

Influence of a Positive Proximal Margin on Oral Intake in Patients with Palliative Gastrectomy for Far Advanced Gastric Cancer

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Abstract

Background Resection margin involvement is one of the most significant risk factors for local recurrence in curative gastrectomy, and local recurrence results in anastomotic stenosis. In the present study, the effects of a positive resection margin in palliative gastrectomy on the symptoms of anastomotic stenosis and the amount of oral intake were analyzed.

Methods Between September 2002 and December 2009, 2,228 patients underwent resection for gastric cancer at Shizuoka Cancer Center, Japan, of whom 18 underwent palliative gastrectomy with a positive proximal margin because of urgent symptoms such as tumor bleeding, stenosis, or perforation. These 18 patients were analyzed retrospectively in this study.

Results Twelve patients had a positive proximal margin, and six patients had both proximal and distal margin involvement. Anastomotic leakage occurred in 2 patients. The median overall survival was 7.5 months, and the median time from operation to a decrease in oral intake was 5.5 months. Anastomotic recurrence developed in 3 patients, and in all of them, anastomotic stricture was found 2–3 months after gastrectomy. One of these patients, who was in good general condition, was treated by endoscopic balloon dilatation. The other 2 patients did not undergo balloon dilatation because their general condition was poor, with peritonitis carcinomatosa.

Conclusions It does not appear necessary for palliative gastrectomy to achieve a negative proximal margin, because salvage therapies resulted in maintaining a tolerable oral intake in patients who were in good general condition.

Introduction

Gastric cancer is a very common disease worldwide and the second most frequent cause of cancer death, affecting about one million people per year [1]. Surgery is the only curative therapy for advanced gastric cancer, and this involves removing the primary lesion with an adequate tumor-free margin [2, 3]. However, the prognosis of advanced gastric cancer patients with noncurable factors, such as hepatic or peritoneal metastasis, is extremely poor [4]. The role of noncurative gastrectomy in patients with far advanced gastric cancer remains unclear. The rationale for offering palliative gastrectomy to patients with far advanced gastric cancer is that the primary tumor will result in gastric obstruction, perforation, or tumor bleeding [5, 6]. Several studies have suggested that the morbidity after palliative gastrectomy for far advanced gastric cancer that needs urgent treatment may be higher [7–10]. Patients who undergo palliative gastrectomy have only a short time to live, so postoperative morbidity is directly related to the quality of the rest of their life. On the other hand, patients who require palliative gastrectomy are those with advanced locoregional disease, so patients with severe tumor invasion into the esophagus from the stomach are not unusual [11–13]. It is difficult and risky to achieve a negative proximal margin in gastric cancer with wide spread into the esophagus, because a highly placed anastomosis in a narrow working space is required. Resection margin

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involvement is one of the most significant risk factors for local recurrence in curative gastrectomy, and local recurrence results in anastomotic stenosis [14, 15]. However, in palliative gastrectomy, a positive resection margin might not be a risk factor for anastomotic recurrence, because patients who undergo palliative gastrectomy usually succumb to metastatic disease before anastomotic recurrence develops. One of the outcomes of palliative gastrectomy is the prolongation of oral intake, but anastomotic stenosis caused by local recurrence might prevent oral intake. Some reports have shown that a positive resection margin has no predictive value for survival in patients with late-stage gastric cancer [16, 17]. However, the effects of a positive resection margin in palliative gastrectomy on the symptoms of anastomotic stenosis and the amount of oral intake are unknown. In the present study, the clinical course, focusing mainly on the amount of oral intake, of patients who underwent palliative gastrectomy with a positive proximal margin was analyzed.

