

Gastric perforation during endoscopic resection for gastric carcinoma and the risk of peritoneal dissemination

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Background: The potential risk of peritoneal seeding following perforation caused by endoscopic mucosal resection (EMR) or endoscopic submucosal dissection (ESD) is unknown.

Methods: Between January 1991 and December 2003, 90 patients suffered gastric perforation during EMR or ESD at the National Cancer Centre Hospital, Tokyo. The clinical and pathological evidence for peritoneal dissemination in these patients was assessed retrospectively.

Results: Eighty-four patients were followed up at this hospital for a median of 53.6 (range 7.0–136.6) months; the remaining six patients were followed up at other institutions. In 83 patients the perforation was repaired by endoscopic clip application and seven patients underwent emergency surgery. Gastrectomy was carried out in 33 patients who had non-curative endoscopic surgery. Among these, peritoneal fluid was sampled during operation in nine patients and was cytologically negative for malignancy. The other 24 patients who had a gastrectomy did not have ascites so cytology was not performed. No peritoneal dissemination was noted during follow-up.

Conclusion: This study suggests that perforation associated with EMR and ESD does not lead to peritoneal dissemination even in the long term.

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Introduction

Endoscopic resection for early gastric cancer (EGC) is a well-established treatment for selected patients in Japan. With the development of new techniques, such as endoscopic submucosal dissection (ESD), removal of larger EGC lesions is possible¹.

Perforation is a major complication of endoscopic resection, especially of ESD. The reported incidence of perforation at the National Cancer Centre Hospital (NCCH), Tokyo is 4 per cent, but higher rates have been reported, in particular when the strip biopsy method is used². Until recently, surgical intervention was the standard approach for sealing the perforation, but this can now be achieved by application of endoscopic clips³.

Peritoneal seeding after fine-needle aspiration (FNA) biopsy or ethanol injection therapy for hepatocellular carcinoma has been reported⁴, as well as port-site seeding after laparoscopic surgery⁵. Inadvertent seeding of malignant cells in the peritoneum could occur

after endoscopic mucosal resection (EMR)/ESD-related perforation. The present study investigated outcome after gastric perforation during EMR and ESD at the NCCH.

Methods

All patients who have endoscopic resection of gastric cancer are prospectively recorded in a database. Of a total of 1629 patients who underwent endoscopic resection between 1991 and 2003, gastric perforation occurred in 90 (5.5 per cent). The clinical records of these 90 patients were reviewed and information obtained on pathology, clinical course and any evidence of peritoneal dissemination.

Indication for endoscopic resection

The Japanese Classification of Gastric Carcinoma⁶ was used to classify tumours. The indications for EMR and ESD have changed over the years. When EMR was introduced to the NCCH in 1987, the indication was

a lesion of 15 mm or less in diameter, and piecemeal resection was not accepted. Based on a series of 5265 patients who had undergone gastrectomy with D2 level lymph dissection, it has been possible to clarify further the risks associated with different lesions and the criteria for local treatment without lymph node dissection have been expanded⁷. As it is sometimes difficult to assess the depth of invasion before endoscopic resection, the authors are prepared to remove any lesion that appears to be confined to the mucosa if it is a differentiated type, less than 3 cm with ulcer findings (any size without ulcer findings) and no evidence of invasion.

Evaluation of resected specimens and resectability

Resected specimens were evaluated both endoscopically and histopathologically in slices cut at 2-mm intervals according to the Japanese Classification of Gastric Carcinoma⁶. Deep submucosal invasion, vessel involvement and positive margins were regarded as indicative of a high risk of nodal involvement or distant metastasis. In these situations, complementary surgical intervention was strongly recommended.

Endoscopic clip technique

Perforations were closed with endoclips (HX-600-090; Olympus Optical, Tokyo, Japan), using the single-closure method for small defects (*Fig. 1*) and the omental patch method⁷ for larger defects. The first few patients with a perforation were fasted for 9 days with nasogastric tube drainage for the initial 3 days. Oral diet was not introduced until a contrast study showed no leakage and so these patients all required parenteral nutrition. The treatment plan later changed to 1 day of nasogastric tube drainage,

fasting for 2 days, and oral diet thereafter if the clinical course was unremarkable.

Follow-up

After complete resection, follow-up consisted of endoscopic examination at 3 months and 1 year, and annually thereafter to check for local recurrence or the presence of metachronous lesions. Abdominal ultrasonography or computed tomography was also performed yearly.

