

Relationship between quality of life and side effects of neoadjuvant cytostatic treatment in patients with non-metastatic breast cancer and their evolution over time

Larisa Morar¹, Vladimir Poroch^{1,2}, Daniela Mosoiu^{3,4}

¹Institutul Regional de Oncologie Iași, România

²Universitatea de Medicină și Farmacie "Gr. T. Popa", Iași, România

³Universitatea Transilvania Brașov, România

⁴Fundația HOSPICE Casa Speranței, Brașov, România

Received: 03.07.2023 • Accepted for publication: 19.07.2023

Abstract

Breast cancer is the leading cause of cancer death in women, with an increasing incidence and predominantly affecting middle-aged people. Both cancer diagnosis and cancer treatment have a major impact on patients' quality of life.

From January to December 2022, we conducted a prospective longitudinal observational quantitative study at the Regional Institute of Oncology Iasi, with the aim of identifying how neoadjuvant chemotherapy (NAC) influences the quality of life of these patients, using the EORTC QLQ-C30 and BR23 questionnaires in dynamics (at the initiation of NAC, at 3 months and at 6 months of treatment). Seventy-six patients were included in the study.

We found a significant difference in scores prior to initiation of cancer treatment and at 3 months and 6 months of NAC, respectively. Patients' quality of life (QoL) was decreased during neoadjuvant chemotherapy. The lowest QoL values were recorded at 6 months in younger patients under 49 years (QoL 51.19 points, $p=0.054$). The most common symptoms affecting QoL among respondents were fatigue, insomnia, anorexia and financial difficulties - especially in rural respondents. The most serious symptom from the patients' perspective is alopecia, contributing to impaired body image and outlook on the future and withdrawal from social activities

Cancer patients require a holistic approach from the moment of diagnosis, requiring physical, psycho-emotional, social and spiritual support.

Rezumat

Cancerul mamar reprezintă principala cauză de deces prin cancer la femei, având incidență în creștere și afectând preponderent persoanele cu vârstă mijlocie. Atât diagnosticul de cancer cât și tratamentul oncologic au o influență majoră asupra calității vieții pacienților.

În perioada ianuarie – decembrie 2022 s-a realizat un studiu cantitativ observațional longitudinal prospectiv în cadrul Institutului Regional de Oncologie Iași, cu scopul de a identifica modul în care chimioterapia neoadjuvantă (NAC) influențează calitatea vieții acestor pacienți, utilizând chestionarele EORTC QLQ-C30 și BR23 în dinamică (la inițierea NAC, la 3 luni și la 6 luni de tratament). Au fost incluși în studiu 76 de pacienți.

S-a constatat o diferență semnificativă a scorurilor obținute anterior inițierii tratamentului oncologic și la 3 luni respectiv la 6 luni de NAC. Calitatea vieții (QoL) pacienților a fost scăzută pe perioada administrării chimioterapiei neoadjuvante. Cele mai mici valori ale QoL au fost înregistrate la 6 luni, la pacienții tineri sub 49 ani (QoL 51.19 puncte, $p=0.054$). Cele mai frecvente simptome care au afectat QoL în rândul respondenților au fost: obosealitatea, insomnia, anorexia și dificultățile financiare - în special la respondenții din mediul rural. Cel mai grav simptom din perspectiva pacienților este alopecia, aceasta contribuind la afectarea imaginii corporale și a perspectivei asupra viitorului și la retragerea din activitățile sociale

Pacienții oncologici necesită o abordare holistică încă de la stabilirea diagnosticului, necesită susținere atât din punct de vedere fizic, cât și psiho-emoțional, social și spiritual.

Introduction

Cancer is by far one of the leading causes of death in Romania [1]. Most often diagnosed in middle and old age, the number of people suffering from this disease is increasing and the incidence of cancer is rising [2]. According to statistics, breast cancer is the most common of all neoplasms in women and is the leading cause of cancer death in European women, according to the European Society of Medical Oncology [3, 4]. In 2020 in Romania almost 4,000 women will have lost their battle with breast cancer, which means 11 women per day [5].

In the records of the Regional Institute of Oncology (IRO) Iasi there were 15,934 patients in 2021, of which 3,020 were new cases [5]. The most cancer cases in the IRO Iasi records are breast cancers - 3,526 cases of which 303 were new cases (in 2021) [5, 6]. Given the very large number of breast cancer patients diagnosed and treated at IRO Iași, we conducted a prospective quantitative observational study investigating how neoadjuvant chemotherapy (NAC) influences the quality of life of these patients.

The aim of is to study how the quality of life of breast cancer patients is influenced and how it could contribute to improving their quality of life. The study aims to answer the research question: How does neoadjuvant chemotherapy influence the quality of life of breast cancer patients?

