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INCIDENCE, NATURAL HISTORY, AND PATTERNS OF LOCOREGIONAL RECURRENCE IN GASTRIC CANCER PATIENTS TREATED WITH PREOPERATIVE CHEMORADIATION

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Abstract

Purpose—To retrospectively determine the incidence and patterns (in-field, marginal, or out-of-field) of locoregional recurrence of gastric cancer in patients who received preoperative chemoradiotherapy and to determine the outcome in these patients.

Methods and Materials—Between 1994 and 2004, 149 patients with gastric carcinoma were treated on institutional protocols with preoperative chemoradiation. Ultimately, 105 patients had an R0 resection. Sixty-five of these patients received preoperative chemotherapy followed by chemoradiotherapy and 40 patients received preoperative chemoradiotherapy. Most (96%) of these patients received 5-fluorouracil-based chemotherapy during radiation, and the median dose of

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CONFLICTS OF INTEREST NOTIFICATION

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radiation administered was 45 Gy. We retrospectively identified and classified the patterns of locoregional recurrences.

Results—The 3-year actuarial incidence of locoregional recurrence was 13%, with locoregional disease recurring as any part of the failure pattern in 14 patients. The majority (64%) of evaluable locoregional recurrences were in-field. Two of the four patients with marginal recurrence had inadequate coverage of regional nodal volumes on their oblique fields. The pathologic complete response rate was 23%. A pathologic complete response was the only statistically significant predictor of locoregional control.

Conclusions—Patients with gastric cancer who received preoperative chemoradiotherapy had low rates of locoregional recurrence. This strategy merits prospective multi-institutional and randomized evaluation.

Keywords

Locoregional recurrence; Patterns; Gastric cancer; Preoperative; Chemoradiation

INTRODUCTION

Several clinical follow-up, reoperation, and autopsy series, have shown a high rate of locoregional recurrence after surgical resection for gastric cancer.^{1,2,3} Various adjuvant treatment strategies have been used to address this risk. In a recent prospective randomized trial, postoperative chemoradiotherapy has been shown to improve locoregional control rate and overall survival time.⁴ However, many patients are unable to receive all of the planned postoperative therapy in a timely manner because of surgical complications or delayed postoperative recovery in performance and/or nutritional status.⁵

An alternative approach is preoperative chemoradiotherapy. This therapy has the potential advantage of ensuring that a greater proportion of patients receive all components of multimodality therapy and that those with rapidly progressive disease (assessed at restaging before surgery) can be spared the morbidity associated with major surgery. Chemoradiation may be more effective in the preoperative setting, due to the potential increased penetration of chemotherapeutic agents in tumors with intact vasculature, and the greater radiosensitivity of vascularized nonhypoxic tumors. In contrast to the difficulties encountered in trying to define accurate radiation fields in the postoperative setting, preoperative chemoradiotherapy allows more precise definition of tumor location, leading to more accurate and possibly smaller radiation fields. Another advantage of preoperative chemoradiotherapy is that it may increase the likelihood of an R0 resection and decrease the chance of peritoneal seeding at the time of surgery.

Over the past decade, more than 100 patients with gastric cancer have been treated at our institution using successive preoperative chemoradiotherapy protocols. The patterns of locoregional recurrence after surgical resection have been defined spatially and/or anatomically in prior series, making a compelling argument for locoregional radiotherapy in this disease. Hence, we herein report the experience on the patterns of locoregional recurrence after surgical resection in patients who have received preoperative

chemoradiotherapy within a large, multidisciplinary, tertiary care cancer center. We retrospectively reviewed the medical records of patients with gastric cancer who received preoperative chemoradiotherapy, with specific aims to: 1) identify the incidence and patterns of locoregional recurrences and 2) determine the outcomes in these patients, with particular emphasis on correlating these findings to the radiation fields used.

METHODS AND MATERIALS

Patient identification and selection

We identified 149 patients with gastric cancer who received preoperative chemoradiotherapy on institutional protocols between 1994 and 2004. One hundred and five patients had an R0 resection and were included in this analysis, as shown in Fig. 1. Eligible patients were at least 18 years old and had had biopsy-proven gastric adenocarcinoma clinically staged as at least T2 (American Joint Committee on Cancer TNM staging, 6th edition),⁶ or as node positive. All patients signed a study-specific consent form. Tumors that involved the gastroesophageal junction (GEJ) were included in this study if the bulk of the tumor was within the stomach rather than in the distal esophagus.

