Functional Outcomes According to the Size of the Gastric Remnant and the Type of Reconstruction Following Distal Gastrectomy for Gastric Cancer: An Investigation Including Total Gastrectomy

Eiji Nomura1,*, Sang-Woong Lee2, Takaya Tokuhara2, Toshikatsu Nitta2, Masaru Kawai2 and Kazuhisa Uchiyama2

1Department of Gastroenterological and General Surgery, Tokai University Hachioji Hospital, Tokyo and 2Department of General and Gastroenterological Surgery, Osaka Medical College, Osaka, Japan

*For reprints and all correspondence: Eiji Nomura, Department of Gastroenterological and General Surgery, Tokai University Hachioji Hospital, 1838 Ishikawa-machi, Hachioji, Tokyo 192-0032, Japan. E-mail: nomura@hachioji-hosp.tokai.ac.jp

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Objective: In gastric cancer, various methods of gastric resection have been devised according to the location of the primary tumor and the depth of invasion. Functional outcomes were compared among different types of reconstruction following open 2/3- or 4/5 distal gastrectomy for gastric cancer.

Methods: Resection and reconstruction were performed by one of the following three methods, depending on the depth of cancer invasion and the date of the procedure relative to the introduction of Roux-en-Y reconstruction: distal 2/3 gastrectomy with Roux-en-Y reconstruction (1/3 Roux-en-Y, n = 30); distal 4/5 gastrectomy with Roux-en-Y reconstruction (1/5 Roux-en-Y, n = 15) and distal 2/3 gastrectomy with Billroth I reconstruction (1/3B1, n = 30). Open total gastrectomy with Roux-en-Y reconstruction (total gastrectomy with RY reconstruction, n = 30) was taken as the control procedure.

Results: Comparison of postoperative/preoperative body weight ratios and food intake ratios revealed better preservation among patients with a larger remnant stomach (the 1/3 Roux-en-Y and 1/3B1 groups), regardless of the reconstruction. The gastric emptying pattern in larger remnant stomach groups was milder than in the 1/5 Roux-en-Y and total gastrectomy with RY reconstruction groups. Reflux esophagitis was often observed on endoscopy in the 1/3B1 group.

Conclusions: Better functional outcomes were observed in patients with a large remnant stomach regardless of the reconstruction.

Key words: gastric cancer – distal gastrectomy – quality of life – reconstruction – gastric remnant size

INTRODUCTION

The incidence of early gastric cancer has increased in recent years (1), but the numbers of advanced gastric cancer patients remain high. Advanced gastric cancer patients are expected to survive for a longer period after surgery with chemotherapy, and there has been increasing demand for improved postoperative quality of life (QOL) (2). For primary gastric cancer located in the middle or lower third of the stomach, we perform distal gastrectomy. Various methods of resection with reconstruction have been devised over time, primarily for early gastric cancer (3–5). Standard distal gastrectomy for advanced gastric cancer, as defined by the Japanese gastric cancer treatment guidelines (6), requires resection of more than two-third of the stomach. According to the location of the primary tumor, the extent of the gastric resection is altered, and the manner of reconstruction has been changing.

We used to perform Billroth I (B1) reconstruction following distal gastrectomy in principle. Since 2006, a laparoscopic approach has been regularly adopted for a wide-extent distal gastrectomy for early gastric cancer. When four-fifth of the distal
stomach is resected, Roux-en-Y (RY) reconstruction has been used to reduce the tension at the anastomotic site. Based on the Japanese gastric cancer treatment guidelines (6), laparoscopic gastrectomy has been recommended as treatment for early gastric cancer. At present, for advanced gastric cancer patients, we are performing an open, wide-extent, distal gastrectomy with RY reconstruction. In the present study, functional outcomes were retrospectively compared between two different types of reconstruction: B1 vs. RY following open 2/3 or 4/5 distal gastrectomy for advanced gastric cancer.

