

ORIGINAL PAPER

**CORRELATIVE ASPECTS REGARDING THE GASTRIC STUMP CANCER
CLINICAL PRESENTATION AND IMAGISTIC STADIALIZATION****Mihaela Handaric¹, D.N. Păduraru^{2,3}, O. Andronic², Elena Gologan^{1,4}**¹Gr. T. Popa” University of Medicine and Pharmacy, Iași, Romania²Carol Davila” University of Medicine and Pharmacy, Bucharest, Romania³3rd Department of General Surgery, The University Emergency Hospital Bucharest, Romania⁴ The Gastroenterology and Hepatology Institute of Iasi

Corresponding author: Dan Nicolae Păduraru
Phone no. 0040744756443
E-mail: dan.paduraru.nicolae@gmail.com

Abstract

The gastric stump cancer (GSC) is a last stage subdiagnosed or diagnosed pathologically, when the therapeutic options are limited. The research that aimed the evaluation of patients with stomach surgical interventions related to the development of gastric stump neoplasias is based on a retrospective observational study of a group of 52 patients, institutionalized and diagnosed within the Gastroenterology and Hepatology Institute of Iasi between January 2004 and December 2015. In order to identify which of the clinical elements are most relevant in guiding the stage of the diagnosis, we considered it suitable, in the absence of a witness group, to realize correlations between the clinical elements and the stadialization of the imagistic quantified tumoral formation.

Keywords: *gastric stump cancer, gastric stump neoplasia, stomach surgical intervention*

Introduction

The gastric stump cancer (GSC) is a last stage subdiagnosed or diagnosed pathologically, when the therapeutic options are limited. This is what makes us regard the gastric neoplasia identified in a previously operated area with keen interest, especially related to the early diagnosis and to the monitoring of the patients in high risk for gastric neoplasia. In order to identify which of the clinical elements are most relevant in guiding the stage of the diagnosis, we considered it suitable, in the absence of a witness group, to realize correlations between the clinical elements and the stadialization of the imagistic quantified tumoral formation.

GSC is the malign tumor developed in the remaining stomach after the subtotal

gastrectomy performed both for benign and malignant lesions [1].

Materials and methods

The research that aimed the evaluation of patients with stomach surgical interventions related to the development of gastric stump neoplasias is based on a retrospective observational study of a group of 52 patients, institutionalized and diagnosed within the Gastroenterology and Hepatology Institute of Iasi between January 2004 and December 2015. The group was established by identifying all the patients who attended the clinic where the research was performed and who met all the inclusion criteria and none of the exclusion criteria hereafter presented.

Inclusion criteria:

- Institutionalized patient in the Gastroenterology and Hepatology Institute of Iasi with gastric stump cancer as the final discharge diagnosis

- Patients with previous surgical interventions like subtotal gastrectomy, irrespective of the operative indication that the diagnosis was based on

- The presence of all the medical, biological and imagistic data that we have quantified in order to evaluate the patient with gastric stump cancer, according to the established protocol

- Minimum age of 18 years old

Exclusion criteria:

- Patients who have been initially operated in another medical unit and whose medical records (MR) did not contain precise evidence of the therapeutic attitude and/or of the preoperative imagistic assessment with a view to a stadialization as accurate as possible.

- Patients with gastric pathology who were operated without having suffered a gastric resection or who have suffered a total gastric resection.

- Patients who did not have a precise record of all the clinic, biological and imagistic data that we have quantified along our research and our activity.

On the basis of these criteria we have identified a number of 52 patients who were our sample group.

The assessment of the data included in the study was performed on the basis of demographic, anamnestic, clinic, biological and imagistic data contained in the medical records. The evaluation was completed with data from the anatomopathological exam containing information regarding the microscopic features of the tumoral segments resulted from the endoscopic biopsy.

Results

Regarding the structure of the general lot, based on gender, the male subjects have a larger percentage (37 male subjects), compared with the female subjects (15 subjects).