Results

Clinicopathological characteristics of the 90 patients who had gastric perforation are summarized in *Table 1*. Twenty-nine patients underwent standard EMR and 61 had ESD. There was no significant difference in perforation rate between the two procedures. Data on resection margin status are shown in *Table 2*. Forty-one patients (46 per cent) had a curative resection and 34 (38 per cent) a non-curative procedure; 15 specimens (17 per cent) could not be evaluated histologically because of diathermy burn, mechanical damage or failure to retrieve multiple fragments. In 58 patients (64 per cent), both the lateral and vertical margins were negative.

Perforation during endoscopic resection was recognized and treated immediately by endoscopic clip application in 83 patients (92 per cent). The remaining seven underwent emergency surgery. Eighty-four patients were followed up at this hospital and six patients at other institutions (*Fig. 2*). Median follow-up for NCCCH patients was 53.6 (range 7.0–136.6) months.

Twenty-nine patients who had non-curative endoscopic treatment underwent additional surgery (gastrectomy with lymph node dissection). Two patients underwent laser

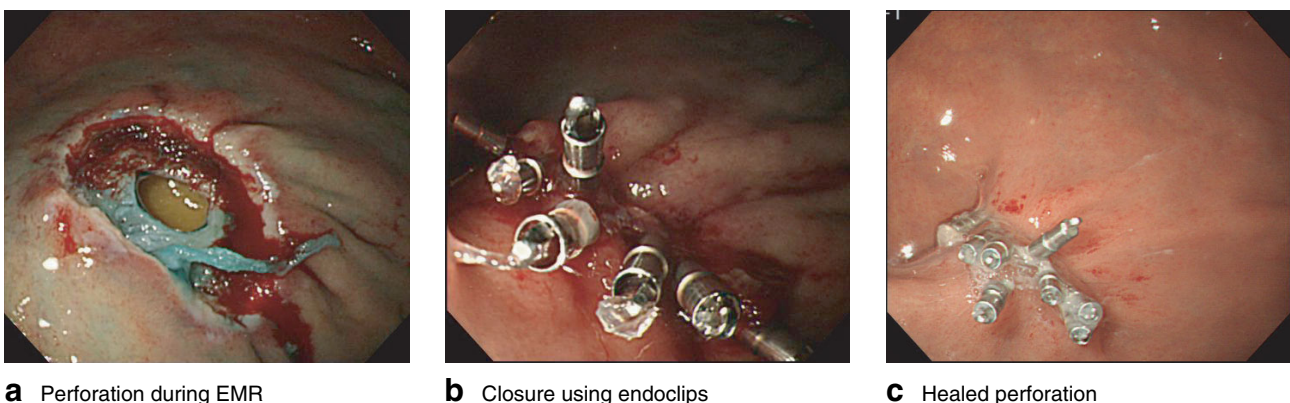


Fig. 1 a Gastric perforation created during endoscopic mucosal resection. b Small perforation treated by single-closure method using endoclips only. c Healed perforation 2 months after endoscopic closure

Table 1 Clinicopathological characteristics

| | No. of patients (n = 90) |
|----------------------------------|-----------------------------|
| Sex ratio (M : F) | 74 : 16 |
| Median (range) age (years) | 66.8 (36–84) |
| Tumour location | |
| Upper | 31 |
| Middle | 45 |
| Lower | 14 |
| Tumour size (mm) | |
| < 20 | 61 |
| 21–30 | 19 |
| > 30 | 10 |
| Histological diagnosis | |
| Differentiated | 79 |
| Undifferentiated | 11 |
| Depth of tumour invasion | |
| Intramucosal | 56 |
| Submucosal | 31 |
| ≥ T2 | 3 |
| Endoscopic procedure | |
| Endoscopic mucosal resection | 29 |
| Endoscopic submucosal dissection | 61 |

treatment as the EMR specimen showed a positive lateral margin. Of the remaining patients, six were followed-up at a different institution. Fifty-three patients were followed up, 33 of whom had a curative endoscopic resection, 11 a non-curative procedure and nine for whom histological evaluation was not available. During follow-up, four patients underwent salvage surgery for local recurrence.

