Original Article doi: https://doi.org/10.1590/1983-1447.2022.20210123.en

# Evaluation of fatigue and quality of life of colorectal cancer patients in chemotherapy

Avaliação da fadiga e da qualidade de vida de pacientes com câncer colorretal em quimioterapia

Evaluación de la fatiga y la calidad de vida de los pacientes con con cáncer colorrectal en quimioterapia

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### How to cite this article:

Silva RC, Goncalves MC, Mendes AS, Cardoso MRR, Nicolussi AC. Evaluation of fatigue and guality of life of colorectal cancer patients in chemotherapy. Rev Gaúcha Enferm. 2022;43:e20210123. doi: https://doi.org/10.1590/1983-1447.2022.20210123.en

### ABSTRACT

**Objective:** To evaluate fatigue and health-related guality of life of colorectal cancer patients undergoing chemotherapy.

Method: Descriptive study conducted with 69 patients between January and September/2019 in a public hospital in Minas Gerais. Instruments used: sociodemographic and clinical questionnaire, Quality of Life Questionnaire-Core30 and Piper Fatique Scale, analyzed according to measures of frequency, mean and standard deviation by the software PSPP.

Results: Most patients were women over 60 years old, married, retired and housewives, with an average level of education. The scores of general health status, social, physical, emotional and role functioning were considered satisfactory (means 50 to 70), cognitive function was good (mean higher than 70); the most prevalent symptoms were loss of appetite, fatigue, pain and insomnia. As for fatigue, all dimensions had a mean value <4, considered mild fatigue.

**Conclusion:** Quality of life had satisfactory scores and fatigue was classified as mild in patients undergoing chemotherapy. Keywords: Colorectal neoplasms. Quality of life. Fatigue. Drug therapy.

### RESUMO

**Objetivo:** Avaliar a fadiga e a qualidade de vida relacionada à saúde de pacientes com câncer colorretal em quimioterapia.

Método: estudo descritivo, realizado com 69 pacientes entre janeiro a setembro/2019, em um hospital público de Minas Gerais. Instrumentos utilizados: questionário sociodemográfico e clínico. *Quality of Life Questionnaire-Core30* e Escala de Fadiga de Piper. analisados segundo medidas de freguência, média e desvio padrão pelo softwarePSPP.

Resultados: A maioria era mulheres, acima de 60 anos, casadas, aposentadas, donas de casa, com médio nível de escolaridade. Os escores de estado geral de saúde, das funções social, física, emocional e desempenho de papel foram considerados satisfatórios (médias50-70), da função cognitiva foi boa (média>70); sintomas mais prevalentes foram perda de apetite, fadiga, dor e insônia. Quanto à fadiga, todas as dimensões tiveram média <4, considerado fadiga leve.

Conclusão: A qualidade de vida apresentou escores satisfatórios e a fadiga foi classificada como leve nos pacientes em quimioterapia. Palavras-chave: Neoplasias colorretais. Qualidade de vida. Fadiga. Tratamento farmacológico.

### RESUMEN

Objetivo: Evaluar la fatiga y la calidad de vida relacionada con la salud de los pacientes con cáncer colorrectal sometidos a quimioterapia.

Método: Estudio descriptivo, realizado con 69 pacientes entre Enero y Septiembre/2019 en un hospital público de Minas Gerais. Instrumentos utilizados: cuestionario sociodemográfico y clínico, Quality of Life Questionnaire-Core30 y Piper Fatigue Scale, analizados según medidas de frecuencia, media y desviación estándar por el software PSPP.

Resultados: La mayoría eran mujeres, mayores de 40 años, casadas, jubiladas y amas de casa, con un nivel medio de educación. Los puntajes del estado general de salud, las funciones social, física, emocional y desempeño del papel se consideraron satisfactorias (media 50 a 70), la función cognitiva fue buena (media superior a 70); los síntomas más prevalentes fueron pérdida de apetito, fatiga, dolor e insomnio. En cuanto a la fatiga, todas las dimensiones tienen una media de <4, considerada fatiga leve.

Conclusión: La calidad de vida presentaba puntuaciones satisfactorias y la fatiga se clasificó como leve en pacientes sometidos a guimioterapia.