Patient characteristics

The baseline patient characteristics are shown in Table 1. Of the 105 patients included in our analysis, 81 (77.1%) had T3 disease and 52 (49.5%) had N1 disease on endoscopic ultrasonography. Twenty-four patients (22.9%) had a pathologic complete response to treatment. The median follow-up time was 35 months and the minimum follow-up time was 3 months.

Pretreatment evaluation

Pretreatment staging was based on a complete physical examination, computed tomography (CT) of the abdomen (and pelvis and chest when indicated), endoscopic ultrasonography (EUS), and laparoscopy. Patients with positive peritoneal washings in the absence of visible peritoneal disease were eligible in earlier institutional protocols.⁷

Treatment

Patients in this study underwent preoperative chemotherapy followed by chemoradiotherapy (n = 65) or preoperative chemoradiotherapy (n = 40) prior to surgery. For patients who initially received chemotherapy, a median of two cycles (range: one to five) were administered. Most patients received either 5-fluorouracil (5-FU), cisplatin, and paclitaxel (n = 33) or 5-FU, cisplatin, and leucovorin (n = 30). The schedule and doses for these regimens have been published elsewhere.^{8,9,10}

Typical radiation fields encompassed the stomach and regional lymph nodes employing a multiportal technique with customized blocking that included oblique or lateral fields. Thirty-five percent of patients were treated with use of three-dimensional conformal radiation planning. Radiation was delivered by 6–18-MV photons. The median radiation dose was 45 Gy (range: 9–45 Gy) delivered at 1.8 Gy per fraction. For patients who received electron beam intraoperative radiotherapy (IORT), the median dose was 10 Gy (range: 10–

15 Gy). During radiotherapy, patients received either a continuous infusion of 5-FU (300 mg/m²/day, usually starting on a Monday and ending on a Friday after radiotherapy), or the same regimen of 5-FU plus paclitaxel (45 mg/m² each Monday), or irinotecan each Monday (median 65 mg/m²; range: 30–70 mg/m²).

The type of surgery depended on the location and extent of the primary tumor. A luminal gastric margin of at least 5 cm was obtained when feasible. A spleen-preserving D2 type nodal dissection was recommended but not required. Thirty-one patients received electron beam IORT according to the specifications of earlier protocols.⁷ The mean dose was 10 Gy delivered to the gastric bed and para-aortic lymph nodes using a 7- to 8-cm cone prescribed to the 90% isodose line.

Analyses of the incidence and patterns of locoregional recurrence

We reviewed the patients' medical records and documented evidence of locoregional recurrence. A diagnostic radiologist (P.R.B.) reviewed the imaging studies showing locoregional recurrence and correlated the area of recurrence with bony landmarks. Local recurrences were defined as anastomotic or gastric remnant recurrences. Regional recurrences were defined as nodal recurrences in the porta hepatis, celiac axis, superior mesenteric artery/vein, para-aortic (from vertebral level T11 to L3), or gastrohepatic nodal regions. Mediastinal recurrences were considered locoregional in patients with GEJ tumors. Peritoneal recurrences were not considered locoregional. Two radiation oncologists (V.K.R. and S.K.) simultaneously reviewed the simulation films of the patients with locoregional recurrences and determined whether these recurrences were in-field, marginal, or out-of-field. In-field recurrences were those at least 2 cm within the field border, marginal recurrences included those within 2 cm of the field border (inside or outside), and out-of-field recurrences included those more than 2 cm outside of the field border.

Statistical analyses

The time to locoregional recurrence and overall survival time were calculated from the date of first treatment. Dates of locoregional failure were determined using imaging studies, primarily abdominopelvic CT scans. The frequency of post-treatment follow-up CT scans likely varied over time, such that the time to locoregional recurrence for a given patient may be dependent on this inconsistency. Survival probabilities were estimated using Kaplan-Meier's product limit method, and groups were compared using a log-rank test.^{11,12} All tests were two-sided, and a *p* value of 0.05 was considered statistically significant.