It is a **prospective longitudinal observational quantitative study**. Patients signed the informed consent (attached at the end of the paper) and completed the EORTC QLQ-C30 and BR23 questionnaires in three successive steps:

1. At the initiation of chemotherapy;
2. At 3 months after initiation of treatment (during which time they received anthracycline-based regimens: Cyclophosphamide 600mg/mp + Epirubicin 100mg/mp at 3-week intervals (q3w) or Cyclophosphamide 600mg/mp + Adriamycin 60mg/mp q3w or q2w for dose-dense regimens, a total of 4 cycles).
3. At 6 months after treatment initiation, i.e. - quality of life under taxane treatment (Docetaxel 100mg/mp, q3w (4 cycles) or Paclitaxel 80mg/mp q1w (12 weeks). Her2+ patients received at this stage a combination of taxanes with anti-Her biologic therapy (Pertuzumab 420mg i. v and Trastuzumab 600mg s.c. q3w, 4 cycles) , and the side effects of the therapeutic combination in this category of patients were followed up

The study was conducted at the Regional Institute of Oncology Iasi (Romania) and was a single-centre study. The study group included patients with non-metastatic breast cancer diagnosed and treated at the Regional Institute of Oncology Iasi between January and December 2022. The study was conducted under the condition of conclusive biopsies (confirming the diagnosis). After obtaining informed consent from the subjects, they completed questionnaires.

The QLQ-C30 questionnaire has 30 questions. Scales for different functions are calculated on the basis of the questionnaire, so five functional scales, three symptom scales, a general health scale (QoL scale) and six single items are included. Each response is used only once on one scale, not repeated. A high score for the functional scales represents a high level of functioning, and a high score for a symptom/symptom scale represents a significant symptomatology/high problem. High score for general health represents good QoL.

Breast Cancer Module: QLQ-BR23 is a 23-question questionnaire that assesses symptoms of the disease, treatment side effects, body image, sexual function and future outlook. This breast cancer module includes 5 multiple item scales and 3 single items.

Table 1 - EORTC QLQ-C30 and BR-23: number of function-specific questionnaire questions and symptoms

	Scale	Number of items	Question number in the questionnaire
EORTC QLQ-C30			
General state of health			
QoL	QoL	2	29, 30
Functional scales			
Physical function	PF2	5	1, 2, 3, 4, 5
Functional role	RF2	2	6, 7

Emotional function	EF	4	21, 22, 23, 24
Cognitive function	CF	2	20, 25
Social function	SF	2	26, 27
Symptom scale			
Fatigability	FA	3	10, 12, 18
Nausea and vomiting	NV	2	14, 15
Pain	PA	2	9, 19
Dyspnoea	DY	1	8
Insomnia	SL	1	11
Anorexia	AP	1	13
Constipation	CO	1	16
Diaree	DI	1	17
Financial difficulties	FI	1	28
QLQ-BR23			
Functional scales			
Body image	BRBI	4	39, 40, 41, 42
Sexual function	BRSEF	2	44, 45
Sexual satisfaction	BRSEE	1	46
Future outlook	BRFU	1	43
Symptom scale			
Side effects of systemic therapy	BRST	7	31, 32, 33, 34, 36, 37, 38
Breast symptoms	BRBS	4	50, 51, 52, 53
Symptoms of the upper limb	BRAS	3	47, 48, 49
The impact of alopecia	BRHL	1	35

Study population

Inclusion criteria

- women/men diagnosed (histologically) with non-metastatic breast cancer;
- unilateral or bilateral breast cancer;
- persons capable of signing informed consent;
- patients over 18 years of age at the time of enrolment in the study;
- ECOG performance index 0-2;

Exclusion criteria

- patients diagnosed with other neoplasia;
- inability to consent and take cognisance;
- minor patients (under 18 years of age);
- Patients who have given up chemotherapy after the first cycles for personal reasons;
- Patients who are stage IV at diagnosis or who have undergone hormonal/radiotherapy treatment;
- patients who progress under treatment (become stage IV/inoperable);
- patients with cognitive impairment;
- impaired performance status (ECOG ≥ 3);
- patients with psychiatric pathology, neuromuscular diseases, bronchial asthma, COPD;
- pregnant patients;
- Patients who refuse to complete the dynamic questionnaire or withdraw from the study for personal reasons;

Results

1. Validation of the EORTC QLQ-C30 and BR23 questionnaire (checking the internal consistency of the scales)

To begin with, internal consistency analysis was applied using Cronbach's alpha to identify whether the scales used are statistically reliable. The indicator measures the internal consistency between the items of a scale and must have the same response variants (e.g. 1 - a little; 2 - medium; 3 - a lot; 4 - very much). The basic criterion for this operation is the value of Cronbach's alpha, which has a range between 0 and 1. A scale, to be considered consistent, must reach a value as close as possible to 1, with 0.70 being accepted as the cut-off level by most researchers. However, Cronbach's alpha cannot be less than 0.60.

