THE SURGICAL TREATMENT OF ESOPHAGEAL CANCER. INDICATIONS, COMPARATIVE ANALYSIS OF SURGICAL TECHNIQUES.

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KEY WORDS:

✓ esophageal cancer
✓ surgical treatment
✓ surgical techniques
✓ complications
ACTUAL KNOWLEDGE

The esophagus is the narrowest portion of the digestive system, represented by a muscular pipe that extends from the pharinx to the stomach. It’s function, although seemingly simple - virtually unchanged transport of the food to the stomach - is of huge importance in the alimentation.

Romania has a low incidence of esophageal cancer compared with other countries, with a mortality rate of 1.6 per 100,000 in men and 0.3 per 100,000 women (Zatonski et al., 1996).

More recent data (European Cancer Observatory website, 2008) estimated for Romania 744 annual new cases (incidence rate of 3.1 per hundred thousand inhabitants, for both sexes combined) and 681 annual deaths from cancer of the esophagus (mortality rate of 2.8 per 100,000 population).

There are two major histological types most frequently encountered in esophageal cancer: squamous (epidermoid) and adenocarcinoma.

The main risk factors contributing to the development of esophageal adenocarcinoma, either directly or via GERD - Barrett's esophagus - adenocarcinoma, are: obesity, absence of H. pylori, diet, drugs, smoking and genetic predisposition.

Although most patients with esophageal cancer presents to the doctor for the first time with locally advanced disease, leaving few therapeutic options for radical treatment, many symptoms are present for months in advance and can be revealed by a thorough history.
Clinical diagnosis of esophageal cancer is mainly based on a careful history and examination of the patient. Physical examination is in turn less contributory to the diagnosis, showing only signs of extension of disease: supraclavicular lymph nodes or metastatic hepatomegaly.

Paraclinical diagnosis is based on the following investigations:

- Barium examination
- Computer tomography
- Endoscopy (Esophagoscopy)
- Echoendoscopy (EUS)
- Bronchoscopy
- Abdominal ultrasound
- Positron emission tomography (PET-CT)

For localized esophageal cancer resection surgery remains the gold standard. Were combined various methods of treatment: chemotherapy followed by surgery, radiotherapy followed by surgery, chemotherapy and radiotherapy followed by surgery. It is now mainly used concomitant chemotherapy and radiotherapy followed by surgery.

After assessing resectability, tumor location is the most important factor that decides the way of approach, type of resection and the assembly way after reconstruction.

Esophagectomy is generally practiced for esophageal tumors located in the chest portion of the esophagus.

For thoracic esophageal cancer there are two types of esophagectomy (standard and transhiatal), with several variants of the approach path, depending on tumor location.
Cancers located in the upper third thoracic esophagus can be resected by triple approach (Mc Keown): right posterolateral thoracotomy, laparotomy and left laterocervical incision.

Cancers located in the middle and lower thirds of the thoracic esophagus can be addressed either by transhiatal surgery (laparotomy) or double thoraco-abdominal approach.

Thoraco-abdominal laparoscopic technique was described by Ivor-Lewis (1946) and Tanner (1947). This is the median laparotomy followed by a right posterolateral thoracotomy.

For the lower third tumors and those at the esogastric junction is preferred the approach through left thoracotomy (Adam and Phemister, 1938, Churchill and Sweet, 1942). The incision can be extended and transformed in thoraco-abdominal incision.

Transhiatal esophagectomy has generated since its first description (Turner 1933) multiple controversies, is considered feasible by some or a surgical nonsense by others. The technique was modified by Orringer and Sloan (Orringer 1984).

Extension and thoroughness of limbadenectomy is the key factor that significantly increase the success of esophagectomy for esophageal cancer, contributing to the improved survival and better quality of life.

The esophagus is a less elastic tubular organ so resection of any part of it can not get a simple end-to-end anastomosis as possible in the rest of the digestive tract.

It should therefore be followed almost without exception after esophagectomy a reconstruction of the resected portion. The difficulty of this goal is comparable to performing a duodenopancreatectomy.
The ideal substitute for the esophagus should have many of its features and some additional attributes: to be large enough to carry the food, to have antireflux barrier against aspiration, should not take up much room in the chest, to be easily ascended intrathoracic, to have a sufficient vascularization even after mobilization and to impose as few anastomoses as possible.

There are several options for replacing the esophagus, each with advantages and disadvantages. Not infrequently, however, selection substitution is chosen based on surgeon experience or habit.

The stomach is the first choice for many surgeons for reconstruction due to the multiple advantages of this substitute. In a study published in 2000 on a total of 1874 patients, Huang reported use of stomach in 98.2% cases.