Palabras clave: Neoplasias colorrectales. Calidad de vida. Fatiga. Quimioterapia.

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According to estimates of incidence in Brazil, except for non-melanoma skin cancer, Colorectal Cancer (CRC) is the second most frequent cancer in females, after breast cancer and the second most common in males after prostate cancer<sup>(1)</sup>. Its etiological factors involve genetic issues and aging. However, they are related to an inadequate lifestyle of individuals, such as obesity, alcoholism, smoking, processed foods and high intake of red meat. Protective factors are associated with regular physical activity and maintenance of healthy body weight<sup>(2)</sup>.

The CRC diagnosis generates physical, functional, socioeconomic, cognitive/psychological and spiritual changes due to feelings of fear, stress, anxiety and uncertainties about the future. Likewise, the type of treatment selected, such as chemotherapy, surgery and radiotherapy, associated or not, can maximize these feelings, in addition to causing symptoms and impacting the Health-Related Quality of Life (HRQOL)<sup>(3-4)</sup>.

Chemotherapy treatment causes several side effects due to the non-specific and unrestricted elimination of cells, which in turn, has a negative impact on HRQOL and patients' daily activities<sup>(3-4)</sup>.

The concept of HRQOL is comprehensive, subjective and related to individual's perceptions of their position in life, in the context of the culture and value systems in which they live, as well as in relation to their goals, expectations and concerns<sup>(5)</sup>. Their interactions are complex and can be affected by their physical and mental health status, level of independence, social relationships and environmental characteristics. Furthermore, its measurement during chemotherapy is essential to assess the clinical-therapeutic repercussions of the treatment, including tissue tolerance and side effects<sup>(5-6)</sup>.

Cancer-Related Fatigue (CRF) is one of the most prevalent effects of the disease and its treatment. It is one of the most common symptoms in all stages of the disease, including after the end of treatment and cure of the malignancy<sup>(3)</sup>. Moreover, their levels tend to fluctuate according to the protocol and number of days of chemotherapy infusion, reaching a peak immediately after chemotherapy administration<sup>(7)</sup>.

CRF is a complex and distressing symptom that is rarely isolated and can be defined as a subjective feeling of tiredness or physical, emotional and/or cognitive exhaustion, related to the disease or treatment itself, which is independent of the level of recent physical exertion and impacts the ability to perform activities of daily living<sup>(8)</sup>.

The mechanisms of CRF pathophysiology are complex and have not yet been well defined. However, it is believed that the factors related to its occurrence involve immunological, inflammatory, metabolic, neuroendocrine and genetic biomarkers, in addition to the hypothalamic-pituitary-adrenal axis<sup>(9)</sup>. Fatigue can also be influenced by the type and stage of cancer, treatment modality, associated comorbidities, medical complications such as anemia, interactions and side effects of other medications, as well as physical and psychological factors<sup>(4,9)</sup>.

Given the disorders resulting from CRC and chemotherapy, which tend to intensify CRF and negatively impact HRQOL, it is essential to evaluate and monitor patients for early detection of these disorders. This is done through active and decisive nursing action in planning and implementing evidence-based strategies that meet the individual needs of each patient, in order to improve HRQOL and reduce the symptom of fatigue.

Thus, the present study aims to assess fatigue and health-related quality of life in patients with colorectal cancer undergoing chemotherapy.

## METHOD

Descriptive study carried out at the chemotherapy center of a teaching hospital in the Triângulo Mineiro region, in Minas Gerais, where about 400 monthly outpatient appointments in the various oncological specialties are done.

Non-probabilistic convenience sampling was performed, that is, adult patients diagnosed with CRC who were present at the chemotherapy center undergoing outpatient treatment during the period in which the researchers were on site for data collection were selected to participate in the study.

Inclusion criteria were patients aged 18 years or older, of both genders, diagnosed with CRC and undergoing outpatient chemotherapy, assisted by the Unified Health System (SUS).

Patients who had difficulty answering three out of four adjusted questions from an instrument: their age, day of the week and the month and place where they were<sup>(10)</sup> were excluded, since divergence could suggest some cognitive deficit, as the answers of these patients to the other instruments could be incompatible with the clinical reality experienced.

