Nodes or No Nodes? The Lymph Node Metastasis Risk of T1 Esophageal Cancer Revisited

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Endoscopic treatment of early Barrett's neoplasia has gained more and more acceptance over the past 10 years. It is well known that the risk for lymph node and distant metastasis is absent in high-grade dysplasia (HGD) and very low in mucosal Barrett's cancer (T1a) (1,2). However, when the cancer is invading into the submucosal layer (T1b), the risk for lymphatic spread rises substantially (1,2). Therefore, recent guidelines recommend endoscopic treatment for HGD and mucosal adenocarcinoma and esophageal resection for submucosal cancer (3). There seems to be a subgroup of patients with submucosal invasion having a very low risk for lymph node metastasis—well and moderately differentiated adenocarcinoma infiltrating only the upper third of the submucosal layer (≤500 μm) without lymphatic or vascular invasion (4). In these cases, endoscopic resection could be an alternative to surgery (3,4). In squamous cell cancer of the esophagus, the risk for lymphatic spread is known to be higher. When the cancer invades the deep mucosal layer (T1m3) the risk rises markedly, up to greater than 10% (5).

In the current issue of JNCI, Merkow et al. publish a large retrospective analysis of data from the National Cancer Database, in which they identify 5390 patients with T1 esophageal cancer treated in 824 hospitals in the US between 2004 and 2010 (6). Surgical resection was performed in 73.5% and endoscopic treatment in 26.5%. The vast majority of the tumors were adenocarcinomas (89%). Interestingly, the authors find that 5% of patients who received esophagectomy for T1a esophageal cancer had at least one positive lymph node. The rate decreased to 0.5% for low-grade lesions smaller than 2 cm in diameter. There was no difference between adenocarcinoma and squamous cell carcinomas. These results are very surprising, because they are contradictory to most recent publications; Hölscher et al. reported a 0% lymph node metastasis rate (0 of 124 patients) for T1a esophageal cancers. In the same issue, Griffin et al. reported a lymph node metastasis rate of 0% (0 of 54 patients) for mucosal esophageal cancers (1,2).

In accordance with those findings, our group recently published a large series of 1000 patients with T1a Barrett's adenocarcinoma treated by endoscopic resection (ER) (7). The long-term outcome was excellent, with a complete remission rate of neoplasia of 93.8% after almost 5 years of follow-up. More than half of the tumors were larger than 2 cm, and 54 patients even revealed a poorly differentiated adenocarcinoma. All patients were followed with CT scan and endoscopic ultrasonography every six months during the first two years of follow-up and yearly afterwards. However, lymph node metastasis was only found in two out of 1000 patients who were referred to surgery because of mucosal adenocarcinoma with lymph vessel infiltration. Two other patients died from metastatic esophageal cancer. Applying the lymph node metastasis rate of 5% found by Merkow et al., 50 patients in our series would have died from metastatic disease (6).

One possible explanation for this contradictory data might be the quality of the histopathological work up of the operation specimen in the series by Merkow et al. (6).

In contrast to surgical treatment, after ER, the specimen is pinned on cork, the margins are marked, and then cross sections of the ER specimens are performed every 2 mm, resulting in a meticulour histopathological work up of the whole tumor. Therefore, the chance to miss the deepest point of infiltration or a focal lymph vessel infiltration is very low. The work up of surgical specimens is not that exact: Usually cross sections every 5 to 10 mm are performed. In those cases, the chance to miss deeper infiltrating cancer or lymph vessel infiltration in the area between the sections is substantially higher. In addition, the diagnostic focus of the pathologists after esophageal resection is not the differentiation between mucosal or submucosal infiltration in T1 esophageal cancers. The focus after esophagectomy is usually on the detection of positive lymph nodes, because a positive lymph node status has an important impact on the prognosis of the patient. Regarding the evaluation of the ER specimen, the situation is completely different: The main task of the pathologist here is the differentiation of mucosal or submucosal infiltration. Therefore, it could be possible that patients diagnosed with T1a esophageal cancer after surgery might have been understaged and had deeper infiltrating cancer.

The low rate of dissected lymph nodes of a median of 10 per patient in the series by Merkow et al. also questions the quality of the histopathological work up (6). According to the worldwide esophageal cancer collaboration (WECC) a minimum of 23 regional lymph nodes should be removed (9). The number reported by Merkow et al. is far below the required standard (6).

A further important finding of Merkow et al. was the 30-day mortality rate of 0.5% for endoscopic treatment (6). Expert centers have not reported ER-related mortality yet, but a wide use of this technique in less experienced hands seems to result in a notable mortality and complication rate.
In summary, the interesting article by Merkow et al. demonstrates the shift from surgical to endoscopic treatment for T1 esophageal cancer during the last 10 years (6). It sheds light on the current status of treatment of early esophageal carcinomas and gives several important insights. However, the high rate of lymph node metastasis for T1a esophageal cancers reported needs to be interpreted with caution.

**References**


**Notes**
The authors declare no conflict of interest.

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