



Endoscopic resection for esophageal or gastroesophageal junction adenocarcinoma

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Comment on: Abe S, Ishihara R, Takahashi H, *et al.* Long-term outcomes of endoscopic resection and metachronous cancer after endoscopic resection for adenocarcinoma of the esophagogastric junction in Japan. *Gastrointest Endosc* 2018. [Epub ahead of print].

Received: 31 March 2019; Accepted: 18 April 2019; Published: 22 April 2019.

doi: 10.21037/dmr.2019.04.01

View this article at: <http://dx.doi.org/10.21037/dmr.2019.04.01>

Endoscopic resection is a treatment option for the superficial carcinoma in gastrointestinal tract. The strategy of endoscopic resection for gastric adenocarcinoma (GAC) and esophageal squamous cell carcinoma (ESCC) has been well established in Japan, but not so much for esophageal adenocarcinoma (EAC) (1-3). EAC has become prevalent especially in North America and Western Europe, but it is still uncommon in east Asia (4). Therefore, the evidence of endoscopic resection for EAC has been based on studies performed in Western countries (5,6). In 2017, Ishihara *et al.* conducted a multicenter retrospective study in 13 high-volume centers in Japan and assessed the risk factor for metastases in 458 patients with T1 (T1a and T1b) EAC (7). This study concluded that the presence of lymphovascular involvement (LVI), poorly differentiated component, and >3 cm tumor size are risk factor for metastases. Patients with T1a or superficial submucosal (SM) invasion (1–500 µm) tumor without these risk factors are least likely to develop lymph node metastases and thus seem ideal candidates for endoscopic resection (7). However, long-term outcome after endoscopic resection remains unclear.

Abe *et al.* evaluated long-term outcomes in 372 patients after endoscopic resection based on the risk factor which Ishihara *et al.* suggested; 277 low-risk patients (T1a or SM1 with less than 3 cm tumor diameter, no LVI, and no poorly differentiated component) and 95 high-risk patients (T1 tumor with over 3 cm, presence of LVI, and poorly differentiated component or SM tumor invading into submucosa more than 500 µm) (8). In the low risk group,

3 patients had local recurrence, but no distant metastases. On the other hand, in high risk group, 9 patients (9.5%) developed metastases. The 5-year disease-specific survival rates in the low-risk group, the high-risk group with additional treatment, and the high-risk group without additional treatment were 100%, 94.4%, and 92.8%, respectively. This study strongly suggests that endoscopic resection might be valuable for the low risk group.

Indication for endoscopic resection in patients with EAC has been evaluated in Western countries. Westerterp *et al.* evaluated surgical specimen of EAC and showed that only 1 of 79 patients with T1a or SM1 EAC had lymph node metastases (9). Lee *et al.* evaluated 258 patients with T1 EAC who underwent esophagectomy without preoperative therapy and showed that the incidence of LN metastases was 7% for T1a and 26% for T1b (10). Moreover, tumor size, poor differentiation, and the presence of LVI were risk factors for LN metastases, being consistent with the Ishihara report (7,10). Manner *et al.* showed that only 1 of 53 SM1 patients with no LVI and no poorly differentiated developed lymph node metastases following endoscopic resection (11). Alvarez Herrero *et al.* showed that 69 patients with T1a-muscularis mucosae (MM) and SM1 have no LN metastases after endoscopic resection (12). Leggett *et al.* showed that the presence of LVI in endoscopic specimen is a significant prognostic factor (13). Based on these reports, the European Society of Gastrointestinal Endoscopy recommended endoscopic resection for patients with T1a or low risk SM1 (less than 500 µm invasion, well or

moderate differentiation, and no LVI) (5). NCCN guideline recommend endoscopic resection for T1a or superficial pT1b tumor with no LVI and no poor differentiation (6). This indication is similar with recommendation which Ishihara *et al.* and Abe *et al.* provided in Japan (7,8).

