

• RAPID COMMUNICATION •

## Treatment for isolated loco-regional recurrence of gastric adenocarcinoma: Does surgery play a role?

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### Abstract

**AIM:** To evaluate the role of surgical treatment for isolated loco-regional recurrences of operated gastric adenocarcinoma.

**METHODS:** Among the 837 patients operated for gastric adenocarcinoma between December 1979 and April 2004, 713 (85%) underwent resection with curative intent. A retrospective review of a prospectively collected gastric cancer database was carried out. Overall recurrence rate was 44% (315 cases), with 75% occurring within the first 2 years from the operation. Isolated L-R recurrences were observed in 38 (12%) patients. Symptomatic lesions were observed in 27 (71%).

**RESULTS:** Six (16%) patients were macroscopically resected with curative intent. The recurrence was located in the gastric stump after a STG in three patients, in the esophagojejunal anastomosis after a TG in two patients and in the gastric bed after a TG in one patient. Surgical procedures consisted of three secondary TG, two esophagojejunal resection and one excision of an extraluminal recurrence. Postoperative complications occurred in two patients (33%), including one anastomotic leakage and one hemorrhage. The latter patient died of sepsis 35 d after the surgery (mortality rate 17%). All patients died of recurrent gastric cancer: 2 within 1 year from surgery (8 and 11 mo, respectively), 2 after 16 and 17 mo respectively and 1 after 28 mo from the second operation.

**CONCLUSION:** Surgery plays a very limited role in the treatment for isolated loco-regional recurrence of gastric adenocarcinoma.

### INTRODUCTION

Despite the decreasing overall incidence, gastric adenocarcinoma is still one of the most common causes of death for cancer worldwide. Even after curative gastrectomy, disease recurrence occurs in 22-50% of patients, mostly within two years from the operation<sup>[1-5]</sup>.

Loco-regional (L-R) recurrence results from lymphatic spread or direct tumor propagation within the abdominal cavity<sup>[6]</sup>. Several series tried to clarify the relationship between clinicopathologic features of the primary tumor and failure patterns<sup>[1-5,7-11]</sup>. In any case, effective therapies are lacking and surgical resection is only rarely possible.

The aim of this study was to retrospectively analyze our experience with the surgical treatment of L-R recurrence in patients operated for gastric cancer.

### MATERIALS AND METHODS

Out of the 905 patients submitted to gastric resections between December 1979 and April 2004, 837 with adenocarcinoma were entered and followed in a prospectively recorded database. Among these, 713 (85%) underwent resection with curative intent, consisting of 392 total gastrectomies (TG) and 321 proximal or subtotal distal gastrectomies (STG). Standard D2 lymph node dissection was performed in most patients, with D3 dissection performed for curative intent in selected cases. Pathologic stage distribution, according to the 1997 TNM classification<sup>[12]</sup>, included stages IA (11%), IB (13%), II (14%), IIIA (15%), IIIB (16%), and IV (31%). All stages up to IV were due to N category or T4 classification in the presence of positive nodes. The most common histological type was intestinal (53%), according to Lauren's criteria.

All patients were included in a prospectively collected database. Follow-up examinations were performed 1 mo

**Table 1** Resected patients' background at the time of the primary operation

Sex	Age	Staging	Operation	Adjuvant therapy	Histology	Tumor-free interval (mo)
1 M	72	T3N2M0	STG	CHT	Diffuse	9
2 F	60	T3N0M0	STG	-	Diffuse	21
3 M	49	T3N2M0	STG	CHT	Intestinal	12
4 M	63	T3N2M0	TG	CHT	Diffuse	16
5 M	66	T4N1M0	TG	CHT	Diffuse	24
6 F	58	T2N1M0	TG	-	Intestinal	50

after the surgery, once in every 3 mo during the first 2 years, every 6 mo for the first 5 years and yearly thereafter. Follow-up program included physical examination, laboratory analysis including serum tumor markers (CEA, CA 19-9, and CA 72-4) at each visit, abdominal ultrasound or computed tomography (CT) and chest radiograph every 6 mo and endoscopy once a year. Follow-up information was regularly obtained from outpatient clinical visits, from the time of surgery to May 2004 or until death. Median follow-up was 13 mo (range 1 mo to 163 mo).