Materials and methods

Between September 2002 and December 2009, 2,228 patients underwent resection for gastric cancer at Shizuoka Cancer Center, Japan. A positive proximal margin was found on final pathological analysis of the resected specimen in 20 patients who underwent palliative gastrectomy. In all of them, the status of the proximal margin was negative on macroscopic examination. Of the 20 patients, 2 were lost to follow-up. Therefore, 18 patients with urgent symptoms, such as tumor bleeding, stenosis, or perforation, were analyzed retrospectively in this study. All 18 patients were routinely followed at Shizuoka Cancer Center at least once a month postoperatively, and the patients were asked detailed questions about the amount of oral intake and the presence of symptoms of anastomotic stenosis. Endoscopic examination was not performed routinely; it was performed only when the patients complained of obstructive symptoms. We investigated the time between the operation and the decrease in oral intake. The time to decrease in oral intake was defined as the time when total parenteral nutrition or tube feeding was required. The data collected included patient demographics, clinicopathologic features, and clinical course. To compare this study population with patients who underwent palliative gastrectomy with a negative proximal margin, the data of 46 patients who underwent palliative gastrectomy with a negative proximal cut end were collected. Stage was reported according to the Seventh Edition of the tumor-node-metastasis (TNM) classification of malignant tumor established by the International Union Against Cancer (UICC) classification [18].

Results

The patients ranged in age from 49 to 85 years, with a median age of 70 years. Overall, 8 patients were male, and 10 patients were female. The patient characteristics are shown in Table 1. Twelve patients had a positive proximal margin, and 6 patients had both proximal and distal margin involvement. The symptoms leading to palliative gastrectomy were gastric outlet obstruction and/or tumor bleeding. Ten patients suffered from gastric outlet obstruction, 3 patients had severe anemia caused by tumor bleeding, and 5 patients had both. No patients underwent palliative gastrectomy for tumor perforation. Noncurable factors included liver metastasis in 4 cases, lymph node metastasis in 9 cases, peritoneal metastasis in 14 cases, and positive peritoneal cytology in 18 cases. Operative data are shown in Table 2. Total gastrectomy was performed in 14 patients, distal gastrectomy was performed in 3, and 1 patient underwent proximal gastrectomy. Systematic lymph node dissection was not performed in any of the patients. All patients underwent D1 lymphadenectomy, 14 underwent R2 resection, and 4 underwent R1 resection. Postoperative complications occurred in 5 patients.

Anastomotic leakage occurred in 2 patients: 1 patient in an esophagojejunostomy with tumor involvement after total gastrectomy, and 1 patient in a duodenal stump that

Table 1 Patient characteristics ($n = 18$)

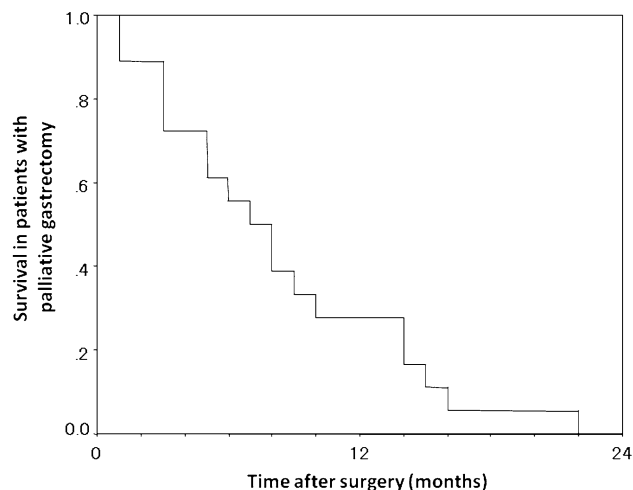
| Characteristic | |
|-------------------------------|------------|
| Age, years, median (range) | 70 (49–85) |
| Sex | |
| Male | 8 (44%) |
| Female | 10 (56%) |
| Symptoms | |
| GOO | 10 (56%) |
| Tumor bleeding | 3 (17%) |
| GOO and tumor bleeding | 5 (28%) |
| Noncurable factors | |
| Peritoneal lavage cytology | |
| Positive | 18 (100%) |
| Negative | 0 |
| Peritoneal metastasis | |
| Positive | 14 (78%) |
| Negative | 4 (22%) |
| Liver metastasis | |
| Positive | 4 (22%) |
| Negative | 14 (78%) |
| Distant lymph node metastasis | |
| Positive | 9 (50%) |
| Negative | 9 (50%) |