The jejunum can be used as esophageal substitute especially for the lower esophagus due to the length of vascular pedicle that can be mobilized, but also in higher areas as free loop with microvascular anastomosis in the cervical region.

The left colon is a good alternative when the stomach is unavailable due to a preexisting gastric pathology (previous gastric resection, gastric ulcers, caustic strictures) or after a failure of reconstruction with stomach. Unlike the left colon, the right colon is used only in rare cases for esophageal reconstruction.

Are used less often: free graft jejunum, stomach, skin or musculocutaneous flap.

There are 5 ways to place the conduct, each with advantages and disadvantages:

- the posterior mediastinal route (the bed of esophagus)
- the retrosternal way
- the presternal way (subcutaneous)
• the transpleural way
• the endoesophagian way

With the development of laparoscopic and thoracoscopic techniques and instruments appropriate for these procedures, increasingly often minimally invasive techniques are used for esophageal resection and reconstruction, both for benign pathology and esophageal neoplasms. Such procedures are known as Minimal Invasive Esophagectomy (MIE) and began to be practiced 20 years ago.

Surgery for esophageal cancer is challenging both by the complexity of operations and the complications that may be encountered. Getting an appropriate biological status of the patient preoperatively, applying a rigorous anastomotic techniques, avoiding any tension on the anastomosis, providing a well vascularized graft, gentle handling of substitution during surgery, applying a clear re-feeding protocol are the most important factors to reduce the risk of postoperative complications.

The most important prognostic factor in esophageal cancer was found to be the tumor stage at diagnosis. So far the best strategy to improve survival is considered to be early diagnosis.
The statistical study of this work was based on a total of 170 patients admitted and operated on in four surgical clinics in Craiova and Bucharest, with the clinical diagnosis, later confirmed histopathologically, of malignant tumor located in the esophagus.

The four clinics were The Clinics of Surgery I and II of the County Emergency Hospital Craiova, The Clinic of Surgery of Hospital CFR Craiova IV and The Thoracic Surgery Clinic I of The Institute of Pneumology "Marius Nasta" Bucharest.

The period of the study was 5 years (01.06.2005 - 31.05.2010). Of the total number of patients 4 groups were individualized represented by the patients of each of the clinics listed:

• Lot 1, consisting of 31 patients admitted and operated in Surgical Clinic I of Emergency County Hospital of Craiova. (Clinic C1).

• Lot 2, consisting of 54 patients admitted and operated in Surgical Clinic II of Emergency County Hospital of Craiova. (Clinic C2).

• Lot 3, consisting of 30 patients admitted and operated in Surgical Clinic IV of Hospital CFR Craiova. (Clinic C4).

• Lot 4, consisting of 55 patients admitted and operated in Surgical Clinic I of The Institute of Pneumology Thoracic "Marius Nasta" Bucharest. (Clinic B1).

If the demographics and general clinical study was performed on the whole group of patients, for the rest of the analysis (staging, treatment, surgical
technique, complications) studies were limited to cases radically operated in each of the four clinics examined (a total of 105 patients).

We conducted a multicenter, multioperator, allowing the definition of current attitudes in the treatment of esophageal cancer in the Dolj county (and implicitly in the Oltenia region), as a comparison with one of the most active centers of esophageal surgery in Bucharest and the country (Surgical Clinic I of The Institute of Pneumology Thoracic "Marius Nasta" Bucharest).

The study was retrospective, including 170 consecutive cases of esophageal cancer patients diagnosed and operated in the clinics listed above in the period 01.06.2005 - 31.05.2010 and was divided into four chapters:

• Analysis of general data

• Analysis of esophageal tumors operated

• The study of correlations between clinical parameters

• Comparative study of surgical treatment
RESULTS AND DISCUSSIONS

CHAPTER 2. GENERAL CLINICAL DATA ANALYSIS

The first evaluated clinical parameter was the sex ratio distribution. The esophageal cancer was more frequently encountered in men, with a sex ratio of 5.3:1.

<table>
<thead>
<tr>
<th>Sex</th>
<th>Nr. of cases</th>
<th>%</th>
<th>Ratio M/F</th>
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<tbody>
<tr>
<td>Men</td>
<td>143</td>
<td>84</td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>27</td>
<td>16</td>
<td>5.3</td>
</tr>
<tr>
<td>TOTAL</td>
<td>170</td>
<td>100</td>
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</table>

The sex ratio distribution was almost the same for the defined lots, with a male predominance between 4.3 and 6.7.

The patients included were adults in general and mainly older people. The age interval was between 21 years (the youngest patient) and 84 years (the oldest patient).

