THE STUDY OF RISK FACTORS AND THE CONTRIBUTIONS OF IMAGISTIC EXPLORATIONS IN DIAGNOSIS AND STAGING ESOPHAGEAL CANCER

ABSTRACT

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INTRODUCTION

The esophageal cancer represents the eight most common cancer worldwide and the sixth leading cause of death from cancer, being one of the four cancers with the most unfavourable prognosis, along with the hepatic, pancreatic and lung cancers. The epidemiology of the esophageal carcinoma has changed significantly in the last decades worldwide, the most common forms of esophageal cancer being represented by the squamous-cell carcinoma and the esophageal adenocarcinoma.

PURPOSE AND OBJECTIVES

The purpose of this research is to demonstrate the increased incidence of the esophageal cancer, under the action of various risk factors (alcohol – smoking and obesity – gastroesophageal reflux disease – Barrett’s esophagus).

The objectives of this study consist of:

1. Demographic study of the patients with esophageal neoplasm, diagnosed during 2006-2010;
2. Assessment of risk factors implied in the appearance of esophageal cancer (smoking, alcohol, obesity, GERD, BE);
3. Assessment of the ratio squamous cell carcinoma/ esophageal adenocarcinoma, as well as the risk factors linking the two histological types of cancer;
4. Assessment of the imaging aspects used in esophageal cancer diagnosis and staging;
5. Assessment of esophageal cancer patients’ survival.
MATERIAL AND METHODS

The study has been conducted in the Gastroenterology Clinic of the UMF Craiova, the Gastroenterology and Hepatology Research Centre of Craiova, between 2006-december 2010. During this period of time, there have been included in the study 143 patients endoscopically diagnosed and histopathologically confirmed with esophageal cancer, to whom thoroughly demographic, clinical and imagistic studies have been conducted.

DISCUSSIONS AND INTERPRETATION OF RESULTS

**General clinical data**

The esophageal cancer has been obviously more common in men, with a men/female ratio of 4.1.

Out of the total number of 143 patients, 79 patients came from the urban area while 63 patients came from the rural area.

The rage of the dispersion age was between 29 and 87 years old, the age of the youngest patient and the age of the oldest one.

From the main group two subgroups were individualized, according to the histopathological form: subgroup I comprising 85 patients with squamous cell carcinoma (59.44%) and subgroup II consists of 58 patients with adenocarcinoma (40.56%), with a ratio of 1.46 / 1 in favor of esophageal squamous cell carcinoma.

**Demographic and risk factors study in subgroup I**

Subgroup I consisted of 85 patients histopathologically confirmed with squamous cell esophageal carcinoma, with a male / female ratio of 4/1.

Patient distribution according to the area of origin showed a slight predominance of the urban area, with an urban / rural area ratio of 1.3 / 1.

According to the placement under the age of squamous cell esophageal cancer patients, the highest frequency of cases was found between 50-69 years.

Out of the 85 patients 63 patients (74.12%) were smokers, with a smoking / non-smoking ratio of 2.86 / 1.

The esophageal consumption of alcohol was noticed in 60 patients, with a ratio of consumers of alcohol / non-consumers of 2.4 / 1.

The combined analysis regarding smoking and alcohol consumption in patients with esophageal squamous cell carcinoma showed that over 55% of men recognized the simultaneous presence of both risk factors, whereas for women the percentage being of only 17.65%, which shows a statistically significant difference of the distribution of the two factors among patients of this group (p = 0.0467).

The analysis of body mass index of patients belonging to subgroup I showed that 50 patients had BMI below 25 kg/ m², (39 men and 11 women), 28 patients were overweight with a BMI between 25 - 30 kg / m², (22 men and 6 women), only 7 patients presenting BMI above 30 kg/ m², all patients within the obese category were men.

The abdominal circumference measurement showed that out of the 68 men 23 had values greater than 94 cm, and out of the women 10 were above 80 cm.

The study prevalence of specific symptoms of gastroesophageal reflux disease revealed that only 13 patients of subgroup I, 11 men and 2 women had symptoms for GERD.