Recurrences were classified according to the definition of Lenhart *et al*<sup>[6]</sup> as distant metastasis and L-R recurrences, including local lymph nodes metastasis, extraluminal recurrence, recurrence within the gastric remnant after STG and esophagojejunal anastomosis recurrence after TG.

Overall recurrence rate was 44% (315 cases), with 75% occurring within the first 2 years from the operation. Disease recurrence was rare after 5 years (5%). Isolated L-R recurrences were observed in 38 (12%) patients, while distant metastasis only in 167 (53%) and combined in the remaining 110 (35%). Symptomatic lesions were observed in 27 (71%), mostly including upper digestive obstruction and pain. In the asymptomatic patients, the recurrence was incidentally discovered during routine follow-up, most commonly by CT scan and occasionally by endoscopy or tumor markers elevation.

## RESULTS

Six (16%) patients were macroscopically resected with curative intent, representing 4% only of all observed L-R recurrences. The other 32 patients underwent conservative treatment in 25 cases (66%), laparotomy only in five cases (13%) and by-pass procedure in two cases (5%). Resected patients' background at the time of the primary operation is shown in Table 1. Mean tumor-free interval was 22 mo.

The recurrence was located in the gastric stump after a STG in three patients, in the esophagojejunal anastomosis after a TG in two patients and in the gastric bed after a TG in one patient. Surgical procedures consisted of three secondary TG, two esophagojejunal resection and one excision of an extraluminal recurrence. Postoperative complications occurred in two patients (33%), including one anastomotic leakage and one hemorrhage. The latter patient died of sepsis 35 d after the surgery (mortality rate 17%). Three patients received adjuvant chemotherapy (CHT) after the second operation, in two combined with

**Table 2** Clinical course in resected cases

Case	Recurrent site	Operation	Adjuvant therapy	Survival (mon)	Recurrence
1	Gastric stump	TG-liver segmentectomy	-	16	Distant
2	Gastric stump	TG-splenectomy	CHT+IORT	28	Distant
3	Gastric stump	TG-liver segmentectomy	CHT+IORT	17	Combined
4	Esophagojejunal anastomosis	Resection	-	1	-
5	Esophagojejunal anastomosis	Resection	-	8	Combined
6	Gastric bed	Excision	CHT	11	Loco-regional

intraoperative radiation therapy (IORT). Clinical course of the resected cases is described in Table 2.

All patients died of recurrent gastric cancer: 2 within 1 year from surgery (8 and 11 mo, respectively), 2 after 16 and 17 mo respectively and 1 after 28 mo from the second operation (Table 2). Mean survival of the palliated or non-resected patients was 8 mo.

## DISCUSSION

Despite considerable improvement in the surgical treatment of gastric adenocarcinoma, recurrences still constitute the main cause of death in operated patients. Recent series showed overall incidence rates of 22-50% after curative surgery, mostly (75-80%) occurring within 2 years<sup>[1-5,7-11]</sup>. Our 44% recurrence rate is probably due to the high incidence (62%) of advanced operated gastric cancer cases, as for most Western experience. Moreover, our results confirm that recurrences beyond 5 years are rare (3-9%)<sup>[1,4,5,10,13]</sup>. Median survival from the time of recurrence is approximately 6 mo<sup>[1,2,7,10,13]</sup>.

