

Analysis of quality of life and functional capacity in cancer patients receiving chemotherapy in Paraná Southwest, Brazil.

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Abstract: Understanding psychosocial responses in cancer patients is fundamental for prognosis and quality of life (QoL). Chemotherapy is the primary and essential treatment for cancer. However, patients submitted to chemotherapy frequently show emotional and cognitive disruptions, which negatively influence the overall QoL. Here we evaluated the relationship between the functional capacity (FC) and QoL of cancer patients submitted to chemotherapy in a public health hospital in Paraná southwest, Brazil. We included 101 patients with cancer receiving chemotherapy who were enrolled from June to December 2017. Karnofsky Performance Status Scale (KPS) and European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30) were used to evaluate FC and QoL, respectively. Patients presented a mean age of 59.6±13 years and were predominantly female. Breast cancer was the most common neoplasia (43.56%), and most patients exhibited advanced disease (73%) and distant metastasis (66.33%) at diagnosis. The global health score evaluated by EORTC QLQ-30 was 67.5%, and about 63% of patients presented a KPS of 80%. The working function was the one most affected FC ($R=0.515$; $p<0.05$). Emotional and social functions were strongly associated with patients' global health status ($R=0.960$; $p<0.05$). Our data showed that the KPS is an excellent tool for evaluating the QoL in patients undergoing chemotherapy, which correlates positively with their global health and is affected by the emotional and social functions of patients.

Keywords: cancer, quality of life, KPS, chemotherapy, EORTC QLQ-C30.

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Análise da qualidade de vida e capacidade funcional em pacientes oncológicos em tratamento quimioterápico no Sudoeste do Paraná, Brasil

Resumo: A compreensão das respostas psicossociais em pacientes com câncer é fundamental para o prognóstico e a manutenção da qualidade de vida (QV). A quimioterapia é o tratamento primário e essencial para o câncer. No entanto, os pacientes submetidos à quimioterapia frequentemente apresentam rupturas emocionais e cognitivas, que influenciam negativamente a QV geral. Avaliou-se a relação entre a capacidade funcional (CF) e a QV de pacientes oncológicos submetidos à quimioterapia em um hospital público de saúde do sul do Brasil. Um total de 101 pacientes com câncer que receberam quimioterapia foram inscritos de junho a dezembro de 2017. A Karnofsky Performance Status Scale (KPS) e o European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30) foram utilizados para avaliar a CF e a QV, respectivamente. Os pacientes apresentaram média de idade de $59,6 \pm 13$ anos e eram predominantemente do sexo feminino. O câncer de mama foi a neoplasia mais comum (43,56%), e a maioria das pacientes apresentou doença avançada (73%) e metástase à distância (66,33%) ao diagnóstico. O escore de saúde global avaliado pelo EORTC QLQ-30 foi de 67,5%, e cerca de 63% dos pacientes apresentaram KPS de 80%. A função de trabalho foi a que mais afetou a CF ($R=0,515$; $p<0,05$). As funções emocionais e sociais foram fortemente associadas ao estado de saúde global dos pacientes ($R=0,960$; $p<0,05$). Nossos dados mostraram que a KPS é uma excelente ferramenta para avaliar a QV em pacientes submetidos à quimioterapia, o que se correlaciona positivamente com sua saúde global e é afetado pelas funções emocionais e sociais dos pacientes.

Palavras-chave: câncer, qualidade de vida, KPS, quimioterapia, EORTC QLQ-C30.

Análisis de la calidad de vida y capacidad funcional en pacientes oncológicos en quimioterapia en el Sudoeste de Paraná, Brasil

