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ORIGINAL ARTICLE

Surgery for patients with gastric cancer in the terminal stage of the illness – TNM stage IV

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Summary

Purpose: *To assess any survival advantage in patients with incurable gastric cancer who had undergone resection, bypass or exploratory surgery. In nonresectable patients with pain, the effect of celiac plexus neurolysis was assessed.*

Methods: *We retrospectively analysed data of 330 patients, operated between 1992 and 2006. The patients were followed until death or last examination. Incurable gastric cancer was defined as TNM stage IV disease: locally advanced (LA), with solitary distant metastasis (SM) or with multiple metastases and/or peritoneal carcinomatosis (MMC). The patients were divided into these 3 groups. Their postoperative survival was calculated and compared in relation to the surgical technique used. Factors which influenced mortality and survival were identified.*

Results: *131 patients (39.7%) had locally LA cancer, 98 (29.7%) SM, and 101 (30.6%) belonged to the MMC group. The surgical procedures included 138 (41.8%) exploratory laparotomies, 84 (25.5%) bypass procedures and 108 (32.7%) resections. Thirty-three (10%) unresectable patients with pain underwent celiac plexus neurolysis. The mean survival was 21.8 months after resections, 7 months after bypasses and 4.8 after exploratory laparotomies ($p = 0.0001$). It was 14.57 months ($p=0.001$) in the LA group, 12.53 ($p = 0.005$) in the SM group, and 5.2 in the MMC group. Survival was shorter in patients with preoperative weight loss of more than 20 kg (3.2 months, $p <0.0001$). Postoperative 30-day mortality was 23.2% after exploratory laparotomies, 23.8% after bypasses and 20.4% after resections. Increased mortality was observed in the MMC group (27.7%) and in multivisceral resections (41%, $p > 0.05$), while significantly increased mortality occurred in patients with weight loss of over 20 kg (32%, $p=0.03$). Celiac plexus neurolysis was immediately effective in 30 out of 33 (91%) patients ($p=0.0001$), while 3 months later it was still effective in 15 (45.5%) patients ($p=0.08$).*

Conclusion: *Resections are suggested in the LA and SM groups, and neurolysis in all nonresected patients with pain.*

Key words: gastric cancer, pain, palliative care, surgery, survival

Introduction

Gastric cancer was until recently the second most common cancer worldwide, but its incidence is declining steadily, and nowadays it ranks 4th among cancers, with 934,000 new cases per year, in 2002. In eastern Europe it is still frequent, with an incidence of 29.6 males and 12.8 females per 100,000 [1].

Stage IV gastric cancer is regarded as the terminal phase of the illness. According to the International Union Against Cancer (UICC) TNM classification for gastric cancer, stage IV disease includes all patients with distant metastasis, regardless of the depth of tumor penetration of the gastric wall (T) and regardless of the number and status of lymph nodes (N); all patients with metastasis in more than 15 regional lymph nodes (N3), regardless of the depth of tumor penetration of the gastric wall (T1-T4); and patients with tumor penetrating the surrounding tissues (T4), combined with positive regional lymph nodes (N1 or N2) [2].

The prognosis of stage IV patients is poor, somewhat better in the case of patients with involvement of

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lymph nodes alone than in those with distant extranodal metastasis. The majority of patients submitted to surgery at our Institute during the observed period had TNM stage IV gastric cancer [3]. Patients in this stage usually have a long history of complaints. They tend to be wasted, malnourished, anemic and hypoproteinemic. A certain number of them may experience problems caused by obstruction, which could produce electrolytic disbalance.

Resections remain the best palliative modality for patients with stage IV gastric cancer which may prevent possible obstruction, bleeding, pain and the possibility of perforation or infection. Tumor volume reduction diminishes the patient's metabolic demands, so wasting is slowed down, and, finally, a resected patient should be more responsive to chemotherapy. On the other hand, resections could result in increased morbidity and mortality compared to nonresections, since the procedure demands greater expertise to perform, the operating time is longer and the extent of surgery-induced trauma is greater. Debilitated patients often deny resection because of poor performance status. In such patients, poor survival and increased mortality could be ascribed to the same factors which have precluded resection – advanced disease. The majority of surgeons would prefer resections in localized disease, when the disease seems controllable. When the disease is generalized the question whether to resect tumor is still a matter of debate since survival benefit of such patients, as well as their postoperative quality of life, are not clearly defined. In nonresected patients, pain is often overlooked by the surgeon.

The aim of this study was to assess and compare survival and overall postoperative mortality rates in patients who had undergone resections, bypass or exploratory surgery, and to compare survival and postoperative mortality in the 3 groups of the TNM stage IV patients, in order to detect any survival advantage, either for a particular group or for a particular surgical procedure. This study also tried to investigate the effectiveness of pain control achieved with celiac plexus neurolysis in nonresected patients, who had severe pain preoperatively.

