Original article

Nodal abdominal spread in adenocarcinoma of the cardia. Results of a multicenter prospective study

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Abstract:

Background. Precise knowledge of the abdominal nodal spread of cardia adenocarcinoma in relation to the depth of invasion of the tumor and its longitudinal extension may be very important for the surgeon as a guide in choosing the type of resection and lymphadenectomy.

Methods. The frequency of node metastases in each abdominal station of the first and second tier was prospectively studied in 101 patients with type II and III cardia cancer (defined as approved by the consensus conference held during the second International Gastric Cancer Conference in Munich in April, 1997) who underwent total gastrectomy with D2 lymphadenectomy during the period January 1994 to April 1998. Lymph nodes were retrieved immediately after operation by the surgeon and assigned to the appropriate station according to the classification of the Japanese Research Society for Gastric Cancer.

Results. In early gastric cancer, of both type II and type III, lymph node involvement was limited to the perigastric nodes of the upper half of the stomach and to the lymph node station of the celiac trunk. In advanced cancers, whether of type II or type III, there was a fairly high frequency of metastases to the perigastric nodes of the lower half of the stomach; there was also high frequency of metastases at N2 stations, without differences in frequency between pT2 and pT3 tumors (staged according to the classification of the Japanese Research Society for Gastric Cancer).

Conclusions. The results of our study provide evidence for the need to perform a total gastrectomy with D2 lymphadenectomy in all patients with advanced cardia cancer type II or type III. In early cancers, a less extensive resection (proximal gastrectomy) with D2 lymphadenectomy may be indicated.

Key words: cardia cancer, lymph node metastasis, surgery, extended lymphadenectomy

Introduction

Recent studies reported in the literature have revealed that, despite the decreasing overall incidence of gastric cancer in Western countries, there has been an increase in adenocarcinomas localized in the proximal stomach, particularly at the level of the cardia [1–5].

There is a great deal of controversy regarding the definition, classification, and staging of this type of cancer [6,7]. Moreover, the extent of gastric and esophageal resection and the therapeutic value of extended lymphadenectomy are still much debated issues [8–12].

A thorough knowledge of the ways such tumors spread, both at organ and lymph node level, would undoubtedly be of great help as a guide to the surgeon in choosing the most appropriate type of resection and lymphadenectomy in these malignancies.

We therefore conducted a prospective multicenter study in order to assess the abdominal nodal spread of cardia adenocarcinoma in relation to the depth of invasion of the tumor and its longitudinal extension.

Patients and methods

Method

In this study, adenocarcinoma was defined according to the classification proposed by Siewert and recently approved during the consensus conference held during the second International Gastric Cancer Congress in Munich in April, 1997 [13].

Type I. Cardia adenocarcinoma extending to the esophagus with the center lying 1–5 cm above the anatomic esophago-gastric junction.

Type II. Cardia adenocarcinoma with the center lying 1 cm above to 2 cm below the anatomic esophago-gastric junction.

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Type III. Cardia adenocarcinoma extending to the stomach with the center lying 2–5 cm below the anatomic esophago-gastric junction.

Tumors were staged according to the classification of the Japanese Research Society for Gastric Cancer (JRS GC) [14], and the histologic classification was based on the Lauren criteria.

Perigastric lymph nodes (N1) were dissected from the excised specimens by the surgeons immediately after gastrectomy, assigned to the appropriate station according to the JRS GC classification, and sent for histologic examination. Among the lymph nodes on the greater curvature, those lying along the right gastro-epiploic artery were isolated from the lymph nodes of the upper half of the greater curvature (along the short vessels and the left gastro-epiploic artery).

To avoid errors due to difficulties in assigning the lymph nodes of the second compartment to the correct lymph node stations after en-bloc resection [15], the N2 nodes were subdivided by the surgeon during lymphadenectomy.

Patients

This prospective study included all patients suffering from type II or type III cardia adenocarcinoma who underwent total gastrectomy with distal esophagectomy, D2 abdominal lymphadenectomy (i.e. dissection of nodes in positions 1–11), and dissection at least of the lower mediastinal nodes, at the First Division of General Surgery, Verona University, at the Institute of Surgical Sciences, Siena University, and at the First Division of General Surgery, Forlì Hospital, Italy during the period January 1994 to April 1998.

