

Long-Term Clinical Efficacy and Safety of Endoscopic Submucosal Dissection for Early Gastric Cancer in Korea

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See “Long-Term Clinical Outcomes of Endoscopic Submucosal Dissection in Patients with Early Gastric Cancer: A Prospective Multicenter Cohort Study” by Sang Gyun Kim, et al. on page 402, Vol. 12, No. 4, 2018

From a global perspective, gastric cancer ranks third in cancer-related mortality despite a substantial decrease in incidence over the past decades and variable incidence in different geographical regions.¹ Especially, the incidence of gastric cancer in East Asia is approximately two-thirds of all gastric cancers worldwide; cancer screening strategies that are aimed at its detection at an early and more curable stage have led to a significant reduction in mortality.² After more than 10 years since the development of endoscopic dissection (ESD), ESD enables treatment of early gastric cancer (EGC) and provides good survival rates and better quality of life compared to surgical modality.^{3,4} Generally, the absolute indication of ESD includes differentiated EGCs less than 20 mm in diameter without ulceration or scarring; moreover, in treating EGC, these lesions must be confined to the mucosa, with no lymphatic or vascular involvement, as established by the Japanese Gastric Cancer Association.⁵ Previous studies reported that ESD has shown excellent *en bloc* and curative resection rate of around 90% and minimal risk of adverse events.⁶ However, there was concern on the long-term outcome of ESD for EGC. Several reasons should be considered why long-term outcomes after ESD are comparable to those after surgery for EGCs that fall under the absolute indication for ESD by the Japanese criteria.⁴ Most of all, the major difference between ESD and gastrectomy is that dissection of lymph nodes can be performed only in surgery. For this reason, the indication of ESD for EGC should be defined as with low risk of lymph node metastasis. In this view, the possibility of lymph node metastasis was very low or absent in patients with EGC, meeting the absolute indication of ESD.⁵ In addition, ESD showed higher

rates of *en bloc* and completion resection in the absolute-indication group compared to endoscopic mucosal resection.³

In this issue of *Gut and Liver*, Kim *et al.*⁷ reported a nationwide multicenter prospective cohort study to evaluate the long-term efficacy of ESD for EGC. Six hundred ninety-seven patients with 722 EGCs treated with ESD were prospectively enrolled and followed for 59 months (median; range, 2–60 months). During the follow-up period, the overall survival rate was 96.6%, and the disease-specific free survival rate was 90.6%. Local recurrence developed in 0.7% in the curative group, and metachronous tumor development occurred in 7.8%. Distant metastasis was observed in 0.2% in the curative resection group and 2.5% in the non-curative resection group ($p=0.01$). This present study showed that the survival rates, including 5-year disease-specific free survival, as primary outcome in the curative group were not significantly inferior to surgery. The major advantage of this study is that this is the first nationwide prospective enrollment and follow-up multicenter study in Korea. Thus, this prospective design could overcome the bias which was usually caused by the retrospective design, frequent loss of follow-up, and heterogeneous criteria of enrollment in previous studies and could maintain homogeneity of risk of recurrence during long-term follow-up.

Recently, a Japanese multicenter retrospective study reported the long-term result of ESD for EGC at 57 months (median; range, 39–76 months).⁸ Local recurrence developed in 0.22% in the absolute-indication group and 1.26% in the expanded-indication group. Metastatic recurrence was not observed in any patient with absolute-indication lesions, but developed in

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six patients with expanded-indication lesions (0.14%).⁸ Taken together, Korean and Japanese multicenter studies showed that ESD has an equivalent long-term outcome for treatment of EGC, and ESD can be accepted as a standard modality for the management of EGC in patients with absolute indication.

In addition, the criteria of enrollment of the studies were similar in absolute indication except that the gross tumor size is 3 cm in the Korean study; some patients had shown that the final pathological result was beyond the absolute criteria.⁷ The author showed that all survival rates were not statistically significantly different according to the criteria and concluded that ESD is expected to be a standard treatment for EGC in the expanded criteria in the final pathology with comparable clinical outcomes. However, the 5-year survival rate after surgical resection of EGC is 99% in patients with mucosal cancer and 96% in those with submucosal cancer; the outcomes of ESD might be equivalent to those of surgical resection.⁶ Thus, patients with EGC with expanded-indication lesions should be followed up according to a stricter protocol than patients with absolute-indication lesions.

In conclusion, this nationwide multicenter study strengthened the evidence of long-term safety outcome of ESD for EGC with absolute indication. However, the long-term outcome of ESD in those with expanded indication should be evaluated through different strategies considering the risk factors for metastatic recurrence, such as pathology, ulceration, and submucosal invasion.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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