Methods

The patients were admitted to the department of surgery with histological diagnosis of gastric cancer. The data were retrieved manually from the medical records kept by the department and included age, sex, weight loss, duration of symptoms, histological findings, operative description and the date of death. Weight loss covered the preoperative period and was expressed in kilograms. The duration of symptoms was expressed in months. The histological findings in resected patients included the type of carcinoma using Lauren's classification, the number of the resected and positive lymph nodes, the depth of tumor penetration of the gastric wall and positive or negative resection margins. A pathologist was responsible for counting the number of the resected lymph nodes, by which the extent of lymphadenectomy was determined. The operative description included the date of operation, type of surgical procedure, description of tumor spread, lymph node status, presence of metastases - with their location and number, and peritoneal carcinomatosis. The date of death of patients who had died at home was obtained from the yearly epidemiological report of the Cancer Registry of Vojvodina [4].

The choice of surgical technique was decided by the operating surgeon, based on the extent of the disease and the patient's general condition. Surgical methods were classified as resections, bypass procedures and explorations. Resections included total gastrectomies, subtotal gastrectomies and distal two-third gastrectomies. They were accompanied by D1, D2 lymphadenectomies, or no lymphadenectomy. Standard D2 lymphadenectomy was performed in patients in whom the surgeon estimated there was a possibility of complete resection.

Nonresected patients, as well as those resected with positive resection margin were postoperatively admitted to the oncology department where they received palliative chemotherapy (FAP, EAP, or ELF combination chemotherapy), depending on their age, general condition, performance status and personal attitude. The effect of chemotherapy was not evaluated in this paper, except survival. Patients were divided as either having had received chemotherapy or not, and, thereafter, comparisons were made if chemotherapy had any impact on survival.

Nonresected patients with preoperative pain were considered for celiac plexus neurolysis. This was defined as a chemical splanchnicectomy of the celiac plexus aiming at ablating the efferent nerve fibers which transmit pain from the intra-abdominal organs. Patients had filled in pain estimation forms (from 1 to 10 scale) to measure the intensity of their pain prior to operation. Those with preoperative pain intensity of 3 or higher were enrolled for celiac plexus neurolysis. In those patients, chemical neurolysis of the celiac plexus was carried out during the operation. This was done by injecting 50 ml of a 75% alcohol solution retroperitoneally, equally divided on both sides of the aorta, paraaortically, at the level of the upper half of the lesser gastric curve at the closing stages of the operation. The pain control effect of neurolysis was classified as effective or non-effective. Pain intensity was assessed preoperatively, postoperatively

at the time of discharge from the hospital, and 3 months after the operation in patients who survived that long. Pain control was effective if there was a decrease of its intensity of 2 or more grades after the procedure. Side effects and complications were sought and recorded until hospital discharge.

Patients were divided into 3 groups on the basis of the disease extension. This was done by combining the data from operative descriptions and the histological findings.

Patients with locally advanced tumor (LA group), had T4 N1 and T4 N2 disease. The SM (solitary metastasis) group included patients who had one solitary visceral metastasis located either in the liver, omentum, ovaries, lungs or bones. This group also included patients with more than 15 positive lymph nodes (N3), as well as patients with positive cytological findings obtained with fine needle aspiration from the left supraclavicular-Virchow's lymph node and/or left axillary lymph nodes, regardless of tumor status, and without further dissemination of the illness. The MMC (multiple metastases, carcinomatosis) group included patients with multiple visceral metastases and those with peritoneal carcinomatosis.

Mortality was defined as lethal outcome during surgery and/or within 30 postoperative days. It was analyzed in percents, by dividing the number of lethal outcomes by the total number of the procedures done, for each surgical procedure and for each group of patients. No effort was made to exclude patients who died as a consequence of the operation, from those who succumbed to the natural course of the disease or from comorbidities. Survival was measured from the date of surgery to the date of death or the date of last examination in the case of living individuals. Survival analysis was carried out for patients who succumbed within the first 30 postoperative days.

Exclusion criteria

All patients with more than one malignancy and all patients who were not registered in the Cancer Registry of Vojvodina were excluded from the survival study. Patients who could not be clearly classified into any of the 3 groups, because they had mixed characteristics of 2 or more of the groups (e.g. locally advanced and metastases), were excluded from the analysis.

Staging criteria

The staging system used was the UICC 2002 6th edition of the TNM classification of malignant tumors.

