

Cardiovascular Disease and Breast Cancer

Mamurov Olimjon Islomovich¹, Gafur-Ahunov Mirza Aliyarovich², Dadamyants Nataliya Gamletovna³

¹Independent Researcher, Center for the Development of Professional Qualification of Medical Workers, Uzbekistan

²Center for the Development of Professional Qualification of Medical Workers, Head of Department of Oncology, Uzbekistan

³Republican Scientific Center of Emergency Medical Care, Head of Department of Radiology, Uzbekistan

Abstract In this regard, there is a reasonable increase in alertness regarding the increase in morbidity and mortality among surviving patients due to cardiovascular diseases. This may be a consequence of the side effects of the selected therapy and the acceleration of the development of cardiovascular diseases.

Keywords Patients, Morbidity, Cardiovascular, Therapy, Development, Cancer, Patients

1. Introduction

Center for the Development of Professional Qualifications of Medical Workers. It is known that in the structure of morbidity and mortality in economically developed countries, the leading position is occupied by cardiovascular diseases (CVD) and oncological pathologies.

With the increase in the prevalence of a number of oncological diseases, there is a general trend for many countries of the world to increase the life expectancy of patients. For patients with breast cancer, the increase in survival was eight percent [1,2,3,4].

Increasing the survival and life expectancy of patients than certainly? of course, it is primarily associated with the detection of breast cancer at an early stage due to the widespread introduction of screening methods and programs, as well as with an increase in the effectiveness of complex treatment [3].

In this regard, there is a reasonable increase in alertness regarding the increase in morbidity and mortality among surviving patients due to cardiovascular diseases. This may be a consequence of the side effects of the selected therapy and the acceleration of the development of cardiovascular diseases. This will be especially pronounced if they have risk factors such as arterial hypertension, hyperglycemia, obesity, lack of physical activity, alcohol, smoking [4,23,24].

It is very difficult to overestimate the clinical significance of the comorbidity of cardiovascular diseases and breast cancer. Epidemiological studies have been conducted and data indicate that 1 in 3.3 cases of mortality in patients with breast cancer is associated with cardiovascular diseases. One out of 31.5 deaths is associated with breast cancer [5,6].

It should be emphasized that the absolute risk of death from cardiovascular disease in patients with breast cancer

ranges from 1.6% to 10.4% [6]. A population-based comparative study of cardiovascular complications in patients with and without breast cancer showed that breast cancer survivors had a 1.8- and 1.3-fold increased risk of total and cardiovascular mortality. This increase in risk has been shown to be most pronounced about seven years after the diagnosis of breast cancer [1,27].

There is a commonality of the risk factor for breast cancer and cardiovascular diseases and has been proven in experimental, clinical and epidemiological studies.

Several meta-analyses of epidemiological studies in the female population have shown the dependence of the impact of alcohol on health on the level of its consumption and age.

26 flight observation by M. Jimenez et al. (83,578 women aged 30 to 55 years showed that the risk of stroke was lower in the low-dose groups of women.

M. Roerecke et al. showed that women had the lowest mortality and incidence of coronary heart disease when consuming 11 g of alcohol. The author included 44 cohort and case-control studies in the meta-analysis [20,21].

2. Materials and Methods

A recent meta-analysis found no evidence of a protective effect of alcohol consumption on hypertension in women [22]. Scientists have proven a safe range of alcoholic beverages for women. And so, safe consumption of <1 standard dose per day for women, that is, less than 3.7 g (18 ml) of ethanol, which corresponds approximately to 330 ml of beer, 150 ml of wine or 45 ml of spirits [10].

Currently, a number of biological and epidemiological data suggest that there is a strong, dose-dependent association between alcohol consumption and breast cancer, even at low levels of consumption [23].

How does alcohol cause breast cancer? The effects of alcohol on the formation of an increased risk of breast cancer include an increase in the serum concentration of

endogenous estrogens. Cellular hyperproliferation develops through an increase in the expression of estrogen receptor-dependent genes. Increases the level of insulin-like growth factor 1 further increases the density of breast tissue. All this can happen with moderate alcohol consumption. Reactive oxygen species are formed, this is the primary carcinogen. The reactive oxygen species is formed due to an increase in the level of the main metabolite of ethanol, decreases, a decrease in the concentration of 5-methyltetrahydrofolate due to inhibition of the absorption of folates and an increase in the level of homocysteine [23].

According to some authors, the risk of breast cancer increases by 7-10% for each dose of alcohol per day, which is approximately 25 ml of 40% spirits or 125 ml of 12% wine [15,24].

The following meta-analysis showed that alcohol consumption was associated with a 21% increased risk of breast cancer without a significant effect on overall mortality [25].

