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A new sequential neoadjuvant therapy strategy for gastric cancer patients with pyloric obstruction

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Abstract

Background: The safety and efficacy of neoadjuvant therapy have been proven for advanced gastric cancer. Due to intolerance to oral intake, neoadjuvant therapy of gastric cancer patients with pyloric obstruction remains challenging. This study showed a new sequential treatment model, stomach-partitioning gastrojejunostomy (SPGJ), followed by neoadjuvant therapy and radical gastrectomy.

Methods: From May 2022 to February 2025, 7 patients with histologically confirmed gastric cancer and pyloric obstruction who underwent this new sequential treatment model were retrospectively enrolled. The clinical characteristics, drug adverse events, surgical complications, and pathological responses were collected and analyzed.

Results: SPGJ was performed in all seven patients, and no perioperative complications occurred. All seven patients completed three cycles of neoadjuvant therapy. During the neoadjuvant therapy, all patients took food orally, and no case of gastric retention or upper gastrointestinal bleeding was observed. After neoadjuvant therapy, all patients achieved R0 resection. Two of the patients achieved a complete pathological response.

Conclusion: This new sequential neoadjuvant treatment model was a strategy that should be further explored for resectable gastric cancer with pyloric obstruction.

Key words

Gastric cancer, Pyloric obstruction, Neoadjuvant therapy, Stomach-partitioning gastrojejunostomy

Introduction

Worldwide, gastric cancer was the fifth most common cancer and the fourth deadliest cancer¹. Most patients came from East Asia, and 47% of those came from China². Although the incidence of esophagogastric cancer increased, the gastric antrum was still the predilection site of gastric cancer³. Most of the patients were diagnosed with advanced gastric cancer in these high-incidence areas. For advanced gastric cancer, perioperative therapy was verified as an effective method to improve surgical resection rate and overall survival⁴.

However, these perioperative studies only included patients who could swallow. Up to now, for advanced gastric cancer patients with pyloric obstruction who could not swallow, there was not enough evidence for neoadjuvant therapy. Intolerance of oral taking and malnutrition were the most important limitations on the neoadjuvant therapy for advanced gastric cancer with gastric outlet obstruction. In these previous perioperative studies, intolerance of oral intake or malabsorption was one of these exclusion criterions^{2,5}. So, there was not a criterion of perioperative therapy for these patients with gastric outlet obstruction.

Anyway, the feeding problem was the first thing to resolve before perioperative therapy. Gastrojejunostomy was the most common bypass operation for these patients with gastric outlet obstruction. Conventional gastrojejunostomy (CGJ) could lead to retention of food or bleeding from the tumor⁶⁻⁹. Stomach-partitioning gastrojejunostomy (SPGJ) was comprised of stomach-partitioning transection and gastrojejunostomy from the proximal stomach to the proximal part of the jejunum¹⁰. Compared to CGJ, SPGJ had better gastric emptying performance and reduced the postoperative hospital stay^{8,11}. However, this method was only used for unresectable gastric cancer up to now^{8,11-15}.

In this study, we first introduce a sequential neoadjuvant therapy in patients with

resectable gastric antrum cancer. Firstly, laparoscopy was performed to exclude peritoneal implantation metastasis. At the same time, SPGJ was performed to resolve the eating problem. Secondly, neoadjuvant drug therapy was sequentially performed. Finally, distal gastrectomy was performed.

Methods

Patients

From May 2022 to February 2025, patients diagnosed with advanced gastric cancer with pyloric obstruction were retrospectively included in this study. All patients included in this study met the following inclusion criteria: (1) The diagnosis of distal gastric adenocarcinoma was confirmed histologically; (2) The existence of pyloric obstruction was confirmed by upper gastrointestinal endoscopy; (3) The preoperative clinical stage was T4aN0-3M0. (4) The patient has not received prior therapy, including chemotherapy, radiotherapy, targeted therapy, or immunotherapy. (4) Laparoscopy and SPGJ were performed. The following exclusion criteria: (1) Neoadjuvant drug therapy was not performed after SPGJ surgery; (2) Gastrectomy was not performed after neoadjuvant therapy.

The study protocol was approved by the Ethics Committee of the Hospital (SCCHEC-02-2024-113).

Process of SPGJ

We used SPGJ in the following procedure. A side-to-side anastomosis was performed between the upper segment of the stomach's greater curvature and the small intestine 15cm below the Treitz ligament using a linear stapler. The upper third of the stomach was partitioned at the middle point from the greater curvature side to the lesser curvature (Fig.1). However, the distance between the cutting line and the tumor should be greater than 5 cm. If necessary, intraoperative gastroscopy was used to determine this distance.

