

## Ca 125 IN OVARIAN CANCER DIAGNOSIS AND SCREENING

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**Abstract:** Carcinom ovarii is a malignant disease of the ovarian tissue, which occurs in women over 35 years of age. The risk factors for the occurrence of ovarian cancer are endocrine, genetic and environmental influences. The genetic risk factors are mutations in the BRCA1 or BRCA2 genes at 8- ot chromosome, or other mutations in the genetic profile that increase the risk of ovarian cancer. Early detection of the existence of ovarian cancer increases the degree of success in treatment. To diagnose ovarian cancer, numerous blood tests are performed, such as the tumor marker Ca 125, then an ultrasound method, a CT scan. The final diagnosis is made by taking a biopsy sample from the suspected lesion. However, it is known that the concentration of tumor markers in the serum they increase much earlier than diagnosing the tumor with any screening test. The treatment of ovarian cancers is by chemotherapy, surgically (hysterectomy with bilateral salpingo-oophorectomy – HTA cum BSO) and radiation therapy. Drug therapy for the treatment of Carcinom ovarii is with Avastin (Bevacizumab), which is a monoclonal antibody that specifically binds to VEGF (vascular endothelial growth factor), and prevents tumor angiogenesis. The purpose of the research is to prove the significance of determining the concentration of Ca 125 in monitoring Carcinom ovarii and keeping it under control. This is a reliable method for detecting the presence of ovarian cancer as a suspected diagnosis, and monitoring the effect of anticancer therapy through increase or decrease in the concentration of Ca 125. The tests were carried out in patients aged 25-55 years with a previously established diagnosis of Carcinom ovarii. The patients were divided into three groups: a control group of patients with a normal level of Ca 125 in the circulation (n =35), a group of patients diagnosed with Carcinom ovarii (n=35), a group of patients treated with therapy to reduce the level of Ca 125 in the blood (Avastin), which acts on a platinum basis (n=35). Ca 125 is determined by an enzyme-linked, immunoabsorbent method (ELISA), based on the sandwich principle. Microtiter wells are coated with a monoclonal (mouse) antibody directed against a unique antigenic site on the CA 125 molecule. A portion of the patient sample containing endogenous CA 125 is incubated in the coated well with an enzyme conjugate, which is a rabbit monoclonal anti-CA 125 antibody conjugated with peroxidase. After incubation, the unbound conjugate is washed, and the amount of bound peroxidase, ie the intensity of staining, is proportional to the level of CA 125 in the sample. The obtained results showed that the patients diagnosed with Carcinom ovarii have significantly increased results for the concentration of Ca 125 compared to the patients from the control group whose results range within normal reference values. The patients treated with therapy to reduce the level of Ca 125 (Avastin) have evidently reduced results for the level of Ca 125. There is a visible effect of treatment with Avastin therapy, which reduces the concentration of Ca 125 to normal values, that is, it regulates its level in such a way that it inhibits tumor angiogenesis. By applying anticancer therapy with Avastin, removes the negative effect of carcinogenesis. In conditions of Carcinom ovarii the concentration of Ca 125 significantly increases compared to the control group, in the treated group of patients the level of Ca 125 significantly decreases to values close to the control group of patients, and after the problem was determined the use of appropriate therapy is approached.

**Keywords:** Sa 125, angiogenesis, VEGF, Carcinom ovarii, Avastin.

### 1. INTRODUCTION

Ovaries are paired, almond-shaped female sex glands, located in the depression of the side walls of the pelvis - fossa ovarica on both sides of the uterus. Female sex cells - egg cells - are created in them, and two female sex hormones - progesterone and estradiol. In young women, the ovaries are whitish and smooth, and then with each ovulation, grooves appear as a result of the spraying of the Graff follicle and the release of a mature egg cell. The hormone progesterone is secreted by the ovaries throughout the woman's life, while progesterone it is secreted during the luteinizing phase of the menstrual cycle and during pregnancy. Carcinom ovarii is a malignant disease of the ovarian tissue, which occurs in women over 35 years of age. The risk factors for the occurrence of ovarian cancer are endocrine, genetic and environmental influences. The genetic risk factors are mutations in the BRCA1 or BRCA2 genes at 8- chromosome, or other mutations in the genetic profile that increase the risk of ovarian cancer, but also increase the sensitivity of platinum-based chemotherapy, which are targeted drugs in the therapy of these cancers.

