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Relationship between systemic treatment of breast cancer and body mass index

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ABSTRACT

For many years, patient age, axillary lymph node status, tumor size, histological features (especially histological grade and lymphovascular invasion), hormone receptor status, and HER2 status have been the major factors used to categorize patients with breast cancer in order to assess prognosis and determine the appropriate therapy. These factors are most often viewed in combination to group patients into various risk categories. Although these risk categories are useful for assessing prognosis and risk in groups of patients with breast cancer, their role in determining prognosis and evaluating risk in an individual patient is more limited. Therefore, better methods are required to help assess prognosis and determine the most appropriate treatment for patients on an individual basis. Recently, BMI particular, have been used to help refine breast cancer doses and to assess prognosis and response to therapy, it is clear that they have the potential to provide value above and beyond that provided by the traditional clinical and pathological prognostic and predictive factors.

Keywords: breast cancer; classification; prognosis; molecular; BMI,

INTRODUCTION:

The incidence of breast cancer in the world in general and in Ukraine in particular is growing. In 2016, in Ukraine the incidence reached 70.0 per 100 thousand female population.

According to the Ministry of Health in Ukraine 26% of the female population for 2016 was overweight or obese. Obesity - a chronic metabolic character, which is the result of the interaction of the endogenous factors, environmental conditions and lifestyle. Endogenous factors could be considered a violation of the genetic and hormonal balance. The external conditions include irregular rhythm nutrition, use of substandard products. By disorders include sedentary lifestyle lifestyles.

Obesity is the first risk factor for metabolic syndrome, diabetes type II, cardiovas-

cular disease and some forms of cancer, including breast cancer.

Since overweight is a risk factor for breast cancer, there is reason to believe that among patients with breast cancer the percentage of obese women is higher than in the population. The risk of breast cancer in postmenopausal women by 30% more than in premenopausal, women with obesity - 50%. Furthermore it was proven that obesity is associated with poor prognosis in patients with breast cancer, regardless of menopausal status. [1]

The leading role in achieving long-term results of treatment with systemic methods, such as chemotherapy or hormone therapy. The purpose of systemic therapy is the eradication of micrometastases in the case of radical surgical treatment or reduction of tumor load in case of treatment of locally advanced or metastatic cancer.

The calculation of the dose of chemotherapy conducted mainly in the area of the body. [2] Thus to avoid complications associated with overdose of chemotherapy, the standard practice is to calculate the dose of 2.0 m2 patients whose body area more than this. Preparations hormonal action used in standard dosage for an adult without constitutional features. Along with this recent literature there is information that women are overweight effectiveness of systemic treatments may be lower than expected. Other data refute this information. [3]

In view of the above, the study on the impact of body mass index on the effectiveness of systemic treatment for breast cancer is an actual scientific problem and promising area of research.

Overexpression of Her-2/neu in ER-positive breast cancer cells can cause tamoxifen to behave as an

agonist and stimulate cell growth. Implicit in this mechanism for resistance is cross-talk activation between the ER and the epidermal growth factor receptor (EGFR/Her-2/neu) pathways [3]. Treatment with various signal transduction inhibitors has been used in combination with endocrine therapy to overcome resistance, such as gefitinib, which targets the internal tyrosine kinase domain of EGFR, and trastuzumab, which blocks the external domain of Her-2/neu [4].

Recently, complementary and alternative medicine (CAM) is widely accepted among patients with breast cancer, which may provide several beneficial effects including reduction of therapy-associated toxicity, improvement of cancer-related symptoms, fostering of the immune system, and even direct anticancer effects [5].

Carnitine is a trimethylated amino acid, naturally synthesized in the liver, brain and kidney from protein-bound lysine and methionine. Several factors such as sex hormones and glucagon may impact on carnitine distribution and level in tissues

[6]. L-carnitine plays an important role in cell energy metabolism through mediating the transport of long chain fatty acids across the inner mitochondrial membrane. Carnitine has a modulating effect on the function of acetylcholine excitatory neurotransmitter, glutamate excitatory amino acid,insulin growth factor-1 (IGF-1) and nitric oxide (NO). L-carnitine may have a dual protective effect by enhancing the energy dynamics of the cell and inhibiting cell membrane hyperexcitability[15]., which make it an ideal nutrient for cancer prevention and treatment [7]. ex hormones, especially estrogens, have been implemented in the development of breast cancer. Breast cancer risk increases after menopause, where aromatization of androgens to estrogens in adipose tissue is the most important source of estrogen in blood and peripheral tissues [11]. Weight increase and obesity subsequent to menopause have been identified as the most important risk and negative prognostic factors for breast cancer in postmenopausal women. Obesity results in increased circulating levels of insulin and insulin-like growth factor, which by acting as mitogens for epithelial breast cells, stimulate their growth and neoplastic degeneration. Mechanisms may combine to explain the association which links together menopause, the subsequent body weight increase, and hormone-dependent breast cancer [12]. Body mass index of letrazol-treated breast cancer patients included in the present study was positively correlated with estrogen level (E2) which is consistent . [11], who showed that the increased breast cancer risk seen in postmenopausal women with adiposity might be related to elevated sex hormone level.

