Prognostic factors in gastric carcinoma after R0 resection with DII lymph node dissection. Tunisian experience.

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Facteurs pronostiques après résection R0 et curage ganglionnaire des cancers de l'estomac: Expérience tunisienne.

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RÉSUMÉ

Prérequis : La résection à visée curative avec curage ganglionnaire adéquat est le traitement de choix pour le cancer gastrique.
But : Déterminer les facteurs pronostiques après résection R0 avec curage ganglionnaire
Méthodes: Sur une période de 15 ans ; entre 1991 et 2006, nous avons colligé rétrospectivement 126 patients ayant eu une résection R0 avec curage ganglionnaire DII pour cancer gastrique (à l'exclusion du tiers supérieur de l'estomac). Le suivi médian était de 38,5 mois (6-219). Grace à une étude statistique (modèle de Cox), nous avons essayé de déterminer les facteurs pronostiques.
Résultats: On a colligé 45 femmes et 81 hommes. L'âge médian était 60 ans (21 - 87). Quatre patients sont décédés (3,2%). La morbidité postopératoire était de 16,7%. L'examen anatomopathologique des pièces de résections avait révélé que 50% des tumeurs étaient de stade T3 (63 cas). Le nombre médian d'adénopathies prélevés était de 11 (8-40). Cinquante % étaient envahis. Les taux de survie à cinq et 10 ans étaient respectivement de 56,9% et 40,2%. En analyse multi variée, l'envahissement en profondeur, l'envahissement ganglionnaire et plus de 15 ganglions lymphatiques prélevés étaient des facteurs pronostiques indépendants.
Conclusion: Après résection R0 avec lymphadénectomie DII, l'envahissement en profondeur, l'envahissement ganglionnaire et plus de 15 ganglions lymphatiques prélevés étaient des facteurs prédictifs indépendants de survie.

SUMMARY

Background: Curative resection with adequate lymph node dissection is the treatment of choice for gastric cancer.
Aim: To determine the prognostic factors after R0 resection with DII lymph node dissection.
Methods: We retrospectively assessed 126 patients who underwent R0 resection with DII lymph node dissection for gastric cancer (excluding the upper third of the stomach) in a single institution between 1991 and 2006 with median follow-up of 38.5 months (6 – 219). Prognostic factors were assessed by Cox proportional hazard model.
Results: There were 45 women and 81 men. The median age was 60 years (21 – 87). Four patients died (3.2 %). Postoperative hospital morbidity was 16.7 %. The pathologic review of the slides revealed that 50% of the tumors were stage T3 (63 cases). The median number of lymph node removed was 11 (8-40), 50% were involved. Five and 10 years survival rates were respectively 56.9 % and 40.2 %. In multivariable analysis, depth of wall invasion, lymph node involvement and more than 15 retrieved lymph nodes were found to be independent prognosis factors.
Conclusion: After R0 resection with DII lymphadenectomy, depth of wall invasion, lymph node involvement and more than 15 retrieved lymph nodes were independent predictive factors for survival.

Mots-clés

Chirurgie du cancer gastrique, résection curative, lymphadénectomie

Key-words

Cancer stomach surgery, curative resection, lymphadenectomy

Cancer of the stomach is the second most common cancer in the world and remains one of the most relevant health problems in Tunisia. Prognosis is poor perhaps because of delayed diagnosis and frequent local and regional recurrences [1]. Gastrectomy with regional lymphadenectomy (DII) is the mainstay of curative treatment with satisfactory survival. Several prognostic factors have been evaluated in order to assess their value in predicting patients' outcome. Radical resection (R0) has been found to be the most statistically significant predictive factor of survival [2-6].

The aim of this study was to determine the prognostic factors in patients undergoing curative resection for carcinoma of the middle and the lower thirds of the stomach. Cancer of the upper third of the stomach was excluded due to its poor prognosis in comparison with other locations [7].