Mutations of these genes are found in 20% of the cases of ovarian cancer. There are several types of ovarian cancer, namely malignant epithelial tumors (serous and mucinous adenocarcinomas, endometrioid malignant tumors), malignant tumors of the germinal epithelium (disgerminoma, malignant teratoma, horikarcinom, gonadoblastoma), malignant tumors of the gonadal stroma (granuloza tumori, Sertolijevi tumori, Sertoli Lajdgovi tumori). Symptoms of ovarian cancer are nausea, vomiting, constipation, constant dull pain in the abdomen, difficulty urinating, loss of appetite, weight loss, difficulty breathing, irregular menstruation, loss of menstruation, acne. Early detection of ovarian cancer is of great importance because it increases the degree of success in its treatment.

Diagnosis of Carcinom ovarii. To establish a diagnosis of ovarian cancer, numerous blood tests are performed, tumor marker Ca 125 as a protein product of the cancer, then an ultrasound method, CT examination. The final diagnosis is established by taking a biopsy sample from the suspected lesion. Treatment of ovarian, fallopian tube and peritoneum cancers is basically the same, with chemotherapy, surgery (hysterectomy with bilateral salpingo-oophorectomy – HTA cum BSO) and radiation therapy. Drug therapy for the treatment of Carcinom ovarii is usually Avastin (Bevacizumab), Olaparib or Niraparib. Avastin is a monoclonal antibody that specifically binds to VEGF (vascular endothelial growth factor), and prevents tumor angiogenesis, which tumors need to grow and spread, i.e. metastasize to other parts of the body. The mechanism of action of Avastin allows it to be effectively combined with a wide range of chemotherapeutics in a way that controls the growth of tumors, which prolongs the survival of patients, and has a small number of side effects.

Tumor markers are specific biomolecules that the body creates as a metabolic or immune response to healthy cells due to the presence of malignant cells in the body, or they are produced by malignant tumor cells. They can be enzymes, specific proteins, various antigens, hormones, specific receptors, which do not have sufficient specificity and sensitivity to be screening tests for establishing a diagnosis. Determining their concentration is for precisely monitoring the success of therapy. The concentration of the tumor marker Ca 125 is used to monitor ovarian epithelial cell carcinoma, but it is not precise screening test. A continuous increase in the concentration of the protein tumor marker Ca 125 means the presence of malignancy and a poor response to the therapy used in Carcinom ovarii, while a decrease in the concentration means a favorable response to the therapy. A small increase in the concentration of Ca 125 can also occur in inflammatory processes of the ovaries, third trimester of pregnancy, autoimmune diseases, cirrhosis and hepatitis. However, it is known that the concentration of tumor markers in the serum increases much earlier than diagnosing the tumor with any screening test and therefore they are used as a screening for a suspicious diagnosis and further follow-up and testing with other methods to make a definitive diagnosis. The purpose of this research is to prove the significance of determining the concentration of the tumor marker Ca 125 as an initial sign of the existence of ovarian cancer and with the help of other investigations such as gynecological ultrasound, CT, MR, biopsy of a suspicious region, to set a final diagnosis. After establishing the diagnosis, the tumor marker Ca 125 is very important in determining its concentration, in order to monitor the success in applying the therapy with which the patients are treated.

## 2. MATERIALS AND METHODS

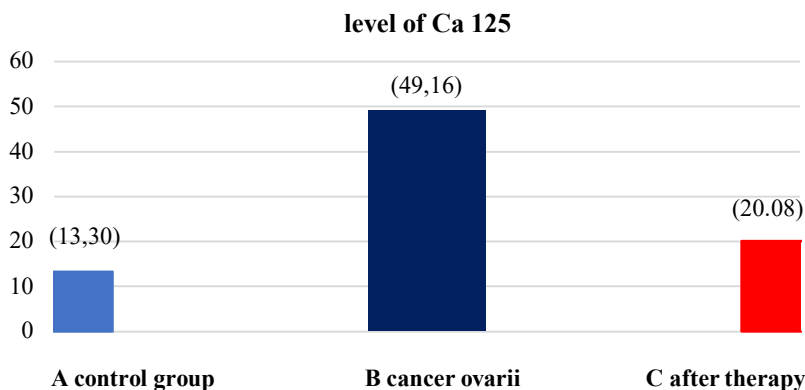
In order to prove the importance of determining the concentration of Ca 125 for monitoring and prescribing the correct therapy in patients with Carcinoma ovarii, the tests (determination of Ca 125) were carried out in patients aged 25-55 years with a previously established diagnosis of Carcinoma ovarii. The patients were divided into three groups:

- control group of patients with a normal level of Ca 125 in the circulation (n=35)
- group of patients diagnosed with Carcinom ovarii (n=35)
- a group of patients treated with therapy to reduce the level of Ca 125 in the blood (Avastin) which acts on the basis of preventing tumor angiogenesis (n=35)

Principle of the method: Ca 125 is determined by an enzyme-linked, immunoabsorbent method (ELISA), based on the sandwich principle. The microtiter wells are coated with a monoclonal (mouse) antibody directed to a unique antigenic site of the Ca 125 molecule. The antigenic determinant Ca 125 has a protein structure with attached carbohydrate side chains. A portion of the patient sample containing endogenous Ca 125 is incubated in the coated well with the enzyme conjugate, which is a peroxidase-conjugated rabbit anti-Ca 125 monoclonal antibody. After incubation, the unbound conjugate is washed away. The amount of bound peroxidase is proportional to the concentration of Ca 125 in the sample. After the addition of the substrate solution, the intensity of the color developed is proportional to the concentration of Ca 125 in the patient sample. The total duration of the analysis is 18 minutes and 20  $\mu$ L of patient serum is used. The reference values for Ca 125 are: > 35 U/L. Ca 125 ELISA is an assay for the detection of OC 125 reactive determinants of heterogeneous high molecular weight glycoprotein (200 - 1000 kDa) in serum. OC 125 reactive determinants can be found in a high percentage of non-mucinous epithelial ovarian tumors and are found in the serum of women bearing such tumors.

### 3. RESULTS

The results obtained from the examination of the level of concentration of Ca 125 in patients from the control group, the group of patients with Cancer ovarii and the treated group of patients with Avastin are shown in graph number 1.



Picture nu. 1. Level of Ca125 in the serum of a control group in Cancer ovarii and in a group after therapy

**Legend:**

- group A, patients with a normal level of Ca 125 in the serum (control group)
- group B, patients diagnosed with Carcinom ovarii
- group C, patients treated with therapy to reduce the level of Ca 125 in the serum (Avastin)

From the obtained results, it can be seen that the patients diagnosed with Carcinom ovarii have significantly increased results for the concentration of Ca 125 compared to patients from the control group whose results are within the normal reference values for Ca 125. The group of patients treated with therapy to reduce the level of Ca 125 in the blood i.e. with Avastin have evidently reduced results for the level of Ca 125 to a level close to the control group. The graph number 1 shows the visible effect of treatment with Avastin therapy in reducing the concentration of Ca 125 in the blood i.e. successful treatment of Carcinom ovarii, as a condition that significantly impairs the quality of life of patients.

### 4. DISCUSSIONS

Carcinom ovarii is a malignant disease of the epithelial tissue of the ovaries and occurs as a result of mutations in the BRCA1 or BRCA2 genes on the 8th chromosome in the human organism. For its suspicious diagnosis and as an initial signal for a possible disease of the ovaries, determination of the concentration of the tumor marker Ca 125. This tumor marker is a protein product that is secreted by the tumor of the ovaries and determining its concentration in the body is mostly used to monitor the effect of the treatment with the medication Avastin to suppress the tumor. For the growth and development of the tumor and its metastasis, it is necessary for him to develop his own network of blood vessels in the process of angiogenesis, during which vascular endothelial growth factor (VEGF) is released. The drug Avastin is a monoclonal antibody that specifically binds to vascular endothelial growth factor (VEGF), and performs its inhibition, which prevents the development of the network of blood vessels of the tumor, thereby preventing metastasis and its development. A continuous increase in the concentration of the protein tumor marker Ca 125 means the existence of malignancy and a poor response to the therapy used in Carcinom ovarii, while reduction of its concentration means a favorable response to therapy.

### 5. CONCLUSIONS

From the research done on the effect of treatment with platinum-based anticancer therapy with Avastin, it can be concluded that: is

- a reduced quality of life was found in patients diagnosed with Carcinom ovarii,
- by applying anticancer therapy with Avastin, the negative effect caused by the influence of the presence of ovarian cancer is removed,
- in conditions of Carcinom ovarii the concentration of Ca 125 increases significantly compared to the control group,
- with the use of anticancer therapy in the treated group of patients, the level of Ca 125 significantly decreases to values close to the control group of patients,

- after the problem is determined, appropriate anticancer therapy is used to reduce the concentration of Ca 125 in the blood, i.e. inhibition of the endothelial growth factor (VEGF), by binding it to Avastin, which prevents angiogenesis and thus growth and development of the tumor.

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