The age group that included the most patients (71 patients or 42% of cases) was between 61 and 70 years.
Analysing patients by age periods, we found that more than half (56%) were 60 years older, resulting in a mean age of 61 years and an aglomeration interval between 60 and 80 years.

The age periods distribution maintained, in general, for the 4 lots, remarking anyway a bigger proportion of youngest patients in the lot B1.

Analysing the distribution of patients by the environment of origine, we did not pointed out a significant difference between urban and rural areas, noting just a slightly preponderence of rural patients (1.3/1 ratio).

We noted a slight increase tendency of the number of esophageal cancer both for the entire lot and for each of the studied clinics.

We found a balanced distribution of radically operated cases for the 5 years of the study, demonstrating that despite the slightly increase of the number of operated cases, from those patients was not possible to select more for radical surgery due to the advanced stage of disease.

The number of cases operated annually included both radically operations (esophagectomy with reconstruction) and palleative operations (mostly feeding gastrostomy).

We consider that this indicator reflects the best the incidence of esophageal cancer in the 4 clinics.

The esophageal cancer is not one of the most frequent malignancies, being surpassed in terms of incidence by colon, lung, stomach, breast, uterin cervix and prostate cancers.

Even in Romania the incidence of this type of cancer is not important, resulting in a not so big number of radical interventions.
Because of the late diagnosis a relatively small number of patients can be operated radically.

For the entire lot we found that 62% of operations were radical.

Analysing this aspect for each of the studied clinics, we observed that radical operations represented major proportions from the total number of operated cases, ranging from 54% (Clinic C2) and 76% (Clinic B1).

We can affirm so that for every of the above mentioned clinics most of the cases were radically operated, representing a positive issue in the treatment of esophageal cancer.

CHAPTER 3. ANALYSIS OF THE OPERATED TUMORS OF THE ESOPHAGUS

Regarding the tumor site for the entire lot, we found that most of the cancers were situated at the esogastric junction (40 cases or 38%). The next location in our study was the medium third of the thoracic esophagus (28 cases).

Tumor location was different for the 4 Clinics. We noticed a concordance between the specific of each clinics and the site of the operated tumors.

The analysis of histological type of resected tumors showed for the entire lot a relatively balanced distribution between the most common types (adenocarcinoma and squamous carcinoma), with a slight predominence of the first.
For 3 cases we noticed rare types of esophageal cancer (one each of adenosquamous carcinoma, anaplastic poor differentiated carcinoma, signet-ring cell carcinoma).

Regarding the TNM stage distribution of radically operated cases, we observed that most of the cases (96 patients or 91%) were in stages II and III.

<table>
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<tr>
<th>TNM Stage (entire lot)</th>
<th>Nr. of cases</th>
<th>%</th>
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<tbody>
<tr>
<td>Stage IB</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Stage IIA</td>
<td>10</td>
<td>9</td>
</tr>
<tr>
<td>Stage IIB</td>
<td>22</td>
<td>21</td>
</tr>
<tr>
<td>Stage IIIA</td>
<td>24</td>
<td>23</td>
</tr>
<tr>
<td>Stage IIIB</td>
<td>29</td>
<td>28</td>
</tr>
<tr>
<td>Stage IIIC</td>
<td>11</td>
<td>10</td>
</tr>
<tr>
<td>Stage IV</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>TOTAL</td>
<td>105</td>
<td>100</td>
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Studying the TNM stage distribution for each of the clinics, we founded the same medium advanced stage of the most of the cases.

CHAPTER 4. CORRELATIONS BETWEEN CLINICAL PARAMETERS

The comparation between age periods of women and men showed that if for the women the esophageal cancer was almost equal for mature adult and young elder, for the men most of the patients were over 60 years.

Analysing the correlation between the sex and the environment of origine revealed that if for men the number of patients from rural areas is slightly greater
than for urban area, for women the number of patients from rural areas is almost twice than those from urban areas.

Analysis of patient distribution by age in the two areas of origin reveal a higher proportion of patients aged over 65 in rural areas, with a rate of almost 60% of cases, compared to urban areas where the percentage was a little lower, respectively 55.7%.

In our study we found a higher incidence of squamous cell carcinoma in women with a ratio of 1.5:1 to adenocarcinoma.

In men we found a slight predominance of adenocarcinoma, with a ratio of 1,1:1 to squamous cell carcinoma.

Of the few cases found in stage I, two were located in the lower third and one in the upper third of esophagus.

Advanced stages were found in lower areas of the esophagus, of the 6 cases in stage IV two being located in the lower third and 4 at the esogastric junction.

It is known that the majority of squamous carcinomas are found in cranial esophagus while adenocarcinoma in lower positions, near the stomach.