Resumen: Comprender las respuestas psicossociales en pacientes con cáncer es fundamental para el pronóstico y el mantenimiento de la calidad de vida (CdV). La quimioterapia, es el tratamiento primario y esencial para el cáncer. Sin embargo, los pacientes sometidos a quimioterapia con frecuencia muestran trastornos emocionales y cognitivos, que influyen negativamente en la CV general. Aquí evaluamos la relación entre la capacidad funcional (CF) y la CV de pacientes con cáncer sometidos a quimioterapia en un hospital de salud pública del sur de Brasil. Un total de 101 pacientes con cáncer que recibieron quimioterapia se inscribieron de junio a diciembre de 2017. Se utilizaron Karnofsky Performance Status Scale (KPS) y European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30) para evaluar la CF y la CdV, respectivamente. Los pacientes presentaron una edad promedio de $59,6 \pm 13$ años y fueron predominantemente del sexo femenino. El cáncer de mama fue la neoplasia más frecuente (43,56%), y la mayoría de las pacientes presentaron enfermedad avanzada (73%) y metástasis a distancia (66,33%) en el momento del diagnóstico. El puntaje de salud global evaluado por EORTC QLQ-30 fue de 67,5%, y cerca de 63% de los pacientes presentaron un KPS de 80%. La función de trabajo fue la que más afectó a la CF ($R=0,515$; $p<0,05$). Las funciones emocionales y sociales se asociaron fuertemente con el estado de salud global de los pacientes ($R=0,960$; $p<0,05$). Nuestros datos mostraron que el KPS es una excelente herramienta para evaluar la CV en pacientes sometidos a quimioterapia, lo que se correlaciona positivamente con su salud global y se ve afectado por las funciones emocionales y sociales de los pacientes.

Palabras clave: cáncer, calidad de vida, KPS, quimioterapia, EORTC QLQ-C30.

Introduction

Cancer is a public health problem worldwide, especially in developing countries. According to estimates from the World Cancer Report, in 2025, more than 20 million new cancer cases will be reported worldwide (FERLAY et al., 2012; INCA, 2015). Furthermore, reported cancer prevalence in the BRICS (Brazil, Russia, India, China, and South Africa) countries seemed to exceed the prevalence reported by the International Agency for Research Against Cancer, estimated between 1.3% and 1.6%. The Brazilian National Cancer Institute (INCA) estimates the occurrence of about 420 000 new cases of cancer from 2018 to 2019 (except non-melanoma skin cancers), which would account for more 170 000 new cases of this disease (INCA, 2017).

Chemotherapy is a more common treatment for many cancer subtypes, being able to kill cancerous cells, block their growth, and increase survival rates. However, due to their frequent toxic physiologic effects (nausea, vomiting, anemia, neutropenia, alopecia, fatigue), chemotherapy frequently negatively impacts emotional and cognitive states (GALMARINI, GALMARINI, GALMARINI, 2012). According to several studies, patients with cancer submitted to chemotherapy (ZAMEL et al., 2021; BRAGA MENDONÇA et al., 2022; ROQUE, FORONES, 2006) show poor quality of life (QoL), as well as present deleterious effects in functional capacity (FC). Chemotherapy and other surgical and pharmacological strategies for cancer therapy have extended the life of patients with cancer making it essential to provide for the maintenance and improvement of the QoL of cancer patients (GALMARINI, GALMARINI, GALMARINI, 2012; ZAMEL et al., 2021[]).

In this regard, evaluating cancer patients' ongoing treatment should not be restricted to their clinical or physical performance issues.

Oncology research has developed surveys and scales to characterize the parameters affecting patients' perception of their QoL and FC. Such approaches are instrumental for scaling specific features concerning patients' physical and emotional capabilities. Patients' performance status is defined as their ability to care for themselves. It reflects their autonomy in daily life activities, such as cognition, mood, mobility, and communication (PEREIRA, SANTOS, SARGES, 2014). Karnofsky Performance Status Scale (KPS) and European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC QLQ-C30) have been well-recognized instruments to evaluate, respectively, FC and QoL in patients with cancer (OKEN et al., 1982; GOMES et al., 2011).

The EORTC QLQ-C30 questionnaire is a validated instrument employed to evaluate the QoL of cancer patients independent of primary neoplasia. It consists of 30 closed questions

organized into domains to facilitate the evaluation of which characteristics or factors are most influenced by disease (FAYERS et al., 2001; FRANCESCHINI et al., 2010). As demonstrated by several data, the EORTC QLQ-C30 is an efficient instrument to evaluate QoL in cancer patients receiving chemotherapy treatment in different cancer subtypes (GEORGAKOPOULOS et al., 2013; UWER et al., 2011; DIJKSTRA et al., 2022). According to Uwer et al. (2011), EORTC QLQ-C30 was a more effective survey to evaluate QoL in patients with colorectal cancer. Moreover, Masey et al. (2007) suggested that an adapted survey from EORTC QLQ-C30 could be used to measure the international clinical trials of high-dose chemotherapy.