PATIENTS AND METHODS

We retrospectively reviewed our database of patients who underwent gastrectomy for gastric cancer from January 1991 to December 2006, in general surgery La Rabta hospital in Tunis, Tunisia. A total of 253 patients underwent gastrectomy for gastric cancer during this period. Among these patients, 126 underwent R0 resection that was defined by the absence of residual tumor after surgical treatment proved by pathologic examination of the resected margins. Patients with cancer of the upper third of the stomach were excluded.

Surgery

Two types of gastrectomy were performed: subtotal (STG) or total (TG). STG was performed for tumors located in the lower third of the stomach if there was a tumor-free proximal margin of 6 cm. All the other patients underwent TG.

STG was associated with DII lymph node (LN) dissection including stations 1,3,4,5,6,7,8 and 9, according to the Japanese Research Society for gastric Cancer guidelines [8]. This technique of DII gastrectomy included the removal of the entire greater omentum, pancreatic capsula and the lesser omentum. The left gastric artery was ligated at its origin. Lymphadenectomy included also the removal of nodes along the celiac trunk, the commun hepatic artery and the origin of spleen artery.

For TG, DII LN dissection did not include removal of the spleen and the tail of the pancreas. This resection was needed because of tumor invasion or intraoperatively suspected LN involvement in stations 10 or 11. If the spleen was removed, the Maruyama technique was recommended and the spleen artery was ligated after the origin of the dorsal pancreatic artery [9].

Statistical analysis

The final date for follow-up was December 2008. Follow-up information was obtained regularly from outpatient clinical visits. Data analysis included relative frequency, median and range values. Five year survival rates and 95 % confidence intervals (CI) were calculated using the Kaplan-Meier method and differences in survival were compared by the Log Rank test. Overall mortality represented all deaths during follow-up. Multivariable analysis was performed using Cox's proportional-hazards regression model. Significance was defined as $p < 0.05$. SPSS 11.5 was used to generate these analyses.

RESULTS

There were 45 women and 81 men. The median age was 58 years (21 – 87). The tumor was located in the lower third of the stomach in 54.8 % of the cases (69 patients). Subtotal gastrectomy was performed in 64 patients (50.8 %) and total gastrectomy in 62 patients (49.2 %). The tumor was locally advanced in 8 cases (6.3 %) and radical resection was extended to the spleen and the tail of the pancreas in one case, to the colon in four cases, to the left liver in one case and to the head of the pancreas in two cases. Thirty eight patients were transfused (30.2 %).

Four patients died (3.2 %). Postoperative hospital morbidity was 16.7 %. Anastomotic leakage was the most common complication (9 cases 7.1%). The patients were discharged after a median period of 10 days (5 to 67 days).

The pathologic review of the slides revealed that 50% of the tumors were stage T3 (63 cases). T1, T2 and T4 tumors represented 15.1, 31 and 4 % of patients, respectively (Table 1).

Table 1: Clinical data

Data		N (%)
Sex (M/F)		81/45
Tumor location	Middle	57 (45,2)
	Lower	69 (54,8)
Type of gastrectomy	TG	62 (49,2)
	STG	64 (50,8)
Transfusion		38 (30,2)
Depth of invasion	T1	19 (15,1)
	T2	39 (31)
	T3	63 (50)
	T4	5 (4)
Lymph node metastasis	N0	63 (50)
	N+	63
Tumor differenciation	Well	35 (27,8)
	Poor	91 (72,2)

The median number of lymph nodes removed was 11 (8-40). LN involvement was found in 50 % of cases. The tumor was well-differentiated in 35 cases (27.8 %).

The median follow-up period was 38.5 months (6 – 219). During the follow-up period, 61 patients died (48.4 %). Five and 10 years survival rates were respectively 56.9 % and 40.2%

(Figure 1). The median survival was 76 months. A 5 year-survival rate of T1 and T2 tumors was significantly superior to T3 and T4 tumors (77.3 % versus 37.1 %, P< 0.0001) (Figure 2). Survival was superior in case of absence of LN invasion (76% versus 36.1 %, P< 0.0001) (Figure 3). Long term survival varied also according to the number of removed LN. In fact, survival was 34% when 15 LN were removed versus 73.3 % when fewer lymph nodes are resected (P< 0.0001) (Figure 4). Survival rate did not differ according to tumor location, the type of gastrectomy, resected adjacent organs, tumor differentiation, the presence of ring cell carcinoma, perinervous or vascular invasion. On multivariable analysis, depth of the wall invasion, LN involvement and a number of resected LN superior to 15 were found to be independent prognostic factors (Table 2).

