

Discussion: In 1978 Weiman and in 1990 Holmgren¹ had separately noted that workplace or work-related stress and stressors are the major reasons for such as sick-leave; physiological and psychological illnesses, work burnout and consequently these issues can cause the individual or organizational problems. We employed the Rice (1999) WPS self-esteem questionnaire because we considered that our study participants will be categorized as relatively healthy, i.e. they never complain about being sick and leave the work. Furthermore, we decided that it would be reasonable if the participants assess themselves whether they are in work-related stress by reading and getting an idea what can be called workplace stress indeed².

It is clear that women dominate nursing around the world, however regardless of the work environment, requirements, or workload, regardless of gender all are exposed to workplace stress. The results of our study agree that it depends only on individuals. Our study gave proof that due to ANOVA the gender differences on workplace stress is absent ($F=0.404$), ($p=0.525$) statistically. According to literature, workplace stress is often treated by the gender of nurses, but the results vary. Certain researchers noted that there is no gender difference in work stress³ and others claimed that female nurses are more vulnerable to various

occupational stresses than men⁴ moreover; some researchers figured out those female nurses are more intended for psychological stress; meanwhile the men tend to physiological stressors.⁵ The results of this study are similar to the results of a 2013 study by Finnish researchers as well as Mauno that found that young nurses are less exposed to workplace stress than older nurses⁶. We agreed with the global studies that the nurses at younger age are less exposed to the work stress because they are working in a fellowship system and they are always relying on co-workers help. Particular researchers, such as Takase, Teraoka, and Yabase, suggested in a 2016 study that nurses over the age of twenty-five who want to keep their workplaces are more stressed than middle-aged and older nurses.⁷ The statistically significant differences in the stress levels ($F = 1.923$) and ($p = 0.105$). Above demonstrated results suggested that the onset of stress in a nurse's workplace depends on many different levels of social factors, such as age, gender, organizational characteristics, organization, place of work, and years of service. And these stressors have different impacts on individuals.

Conclusion: Nursing work-related stress levels were $F=3.071$, $p=0.028$; and it expressed statistical significant differences regarding the ANOVA analysis.

STUDY OF THE POSSIBILITIES OF PREOPERATIVE CHEMOTHERAPY IN MULTIPLE METASTASIS OF COLORECTAL CANCER IN THE LIVER

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SUMMARY

Preoperative chemotherapy (CT) in 35 patients with colorectal cancer (CRC) with liver metastases demonstrated a high frequency of objective effects - in 22 (62.9%) patients, stabilization was noted in 10 (28.6%) cases. With bilobar liver metastases and the use of oxaliplatin-containing regimens, partial regression was 62.9%. Side effects in most cases were clinically insignificant, no deaths were observed. The results obtained demonstrate the possibility of performing extended surgical operations in the majority of CRC patients with multiple liver metastases after preoperative CT.

Key words: colorectal cancer, liver metastases, preoperative chemotherapy

¹ <https://bmcpublihealth.biomedcentral.com/articles/10.1186/s12889-019-7940-5/>

² Rice, P. L. (1992). *Stress & Health* (2nd ed.) Pacific Grove, California: Brooks/Cole Publishing Company. <http://www2.uwstout.edu/content/lib/thesis/2000/2000braate nd.pdf> - research paper

³ Wong S., DeSantici G., Staudemayer N. The relationship between task interdependency and role stress: A revisit of the job demands-control model. *J. Manage. Stud.* 2007;44:284–303. doi: 10.1111/j.1467-6486.2007.00689.x. [CrossRef] [Google Scholar] [Ref list] ². Proost K., de Witte H., de Witte K., Everts G. Burnout among nurses: Extending the job demand-control-support model with work-home interference. *Psychologica Belgica.* 2004;44:269–288. [Google Scholar] [Ref list]

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³. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3564148/>, ⁵ (Burke R. Work stress and women's health: Occupational status effect. *J. Bus. Ethics.* 2002;37:91–102. doi: 10.1023/A:1014734302972. [CrossRef] [Google Scholar] [Ref list])

⁶ Mauno, S., Ruokolainen, M., & Kinnunen U. (2013). Does aging make employees more resilient to job stress? Age as a moderator in the job stressor-well-being 127 relationship in three Finnish occupational samples. *Aging & mental health.* 17(4), 411–412. doi:10.1080/13607863.2012.747077

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In recent decades, there has been an increase in incidence and mortality rates from colorectal cancer (CRC) throughout the world, including in Uzbekistan. The main target for metastasis in colorectal cancer is the liver due to unique portal drainage. In 15-30% of patients with newly diagnosed cancer of the colon or rectum, synchronous liver metastases are revealed, and in 50-75% of patients in subsequent years, secondary (metachronous) liver metastases are diagnosed. The average life expectancy of patients with unresected CRC metastases is less than 1 year, and with synchronous metastases - 4.5 months from the date of diagnosis [1,2,3,8,11,17].