Statistical methods

Statistical analyses were carried out using SPSS for Windows, Realize 8.0 statistical package program (SPSS Inc; Chicago, Illinois) for the IBM mainframe computer system. The data were expressed as percents in case of categorical variables, and as medians in case of continuous variables. Mean values were compared with Student's t-test, while frequencies were compared using the chi-square test. Logistic regression was applied to identify the variables which influenced mortality. Kaplan-Meier method was used for cumulative survival and log-rank test was applied to assess statistical differences between groups. Independently associated factors were identified by applying the Cox proportional hazard regression model. To determine which variables were independent prognostic factors for survival, backward regression was used to select the final fitted model analysis. Differences were considered significant with $p\text{-value} < 0.05$.

Results

Three hundred and thirty stage IV gastric cancer patients operated at the Institute from January 1992 to the end of 2005, were eligible for analysis. There were 215 (65.2%) males and 115 (34.8%) females (male to female ratio 1.87). Their age ranged between 27 and 84 years (mean 60.2). The duration of symptoms ranged from 0 to 48 months (mean 8.1). Mean preoperative total body loss was 14.8 kg (range 0-60). Hospital stay ranged from 6- 61 days (mean 16.5), which included 2-3 days of the preoperative period, the operation day, and the postoperative period which averaged 13.5 days. All operations were performed through an abdominal approach.

Histological findings showed 329 adenocarcinomas and 1 squamous cell carcinoma. In the adenocarcinoma group, there were 148 (44.8%) diffuse, 78 (23.6%) intestinal and 16 (4.8%) mixed types; 87 (26.4%) cases couldn't be classified according to Lauren's classification. These 87 nonresected patients who lacked Lauren's classification had their histology taken at other medical centers, where such a classification was still not obligatory. There were 131 (39.7%) patients in the LA group, 98 (29.7%) patients in the SM and 101 (30.6%) patients in MMC group. One hundred and thirty-eight (41.8%) patients were found inoperable during exploratory laparotomy. Eighty-four (25.5%) patients underwent bypass surgery and 108 (32.7%) were resected, contributing to an overall resectability rate of 32.7%. Resections consisted of 42 total gastrectomies –12.7% of the operated

patients (38.9% of the resections performed), 25 subtotal distal gastrectomies, which equaled 7.6% of the operated and 23.1% of the resected patients, and 41 distal two-third resections – 12.4% of the operated and 38% of the resected. Seventeen out of 108 (15.7%) resections were multivisceral-combined resections, comprising 5.2% of all the operations done. They included resections of either transverse and/or ascending colon, left hepatic lobe, spleen and the pancreatic tail/body, in addition to gastric resection. Ten percent of the operated patients (33/330) had been neurolysed (Table 1). Most of the resections performed – 68.5% (74/108) – were accompanied by lymphadenectomy. There were 49 (45.4%) patients with D1 and 25 (23.1%) with D2, while 34 (31.5%) patients didn't have lymphadenectomy (D0). Bypass surgery consisted of gastroenterotomies.

The mean post resection survival was 21.8 months. This was significantly longer compared to both survival after bypass and exploratory surgery (p = 0.0001). One-year post resection survival was 54.3%, 2-year survival 29.5% and 6.7% of the patients were alive after 5 years. Patients with bypass operation had a mean survival period of 7.0 months; 12.2% of the patients were alive one year after the operation, 2.4% after 2 years and 1.2% after 5 years. Patients who had undergone exploration had a mean survival period of 4.8 months; 8.4% survived for one year while none survived for 2 years after the procedure. The difference in survival between patients who underwent bypass and exploratory surgery was not significant (Table 2).

The majority of resections were performed on the patients in the LA group. In this group, there were 131 operations: 71 (54.2%) resections, 30 (22.9%) bypasses and 30 (22.9%) explorations. In the SM group, 98 operative procedures included: 35 (35.7%) resections, 28 (28.6%) bypasses and 35 (35.7%) explorations. In

Table 1. Main patient clinical and pathological variables (n=330)

Variables			
Gender			
Male	215 (65.2)		
Female	115 (34.8)		
M/F ratio	1.87		
Age, years			
Mean	60.2		
Range and SD	27-84; SD=10.6		
Duration of complaints			
Mean, months	8.1		
Range and SD	0- 48; SD=7.9		
Weight loss			
Mean, kg	14.8		
Range and SD	0 -60; SD=9.9		
In-hospital stay			
Days	16.5		
Range and SD	3-61; SD=7.6		
Histologal type	Number of patients (%)		
Diffuse	148 (44.8)		
Intestinal	78 (23.6)		
Mixed	16 (4.8)		
Not assessed	87 (26.4)		
Patient groups	Number of patients (%)	Mortality (%)	p-value
LA	131 (39.7)	21. 4	NS
SM	98 (29.7)	18. 4	NS
MMC	101 (30.6)	27.7	NS
Type of surgery	Number of patients (%)	Mortality (%)	p-value
Resections	108 (32.7)	20.4	NS
Total gastrectomy	42 (12.7)	16.7	NS
Subtotal gastrectomy	25 (7.6)	28.0	NS
Distal gastric resections	41 (12.4)	19.0	NS
Combined resections*	17 (5.1)	41.0	NS
Bypasses	84 (25.5)	23.8	NS
Explorations	138 (41.8)	23.2	NS
Neurolysis§	33 (10)		

