



Effect of surgery in patients after non-curative endoscopic submucosal dissection

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Over the past decade, endoscopic submucosal dissection (ESD) has emerged as the preferred treatment for patients with early gastric cancer (EGC) without lymph node metastasis (LNM). Favorable long term outcomes have been reported for patients meeting absolute (AI) or expanded indications (EI) (1-3). Endoscopic resection has been reported to be comparable to surgery with respect to overall survival in patients who meet AI or EI (4,5). However, it is impossible to accurately predict tumor size or depth of EGC. Pretreatment diagnostic classification has been reported to be upgraded in 15.9% (6). Non-curative results with considerable risk of LNM have been reported to account for 15.3–16.7% of all endoscopic resections for EGC (7,8). Additional surgery with lymph node dissection is generally recommended for these non-curative patients. However, factors such as age, co-morbidity, and quality of life should be considered in these patients. Kawata *et al.* have examined the long-term outcomes after non-curative ESD in their study “Risk factors for lymph node metastasis and long-term outcomes of patients with early gastric cancer after non-curative ESD” (9). In that study, patients who were judged to have had non-curative ESD were classified into two groups: (I) those who subsequently underwent surgical resection; and (II) those who did not receive additional surgical resection. Pathologic risk factors associated with LNM was analyzed in the surgical resection group. Primary outcomes were pathological risk factors for LNM. Secondary outcomes were long-term prognosis among patients in the surgical group and nonsurgical group.

A total of 642 patients with 707 primary EGCs were judged to have had non-curative resection after ESD. After applying exclusion criteria, a total of 506 patients with 506 EGCs were included in this study, including 323 patients who underwent additional surgical resection and 183 patients who were followed up without additional surgical resection. Pathological LNM was found in 30 patients (9.3%) after additional surgical resection. Multivariate logistic regression analysis revealed that lymphovascular invasion (LVI) was an independent risk factor for LNM.

There was a significant difference in 5-year overall survival rate between the surgical group and the nonsurgical group (90.0% *vs.* 72.0%, $P < 0.0001$). However, the 5-year cause-specific survival rates in the two groups were not significantly different (98.7% *vs.* 96.5%, $P = 0.07$). Subgroup analysis revealed that the 5-year cause specific survival rate of patients with LVI was significantly higher in the surgical group compared to that of the non-surgical group (98.1% *vs.* 79.3%, $P < 0.0001$). Results of that study revealed that LNM rates were 9.3% after non-curative resection and that LVI was an independent risk factor of LNM. Although 5-year cause-specific survival rates were not increased in the surgical group, survival rate was increased in patients with LVI, suggesting that patients with LVI after non-curative resection should be recommended to receive surgery. Patients without LVI can cautiously be managed without surgery if patient has associated comorbidity. However, the results of that study should be interpreted with caution. The surgical group was significantly younger with a deeper tumor

depth, a higher positive vertical margin positive rate, and more non-curative factors. The authors rightfully mention that the overall survival rates in these two groups might have been biased. Patients with high risks of LNM might have received additional surgery and patients with low risks might not have received surgery. The survival benefit of surgery in patients who receive non-curative endoscopic resection still remains controversial. A previous study has reported that the five-year overall survival rates in the surgery group and observation groups are 94.3% and 85%, respectively ($P=0.028$) (10). Rescue surgery was identified as an independent predictor of overall survival after non-curative endoscopic resection. However, the authors of that study did not provide data on disease specific survival rates (10). A more recent study has reported similar results (11). The overall survival rate was higher in the surgery group when compared to that in the non-surgery group (93.3% *vs.* 76.25%, $P=0.028$) (11). However, disease specific survival rates did not differ between the two groups (97.8% *vs.* 100%, $P=0.495$) Altogether, careful observation without surgery may be possible in a selected group of patients. Further studies focusing on the risk factors of LNM and selection of patients who need additional surgery are warranted.

In conclusion, the authors should be commended for their efforts on identifying risk factors of LNM after non-curative endoscopic submucosal dissection. Patients with LVI have a high risk of LNM. Therefore, surgery should be strongly recommended in these patients. Careful observation may be an alternative for patients without LVI and those with advanced age and comorbidities.

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to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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