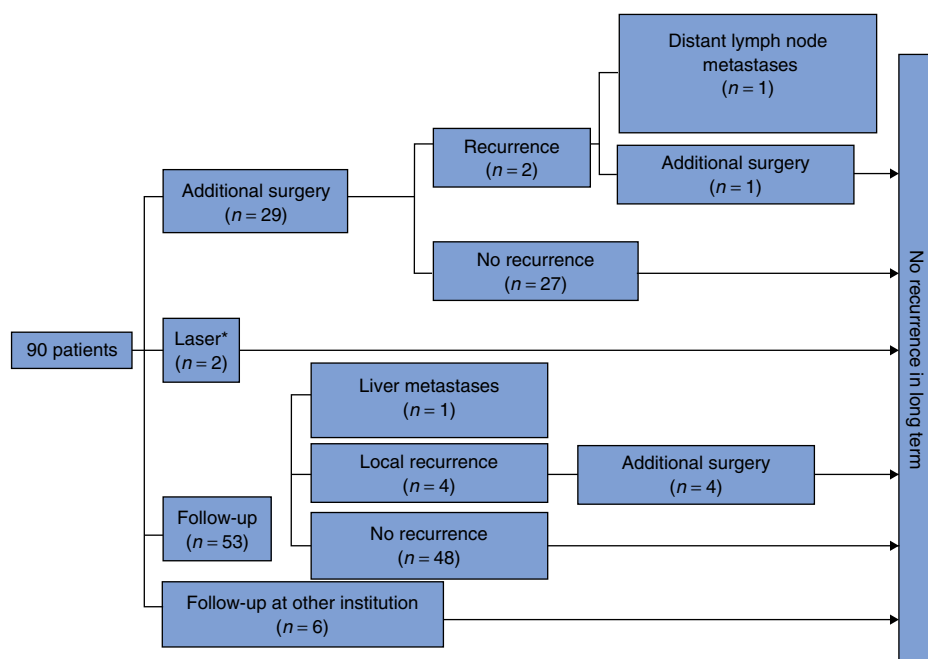
Table 2 Resection margin status after endoscopic surgery

| | Positive | Negative | Unknown |
|-----------------|----------|----------|---------|
| Lateral margin | 9 (10) | 63 (70) | 18 (20) |
| Vertical margin | 8 (9) | 79 (88) | 3 (3) |

Values in parentheses are percentages.

All tumour recurrences were on the mucosal side, and no serosal or peritoneal deposits were found during surgery. Cytological examination of ascites was performed in nine of the 33 patients who had further surgery, and was negative in all cases. The other 24 patients did not have ascites and cytology was omitted. No patients received adjuvant chemotherapy or radiotherapy.

Two patients whose ESD specimen had shown deep submucosal invasion died from distant metastasis during follow-up. The first patient had additional surgery, which revealed lymphatic dissemination (six of 40 nodes were positive), and lymph node recurrence was detected during follow-up examination 9 months later. The patient died with widespread intra-abdominal lymph node disease. The second patient refused further surgery after ESD, and 2 years later follow-up examination showed tumour recurrence and liver metastasis. Eight additional patients died from unrelated causes without peritoneal disease at the time of death. There was no evidence of peritoneal seeding in any of the survivors.

**Fig. 2** Clinical course after endoscopic resection-related perforation. No serosal tumour involvement or peritoneal metastasis was found

Discussion

The development of ESD has made possible the removal of large EGC lesions. Until recently, perforations caused by endoscopic resection necessitated emergency surgical repair, but complete closure of the defect can now be achieved by endoscopic clipping⁸. Two major endoscopic clipping methods have been described, simple closure and the omental patch method⁹. Most perforations resulting from ESD are small and can be treated by simple closure.

The possibility of disseminating malignancy in the peritoneal cavity is a fear associated with any diagnostic or therapeutic minimally invasive procedure. Peritoneal seeding has been reported after percutaneous diagnostic FNA biopsy⁴ and port-site metastasis after laparoscopic surgery for gastrointestinal malignancy¹⁰. It is possible that disruption of the gastric wall in an area containing malignant cells during endoscopic resection may lead to peritoneal seeding. However, the present series has provided no evidence of this as none of the patients who had endoscopic clip closure of a gastric perforation developed signs of peritoneal disease. This good outcome may also be related to the high rate of one-piece resection achieved in this study, even though eight patients had a positive vertical margin and nine had a positive lateral margin. The implication of positive margins combined with gastric perforation could not be assessed in this study, as the number of patients fulfilling both conditions was small.

If EMR or ESD is performed in appropriately selected patients the rate of positive margins should be minimal. The present results indicate that peritoneal dissemination is unlikely to occur after gastric perforation during endoscopic resection.

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