Thus, using SPSS, we calculated the coefficient given for the EORTC QLQ C-30 and EORTC QLQ BR23 scales, apart from the independent items, to which it is not applicable, obtaining the following results:

Table 2 - Cronbach's alpha values and validation of the EORTC QLQ-C30 and BR-23 questionnaires

EORTC	Scala (the questions)	Cronbach alpha
QLQ-C30	General state of health (29, 30)	0,857
	Physical functionality (1-5)	0,837
	Personal affirmation (6, 7)	0,865
	Emotional functionality (21-24)	0.910
	Cognitive functionality (20, 25)	0,860
	Social functionality (26, 27)	0,856
	Fatigue (10, 12, 18)	0,869
	Nausea and vomiting (14, 15)	0,500
	Pain (9, 19)	0,834
QLQ-BR23	Body image (39-42)	0,942
	Sexual function (44, 45)	0,513
	Side effects of treatment (31-34, 36-38)	0,861
	Breast symptom (50-53)	0,802
	Upper limb symptoms (47-49)	0,807

We note that the internal consistency of the scales was affirmed, with the exception of the Nausea and Vomiting scale ($\alpha = 0.5$) and the Sexual Function scale ($\alpha = 0.513$). Due to the short period of patient enrolment in the study (January to May 2022, with follow-up until December 2022), the number of participants was reduced. Out of a total of 87 patients diagnosed and treated in the IRO Iasi Medical Oncology Clinic who initially agreed to be enrolled in the study,

5 were lost to follow-up, 4 refused to complete the questionnaire repeatedly, and 2 were excluded due to progression (becoming stage IV - metastatic) and a change in therapeutic strategy. Thus only 76 patients (73 women and 3 men) who completed the EORTC QLQ-C30 and BR23 questionnaires dynamically were included in the study.

Distribution of patients by age group

Table 3 - Distribution of patients by age group

		Age range			
		Frequency (n)	Percent %	Valid Percent %	Cumulative Percent
Age	30-39	9	11.8	11.8	11.8
	40-49	14	18.4	18.4	30.3
	50-59	23	30.3	30.3	60.5
	60-69	20	26.3	26.3	86.8
	>=70	10	13.2	13.2	100.0
Total		76	100.0	100.0	

It can be seen that most patients in the study group (23/76) are aged between 50-59 years. Average age: 55 years (35-77 years). Standard deviation (SD) = 11.19

2. EORTC QLQ-C30 development over time of functions and general health status

Both cancer diagnosis and cancer treatment have a major influence on patients' quality of life. If we refer to the functions and symptoms dynamically assessed with the EORTC questionnaires we can observe that after the initiation of neoadjuvant chemotherapy patients showed a deterioration of the general health status, but with improvement towards the end of the treatment with taxanes +/- antiHer therapy. Patients' physical and social functioning was relatively good during the period of cytostatic treatment, with moderate decreases over the 6 months of follow-up, thus the mean for initial physical functionality (T1) of patients was 82.63 and 60.53 at 6 months, respectively, and social functionality decreased from 85.09 (T1) to 56.58 (T3). If we were to refer to personal affirmation, it decreased significantly from 76.75 to 51.53 at the initiation of cancer treatment, but subsequently remained constant during the 6 months of neoadjuvant chemotherapy.

It is found that in the studied group, the cognitive functionality and emotional state of the patients were most influenced during the treatment period with the lowest and continuously decreasing values during the 6 months of regular monitoring.

Table 4 - EORTC QLQ-C30: time evolution of functions, mean values +/- Standard Deviation (SD)

Response time: average +/- DS	EORTC QLQ-C30 - Functions					
	General state of health	Physical functionality	Personal affirmation	Emotional functionality	Cognitive functionality	Social functionality
Initial time (T1)	89.80 +/- 17.45	82.63 +/- 14.11	76.75 +/- 26.26	77.85 +/- 21.84	80.48 +/- 17.72	85.09 +/- 19.74
At 3 months of treatment (T2)	60.96 +/- 22.62	65.35 +/- 16.97	51.53 +/- 29.59	51.10 +/- 28.03	58.55 +/- 30.61	63.16 +/- 26.71
At 6 months of treatment (T3)	63.49 +/- 21.90	60.53 +/- 21.22	51.54 +/- 30.57	41.67 +/- 31.97	47.81 +/- 31.43	56.58 +/- 32.56
Media	71.42 +/- 27.47	69.50 +/- 20.00	59.94 +/- 31.11	56.87 +/- 31.48	62.28 +/- 30.42	68.27 +/- 29.39