Among the risk factors involved in esophageal squamous cell cancer appearance, our study also included one patient to whom was mentioned in his medical history, the
accidental ingestion of caustic soda, 22 years ago, and a patient who performed radiotherapy for right breast neoplasm 16 years ago.

No patient with esophageal squamous cell carcinoma has been diagnosed with Barrett's esophagus.

**Demographic and risk factors study in subgroup II**

The demographic analysis of subgroup II of 58 patients with esophageal adenocarcinoma showed male predominance, with a male / female ratio of 4.27 / 1.

Patient distribution according to area of origin showed a slight predominance of the urban area, with an urban / rural area ratio of 1.3 / 1.

The maximum age of patients was of 87 years and the minimum age of 29 years, both extremes being male patients belonging to the urban area.

In terms of smoking statistics of patients belonging to subgroup II showed that 30 patients were smokers and 28 patients were non-smokers.

The alcohol consumption in patients with esophageal adenocarcinoma was noticed in 31 of the patients, with a ratio of consumers of alcohol / non-consumers of 1.14.

Correlating the two risk factors, smoking and alcohol, according to the gender of the patients with esophageal adenocarcinoma, revealed that only 31.91% of men smoked and drank alcohol and no female patient admitted the presence of both faults, the difference being statistically significant (p = 0.0086).

The analysis of body mass index of patients belonging to subgroup II showed that 18 patients had BMI below 25 kg/ m², (12 men and 6 women), 24 patients were overweight with a BMI between 25 - 30 kg / m², (20 men and 4 women), 16 patients with BMI above 30 kg/ m², 15 men and one woman.

The abdominal circumference measurement showed that from the 47 men diagnosed with esophageal adenocarcinoma, 31 had values greater than 94 cm at the waist level and nine women were above 80 cm at the waist level.

The specific symptoms of gastroesophageal reflux disease were present in 45% of the patients belonging to the subgroup II, the patients presenting a medical history of heartburn, acid regurgitation, retrosternal pain, impaired quality of sleep due to night-time heartburn.

Most of the patients who had symptoms of gastroesophageal reflux were patients with BMI greater than 25 kg/m², 20 men and 2 women, ascertaining a statistically significant difference regarding the distribution of the two parameters within the subgroup II (p = 0.0478).

Assessing Barrett's esophagus presence within patients belonging to subgroup II this was recorded in 8 patients, 5 in the urban area and 3 in the rural area.

The reflux symptoms were present in most patients diagnosed with Barrett's esophagus, 7 of the 8 patients diagnosed or acknowledged with Barrett’s esophagus.

**Group comparison**

During the period of study the number of patients diagnosed with esophageal squamous cell carcinoma was higher than the number of patients with esophageal adenocarcinoma, except in 2007 when the number of patients was equal, with a general ratio squamous cell carcinoma / adenocarcinoma esophageal of 1.46 / 1.

The gender distribution showed the male predominance, the male/female ratio being of 4/1 both for squamous esophageal cancer patients and for patients with esophageal adenocarcinoma, not being noticed statistically significant differences of gender distribution in patients between the two subgroups (p = 0.8783).
As far as the area of origin of patients is concerned, we have noticed the predominance of the urban area both in patients with squamous esophageal cancer and in patients with esophageal adenocarcinoma, with no statistically significant difference of the distribution of patients belonging to the two subgroups according to the area of origin (p = 0.7212).

The comparative analysis of the distribution of patients by age groups, showed that if for the subgroup I, the maximum number of patients was noted in the age group 50-59 years, with 30 patients, for the subgroup II the age group 70-79 years was best represented including 22 patients, being noticed the larger number of patients with esophageal adenocarcinoma compared with that of patients with squamous cell carcinoma at the extremes of age range (p = 0.0530).

The comparative analysis of alcohol consumption in the two subgroups of patients revealed that 70% of the patients with esophageal squamous cell carcinoma have consumed alcohol, compared with 46% of the patients with esophageal adenocarcinoma who admitted the alcohol consumption (p = 0.0038).

Also for smokers, the comparative analysis of the two subgroups showed the predominance of the smoking patients belonging to the subgroup I with esophageal squamous cell carcinoma (p = 0.0058).