Data were collected between January and September 2019. The interviews were carried out by assistant researchers (undergraduate nursing students) in private rooms. The students attended the unit twice a week, in the morning, during the period of greatest concentration of care, and clarified doubts and interviewed the patients who were receiving outpatient chemotherapy treatment on that particular day. However, as this was a part of a larger project, there were weeks when there were no subjects with CRC to participate in the study, and due to the chemotherapy protocol used, some patients were interviewed more than once in subsequent months.

Three questionnaires were used. The first covered questions related to gender, age group, marital status, occupation, educational level, diagnosis, presence or absence of metastasis, type of surgery performed, radiotherapy, chemotherapy protocol, for the characterization of sociodemographic and clinical data.

The second instrument applied was the Quality of Life Questionnaire-Core30 (QLQ-C30), validated in Brazil, which assesses the specific quality of life for cancer patients. It addresses domains related to General Health Status/Quality of Life; five symptom items: dyspnea, loss of appetite, insomnia, constipation and diarrhea, and one item assessing the financial impact of treatment and illness; three symptom scales: fatigue, pain and nausea and vomiting, and five functional scales: physical, emotional, cognitive, social and role functioning<sup>(11)</sup>.

It consists of 30 questions, and the answers are converted to scores (0-100 scale), according to the guidelines of the European Organization for Research and Treatment of Cancer (EORTC), where zero is the worst score and 100 the best score on the General Health Status/Quality of Life (GHS/ QL) scale and on the functional scales. On the other hand, in the item financial difficulty and in the symptom scales and items, zero represents no symptoms and 100 indicates the maximum number of symptoms<sup>(11)</sup>.

The last instrument was the Piper Fatigue Scale – revised, which assesses the intensity of the fatigue symptom, through the analysis of 22 quantitative items that comprise three dimensions: behavioral (items 2 to 7), affective (8 to 12) and sensory/ psychological (13 to 23). The total score is calculated by the mean score of all the items of the instrument (2 to 23) and the dimension scores are calculated by the mean score of the items in each dimension, and the higher the value, the greater the fatigue<sup>(12)</sup>.

For the analysis of the results, a score of 0 indicates absence of fatigue, a score greater than 0 and lower than 4 indicates mild fatigue, while a score equal to 4 and lower than 6 indicates moderate fatigue, and a score equal to and greater than 6 indicates intense fatigue. Based on this classification, four (4) was the cut-off point to discriminate between fatigued and non-fatigued patients, so that patients classified without fatigue were those who had no fatigue or only mild fatigue, whereas the group classified as having fatigue included patients with moderate and severe fatigue<sup>(12)</sup>.

In this scale, in addition to the 22 items with closed-ended questions, there are five additional open-ended questions (items 1 and 24 to 27) that are not computed to calculate the score of the instruments<sup>(12)</sup>. These items provide an additional, more qualitative assessment of fatigue, which will not be addressed in this study.

The data obtained were entered into an electronic spreadsheet (Microsoft Office Excel for Windows®), and double typing was used to check the data. Analysis was performed using PSPP version 1.2.0 software. Absolute and relative frequencies of sociodemographic and clinical variables and mean and standard deviation for the HRQOL and fatigue domains were calculated.

This study was registered in Plataforma Brasil – CAAE: 52529116.3.0000.5154 and approved by the Research Ethics Committee of the responsible institution, under protocol number 1,715,819. The confidentiality of the subjects' identity was maintained, and these individuals were identified by codes. Copies of the Free and Informed Consent Form were signed and delivered, in accordance with Resolution no. 466/12, of the National Health Council.

### **RESULTS**

A total of 72 subjects with CRC were approached. Of these, three were excluded because they did not meet the inclusion criteria. Therefore, the sample consisted of 69 patients with CRC, predominantly women, over 60 years of age, married, retired and housewives, with a low level of education (Table 1).

Regarding their origin, most patients lived in the city where the chemotherapy center was located (49 – 71.0%), in other cities in the Triângulo Sul area of Minas Gerais (16 – 23.2%), in other cities in Minas Gerais (3 - 4.4%) and in other states (4 - 1.4%).