To date, liver resection has been the only treatment to achieve long-term survival in patients with liver metastases of CRC. However, only a small group of patients (15-20%) can count on a potentially radical treatment, including removal of the primary tumor of the colon and liver resection. Traditional liver resection in operable patients allows a 5-year survival rate of 21-37% to be achieved [4,12-16].

Currently, the standard treatment regimens for patients with colorectal cancer with liver metastases are cytotoxic drugs (oxaliplatin or irinotecan) in combination with 5-fluorouracil and leucovorin [7,10]. There is still no consensus on the effect of preoperative chemotherapy on postoperative complications. In a number of studies, no effect of preoperative chemotherapy on the postoperative course was found. On the other hand, many studies have shown a clinically significant prevalence of the incidence of postoperative complications in the group with preoperative chemotherapy in relation to the group of surgical treatment. Values range from 13-16% in the surgical treatment group and up to 25-37% in the neoadjuvant chemotherapy group [6,18]. In this case, preoperative chemotherapy can cause toxic damage to the liver, and thereby limit the resectability of the tumor, increasing the likelihood of postoperative complications, in particular, liver failure. The effect of preoperative chemotherapy is not so obvious in the case of a greater number of liver metastases (more than four), since at the moment there are no prospective data that could help in making a decision on prescribing chemotherapy [5,9,10, 19-22].

The aim of the study

To study the possibilities of modern preoperative chemotherapy regimens in the combined treatment of CRC metastases in the liver.

Materials and methods.

The present study included 35 patients with CRC with liver metastases who were examined and treated in the chemotherapy department of the Republican Scientific and Practical Medical Center of Oncology and Radiology of the Ministry of Health of the Republic of Uzbekistan in the period from 2018 to 2020. between the ages of 34 and 73. All patients had a morphologically verified diagnosis of colon adenocarcinoma after removal of the primary tumor. According to the morphological study, in 26 (74.3%) patients, moderately differentiated adenocarcinoma prevailed, highly and poorly differentiated variants were encountered much less frequently - in 5 (14.3%)

and 4 (11.4%) patients, respectively. Liver metastases met the following criteria of resectability: preservation of at least 25% of the liver parenchyma formed by at least two adjacent segments, with adequate bile duct and vascular blood supply. In the majority of patients - 28 (80.0%) were diagnosed with a primary metastatic process, in 7 (20.0%) liver metastases were detected after colon resection in the period from 5.5 to 44 months, on average after 22 ± 4.3 months. In most cases, 23 (65.7%) patients had bilobar liver damage. The sizes of metastases varied from 0.3 to 12.7 cm, and the number of metastases ranged from 1 to 15 (on average, 5.1 ± 0.5). At the time of enrollment in the study, all patients were in satisfactory condition (WHO ECOG 0-1), normal hematopoiesis, liver and kidney indices, and no serious comorbidities.

In terms of combined treatment, all patients underwent preoperative chemotherapy for an average of 3.5 ± 0.12 months. followed by surgery. 32 (91.4%) patients underwent preoperative chemotherapy with fluoropyrimidines and oxaliplatin (XELOX, CAPOX, FOLFOX); the remaining 3 (8.6%) patients received the FOLFIRI regimen. The effect of chemotherapy was assessed by computed tomography (CT) data, every 6-8 weeks. treatment. The severity of side effects was determined using the NCI CTCAE Toxicity Scale, version 4.0 (2009).

Results and discussion.

After courses of preoperative chemotherapy, 27 (77.1%) patients underwent radical surgery, the volume of which was determined by the initial metastatic lesion of the liver. More often than others, standard hemihepatectomy was performed - in 14 (51.9%) of 27 patients, 11 (40.7%) underwent extended hemihepatectomy, which included removal of the lobe and adjacent liver segments, and in 2 (7.4%) patients, radical resection was limited to removal 1-3 liver segments.

All patients underwent a morphological examination of the surgical material. In no case were tumor cells found in the margin of liver resection. Signs of grade I drug pathomorphosis were detected in 5 (18.5%) cases; II degree - in 10 (37.0%) cases; III degree - 7 (25.9%) and IV degree - 3 (11.1%). In 2 (7.4%) patients with disease progression on the background of CT, no signs of therapeutic pathomorphosis were found in the surgical material.