Reconstruction was performed in all patients by means of an intrathoracic or transhiatal Roux-en-Y esophagojejunostomy.

A superextended lymphadenectomy (D4, dissection extended to nodes in positions 12–16) was performed in 15 patients with cardiac malignancies spreading to the stomach.

Patients with type I adenocarcinoma of the cardia ($n = 33$) were excluded from the study.

A total of 101 patients were recruited into the study (43 with type II and 58 with type III). The demographic data and tumor characteristics of these patients are summarized in Table 1.

Results

Seven patients died within the first 30 postoperative days (operative mortality rate, 6.9%) and 25 patients (24.7%) developed postoperative general and surgical complications, such as pneumonia, anastomotic leakage, pancreatic fistula.

Table 1. Main demographic and clinical characteristics of all 101 patients in our series who underwent total gastrectomy for cardia cancer between January 1994 and April 1998^a

	Type II ^b ($n = 43$) ^c	Type III ^b ($n = 58$) ^c
Mean age (years) (sd)	60 (11.7)	62 (11.2)
Sex		
Male	34	42
Female	9	16
Depth of invasion ^d		
pT1	12 (28)	4 (7)
pT2	13 (30)	20 (34)
pT3	16 (37)	23 (40)
pT4	2 (4)	11 (19)
Borrmann classification (advanced tumors)		
B I	6 (14)	16 (28)
B II	19 (44)	25 (43)
B III	6 (14)	11 (19)
B IV	0	2 (3)
Lauren classification		
Intestinal type	32 (75)	31 (53)
Diffuse type	7 (16)	20 (35)
Mixed type	4 (9)	7 (12)
Histological grading		
Well differentiated	4 (9)	4 (7)
Moderately differentiated	19 (44)	20 (35)
Poorly differentiated	16 (37)	22 (38)
Not classified	4 (9)	12 (20)

^aInstitutions in the series were: First Division of General Surgery, Verona University; Institute of Surgical Sciences, Siena University; and First Division of General Surgery, Forlì Hospital, Italy

^bSee text for definitions of type II and type III

^cValues in parentheses are percentages

^dStaged according to the classification of the Japanese Research Society for Gastric Cancer [14]

The total number of lymph nodes dissected in the 101 patients, was 3114. The mean number of nodes dissected per patient was 31.2 ± 14.7 (range, 10–108), and the mean number of metastatic nodes was 6.2 ± 6.7 (range, 0–39).

The frequency of lymph node involvement in relation to depth of tumor invasion is given in Table 2 for the pure cardiac tumors (type II) and in Table 3 for the subcardial tumors with invasion of the cardia (type III). As shown, there was a high frequency of patients with lymph node metastases in both types of malignancies (70% of patients with type II tumors and 83% of patients with type III tumors). The frequency of lymph node metastases in type II adenocarcinomas appeared to be very high right from stage pT1, whereas in type III pT1 tumors, the lymph node spread of the malignancies closely resembled that of early stomach cancers at other gastric sites.

No significant differences in frequency of lymph node metastases could be discerned between pT2 and pT3 tumors among either the type II or type III

adenocarcinomas. As postulated by Siewert et al. [16], in gastric tumors of the upper third of the stomach this may be because T2 tumors at this site involve the full thickness of the gastric wall in most instances, thus resembling T3 malignancies, despite there being no

Table 2. Frequency of lymph node metastases in relation to depth of tumor invasion in the 43 patients with type II adenocarcinoma of the cardia

	pN0 ^a	pN+ ^a	pN1 ^a	pN2 ^a
pT1 (<i>n</i> = 12)	8 (67)	4 (33)	3 (25)	1 (8)
pT2 (<i>n</i> = 13) ^b	2 (15)	11 (85)	5 (38)	6 (46)
pT3 (<i>n</i> = 16)	3 (19)	13 (81)	5 (31)	8 (50)
pT4 (<i>n</i> = 2)	0	2 (100)	0	2 (100)
Total	13 (30)	30 (70)	13 (30)	17 (40)

^a Values in parentheses are percentages

^b Patients with transmural growth and invasion of the subserosa or perivisceral fat