Clinical outcomes

The Clavien-Dindo classification system was used to classify complications. Clinical characteristics, drug complications, surgical outcomes, and pathological characteristics of patients were collected. The following surgical outcomes were obtained: lymphadenectomy type, retrieved lymph nodes, and complications. Pathological characteristics included preoperative clinical stage, postoperative pathological stage, and pathological TRG score. The TRG score was defined following the recommendations of the College of American Pathologists¹⁶.

STROCSS GUIDELINE CHECKLIST

The work has been reported in line with the STROCSS criteria.

Results

From May 2022 to February 2025, 7 patients were retrospectively included in this study. These clinicopathological characteristics were retrospectively collected (Table.1).

Surgical outcomes

7 patients underwent laparoscopic exploration, and no peritoneal metastases were found. Then, SPGJ was performed, and no major operative complications were observed during the procedure. Following SPGJ, oral intake was successfully initiated in all patients. This was confirmed via postoperative gastrointestinal contrast imaging, which demonstrated adequate patency at the anastomotic site without signs of leakage or obstruction (Fig.2).

No major postoperative complications, such as gastric retention or upper gastrointestinal bleeding, were observed. Following neoadjuvant therapy, all patients successfully underwent distal gastrectomy, with an R0 resection achieved in all cases (Table.2).

Complications of neoadjuvant therapy

Neoadjuvant therapy was well-tolerated by all patients, and the full course was completed as scheduled. Treatment-related adverse events comprised hematologic toxicity (leukopenia, erythrocytopenia, neutropenia, and thrombocytopenia), gastrointestinal toxicity (nausea and vomiting), and hepatotoxicity. Most drug toxicities were grade 2. However, two of these patients developed grade 3 toxicity, which showed marked improvement following antiemetics (Table.3).

Pathological findings

The study cohort comprised seven patients, in whom a diagnosis of clinical stage III was established prior to the initiation of therapy. Tumor downstaging was observed across all patients, with a significant reduction in T stage universally noted and a corresponding N stage reduction in five of the seven individuals. An R0 resection was accomplished in every case. Pathological complete response (TRG 0) was achieved in two patients (Table.4).

Discussion

For advanced gastric cancer, perioperative therapy is an effective strategy to improve patient prognosis. Clinical evidence from the MAGIC⁴, FLOT¹⁷, JCOG0405¹⁸ and RESOLVE trials ² has confirmed the efficacy and safety of neoadjuvant therapy. Compared with surgery alone, neoadjuvant therapy can improve overall survival in patients with resectable gastric cancer.

Pyloric obstruction is a common complication in patients with distal gastric cancer ¹⁹. At initial diagnosis, 15% to 30% of distal gastric cancer presents with symptomatic pyloric obstruction ^{20,21}. Moreover, pyloric obstruction in patients with advanced gastric cancer impairs oral intake, often resulting in progressive malnutrition characterized by hypoalbuminemia and significant weight loss ²². Consequently, these patients develop intolerance to chemotherapy, and were unsuitable candidates for neoadjuvant therapy ^{2,5,23}. As a result, the 5-year overall survival among patients with pyloric obstruction is significantly lower compared to non-obstructed cohorts ²⁴⁻²⁶. In

addition, gastric cancer patients with pyloric obstruction frequently exhibit deeper tumor invasion and higher lymph node metastasis rates ^{26,27}, which constitute key pathological determinants of their poor prognosis. So, these gastric cancer patients with pyloric obstruction usually have a poorer prognosis ^{24,25}. Therefore, the treatment of these patients still presents a distinct clinical challenge.

However, oral feeding is the most important condition for neoadjuvant therapy. Consequently, gastrojejunostomy has become the standard palliative procedure for relieving malignant gastric outlet obstruction in patients with advanced unresectable gastric cancer ²⁸. With ongoing advancements in surgical techniques, SPGJ may represent a promising alternative. This approach not only significantly reduces the risk of delayed gastric emptying (DGE) compared to LGJ ^{11,28}, but also lowers the risk of bleeding caused by food stimulation¹².