Ying Liu *et al.* showed that regular alcohol consumption between menarche and first pregnancy was associated with an increased risk of breast development [12,18].

A low level of physical activity is also a significant risk factor for cardiovascular and oncological diseases. It was found that regular physical activity, regardless of gender and age, has a positive effect on blood pressure, dyslipidemia, hyperglycemia, and BMI [10,11].

At the same time, large studies among women have confirmed the general trend, with moderate physical activity being associated with a lower risk of developing coronary heart disease and other cardiovascular diseases, and low physical activity increases the risk of cardiovascular disease [10,16].

Adequate physical activity between the ages of 14 and 17 was associated with a 15% lower risk of perimenopausal breast cancer, according to the NHSII survey.

Researcher Rulla M. Tamimi *et al.* also studied risk factors for breast cancer in women aged 30-50 years and found no association between low levels of physical activity and the risk of developing breast cancer.

A systematic review of 10 studies looking at risk factors for breast cancer in women aged 40-49 also found no statistically significant difference in breast cancer risk with physical activity. On the contrary, in postmenopausal women, a decrease in the risk of breast cancer against the background of increased physical activity has been shown [19].

3. Result and Discussion

The positive role of physical activity is associated with a decrease in the level of androgens, inflammatory markers, estrogen, insulin, a change in the level of sex hormone-binding globulin, including in women who are not yet obese or insulin resistant. Unhealthy and malnutrition is a modifiable risk factor for arterial hypertension, dyslipidemia, diabetes mellitus and obesity [9]. Compliance with the general principles of a healthy diet reduces the risk of

cardiovascular diseases by 28% reduces mortality from cardiovascular diseases by improving the control of blood pressure, insulin, glucose and lipids [10,12].

Numerous authors have established a link between nutrition and breast cancer. For example, in the NHS (Health Health Study) study, 86,261 women whose diet consisted of fruits, vegetables, vegetable protein and fat, but with a moderate content of carbohydrates, had significantly fewer estrogen-negative breast cancer subtypes [7,13].

According to the results of a recent study, a more pronounced increase in the risk of breast cancer, that is, by 35%), compared with non-smokers among women with a hereditary burden of breast cancer [20] was noted. Another fact proved an increase in the risk of breast cancer only in women who smoke without a family history of breast cancer [20].

There are facts about the role of vitamin D deficiency in the development of breast cancer. In many countries of the world, vitamin D deficiency occurs in all age groups [10]. Many prospective studies have demonstrated the effect of vitamin D in increasing the risk of cardiovascular disease, especially arterial hypertension. This is due to the fact that vitamin D tends to suppress the expression of renin in the juxtaglomerular apparatus of the kidneys and the proliferation of vascular smooth muscle cells.

J. P. Forman *et al.* noted a 3-fold increase in the risk of arterial hypertension in women at a level of 25 ng / ml. The incidence of vitamin D deficiency among women with breast cancer ranges from 23% to 95.6%.

Most studies examining the relationship between vitamin D levels and breast cancer risk show an inverse relationship [25]. According to them, for every 10 ng / ml increase in serum vitamin D concentration, the risk of breast cancer decreases by 3.2%. Stoll *et al.* a review of 37 studies showed a reduction in the risk of breast cancer with more than 400 IU per day of vitamin D in food. But there is conflicting evidence, including a meta-analysis that showed an increase in the risk of breast cancer with a higher concentration of vitamin D.

One possible explanation could be the phenomenon of VDR heterogeneity in breast cancer. This can be explained by differences in the sensitivity of tumor tissue to vitamin D and its uptake, accumulation, and metabolism [27].

Recent clinical studies have shown that hyperhomocysteinemia is also a risk factor for cardiovascular disease and breast cancer. hyperhomocysteinemia is found in about 5% of people, and it is associated with neurodegenerative, malignant tumors, vascular diseases, autoimmune disorders.

Hyperhomocysteinemia can serve as a diagnostic marker for the development of a particular pathology in the human body. Clinical studies have also shown that a moderate increase in homocysteine levels by 3-5 $\mu\text{mol/l}$ increases the risk of cardiovascular disease by 10-80% [11,12].

The results of two large meta-analyzes have shown that a decrease in plasma homocysteine by 3 $\mu\text{mol/l}$ is associated with an 11-16% reduction in the risk of coronary heart disease and a 19-25% reduction in stroke [24].

The authors proved that disturbances in the processes of homocysteine and folic acid metabolism can lead to abnormal DNA methylation, incorrect inclusion of uracil in DNA, this will lead to chromosome breakage and DNA destruction, and increased mutagenesis and apoptosis [9].