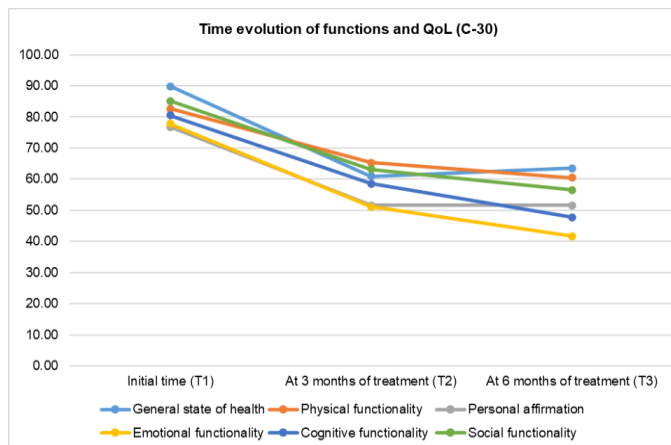


Figure 1 - EORTC QLQ-C30: time evolution of functions

i.EORTC QLQ-C30 time course of symptoms

Table 5 - EORTC QLQ-C30: time course of symptoms

EORTC QLQ-C30 - Symptom									
Response time +/- DS	Fatigability	Nausea/vomiting	Pain	Dyspnoea	Insomnia	Anorexia	Constipation	Diarrhea	Financial difficulties
Initial time (T1)	22.07 +/- 18.99	3.29 +/- 8.17	18.64 +/- 17.63	9.21 +/- 16.86	21.49 +/- 24.16	17.54 +/- 27.47	11.84 +/- 18.62	3.51 +/- 10.30	21.05 +/- 27.67
At 3 months of treatment (T2)	50.73 +/- 20.32	37.50 +/- 23.75	29.39 +/- 24.17	20.61 +/- 23.07	55.26 +/- 32.00	49.56 +/- 29.06	36.84 +/- 25.29	18.86 +/- 20.61	47.81 +/- 35.00
At 6 months of treatment (T3)	59.50 +/- 27.44	25.22 +/- 19.72	33.33 +/- 29.19	19.74 +/- 25.05	62.72 +/- 34.41	60.09 +/- 33.56	33.33 +/- 31.27	17.98 +/- 25.21	57.02 +/- 39.18
Average +/- SD	44.10 +/- 27.58	22.00 +/- 23.19	27.12 +/- 24.82	16.52 +/- 22.45	46.49 +/- 35.29	42.40 +/- 35.06	27.34 +/- 27.78	13.45 +/- 20.86	41.96 +/- 37.40

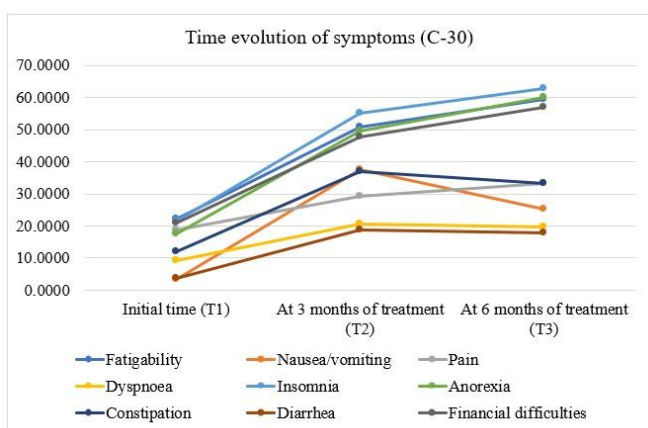


Figure 2 - EORTC QLQ-C30: time course of symptoms

As more severe symptoms, according to the patients' statements, insomnia, fatigue and anorexia are noted, which worsened during the 6 months of treatment. Some patients

also reported financial difficulties, which were accentuated throughout the treatment period, especially in patients who lived in other counties and travelled to the hospital for weekly administration of taxanes (Paclitaxel). Diarrhoea and dyspnoea appeared immediately after the initiation of anthracycline treatment with moderate frequency and remained constant thereafter. Nausea and vomiting were more severe during anthracycline treatment and had a much lower frequency during taxane administration. Some patients experienced constipation during the first 3 months and decreased in frequency thereafter.

ii.EORTC QLQ-BR23 evolution over time of function averages

Table 6 - EORTC QLQ-BR23: time course of mean functions (N = number of patients; SD = standard deviation)

EORTC QLQ-BR23: Evolution over time of function averages					
Moment of response		Body image	Sexual function	Sexual satisfaction	Future outlook
Initial time (T1)	Media	89.25	37.69	45.65	65.35
	N	76	65	46	76
	DS	16.544	21.506	26.630	34.616
At 3 months of treatment (T2)	Media	61.51	12.05	18.52	31.14
	N	76	65	27	76
	DS	32.801	13.663	19.244	31.896
At 6 months of treatment (T3)	Media	53.18	8.21	15.79	20.18
	N	76	65	19	76
	DS	38.030	11.830	17.098	33.590
Total	Media	67.98	19.32	31.52	38.89
	DS	34.097	20.797	26.779	38.427

Only 65 patients in the study group agreed to answer questions about sexual function and a decreasing number answered questions about sexual satisfaction. Perhaps because it is still a taboo subject or because self-image suffers greatly, especially for young women. Sexual activity is low among sufferers, partly because of symptoms, but also because of treatment, which sometimes leads to low libido.

According to the mean results of the EORTC QLQ-BR23 questionnaire, if we refer to functions, we can easily see that body image is the most affected during the whole treatment period, but especially during the first 3 months after the initiation of therapy. The patients' future outlook also undergoes significant changes, especially in younger patients.

