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Long-term survival after endoscopic resection for early gastric cancer in the remnant stomach: comparison with radical surgery

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Gastric cancer is still one of the most common causes of death from cancer causing more than 700,000 deaths worldwide annually. The implementation of endoscopic screening, surveillance programs and the development of new advanced endoscopic imaging techniques have increased the diagnosis of gastric cancer at earlier stages. Early gastric cancer is clearly associated with a better prognosis, with reported 5-year survival rates greater than 85%.

Endoscopic resection techniques can offer a curative treatment with minimal invasiveness compared with the conventional surgical approach. Since Tada *et al* [1] introduced back in 1984 the use of "strip-off biopsy" for treatment of early gastric cancer to the initial development of the endoscopic mucosal dissection (ESD) in 1994 with the design of a new endoscopic device, the insulated-tip knife (*IT-knife*), by Muto *et al* [2], endoscopic resection has become the treatment of choice for early gastric cancer, mainly in Eastern countries.

Despite being a technically challenging procedure, time consuming and associated with higher complications, ESD has been shown to have significant advantages compared with endoscopic mucosal resection (EMR) for *en bloc* and curative resection. It is also associated with lower local recurrence risk [3,4].

Current guidelines [5] recommend endoscopic treatment for differentiated type gastric cancer in non-ulcerated lesions regardless of tumour size and depressed/ulcerated lesions ≤3 cm and for undifferentiated type gastric cancer in non-ulcerated lesions ≤2 cm. For a curative resection, histological analysis must confirm negative lateral and deep resection margins (R0), absence of lymphatic or vascular invasion and presence of the lesion not beyond the mucosa layer (pT1a lesions). For differentiated-type cancer within lesions ≤3 cm, invasion into the superficial submucosal layer (<500 μm from the muscularis mucosae) can be also considered curative. These lesions have shown to have a negligible risk of lymph node metastasis and thus suitable for curative endoscopic treatment [6]. EMR and ESD for early gastric cancer have shown excellent results after short and long-term follow-up periods favoring endoscopic resection over the standard surgical treatment in the intact stomach.

In this issue, Yamashina *et al* [7] are presenting the results of one of the first published case series reporting long-term outcomes of the endoscopic resection of early gastric cancer in the remnant stomach compared to the classical surgical treatment.

The remnant stomach after a previous partial gastrectomy has obviously limited space that makes it more challenging to perform endoscopic resection of metachronous early neoplastic lesions. Depending upon the location of the lesion, due to the potential presence of scarring, fibrosis or surgical clips, the procedure could be even more difficult. This may have more relevance in western countries, because of the limited experience and expertise in this technique.

There is a lack of publications regarding the most appropriate therapeutic approach for early gastric cancer in the remnant stomach, but several feasibility studies have already reported a high *en bloc* resection rates with EMR and ESD, similar to those achieved in non-previously operated stomach. We also should keep in mind that, because of the already mentioned technical difficulties, endoscopic resection in the remnant stomach can be associated with a higher incidence of complications, as some of these studies have already suggested [8-12].

Yamashina *et al* [7] did not show in their study statistical significant differences in long-term outcomes between endoscopic and surgical treatment. The reported 89% overall 5-year survival rate and 100% disease-specific 5-year survival rates in the endoscopic resection group for ≤sm1 lesions are very similar to those from previously published studies with 5-year overall and disease-specific survival rates ranging from 88% to 97% and nearly 100% respectively [13-18]. These results are also comparable to the reported >90% 5-year overall survival rate after gastrectomy with lymph node dissection for early gastric cancer [19,20].

As has been previously published, procedure time, hospital stay length and complications rate are higher in the surgical group.

An appropriate selection of the case is the first and most relevant step in decision making for endoscopic treatment of early gastric cancer. If the endoscopic features of the lesion are suspicious of deep submucosal involvement, the most adequate approach should be offering surgical treatment. We also know that the endoscopic resection techniques, especially ESD with its capability to obtain *en bloc* resection almost regardless of the size of the lesion, are excellent

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diagnostic tools. This allows obtaining optimal specimen for an accurate histopathological evaluation, which may change differentiation grade and local staging of early neoplasia from initial biopsies and endoscopic imaging and thus may change the therapeutic approach.

The reported long-term outcomes after endoscopic resection of mucosal and superficial submucosal lesions (≤sm1) are excellent, with a 3-year cause specific survival rate of 100% (34/34 patients), and this type of lesions are a clear indication for endoscopic treatment [21].

On the other hand, this report has showed a cause specific 3-year survival rate for lesions with invasion into the deep submucosal layer (≥sm2 lesions) in the endoscopic group as poor as 47.6%, compared with the 100% from those in the surgical group. We could expect a lower distant metastasis as all these patients had undergone a previous gastric surgery with regional lymph nodes dissection, but 3 of 8 patients with ≥sm2 lesions treated by endoscopic resection died of metastatic gastric cancer. These results confirm the data from previously reported studies, and the presence of deep submucosal involvement is a strong indication for surgery and this needs be offered to any patient.

Additional treatment, ideally surgery, should be offered to all patients with non-curative endoscopic resection. We should also consider and keep in mind the reason for non-curative resection. There is a lack of studies and the scanty published data are not very promising with 5-year survival rates of 64%, but photodynamic therapy may have a role in selected cases, like those with positive lateral margins or lymphovascular invasion, patients with severe co-morbidities or contraindication for surgery or patients who refused surgical treatment [22].

In conclusion, endoscopic resection in the remnant stomach is feasible and a safe procedure. Endoscopic treatment for early gastric cancer with invasion not beyond the superficial submucosal (≤sm1) layer is associated with comparable long-term survival rates than surgery. The presence of submucosal invasion ≥500 μm from the muscularis mucosae (≥sm2) is a definitive indication for subsequent surgical treatment.

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