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Review Article

Controversies in management of gastric cancer



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ABSTRACT

The rates of relapse and death remain high in gastric cancer patients especially in advanced stages. Local relapses in the tumor bed and regional lymph nodes and distant spread result in a failure after a R0 resection. Even following significant advances in chemotherapy, survival rates continue to be dismal. A multidisciplinary team approach is the way forward and could possibly reduce the recurrence rates and hence improve survival. As a result of several prospective, randomized trials, many surgeons view the large volume of international opinion concerning optimal gastric cancer treatment as having been filtered clean. But does this view withstand detailed scrutiny? This new therapeutic approach in gastric cancer is rapidly evolving and has led to a series of controversies on the best strategy to follow. Emphasizing existing trial findings and controversies, this review hopes to illuminate the topic, so the reader can reach his own conclusions.

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1. Introduction

Management of gastric cancer is a challenging and contemporary topic in modern oncology. Despite a declining incidence in Western countries, gastric cancer is often diagnosed at advanced stages and its mortality remains high. Surgery is the only possible curative treatment, but the 5-year survival rate is still poor, even when extended lymphadenectomy is performed. The aim of this paper is to answer questions dealing with diagnosis and treatment currently debated in the scientific meetings and literature of gastric carcinoma in the

light of the best evidence available. The questions put forward in this manuscript are the following:

1. What is the best treatment of early gastric cancer?
2. What is the current role of endoscopic ultrasound (EUS) and staging laparoscopy in staging and management of gastric cancer?
3. Which treatment strategy can be followed for patients with a positive peritoneal lavage?
4. What should be the ideal reconstruction?
5. What kind of lymphadenectomy should be performed?
6. What is the role of pancreaticosplenectomy?

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7. What is the role of para-aortic lymphadenectomy?
8. Is the laparoscopic approach an alternative to the open approach?
9. What should the reference chemotherapy combination for perioperative treatment in patients with resectable disease?
10. Is there a place for neoadjuvant chemotherapy and chemoradiation?
11. What is the role of radiotherapy after surgical resection?
12. What treatment strategy should be followed for patients with R1 resections after neoadjuvant chemotherapy?
13. Which chemotherapy regime should be considered standard for stage IV gastric cancer?
14. What is the current status of Omentectomy and Omentobursectomy?

1.1. What is the best treatment of early gastric cancer (EGC)?

Much of the data available regarding EGC is from Japanese centers because of a higher incidence of gastric cancer and use of screening endoscopy in Japan to diagnose such cancers. With the excellent prognosis of EGC, which has a 5-year survival rate of greater than 85%, endoscopic therapies are becoming increasingly popular for its treatment.¹ This is partially due to the concern of subjecting patients to greater-than-necessary risk of morbidity following gastrectomy which, in some reports, is as high as 32%.^{2,3} For a selected superficial early gastric cancer (i.e., Tis or T-1 tumor), endoscopic mucosal resection (EMR) has emerged as a reasonable option.^{4–9} Selection of cases suitable for EMR/ESR depends on the absence of disease in the regional lymphatics. Criteria for appropriate use of endoscopic therapy for the treatment of EGC have been outlined in the gastric cancer treatment guidelines published by the Japanese Gastric Cancer Association.¹⁰ The indications are based on the principle that endoscopic therapy should be reserved for tumors having a size and morphology that are amenable for resection and that carry a very low probability of lymph node metastasis (LNM). For the absolute indications, the tumor must meet all of the criteria listed in the guidelines, as shown in [Table 1](#). The expanded criteria are a modified set, taking into account the improved resection capabilities of endoscopic mucosal dissection (ESD), as compared with EMR, and are based more particularly on the principle of low likelihood of LNM.

Gotoda and colleagues¹¹ studied 5265 surgically treated T-1 cases from the National Cancer Center Hospital and the Cancer Institute Hospital in Tokyo. For intramucosal tumors, none of the 1230 well-differentiated cancers of less than

30-mm diameter, regardless of ulceration findings, were associated with nodal involvement. Regardless of tumor size, for completely intramucosal tumors, none of the 929 cancers without ulceration were associated with nodal metastases. For submucosal cancers, there was a significant correlation between tumor size more than 30 mm and lymphatic-vascular involvement. However, none of the 145 well-differentiated adenocarcinomas of less than 30-mm diameter without lymphatic or venous permeation were associated with nodal involvement, provided that the lesion had invaded less than 5 mm into the submucosa.¹¹ In an 11-year, 445-case series by Ono and colleagues⁴ from the National Cancer Center Hospital in Tokyo, there were no gastric cancer-related deaths during a median follow-up period of 38 months (3–120 months). Although bleeding and perforation occurred in 5% of cases, there were no treatment-related deaths.⁴ If a perforation occurs and is immediately recognized, it can be repaired with intraluminal application of endoclips; the risk of intraperitoneal seeding associated with such an event seems negligible.¹² For selected superficial T-1 cancers, EMR performed by experienced personnel can generate excellent results and can be recommended, especially because any local recurrences can be addressed with salvage gastrectomy. In cases of recurrence or incomplete resection, either repeat endoscopic resection (in cases of local recurrence) or gastrectomy is indicated.^{2,11,13,14}

Close follow up with endoscopic surveillance and computed tomographic (CT) scanning is universally required in all patients, including those undergoing complete resection. There is some concern regarding a delay in diagnosis as a result of performing endoscopic therapy as a primary treatment, as this necessarily delays the time to gastrectomy in patients who have incomplete resection and delays diagnosis for those who may develop lymph node metastasis. Lee et al retrospectively studied 13 patients who required gastrectomy following an incomplete endoscopic resection by either EMR or ESD.¹³ Three out of the 13 cases were found to have lymph node metastasis and all three had submucosal invasion into the stomach. The authors concluded that all patients with incomplete resection should undergo gastrectomy—and not a repeat endoscopic procedure—due to the high risk of lymph node metastasis.¹³

It is estimated that the risk of lymph node metastasis is 3% if the tumor is localized within the mucosa and increases to 20% when the tumor has invaded the submucosal layer. In most EGC patients, the metastatic lymph nodes are localized within the group 1 lymph nodes. Therefore, for EGC patients who are not eligible for endoscopic resection, dissection of the above lymph node stations alone can achieve good outcomes. Laparoscopic resection with D1 lymphadenectomy and pylorus-preserving gastrectomy can be performed for T1 tumors not meeting EMR/ESD criteria.⁹ However, for all T1

Table 1 – The absolute and expanded indications for EMR/ESD.

Absolute indications	Expanded indications
1. A differentiated-type adenocarcinoma without ulcerative findings.	Tumors clinically diagnosed as T1a and:
2. The depth of invasion is clinically diagnosed as T1a	(a) of differentiated-type, but >2 cm in diameter
3. The diameter is less than 2 cm.	(b) of differentiated-type, and <3 cm in diameter
	(c) of undifferentiated-type, and <2 cm in diameter

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