RESULTS

Actuarial incidence of locoregional recurrence

The 3-year actuarial incidence of locoregional recurrence was 13%, with 14 patients having locoregional recurrence as any part of their failure (Fig. 2). Twelve patients had a locoregional recurrence as a component of their first recurrence. Four patients had isolated locoregional recurrence as their first site of recurrence, but two of these four patients eventually failed elsewhere. There were no statistically significant differences between locoregional recurrence and tumor stage, nodal stage, IORT status, use of taxane-based

chemotherapy, or treatment sequence (Table 2). The effect of radiation dose on locoregional recurrence rates could not be evaluated because most patients had received an external beam radiation dose of 45 Gy. A pathologic complete response was the only statistically significant predictor for decreased locoregional recurrence rates ($p = 0.02$). Taxane-based chemotherapy did not predict for pathologic complete response (data not shown). The 3-year actuarial incidence of overall survival was 65%, respectively (Fig. 3).

Patterns of locoregional recurrence

Twelve patients with 14 locoregional recurrences had both diagnostic radiologic and simulation films available for review. CT films were not available for one patient with a GEJ tumor, but a CT report for that patient described enlarged retroperitoneal and mediastinal nodes. Another patient had had a peripancreatic nodal recurrence confirmed by our diagnostic radiologist, but the simulation films were not available. We coded both patients as having had a locoregional recurrence, but the relationship between the recurrence and the radiation field for these patients could not be determined.

Table 3 and Fig. 4 show the correlation between recurrence sites and the radiation field. Three patients had a recurrence in the anastomosis, and 11 patients had nodal recurrences. One patient with a proximal tumor had had a recurrence in the gastric remnant after undergoing an esophago-proximal gastrectomy at another institution. Most of the evaluable recurrences (9 of 14; 64%) were defined as in-field. Of the 38 patients with GEJ locations, one had a marginal mediastinal recurrence.

Outcomes of patients with locoregional recurrence

The median time to locoregional recurrence was 16 months (range: 5–61 months). The median overall survival time after locoregional recurrence was 5 months (range: 0.2–82 months).

Three patients with anastomotic recurrences underwent reoperations for these recurrences. One died 9 months after surgery of unknown cause. Another had had a long disease-free interval but had developed mediastinal and peritoneal disease 6 years after the reoperation. The third developed a second anastomotic recurrence nearly 2 years after the reoperation for the first anastomotic recurrence; during surgery for the second anastomotic recurrence, peritoneal disease had been discovered.

One patient had undergone a reoperation for a nodal recurrence but died 6 weeks later of multiple-organ system failure from sepsis.

DISCUSSION

This study systematically analyzes the incidence and patterns of locoregional recurrence after preoperative chemoradiotherapy for gastric cancer. Studies outlining the patterns of failure after surgery for gastric cancer have shown a high rate of locoregional recurrence after surgical resection for gastric cancer.^{1,2,3} In the University of Minnesota reoperation series of 86 patients, 87.8% of patients were found to have a locoregional recurrence (including isolated peritoneal recurrence).² In the Massachusetts General Hospital series, the

locoregional recurrence rate was 38% in 130 patients who had undergone curative resection.¹ Furthermore, an autopsy series demonstrated an 80.4% locoregional recurrence rate in 92 patients after curative subtotal gastrectomy.³ The high rates of recurrence have been attributed to the abundant lymphatic channels within the gastric wall, providing channels for mucosal skip lesions and numerous potential pathways of lymphatic drainage away from the stomach. The 13% actuarial incidence of any locoregional recurrence at 3 years in the current study compares favorably with that of previous series of surgery alone. However, given that these series date back many years, the relative contributions of improved preoperative staging, near-uniform D2 node dissection, and preoperative chemoradiotherapy to the favorable local control observed in these patients cannot be determined. In a more recent series of 2038 patients treated with surgery alone, 25% developed recurrences, a third of which were locoregional.¹³ While these patients underwent modern surgical resections with extended lymphadenectomies, they did not receive adjuvant therapy. In a similar analysis of 1172 patients with gastric cancer who underwent resection with modern surgical techniques with/without adjuvant therapy, the first site of failure was locoregional in 17% of patients.¹⁴ The authors did not analyze the impact of adjuvant therapy on the patterns of failure since patients received heterogeneous treatments in an inconsistent manner.

To analyze the relative influence of adjuvant therapy on locoregional recurrence patterns following surgery, the Intergroup 0116 study reported local and regional recurrence information after surgery alone and after surgery with postoperative chemoradiotherapy. In this study, local recurrence occurred in 19% of the patients in the postoperative chemoradiotherapy arm compared to 29% in the surgery alone arm, and this improved local control appeared to contribute to the 10% improvement in overall survival rate at 3 years in the arm that received postoperative chemoradiotherapy. In contrast to the Intergroup study which reported only the first sites of recurrence, the local recurrence rate of 4% in the current study reflects all local recurrences (three anastomosis recurrences and one gastric remnant recurrence). Furthermore, regional recurrence rates were defined differently in INT 0116 and recurrences in the liver, intra-abdominal lymph nodes, and peritoneum were considered regional failures. Thus, we were unable to compare the regional recurrence reported in the current study to INT 0116.