The comparative analysis of the association of the two risk factors in patients belonging to the studied subgroups, showed the greater importance of smoking and alcohol consumption in the patients with esophageal squamous cell carcinoma compared to the patients with esophageal adenocarcinoma (p = 0.0002).

Obesity and overweight were better represented in the patients with esophageal adenocarcinoma, over 70% of the patients in subgroup II having a BMI above 25 kg/ m².

The number of patients with elevated abdominal circumference is better represented in the subgroup II, over 68% of the patients with esophageal adenocarcinoma having an increased abdominal circumference, compared to only 39% of the patients with esophageal squamous cell carcinoma.

The comparative analysis of the presence of GERD revealed the fact that the reflux symptoms prevailed in patients belonging to the subgroup II, with a highly statistically significant difference of the distribution of reflux disease between the two subgroups (p = 0.0001).

Barrett’s esophagus was found exclusively in patients belonging to the subgroup II.

**Imagistic study**

*Upper gastrointestinal endoscopy*

The upper gastrointestinal endoscopy, except that it represented the major criterion for inclusion of patients in this study, allowed the evaluation of macroscopic appearance of the lesions and their location.

Most of the examined lesions were classified into one of the four macroscopic aspects of the advanced esophageal cancer forms, except the five cases of early cancer.

**Modern endoscopic techniques**

33 patients received modern endoscopic explorations. 19 patients were explored in a tri-modal way and 14 patients were explored by confocal laser endomicroscopy.

With modern imaging techniques we could reveal the suggestive appearance of malignancy in a number of 4 cases; the histopathological examination confirmed the diagnosis of esophageal squamous cell carcinoma in one case and esophageal.
adenocarcinoma in three cases, two of which were developed on Barrett's mucosa. The presence of Barrett's esophagus adjacent to the tumor was confirmed in four cases.

Eco endoscopic study

In this study, the eco endoscopy allowed the assessment of the esophageal wall invasion level (T), the damage of regional lymph nodes (N) and remote invasion (M). Eco endoscopic examinations were performed in 63 patients.

Computed tomography study

Native thoraco-abdominal CT scan examination and examination with contrast revealed the presence of the tumor, of the loco-regional adenopathies, the invasion of the tumor in adjacent structures and the presence of metastases in a subgroup of 61 patients initially investigated endoscopically.

Ultrasonographic study

The sequential ultrasound examination according to the work protocol, has brought important information on malignant lesion extension both at liver parenchyma level, at serous peritoneal, as well as at the level of the main groups retroperitoneal and laterocervical lymph nodes.

Comparisons between the assessments of TNM stage invasion with imaging techniques

Computed Tomography vs. Eco endoscopy

The comparison of the results of the assessment of various components of TNM invasion score was possible at a group of 40 patients to whom both imaging explorations were performed.

Staging the patients with esophageal cancer

Following the imaging examination staging TNM was performed in 84 patients. As expected, the high percentage of tumors in stages T3 and T4 of invasion, the similar percentage of patients with nodal determinations and the significant percentage of cases with metastases highlighted through imaging, led to the shaping of a majority group of patients who met the criteria for admission into stages III and IV TNM.

Histopathological study

The subgroup analyzed included 143 pieces of biopsies taken endoscopically. Following the histopathological examination 85 results were squamous cell carcinomas and 58 esophageal adenocarcinomas.

Survival of patients with esophageal cancer

The assessment of the survival period in the entire group revealed that out of 143 patients enrolled in the study, only 34 patients were alive at the end of it, the average survival period being of 14 months.

The statistical analysis of survival correlation with patients gender showed an average value of the survival of 3 months higher in women than in men without statistically significant differences between the survival rates for men and for women (p = 0.300).
The analysis of correlation of survival and the area of origin of patients showed that both for the urban and the rural areas, the average survival period was equal, more precisely of 13 months, without significant differences between survival rates for patients in urban areas and those in rural areas (p = 0.650).

The survival analysis according to the smoking status of patients with esophageal malignancy shows a significantly higher average survival of non-smokers, these ones showing a nine-month-longer survival period than smokers, the statistical difference being close to the limit significance (p = 0.053).

