ESD for EGC with Undifferentiated Histology

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Risk of lymph node metastasis

The risk of LN metastasis is known to increase in EGC with undifferentiated type histology due to lymphovascular invasion. However, we have identified EGC with undifferentiated type histology as a group with a low risk of LN metastasis. In addition, Hirasawa et al. reported that from the analysis of 3,843 patients who underwent gastrectomy with LN dissection for solitary EGC with undifferentiated type histology, none of the 310 intramucosal cancers 2 cm or less in size without lymphovascular invasion and ulcer findings were associated with LN metastases. Therefore, Japanese gastric cancer treatment guidelines 2010 (ver. 3) state that ER for EGC with undifferentiated type histology with these characteristics is regarded as an EI, and that ESD, not EMR, should be employed. A few reports exist on the outcomes of ER for EGC with undifferentiated type histology. However, the data were limited regarding long-term outcomes.

To improve the curative resection rate, accurate determination of depth and extent of tumor is pursued. Unfortunately, this can be difficult. The accuracy of depth diagnosis by endoscopic ultrasound in EGC patients with undifferentiated type histology has been known to be worse than that in EGC patients with differentiated type histology. At first, therefore, EGC with undifferentiated type histology in tumors smaller than 20 cm needs to be considered for ESD, and when ESD is carried out, marks should be placed farther away from the endoscopically determined margins than in EGC with differentiated type histology. Nevertheless, more data are necessary to confirm the feasibility of ESD for EGC with undifferentiated type histology.

Discrepancy between pre- and post-treatment diagnoses

A histologic discrepancy may exist between pre- and post-treatment diagnoses, making it difficult to know whether a lesion is compatible with EI prior to ER. Therefore, the strict meaning of EI, rather than an indication, may be criteria for determining if a curative resection is achieved after evaluating the resected specimen. Despite advanced techniques and development of new diagnostic methods, the precise pre-treatment evaluation of gastric neoplasm is somewhat limited. In a recent Korean single-center retrospective study, 80/236 (33.9%) biopsy-proven, low-grade gastric adenomas/dysplasias (category 3 of the Vienna classification) turned out as invasive carcinoma (category 5) in 71 (30.1%) and high-grade gastric adenomas/dysplasias...
(category 4) in 9 (3.8%) after resection. In a Japanese multicenter retrospective study, among 468 biopsy-proven gastric noninvasive neoplasias (equivalent to category 3 or 4.1 of the Vienna classification), 205 (43.8%) were diagnosed with adenocarcinoma after ESD. However, most studies presenting the clinical outcomes of ER for EGC were based on the post-treatment diagnoses.

To analyze the discrepancy between pre- and post-treatment diagnoses of gastric neoplasm, we performed a retrospective study involving a total of 2,056 patients with gastric adenoma or cancer who underwent a curative ER or surgery at Samsung Medical Center in 2012. According to our results, about one third of pre-treatment AI-EGC (131/396) was shifted to post-treatment beyond AI-EGC, and 42.8% of the changes (56/131) were beyond EI for ESD. This observation suggests that applying EI in selecting the treatment method for EGC could be risky. Moreover, among the post-treatment beyond AI-EGC patients (n = 876), 185 patients initially received ESD and 73 patients (40%) were identified as not satisfying EI. Considering the discrepancy between pre- and post-treatment diagnoses of gastric neoplasms and the significant number of patients not receiving additional surgery, applying EI in selecting ESD for EGC could be risky.

Clinical simulation based on surgical database

Using a non-selected surgical cohort of endoscopically suspected early gastric cancer, we simulated the selection of endoscopic submucosal dissection candidates, and evaluated the pathologic outcomes. Patients and Methods: Among 1,336 surgery patients with gastric cancer, 802 cases with poorly differentiated adenocarcinoma (PD) or signet ring cell carcinoma (SRC) in the forceps biopsy before surgery were screened. By reviewing the endoscopic images before the surgery, 537 cases of endoscopically suspected EGCs were enrolled. ESD candidates were selected by the expanded indications of ESD, such as 2 cm or smaller in diameter, without ulceration, clinically mucosal lesion and no evidence of lymph node metastasis in abdominal computed tomography. On condition of technically successful resection, expected pathologic outcomes were analyzed. ESD candidates meeting the expanded indications were 51.1% (280/557)-50.5% (104/206) in PD, and 53.2% (176/331) in SRC. Rate of curative resection was 42.1% (118/280), but the rate in PD was lower than in SRC (31.7% vs 48.2%, respectively, p = 0.007). In 120 patients within curative resection criteria, lymph node metastasis was found in 3 patients (2.5%). When the indication was narrowed to 1 cm in diameter, the number of ESD candidates decreased to 25.3% (136/537), but the rate of curative resection increased to 53.6% (73/136)-34.7% (16/46) in PD and 63.3% (57/90) in SRC. In 73 patients within curative resection criteria, lymph node metastasis was found in 1 patient (1.3%). When the indication was narrowed to 0.6 cm in diameter, there was no improvement in the rate of curative resection. In our simulation using current expanded indications with unselected surgical cohort, the overall rate of curative resection was less than 50% for undifferentiated-type EGCs. ESD should be considered in more selected patients, such as tumor size smaller than 1cm with the histology of SRC to achieve better outcome.
References