There were some possible biases in our study. First, 41 enrolled patients had received preoperative therapy but had not undergone surgery or an R0 resection, usually because of progressive disease found during treatment. This could have led to our inclusion of patients with more favorable prognoses in this study, relative to the patient populations in other series examining patterns of postoperative recurrence of disease. Also, although the patients had been monitored prospectively according to institutional protocols, we determined the patterns of recurrence retrospectively through medical record review, which could have resulted in an underestimation of locoregional recurrence. There were also some limitations to our study. Since most patients had received an external beam radiotherapy dose of 45 Gy, the effect of radiotherapy dose on locoregional recurrence rates could not be evaluated. Similarly, because of our small sample size, we were unable to draw firm conclusions about the use of IORT.

Three important issues are worth noting in the current study. First, the rates of locoregional recurrence (as the first site of failure and/or as any site of failure) were low and compare favorably with those of other series. In our series, 105 (95%) of the 110 patients who underwent surgery had an R0 resection. This rate of R0 resections is comparable to that of other series.^{15, 16, 17} While it is generally believed that postoperative chemoradiotherapy may not improve overall survival after margin-positive resections, the relative contribution of preoperative chemoradiotherapy to the observed low R0 resection rate remains to be defined.¹⁷ Second, in the current study, pathologic complete response was the only statistically significant predictor of locoregional control. This correlation between pathologic complete response and lower locoregional recurrence rate is noteworthy because chemoradiotherapy may result in higher rates of pathologic complete response than chemotherapy alone. For instance, there were no pathologic complete responses noted among the patients randomized to receive perioperative chemotherapy (epirubicin, cisplatin, and fluorouracil) in the Medical Research Council Adjuvant Gastric Infusional Chemotherapy (MAGIC) trial.¹⁸ In our own experience, the pathologic complete response rate of merely 4% with neoadjuvant chemotherapy alone⁷ led to the incorporation of radiotherapy into neoadjuvant regimens. Furthermore, a pathologic complete response predicted for overall survival and provides a simple surrogate measurement of prognosis until molecular techniques become available.⁸ Therefore, we believe this pathologic complete response rate of 22.9%, which predicts for improved locoregional control, is clinically relevant. Third, the low rate of marginal recurrence is noteworthy because this is likely due to the relative ease of designing radiation fields for intact tumors, which can be readily visualized, minimizing the possibility of geographic misses. Despite this relative ease of field-design, of the four patients who had marginal recurrences, two were within the anteroposterior fields but outside the oblique fields, which did not have enough anterior coverage. This relationship between marginal failures and oblique radiation beams suggests that careful contouring of the regional nodal regions at risk may be an important component of three-dimensional planning. Regarding the one patient who had a marginal mediastinal recurrence, the treatment field had adequate cranial mucosal coverage of the distal esophagus (at least 5 cm). On the basis of only this one patient, we do not recommend increasing the treatment field to cover the mediastinum in all patients with GEJ carcinomas because this could greatly increase treatment toxicity. Two of the three patients with anastomotic recurrences had close surgical margins at the time of resection. One of these patients had had a 7-mm proximal margin. The other had had foci of carcinoma in close proximity to the distal margin. Since the pathologic margin status was not routinely reported in all patients, we were unable to determine a relationship between locoregional recurrence and margin size. However, two patients had atypical cells at either the proximal or distal resection margin, and both of these patients had no evidence of recurrent disease at four and six years after surgery.

The ideal adjuvant or neoadjuvant strategy for gastric cancers is yet to be defined. Until randomized trials are performed comparing preoperative chemoradiotherapy with perioperative chemotherapy and postoperative chemoradiotherapy, preoperative chemoradiotherapy will remain one of several potential investigational strategies for patients with higher risk localized gastric cancer. Despite the theoretical advantages of preoperative

chemoradiotherapy discussed above, the majority of locoregional failures (64%) were in-field. Given that further dose escalation using external beam radiotherapy is constrained by gastrointestinal mucosal tolerance and the tolerance of surrounding structures, further reduction in locoregional recurrence may require the use of novel radiosensitizing strategies. The impact of the incorporation of novel radiosensitizers to increase the therapeutic ratio would be best evaluated in trials designed for the highest risk patients.