PATIENTS AND METHODS

This study evaluated 30 patients who underwent distal 2/3 gastrectomy with B1 reconstruction (1/3B1) and 30 patients who underwent total gastrectomy with RY reconstruction (TG) between April 2001 and June 2005. They were the selected cases who underwent D2 lymph node dissection according to the preoperative diagnosis as advanced gastric cancer and Stage II. A total of 45 patients underwent distal gastrectomy with RY reconstruction for advanced gastric cancer between April 2006 and June 2010 at our institution. The 45 patients were divided into two groups according to the size of the resected stomach: 30 patients who underwent 2/3 distal gastrectomies were included in the 1/3RY group, and 15 patients who underwent 4/5 distal gastrectomy were included the 1/5RY group. Overall, 30 patients in the 1/3B1 group and 30 patients in the TG group prior to June 2005, and 30 patients in the 1/3RY group and 15 patients in the 1/5RY group after April 2006 were consecutively selected without intensive selection in accordance with the location and stage of the tumor. Until now, we performed open resection of over two-thirds of the distal stomach with D2 lymph node dissection for advanced gastric cancer. When their stages are greater than Stage II, they are supposed to receive chemotherapy with S-1 (6). In our institute, each operator was expected to measure the ratio of the size of the resected stomach to the whole stomach and record it intraoperatively. In practice, they put a circle around the appropriate size: 1/2, 2/3, 4/5 and others. The cases recorded as others were excluded.

The primary outcome measure was postoperative digestive function measured by the postoperative/preoperative body weight ratio, postoperative/preoperative meal intake ratio and the degree of postprandial abdominal symptoms. The postoperative/preoperative meal intake ratio was estimated by the mean of the whole meal intake per day compared with the preoperative intake. These data were acquired at one time point, 12 months postoperatively, through an in-house questionnaire (Table 1). In addition, the findings of patients who underwent endoscopy postoperatively at our outpatient clinic were analyzed to investigate the incidence of remnant gastritis and esophagitis. Endoscopic findings of the gastric remnant were evaluated according to the ‘residue, gastritis, bile’ classification (7), and the esophagitis was evaluated by the Los Angeles classification (8). The incidence of gastritis, residue Grade 2 or more and esophagitis Grade A or more were considered to be the findings of clinical significance.

In addition, functional evaluation was performed for patients who were undergoing regular follow-up at our hospital and agreed to be involved in the study. The course of gastric emptying was investigated with acetaminophen in 10 patients of the 1/3RY group, 5 patients of the 1/5RY group, 10 patients of the 1/3B1 group and 5 patients of the TG group. Acetaminophen is not absorbed in the stomach but is absorbed in the duodenum or jejunum, through which it enters the blood stream (9). Patients swallowed an alimentary liquid (200 ml of Ensure liquid mixed, Meiji, Tokyo, Japan) containing 1.5 g of acetaminophen, and the concentration of acetaminophen in the blood was measured every 15 min for 60 min (5,10).

Twelve months after the surgery, mail questionnaires were completed to exclude influence from the researchers. Questionnaire forms sent to patients were returned to the researchers. Subsequently, within 1 month, endoscopic examinations and gastric emptying tests using acetaminophen were performed.

This study protocol was approved by the Human Ethics Review Committee of Osaka Medical College. A written, informed consent was obtained from each enrolled patient before study entry in accordance with the Declaration of Helsinki.

Clinicopathological findings of the gastric resections were recorded according to the Japanese Classification of Gastric Carcinoma, second English edition (11).