Recent clinical studies have shown positive associations between homocysteine levels and breast cancer risk. A significant number of international studies show that polymorphic genes of folate-methionine-homocysteine metabolism can be risk factors for the development of breast cancer, but the results of the work are contradictory [20]. It should be noted that the authors emphasize associations between polymorphisms of the folate-methionine-homocysteine metabolism genes and the lack of folates, B vitamins and the risk of developing breast cancer or its individual subtypes [20].

In a Japanese study of 456 breast cancer patients and 912 control women, the risk of breast cancer was associated with folic acid intake and was inversely proportional to the amount in the body. The association of the polymorphic marker A66G of the MTRR gene and the TT genotype of the MTHFR gene with an increased risk of breast cancer, and the correlation of these markers with the level of folic acid consumption, has been proven.

Acute and chronic stress, low social support, anxiety and depressive states are independent factors in the development of cardiovascular diseases, adverse outcomes, and death from this pathology [10].

Women with breast cancer often attribute the origin of the disease to psychological disorders, although scientific evidence is currently insufficient [25]. But the results of a recent meta-analysis of 15 prospective studies do not rule out an association between stress and breast cancer [25]. Thus, the analysis shows that in the female population, cardiovascular disease and breast cancer do share modifiable risk factors. This determines the prospects for additional benefits of non-pharmacological preventive measures.

4. Conclusions

It should be emphasized that in breast cancer, we still do not have insufficient data on the effectiveness of certain preventive interventions focused on the discussed risk factors. Identification of risk factors and study of their mechanisms of action in the development of cardiovascular diseases and breast cancer will certainly contribute to a better understanding of the pathogenesis, a differentiated approach to the treatment of cardiovascular diseases and breast cancer, and how to prevent these diseases.

REFERENCES

[1] Муромцева Г. А., Концевая А. В., Константинов В. В. и др. Распространенность факторов риска неинфекционны

х заболеваний в российской популяции в 2012-2013 гг. Результаты исследования ЭСЦЕ-РФ // Кардиоваскулярная терапия и профилактика. 2014; 13 (6): 8.

[2] Муромцева Г. А., Концевая А. В., Константинов В. В. и др. Распространенность факторов риска неинфекционных заболеваний в российской популяции в 2012-2013 гг. Результаты исследования ЭСЦЕ-РФ // Кардиоваскулярная терапия и профилактика. 2014; 13 (6): 8.

[3] Gernaat S. A. M., Ho P. J., Rijnberg N. et al. Risk of death from cardiovascular disease following breast cancer: a systematic review // *Breast Cancer Research and Treatment*. 2017; 164 (3): 537-555. DOI: 10.1007/s10549-017-4282-9.

[4] Bradshaw P. T., Stevens J., Khankari N., Teitelbaum S. L. et al. Cardiovascular Disease Mortality Among Breast Cancer Survivors // *Epidemiology (Cambridge, Mass)*. 2016; 27 (1): 6-13. DOI: 10.1097/EDE.0000000000000394.

[5] Кардиоваскулярная профилактика 2017. Национальные рекомендации. Комитет экспертов. 2017; 289 с. <http://scardio.ru/content/Guidelines/Cardiovascular-prof-2017.pdf>.

[6] Hashemi S. H. B., Karimi S., Mahboobi H. Lifestyle changes for prevention of breast cancer // *Electronic Physician*. 2014; 6 (3): 894-905. DOI: 10.14661/2014.894-905.

[7] Zheng J. S., Hu X. J., Zhao Y. M., Yang J., Li D Intake of fish and marine n-3 polyunsaturated fatty acids and risk of breast cancer: meta-analysis of data from 21 independent prospective cohort studies // *BMJ*. 2013; 346: f3706.

[8] Kushi L. H., Doyle C., McCullough M., Rock C. L. et al. American Cancer Society guidelines on nutrition and physical activity for cancer prevention // *CA: A Cancer Journal for Clinicians*. 2012; 62: 30-67. DOI: 10.3322/caac.20140.

[9] Papaioannou M. D., Koufaris C., Gooderham N. J. The cooked meat-derived mammary carcinogen 2-amino-1-methyl-6-phenylimidazo[4,5-b]pyridine (PhIP) elicits estrogenic-like microRNA responses in breast cancer cells // *Toxicol Lett*. 2014; 229 (1): 9-16.

[10] Knott C. S., Coombs N., Stamatakis E., Biddulph J. P. All cause mortality and the case for age specific alcohol consumption guidelines: pooled analyses of up to 10 population based cohorts // *BMJ*. 2015; 350: h384. DOI:10.1136/bmj. h384.

