

UNIVERSITY OF MEDICINE AND PHARMACY OF CRAIOVA

SUMMARY OF THE DOCTORAL THESIS

**THE ROLE AND PLACE OF STAGING LAPAROSCOPY IN
GASTRIC CANCER**

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THE ROLE AND PLACE OF STAGING LAPAROSCOPY IN GASTRIC CANCER

Key words: epidemiological study, gastric cancer, diagnostic laparoscopy, peritoneal cytology.

The present paper is divided in two parts: the general part (the current stage of knowledge) and the special part (the personal contribution).

In the first part, of 49 pages, we present the theoretical part of the current aspects regarding the gastric cancer epidemiology, the clinical background, the natural evolution and prognostic factors, the iconic diagnose and the iconic investigations of the staging strategy, the chirurgical and non-chirurgical treatment.

The special part, of over 160 pages, is allocated to the personal investigation in which we research the “Role and place of laparoscopy in staging the gastric cancer”.

Introduction

The gastric cancer staging, as well as the one of other cancers with different localizations, represent the key-point in the strategy of treatment of patients suffering from this disease. The disease staging aids establishing the treatment algorithm, which concurrently delineates the patient’s prognostic.

Goal

The present study proposes the investigation of the role of intraoperative laparoscopy in the completion and correction of the staging and the gastric cancer’s diagnostic, compared to the traditional preoperative techniques used for determining the staging, in order to entail a proper therapeutic conduit.

Specific objectives

1. To extend the knowledge regarding the epidemiologic and clinical-pathological factors which intervene in the stomach's tumorigenesis

2. To identify the role of laparoscopy in the detection of tumor infiltration of gastric serosa, as well as of the T₃, in order to orient certain patients towards neoadjuvant therapy protocols;

3. To master the role of laparoscopy in the detection of distant tumoral spread, which have not been highlighted or cannot be highlighted by the conventional preoperative investigations, a fact which can reduce the number of needless laparotomies, as well as their associate mortality and morbidity.

4. To evaluate the role of laparoscopy in the detection of metastatic adenopathies in order to direct these patients towards other treatment methods.

5. To establish the role of laparoscopy in the correct evaluation of the resectability of the local advanced gastric cancer in order to reduce to zero the exploratory laparotomies.

Working hypothesis

1. The gastric cancer prognostic is tightly related to the tumoral stage at the time of diagnostic.

2. The pre-therapeutic evaluation performed with standard techniques can be sometimes inexact, leading to unnecessary laparotomies.

3. A proper preoperative staging represents an important aspect in establishing the ulterior treatment protocol for the patient.

4. Laparoscopy can improve the accuracy of the staging process.

Material and methods

Studied material

In order to attain the previously mentioned objectives, I have conducted an analytical, retrospective study regarding the role of diagnostic laparoscopy in the completion of gastric cancer staging for the patients who present an apparently localized gastric cancer, diagnosed by endoscopic confirmed by histopathologic examination of the biopsy sample as gastric

adenocarcinoma, hospitalized between 2008-2012 in the Clinical Surgery I of the Emergency Clinical County Hospital Craiova.

The study had a base of 190 patients.

The criteria of inclusion in the study were: endoscopic exploration together with the biopsy and histopathologic diagnosis of adenocarcinoma.

The criteria of exclusion from the study were: the patient's refusal to comply with the investigation algorithm and contraindications in applying different stages of the investigation algorithm.

On the main group (190 patients) I have studied the epidemiological, clinical and pathological factors which intervene more frequently in the stomach tumorigenesis.

The main group has been subsequently divided into the following sub-lots:

The sub-group formed out of 76 patients who were excluded in the beginning of our study, after preoperative evaluation (abdominal ultrasound exam, pulmonary radiological exam, echo-endoscopy exam, computer tomography exam). In the first phase, these patients underwent a primary laparotomy.

The sub-group formed out of 114 patients who were initially eligible for a curative gastrectomy, patients for whom the preoperative iconic complex evaluation revealed a localized gastric tumor, apparently without any distant spread and for whom the anamnesis didn't indicate previous surgeries which could cause aderenial syndromes and therefore counterindicate a laparoscopy. These patients had indication for diagnostic laparoscopy.

