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Incidence of symptoms of fatigue, pain and sleep disorders in patients with a malignant disease who are actively involved in the rehabilitation process

Pojavnost simptoma umora, boli i poremećaja sna kod osoba s malignim oboljenjem, aktivno uključenih u rehabilitacijski proces

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Summary

The incidence of symptoms of chronic fatigue in cancer patients (cancer-related fatigue, CRF) is a significant factor in the assessment of quality of life, and occurs during and after the implementation of oncological treatment. The aim of this study was to investigate the incidence of symptoms of fatigue, pain and sleep disorders in patients with a malignant disease in relation to the involvement in the rehabilitation process and sport activity. The study included 129 people with malignant diseases. We used the EORTC QLQ-C30 questionnaire version 3.0 for self-assessment of quality of life that in subscales examine fatigue, pain and sleeping disorder. Research results confirm that people with malignant diseases who are active participants in the rehabilitation process and active in sports estimate a significantly lower fatigue than those who are not involved in sports. Education, active participation of people with malignant diseases in a rehabilitation process with a strictly individualized approach to inclusion of oncology patients in physical activity are the most important strategies in the battle against the symptoms of fatigue.

Key words: fatigue, EORTC QLQ, rehabilitation, physical activity

Sažetak

Pojavnost simptoma kroničnog umora kod onkoloških bolesnika značajan je čimbenik u procjeni kvalitete života, a javlja se tijekom i nakon provođenja specifičnog onkološkog liječenja. Cilj ovoga istraživanja bio je ispitati pojavnost simptoma umora boli i poremećaja sna kod osoba s malignim oboljenjem u odnosu na uključenost u rehabilitacijski proces i sportsku aktivnost. U istraživanju je sudjelovalo ukupno 129 osoba s malignim bolestima. Upotrijebili smo upitnik EORTC QLQ-C30 verzije 3.0 za samoprocjenu kvalitete života koji u subskalama ispituje pojavnost simptoma umora boli i poremećaja sna. Rezultati istraživanja potvrđuju da osobe s malignim oboljenjem koji su aktivni sudionici rehabilitacijskog procesa, te aktivni u sportu, procjenjuju značajno manji umor u usporedbi s onima koji se ne bave sportom. Edukacija, aktivno sudjelovanje osobe s malignim oboljenjem u rehabilitacijskom procesu, uz strogo individualiziran pristup kod uključivanja onkoloških bolesnika u tjelesnu aktivnost, najvažnije su strategije u borbi protiv simptoma umora.

Ključne riječi: umor, EORTC QLQ, rehabilitacija, tjelesna aktivnost

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Introduction

Malignant diseases are one of the biggest health problems in the world today, with 14 million new diagnoses and 8.2 million deaths.[1,2] The healthcare profession invests a great deal of intention into solving oncological problems that disturb the quality of life and everyday activity of an individual. The most common incidence of symptoms such as fatigue, pain and sleep disorders, which are associated to comorbidity with cancer, decrease the quality of life of a person, thus affecting the outcome of the disease, increasing morbidity and mortality, and, according to literature, it is considered that they occur in most patients with the diagnosis of cancer. [3]

Cancer-Related Fatigue (CRF) has several definitions. Most commonly used is the one given by the *National Comprehensive Cancer Network* (NCCN), which defines fatigue in malignant diseases as a disturbing, persistent, subjective sense of physical, emotional and/or cognitive tiredness or exhaustion related to cancer or cancer therapy, which is not proportionate with the patients' activity and hampers their daily functioning.[4] It is characterized by a sense of exhaustion, weakness and lack of energy. In healthy people, fatigue is the functional and defensive response of the body to physical and emotional stress, while in oncologic patients it has lost its protective role and does not disappear after rest.[5]

The appearance of fatigue in these patients may also result in a sleep disorder as well as the appearance of pain symptoms that disturb the daily functioning of the individual. Sleep disorders, such as difficulty with falling asleep, problems with the maintenance of sleep, poor sleep, premature awakening and excessive drowsiness during the day, are common in people treated for cancer.[6]

Pain occurs in about 70% of patients with advanced malignancy. In oncologic patients the cause of the pain is most often the result of changes caused by tumor growth and tumor metastasis. It is rarely caused by treatment (side effects of treatment) or dysfunction of the nervous system (neuropathic pain). In oncological patients, due to the nature and extent of the tumor disease, the pain is very often of a chronic type. Pain lasts for a long time and the cause of pain (advanced tumor disease) cannot be removed. In such conditions, the pain negatively changes the molecular processes and the functioning of the nervous system or the quality of life of an individual. The correct approach to the treatment of malignant pain is based on the understanding of symptoms as a psychosomatic phenomenon whose seriousness is not only determined by the degree of physical disability but also by the mental state of the person at that time.[6,7]