The age range for the subjects varies from 35 to 84 years old, having an average of

65.6 years. After an analysis by gender comparison, it could be observed that there is a minimum age for the onset of cancer by gastric blunt - 48 for female subjects, respectively 35 for the male subjects. The maximum age for the female lot was 84 years old, while for male 81 years old. (Table 1)

	General	Female	Male
Sample size	52	15	37
Lowest value	<u>35</u>	<u>48</u>	<u>35</u>
Highest value	<u>84</u>	<u>84</u>	<u>81</u>
Arithmetic mean	65,5000	65,6667	65,4324
95% CI for the mean	62,667 to 68,332	60,393 to 70,939	61,913 to 68,950
Median	65,50	66,00	65,00
95% CI for the median	63,465 to 70,068	61,529 to 70,470	62,077 to 71,000
Variance	103,5098	90,6667	111,3634
Standard deviation	10,174	9,521	10,552
Relative standard deviation	0,1553 (15,53%)	0,1450 (14,50%)	0,1613 (16,13%)
Standard error of the mean	1,4109	2,4585	1,7349

Table 1 - Statistical data on patient age

The analysis in graph Figure 1 highlights two points outside the area in which the data values are considered to be statistically accurate. These two points are determined by the male subjects having an age range between 35, respectively 41 years. The remaining male subjects have an age varying between the interval of 45-81 years.

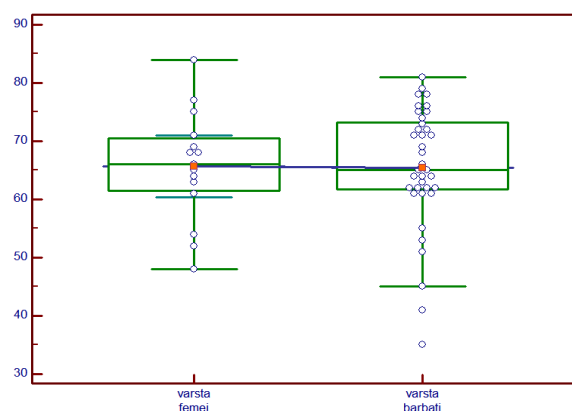


Figure 1 - Comparison of statistical data on age by gender

Among the hospitalization reasons recorded in the observation sheets, we have identified a number of symptoms, predominantly oriented diagnosis and need for hospitalization of the patients in the gastroenterology service where the study was conducted. The most frequent and dominant symptom was the abdominal pain, located in the epigastrium, for 16 of the patients (this representing 30.76 from the total number of patients). Of the 12 patients – representing 23.07% - having deglutition pain, 11 (representing 21.15%) presented dysphagia as the dominant symptom (Figure 2). Besides, although a majority number of patients (37 cases, representing 71.15%) accused nausea at the time of admission, the symptoms were not able to dominate the clinical picture of the patients, this not being considered for anyone a dominant symptom.

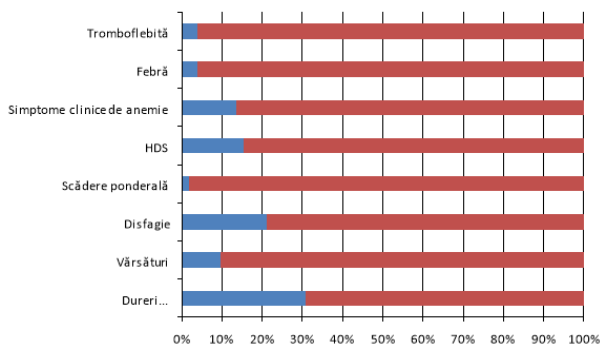


Figure 2 - Distribution of the dominant symptom

The physical exam, conducted at the time of the diagnosis and recorded in the observation sheets, detected wanness for the majority of patients (47 cases, representing 90.38%), weight deficit (45 cases, accounting for 86.53%) and abdominal pain on palpation, mainly in the epigastrium (41 cases, accounting 78.94%). The hepatomegaly was identified in a total of 12 clinical patients, accounting for 23.07%, and the ascites fluid could be detected in 8 patients, accounting for 15.38% (Figure 3).