CONCLUSION

Preoperative chemoradiotherapy resulted in a 3-year actuarial locoregional control rate of 87%, which compares favorably with those of other series. A pathologic complete response was the only statistically significant predictor of locoregional control. Despite the low rate of marginal recurrences after preoperative chemoradiotherapy, careful contouring of the regional nodal regions at risk using three-dimensional planning may permit improved target-coverage. Multidisciplinary coordination of preoperative chemoradiotherapy is feasible and is associated with good pathologic complete response rates, locoregional control rates, and overall survival rates. This strategy merits prospective multi-institutional and randomized evaluation.

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REFERENCES

- Landry J, Tepper JE, Wood WC, et al. Patterns of failure following curative resection of gastric carcinoma. *Int J Radiat Oncol Biol Phys*. 1990; 19:1357–1362. [PubMed: 2262358]
- Gunderson LL, Sosin H. Adenocarcinoma of the stomach: areas of failure in a re-operation series (second or symptomatic look) clinicopathologic correlation and implications for adjuvant therapy. *Int J Radiat Oncol Biol Phys*. 1982; 8:1–11. [PubMed: 7061243]
- McNeer G VH, Dong FY, et al. A critical evaluation of subtotal gastrectomy for the cure of cancer of the stomach. *Ann Surg*. 1957; 134:2–7. [PubMed: 14838535]
- Macdonald JS, Smalley SR, Benedetti J, et al. Chemoradiotherapy after surgery compared with surgery alone for adenocarcinoma of the stomach or gastroesophageal junction. *N Engl J Med*. 2001; 345:725–730. [PubMed: 11547741]
- Allum WH, Hallissey MT, Ward LC, et al. A controlled, prospective, randomised trial of adjuvant chemotherapy or radiotherapy in resectable gastric cancer: interim report. *British Stomach Cancer Group. Br J Cancer*. 1989; 60:739–744. [PubMed: 2508737]
- Green FL, PD.; Fleming, ID., et al. *AJCC Cancer Staging Manual*. Springer-Verlag; New York: 2002.
- Lowy AM, Feig BW, Janjan N, et al. A pilot study of preoperative chemoradiotherapy for resectable gastric cancer. *Ann Surg Oncol*. 2001; 8:519–524. [PubMed: 11456051]
- Ajani JA, Mansfield PF, Crane CH, et al. Paclitaxel-based chemoradiotherapy in localized gastric carcinoma: degree of pathologic response and not clinical parameters dictated patient outcome. *J Clin Oncol*. 2005; 23:1237–1244. [PubMed: 15718321]
- Ajani JA, Mansfield PF, Janjan N, et al. Multi-institutional trial of preoperative chemoradiotherapy in patients with potentially resectable gastric carcinoma. *J Clin Oncol*. 2004; 22:2774–2780. [PubMed: 15254045]

10. Ajani JA, Winter K, Okawara GS, et al. Phase II trial of preoperative chemoradiation in patients with localized gastric adenocarcinoma (RTOG 9904): quality of combined modality therapy and pathologic response. *J Clin Oncol*. 2006; 24:3953–3958. [PubMed: 16921048]
11. Kaplan E MP. Non-parametric estimation for incomplete observations. *J Am Stat Ass*. 1958; 53:457–481.
12. Peto R PJ. Asymptotically efficient rank invariant procedures (with discussion). *J Royal Stat Soc*. 1972; 135:185–207.
13. Yoo CH, Noh SH, Shin DW, et al. Recurrence following curative resection for gastric carcinoma. *Br J Surg*. 2000; 87:236–242. [PubMed: 10671934]
14. D'Angelica M, Gonen M, Brennan MF, et al. Patterns of initial recurrence in completely resected gastric adenocarcinoma. *Ann Surg*. 2004; 240:808–816. [PubMed: 15492562]
15. Cunningham SC, Kamangar F, Kim MP, et al. Survival after gastric adenocarcinoma resection: eighteen-year experience at a single institution. *J Gastrointest Surg*. 2005; 9:718–725. [PubMed: 15862270]
16. Jahne J, Piso P, Meyer HJ. 1114 total gastrectomies in the surgical treatment of primary gastric adenocarcinoma--a 30-year single institution experience. *Hepatogastroenterology*. 2001; 48:1222–1226. [PubMed: 11677935]
17. Kim SH, Karpeh MS, Klimstra DS, et al. Effect of microscopic resection line disease on gastric cancer survival. *J Gastrointest Surg*. 1999; 3:24–33. [PubMed: 10457320]
18. Cunningham D, Allum WH, Stenning SP, et al. Perioperative chemotherapy versus surgery alone for resectable gastroesophageal cancer. *N Engl J Med*. 2006; 355:11–20. [PubMed: 16822992]