*Combined resections were already calculated in Total, Subtotal or Distal gastric resection.
§Neurolysis was distributed and calculated in Bypasses and Explorations.
SD: standard deviation, LA: locally advanced, SM: solitary metastasis, MMC: multiple metastases/peritoneal carcinomatosis, NS: non significant

Table 2. Surgery type, age of patients and postoperative mean survival

Operation type	*Number of patients (%)*	*Mean patient age, years (range and SD)*	*Mean postoperative survival (months)*
Resections	108 (32.7)	59.3 (36-83; SD=9.4) p=NS	21.8 (0.1-155; SD=30.7) p=0.0001 vs. non resections
Bypasses	84 (25.5)	64.6 (30-84; SD=9.2) p=NS	7.0 (0.1-107;SD=13.2) p=0.0001 vs. resections p=NS vs. explorations
Explorations	138 (41.8)	58.3 (27-82; SD=11.5) p=NS	4.8 (0.1-36.6; SD=6) p=NS vs. bypasses

NS: non significant

the MMC group only 2 (2%) resections were done. In that group there were 26 (25.7%) bypasses and 73 (72.3%) explorations. The resectability rate declined from 54.2% in the LA group to 35.7% in the SM and to 2% in the MMC group (p = 0.0001). Lymphadenectomies which accompanied resections fell from 91.6% in the LA group to 35.7% in the SM group and to 0% in the MMC group, where all resections were performed without lymphadenectomy. In the LA group most of the resections (45/71, 63.4%) were done with D1 lymphadenectomy, followed by 28.2% (20/71) with D2 and 8.4% (6/71) without any. In the SM group the majority of the resections (74.5%; 26/35) were performed without lymphadenectomy, while 11.4% (4/35) were done with D1 and 14.3% (5/35) with D2 (Table 3).

Twelve percent (13/108) of the resections had histologically positive resection margin. As these findings came postoperatively, patients were not submitted to reoperation; they rather underwent chemotherapy or were just followed regularly in order to obtain information about the progression rate of the tumor. The survival of patients with clear resection margin was longer (mean 22.6 months; range 0.1-155: standard deviation/ SD = 31.1) than of those with positive margin (mean 17.8 months; range 0.1-58.2; SD = 18.5). However, this survival difference was not significant. Overall mean survival for patients in the LA group was 14.57 months (range 0.1-155; SD = 23.6). It was longer, but not significantly than in patients from SM group in whom it was 12.53 months (range 0.1-135; SD = 23.4), and significantly longer than 5.2 months (range 0-50.6; SD=7.6), observed in the MMC group. MMC group patients had significantly shorter survival, both in comparison to the LA (p = 0.001) and the SM (p = 0.005) group. Mortality rates between patients of these groups were not significantly different (Table 4).

Univariate analysis of the association of individual risk factors that could influence survival, using the independent samples t-test, showed a mean survival advantage for patients who underwent resection, did not undergo combined resection, lost < 20 kg of their preoperative weight, were younger than 70 and belonged to the LA group compared with patients who underwent explorations and bypasses, patients in the MMC group, those with combined resections, and those older than 70 showed significantly shorter survival as follows: the mean survival in patients who underwent combined-multivisceral resections was 10.8 months (range 0.1-

Table 3. Surgery in the 3 groups of TNM stage IV patients; p=0.0001

	Number (%) of procedures done in 3 groups of patients according to the spread of cancer				*Total*
	LA n (%)		*SM n (%)*	*MMC n (%)*	
Resection	71	(54.2)	35 (35.7)	2 (2)	108
Lymphadenectomy					
D0	6/71	(8.4)	26/35 (74.5)	2 (100)	
D1	45/71	(63.4)	4/35 (11.4)	0	
D2	20/71	(28.2)	5/35 (14.3)	0	
Bypass	30	(22.9)	28 (28.6)	26 (25.7)	84
Exploration	30	(22.9)	35 (35.7)	73 (72.3)	138
Total	131		98	101	330