Also the survival period of patients who have not consumed alcohol was superior to the survival period of patients consuming alcohol, with an average difference of 6 months.

By correlating the concomitant presence of smoking and alcohol consumption in patients with esophageal cancer, patient survival data to whom were present both risk factors showed a dramatic decrease in the survival, with an average survival period of 6 months, much lower than the survival period of patients who were non-smokers and non-consumers of alcohol.

The Kaplan-Meier curves achievement emphasizes the lower net trajectory of the curve reflecting the survival of patients to whom it was noted the presence of the two risk factors, being noticed a statistically significant difference between the two curves (p = 0.014).

The correlation of the survival period with the presence of gastroesophageal reflux disease did not show a great aspect, the average survival period of patients without GERD being three months longer than the survival period of patients with reflux symptoms.

The Kaplan-Meier curves determination of estimating the survival period according to the presence or the absence of gastroesophageal reflux disease showed a similar appearance of the two curves, without statistically significant differences (p = 0.999).

The correlation of the survival period with the two histological types of cancer showed that patients with esophageal adenocarcinoma had an average survival period twice longer than those ones with squamous cell carcinoma.

The analysis of the survival period correlation in patients with the TNM stage of disease showed a linear regression trend of the values of the average survival period compared with TNM staging, starting from an average survival period of 19 months and reaching a survival period of 5 months.

**CONCLUSIONS**

1. During the period of study the number of patients diagnosed with esophageal squamous cell carcinoma was higher than the number of patients with esophageal adenocarcinoma, with a squamous cell carcinoma/esophageal adenocarcinoma ratio of 1.46/1.
2. Gender distribution of the study group showed an increased incidence of esophageal cancer in male patients, with a ratio male / female of 4/1.
3. The distribution by area of origin showed predominant the urban area, both to the entire group, as well as to the subgroups, with no statistically significant difference regarding the distribution of patients according to the two areas of origin.
4. The age distribution of male patients showed predominant the age groups 50-59 years and 60-69 years for patients diagnosed with esophageal squamous cell carcinoma and the group 70-79 years for those with esophageal adenocarcinoma.
5. The most important risk factors studied for patients with esophageal squamous cell carcinoma were smoking and alcohol consumption, and for those diagnosed with...
esophageal adenocarcinoma were obesity, gastroesophageal reflux disease and Barrett’s esophagus.

6. By using modern endoscopic techniques, the esophageal neoplasms diagnosed at an early stage have increased.

7. The number of patients with Barrett’s esophagus has increased, and this demonstrates that it is underdiagnosed, requiring extensive screening programs to the population at risk.

8. Computed tomography investigation is the examination of choice for remote evaluation of the tumor process.

9. Eco endoscopic exploration is sovereign in determining the invasion degree of the esophageal wall, with a slight tendency to overestimate the lymph nodes damage.

10. Most patients included in the study were diagnosed in advanced stages of disease, with a reduced survival period, the average survival period being of 14 months.

REFERENCES


Personal information

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Work experience

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Teaching staff - Supervise, monitor students individually or in small groups and conduct demonstrations

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Health
**Education and training**

- 2010 Graduated from Master studies, University of Medicine and Pharmacy Craiova
- 2008 - 2010 Master studies in “Management of Health Units”, University of Medicine and Pharmacy Craiova
- 2005 - Internal Medicine specialist
- 2005 – present Doctoral Studies, University of Medicine and Pharmacy Craiova
- 2000 - 2005 Internal Medicine Resident
- 1999 - 2000 Internship, Emergency County Hospital Craiova
- 1998 - Graduated from Faculty of Medicine - University of Medicine and Pharmacy Craiova
- 1992 - 1998 Student at the University of Medicine and Pharmacy Craiova, Faculty of Medicine

**Personal skills and competences**

- 2011 Certificate in “Management of Health Units”
- 2004 Certificate in General Ultrasonography
- 2005 Specialist in Internal Medicine
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**Self-assessment**

- **European level**
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- Social skills and competences
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