SURGICAL PROCEDURES

Resection and reconstruction were performed by one of the following four methods, depending on the location of the cancer and the date of the procedure relative to the introduction of laparoscopic gastrectomy: distal 2/3 gastrectomy with

Table 1. Questionnaire survey on postoperative body weight, meal intake and abdominal symptoms

<table>
<thead>
<tr>
<th>Question</th>
<th>Percentage</th>
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<tbody>
<tr>
<td>(1) Please describe your body weight at present. _____kg.</td>
<td></td>
</tr>
<tr>
<td>(2) Please put a circle around the number below that fits your present postoperative whole amount of meal intake per day compared with your preoperative whole meal intake.</td>
<td></td>
</tr>
<tr>
<td>(1) 20%</td>
<td></td>
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<tr>
<td>(2) 40%</td>
<td></td>
</tr>
<tr>
<td>(3) 60%</td>
<td></td>
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<tr>
<td>(4) 80%</td>
<td></td>
</tr>
<tr>
<td>(5) 100%</td>
<td></td>
</tr>
<tr>
<td>(6) Other _ _ _ _ _ _ _ _ _ %</td>
<td></td>
</tr>
<tr>
<td>(3) Please put a circle around the number below that fits your description of abdominal symptoms often occurring especially after meals at present.</td>
<td></td>
</tr>
<tr>
<td>(1) Borborygmi</td>
<td></td>
</tr>
<tr>
<td>(2) Abdominal pain</td>
<td></td>
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<tr>
<td>(3) Diarrhea</td>
<td></td>
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<tr>
<td>(4) Nausea or vomiting</td>
<td></td>
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<tr>
<td>(5) Abdominal sensation of feeling full</td>
<td></td>
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<tr>
<td>(6) Abdominal discomfort</td>
<td></td>
</tr>
<tr>
<td>(7) Heart burn or reflux</td>
<td></td>
</tr>
<tr>
<td>(8) No symptoms</td>
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B1 (1/3B1), distal 2/3 gastrectomy with RY (1/3RY), distal 4/5 gastrectomy with RY (1/5RY) and TG. Total gastrectomy for advanced cancer located in the upper or middle third of the stomach was considered to be the control procedure. Combined resection of the spleen was performed in 10 cases.

For RY following distal gastrectomy, we fashion a side-to-side anti-peristaltic gastrojejunostomy 30 cm from the ligament of Treitz, after which the jejunum is divided and the enterotomy closed using a further firing of the linear stapler (12). While we perform a side-to-side peristaltic gastrojejunostomy, the enterotomy is closed by hand-sewing (13). The jejunojejunostomy is subsequently created, either by hand-sewing or by using the stapler to complete the reconstruction. As a result, a 25 cm segment of jejunum is interposed between the remnant stomach and the jejunojejunalostomy. The figures for anti-peristaltic/peristaltic gastrojejunostomy were 21:9 in the 1/3RY group and 9:6 in the 1/5RY group, respectively (Fig. 1). The figures for those who underwent the gastric emptying test with acetaminophen for anti-peristaltic/peristaltic gastrojejunostomy were 5:5 in the 1/3RY group and 5:0 in the 1/5RY group (all patients underwent peristaltic gastrojejunostomy).

Statistical analysis was performed using Student’s t-test and the χ² test. A P value of < 0.05 was considered significant.

RESULTS

All patients completed the questionnaires on digestive function. Patient demographics stratified according to the surgical procedure are presented in Table 2. Because significant differences among the four experimental groups undergoing different procedures were observed in the final clinical stage, the rate of receiving chemotherapy was significantly higher in 1/3RY and 1/5RY than in 1/3B1, and that in 1/3RY was significantly higher than in TG. On follow-up, there was no evidence of recurrence 2 years after surgery in any of the patients.

FUNCTIONAL OUTCOMES AT 12 MONTHS

A comparison of postoperative/preoperative body weight ratios (Fig. 2) revealed better preservation of postoperative body weight among those with a larger remnant stomach (the 1/3B1 and 1/3RY groups). The postoperative/preoperative food intake ratio was also higher in the 1/3B1 and 1/3RY groups than in the other groups (Fig. 3).

Abdominal pain and diarrhea (26.7%, 8 of 30) were frequent in the 1/3B1 group, and borborygmi (33.3%, 10 of 30), abdominal heavy feeling (23.3%, 7 of 30) and abdominal discomfort (30.0%, 9 of 30) were frequent in the TG group, though there were no significant differences among these four groups. Petersen’s hernia cases were not seen, but two cases that were thought to be Roux stasis syndrome were reported in the 1/3RY group. Nausea and an abdominal fullness sensation were reported after the beginning of meal intake, but these disappeared within 1 month by conservative therapy, such as fasting.