GOO gastric outlet obstruction

Table 2 Operative data from patients undergoing palliative gastrectomy ($n = 18$)

| Characteristics | |
|--------------------------|-----------|
| Surgical procedure | |
| Total gastrectomy | 14 (78%) |
| Distal gastrectomy | 3 (17%) |
| Proximal gastrectomy | 1 (6%) |
| Lymph node dissection | |
| ≤D1 | 18 (100%) |
| >D1 | 0 |
| Sites of positive margin | |
| Proximal only | 12 (67%) |
| Proximal and distal | 6 (33%) |
| Residual tumor | |
| R1 | 4 (22%) |
| R2 | 14 (78%) |
| Complications | |
| Anastomotic leakage | 2 (11%) |
| Anastomotic hemorrhage | 1 (6%) |
| Intra-abdominal abscess | 1 (6%) |
| Pneumonia | 1 (6%) |

was not margin-positive after Roux-en-Y reconstruction. In these patients with anastomotic leakage, oral intake was not resumed up to the time of death. Anastomotic hemorrhage, intra-abdominal abscess, and pneumonia occurred in 1 patient each. These 3 patients recovered with conservative treatment and maintained oral intake during their remaining survival time. Of the 5 patients who developed a postoperative complication, 4 had undergone total gastrectomy, and 1 had undergone distal gastrectomy. The complication in 1 patient who underwent distal gastrectomy was duodenal stump leakage that was not margin-positive after Roux-en-Y reconstruction. To achieve a negative proximal margin, the risk of surgery is considered to differ between distal gastrectomy and total gastrectomy. All 18 patients presented with cancer progression and died during follow-up. The median overall survival was 7.5 months (Fig. 1). The median time from operation to decrease in oral intake was 5.5 months (Fig. 2). Anastomotic recurrence developed in 3 patients, and all of whom had anastomotic stricture 2–3 months after gastrectomy (Table 3). Of these 3 patients, 2 had undergone total gastrectomy, and 1 had undergone distal gastrectomy. Anastomotic stricture due to anastomotic recurrence occurred in the patients after palliative distal gastrectomy. One of these three patients was treated by endoscopic balloon dilatation and maintained oral intake for 2 months after balloon dilatation. This patient had undergone total gastrectomy. The other 2 patients had peritonitis carcinomatosa when anastomotic recurrence was found. Balloon dilatation was

**Fig. 1** Survival in patients with palliative gastrectomy

not performed for these 2 patients, because we considered that oral intake could not be resumed even with anastomotic stricture dilatation. One patient after distal gastrectomy did not undergo balloon dilatation because of poor general condition owing to peritonitis carcinomatosa.

In all 18 patients, the status of the proximal margin was negative on macroscopic examination, because the goal of all surgeries, even palliative, was to obtain a macroscopic negative margin. Therefore, patients with a microscopic-positive margin cannot be compared with those with a macroscopic-positive margin.

In 46 patients with a negative proximal margin, the median overall survival was 8.5 months, and the median time from operation to a decrease in oral intake was 7 months. There was no significant difference between proximal margin-positive and proximal margin-negative patients in the time between gastrectomy and death ($p = 0.26$) and a decrease in oral intake ($p = 0.12$).

Discussion

Radical resection is the primary treatment for gastric cancer, but the benefit of noncurative gastrectomy for metastatic gastric cancer patients is still debatable. The prognosis of patients who undergo noncurative gastrectomy is extremely poor [7, 19, 20]. Palliative gastrectomy is not the same as noncurative gastrectomy. Noncurative gastrectomies have been classified as either palliative or nonpalliative. Palliative care has been defined by the World Health Organization as “the total active care of patients whose disease is not responsive to curative treatment. Control of pain, of other symptoms, and of psychological, social, and spiritual problems is paramount. The goal of palliative care is the achievement of the best quality of life

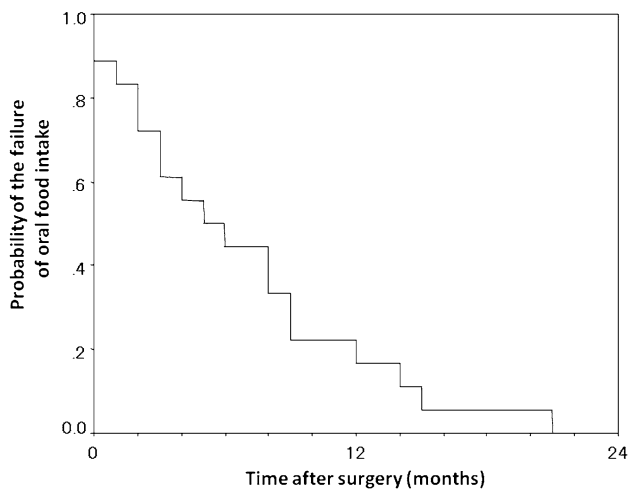


Fig. 2 Cumulative incidence of failure of oral food intake. Kaplan-Meier curve showing the time to failure of oral food intake after operation