Frequency of LN metastasis in EAC differ from ESCC, therefore indication of endoscopic resection for EAC should be independent with ESCC. In ESCC, Japanese esophageal cancer guideline recommended endoscopic resection for only T1a tumor (1,2). LN metastases of pT1a-epithelium (EP)/lamina propria mucosae (LPM), is very rare. However, pT1a-MM is possible to develop metastases; Akutsu *et al.* reported that the overall risk of metastasis in T1a-MM ESCC was 16%, especially in patient with the presence of LVI (14). Definitely, pT1b tumor have higher frequency of metastases, therefore T1b tumor is not appropriate for the endoscopic treatment. Yamashita *et al.* evaluated the long-term outcome after endoscopic resection for ESCC and reported that the cumulative 5-year metastatic rates in patients with EP/LPM, MM, SM1, and SM2 cancer were 0.4%, 8.7%, 7.7%, and 36.2%, respectively (15). Therefore, for patient with pT1a-MM and pT1b ESCC after endoscopic resection, additional surgical treatment and/or chemoradiation should be considered (1,2). However, necessity of additional treatment for pT1a-MM without LVI is still controversial.

Indication for endoscopic resection for gastric cancer are more precisely investigated in Japan and have more detail criteria. Endoscopic resection for GAC had been indicated to T1a differentiated-type with less than 2 cm without ulcerative findings (UL). According to the JCOG0607 results, following pathological status with margin negative and LVI negative have been considered as curative; (I) tumor diameter over 2 cm, differentiation, pT1a, UL negative, (II) Tumor size less than 3 cm, differentiation, pT1a, UL positive, and (III) tumor size less than 3 cm, differentiation, pSM1 invading 1–500 um into submucosa (16). Indication for undifferentiated or mixed type (accompanied with differentiated area and undifferentiated area) is still insufficient and assessed in ongoing study (JCOG1009/1010).

Study performed by Abe *et al.* contained the largest sample size and showed very favorable prognosis after endoscopic resection in the low-risk EAC patients, thus leading to a high evidence of endoscopic resection for low-risk EAC patients in Japan. Endoscopic resection in Japan has any differences from that in West. *En bloc* resection with endoscopic submucosal dissection (ESD) is performed well in Japan, resulting in accurate pathological evaluation. Long

segment Barrett's esophagus is still rare in Japan. Most of EAC in Japan located near esophagogastric junction.

In conclusion, indication of endoscopic resection should be considered in balance with the risk of LN metastases after endoscopic resection and the morbidity from esophagectomy. The Abe *et al.* paper suggests possibility of endoscopic resection for low risk EAC patients. Further prospective studies were warranted.

Acknowledgments

Funding: This work was supported by the Caporella, Dallas, Sultan, Park, Smith, Frazier, Oaks, Vanstekelenberg, Planjery, and Cantu families, as well as from the Schecter Private Foundation, Rivercreek Foundation, Kevin Fund, Myer Fund, Dio Fund, Milrod Fund, and The University of Texas MD Anderson Cancer Center (Houston, Texas, USA) multidisciplinary grant program. This research was also supported in part by National Cancer Institute grants CA129906, CA127672, CA138671, and CA172741 and by Department of Defense grants CA150334 and CA162445 (JA Ajani), and by a grant from the Japan Society for the Promotion of Science Overseas Research Fellowships and Program for Advancing Strategic International Networks to Accelerate the Circulation of Talented Researchers (K Harada).

Footnote

Provenance and Peer Review: This article was commissioned and reviewed by the Section Editor by Xueru Song (Clinical Cancer Institute of Nanjing University, Nanjing, China).

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <http://dx.doi.org/10.21037/dmr.2019.04.01>). JAA serves an unpaid editorial board member of *Digestive Medicine Research* from Nov. 2018 to Nov. 2020. The other authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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doi: 10.21037/dmr.2019.04.01

Cite this article as: Harada K, Zhao M, Baba H, Ajani JA. Endoscopic resection for esophageal or gastroesophageal junction adenocarcinoma. *Dig Med Res* 2019;2:7.