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Editorial

Pitfalls in Endoscopic Submucosal Dissection for Early Gastric Cancer with Papillary Adenocarcinoma

Gwang Ha Kim

Department of Internal Medicine, Pusan National University School of Medicine and Biomedical Research Institute, Pusan National University Hospital, Busan, Korea

Corresponding Author
Gwang Ha Kim
ORCID https://orcid.org/0000-0001-9721-5734
E-mail doc0224@pusan.ac.kr

See "Clinical Outcome of Endoscopic Submucosal Dissection for Papillary Type Early Gastric Cancer: A Multicenter Study" by Hyun-Deok Shin, et al. on page 426, Vol. 18, No. 3, 2024

Papillary adenocarcinoma is an uncommon histologic type of gastric cancer accounting for approximately 1% to 3% of early gastric cancers (EGC).[1] Histopathologically, the Japanese classification categorizes it as a differentiated type, and the Lauren classification as an intestinal type.[2] Therefore, endoscopic submucosal dissection (ESD) is suggested to be a safe therapeutic approach for EGC with papillary adenocarcinoma (EGC-P). However, patients with papillary adenocarcinoma have a poor prognosis compared with those with other differentiated-type histologies; patients with papillary adenocarcinoma have a higher rate of lymph node (LN) and liver metastases and a lower 5-year overall survival rate than those with non-papillary adenocarcinoma.[3] In my previous study including 1,583 patients who underwent gastrectomy for EGC, the rate of submucosal invasion was significantly higher in EGC-P than in EGC with non-papillary adenocarcinoma (EGC-NP) having both differentiated-type and undifferentiated-type histologies (71.4% vs 50.8% and 37.6%, respectively). The rate of LN metastasis in EGC-P was higher than that in both EGC-NP histology types (17.9% vs 9.7% and 11.1%, respectively).[1] In addition, of the 17 patients who met the current ESD indication, four (23.5%) had lymphovascular invasion (LVI) or LN metastasis. When patients with EGC-P who meet the ESD indication would undergo ESD, approximately one-fourth of them would require additional gastrectomy due to non-curative resection.[1]

In the current issue of *Gut and Liver*, Shin *et al.*[4] reported post-ESD outcomes for 97 patients with EGC-P in a multicenter study. EGC-P showed a trend toward distal tumor location and elevated shape. Nine patients (9.3%) had positive resection margins with tumor, and submucosal invasion and LVI were observed in 18 (18.5%) and five (5.2%) patients, respectively; especially, LVI was observed in two patients with mucosal cancers. As the overall curative resection rate was 86.6% (84/97), the authors concluded that ESD was favorable for EGC-P. They also evaluated the risk factors for LN metastasis in 79 patients with EGC-P who underwent surgical resection. Submucosal invasion (odds ratio, 3.735) and LVI (odds ratio, 7.636) were significant risk factors for LN metastasis in multivariate analysis. The fact that the frequency of LVI was not low even in mucosal EGC-P should not be ignored. In another study including 4,140 patients who underwent ESD for differentiated-type EGC, the curative resection rate of EGC-P was 49.4%, which was significantly lower than that of other differentiated-type histologies (82.2%).[5] A recent systemic review including 15 studies also showed that submucosal invasion and LVI were frequent in EGC-P, and the curative resection rate was only 67.0% (95% confidence interval, 43.0% to 84.5%).[6] Accordingly, ESD should be more carefully applied for EGC-P than for EGC with other differentiated-type histologies.

How can papillary adenocarcinoma be accurately diagnosed before ESD? Although papillary adenocarcinoma is present within a tumor, it may not always be detected through pre-ESD biopsy owing to the limited amount of tissue obtained from endoscopic biopsy and tangential sectioning of specimens.[1] Pre-ESD biopsy sometimes reveals a different histology than that observed in the post-ESD

specimen, which can be attributed to inter- and intra-observer variability, as well as the histological heterogeneity of gastric cancer.[7] Magnifying endoscopy with narrow-band imaging is reported to be effective in diagnosing papillary adenocarcinoma.[8-10] The vessels within the epithelial circle pattern on magnifying endoscopy with narrow-band imaging exhibited a sensitivity and specificity of 84.6% and 96.9%, respectively, for diagnosing papillary adenocarcinoma. However, coexisting undifferentiated carcinomas were observed in 22.9% of vessels within the epithelial circle-positive cancers. Therefore, when endoscopic forceps biopsy reveals differentiated-type histology and vessels within the epithelial circle is observed on magnifying endoscopy with narrow-band imaging, papillary adenocarcinoma could be predicted before ESD, even in the absence of typical histopathological features of papillary adenocarcinoma, such as elongated finger-like epithelial projections, in the endoscopic biopsy specimens.

Although the curative resection rate of ESD for EGC-P is lower than that for EGC with other differentiated-type histologies, curative resection shows favorable long-term outcomes.[5] The probability of LN metastasis is a very important factor influencing the success of ESD for EGC; LVI is an especially strong predictive factor of LN metastasis. Therefore, detailed histopathological examination of resected specimens is mandatory, especially to detect the presence of LVI after ESD for EGC-P.

CONFLICTS OF INTEREST

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ORCID

Gwang Ha Kim https://orcid.org/0000-0001-9721-5734

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