for patients and their families” [21]. Palliative gastrectomy should concentrate on relieving symptoms such as gastric outlet obstruction, perforation, or tumor bleeding. Therefore, in the present study, patients without symptoms were excluded, even if a noncurative operation was performed. The morbidity was high after palliative gastrectomy for far advanced gastric cancer with urgent symptoms that needed to be controlled. For patients with short life expectancy, complications of surgery ruin the rest of their lives. In the present study, anastomotic leakage dealt a crushing blow. It is difficult and risky to perform highly placed intramediastinal anastomosis for far advanced gastric cancer with severe esophageal invasion to achieve a negative proximal margin. Palliative resection does not seek to offer cure options, and resection margin involvement was not considered to affect the clinical course after gastrectomy. However, in general, a positive resection margin induces anastomotic recurrence and anastomotic stenosis.

Anastomotic stenosis caused by recurrence might lead to decreasing oral intake. Actually, it is unclear whether a positive proximal margin in palliative gastrectomy affects the amount of oral intake after surgery. In this study, anastomotic recurrence occurred in 3 of 18 patients (16.7%), and recurrence was found at 2 months after gastrectomy. Lee et al. [22] reported that anastomotic recurrence was found in 4.3% of patients who underwent gastrectomy for advanced gastric cancer, and anastomotic strictures were observed at a median interval of 11.9 months. Cho et al. [23] reported that resection margin involvement occurred in 1.8% of gastrectomies with curative intent, and that anastomotic recurrence occurred in 14.3% of patients with positive resection margins. Jakl et al. [24] reported that anastomotic recurrence was found at a median interval of 11 months. The present study showed that a positive proximal margin resulted in a high incidence of early recurrence at the site of anastomosis. In 2 patients, anastomotic stenosis caused by tumor recurrence did not affect their quality of life, because their condition was poor due to peritonitis carcinomatosa. For another patient with anastomotic stricture caused by recurrence, who was in good general condition, endoscopic balloon dilatation was effective in maintaining a reasonable quality of life. We performed endoscopic balloon dilatation for anastomotic stricture as salvage therapy, which was effective for benign esophagojejunal anastomotic stricture [25, 26], but there are other salvage treatments available. Some studies have shown that a self-expandable metal stent provides safe and effective palliation of anastomotic recurrence of gastric cancer [27–30]. If long-term survival is possible, stent insertion is worthwhile, because the effect of balloon dilatation is temporary. At any rate, patients with anastomotic stricture due to tumor recurrence after palliative gastrectomy, if they are in good general condition, can maintain oral intake with balloon bougie or stenting therapy. Therefore, we concluded that it is not

Table 3 Patients with anastomotic stenosis caused by local recurrence

| Case | Noncurable factor | Surgical procedure | Interval between operation and AS caused by local recurrence | Recurrent site except anastomosis | Interval between operation and non-local recurrence | Intervention for AS | Outcome |
|------|-------------------|--------------------|--|-----------------------------------|---|---------------------|----------------|
| 1 | P, CY | Total gastrectomy | 2 months | Peritoneal dissemination | 4 months | Balloon dilatation | 6 months Death |
| 2 | P, CY | Distal gastrectomy | 2 months | Peritoneal dissemination | 2 months | None | 3 months Death |
| 3 | P, CY, M(LYM) | Total gastrectomy | 3 months | Peritoneal dissemination | 3 months | None | 5 months Death |

AS anastomotic stenosis, P peritoneal metastasis, CY peritoneal lavage cytology, M(LYM) nonregional lymph node metastasis

necessary for palliative gastrectomy to achieve a negative proximal margin, because salvage therapies resulted in maintenance of a tolerable oral intake.

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