Endoscopic Therapy for Early Gastric Cancers – from EMR to ESD, from Guideline Criteria to Expanded Criteria

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Endoscopic mucosal resection (EMR) has been established in the treatment of early gastric cancers (EGCs) for more than 20 years. In 1984 EMR was first described by Tada et al. [1] as a new technique called strip biopsy. Inoue et al. [2] developed another resection technique in 1993 using a cap-fitted panendoscope to suck targeted lesions into the cap and resect them with a snare (EMR-C). This technique gained worldwide acceptance over the following years and was considered the treatment of choice for EGCs in Japan and also in the Western world. However EMR has technical limitations. En bloc resections are restricted to lesions with a diameter of 20 mm or less, and the endoscopist's view during resection is limited. In 2006 Chiu [3] concluded: 'Conventional EMR is limited by the blindness of the resection and the size of the specimen'. Resulting piecemeal and incomplete resections lead to difficulties in histopathological assessment of R0 resections and to an increased risk of recurrence. In the era of EMR the Japanese guideline criteria for endoscopic resection of EGCs were therefore restricted to elevated lesions of <20 mm in diameter and depressed lesions without ulceration of <10 mm in diameter. Ulcerated lesions and lesions with undifferentiated histology, lymphatic or vascular involvement and submucosal invasion were excluded due to possible lymph node metastases [4].

In the late 1990s the development of endoscopic submucosal dissection (ESD) using different knives revolutionized the spectrum of endoscopic resection techniques allowing en bloc resections regardless of the lesion's size [5]. In combination with new data on the risk of lymph node metastases in early gastric cancer resection, criteria could be extended [6, 7]. The so-called expanded criteria include mucosal cancers without ulceration regardless of the lesion's size, ulcerated mucosal cancers with a size restriction of 30 mm, and cancers with minute submucosal invasion of <500 μm (also with a size restriction of 30 mm). Lesions with undifferentiated histology and lymphatic or vascular invasion are still excluded [7, 8]. In 2006 Oka et al. [9] confirmed the presumed advantages of the ESD method in comparison to EMR. ESD showed a significant improvement in en bloc resections and complete resections. For lesions without ulceration, the superiority of ESD was significant even for small lesions of <10 mm in diameter where en bloc resection rates were 95.1% for ESD and only 61.9% for EMR [9]. Today, we can conclude that in the last years ESD has revolutionized the endoscopic treatment of premalignancies and early malignancies and should be considered the treatment of choice for EGCs, even when a lesion is small and seems to be easily resected with EMR-C. For lesions fulfilling

the expanded resection criteria, ESD is the only method available allowing en bloc resections and resulting in a better histopathological diagnosis of R0 resections and a reduced recurrence rate. However, so far, clinical long-term follow-up after ESD for expanded criteria lesions has not been widely studied due to its recent introduction. In this issue of *Digestion* Yamaguchi et al. [pp 173–181] report on 551 patients with 589 EGCs treated by ESD and compare subgroups of lesions fulfilling the traditional resection criteria (guideline criteria group) versus lesions fulfilling the expanded criteria (expanded criteria group). En bloc resection rates (98.6 vs. 93%), complete resection rates (95.1 vs. 88.5%) and curative resection rates (97.1 vs. 91.1%) were significantly better in the guideline criteria group but were also excellent in the expanded criteria group. Bleeding (4.9 vs. 0.9%) and perforation (6.6 vs. 2.9%) were significantly more frequent in the expanded criteria group, but acceptable. In patients with a follow-up of more than 2 years, 1 recurrence was observed among the 247 patients of the guideline criteria group (0.4%) and another 1 in 177 patients in the expanded criteria group (0.6%; n.s.). During a mean follow-up of 14 months, metachronous gastric cancers developed in 6 patients in the guideline group (2.4%) versus 4 patients in the expanded group (2.6%; n.s.). The 5-year overall survival rates were 96.9% in the guideline group and 93.4% in the expanded group (n.s.). Disease-specific survival rates were 100% in both groups. Two other recently published studies on ESD for EGCs fulfilling the expanded criteria reported similar results. Isomoto et al. [10], from the same group as Yamaguchi, showed 5-year overall and disease-specific survival rates of 97.1 and 100%, respectively, while Goto et al. [11] reported rates of 96.2 and 100%. The results of Yamaguchi et al., Isomoto et al. and Goto et al. give precious information on the excellent clinical outcome after ESD of EGCs according to the expanded criteria. The data confirm the clinical value of the expanded criteria which were initially based only on his-

topathological studies in gastrectomy specimens [6]. The clinical outcome data of these large studies have become particularly important after a publication in 2007 by Ishikawa et al. [12] who found lymph node metastases in 3 gastrectomy specimens with EGCs fulfilling the expanded criteria and recommended restriction of endoscopic resection to mucosal lesions. However one limitation of the reported studies is a mean follow-up of 30–36 months so far, requiring further long-term observations especially with regard to disease-specific survival and also metachronous lesions. As in other situations where resections of early cancers are performed in persistent precancerous conditions (e.g. resection of early cancer in Barrett's esophagus), the rising frequency of metachronous lesions within long-term follow-up is also to be expected after ESD for EGCs. According to the reported rate of 2.4% in the Yamaguchi et al. study and a similar rate of 2.2% in the Isomoto et al. study, our own limited data show metachronous lesions in 2/44 patients (4.5%) 6 and 16 months after initial ESD [13]. However, all reported metachronous lesions were early cancers that were resectable by ESD and therefore did not compromise the clinical outcome. However, life-long endoscopic surveillance seems mandatory.

In recent years clear progress in endoscopic resection techniques has been made, particularly with the development of ESD. ESD can be considered the treatment of choice for EGCs, and expanded resection criteria are justified by the excellent clinical results as shown now by Yamaguchi et al. in this issue of *Digestion*. However, despite the fascinating development of resection techniques, it should not be forgotten that endoscopic treatment needs recognition of gastric neoplasia at a very early stage. Especially in the Western world detection rates for EGCs are low, and clear improvement in early diagnosis must be achieved to transfer the fascinating improved resection techniques to patients outside Asia and to improve their prognosis.

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