Figure 1 : Survival curve

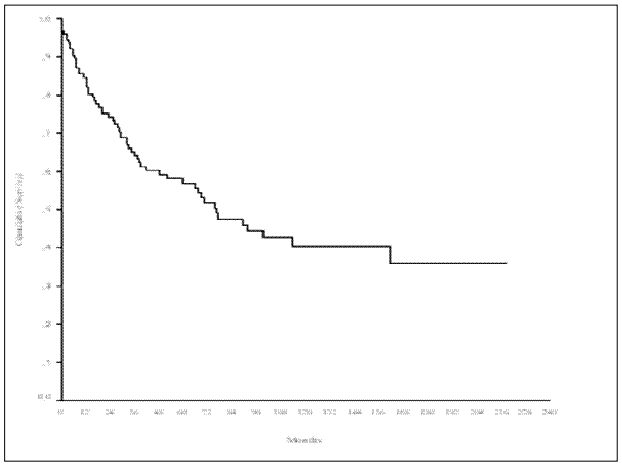

Figure 2 : Survival curve with regard to depth of invasion

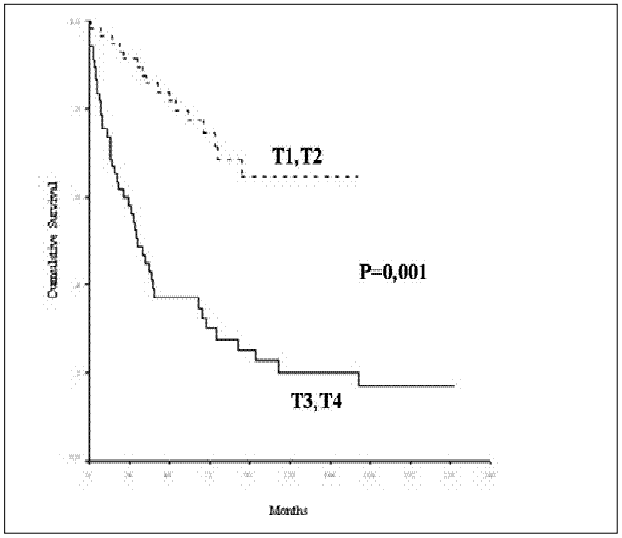

Figure 3 : Survival curve with regard to nodal status

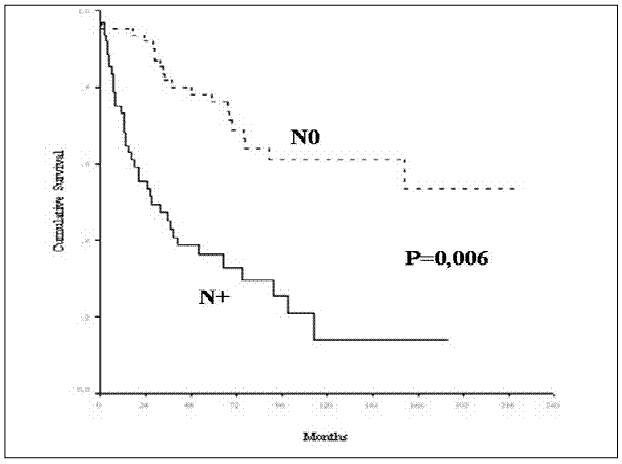

Figure 4 : Survival curve with regard to number of retricvec lymph nodes

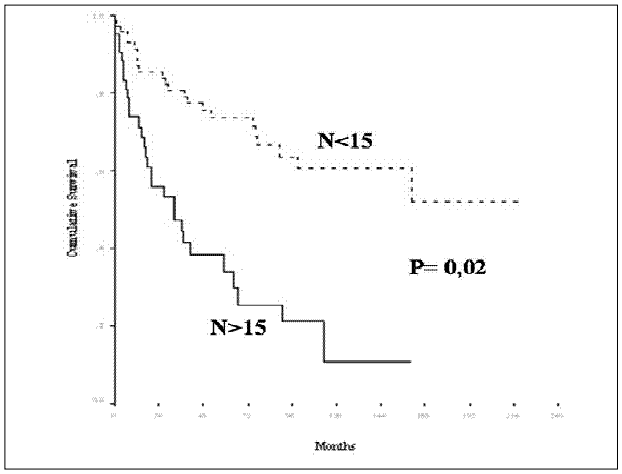

Table 2: Multivariate analysis

Factors	OR	CI	P
Depth invasion	3,1	1,63-5,91	0,001
Lymph node metastasis	2,57	1,3-5,1	0,006
Number of resected LN (>15)	2,03	1,1-3,74	0,02

DISCUSSION

In this highly selected group of patients (R0 resection of tumors of middle and distal third of the stomach), it seemed interesting to identify patient with the poorest prognosis so that could benefit from radiation or chemotherapy [10, 11]. Our retrospective study showed that after R0 resection with DII lymphadenectomy, depth of wall invasion, LN metastasis and the number of retrieved LN were the independent prognosis factors.

Complete loco regional tumor removal with adequate margins of clearance defines the R0 resection and has been widely identified as a major impact factor for reduction of locoregional

and metastatic tumor recurrences. This R0 resection is the first step to improve survival in patient with gastric carcinoma [2-6]. Our 5 and 10 years survival rates were 56.9 % and 40.2 %, respectively. These survival rates are comparable to those reported in the German gastric cancer study [12] and the Memorial Sloan-Kettering cancer center in New York [13] and some other western centers [14-16]. Nevertheless, the survival rates are worse than those reported in Japan [17-19]. Differences in the staging systems, epidemiology, tumor location (upper third tumors were excluded in our study), the stage distribution and the more radical approach toward lymphadenectomy in Japan may explain these differences.