Clinical data are shown in Table 2. Most patients did not have metastasis, underwent oncologic surgery (mostly partial colectomy) and were not treated with radiotherapy. It should be noted that not all patients underwent surgical treatment at the same institution. Therefore, it was not possible to confirm the type of surgery they underwent.

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**Table 1** – Sociodemographic characterization of the patients undergoing chemotherapy treatment (n=69). Uberaba, Minas

 Gerais, Brazil, 2019

Variable	n	%
Gender		
Female	36	52.2
Male	33	47.8
Age range		
18-39 years	9	13.0
40-59 years	23	33.3
60-79 years	30	43.5
>80 years	7	10.2
Marital Status		
Married	37	53.6
Single	16	23.2
Widow(er)	8	11.6
Divorced	8	11.6
Occupation		
Retired	20	29.0
Housewives	15	21.7
Active	34	49.3
Educational level		
Has completed primary education	47	68.2
Has completed secondary education	19	27.6
Has completed higher education	3	4.4

Source: Research data, 2019.

Characteristics	n	%
Metastasis		
No	59	85.5
Yes	10	14.5
Underwent surgery		
Yes	57	82.6
No	12	17.4
Type of surgery		
Partial colectomy	23	33.3
Tumorectomy	13	18.8
Biopsy	6	8.7
Total colectomy	5	7.3
Were unable to inform	10	14.5
Did not undergo surgery	12	17.4
Underwent radiotherapy		
Yes	19	27.5
No	50	72.5

Table 2 – Clinical characterization of patients undergoing chemotherapy (n=69). Uberaba, Minas Gerais, Brazil, 2019

Source: Research data, 2019.

As for the chemotherapy protocol, several medication regimens were found, the most used were: Fluorouracil + Leucovorin + Oxaliplatin in 25 (36.3%) patients; Fluorouracil in 13 (18.8%), Fluorouracil + Leucovorin in 10 (14.5%); Oxaliplatin in three patients (4.5%); Cisplatin in two patients (2.9%); Irinotecan + Fluoracil + Leucovorin in one (1.5%); Irinotecan + Fluorouracil + Leucovorin + Bevacizumab in one (1.5%); Leucovorin + Oxaliplatin in one patient (1.5%); Paclitaxel + Carboplatin in one (1.5%) patient. In 11 (15.9%) subjects, the chemotherapy protocol was not dentified, due to lack of access to the medical records on the day of the interview.

As for HRQOL, Table 3 indicates the mean and standard deviation of the scales of the QLQ-C30 instrument. The scores

of General Health Status (GHS) and of social, physical, emotional and role functioning are considered satisfactory (means between 50.00 and 70.00), while the result obtained for cognitive function was considered good (mean above of 70.00). The most prevalent symptoms were loss of appetite, fatigue, pain and insomnia.

Regarding total fatigue, only four (5.8%) patients answered the 23 Likert-type questions, informing the value/score zero, which indicates the absence of fatigue. Mild, moderate and severe fatigue was reported by 53 (76.8%), six (8.7%) and six (8.7%) patients, respectively. Given the instrument's cutoff score, which considers patients fatigued when the total score of total fatigue is  $\geq$ 4, it can be said that 12 (17.4%) subjects had moderate or severe fatigue.

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Table 4 presents means and standard deviation of the dimensions that make up the Piper Fatigue Scale – revised. The mean scores for behavioral, affective, sensory and total

fatigue ranged from 1.77 to 3.05, indicating that all dimensions of fatigue are mild (scores between 0 and 4).

Scales and Symptoms	Mean	Standard Deviation
General Health Status (GHS)	69.31	23.85
Cognitive Function (CF)	74.18	30.06
Social Functioning (SF)	69.36	35.10
Physical Functioning (PF)	67.95	29.13
Emotional Functioning (EF)	58.24	33.45
Role Functioning (RF)	56.53	42.03
Loss of Appetite (LA)	35.24	41.96
Fatigue (FAT)	28.49	33.45
Pain (PAIN)	27.97	38.16
Insomnia (INS)	27.22	29.26
Nausea and Vomiting (NAV)	25.03	35.35
Constipation (CON)	12.80	22.17
Dyspnea (DYS)	12.53	26.22
Diarrhea (DIA)	8.67	24.64
Financial difficulties (DIF)	6.74	21.03

Table 3 – Mean and standard deviation of the QLQ-C30 instrument scales. Uberaba, Minas Gerais, Brazil, 2019
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Source: Research data, 2019.