Examination by EDS was followed to all patients by harvesting of a biopsy for diagnosis. The result of the pathological fragments biopsy revealed a total of 27 cases (representing 51.92%) for which the diagnosis was adenocarcinoma. In 10 cases (representing 19.23%) the tumor formation was classified histologically as undifferentiated carcinoma, so that seven cases (accounting for 13.46%) were cell carcinoma in signet ring. Anaplastic

carcinoma was found in five cases (representing 9.61%) and colloid carcinoma in 3 patients (representing 5.76%) (Figure 4).

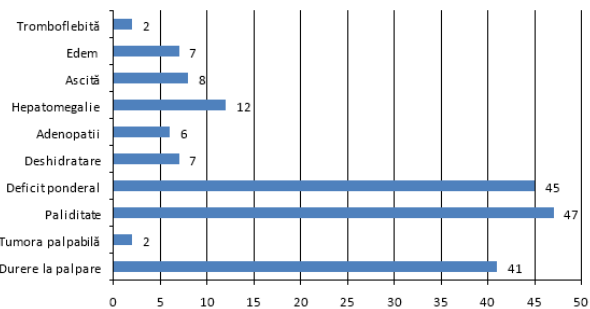


Figure 3 - Distribution for the elements detectable on physical examination

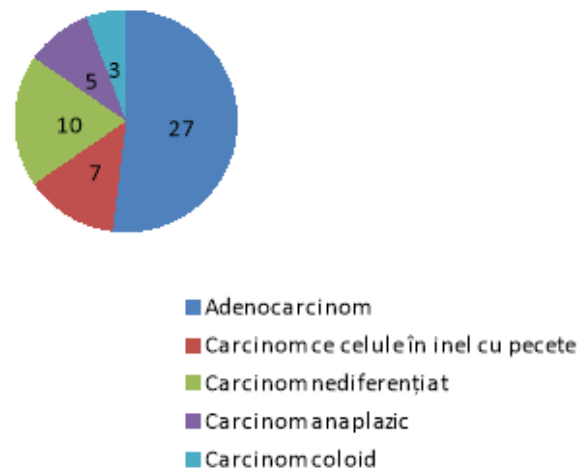


Figure 4 - Distribution of patients according to the histological type of tumor formation, detected by the endoscopic biopsy exam

In the study group, we did not identify patients showing stages 0, IA respectively. Of all stages identified, the highest frequency was for stage IV, for a total of 12 patients (representing 31.57% of the patients who underwent CT) and the lowest frequency was for stage IB - a patient (representing 2.63%). Stage IIIB was found in 10 patients (representing 26.31%) and stage IIIA in a total of 6 patients (representing 15.78%) (Figure. 5).

In order to identify which elements are most relevant to the clinical diagnosis of stage orientation in the absence of a control group, we considered making correlations between clinical elements and the imaging staging of the tumor formation. Thus we identified statistically significant correlations for three parameters of objective clinical examination, ie, hepatomegaly, ascites, and the presence of lymph nodes.

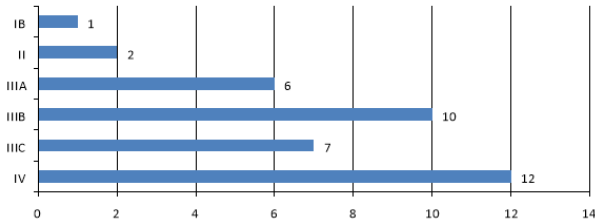
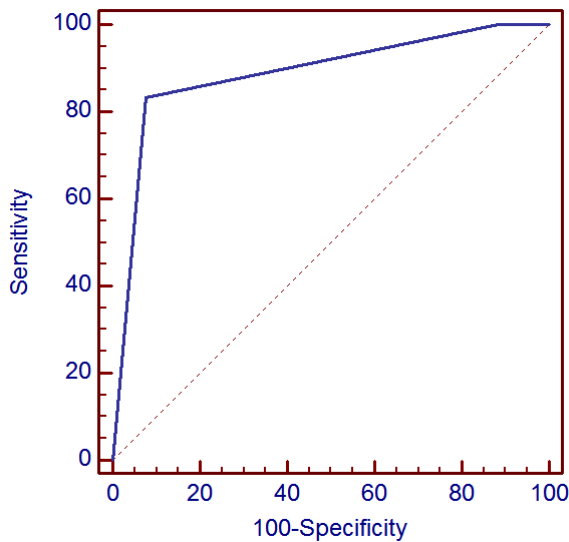