For abbreviations see footnote of Table 1

Table 4. Overall mortality rates and mean survival of patients in the 3 groups of TNM stage IV gastric cancer

	No of patients	*Died in 30 days*	*Overall 30-day mortality % (p-value)*	*Mean survival in months*
LA	131	28	21.4 (NS)	14.57 (SD=23.6) p=0.001 vs. MMC, NS vs. SM
SM	98	18	18.4 (NS)	12.53 (SD=23.4) p= 0.005 vs. MMC
MMC	101	28	27.7 (NS)	5.2 (SD=7.6) p= significant, as above
Total	330	74	22.4 (NS)	

For abbreviations see footnote of Table 1

36.6, SD = 13); this was significantly shorter than in univisceral resections where the survival was 24.6 months (range 0.1-155, SD = 31.9; p = 0.0005).

The mean survival in patients who lost more than 20 kg of their weight was 3.2 months (range 0.1-13.0, SD = 3.7), a period significantly shorter than 11.8 months, which was the case in the remaining patients (p = 0.0001).

The mean survival in patients older than 70 (7.2 months, range 0.1 – 50.6, SD = 10.9) was significantly shorter compared with younger patients (11.8 months, 0 range -155, SD = 21.6; p = 0.023).

No statistical difference in survival was found related to sex, chemotherapy, histological findings, positive resection margin and lymphadenectomy.

Cox regression analysis showed only 2 independent factors adversely related to overall survival. These

Table 5. Influence of clinical factors on survival

Variable	*Mean survival in months (SD)*	*Univariate p-value*	*Multivariate hazard ratio (95%CI)*	*Multivariate p-value*
Gender				
Male	9.9 (19.0)			
Female	13.3 (22.7)	NS		
Weight loss (kg)				
> 20	3.2 (3.7)		2.7 (1.56-4.82)	p=0.0012
< 20	11.6 (12.2)	0.0001		
Age (years)				
> 70	7.2 (10.9)			
< 70	11.8 (21.6)	0.023		p=NS
Chemotherapy				
Yes	14.4 (23.2)			
No	13.7 (15.5)	NS		
Histology (Lauren)				
Diffuse	13.6 (25.3)	NS		
Intestinal	8.7 (10.7)	NS		
Mixed	10.9 (14.2)	NS		
Type of surgery				
Resected	21.8 (9.9)	0.0001	0.2 (0.129-0.504)	0.0001
Bypassed	7.0 (22.1)	NS vs. expl; 0.0001 vs. res		
Explored	5.2 (7.2)	0.0001		NS
Resections				
Margin +	17.8 (18.5)	NS		
Margin –	22.6 (31.3)			
Combined resections	10.8 (13.0)			
Simple resections	24.2 (31.9)	0.005		NS
Lymphadenectomy				
D0	25.6 (39.7)	NS		
D1	19.5 (27.9)	NS		
D2	26.2 (31.6)	NS		
Arms of stage IV				
LA	14.6 (23.5)	0.018		NS
SM	12.4 (23.2)	NS vs. LA; 0.004 vs. MMC		
MMC	5.1 (7.5)	0.0001		NS

For abbreviations see footnote of Table 1

were preoperative total body weight loss > 20 kg (p = 0.0012, relative risk/RR = 2.7, 95% CI 1.56-4.82) and nonresection (p = 0.0001, RR = 0.2, 95% CI 0.129-0.504; Table 5).

A comparison of the mean survival after resections, bypasses and exploratory surgery in the 3 groups is shown in Table 6. Significantly better survival after resections in the LA and SM groups was noted, while in the MMC group no conclusive statistics could be carried out because of insufficient number of resections, although the resected patients lived almost 5 months longer on average than nonresected. Survival after bypasses and explorations was not significantly different in any of the 3 groups. Survival curves depicting survival advantages for resected patients, patients with weight loss < 20 kg, and LA and SM patients are shown in Figures 1, 2 and 3.

Mortality

No statistically significant differences in mortality were found either between various surgical procedures or between the 3 patient groups. Overall 30-day mortality was 22.4%. It was 20.4% in the case of resections, 23.8% in bypass procedures and 23.2% in the case of explorations (p > 0.05). Mortality in the LA group was 21.4%, in the SM group it was 18.4%, while the mortality rate rose to 27.7% (p > 0.05) in the MMC group (Table 1).