Table 3. Frequency of lymph node metastases in relation to depth of tumor invasion in 58 patients with type III adenocarcinoma of the cardia

	pN0 ^a	pN+ ^a	pN1 ^a	pN2 ^a
pT1 (<i>n</i> = 4)	4	0	0	0
pT2 (<i>n</i> = 20) ^b	3 (15)	17 (85)	9 (45)	8 (40)
pT3 (<i>n</i> = 23)	3 (13)	20 (87)	10 (43)	10 (43)
pT4 (<i>n</i> = 11)	0	11 (100)	3 (27)	8 (73)
Total	10 (17)	48 (83)	22 (38)	26 (45)

^a Values in parentheses are percentages

^b Four patients with invasion of the muscularis propria and 16 with transmural growth and invasion of the subserosa or perivisceral fat without perforation of the peritoneum

involvement of the tunica serosa, which, moreover, is present at cardiac level only on the anterior wall.

Below we provide detailed analysis of the tumor spread to the individual stations in relation to the type of malignancy examined.

Type II adenocarcinoma. The nodal spread of type II cardia adenocarcinoma to each abdominal lymph node station of the first and second tiers is shown in Fig. 1.

All the pT2 specimens analyzed showed infiltration of the subserosal layer or of the perivisceral fat; the only two pT4 specimens examined were included in the analysis of the pT3 group.

In the early tumors, the only lymph node stations affected by metastases were the left paracardial (8% of cases) and lesser curvature (17% of cases) stations in the N1 group and the celiac trunk station (13% of cases) in the N2 group.

In the pT2 tumors, in addition to a predictably high frequency of lymph node metastases affecting the perigastric nodes of the upper half of the stomach (right paracardial 50%, left paracardial 31%, lesser curvature 78%), also worthy of note is the presence of metastases affecting the lymph nodes along the right gastroepiploic artery (8% of cases) and the suprapyloric lymph nodes (13% of cases). There were, however, no metastases affecting the infrapyloric lymph nodes. In the N2 lymph node station group, on the other hand, there was a marked lack of metastases to the lymph nodes of the splenic hilus and artery.

In the pT3-pT4 carcinomas, practically all the perigastric stations were found to harbor metastases. Particularly important was the involvement of the lymph nodes of the right gastroepiploic artery (18% of cases) and of the infrapyloric lymph nodes (25% of cases), while metastases to the suprapyloric lymph

Fig. 1. Frequency of metastasis to each lymph node station in patients with type II adenocarcinoma of the cardia. White bars, pT1 tumors; gray bars, pT2 tumors; black bars, pT3-pT4 tumors. See text for definition of type II, pT and lymph node stations classified according to the Japanese Research Society for Gastric Cancer Criteria [14]

Fig 2. Frequency of metastasis to each lymph node station in patients with type III adenocarcinoma of the cardia. *White bars, pT2 tumors; gray bars, pT3 tumors; black bars, pT4 tumors.* See text for definition of type III

nodes were detected in 14% of cases. As regards the N2 stations, a substantial percentage of metastases affected the splenic hilus (20%) and artery (29%).

Type III adenocarcinoma. The nodal spread in type III adenocarcinomas is illustrated in Fig. 2.

No lymph node metastases were detected in pT1 tumors. The number of cases observed, however, was very small ($n = 4$), and the zero metastasis rate cannot therefore be regarded as a definitive finding, although it is, all the same, indicative of very limited nodal spread.

In the stage pT2 tumors, as far as the perivisceral stations were concerned, there was a high frequency of metastases to the lymph nodes along the right gastroepiploic artery (36%), with by no means negligible metastatic spread to the suprapyloric lymph nodes as well (9%). In the N2 group, we should stress the frequency of involvement of the hepatic artery (18%), accompanied, in one case out of six, by involvement of the lymph nodes along the anterior surface of the hepatoduodenal ligament (data not indicated in the graph). The para-aortic station harbored metastases in one of five pT2 patients who had D4 lymphadenectomy.

In the pT3 carcinomas, all the perigastric stations, with the sole exception of the suprapyloric station, were affected by metastases. In particular, the frequency of metastases was 31% in the right gastroepiploic artery station and 4% in the infrapyloric station. Also worthy of note is the presence, in the N2 group, of metastases affecting the splenic hilus (14% of cases).