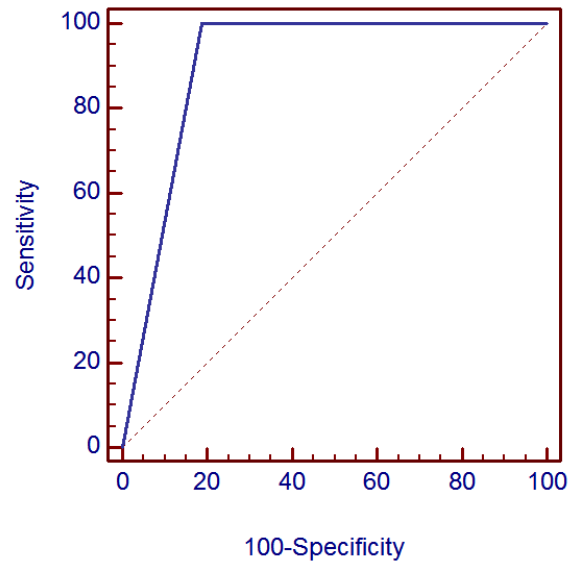
Figure 5 - Distribution of patients according to the stage neoplasia established after examination by CT

Hepatomegaly represented a marker of poor outcome of the neoplastic disease in the group of patients who entered the study. The presence of objective clinical examination after this sign was statistically correlated with neoplastic stage IV, a stage with remote metastases. This correlation was demonstrated statistically by creating the ROC curve and calculating the area under its graph, which highlighted a value of 0.888 (Figure 6).



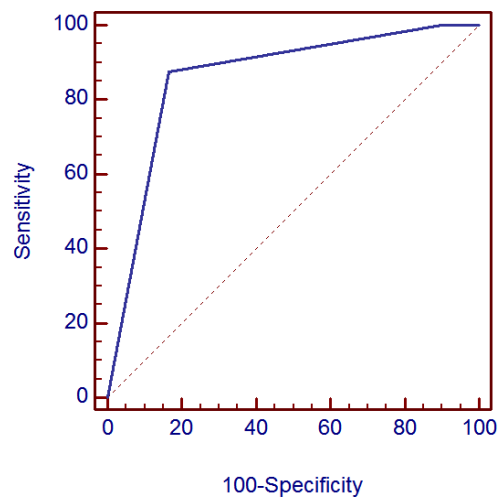
Area under the ROC curve (AUC)	0.888
Standard Error ^a	0.0569
95% Confidence interval ^b	0.743 to 0.967
z statistic	6.815
Significance level P (Area=0.5)	<0.0001

Figure 6 - Statistical correlation between hepatomegaly and staging imaging



Area under the ROC curve (AUC)	0.906
Standard Error ^a	0.0351
95% Confidence interval ^b	0.767 to 0.976
z statistic	11.590
Significance level P (Area=0.5)	<0.0001

Fig. 7 - Statistical correlation between the presence of lymph nodes and staging imaging



Area under the ROC curve (AUC)	0.860
Standard Error ^a	0.0664
95% Confidence interval ^b	0.709 to 0.951
z statistic	5.428
Significance level P (Area=0.5)	<0.0001

Figure 8 - Statistical correlation between ascites and staging imaging

The lymphadenopathies, identified during clinical examination performed at admission, were another negative marker for the evolution of pathology, which was the subject of our study. Thus, we obtained a value of 0.906 area under the ROC curve graph, which was carried out taking into account the presence of lymphadenopathy identified on physical examination and the tumor stage. More specifically, the correlation was determined reported to the stage IV (Figure 7).

Ascites, objectified during the physical exam and confirmed in most cases by imaging investigations, in our study represented an indicator of the presence of metastases in patients with CBG. The correlation between ascites and tumor stage IV was imagistically determined and highlighted by obtaining the ROC curve, which showed an area of 0.860 under its graphic representation (Figure 8).