1/3RY was significantly superior to the 1/5RY and TG procedures in terms of postoperative body weight (P = 0.0210 and 0.0206, respectively). 1/3B1 was significantly superior to the 1/5RY and TG procedures with respect to postoperative body weight (P = 0.00436 and 0.0109) (Fig. 2). 1/3RY was significantly superior to the 1/5RY and TG procedures in terms of preservation of meal intake (P = 0.00341 and 0.00364). 1/3B1 was significantly superior to the 1/5RY and TG procedures with respect to postoperative meal intake (P = 0.00882 and 0.00906) (Fig. 3). Thus, better functional outcomes were observed in patients with large gastric remnants, while no major differences were observed between 1/5RY and TG when the remnant stomach was small or resected.

Furthermore, according to the postoperative/preoperative body weight and food intake ratios, there were no significant differences between the anti-peristaltic and peristaltic gastrojejunostomies among the 1/3RY and 1/5RY groups (body weight ratio, 89.1:91.8% in 1/3RY, 83.3:85.7% in 1/5RY; food intake, 73.3:68.1% in 1/3RY, 51.7:56.7% in 1/5RY). The emptying test using acetaminophen demonstrated that the plasma acetaminophen concentration in the 1/5RY and TG groups increased markedly 15 and 30 min after oral administration, while the increase in the 1/3B1 and 1/3RY groups was gradual; the differences were significant (Fig. 4). For reference, the emptying pattern of five numbered healthy volunteers (HVs) is shown by the black dotted line. There were significant differences between the HV group and the other four groups from 0 to 45 min after the administration of acetaminophen.

Furthermore, there were no significant differences in gastric emptying between peristaltic and anti-peristaltic gastrojejunostomies in the 1/3RY group (Fig. 5).

The incidence of reflux esophagitis on endoscopic examination was 33.3% (10 of 30) in the 1/3B1 group, 6.7% (2 of 30) in the 1/3RY group, 13.3% (2 of 15) in the 1/5RY group and 3.3% (1 of 30) in the TG group. Reflux esophagitis was significantly more common with 1/3B1 than with the 1/3RY and TG procedures (P = 0.0098 and 0.0027, respectively). The incidence of remnant gastritis on endoscopic examination was 46.7% (14 of 30) in the 1/3B1 group, 10.0% (3 of 30) in the 1/3RY group and 13.3% (2 of 15) in the 1/5RY group; the incidence was significantly higher with 1/3B1 than with 1/3RY and 1/5RY (P = 0.0016 and 0.0277, respectively).

DISCUSSION

For early gastric cancer patients, various kinds of function-preserving gastrectomies have been devised and performed. However, these operative procedures have rarely been adopted for advanced gastric cancer patients, and there have been few detailed investigations of the reconstructions reported so far (13, 14). Detailed investigations of reconstruction following distal gastrectomy for advanced gastric cancer should focus.
on the common procedures. In Japan, B1 and Billroth II (B2) have been commonly used as reconstructions for advanced gastric cancer (15). In B2 reconstruction, the passage of meal intake is unphysiological, with detouring around the duodenum, and the incidence of bile reflux to the remnant stomach or esophagus is higher (16). In Japan, B1 accounts for the highest number of reconstructions following distal gastrectomy. B1 reconstruction is very simple, because there is only one anastomosis, with physiological passage through the duodenum, and the pancreato-biliary system can be easily checked postoperatively. On the other hand, the regurgitation of intestinal fluid (bile or pancreatic juice) toward the oral side occurs easily, caused by the resection of the pyloric ring and the increased tension between the stomach and duodenum when the remnant stomach is small (17). In addition, pancreatic juice often has a negative effect on the anastomosis when a pancreatic fistula occurs. It is said that the reconstruction that has the opposite advantages and disadvantages is RY. Namely, RY has three anastomoses, has unphysiological meal passage, and it is difficult to survey the pancreato-biliary system postoperatively (18). On the other hand, anastomotic insufficiency (13) and regurgitation of intestinal fluid occur rarely. Recently, the number of institutes using RY reconstruction has been increasing. This increase has resulted in changes in the prevalence of mechanical suture or anastomosis (12,13). Furthermore, there is little evidence on the nutritional disadvantages due to the detour of the meal around the duodenum (19,20), and the pancreato-biliary system can be easily investigated owing to the mechanical and technological progress in diagnosis (21).