The KPS score has been used to evaluate FC and predict prognostic in some cancer subtypes (MURPHY et al., 2002). The KPS score (0-100) describes increasing levels of activity and independence, where 0 indicates death and 100 means an average physical performance and ability to perform daily activities¹⁰. This scale is the most used instrument in clinics to determine the prognosis of cancer patients undergoing antineoplastic therapy (POLO, MORAES, 2009). In this regard, in patients with primary central nervous system lymphoma (PCNSL), a good KPS score (>70), particularly ≤ 65 years, and adequate organ function should be considered for salvage polychemotherapy (KAULEN, BAEHRING, 2022).

A recent study demonstrated that 84% of Brazilian cancer patients used radiotherapy and/or chemotherapy as a cancer treatment (BUIRET et al., 2022). The EORTC QLQ C-30 instrument was most frequently used to measure QoL in cancer patients receiving chemotherapy in Brazil (SAWADA et al., 2016). However, scarce studies have performed a combined analysis of QoL and FC in Brazilian cancer patients. Thus, the present work evaluated the relationship between KPS and EORTC-QLQ30 as strategies for evaluating QoL and FC in Brazilian cancer patients receiving chemotherapy.

Study design and patients

This study is a descriptive, prospective, and exploratory research enrolling adult cancer patients admitted to a Cancer Hospital located at the 8 Regional of Health of Paraná in Francisco Beltrão, Paraná, Brazil (Ceonc – Hospital do Cancer) in 2017. Overall, 27 municipalities were involved in this study. All individuals signed consent forms, and the research was conducted following institutional ethical guidelines, the Brazilian Council of Ethics in Research (authorization code CAEE 62589816.4.000.0107), and the ethical principles for medical research recommended by the Declaration of Helsinki. Considering that the state of Paraná diagnosed 18,213 new cases of cancer in 2015 and the study site was responsible for the diagnosis of 3.54%

(645) of these cases, the minimum sample size of 73 patients was defined. The sample calculation was performed using the online calculator considering a sampling error of 5% and a confidence level of 95% (SANTOS, 2018).

We included all adult cancer patients undergoing chemotherapy on the first day of their third treatment cycle, independent of the drug schedule adopted for each patient. Data was collected using EORTC QLQ-C30 (FAYERS et al., 2001) and KPS (KARNOFSKY, BURCHENAL, 1949). Medical records were assessed for the obtention of any relevant information. We excluded patients under 18 years or those unable to understand the instrument's consent terms and questions. In this context, we included 101 study participants, as presented in Figure 1.

