possibility of treating EGJ GISTs with enucleation and, if indicated, adjuvant target therapy, thereby reducing esophageal and gastroesophageal resections which undoubtedly result in higher morbidity and mortality rates? A prospective multicenter evaluation focusing on EGJ GIST outcome following different surgical and medical treatments might be the best way to better understand this peculiar pathology.

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