The postoperative management tactics were developed depending on the primary prevalence of the disease, the direct response to CT, and the severity of the therapeutic pathomorphosis. Most - 20 (74.1%) patients in the postoperative period received prophylactic chemotherapy, on average, within 5.7 ± 0.17 months.

A complete response to the ongoing chemotherapy treatment was achieved in 3 (8.6%) of 35 patients, in 19 (54.3%) - a partial effect, stabilization - in 10 (28.6%) patients. Against the background of chemotherapy in 3 (8.6%) patients, the progression of the disease in the form of an increase in metastases by 20-25% was established. These patients were operated on after 2-3 courses of chemotherapy. The maximum effect of preoperative chemotherapy was achieved in patients

with bilobar liver damage who received combinations with oxaliplatin - in 22 (62.9%) cases. Elevated CEA levels before the start of preoperative chemotherapy were observed in 28 (80.0%) patients. The success of preoperative chemotherapy was accompanied by a decrease in the CEA level in all patients with an objective effect and in 6 (60.0%) of 10 patients with stabilization.

In most cases, the side effects of chemotherapy were clinically insignificant and did not exceed I – II degrees. Grade III – IV side effects were associated with 18 (5.4%) treatment courses in 12 (20%) patients. The greatest clinical significance were neutropenia, diarrhea, and palmar-plantar syndrome. There were no cases of discontinuation of chemotherapy due to unacceptable toxicity. At the same time, these complications did not affect the timing of surgical intervention in patients. To date, 32 patients have been followed up for 6-26.4 months, with an average follow-up time of 12.5 months and a median follow-up of 11.2 months. In 5 (15.6%) patients, progression was established, which caused the death of one patient after 6 months. after extended hemihepatectomy, the rest of the patients are alive. The one-year progression-free survival rate was 84.4%.

Conclusion.

To date, treatment of CRC with liver metastases does not have uniform standards, no unified tactics has been developed for this category of patients. The modern literature does not fully reflect the issues related to the possibilities of improving treatment results in patients with liver metastases, as well as the advantages of preoperative chemotherapy. In our studies, preoperative chemotherapy in 35 patients with CRC with liver metastases demonstrated a high frequency of objective effects - in 22 (62.9%) patients, stabilization was noted in 10 (28.6%) cases. With bilobar liver metastases and the use of oxaliplatin-containing regimens, partial regression was 62.9%. Side effects in most cases were clinically insignificant, no deaths were observed. There was also no effect of preoperative chemotherapy on the incidence of postoperative complications. The results obtained demonstrate the possibility of performing extended surgical operations in the majority of CRC patients with multiple liver metastases.

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STEM CELLS IN BREAST CANCER: THE ROLE OF GENDER STEROID RECEPTORS

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СТВОЛОВЫЕ КЛЕТКИ РАКА МОЛОЧНОЙ ЖЕЛЕЗЫ: РОЛЬ ПОЛОВЫХ СТЕРОИДНЫХ РЕЦЕПТОРОВ

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SUMMARY

Breast cancer (BC) is the most common cancer among women, and current treatments available often have high success rates. However, BC can acquire drug resistance and sometimes relapse. Current knowledge about the most aggressive forms of BC indicates the role of specific cells with stem properties located in BC, the so-called "BCSCs" (Breast cancer stem cells). The role of BCSCs in cancer formation, growth, invasiveness, therapy resistance, and tumor recurrence is becoming increasingly evident. The growth and metastatic properties of BCSCs are regulated in a variety of ways that are only partially known. Sex steroid receptors (SSRs), which are involved in the etiology and progression of BC, promote the proliferation, dedifferentiation and migration of BCSCs. However, the literature contains incomplete information about their roles. In particular, there are conflicting findings regarding the expression and role of classic BC hormone biomarkers such as estrogen receptor alpha (ERα), together with scanty, albeit promising, information on the properties of ER-beta (ERβ) and androgen receptor (AR) that control pathways of transduction in BCSC. In this review, we will discuss the role that SRs expressed in BCSCs play in BC progression and relapse, and how these findings have opened up new therapeutic options.

These cells are predictors of BC and promising new therapies are being developed to target these cells and improve BC recurrence.

РЕЗЮМЕ

Рак молочной железы (РМЖ_(рус), ВС_(англ)) является наиболее распространенным раком среди женщин, и современные доступные методы лечения часто имеют высокие показатели успеха. Тем не менее, ВС может приобрести лекарственную устойчивость, а иногда и рецидив. Современные знания о наиболее агрессивных формах ВС указывают на роль специфических клеток со стволовыми свойствами, расположенных в ВС, так называемых «стволовых клеток РМЖ» (BCSCs - Breast cancer stem cells). Роль BCSC в формировании рака, росте, инвазивности, резистентности к терапии и рецидиве опухоли