Out of the sub-group of 114 patients initially eligible for a curative gastrectomy, two comparable sub-groups were selected randomly. Group I was formed out of 52 patients who, before the programmed laparotomy for radical surgery, undertook a diagnostic, exploratory laparoscopy, which, through the video-inspection of the whole peritoneal cavity, confirmed the presence of the tumor and added new elements to the preoperative diagnosis and staging of gastric cancer. The second group, was formed out of the 62 patients who might have undertaken the laparoscopy according to the previous iconic examinations but who were not included in the study since the laparotomy was not preceded by the diagnostic laparoscopy for these patients, because of the above-mentioned motives. Therefore, the results of diagnostic laparoscopy and laparotomy could be compared.

According to the morphological exploration, the primary group was divided into the following sub-groups. A subgroup of 98 patients who undertook a upper GI contrast barium study, a subgroup of 89 patients who undertook an endoscopic ultrasound examination, a subgroup of 57 patients who undertook an abdominal ultrasound examination, a group of 15 patients who undertook a pulmonary x-ray and a subgroup of 89 patients who undertook a CT-scan.

Research methods

In a first phase, I have analyzed the clinical evaluation of the patients from the primary group, considering the following interest parameters: epidemiological data [age, sex, origin, profession, risk factors: heredo-collateral antecedents (neoplastic diseases in the family), personal antecedents (pre-cancerous gastric lesions, local factors), life and work conditions], symptomatology (ulcerous dyspepsia, epigastric pain, weight loss, asthenia and fatigability, diminished appetite, etc.), clinical exam and paraclinical data.

Thenceforth, I have followed the anatomopathological and gastric cancer characteristics (localization of the lesion at the stomach through an endoscopic evaluation, the macroscopic aspect evaluated endoscopically, the invasion of the gastric wall evaluated by abdominal ultrasound, the sentinel lymphnode evaluated by ultrasound, local and regional tumoral extension evaluated through a CT-scan) in all 190 patients from the study.

In order to establish the reliability of the laparoscopical exploration regarding the appreciation of the local possible size and serous gastric infiltration, the hepatic metastasis and the presence of peritoneal carcinomatosis (metastasis), the presence of sentinel lymphnode seeding and gastric tumor resectability I have followed these diagnostic criteria when performing the laparoscopy as a first phase of an elective radical resection for the patients with gastric cancer from the group I (52 patients).

I have used the following investigation techniques: histopathological exam; laparoscopic surgical technique; frozen section; working protocol of the cytology from the lavage liquid.

Results

This chapter contains the results obtained from the investigations of our groups.

When studying the epidemiological data of gastric cancer, I took into consideration the following variables, for the 190 patients hospitalized in the Surgical Clinic I of the Emergency

County Hospital Craiova: study period, age group, sex, origin, professional status, blood type, heredo-collateral antecedents, personal pathological antecedents, life conditions.

When studying the clinical data and anatomopathological characteristics of the gastric cancer, I considered the following indicators: signs and symptoms of gastric cancer, results of the laboratory investigations in gastric cancer. The morphologic aspects of the gastric cancer were evaluated through: radiology, endoscopic-ultrasound, endoscopy, CT-scan.

The role of laparoscopy in staging gastric cancer was studied on 52 patients, following as standard criteria for the reliability of the laparoscopic exploration the following diagnostic aspects: infiltration of gastric serosa, distant spread of the disease, not highlighted by conventional preoperative investigations (peritoneal carcinomatosis and liver metastasis), the presence of metastatic lymphnodes and the evaluation of the resectability. I have also investigated the role of the cytology of the peritoneal lavage fluid which was sampled through laparoscopy.

For the group I and II I have evaluated the complications of laparoscopy/laparotomy, the treatment methods and cost that a laparotomy demands, compared to laparoscopy.

Discussions

The results were analyzed and compared with the results indicated by other authors in similar studies from the specialized literature.