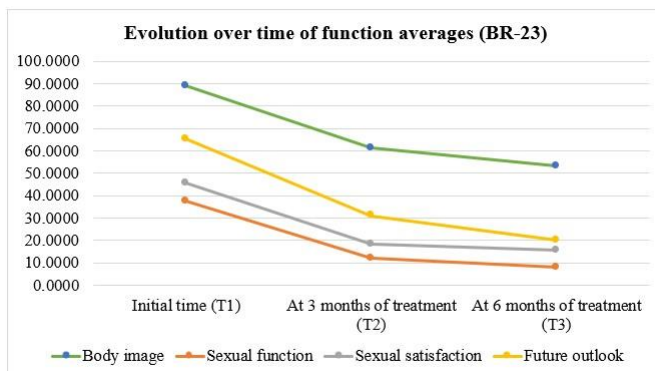


Figure 3 - EORTC QLQ-BR23: evolution over time of function means

iii.EORTC QLQ-BR23 time course of symptoms

Table 7 - EORTC QLQ-BR23: time course of symptoms

EORTC QLQ-BR23: time course of symptoms					
Moment of response		Side effects of treatment	Breast symptom	Upper limb symptoms	Affected by hair loss
Initial time (T1)	Mean	11.34	16.23	13.74	5.70
	N	76	76	76	76
	Std. Deviation	12.072	17.894	16.113	15.765
At 3 months of treatment (T2)	Mean	51.75	17.43	13.30	57.89
	N	76	76	76	76
	Std. Deviation	20.445	13.553	15.923	37.067
At 6 months of treatment (T3)	Mean	54.26	14.80	9.94	65.35
	N	76	76	76	76
	Std. Deviation	23.134	17.084	13.280	39.793
Total	Mean	39.12	16.15	12.33	42.98
	Std. Deviation	27.416	16.250	15.189	42.030

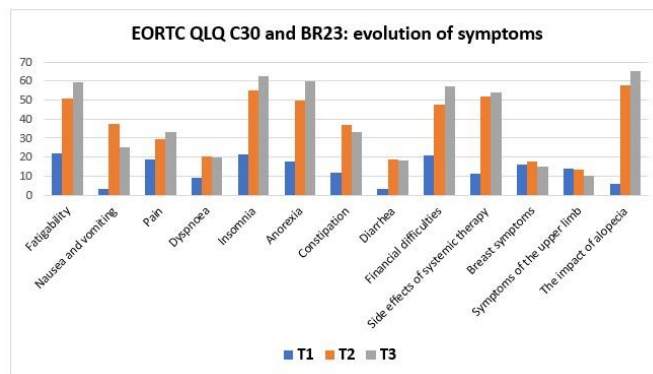


Figure 6 - EORTC QLQ C30 and BR23: evolution of symptoms

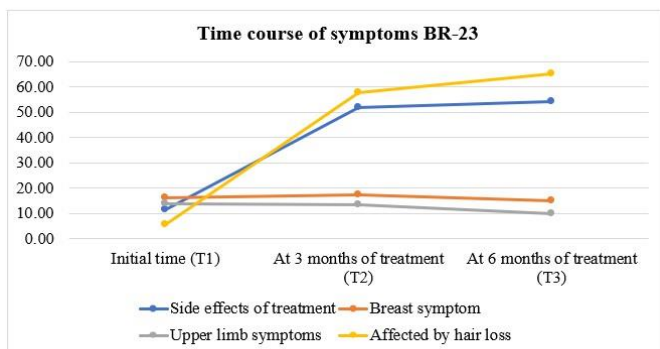


Figure 4 - EORTC QLQ-BR23: Time course of symptoms

The side effects of chemotherapy and alopecia were the most difficult to bear over time having a significant influence on QoL. Since no patients with metastatic breast cancer were included in the study, but only patients with localized disease, breast and upper limb symptoms were somewhat attenuated, present in few patients and improved during the period of cancer therapy.

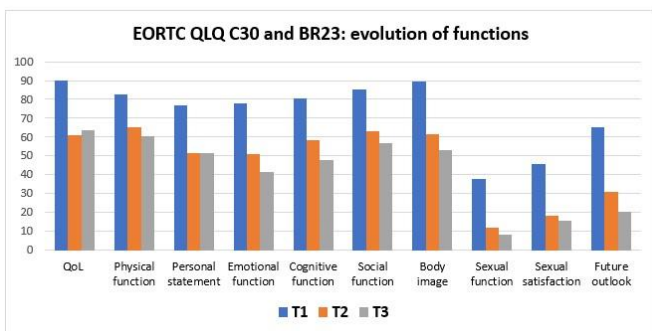


Figure 5 - EORTC QLQ C30 and BR23: evolution of functions

The figures show the averages of functions and symptoms in dynamics. Significant differences that have occurred over time in the patients examined can be seen. Differences of more than 10 points have major clinical significance. Differences occurred in most functions and symptoms, but significant ones were observed especially in sexual function, body image, future outlook and some symptoms - fatigue, nausea and vomiting, insomnia, alopecia, anorexia, financial difficulties.

Decreased physical function and assertiveness can be observed. 1/3 of the patients enrolled in the study report that fatigue, nausea and cognitive disorders (concentration problems, memory disorders) interfere with their ability to work at work 8 hours a day and request sick leave or shorten their work schedule. There are also patients who feel much better when they get involved in social activities and continue to go to work, feel supported, integrated in the collective and have a very good psycho-emotional status.