The same tendency of the two histopathological forms we encountered in this study, noting that all of the upper third esophageal cancers were squamous cell carcinomas, their proportion decreased progressively to 88% in the medium third and 54% average in the lower third, and at the esogastric junction adenocarcinoma become the majority (95% of cases).
CHAPTER 5. COMPARATIVE STUDY OF SURGICAL TREATMENT

From the perspective of the surgical approach for esophageal resection and reconstruction, we met a wide range of surgical techniques, which were chosen depending on the tumor location and depending on the experience and preference of each operator.

We found that the most common surgical approach was the double approach (Ivor Lewis) associating median laparotomy and right posterolateral thoracotomy. This type of surgical approach was found in 53 patients (50% of the entire lot).

The explanation is relatively low locations of the tumors, allowing a relatively easy intrathoracic anastomosis best achieved by the right chest and in the popularity of this surgical approach.

The next surgical approach used was the triple approach (Mc Keown) which consisted of median laparotomy, right posterolateral thoracotomy and cervicotomy for anastomosis in the neck. This technique was encountered in 29 patients (28%).

In the light of the esophageal substitute used for reconstruction is evident in the entire group a preference for use of the stomach (72% of cases), consistent with the literature.

The next preference of surgeons for reconstruction was the jejunum (12%), followed by ileocolon and colon (8% each).

Analyzing the esophageal substitute used for reconstruction in each of the four clinics reviewed, we found various preferences but each of these centers preferred the stomach.
For the entire group of patients we noted a preference for placement in the posterior mediastinum due to the simplicity and the anatomic feature of the assembly and because the location of tumors was low enough, requiring most often relatively easy intrathoracic anastomosis.

This way of placing the substitute was used in 80% of cases.

The next path for reconstruction was retrosternal, used in 20 patients. In one case has been used the right transpleural route.

Looking from this perspective, for each one of the clinics studied, we observed the same preference found for the entire group to use the posterior mediastinum as the site of graft placement.

We encountered the following associated maneuvers for the entire group:

- pilorotomy / pyloroplasty - 25 cases
- tactical splenectomy - 19 cases
- feeding jejunostomy - 16 cases
- omentectomy - 4 cases
- liver metastasectomy - 6 cases
- atypical pulmonary resection - 1 case
- ulceroexcision - 1 case

In our study, for the entire lot we encountered the complications represented in the following graph:

Of the 105 cases radically operated included in the study only 16 were alive at its conclusion, at the end of 2010 (ie 15%) which demonstrates that despite aggressive radical treatment, most patients in the study died before its end.
CONCLUSIONS

1. The esophageal cancer is a major health problem because its incidence is increasing and the prognosis remains reserved despite aggressive surgical treatment integrated into a multimodal algorithm.

2. Advanced stage detection due to less obvious symptoms explains the small degree of operability of malignant esophageal tumors.

3. In this study from a total of 170 cases the radical surgery could be done in 105 patients (62%).

4. The esophageal cancer was found 5.3 times more common in men, and the average age of onset was 61 years.

5. The location at the esogastric junction predominated (38% of cases) and the adenocarcinoma histological type had a minimal predominance compared with squamous cell carcinoma (51 cases versus 50).

6. Most of the radically operated cases (91%) were found in stages II and III of the new TNM classification. The very early stages (stage I) and very advanced stages (stage IV) represented only 3% and 6% of cases.

7. The mainly used approach was the double approach (Ivor Lewis), in 50% of cases. The next preference was for the triple Mc Keown approach (28% of cases). We found no case operated by minimally invasive techniques.

8. The stomach was the most used esophageal substitute for reconstruction (72% of cases), followed in smaller proportions by jejunum, colon and ileocolon.
9. The placement path for reconstruction was predominantly the posterior mediastinum (80% of cases) followed by retrosternal route.

10. The most common associated maneuvers during the interventions were pilorotomy / pyloroplasty (25 cases), tactical splenectomy (19 cases), feeding jejunostoma (16 cases), liver metastasectomy (6 cases).

11. The most common postoperative complications were the respiratory ones (pneumonia, atelectasis, ARDS) - 28 cases and anastomotic fistulas (cervical - 15 and intrathoracic - 10 cases).

12. The overall survival was 15 months, with wide variations between 1 month and 46 months. At the end of the study only 16 patients were alive, confirming the discouraging data from literature.

13. Surgery integrated into a multimodal algorithm including chemotherapy and radiotherapy remains the gold standard in the treatment of the cancer of the esophagus.

14. There are a variety of surgical techniques that are applied effectively both worldwide and in Romania to solve complex situations imposed by esophageal tumors.