

The Asian Perspective on the Surgical and Adjuvant Management of Esophagogastric Cancer



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KEYWORDS

- Gastric cancer • Esophagogastric junctional cancer • D2 dissection
- Adjuvant chemotherapy • Neoadjuvant chemotherapy • Multidisciplinary treatment

KEY POINTS

- D2 dissection without splenectomy has become the global standard for curable advanced gastric cancer except those invading the greater curvature of the upper body.
- Postoperative adjuvant chemotherapy improves overall survival (OS) in East Asia, where high-quality D2 dissection is routinely performed.
- Neoadjuvant chemotherapy is preferred for borderline resectable cases or linitis plastica. Conversion surgery for stage IV tumors remains under active investigation.

INTRODUCTION

Gastric cancer showed a long-term decreasing trend for both incidence and mortality in Japan, mainly due to decreased incidence of *Helicobacter pylori* infection and a Westernized diet of less salty food.¹ The Intergroup Study 0116 was one of the earliest positive adjuvant therapy trials in gastric cancer, proving the efficacy of postoperative chemoradiation therapy.² Its subgroup analysis, together with a small study comparing D1 versus D2 resection, ended the argument that advanced gastric cancer is already a systemic disease and does not benefit from adjuvant therapy.^{3,4} Now it is widely accepted that a good local control is essential to cure gastric cancer. In the guidelines of the Japan Gastric Cancer Association (JGCA), standard surgery for

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resectable gastric cancer is defined as resection of at least two-thirds of the stomach with a D2 lymph node dissection.⁵ Thus, a high degree of local control is achieved by surgery in East Asian countries.⁶ After D2 surgery, the 5-year survival rates for pathologic stage IA and stage IB according to the JGCA classification (13th edition) were 92.3% and 84.7%, respectively.⁷ Contrary to these high survival rates, those for pathologic stages II, IIIA, and IIIB were not adequate—72.1%, 52.8%, and 31.0%, respectively. Thus, patients with stages II–III gastric cancer often have recurrence even after curative surgery, which indicates additional treatment is warranted to improve the prognosis of these patients. This review outlines the Eastern perspective on the surgical and adjuvant management of gastric cancer.

STANDARD SURGERY FOR RESECTABLE GASTRIC CANCER IN THE EAST

In Japan, the standard surgery for resectable gastric cancer has been gastrectomy with a D2 lymph node dissection. Although the Dutch randomized controlled trial (RCT) comparing D1 and D2 dissection could not show a significant survival benefit of D2 dissection in the primary analysis,⁸ it demonstrated a significant reduction in the locoregional recurrence rate and cancer-related deaths after long-term follow-up.⁹ In addition, a Taiwanese RCT demonstrated a significant survival benefit of D2 or more extensive lymph node dissection compared with D1 dissection.⁴ These findings led to the recent revision of the European Society for Medical Oncology guidelines for gastric cancer and the National Comprehensive Cancer Network guidelines for gastric cancer, and they now recommend D2 lymph node dissection for resectable gastric cancer similar to the JGCA guidelines.^{5,10,11} The Japan Clinical Oncology Group (JCOG) conducted a phase III trial (JCOG9501) to investigate the survival benefit of para-aortic nodal dissection (D3 dissection) compared with standard D2 for cT2b–T4 gastric cancer.¹² A total of 523 patients were randomly assigned to either D2 or D3 dissection. D2 plus para-aortic nodal dissection was associated with a longer operation time ($P < .001$), greater blood loss ($P < .001$), and a significant increase in minor complications ($P < .001$). Nevertheless, there was no significant difference in OS and recurrence-free survival (RFS) between the 2 groups. Thus, a clinical benefit of prophylactic para-aortic lymph node dissection for resectable gastric cancer was not shown. Therapeutic para-aortic lymph node dissection for patients with clinically involved para-aortic node metastasis is still considered a recommended surgery in Japan.¹³

In a total gastrectomy with D2 lymph node dissection, the role of splenectomy has been an important topic of debate. A phase III trial (JCOG0110) was conducted to compare D2 with and without splenectomy for proximal gastric cancer that did not invade the greater curvature.¹⁴ The reason for exclusion of tumors invading the great curvature is possible microscopic invasion into the gastrosplenic ligament and 3 times higher incidence of nodal metastasis in the splenic hilum.¹⁵ A total of 505 patients were randomly assigned to either the splenectomy or spleen preservation group. The splenectomy group had higher morbidity ($P < .01$) and larger blood loss ($P = .025$) than the spleen preserving group. The 5-year OS rates were 75.1% and 76.4% in the splenectomy and spleen preservation groups, respectively, and the noninferiority of spleen preservation was demonstrated ($P = .025$). Based on these results, splenectomy should be avoided in total gastrectomy for proximal gastric cancer that does not invade the greater curvature even in Japan.

EVIDENCE FOR POSTOPERATIVE ADJUVANT THERAPY IN THE EAST

Postoperative adjuvant therapy aims to eradicate micrometastasis that exists even after surgery. Accurate staging before surgery in gastric cancer is impossible, whereas

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