Conclusions

The study was performed from 2008 to 2012; it included 190 patients and allowed the following observations:

1. During the study, the gastric adenocarcinoma incidence at the Surgical Clinic I of the Emergency County Hospital Craiova was 22.1⁰/0000.
2. The patients presented an average diagnostic age of 64.8 years, affected men were younger than women, the average age was 64.22 years for men and 66.34 years for women, and the men/women ratio was 2/1.
3. The majority of patients with gastric cancer came from rural area (54.7%).
4. The most affected socio-professional category is represented by seniors and retired (79.0%).
5. The gastric neoplasm's etiology is still considered plurifactorial. The cancerous disease was present in the families of 22,6% of the cases, which suggests the implication of the genetic factor in the disease's etiology ("family aggregation of the

- cancerous disease”), without knowing the involved mechanism yet. The disease’s high incidence among patients with A (II) blood type (53.2%) also pleads for a possible implication of the genetic factor in the occurrence of the gastric neoplasma.
6. A considerable number of cases from our group (54.2%) had personal precancerous lesions with the predominance of gastric benign ulcer (25.8%), chronic atrophic gastritis with present HP (12.1%), gastric ulcer operated more than 20 years ago (8.9%) and adenomatous polyposis with adenomatous polypus of over 2 cm.
 7. I have observed an statistically significant association between the blood groups and the antecedents of neoplastic disease of the digestive tube in the patients’ families.
 8. The role of the alimentary factor in the gastric cancer’s etiology was suggested by the observation that an important numbers of patients had consumed mostly pro-carcinogen aliments, rich in salt or preserved through salting and curing, aliments poor in fibers (70.5%). I have also observed the role of alcohol consumption and smoking, as a possible factor involved in the etiology of gastric cancer, since 78.9% had consumed alcohol or had smoked.
 9. I have also observed, as a characteristic, the low degree of subjective symptoms, and just discrete dyspeptic phenomena of ulcer or gastritis in the stadiums I and II (10.5%) as well as the presence of the following subjective symptoms in the advanced, III and IV stadiums: epigastric pains and weight loss (80.5% and 62.6%), asthenia (43.7%), nauseas and vomit (18.4%), dysphagia (15.8%), altered general condition (12.1%), and the clinical, objective exam revealed: hepatomegaly (12.6%), palpable tumor in the epigastrium (10.0%), icterus and sclerodermic pallor (9.5% and 74.2%).
 10. Among the biochemical examinations currently made, the following were modified significantly: blood sedimentation rate in 88.9% of the cases, alkaline phosphatase and the GT gamma (32.6% and 26.8%) and the carcino-embryonary antigen which were increased in 61.1% of the cases.
 11. The upper gastrointestinal barium examination performed with an adequate technique (balanced compression or double contrast), using a high-density barium, had a radiological diagnostic output of 53.1%, the correspondance degree between the radiological exam and endoscopy was 90.3%; these two examples completed each other.