An increased mortality rate of 32% was found in patients with preoperative weight loss > 20 kg. This was significantly higher compared to other patients (p = 0.03), and was the only independent predictive factor influencing mortality using logistic regression analy-

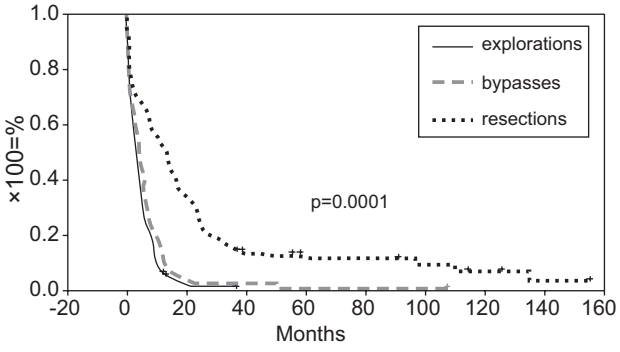

Figure 1. Cumulative postoperative survival for resected, bypassed and explored patients using Kaplan-Meier method and log-rank test. Survival was considerably longer after resections (p=0.0001), while it was not significantly longer if survival after bypasses was compared to survival after explorations.

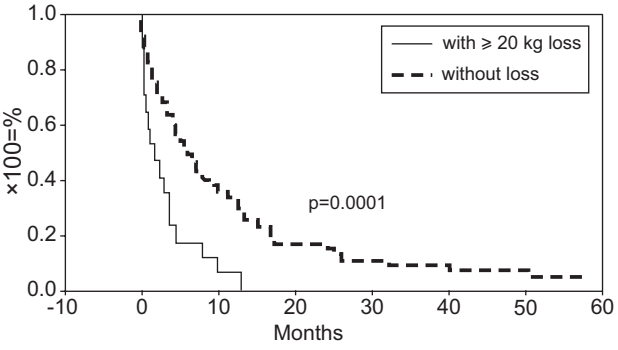

Figure 2. Cumulative postoperative survival for patients with ≥ 20 kg weight loss compared to survival of patients with < 20 kg weight loss, using Kaplan-Meier method and log-rank test (p=0.0001).

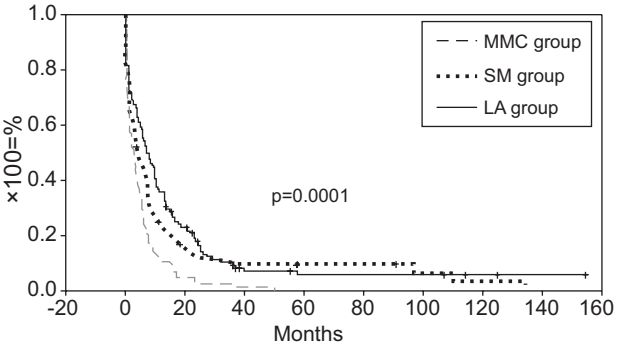

Figure 3. Cumulative postoperative survival for patients with locally advanced disease (LA), solitary metastatic disease (SM) and multiple metastatic disease (MMC) using Kaplan-Meier method and log-rank test. Of the operated LA patients 35.7% were alive one year after the operation, 15.9% after 2 years and 3.2% after 5 years. In the SM patient group there were 22.6% survivors after one year, 11.8% after 2 years and 4.3% after 5 years. From the MMC group 11.3% of the patients were alive one year after surgery, 2.1% after 2 years and none at the end of the 5-year postoperative interval (p=0.0001).

Table 6. Difference in mean survival of the patients after surgery, observed in the 3 groups of patients

Comparison of mean survival between	*LA group (months)*	*SM group (months)*	*MMC group (months; few resections)*
Resected vs. bypassed	20.2 vs. 8.9 p=0.03	26.5 vs. 4.6 p=0.002	12.4 vs. 7.5 p=NS
Bypassed vs. explored	8.9 vs. 6.6 p=NS	4.6 vs. 5.2 p=NS	7.5 vs. 3.9 p=NS

For abbreviations see footnote of Table 1

sis (RR = 3.1, range 1.05-9.6). Increased mortality was not related with age, sex, histological findings, type of operation, or patient group.

Neurolysis

Thirty-three unresectable patients (10% of all patients) underwent this procedure. They were equally distributed between the 3 groups ($p > 0.05$). In the LA group 16 patients underwent neurolysis, it was employed 10 times in the SM group and 7 times in the MMC group. Immediate postoperative positive effect was noticed in 30 patients (91% of all neurolysed patients; $p = 0.0001$). Complete pain control was reported by 14/30 (42.4%) of the patients who needed no further analgesic therapy, while 16 (48.5%) patients reported partial pain control, but still required additional oral analgesics. In 3 (9%) patients, there was no pain control effect. Three months after the procedure, 11 (33%) patients were dead, and of the remaining 22 who were still alive the pain control was still effective in 68.2% (15/22) and ineffective in 31.8% (7/22) of them (Table 7). No side effects including hypotension, diarrhea, pain or hypoxemia were recorded. This may partially be due to general anesthesia, and a postoperative lack of peristaltic activity. Minor bleeding was recorded in 4 (12.1%) patients which was controlled intraoperatively by applying pressure and packing.