Discussions

Breast cancer remains the disease with the highest incidence and mortality among women worldwide. In addition to the well-known risk factors (age, early menarche, late menopause, nulliparity, late delivery of the first child, long-term use of oral contraceptives, family history of breast cancer, genetic factors), sedentary lifestyle, excessive alcohol consumption and exposure to radiation [7, 8].

The average age of patients diagnosed with breast cancer is 50-55 years. If we refer to the mean age of the studied group, it was 55.64 years (35-77 years). Results of studies in the literature give similar results with minor numerical variations: in Horigan et al who studied the quality of life on a group of 1072 patients, the mean age was 53 years [9] ; Lee et al - 52.08 years [10].

It is known that breast cancer mainly affects women, **B/F ratio=1/100**. 3 men (3.95%) and 73 women were included in the study group. In our case the F/B ratio is different due to the exclusion of women with stage I and IV disease, women with multiple neoplasms, those who withdrew from the study during the 12 months, who progressed or who dropped out of therapy. We observed that general health status decreases during the treatment period: initial **QoL** was 89.80, then it decreased significantly below NAC to 60.96 (T2) and improved slightly during the taxane administration period reaching 63.49 (T3). Binotto et al claims that (QoL) general health status is low during the chemotherapy administration period but improves after finishing treatment. It has also been observed that

symptoms worsen in chemotherapy patients and diminish until symptoms disappear after finishing treatment [7, 8]. A decrease in QoL was observed in all patients at 3 and 6 months, respectively, regardless of the neoadjuvant CHT regimen applied. *Rezapour* et al observed that some manifestations such as fatigue, pain, cognitive function and constipation were less troublesome in patients on Cyclophosphamide-Adriamycin compared to the Paclitaxel-Gemcitabine treated group where nausea and vomiting, dyspnea, insomnia and diarrhea were less manifest. No differences in psycho-emotional status and physical performance were observed between the two groups of patients [11, 12].

The study confirmed the **reliability and validity of the EORTC QLQ-C30 and BR23 questionnaires**, with the **Cronbach** alpha indicator showing values above 0.7 (statistically significant) for most scales, except for the nausea and vomiting scale ($\alpha=0.5$) and sexual function ($\alpha=0.513$), where the results are statistically insignificant.

Patients' **quality of life** was decreased during neoadjuvant chemotherapy. The lowest **QoL** values were recorded at 6 months (T3) in younger patients under 49 years of age (QoL 51.19 points, $p=0.054$, statistically significant at 10% variation). Patients also suffered **emotionally**, both immediately after diagnosis (T1, $p=0.050$) and during the first months of anthracycline treatment (T2, $p=0.038$), with emotional functioning being lowest in the 50-59 age group (score 37.68 in T2, $p=0.038$). Also, patients with heart failure (HF) and patients with type 2 diabetes had a low emotional status, which affected their quality of life ($p=0.025$ for HF and $p=0.017$ for type 2 diabetes). Breast cancer patients are at increased risk of altered psycho-emotional status, which negatively influences quality of life [7].

Campora et al: 64-70% of patients surveyed had normal physical activity; 39-45% normal psychological status; 83-90% able to care for themselves and did not require help; 84% had good family relationships; anxiety was reported in 19-28% of patients and depression in 3.9% [13].

If we refer to **social functionality** or integration of patients into society, we find that the lowest values were recorded by patients with CM stage IIB (38.54), $p=0.052$. There are several factors that are associated with breast cancer patients' **withdrawal from social life**. Here we can talk about the social stigmatization of the cancer patient, this directly affects their social relationships. According to studies, the patient's physical condition and oncological treatments have influenced his relationships with his family and his involvement in various social activities [7, 14]. It has been shown that patients who have a large circle of friends and have a wide social network, experience a lot of support from family and friends [15].

Chemotherapy is responsible for exacerbating toxicities such as **diarrhoea**, which alters the quality of life of the CM patient. Another common problem among patients is **insomnia**, this can be caused or aggravated by side effects of cancer treatment such as urinary or digestive symptoms, nausea, gastro-oesophageal reflux [16]. Other side effects of chemotherapy include **changes in taste** and smell, which influence the patient's appetite and the amount of food ingested [7]. These were also present in the study population, but the values obtained were not statistically significant. *Binotto* et al did not observe significant differences in cognitive function, pain, dyspnoea, constipation, financial difficulties and future outlook in the study group [7]. Scales for body image, sexual function and physical functioning show low values

during treatment compared to fluctuating values for psychological aspects and social relationships [7, 8]. *Horigan* et al studied QoL in a group of 1072 patients and found that the lowest values were for appetite, breast symptoms and sexuality [9].

Only 65 patients completed the questions on sexual function and satisfaction. **Sexual function** is influenced both by the psycho-emotional state caused by the cancer diagnosis and by low libido under treatment. It goes without saying that a patient's **sexuality** is greatly influenced after receiving a diagnosis of cancer, primarily by changing hormone levels, but also by changing perceptions of body image [17]. According to the study published by Hall et al systemic chemotherapy frequently compromises women's sex lives in the short or long term [7, 18].