[11] Jimenez M., Chiuve S. E., Glynn R. J., Stampfer M. J. et al. Alcohol consumption and risk of stroke in women // *Stroke*. 2012; 43: 939-945. DOI: 10.1161/STROKEAHA.111.639435.

[12] Roerecke M., Rehm J. The cardioprotective association of average alcohol consumption and ischaemic heart disease: a systematic review and meta-analysis // *Addiction*. 2012; 107: 1246-1260. DOI: 10.1111/j.1360-0443.2012.03780.

[13] Roerecke M., Rehm J. Alcohol consumption, drinking patterns, and ischemic heart disease: a narrative review of meta-analyses and a systematic review and meta-analysis of the impact of heavy drinking occasions on risk for moderate drinkers // *BMC Med*. 2014; 12: 182. DOI: 10.1186/s12916-014-0182-6.

[14] Roerecke M., Tobe S. W., Kaczorowski J. et al. Sex-Specific Associations Between Alcohol Consumption and Incidence of Hypertension: A Systematic Review and Meta-Analysis of Cohort Studies. *Journal of the American Heart Association* //

- Cardiovascular and Cerebrovascular Disease. 2018; 7 (13): e008202. DOI: 10.1161/JAHA.117.008202.
- [15] Shield K. D., Soerjomataram I., Rehm J. Alcohol Use and Breast Cancer: A Critical Review. *Alcoholism // Clinical and Experimental Research*. 2016; 40 (6), 1166-1181. DOI: 10.1111/acer.13071.
- [16] Howell A., Anderson A. S., Clarke R. B., Duffy S. W. et al. Risk determination and prevention of breast cancer // *Breast Cancer Res*. 2014; 16: 446. DOI: 10.1186/s13058-014-0446-2.
- [17] Schwedhelm C., Boeing H., Hoffmann G., Aleksandrova K., Schwingshackl L. Effect of diet on mortality and cancer recurrence among cancer survivors: a systematic review and meta-analysis of cohort studies // *Nutrition Reviews*. 2016; 74 (12): 737-748. DOI: 10.1093/nutrit/nuw045.
- [18] Liu Y., Colditz G. A., Rosner B., Berkey C. S. et al. Alcohol intake between menarche and first pregnancy: a prospective study of breast cancer risk // *J Natl Cancer Inst*. 2013; 105 (20): 1571-1578. DOI: 10.1093/jnci/djt213.
- [19] Armstrong M. E., Green J., Reeves G. K., Beral V., Cairns B. J. On behalf of the Million Women Study Collaborators. Frequent physical activity may not reduce vascular disease risk as much as moderate activity: large prospective study of women in the United Kingdom // *Circulation*. 2015; 131: 721-729. DOI: 10.1161/CIRCULATIONAHA.114.010296.
- [20] Hashemi S. H. B., Karimi S., Mahboobi H. Lifestyle changes for prevention of breast cancer // *Electronic Physician*. 2014; 6 (3): 894-905. DOI: 10.14661/2014.894-905.
- [21] Boeke C. E., Eliassen A. H., Oh H., Spiegelman D., Willett W. C., Tamimi R. M. Adolescent physical activity in relation to breast cancer risk // *Breast Cancer Res Treat*. 2014; 145: 715-724. DOI: 10.1007/s10549-014-2919-5.
- [22] Tamimi R. M., Spiegelman D., Smith-Warner S. A., Wang M. et al. Population Attributable Risk of Modifiable and Nonmodifiable Breast Cancer Risk Factors in Postmenopausal Breast Cancer // *Am J Epidemiol*. 2016 Dec 15; 184 (12): 884-893. DOI: 10.1093/aje/kww145.
- [23] Nelson H. D., Zakher B., Cantor A., Fu R. et al. Risk Factors for Breast Cancer for Women Age 40 to 49: A Systematic Review and Meta-analysis // *Ann Intern Med*. 2012, May 1; 156 (9): 635-648. DOI: 10.1059/0003-4819-156-9201205010-00006.
- [24] Hashemi S. H. B., Karimi S., Mahboobi H. Lifestyle changes for prevention of breast cancer // *Electronic Physician*. 2014; 6 (3): 894-905. DOI: 10.14661/2014.894-905.
- [25] Brenner D. R., Brockton N. T., Kotsopoulos J. et al. Breast cancer survival among young women: a review of the role of modifiable lifestyle factors // *Cancer Causes & Control*. 2016; 27: 459-472. DOI: 10.1007/s10552-016-0726-5.
- [26] Bruno E., Roveda E., Vitale J. et al. Effect of aerobic exercise intervention on markers of insulin resistance in breast cancer women // *Eur J Cancer Care*. 2018; 27: e12617. <https://doi.org/10.1111/ecc.12617>.