**Table 4** – Mean and standard deviation of the dimensions of the Piper Fatigue Scale (revised). Uberaba, Minas Gerais, Brazil, 2019

Dimensions	Mean	Standard Deviation
Behavioral Fatigue	1.77	2.90
Affective Fatigue	2.70	8.36
Sensory Fatigue	3.05	1.72
Total Fatigue	2.57	2.17

Source: Research data, 2019.

# DISCUSSION

The study sample was characterized by the prevalence of women, aged over 60 years, married, retired and with a low level of education. These sociodemographic results are consistent with national studies<sup>(13–14)</sup> and contrast with international studies in which most patients with CRC were men<sup>(7,15–16)</sup>, with a mean age of 59 (23-75) years<sup>(7)</sup>, and higher educational level (>12 years)<sup>(15)</sup>.

On the other hand, regarding the HRQOL, it was found that GHS and the other functions had scores with adequate/ satisfactory results. Cognitive function obtained the highest score and emotional function the worst, along with role functioning. There was a predominance of the symptoms loss of appetite, fatigue, pain and insomnia.

These results are consistent with those obtained in a study carried out in the city of São Paulo<sup>(13)</sup>, which analyzed the relationship between the most prevalent symptoms of cancer and HRQOL, using the QLQ-C30 instrument, and found that the most prevalent cancer was colorectal cancer (49.5%) and GHS and functions scores including role functioning ranged from 68.1 to 78.4 (adequate to good), with cognitive function also having the highest score and emotional function the lowest. Moreover, fatigue, insomnia, pain and loss of appetite were also the four most predominant symptoms, with fatigue being the most intense symptom (mean 29.2)

Compared to an international study carried out in Saudi Arabia, GHS and emotional function (means 67.1 and 66.9, respectively) were identified as satisfactory results, while social and role functioning had the highest scores (means 83.49), considered as good results. Insomnia was considered the most distressing symptom<sup>(17)</sup>.

An integrative review on the QOL of patients with CRC found that in most studies QOL was satisfactory, the social domain was the most preserved and the most affected domains were the psychological/emotional and physical<sup>(18)</sup>.

A study carried out in Petrolina, State of Pernambuco, using the World Health Organization's QOL questionnaire (WHOQOL) found that patients with CRC rated their QOL positively, but their health satisfaction negatively. The psychological domain had the highest score (76.33) and the social domain was the most affected (55.10)<sup>(14)</sup>.

A study carried out in Japan found that the unmet support needs of patients with CRC undergoing outpatient chemotherapy belonged to the psychological domain and were significantly associated with psychological distress and QOL, with the female gender being significantly associated with greater needs for total support. The authors suggest that interventions and strategies to assist in the treatment support needs of health professionals can help to reduce emotional symptoms and consequently improve QOL<sup>(15)</sup>.

Despite the satisfactory scores found in the HRQOL domains, there may be patients with regular to unsatisfactory functions and GHS. Likewise, symptoms may vary from one patient to another, mainly due to the different chemotherapy protocols used. Fatigue measured by the QLQ-C30 instrument was very prevalent. However, it was considered mild by the revised Piper Fatigue Scale, configuring the sample as not-fatigued.

This can be associated with the fact that the QLQ-C30 instrument does not specifically and openly address the fatigue symptom, but addresses its related characteristics such as tiredness, weakness and need for rest<sup>(11)</sup>. Thus, many patients did not realize that they were being asked about fatigue. On the other hand, the revised Piper Fatigue Scale is specific for this symptom and 0 can be chosen by the respondent<sup>(12)</sup>, unlike the QLQ-C30.

Patients often reported fatigue considering only the physical dimension, whose association by common sense is stronger and patients do not always speak openly about this symptom, not even to health professionals, as they consider fatigue a natural symptom of the disease. Therefore, they only reported symptoms that they believed to be relevant to their disease and treatment, and those patients who had some kind of emotional disorder tended not to disclose their concerns to health professionals<sup>(19)</sup>.