Kiebert et al concluded that **alopecia** is the most unpleasant side effect affecting the quality of life of CM patients [19, 20]. And in the respondent's **alopecia** had a significant impact especially in those with stage II breast neoplasm ($p=0.033$).

It was not possible to assess the reversibility of the impact of chemotherapy on the quality of life of patients treated with anthracyclines and taxanes, as long follow-up of the subjects would be required [7]. *Souza* et al observed that nutritional interventions contribute to improvement of muscle strength, relief of inappetence, nausea and vomiting, and contribute to reduction in the frequency of leukopenia and abdominal pain during neoadjuvant CHT [21]. Routine assessment of patients' quality of life increases the quality of care by improving **communication** between doctor and patient, thereby increasing satisfaction on both sides [7].

Quality of life assessment is crucial in everyday clinical practice to identify physical and psycho-emotional problems caused by illness or treatment. Young women (under 45 years of age, approx. 13% of all CM cases) frequently have poorer psycho-emotional status and quality of life compared to older women. It is very likely that their condition is also influenced by their family situation, life partner and sexuality, the presence of young children and the fear of not seeing them grow up, and altered body image [22].

Research limits and directions

Given the small number of participants ($n=76$) from a single cancer institute who were dynamically assessed, this study is somewhat limited, with low statistical power, but the results obtained were reported to data published in the literature. Further research on factors affecting quality of life is needed in order to find effective solutions to improve the quality of life of breast cancer patients.

Possible practical solutions that would improve the quality of life of patients have been sought, such as the successful personalised diet reported by *Lugtenberg* et.al; the potential of digital investigations in sensory-motor rehabilitation called "next generation sensorimotor rehabilitation" by *Axenie* and *Kurz* et.al. Or the exercise and personalized recovery program with rewarding effects described by *Yvonne Anisimowicz* et.al [23, 24, 25].

Conclusions

- Neoadjuvant chemotherapy has negative consequences on patients' quality of life
- There are several tools to measure the quality of life of breast cancer patients, but most commonly used are the EORTC QLQ-C30 questionnaire and the

EORTC QLQ-BR23 breast add-on module translated into Romanian.

- We found a significant difference in scores prior to the initiation of cancer treatment and at 3 months and 6 months of NAC, respectively. The most common symptoms that affected QoL among respondents were fatigue, insomnia, anorexia and financial difficulties - especially in rural respondents. The most serious symptom from the patients' perspective is alopecia, contributing to impaired body image and outlook on the future and withdrawal from social activities

Cancer patients require a holistic approach from the moment of diagnosis, requiring physical, psycho-emotional, social and spiritual support.

