

REVIEWS

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Regarding the dissertation for awarding the degree of Doctor of Medical Sciences, scientific specialty Obstetrics and Gynaecology, Department of Obstetrics and Gynaecology at the Medical University - Varna.

Dissertation topic: "Invasion of lymph and blood vessels in endometrial endometrioid carcinoma - FIGO stage I"

Author: Assoc. Prof. Dr. Elis Hudaim Ismail, MD, PhD

The dissertation submitted for defense contains: 165 pages, included in it: 33 tables and 20 figures. The bibliography lists a total of 211 titles, of which 3 are in Cyrillic, 3 are internet sources and 199 are in Latin.

Relevance of the problem

Endometrial cancer, as a serious and potentially fatal disease of the female genital organs, annually takes thousands of lives worldwide. This makes us look at it not only as a medical but also as a serious social problem, on whose solution many human destinies would depend. At the heart of his favorable prognosis is his timely diagnosis and therapy.

Endometrial cancer is the 14th most common cancer in the world. According to WHO data in 2012, 320,000 new cases have been globally diagnosed.

According to NRC data published in 2017, the incidence of uterine cancer in 2014 was 8.2% and that of cervical cancer was 7.4%. Endometrial carcinoma (EC) does not rank among the top ten most common causes of death. In the NRC data, uterine cancer as a cause of death in women occurs in the age range 45-59 years with a frequency of 10.1%, remains in the same frequency in the 60-74 years group and decreases to 5.5% in women after 75 years.

Assoc. Prof. Ismail is developing a problem of undeniable relevance, especially for Bulgaria.

The review of the literature clearly shows that the dissertation has thoroughly studied a large number of contemporary literary sources. The review has good cognitive value, describing current methods for biochemical screening, treatment and differentiation of endometrioid endometrial carcinoma. This chapter of the dissertation covers 81 pages.

The purpose of the study was to determine the prognostic significance of tumor invasion in lymphatic and blood vessels in patients with endometrial endometrioid stage I carcinoma by FIGO.

The main tasks are 10 in number, of interest are the first, second, third, fifth, seventh and eighth tasks, namely:

- To determine the overall survival of patients in the study;
- Determine the role of lymph node dissection in relation to overall patient survival;
- To determine the incidence of lymphatic metastases in patients with lymph node dissection;
- Present the disease free survival of patients;
- Determine the survival of patients with relapses after treatment;
- To establish the following histological parameters in the operated patients in the studied contingent: lympho-vascular invasion, depth of myometrial invasion over 1/2, G3 - differentiation of the tumor.

Material and methods

The conducted clinical study is retrospective and is for the period 2009 - 2014, involving 159 patients with endometrial cancer, treated and monitored at the Gynaecology Clinic of St. Anna hospital - Varna and Oncology Center - Varna. For a period of 6 years (01.01.2009 - 31.12.2014) 159 patients with endometrioid endometrial carcinoma in the first stage (data on patient epicrises) were operated at the Gynaecology Clinic of St. Anna - Varna. Patients have been diagnosed with prior curetage testing or an accidental finding after hysterectomy for uterine prolapse. All 159 patients underwent revision of postoperative preparations by two expert pathologists. Following the revision of the preparations, the diagnosis of endometrioid endometrial carcinoma in the first stage of FIGO was confirmed in 117 patients. The remaining 42/159 (26.42%) patients were different from the original diagnosis.

Methods:

1. Surgery:

- Lymph node dissection - pelvic and / or paraaortic.
- Simple hysterectomy.

2. Histological examination and revision of operative preparations.

3. Radiation therapy.

4. Statistical methods.
5. Staging.
6. Follow up.
7. Data processing.

Results and discussion

Of the 112 patients with endometrioid endometrial carcinoma, 85 (75.89%) are alive and 27 (24.11%) died. The cause of death in 15/112 (13.4%) patients was not cancer. In 12 patients, the cause of the death was cancer. Relapse rates were 7/12 (58.33%), and the remaining 5/12 (41.67%) had disease progression leading to death. One in 12 patients (8.33%) had vaginal recurrence that was histologically proven, 1/12 (8.33%) patients with pelvic recurrence 5/12 (41.67%) had distant liver and lung metastases. One (8.33%) patient had liver metastases, 1 (8.33%) had lung metastasis and 2 (16.67%) had liver and lung metastases.