Since the introduction of laparoscopic gastrectomy at our unit, we have been performing intra-corporeal RY reconstruction when the remnant is small. In RY, the gastrojejunostomy can be performed without any tension even when the remnant stomach is small, and the anastomoses are distant from any potential pancreatic fistula-related collections that may derive from extensive lymph node dissection (17). Since the

<table>
<thead>
<tr>
<th>Table 2. Characteristics of patients by type of reconstruction</th>
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<tbody>
<tr>
<td>1/3B1</td>
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<td>-------</td>
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<tr>
<td>Age (year)</td>
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<tr>
<td>Sex (male:female)</td>
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<tr>
<td>Stage</td>
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<tr>
<td>I</td>
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<td>II</td>
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<td>III</td>
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<tr>
<td>IV</td>
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<tr>
<td>Administration of anticancer drug (case)</td>
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</table>

\textsuperscript{a}The rate of anticancer drug administration is significantly lower in the 1/3B1 group than in the 1/3RY group (P < 0.001).
\textsuperscript{b}The rate of anticancer drug administration is significantly lower in the 1/3B1 group than in the 1/5RY group (P < 0.001).
\textsuperscript{c}The rate of anticancer drug administration is significantly higher in the 1/3RY group than in the TG group (P < 0.01).
introduction of laparoscopic surgery, we have been performing laparoscopic gastrectomy for early gastric cancer. Because patients who underwent RY reconstruction had a good postoperative course, RY has been introduced for advanced gastric cancer patients. However, there have been few reports on detailed functional investigations of the reconstructions so far. Thus, we investigated the functional outcomes after RY and compared them with those after B1 and total gastrectomy with RY reconstruction. According to the size of the remnant stomach, patients after RY reconstruction were divided into two groups (1/3 RY group and 1/5RY group), limited to the antecolic route. It was found that the 1/3RY and 1/3B1 procedures were significantly superior to the 1/5RY and TG procedures in terms of body weight and meal intake. The emptying test using acetaminophen concentration demonstrated the same tendency. Furthermore, there were no significant differences in gastric emptying between peristaltic and anti-peristaltic gastrojejunostomies in the same size of remnant stomach groups, though the sample size was small. Namely, postoperative functional outcomes were not influenced by the manner of reconstruction, but by the size of the remnant stomach. However, there was no relationship between the occurrence of dumping symptoms in 1/5RY and TG, which showed marked increases in acetaminophen concentration, irrespective of the amount of chemotherapy. This result was thought to be due to the regulation of

Figure 2. Postoperative/preoperative body weight ratios (%).

Figure 3. Postoperative/preoperative meal intake ratios (%).
the manner of meal intake by each patient to decrease the occurrence of dumping symptoms. On the other hand, if patients who underwent RY reconstruction with a small remnant stomach had meal intake within a short time, they would suffer from a similar condition of rapid emptying of the meal as with TG. These results indicate that it is essential for patients to have enough of an explanation about dumping syndrome and adequate instruction to prevent it. Furthermore, if a greater lymph node dissection is needed, TG should be carried out, because RY cases with a small remnant stomach will have almost the same QOL as those with TG.

Given the differences between the peristaltic and anti-peristaltic gastrojejunostomies, further investigations will be needed due to the small sample size.