12. Endoscopy and radiologic examination helped discovery of the gastric neoplasm in stage I and II for 35 cases (18.4%), in stage III for 100 cases (52.7%) and in stage IV for 55 cases (28.8%).
13. Upper gastrointestinal endoscopy allowed tumor localization, assessing of dimensions and anatomopathological evaluation of the tumor:
 - tumor involved the pyloric antrum area in 34.7% of the cases, the small gastric curvature in 27.4%, the gastric body and greater curvature in 16.8% and the esogastric junction in 13.2%.
 - a diameter smaller than 5 cm was observed in 58.9% of the cases and a diameter equal or larger than 5 cm in 41.1% of the cases.
 - according to the Borrmann classification, the ulcero-infiltrative type was predominant (35.8%), according to the OMS classification the predominant type was the tubular carcinoma (40.5%), and according to the Lauren classification the diffuse type was the predominant type (62.1%).
 - well established forms were encountered in 38.8% of the cases, averagely established forms in 27.9% of the cases, frailly established forms in 21.1% of the cases and unestablished forms in 12.6% of the cases.
14. I have indentified a highly significant association between the gastric adenocarcinoma types according to Lauren classification and the histopathological grading.
15. When elaboration the tumor's gravity, endoscopic ultrasound had a diagnostic impact in 65.2% of the cases, and related to highlighting the regional lymphnode spread, it had an impact in 31.4% of the patients. When considering these 2 parameters, the endoscopic ultrasound proved to be inferior to the laparoscopy.
16. The abdominal ultrasound exam registered positive results in 63.2% of the cases, in 50.9% of the cases it has identified correctly the livermetastasis. In 7.0% of the peritoneal metastasis and 5.3% of the metastatic lymphnodes the abdominal ultrasound exam value was proved in the discovery of hepatic metastasis.
17. The CT-scan exam had a diagnostic impact in 55.3% of the patients, by identifying accurately the peritoneal metastasis in 9.2% of the patients, the liver metastasis in 40.8% of the patients and lymphnodes metastasis in 5.3% of the patients. Although it had a significant contribution when establishing the TNM staging, it didn't prove to be the most appropriate method in appreciating the peritoneal and lymphatic spread.

18. The laparoscopy has correctly detected the serous invasion on the gastric wall, as well as the T₃ stage in 86.5% of the cases, which proved its superiority next to CT, from this point of view.

19. An important role of diagnostic laparoscopy was observed in the deceleration detection of distant neoplastic spread, in a percent of 87.5% (92.3% for peritoneal carcinomatosis and 66.7% in the identification of liver metastasis), therefore modifying the treatment strategy in those cases and avoiding an useless laparotomy, which would have significantly increased the degree of morbidity and mortality associated to those particular cases.

20. Laparoscopy was also useful in identifying the lymphnode metastasis, the technique's limitations came from the difficulty of evaluating correctly the adenopathies of the IInd and IIIrd stage.

21. The use of diagnostic laparoscopy has managed to avoid useless laparotomies in 86.2% of the patients with primary localized neoplasm, through a correct appreciation of the resectability.

22. Diagnostic laparoscopy has staged correctly 85.2% of the cases, 14.8% have been sub-staged and any over-staged case, therefore presenting a positive predictive value of 62.5% in detection of Ist and IInd stage, 87.5% in detection of IIIrd stage and 100% in the IVth stage.

23. A re-staging of 44.2% of the cases occurred, 2% with an inferior staging and 42.2% with superior staging; therefore, the diagnostic laparoscopy had also an impact in changing the previously established management of the cases.

24. If the patients from the group II, which did not present any significant change regarding their age, sex and anatomopathological tumoral characteristics from the patients from the group I, would not have refused the diagnostic laparoscopy and would undertake the laparoscopy as a first step of the intervention, while the paraclinical examinations would have allowed it, the laparotomy could have been avoided in 40.3% of the cases, where it proved to be useful only for exploration purposes.

25. The cytological exam of the peritoneal lavage liquid made during laparoscopy for 90.4% of the patients highlighted positive results in 40.4% of the cases, which were quantified as maximum-risk cases for an ulterior development of peritoneal relapses.

26. The laparoscopy procedure didn't register any sort of events, any complications related to it, compared to the exploratory laparotomy which had registered a 11.3% morbidity.

27. From the group I, 69.2% of the patients undertook palliative chemotherapy, whereas 66.5% of the cases from the lot II had an indication for the palliative chemotherapy.

28. I observed, in term of medical care costs (daily hospitalization, drugs, sanitary materials, laboratory investigations, other investigations), and average hospital length of stay, the superiority of the diagnostic laparoscopy compared to the exploratory laparotomy.

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3. **C.L.PĂTRU**, V. ȘURLIN, I. GEORGESCU, EMILIA PĂTRU, D. ALEXANDRU- Epidemiology approach and clinical-pathological features of gastric cancer in the I Surgical Clinic of the county emergency Clinical Hospital of Craiova. Current Health Sciences Journal. Volume 39/2013, suppl. 8, p. 33-39, ISSN 2069-4032.

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