Discussions

Regarding the gender structure of the lot, we found a preponderance of over 70% of the male gender. This is explained primarily by the increased incidence of ulcer disease in men, which was the basis for the indication of the initial gastric resection. Our finding is consistent with the literature, where we have identified a higher frequency in men than in women of 4 to 9 times, respectively Ovaska et al. study [2], where the ratio was 36: 1.

The average age of patients with CGB was 65.5 years, with values in the range 60-80 years. Advanced age at time of diagnosis is due to the fact that most of the patients undergoing surgical cure ulcer require a considerable number of years after the onset of ulcer disease until surgery. Also, the period required from the partial gastric resection until the onset of CGB is higher than 15 years [3], which leads to the diagnosis of neoplastic disease at older ages. Our results are consistent with the literature: in the study of Inom et al. [4] at the time of diagnosis of CBG patients were aged over 60 years, with a mean age between 67-71 years.

Since most patients had multiple symptoms at admission, we considered useful to assess the dominant symptom. Following this assessment, the most common symptom was

abdominal pain, epigastric location (30.76%), followed by swallowing disorders (23.07%), our findings being consistent with the speciality literature [5]. This is explained on the one hand due to tumor growth in a reduced gastric volume and on the other hand due to the proximity to the celiac plexus and rapid invasion of the cardia, generating dysphagia.

Pathological results showed adenocarcinoma in over half the cases, the remainder being undifferentiated cancers of various types (cell carcinoma signet ring, anaplastic carcinoma, colloid). We had not enough data for comparison, but the high share of undifferentiated forms largely explains the aggressive nature of the tumor invasion and the rapid metastasis.

To draw attention to the need of a thorough medical history and of a complete and correct physical examination, we conducted statistical correlations between elements of these two clinical entities and the imaging elements which confirm the diagnosis.

Hepatomegaly detected clinically was correlated with the presence of metastases at CT and with stage IV tumor respectively, a correlation demonstrated by the area under the ROC curve of 0.888 chart.

Adenopathies were also correlated with stage IV tumors (AUC = 0.906), and ascites was correlated with the same stage (stage IV, peritoneal carcinoma) (AUC = 0.860).

Conclusion

There were sure correlations which were identified between the presence of hepatomegaly, ascites and lymph nodes with stage IV, and this leads us to affirm that any patient with history for gastric surgery showing these target signs, should be suspected of the presence of a malignancy gastric stump in an advanced stage and investigated accordingly with this suspicion.

References

- [1]P. Morgagni, A. Gardini, D. Marrelli, V. Giovanni, A. Marchet, G. de Manzoni, M. A. Di Cosmo, G. M. Rossi, D. Garcea, and F. Roviello,

“Gastric stump carcinoma after distal subtotal gastrectomy for early gastric cancer: experience of 541 patients with long-term follow-up,” *Am. J. Surg.*, vol. 209, no. 6, pp. 1063–8, 2015.

[2] J. Ovaska, T. Havia, and H. Kujari, “Retrospective analysis of gastric stump carcinoma patients treated during 1946-1981,” *Acta Chir Scand* 1986, vol. 152, pp. 199–204, 1986.

[3] N. Tanigawa, E. Nomura, S.-W. Lee, M. Kaminishi, M. Sugiyama, T. Aikou, and M. Kitajima, “Current state of gastric stump carcinoma in Japan: based on the results of a nationwide

survey.,” *World J. Surg.*, vol. 34, no. 7, pp. 1540–7, 2010.

[4] M. Inomata, N. Shiraishi, and Y. Adachi, “Gastric remnant cancer compared with primary proximal gastric cancer,” *Hepatogastroenterology*, vol. 50, pp. 587–591, 2003.

[5] A. Di Leo, C. Pedrazzani, M. Bencivenga, and A. Coniglio, “Gastric stump cancer after distal gastrectomy for benign disease: clinicopathological features and surgical outcomes,” *Ann Surg Oncol.*, vol. 21, pp. 2594–2600, 2014.