The current question that an oncology team deals with is whether they have reached all the recommended standards for treating a patient with malignant disease. Oncological rehabilitation requires coordination between the oncological patient, family members and the health care staff. Rehabilitation work model is a model in which professionals from different professions are involved in synergy, where each one works within its area in the direction of achieving the set rehabilitation goals through a targeted improvement of the subjective benefit for the individual. Research suggests that rehabilitation teams in combination with an integrated rehabilitation program are most effective in improving the quality of life of the afflicted person, as well as the family members concerned.[8,9]

The main purpose of this research is to contribute to a better understanding of the symptoms that impair the quality of life of an oncology patient in relation to the involvement in the rehabilitation process and sports activity.

Research methodology

Sample

The study included 129 participants suffering from malignant diseases, members of NGOs and groups based in the city of Zagreb as part of an umbrella organization of the Croatian League Against Cancer. Taking into account the primary disease, respondents were divided into the following categories:

1. persons with colorectal cancer (N = 29),
2. persons suffering from breast cancer (N = 39),
3. laryngectomized persons (N = 35) and
4. persons with leukemia and lymphoma (N = 26)

The youngest patient was 22 years old and the oldest 92 years old with an average age of 55 ± 15 years. Men and women were equally represented (m:f = 58:71, 45%:55%).

Measuring instrument

The Croatian version of EORTC QLQ-C30 (European Organization for Research and Treatment of Cancer's Quality of Life Questionnaire) version 3.0 was used for self-assessment of quality of life and the Croatian translation of the questionnaire that showed good metric characteristics. The questionnaire showed good metric characteristics in many countries including USA, Australia, UK, Northern and Southern Europe and Japan.[10] Through 30 observed items this

questionnaire examines five functional scales: physical functioning, role functioning, cognitive functioning, emotional functioning and social functioning; and three symptom scales: fatigue, pain, nausea/vomiting; general health status/quality of life and six individual symptoms of the disease most commonly associated with malignancy: breathing difficulties, loss of appetite, sleep disturbances, constipation, diarrhea and financial difficulties as a result of the illness and treatment. The quality of life assessment refers to the seven-day period preceding the completion of the questionnaire and all the items were scored on the Likert scale of 1 to 4. The results obtained by this questionnaire are linearly transformed, with the higher result on functional scales indicating better functioning. The good metric characteristics and sensitivity of the questionnaire to differentiate the respondents are the reason for inclusion of this questionnaire in the research.

Procedure

Research was conducted from the beginning of January 2015 till March 2017 on the premises of the Clinic for Tumors, University Hospital Center Zagreb, University Hospital Center Sisters of Mercy and associations and groups of people with malignant diseases registered in the Croatian League Against Cancer. The target sample was subjects who were suffering from a malignant disease and who at the time of the research were members of the associations and groups whose umbrella organization is the Croatian League Against Cancer. For the research to be conducted we asked for the approval of the head of the Clinic for Tumors, University Hospital Center Zagreb and presidencies of organizations and groups that care for people with malignant diseases. The design and process of research was designed and implemented in accordance with the principles of research implementation.

Statistical data processing was carried out with the help of the statistical software Statistica 13.3 (StatSoft Inc., Tulsa, USA). Data are presented by means of the arithmetic mean and standard deviation (SD). Comparative statistical analysis, i.e. difference in the value of the total score depending on (no) sport activity, pre-rehabilitation and rehabilitation are now performed by t-tests for independent samples, and the differences between groups by one-way variance analysis (ANOVA test). Tukey's HSD test was used in post-hoc analysis. Multiple regression analysis was used in the total score to determine the share of examined factors (sport, pre-rehabilitation, rehabilitation now and belonging to a group). In all of these tests, the results were considered statistically significant at $p < 0.05$

Results

The mean values, standard deviations and comparison of mean values for fatigue, sleep and pain with respect to whether sports subjects are involved, whether they have been in rehabilitation before or are currently in rehabilitation are shown in Table 1.