Another reason why patients do not report fatigue is the concern about having the treatment changed, not wanting to bother professionals, fear of being perceived as someone inconvenient who complains excessively, in addition to the belief that there is no treatment for their condition<sup>(8)</sup>.

In addition, health professionals tend to diagnose and prioritize symptoms with observable components – nausea/ vomiting and diarrhea, for example – and later, which results in underestimation of the incidence, severity and distress caused by the symptoms<sup>(19)</sup>.

Fatigue levels fluctuate during the chemotherapy treatment period and the symptom is often underreported in clinical practice. Therefore, it must be evaluated at the beginning, during and after treatment. A study carried out in eight hospitals in Toronto, Canada and in six health facilities in Sydney, Australia, evaluated the severity and duration of fatigue in men and women with CRC and found that fatigue peaked immediately after adjuvant chemotherapy and persisted for up to two years. Fatigue was associated with worse QOL, affective and cognitive symptoms; and these, together with the presence of comorbidities, chemotherapy and baseline fatigue were predictive of long-term fatigue<sup>(7)</sup>. In the referred study, the dimension with the highest score among those included in the revised Piper Fatigue Scale was the sensory/psychological dimension, indicating disorders in the self-perception, emotional and cognitive components that result in different feelings and/or sensations in daily activities, conditions of anxiety and/or depression, disorders in mental functions – memory, concentration and organization of thoughts<sup>(12)</sup>.

The affective dimension has a higher value of standard deviation, indicating that a considerable number of patients had a negative interpretation or meaning attributed to CRF, making it more unpleasant, unacceptable, destructive and abnormal. This is mainly due to the fact that the individuals have never had this experience before<sup>(12)</sup>.

Early detection of fatigue management during the treatment and survival stages of patients with colorectal cancer is important, and health professionals must carry out appropriate interventions to reduce fatigue and consequently improve patients' quality of life<sup>(16)</sup>.

A study carried out in Canada highlighted the role of nursing, as oncology nurses performed a program of standardized interventions to meet the needs of a group of patients with colorectal and breast cancer, and a comparison was made with a control group that received usual care. Although there were no significant differences between the two groups, there was an improvement in terms of unmet needs and QOL for the group that received the intervention<sup>(20)</sup>. Therefore, we emphasize the essential role of nurses in detecting needs and priorities in order to develop strategies to alleviate symptoms and help improve the QOL of these patients.

The present study has the following limitations: it is descriptive and with purposive sampling. A descriptive study does not allow the monitoring of aspects and possible changes in HRQOL and CRF during the treatment, since the collection took place in a single moment of the chemotherapy cycle, and a purposive sampling restricts the study, as the patients received different chemotherapy protocols, and data collection was performed on only two days of the week.

### CONCLUSION

The HRQOL and CRF scores showed a sample of patients with a satisfactory quality of life and non-fatigued. However, this finding does not exclude the need for concise and effective prevention and interventions in the most prevalent dimensions and symptoms found. Changes in HRQOL and the presence of CRF in these patients can negatively impact their ability to perform activities of daily living in all segments, in addition to causing psychological and emotional disorders in the relational dynamics of individuals and their ability to make decisions.

It is essential that nurses ask patients about subjective symptoms such as sensory and affective fatigue, establishing active listening, empathy and trust, and when the presence of CRF and its influence on HRQOL is identified, the professional can carry out an individual planning, with multidisciplinary interventions based on clinical evidence, encompassing pharmacological and non-pharmacological therapies, with the support of family and friends, and permanent evaluation of their effectiveness.

Thus, by ensuring proper management and monitoring of these symptoms and the delivery of systematic and comprehensive care to patients during chemotherapy treatment, nurses will directly contribute to the care provided, as well as expand their knowledge in the areas of teaching, research and care management.

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### Acknowledgments:

In memory of Viviane Aparecida da Silva, who collaborated effectively in the curation and validation of data from this research.

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The authors declare that there is no conflict of interest.

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> Associate editor: Cecília Helena Glanzner

Editor-in-chief: Maria da Graça Oliveira Crossetti

Received: 05.17.2021 Approved: 05.16.2022