References

1. Ministry of Health - Cancer Situation Analysis 2022. Campaign: "Healthy lifestyle and control of behavioural risk factors increase the chances of not becoming a cancer patient! Take care of your health!" <https://view.officeapps.live.com/op/view.aspx?src=https%3A%2F%2Fms.ro%2Fmedia%2Fdocuments%2FANALIZ-A-SITUATIE-CANCER-2022.doc&wdOrigin=BROWSELINK>
2. Globocan 2020: <https://gco.iarc.fr/today/data/factsheets/populations/642-romania-fact-sheets.pdf>
3. World Cancer Research Found - Breast cancer statistics, <https://www.wcrf.org/dietandcancer/breast-cancer-statistics/>
4. European Society of Medical Oncology <https://www.esmo.org/>
5. Iasi: Online support group offered to cancer patients in Moldova by specialists from the Regional Institute of Oncology <https://www.romedic.ro/iasi-grup-de-suport-online-oferit-bolnavilor-de-cancer-din-moldova-de-specialistii-de-la-institutul--0N92473>
6. Activity Report of the Regional Institute of Oncology Iasi for 2021 <https://www.iroiasi.ro/userfiles/files/administrativ/raport-activitate-management-2021.pdf>
7. Binotto M, Reinert T, Werutsky G, Zaffaroni F, Schwartzmann G. Health-related quality of life before and during chemotherapy in patients with early-stage breast cancer <https://doi.org/10.3332/ecancer.2020.1007>
8. Binotto M, Schwartzmann G. Health-related quality of life of breast cancer patients: integrative literature review, 2020 DOI: <https://doi.org/10.32635/2176-9745.RBC.2020v66n1.405>
9. J. L. Horigan , R. J. Gralla , B. J. Davis , P. J. Hollen , J. A. Petersen , K. Burg Determining issues of importance for patients with breast cancer: Results of a web-based study in 1,072 patients to enhance the content validity for the development of a new health-related quality of life (QL) instrument, the Breast Cancer Symptom Scale (BCSS) *Journal of Clinical Oncology* 27(15_suppl):e20615-e20615 https://ascopubs.org/doi/10.1200/jco.2009.27.15_suppl.e20615
10. Lee Y, Jeon YW, Im EO, Baek JM. Causal Attributions and Quality of Life of Korean Breast Cancer Survivors. *Asian Nursing Research* 2020. DOI: <https://doi.org/10.1016/j.anr.2020.11.002>
11. Zhao Y, Chen L, Zheng X, et al Quality of life in patients with breast cancer with neoadjuvant chemotherapy: a systematic review *BMJ Open* 2022;12:e061967. doi: 10.1136/bmjopen-2022-061967
12. Rezapour A, Javan-Noughabi J, Faramarzi A. Quality of life in breast cancer patients using neoadjuvant AC (doxorubicin and cyclophosphamide) in comparison with PG (paclitaxel and gemcitabine) therapy. *Middle East J Cancer* 2018;9:41-7 https://mej.sums.ac.ir/article_42103.html
13. E Campora, C Naso, M T Vitullo, S Giudici, A Camoirano, L Repetto, R Rosso The impact of chemotherapy on the quality of life of breast cancer patients *J Chemother.* 1992 Feb;4(1):59-63. doi: 10.1080/1120009x.1992.11739141. <https://pubmed.ncbi.nlm.nih.gov/1383437/>
14. Gatton-Johansson F, Watkins CC, Kanu IK, et al. The effects of symptoms on quality of life during chemotherapy in African-American women with breast cancer. *J Natl Black Nurses Assoc.* 2015;26:7-16. <https://pubmed.ncbi.nlm.nih.gov/27045153/>
15. Kroenke CH, Kwan ML, Neugut AI, et al. Social networks, social support mechanisms, and quality of life after breast cancer diagnosis. *Breast Cancer Res Treat.* 2013;139:515-527. <https://pubmed.ncbi.nlm.nih.gov/23657404/>
16. Savard J, Ivers H, Savard M-H, et al. Cancer treatments and their side effects are associated with aggravation of insomnia: results of a longitudinal study. *Cancer.* 2015;121:1703-1711. PMID: 25677509 <https://acsjournals.onlinelibrary.wiley.com/doi/10.1002/cn.cr.29244>
17. Lindau ST, Abramssohn EM, Baron SR, et al. 2016 Physical examination of the female cancer patient with sexual concerns: what oncologists and patients should expect from consultation with a specialist. *CA Cancer J Clin.* 2016;66:241-263. <https://acsjournals.onlinelibrary.wiley.com/doi/full/10.3322/caac.21337>
18. E. Hall, D. Cameron, R. Waters, J.M. Bliss, P. Hopwood et al (2014) Comparison of patient reported quality of life and impact of treatment side effects experienced with a taxane-containing regimen and standard anthracycline based chemotherapy for early breast cancer: 6year results from the UK TACT trial (CRUK/01/001) *Eur J Cancer* 50: 2375-2389 DOI: <https://doi.org/10.1016/j.ejca.2014.06.007>
19. Kiebert GM, J Hanneke, C J de Haes, J Kievit, C J van de Velde Effect of peri-operative chemotherapy on the quality of life of patients with early breast cancer *Eur J Cancer.* 1990;26(10):1038-42. PMID: 2148877 DOI: 10.1016/0277-5379(90)90046-v
20. Choi EK, Kim IR, Chang O, Kang D, Nam SJ, Lee JE, Lee SK, Im YH, Yeon Hee Park, Yang JH, Juhee Cho Impact of chemotherapy-induced alopecia distress on body image, psychosocial well-being, and depression in breast cancer patients. *Wiley Online Library* 2014. <https://onlinelibrary.wiley.com/doi/10.1002/pon.3531>
21. Souza APSde, Silva LCda, Fayh APT. Nutritional intervention contributes to the improvement of symptoms related to quality of life in breast cancer patients undergoing neoadjuvant chemotherapy: a randomized clinical trial. *Nutrients* 2021;13:589. <https://pubmed.ncbi.nlm.nih.gov/33579050/>
22. Christophe, V., Duprez, C., Congard, A. et al. The subjective experience of young women with non-metastatic breast cancer: the Young Women with Breast

- Cancer Inventory. *Health Qual Life Outcomes* 13, 73 (2015). <https://doi.org/10.1186/s12955-015-0273-x>
23. Lugtenberg, R.T.; Groot, S. de; Kaptein, A.A.; Fischer, M.J.; Kranenbarg, E.M.K.; Duijm-de Carpentier, M.;...; Dutch Breast Canc Res Grp BOOG (2020): *Quality of life and illness perceptions in patients with breast cancer using a fasting mimicking diet as an adjunct to neoadjuvant chemotherapy in the phase 2 DIRECT (BOOG 2013-14) trial*
<https://scholarlypublications.universiteitleiden.nl/handle/1887/3182286>
 24. Cristian Axenie, Daria Kurz: *Role of Kinematics Assessment and Multimodal Sensorimotor Training for Motion Deficits in Breast Cancer Chemotherapy-Induced Polyneuropathy: A Perspective on Virtual Reality Avatars*
<https://pubmed.ncbi.nlm.nih.gov/32903366/>
 25. Yvonne Anisimowicz, Lauren Rudy *Experiences of an Exercise Program: Perspectives from Breast Cancer Survivors*
<https://nsuworks.nova.edu/cgi/viewcontent.cgi?article=4824&context=tqr>