Therefore, our study innovatively proposes this sequential treatment strategy. In our study, no significant surgical complication was observed in all 7 patients. All patients completed neoadjuvant therapy, and no serious drug event was observed. Notably, all resections were R0, and a pathologic complete response was observed in 28.6% (2/7) of patients. These outcomes demonstrate that our strategy serves as a potential effective bridging method to perform neoadjuvant therapy for these gastric cancer patients.

However, our study also has certain limitations. The retrospective nature and small sample size restrict the generalizability of our conclusions. Consequently, the findings should be viewed as preliminary. Moreover, the lack of long-term follow-up leaves the durability of the observed effect uncertain. Secondly, the lack of long-term follow-up data hinders the assessment of efficacy, safety, and potential long-term adverse effects. To address these limitations, future research should prioritise multicentre, prospective randomised controlled trials.

In conclusion, this sequential neoadjuvant treatment model was a new strategy that

should be further explored for resectable gastric cancer with pyloric obstruction.

Data availability statements

All data generated or analyzed during this study are included in this published article and its supplementary information files. Consent was obtained.

Conflicts of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Fundings

There is no financial help.

Ethical approval

The study protocol was approved by the Ethics Committees of the Hospital and complied with the principles of the Declaration of Helsinki.

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Provenance and peer review

Not commissioned, externally peer-reviewed.

Data statement

We declare that all data can be obtained in the article.

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Figure Legend

Figure.1. Process of SPGJ. The upper third of the stomach was partitioned at the middle point from the greater curvature side to the lesser curvature.

Figure.2. Surgical outcomes. The results indicated free passage of contrast medium through the anastomosis.

Table.1. Clinical characteristics of included patients.

Table.2. Surgical outcomes of SPGJ and gastrectomy.

Table.3. Drug adverse events of neoadjuvant therapy.

Table.4. Pathological characteristics.

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Figures

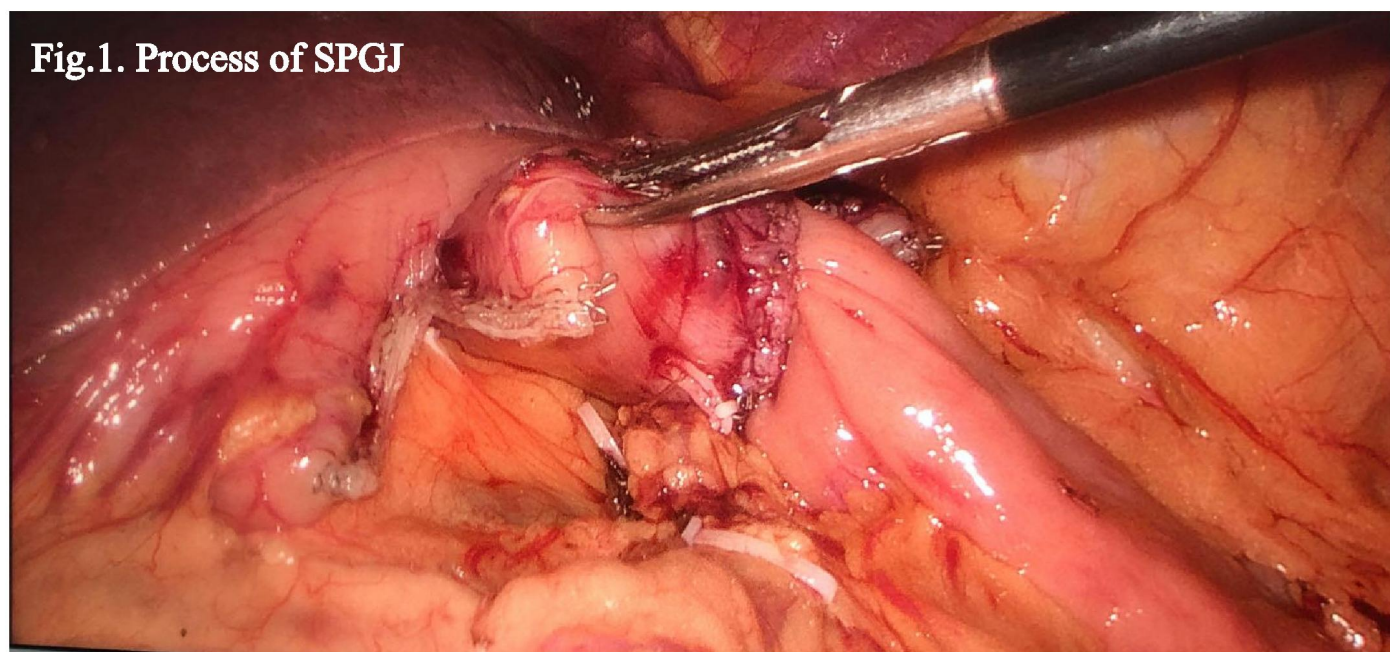


Figure 1

Process of SPGJ. The upper third of the stomach was partitioned at the middle point from the greater curvature side to the lesser curvature.