LN involvement and the depth of wall invasion are now considered as the two most important prognostic factors in gastric cancer especially after R0 resection [12, 13, 15, 20-24]. These data have been reported in 1987 by Maruyama and coworkers in a multivariable analysis of 4710 patients resected between 1962 and 1984. In this study T and N stage had the most powerful prognosis factor of more than 4.0 Odds Ratio [23]. The greater the number of LN analysed, the greater the probability of finding positive LN. In fact in our study there are significantly more invaded LN when 15 or more were retrieved (71.4 % versus 38.9 % Positive LN P=0.03). Analyses of a small number of LN increases the risk of understaging patients who can benefit from adjuvant therapy. The survival rate of our patients with more than 15 LN retrieved were very poor (34% versus 73.3 %, P< 0.0001). A different staging system has been used in the past to improve the assessment of the prognosis of gastric cancer. In 1997, after examination of the study carried out by the German Gastric Study Group and the Erlangen group, [12] the UICC classification recommended the examination of at least 15 LN for a lymphadenectomy of any type for gastric carcinoma. Three years later, Karpeh and colleagues compared the impact of different staging systems (UICC 1988 that used the location of LN versus UICC 1997 that used the number of LN) on the survival of 1038 patients with gastric cancer undergoing resection [13]. They found that the number of positive nodes assesses prognosis more than their location. The authors concluded that the number of LN is more important than their location to predict survival.

CONCLUSION

This study showed that after R0 resection for cancer of the middle and distal thirds of the stomach, depth of wall invasion, lymph nodes involvement and the number (>15) of retrieved LN predict survival. To improve the survival in patients with these poor prognosis factors, we emphasize the necessity of adjuvant therapy and early detection of gastric cancer by increasing the use of upper endoscopy for digestive symptoms.

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