Table 1 The mean values, standard deviations and comparison of mean values for fatigue, sleep and pain in relation to examined variables in all subjects
Tablica 1. Prosječne vrijednosti, standardne devijacije i usporedbe prosječnih vrijednosti za umor, san i bol u odnosu na ispitane varijable kod svih subjekata

	Fatigue / *Umor*	Sleep / *San*	Pain / *Bol*
	Score/Mean ± SD / *Bodovi/Prosjek* ± SD		
Sport			
Yes / *Da* (N = 36)	37 ± 33	38 ± 34	31 ± 37
No / *Ne* (N = 93)	54 ± 31	50 ± 39	39 ± 36
P	0.008*	0.134	0.282
Rehabilitation Before /*Ranija rehabilitacija*			
Yes / *Da* (N = 44)	38 ± 33	45 ± 40	33 ± 40
Yes / *Da* (N = 59)	56 ± 31	50 ± 40	38 ± 33
P	0.006*	0.598	0.499
Rehabilitation Now / *Sadašnja rehabilitacija*			
Yes / *Da* (N = 24)	27 ± 21	37 ± 40	22 ± 32
Yes / *Da* (N = 79)	54 ± 33	51 ± 40	40 ± 36
P	<0.001*	0.150	0.036*

* indicates a statistically significant value of P / *prikazuje statistički značajnu vrijednost za P*

Participants with malignancy who are engaged in sports activities show significantly lower fatigue than those who are not engaged in sports activities ($p = 0.008$). Participants with malignancy who were previously in rehabilitation and those who are currently in rehabilitation show lower fatigue levels compared to patients who were not in rehabilitation before or are not in rehabilitation now (rehabilitation before $p = 0.006$; rehabilitation now $p < 0.001$).

The differences between mean values determined for fatigue depending on sports activity, previously performed rehabilitation, and the difference between mean values for pain depending on the implementation of the current rehabilitation were investigated using ANOVA among the groups whose results are shown in Table 2.

Additional analysis has shown significantly higher fatigue levels in patients with breast cancer compared to fatigue in patients with laryngeal cancer ($p = 0.010$) and significantly higher fatigue levels in patients with leukemia/lymphoma than fatigue in patients with laryngeal cancer ($p = 0.026$). In patients who are not engaged in sports activities, there are significantly higher fatigue levels in breast cancer patients compared to fatigue in patients with laryngeal cancer ($p <0.001$), and significantly greater fatigue in patients with leukemia/lymphoma than fatigue in patients with laryngeal cancer ($p = 0.023$). In patients who were in rehabilitation, there was significantly greater fatigue in patients with colorectal cancer compared to fatigue in breast cancer patients ($p = 0.008$), and significantly higher fatigue levels in breast cancer patients compared to fatigue in patients with laryngeal cancer ($p < 0.001$).

In patients who did not undergo rehabilitation, there was significantly greater fatigue in breast cancer patients compared to tiredness in patients with laryngeal cancer ($p = 0.010$). In patients who were not in the process of rehabilitation at the time of the research there was significantly more fatigue in breast cancer patients compared to patients with colorectal cancer ($p = 0.005$), and significantly a higher level of fatigue in breast cancer patients compared to patients with laryngeal cancer ($p < 0.001$). In patients who did undergo rehabilitation, there was significantly greater pain in breast cancer patients compared to pain in patients with laryngeal cancer ($p = 0.010$).

The impact of investigated factors: sports activity, conducting rehabilitation before and now were tested on fatigue by multiple regression analysis (see Table 3).

A statistically significant multiple regression coefficient $R = 0.395$ ($p = 0.043$) was determined, i.e. $R^2 = 0.156$, which means that the total contribution from these test factors to the total score of fatigue was 15.6%, i.e. these investigated factors with 15.6% contribute to the total fatigue score. Rehabilitation now has a significant influence ($p = 0.047$).

Table 2 Distribution of mean values for fatigue and pain in relation to the examined variables by individual cancer groups (ANOVA)
Tablica 2. Raspodjela prosječnih vrijednosti za umor, san i bol u odnosu na ispitane varijable pojedinačnih skupina karcinoma (ANOVA)

	CRS *Kolorektalni karcinom*	Breast cancer *Karcinom dojke*	Laryngeal cancer *Karcinom grkljana*	Lymphomas / Leukemia *Limfom / Leukemija*	P
	Fatigue/Score (Mean ± SD) / *Umor/Bodovi (Prosjek ± SD)*				
Sport					
Yes / *Da*	19 ± 23	69 ± 21	21 ± 20	54 ± 37	0.003*
No / *Ne*	51 ± 30	69 ± 27	29 ± 28	57 ± 24	< 0.001*
Rehabilitation before / *Ranija rehabilitacija*					
Yes / *Da*	39 ± 33	76 ± 23	22 ± 22		< 0.001*
No / *Ne*	49 ± 31	67 ± 26	34 ± 33		0.008*
Rehabilitation now / *Sadašnja rehabilitacija*					
Yes / *Da*	22 ± 31	33 ± 0	27 ± 22		0.884
No / *Ne*	48 ± 31	71 ± 25	23 ± 30		< 0.001*
	Pain/Score (Mean ± SD) / *Bol/Bodovi (Prosjek ± SD)*				
Rehabilitation now / *Sadašnja rehabilitacija*					
Yes / *Da*	0 ± 0	0 ± 0	27 ± 34		0,348
No / *Ne*	33 ± 35	52 ± 35	22 ± 31		0,010*