Since administration of S-1 is performed within 12 months in our institute, its administration was almost completed and its effect was less at the time of questionnaire completion. In the functional study, three patients in the 1/3RY group and one patient in the 1/5RY group received chemotherapy; the absorption of acetaminophen from the small intestine is thought to be less affected by S-1 administration, but there was no evidence for this in the present study.

There is a potential weakness in the present study, in that internationally recognized questionnaires were not used to evaluate the patient-reported outcomes. The patients were evaluated with the format shown in Table 1 at this time since the established instruments are not necessarily focused on specific postgastrectomy symptoms such as the dumping syndromes that we often encounter, and they may not be sufficiently sensitive to detect subtle differences caused by small differences in the mode of reconstruction.

On the upper esophagogastric endoscopic findings, the occurrence of esophagitis and remnant gastritis was significantly less in RY than in B1, irrespective of the size of the remnant stomach. Fukuhara et al. (16) reported that RY is superior to
either B1 or B2 reconstruction for preventing bile reflux into the gastric remnant and esophagus after open distal gastrectomy, based on the analysis of 92 patients who underwent curative distal gastrectomy. Kojima et al. (20) reported that endoscopic findings showed that the incidence of remnant gastritis was significantly lower in the RY group than in the B1 group after laparoscopic distal gastrectomy based on their analyses of 133 patients who underwent curative distal gastrectomy. Tanigawa et al. (22) reported that the comparisons between B2 and B1 were performed among 887 newly developed remnant cancer patients 10 years after the first operation for primary gastric cancer. The occurrences of remnant cancer were seen at the anastomotic site of B2 reconstruction. In B2, the bile juice returns to the remnant stomach easily, and the anastomotic site can be affected by the bile juice, and this is supposed to be a common site of remnant gastric cancer. Therefore, RY reconstruction might have depressive effects on the development of cancer in the remnant stomach. It might also be better for patients with esophageal hiatal hernia not to perform B1 reconstruction in order to prevent reflux esophagitis. On the other hand, RY has had some problems, including Roux stasis syndrome and Petersen’s internal hernia (23). Petersen’s hernia cases were not seen in the present study, but two cases that were thought to be Roux stasis syndrome were seen in the 1/3RY group. Nausea and an abdominal fullness sensation were reported, but they disappeared between 1 and 2 months later with conservative therapy, such as fasting.

In our previous experience, RY with a large remnant stomach was often associated with early postoperative gastric stasis. The ‘Roux stasis syndrome’ that reportedly occurs in ~30% of patients who undergo this mode of reconstruction (24) has been attributed to a disturbance of jejunal peristalsis (25). This observation may be important when considering stasis from RY with large remnants, where gastric emptying occurs predominantly by gravity. When the remnant stomach is filled with food, it is apt to descend below the antecolic gastrojejunosotomy, rendering gastric emptying through gravity difficult in a sitting position. Weakness in the peristalsis of the jejunum immediately aboral to the anastomosis would further hinder adequate food passage, while the stasis improved as time passed and disappeared gradually. On the other hand, Fujita et al. (13) analyzed 701 patients who underwent standard distal gastrectomy (defined as resection of more than 2/3 of the stomach) with RY reconstruction by open surgery, and they reported that delayed gastric emptying occurred in only 14 (1.9%) patients. The present results also suggest that gastric emptying is unlikely to be a problem when the gastric remnant is small. Because we focused on patients more than 12 months after surgery, no cases with Roux stasis syndrome were seen at the time of investigation.

In summary, several researchers have reported similar results so far, and the present results confirmed their conclusions that each reconstruction has specific advantages or disadvantages. A functional study using acetaminophen as an objective evaluation, body weight as a nutritional evaluation and meal intake by questionnaire as a subjective evaluation were most affected by the size of the remnant stomach. Postoperative functional outcomes were not affected by the manner of reconstruction, but by the size of the remnant stomach. Further randomized clinical trials between B1 and RY with a uniform size of the remnant stomach will be needed in order to verify these functions in detail.

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Conflict of interest statement
None declared.

References