In the clinical contingent study, lymph node dissection was performed in 57 patients and only 3 (5.3%) had pelvic lymph node metastases. The analysis of Kaplan-Mayer patient survival showed a lower median survival (by about 1 month) of those with lymph node dissection than those who did not (110.63 median survival per month for patients without LND and 109.46 months for patients with LND).

In addition to surgical treatment, 55/112 patients underwent postoperative radiotherapy. Of the lethal patients, PRT was performed in 8 (66.67%) / 12, and PRT was not performed in 4/12 (33.33%).

Conclusions and Contributions

14 conclusions and 13 practical contributions have been formulated, six of which are original and confirmatory.

Contributions of original character

1. A retrospective clinical and epidemiological study was performed, covering 112 patients with endometrioid endometrial carcinoma - stage I, diagnosed, treated and monitored at the Gynaecology Clinic of St. Anna hospital- Varna and the Oncological Center - Varna for the period 2009 - 2014 (for the first time in Bulgaria).
2. A ranked quantitative assessment of the risk factors for overall survival (for the

first time in Bulgaria).

3. The localization of the recurrence occurred (for the first time in Bulgaria).
4. The overall survival after relapse are analyzed (for the first time in Bulgaria).
5. Frequency distribution of unfavorable histological parameters was performed in patients in stage I EEC (for the first time in Bulgaria).
6. Adverse histological factors for affecting relapse-free survival were investigated (for the first time in Bulgaria).

Contributions of a confirmatory nature:

1. An input document was created to build a database for women with stage I endometrial cancer by FIGO.
2. The frequency distribution of demographic and clinical characteristics of the sampled patients is presented.
3. The peculiarities of the overall survival of the studied contingent are analyzed.
4. Factors affecting overall survival have been identified.
5. The features of disease-free survival are analyzed.
6. Recommendations for behavior in primary diagnosis of endometrial carcinoma have been given.

The recommendations made by Assoc. Prof. Ismail about the behavior in the diagnosis of endometrial carcinoma, namely:

1. Revision of histological preparations of curettage material with accents: is it carcinoma, sarcoma, mixed tumor, hyperplasia, EIN; histologic type (endometrioid, various components; nonendometrioid-serous, clear-cell, adenosquamous), G3 and LVSI.
2. All cases with the exception of pure endometrioid carcinoma, G1-2 without LVSI, are subject to expert imaging of the abdomen and lung (preferably PET / CT).
3. In the absence of distant or lymphatic metastases from imaging, the volume of surgical treatment is total hysterectomy with adnexa and exploration of the abdominal cavity and palpation of the retroperitoneal lymph nodes (pelvic and paraaortic). Lymph node dissection is recommended only for large lymph nodes .
4. Chemotherapy and brachytherapy are recommended postoperatively in the presence of lymph node metastases, positive LVSI, G3. In the presence of MI> 1/2, TGT and brachytherapy are recommended, and in the absence of the aforementioned adverse factors, observation or vaginal brachytherapy alone.

Short biographical information

Dr. Elis Hudaim Ismail, MD, PhD was born in 1983 in Shumen. She graduated from high school in 2001 in the town of Shumen. In 2008 she graduated in medicine at the Medical University - Varna. In 2011 she started specializing in obstetrics and gynaecology, and from that year she was appointed as a full-time assistant at the Department of Obstetrics and Gynaecology at the Medical University - Varna. Since February 2011 she has been appointed as a doctor in the Gynaecological Clinic of the Hospital "St. Anna" - Varna.

In May 2012, Dr. Ismail was admitted to a free doctorate at the Department of Obstetrics and Gynaecology at the Medical University – Varna, successfully defends her thesis. She acquired a specialty in Obstetrics and Gynecology in 2015. From 2017 until now holds the academic position of Assistant Professor in the Department of Health Care at the Branch Shumen - Medical University - Varna.

Conclusion

Assoc. Prof. Ismail's thesis "Invasion of the lymph and blood vessels in endometrial endometrioid carcinoma - stage I by FIGO" is up-to-date and meets the scientific criteria, as well as the rules for academic development of MU - Varna for the award of the scientific degree " Doctor of Medical Sciences ”.

After considering the critical remarks with deep respect, I recommend to the Honorable Members of the Scientific Jury to vote positively for the award of the Doctor of Medical Sciences degree in Obstetrics and Gynaecology by Assoc. Prof. Dr. Elis Hudaim Ismail, Ph.D.

Date: 02/09/2019

Reviewer

Prof. Dr. E. Kovachev, MD, PhD, DSc.