Discussion

The purpose of staging patients with carcinoma is to bring together similar patient groups considering their extent of the disease, treatment, prognosis and outcome. TNM stage IV gastric cancer includes patients with a resectable tumor which is locally advanced and accompanied by locally involved lymph nodes, as well as patients with multiple and diffuse metastases, and sometimes peritoneal carcinomatosis. The criteria for deciding which patient may benefit from resection are still not fully established and they are still a matter of debate and controversy. Few authors reported their experience concerning survival after gastric resections in relation to TNM stages. Usually reported survivals are related to an ill-defined and imprecise term (palliative resection), the meaning of which may vary from author to author. Resections were considered palliative by some if they achieved radicalism less than R0, or performed in cases with peritoneal, liver or distant lymph node metastasis by others [6,7]. Some authors have classified the resection as palliative if the resection margin was histologically positive, or if it was in the vicinity of the tumor [8-10]. As these determining factors are not uniformly accepted, the same resection could be interpreted differently, depending on the individual author. American authors tried to solve this by defining palliative intervention only when medical records clearly documented palliative intent, or when it was verbally confirmed by the attending surgeon [11]. Hartgrink et al. included in palliative resections only patients with metastasis or those being nonresectable, considering T4 N1 or T4 N2 resected patients as potentially curable, and eliminating them from their analysis [12]. Others included resections in stages III and IV as palliative [13]. We believe that the TNM stage of disease is, up to now, the most reliable predictive factor in the treatment of malignant diseases and we regard TNM stage IV as noncurable state.

Operative mortality of 10-33% was commonly reported by European authors, which sharply contrasts a mortality rate of 2-3%, reported by Asian authors [13,14]. Ekbom and Gleysteen [15] reported mortality of 15% for resections and 25% for bypasses. In his classical paper, Allum et al. [16] reported increased mortality rates after resections in advanced stages that surpassed 23% in the case of partial gastrectomies and 36.6% in total gastrectomies performed in stage IV disease. In their retrospective study, Hartgrink et al. reported recently mortality of 12% rising up to 20% in patients over 70 years of age [12]. Recent American papers reported mortality of 4-10% [17,18]. The explanation for this different rates could be that the term "mortality" does not seem to be precisely defined, having included different categories of mortality causes in the papers of different authors. Some of the authors make a distinction between specific and nonspecific mortality, referring to lethal outcomes caused by surgery as specific and reporting this as mortality, excluding all other causes as nonspecific. These percentages could sometimes be drastically dissimilar, as was for example in Eguchi et al. paper which

Table 7. Pain control after intraoperative celiac plexus neurolysis with 75% alcohol

Number of patients (%)	33	(100)	
Bypassed	12	(36.4)	
Explored	21	(63.6)	
Immediate pain control	*Patients, n (%)*		
Effective	30	(90.9)	p=0.0001
Complete pain control	14	(42.4)	
Partial pain control	16	(48.5)	
Non effective	3	(9.1)	
Pain control after 3 months			
Effective	15	(45.5)	p=0.08
Non effective	7	(21.2)	
Dead	11	(33.3)	

showed postoperative death of 3.8% related to surgery, and a 16.3% death rate from other diseases [14]. Others have discussed "in-hospital" mortality, "surgical" mortality, "perioperative" mortality – not always precisely explaining what happens with their patients after hospital discharge. In-hospital mortality would always be lower than overall 30-day mortality, unless patients are held in hospital for that period, since there would always be patients who would die at home after hospital discharge in this one-month period. This is particularly characteristic for European and American hospitals, where postoperative intrahospital period in patients without complications rarely exceeds 2 weeks. These figures usually do not include death rates presumably caused by the natural course of the disease or comorbidities, and are lower than the percentage of survivors.

Overall 30-day mortality in our series was over 20% in all procedures done, without significant differences between the different kinds of procedures. Mortality included all demises in the period of 30 days after surgery. Our opinion is that overall 30-day postoperative mortality, of whatever cause, is a good guide for obtaining a prognosis in such patients, giving a more realistic approach to what could be expected.

Our analysis showed that preoperative weight loss was an independent prognostic factor, directly related both to mortality and survival. A correlation between malnutrition and increased operative mortality has been recognized earlier [19], and preoperative weight loss was already reported to exert a significant impact to operative mortality [20].