The aim of this retrospective study the effect of body mass index on the efficiency of treatment of breast cancer, improve treatment outcomes for breast cancer by individualization of treatment measures taking into account the characteristics of the metabolism of the patient..

<u>Materials and Methods</u> The study included 800 patients with breast cancer between the ages of 30 and 77 (57,6 ± 1) years of age who were treated according to our clinic, department of oncology and medical radiology . Dnipropetrovsk medical academy at Municipal Institution "Dnipropetrovsk City Multi-field Clinical Hospital #4", Dnepropetrovsk state medical academy from 2005-2016. All patients were evaluated according to the following data: stage of the disease, age and BMI at the time of diagnosis, the size, histological type and metastases. IHC type ,MRI methods, Bioelectrical impedance analysis, Ultrasounds analysis.

Tumor size was evaluated after measuring its maximal diameter and distributed in accordance with the International TNM-classification (7th edition, 2009). The histological type and degree of differentiation of the tumor was evaluated respectively by the National Standards of diagnostics and treatment of malignant neoplasms, reflecting the recommendations of leading international organizations. BMI is calculated by the formula: $I = m \times h^2$, where m - body weight (kg); h - height (m). According to these calculations the patients were divided in accordance with the WHO criteria into the following groups: those with a BMI <25 kg/m^2 - normal or underweight; from 25 to 29.9 kg/m^2 - overweight; > 30 kg/m^2 - obese. The material for the histopathological study was obtained during surgery. We examined the relative risk of relapse and death with regard to the BMI categories adjusting for eight factors known to be predictors of disease-free survival (DFS) and overall survival (OS): menopausal status, nodal status tumor size, vessel invasion, estrogen receptor (ER) status, progesterone receptor status, tumor grade and treatment regimens.ECOG.

By analyzing archival material to consider the particular response to systemic treatment of breast cancer women with deficiency of body weight, normal, high and overweight. Explore options for determining the individual characteristics of lipid metabolism of patients with breast cancer and their possible use for predicting the effectiveness of treatment. To determine the lipid metabolism will be applied anthropological research methods, bioimpedansnoho measurement, CT.lab test biochemistry every curs chemotherapy and control the interval between each curs .

Results

In this retrospective study, among 754 patients with breast cancer, 45% were identified with excess body weight, and 31% - of various obesity degree. Patients with a BMI <25 kg/m^2 were significantly more diagnosed with stage 2 breast cancer triple negative. BMI> 30 kg/m^2, 10 % more often associated with metastatic RLN, which is an indirect sign of higher metastatic potentials. Patients with normal BMI had significantly longer overall survival (OS) and disease-free survival (DFS) than patients with intermediate or obese BMI in pairwise comparisons adjusted for other

factors. We found a strong correlation between obesity and lymph node involvement These observations suggest that obesity may potentiate the metastatic spread of breast tumors. Distant metastases were also found more often in obese patients in bone or visceral sites in patients <45 years of age at diagnosis. Patients with normal mass by IHC with triple negative cancer 45% and 20% with BRCA + and patients with obesity 55% that's with IHC luminal A.B but 2 group receive L carnitine in group with L carnitine by ECOG better and calendar Chemotherapy was as planed and less Adverse Advents than group Patients without support L Carnitine And less hematological complication .by CT scan cheek RECICT 1,1
Was positive results thats patients get chance to operation , from stage 4 to stage 3 and no metastasis thats was more response to chemotherapy , after get material of histology was not possible for IHC results as 4th patmoarphosisi

Discussion/ Conclusion. In conclusion, this retrospective investigation of our patient demonstrates that BMI is an independent prognostic factor for OS in patients with breast cancer. We have supporting evidence that obese BMI represents a poor risk feature for outcome, especially in pre-/premenopausal patients, most of whom received chemotherapy without hormonal therapy. A lifestyle intervention reducing dietary fat intake, with modest influence on body weight, may improve relapse-free survival of breast cancer patients receiving conventional cancer management. Longer, ongoing nonintervention follow-up will address original protocol design plans, which requires 3 years of follow-ups after completion of recruitment. The prominent role of L–carnitine in the present study belongs to the level of Her-2/neu,Ki67, which weresignificantly reduced after L-carnitine supplementation. Thus, L-CAR as add on therapy to TAM, in addition to its ability to foster the immune system and improve the patients` fatigue and quality of life, may offer better cancer prognosis, which may be, in part, a prospective trial to overcome Chemotherapy and letrazol resistance.

Taking into account the data presented in this review at the experimental and clinical levels, L-carnitine should be considered as one of the main drugs in the treatment of cancer patients and it should be prescribed in combination with doxorubicin, cisplatin, carboplatin, oxaliplatin, cyclophosphamide and ifosfamide to reduce them Toxicity to many organs, as well as the ability to inject higher doses of these antitumor drugs, thereby killing more cancer cells and increasing the chances of the patient's survival

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