Fig. 1.
Flow of patients according to medical records.

Fig. 2.
Locoregional control in all patients.

Fig. 3.
Overall survival in all patients.

Fig. 4.
Location of locoregional recurrences. One patient with a mediastinal recurrence had involvement in three separate sites within the mediastinum.

Table 1

Patients' characteristics

Age, in years	
Median	59
Range	24-84
Gender	
Male	71 (67.6%)
Female	34 (32.4%)
Tumor location	
Body or antrum	52 (49.5%)
Gastroesophageal junction	38 (36.2%)
Cardia	11 (10.5%)
Linitis plastica	3 (2.9%)
Gastric remnant	1 (0.9%)
EUS T-stage	
T2	15 (14.3%)
T3	81 (77.1%)
T4	5 (4.8%)
TX	4 (3.8%)
EUS N-stage	
N0	46 (43.8%)
N1	52 (49.5%)
NX	7 (6.7%)
M-stage	
M0	103 (98.1%)
M1	2 (1.9%)
Pathology differentiation	
Well	1 (0.9%)
Moderate	31 (29.5%)
Poor	58 (55.2%)
Unknown	15 (14.3%)
Treatment sequence	
Preoperative chemotherapy, then chemoradiation	65 (61.9%)
Preoperative chemoradiation	40 (38.1%)
Taxane-based chemotherapy (neoadjuvant and/or concurrent)	42 (40.0%)
External beam radiation dose	
Median	45 Gy
Range	9-45 Gy
Intraoperative radiation therapy	31 (29.5%)
Type of surgery	

Total gastrectomy	51 (48.6%)
Distal subtotal gastrectomy	32 (30.5%)
Esophago-proximal gastrectomy	15 (14.3%)
Proximal subtotal gastrectomy	6 (5.7%)
Esophago-total gastrectomy	1 (0.9%)
Lymphadectomy	
Unknown	1 (0.9%)
D1	10 (9.5%)
D2	94 (89.5%)
Mediastinal	10 (9.5%)
Pathologic response	
Complete pathologic response	24 (22.9%)
No complete pathologic response	81 (77.1%)

Abbreviations: EUS = endoscopic ultrasonography.

Table 2

Actuarial 3-year locoregional recurrence-free survival according to patients' characteristics

Factor	No. of patients	3-yr LRR-free rate (%)	<i>p</i> value
Tumor stage			
T2	15	100	0.30
T3, T4, or TX	90	85	
Nodal stage			
N0	46	88	0.90
N1	52	87	
NX	7	86	
Pathologic response			
Complete response	24	100	0.02*
Less than complete response	81	83	
Use of taxane-based chemotherapy			
Yes	42	91%	0.41
No	63	84%	
Use of intraoperative radiotherapy			
IORT	31	96	0.15
No IORT	74	83	
Use of 3D conformal radiotherapy			
Yes	36	90	0.50
No	69	86	
Sequencing of therapy			
Chemoradiotherapy	40	87	0.63
Chemotherapy and then chemoradiotherapy	65	87	

Abbreviations: IORT = intraoperative radiotherapy; LRR = locoregional recurrence

* Statistically significant predictor of locoregional control.

Table 3

Correlation of the site of locoregional recurrence to the radiation field. Some patients had more than 1 recurrence.

<i>In-field</i>		<i>Marginal</i>		<i>Out-of-field</i>		<i>Cannot evaluate</i>	
Site	n	Site	n	Site	n	Site	n
Anastomosis	3	Mediastinal node	1	Mediastinal node	1	Retroperitoneal node	1
Celiac axis node	2	Para-aortic node	2			Peripancreatic node	1
Gastric remnant	1	Gastrohepatic node	1			Mediastinal node	1
Para-aortic node	1						
Portacaval node	1						
Superior mesenteric vein node	1						