Gastric cancer recurrence include: L-R recurrence (regional lymph nodes, perianastomotic region, gastric bed, and stump), peritoneal recurrence and hematogenous metastasis (liver, lungs, bones, brain, and skin)<sup>[2,3,5,7-11]</sup>. As confirmed by our experience, combined recurrences are frequently observed and hematogenous or lymphatic spread without intra-abdominal metastases occur rarely<sup>[2,6-8]</sup>. An isolated L-R recurrence is reported in 6-46% of patients<sup>[1-3,7,8,10,11,13]</sup> and they were 12% in our series. Such differences may be explained by variations in the presentation of data, the definition of recurrence, as well as the mode and timing of detection<sup>[6,7,10,11]</sup>.

Clinicopathologic features of the primary tumor that predict L-R recurrences are: proximal location, older age and male gender, advanced stage of disease (T3-4, N+), infiltrative growth, diffuse type and stromal reaction<sup>[2,5,7-11]</sup>. Although not statistically significant, almost all our cases were males, with advanced age (median 61 years), T4 N+ and diffuse type. Even though advanced stage of the disease is a common risk factor, early gastric cancer (EGC) may relapse in 1.4-6.4% of patients, mostly being hematogenous metastasis, but in approximately 20% of cases, L-R recurrences<sup>[2,14]</sup>.

Diagnosis is improved with modern imaging and

mainly suggested by tumor markers elevation, endoscopy, and CT scan. As occurred in our experience, most patients are symptomatic and diagnosis is earlier in such cases<sup>[10,13]</sup>. Since early detection of recurrence do not improve overall survival of patients; however, according to some authors, until the development of a more effective treatment, routine follow-up is not indicated and should be reserved for symptomatic patients and to provide psychological support<sup>[1,13,15]</sup>.

Some retrospective and small series showed the usefulness of CEA, CA 19-9 and CA 72-4 monitoring in detecting the recurrence of operated gastric cancer<sup>[16,17]</sup>. However, their elevation is often seen much later than detection of recurrence by imaging, especially in patients with low preoperative levels.

Endoscopic surveillance is the most accurate method to identify anastomotic or gastric stump recurrences after STG, allowing early diagnosis and radical treatment in highly selected cases<sup>[18]</sup>, as it occurred for one patient of our series. Helical CT scan is the most commonly employed diagnostic tool in such cases, but its sensitivity is very low because of the limit in differentiating recurrent tumor from postoperative fibrotic and inflammatory changes<sup>[1,19,20]</sup>.

Once the diagnosis of L-R recurrence has been made, curative surgical resection is only rarely possible. Available data in the literature do not allow a valid interpretation with respect to the different types of recurrence<sup>[6]</sup>. Excluding anecdotal cases of local lymph nodes or extraluminal recurrence excision<sup>[21-23]</sup>, it appears that a curative resection is possible when a partial gastrectomy was previously performed. Approximately 20% of patients undergo surgical resection but in 2-6% only it may be considered curative, with a mean survival lower than 2 years<sup>[1,2,6,13,17,21]</sup>. In our series, the resection rate was extremely low. In fact, considering the 38 patients with isolated L-R recurrence, only six (16%) were resected. The remaining group was excluded from surgery mostly because the recurrences were not considered amenable to a curative resection or to the poor general condition. According to some authors, adjuvant chemoradiotherapy has a potential effect on improving prognosis<sup>[6,21,23]</sup>.

Palliative resections are indicated in highly selected symptomatic patient, mainly to restore the food passage, while tumor reduction is of minor importance<sup>[2,6]</sup>. In those with poor general conditions and a short life expectancy, placement of covered expandable metallic stents is technically feasible and clinically effective<sup>[24,25]</sup>.

In conclusion, surgery plays a very limited role in the treatment for isolated L-R recurrences of gastric cancer. In low-risk patients, especially if symptomatic, an attempt at resection may be justified in specialized center with acceptable postoperative mortality and morbidity, as there are no effective alternative therapies. At present, however, prevention or reduction of the frequency of recurrence, with more extended lymph nodal resection and the combination of perioperative adjuvant treatment<sup>[2,4,6,7,10,11]</sup>, seem more important than the early detection and surgical treatment.

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