Fig.2. Surgical outcomes

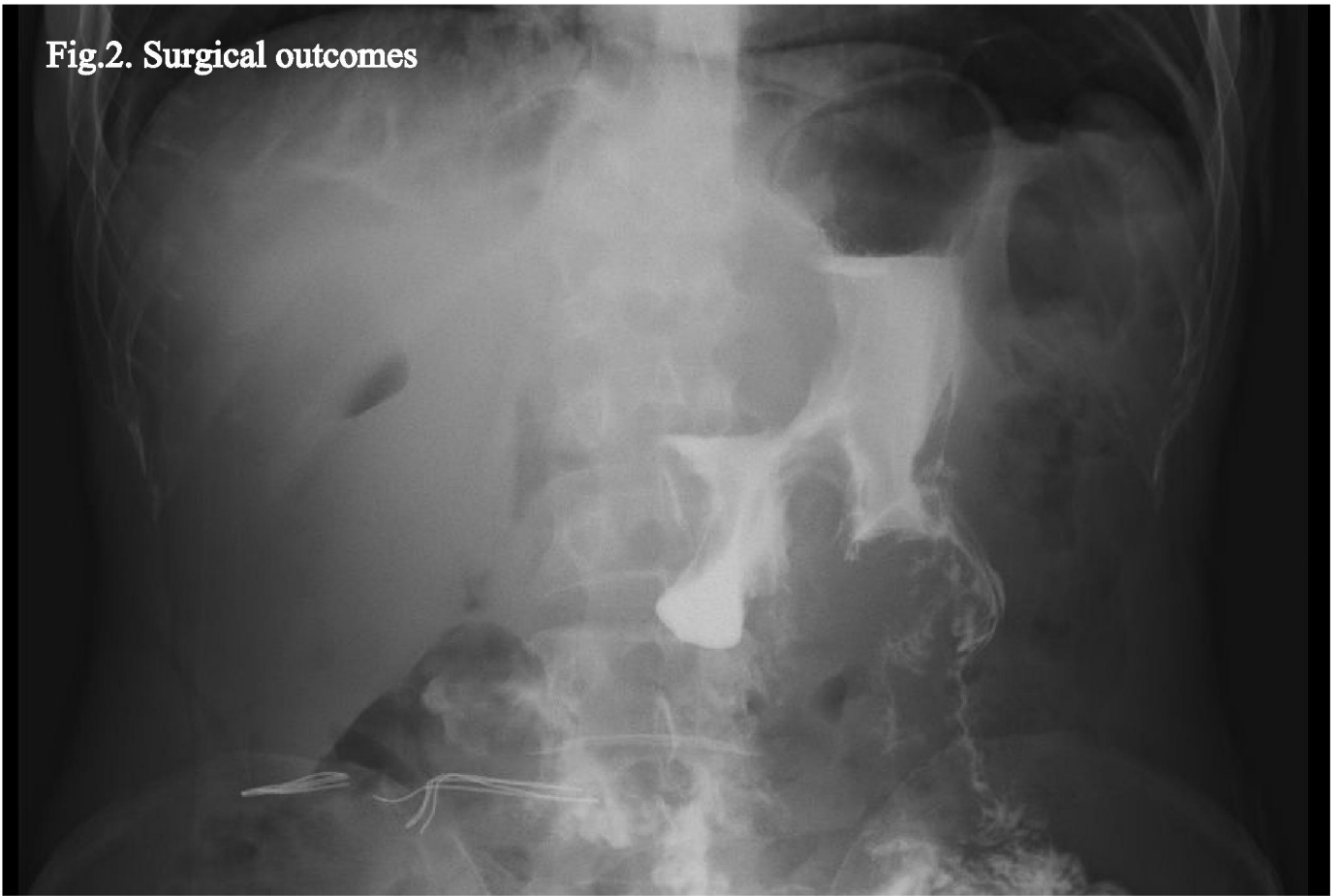


Figure 2

Surgical outcomes. The results indicated free passage of contrast medium through the anastomosis.

Supplementary Files

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