* indicates a statistically significant value of P / **prikazuje statistički značajnu vrijednost za P*

Table 3 Influence of sports activities, conducting rehabilitation before and now on fatigue
Tablica 3. Utjecaj sportskih aktivnosti, vođenje rehabilitacije prethodnog i sadašnjeg umora

Factor / *Faktor*	β	$SE_β$	P
Sport / Sport	0.171	0.105	0.105
Rehabilitation before / *Ranija rehabilitacija*	0.093	0.108	0.393
Rehabilitation now / *Sadašnja rehabilitacija*	0.224	0.112	0.047*

β - coefficient of regression / *koeficijent regresije*
$SE_β$- standard error of the β coefficient of regression / *$SE_β$ – standardna greška β koeficijenta regresije*
* - statistically significant P / * - *statistički značajan P*

Discussion

Based on the results obtained in this research it can be concluded that the occurrence of symptoms that impair the quality of life of participants with malignancy in this study is lesser if they participate in the rehabilitation process or are active in some of the sports activities. This result suggests that strategies for dealing with people with malignant diseases should focus precisely on this examined variable. Of all non-pharmacological methods, physical activity has the strongest evidence to support its effectiveness in treating fatigue.[11,12,13,14] In the rehabilitation process, people with malignancy are taught of various methods of conservation and careful planning of the use of physical energy on essential activities, along with keeping a diary to determine a specific pattern of fatigue or to identify certain activities associated with increased levels of fatigue. On the basis of this information, changes in the organization of specific activities are proposed with the introduction of appropriate rest periods in order to preserve the necessary level of physical energy.[15]

Physical activity has to be carried out under the supervision of a health professional and must be individually tailored to each individual in order to reduce the occurrence of symptoms present when dealing with activities of longer duration or higher intensity. Numerous studies have shown the effectiveness of physical activities and quality of life in patients with different types of cancer, with particularly good results being reported in breast cancer patients. Cochrane Systematic Review, published in 2012, analyzed the data of 56 randomized studies of patients suffering from fatigue and have achieved results that confirmed physical activity as significantly more effective than other interventions in the control group, regardless of whether they were involved during therapy or after it.[16]

During physical exercise, there is a reduction in the compensatory ability of the cardiorespiratory system to meet the metabolic needs of organisms that are more pronounced in people with malignant diseases. As a baseline orientation value for assessing the condition and ability of a person with malignancy to perform an effort, it is primarily necessary to measure blood pressure and pulse before, during and after the activity, and compare the obtained values. In the aforementioned assessment, a framework assessment of the demandingness of physical activity must be taken, which implies its intensity and duration.[17,18,19]

If there is no contraindication (significant thrombocytopenia, anemia, high temperature, infection, presence of extensive lithic bone metastases), in the majority of patients (those on therapy and those who have completed therapy) individualized moderate aerobic activity programs are recommended. American Society of Clinical Oncology (ASCO) guidelines for fatigue treatment recommend 150 minutes of moderate aerobic activity per week with additional 2 to 3 strength trainings.[20] Preserving the vital functions of the organism at an optimal level through recreational sports activities of persons with malignant diseases is a prerequisite for good mood, feeling useful, optimistic and resulting in good quality of life, which is also the ultimate goal of the rehabilitation process.

Conclusion

According to the set goals in this study, it was established that people with malignancy who are active participants in the rehabilitation process and active in sports activities are estimated to have a significantly lower fatigue than those who are not engaged in sports. The practical value of the work is the specificity of the samples of people with malignant diseases and the size of the sample, which gives the relevance to all the statistical procedures carried out on the results. The advantage of the study was the use of a quota sample,

which involved approximately the same number of participants in all the examined categories of persons with malignant diseases. This research contributes to the development of clinical guidelines for the oncologic population and the development of rehabilitation programs that will result in an increase in the quality of life of oncological patients and their families. Future studies should include other categories of persons with malignant diseases as well as additional variables that would contribute to the differentiation of participants such as the use of medication therapy and the time passed since the diagnosis.

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