In the six patients in whom a superextended D4 lymphadenectomy was performed, the hepatoduodenal ligament station was unaffected by metastases, whereas the para-aortic lymph nodes presented metastatic involvement in one patient.

In the pT4 tumors, too, the only perigastric station which was metastasis-free was the suprapyloric station, while metastases to the right gastroepiploic artery station were present in 36% of cases and to the infrapyloric lymph nodes in 10%. In the N2 group, there was a particularly high frequency of metastatic spread to the lymph nodes of the splenic hilus (50%). In the four patients who had D4 lymphadenectomy, the hepatoduodenal ligament station was positive in one and the para-aortic station was in two positive.

Discussion

The data reported in the literature regarding the spread of adenocarcinoma of the cardia are scanty and hard to compare, both because of the frequent pooling of squamous-cell carcinoma of the distal esophagus and cardia adenocarcinoma [17], and because of the lack of any overall consensus as to the definition and staging of the latter type of tumor [18]. Abdominal nodal spread in cancer of the cardia has been studied in a number of recent reports which, however, present no analysis of the involvement of the individual abdominal lymph node stations in relation to the pT stage and longitudinal extension of the tumors [18–21]. Precise knowledge of these data may be very important for the surgeon as a guide in choosing the type of resection and lymphadenectomy. This prospective multicenter study was undertaken, therefore, with the aim of collecting, within a short period of time, a sizeable number of patients in whom the abdominal nodal spread could be studied thoroughly for each regional lymph node station and related not only to the depth of tumor invasion

but also to the type of longitudinal extension, as described in the Siewert classification.

The main findings of the present study are:

- (1) in early malignancies, of both type II and type III, abdominal lymph node involvement is limited and confined to the perigastric lymph nodes of the upper half of the stomach (right paracardial and lesser curvature) and the lymph nodes of the celiac trunk.
- (2) In advanced adenocarcinomas, whether of type II or type III, we found a fairly high frequency of metastases to the perigastric stations of the lower half of the stomach (lymph nodes of the distal portion of the greater curvature, infrapyloric and suprapyloric lymph nodes). As regards the second-tier stations, the frequency of metastases, as also reported by other investigators, was high in both types of adenocarcinoma. Moreover, the patients who had had D4 lymphadenectomy presented metastases to the lymph nodes of the hepatoduodenal ligament and to the para-aortic lymph nodes in all pT stages (pT2, pT3, and pT4).
- (3) There were no differences in frequency of overall lymph node metastases, either at the N1 or N2 stations, between pT2 and pT3 tumors in either of the types of cardia adenocarcinoma studied. The uniformity of the nodal spread of these two types of tumors (pT2 and pT3) is even more marked if we eliminate from the pT2 group the very few patients ($n = 4$) with invasion of the tunica muscularis alone, which invasion is present only in type III malignancies.

We can conclude by saying that, the results of this study provide evidence for the need to perform a total gastrectomy in all patients with advanced type II or III adenocarcinomas of the cardia, to avoid leaving infiltrated lymph nodes along the greater curvature of the stomach in a substantial percentage of these patients. An exception to this rule of thumb may be in those individuals with early malignancies in whom non-involvement of the lymph node stations in the lower half of the stomach may allow a less extensive resection (proximal gastrectomy), as suggested by other authors [22,23].

As far as lymphadenectomy is concerned, the high percentage of involvement of second-tier lymph node stations makes the performance of D2 lymphadenectomy mandatory. Indeed, in our experience [24], as well as that of other groups in the West [25,26], the mortality and morbidity rates after D2 dissection were similar to or even lower than those after the limited D1 dissection in the Dutch [27] and British [28] trials. Furthermore, the presence of metastases to para-aortic lymph nodes in 17%–25% of our patients with a D4 lymphadenectomy suggests that the degree of involvement and the precise role of this station should be examined more thoroughly with studies in larger D4 patient samples.

Lastly, our results reveal a substantial measure of uniformity of nodal spread in tumors that infiltrate the full thickness of the wall of the organ regardless of the absence (pT2) or presence (pT3) of serosal invasion. This finding, as we see it, may lead to modifications of the TNM staging in cardiac tumors and to grouping these pT2–pT3 tumors together in a single group, as has been proposed by Skinner et al. for esophageal cancer [29].

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