Since mortality was similar in all resective procedures done with the exception of multivisceral-combined resections, this should encourage even total gastrectomy in selected cases of stage IV patients, which is in accordance with our earlier work [21]. It has already been stated that combined resection should be performed cautiously in advanced cancer, since it does not provide prolonged survival compared to gastrectomy alone [13,17]. In both of those papers mortality rates for combined resections and gastrectomies were similar, which was not found in our patients where it was higher after combined resections. Although mean survival calculated for all patients with combined resection (10.8 months) was significantly shorter ($p = 0.0005$) than in those who had only gastric resection (24.6 months), the mean survival for the patients who survived one month postoperatively (calculation made without the patients who contributed to 30-day mortality) was 33.4 months (range 12.2-36.5), which was comparable with the survival in other resected patients. This would suggest that multivisceral resections could be considered if 30-day mortality could be reduced.

The issue of resection margins deserves special attention. It has been reported that a microscopically positive histological resection margin could influence survival. Kim et al. published results showing that it was significant in terms of survival only in resections with 5 or less positive lymph nodes [22]. Our study covered stage IV patients who could be regarded similar to patients with more than 5 positive lymph nodes in the Kim's group, since N2 includes patients with more than 7 positive lymph nodes. Although we found better survival in the patients resected with histologically healthy margins compared to those with positive ones, this survival gain did not prove significant. A possible explanation for this could be that microscopically positive margins would need a longer time to develop into a fully-fledged tumor, which is deficient in patients with limited life expectancy. These results could resolve the clinical dilemma of considering reoperation in the cases of resected gastric cancer in stage IV patients, where resection margins were found positive on final histological report, obtained a couple of days after surgery. Survival advantage in these patients could easily disappear with calculation of additional operative mortality.

Neurolysis was seldom reported in surgical literature addressing gastric cancer as a procedure performed intraoperatively. When discussing the problem of pain, surgeons usually report procedures aimed at controlling pain by tumor reduction or resection. They infrequently mention nonresectable patients with pain [11], which leaves a certain share of operated gastric cancer patients with postoperative pain, uncontrolled by surgical methods. In such patients, only a further increase in pain could be expected in the future, due to the progression of disease. Direct injection of alcohol in the vicinity of celiac plexus during surgery is simple, safe and effective, and does not seem to have any adverse effects except minor bleeding. Although the efficiency of pain control have had declined with the passage of time, it was still efficient 3 months after the procedure. In circumstances where survival of 4-7 months is to be expected, 90 days seem to be a significant percentage of life expectancy. As palliation is sought for these patients, and the goal of palliative care, according to the World Health Organization's definition, is "achievement of the best quality of life for patients and their families", this could largely be achieved through the pain control. With neurolysis done, these patients could be spared of additional postoperative increased analgesics consumption.

Survival

It is generally accepted that resections in locally advanced disease result in longer survival. This has been

confirmed in this paper - resection is the best palliation. When patients with metastatic disease are concerned, there is no consensus on the best treatment choice yet. If such patients are treated surgically, the surgeon should be aware that the usually reported survival after bypass or exploratory surgery is not longer than 3-6 months [5,9,25], and that it could be considerably prolonged by palliative resections - reaching 9.5 - 16.3 months [13,27]. Recent papers advocate resections for solitary metastatic disease [12,13], as well as in the cases of multiple metastases and carcinomatosis [23,28] documenting this approach with prolonged survival. In cases with solitary metastasis, further resections of metastasis could be indicated. In their recent paper, Sakamoto et al. documented median survival of 21 months and a 5-year survival of 38% in patients reoperated for single hepatic metastasis of gastric origin [26]. Our results strongly support this approach.

Conclusions

This retrospective, hospital-based study has shown increased survival after resections in stage IV gastric cancer for patients who had locally advanced cancer, as well as for those with a solitary metastasis. It was also documented increased mortality and shorter survival in patients with preoperative total body weight loss of more than 20 kg. The study demonstrated considerable effects of pain control after intraoperative celiac plexus neurolysis. Operative mortality of resections was very similar to other less aggressive procedures, whereas resections resulted in significantly longer survival. All types of resective surgery should be encouraged, including total gastrectomy. Multivisceral resections should be done very cautiously since they yield increased morbidity and mortality. A visually clear resection margin seems to be sufficient to provide longer survival.

In this study, longer mean survival was found in resected patients compared to nonresected patients in all 3 patient groups regarding the extent of disease. Survival advantage after resections was found in patients with locally advanced disease and in those with solitary metastasis. In patients with multiple metastases or carcinomatosis only 2 resections were performed and, although these patients survived longer than nonresected patients, resection was performed too seldom to lead to any conclusion. Whether this MMC group of patients should be resected or left without any surgical intervention and offered other treatment modalities remains to be answered in the future.

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