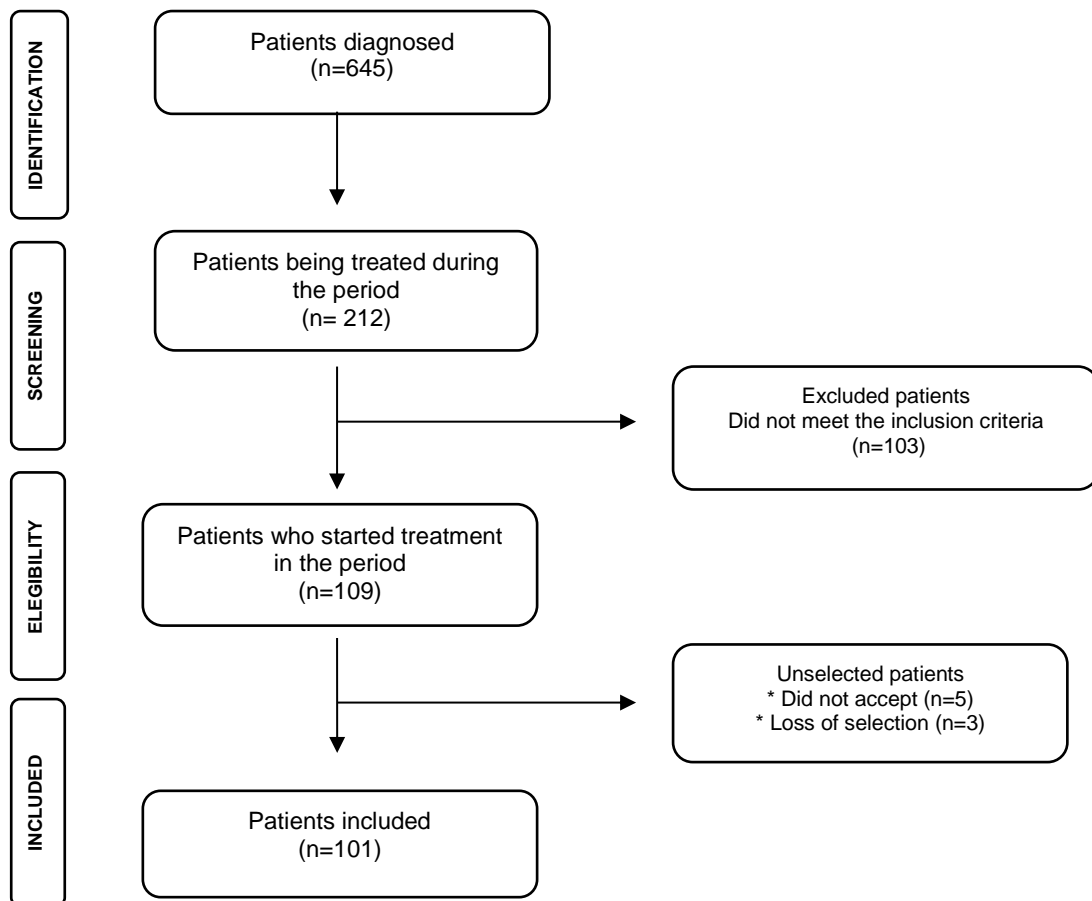


Figure 1 - Study Design.

KPS data were classified into Category 1 for scores between 10 and 40%, category 2 for scores between 50% and 70%, and Category 3 for scores between 80% and 100%. EORTC QLQ-C30 was described as a percentage after linear transformation, as defined by the EORTC QLQ-C30 Scoring Manual (FAYERS et al., 2001).

All data obtained were categorized and analyzed using the statistical software IBM SPSS 22.0.0. Correlations among variables were investigated using Chi-Square and linear regression tests. They included the presence of metastasis at diagnosis, disease staging, outcome, global health status, functional scale, and symptoms and the impact of such associations on patients' subjective QoL. The results were considered significant if p values were <0.05. Data are presented as a beta index, association R values, and p values.

Results and discussion

This study included 101 patients diagnosed with cancer and submitted for chemotherapy. Table 1 shows the clinicopathological data of cancer patients.

Table 1 – Sociodemographic characteristics of patients.

Variables	N	%	
Sex	Female	78	77.23
	Male	23	22.77
Age (years)	< 30	0	0.00
	30-39	5	4.95
	40-49	21	20.79
	50-59	24	23.76
	60-69	27	26.73
	70-79	15	14.85
	> 80	9	8.91
Schooling	Illiterate	7	6.93
	Incomplete Fundamental	58	57.43
	Complete Fundamental	12	11.88
	Full Medium	16	15.84
Occupation	Superior	8	7.92
	Services	29	28.71
	Housewife	28	27.72
	Agriculture	21	20.79
	Retired	15	14.85
	Trade	6	5.94
Marital status	Education	2	1.98
	Single	7	6.93
	Married	75	74.26
	Widowhood	15	14.85
	Divorced	4	3.96

Most patients were women (77.23%, n = 78), married (74.26%, n = 75), with a mean age of 59.64 ± 12.97 years. The most frequent topography of cancer found in this study was breast cancer (43.56%, n = 44), followed by cancers of the gynecologic organ (15.84%, n = 16) and gut (15.84%, n = 16). The prevalence of breast cancer in our study corroborates the data published by INCA for Brazil and the State of Paraná in 2015 (INCA, 2015).

Regarding the disease staging, 72.27% of patients (n = 73) were in stages III/IV, and 45.54% (n = 46) were under palliative care. These data agree with the Brazilian Hospitalar Registry of Cancer, which reports that 23.33% of the patients are diagnosed in Brazil at stage III or above. Our results also demonstrate that 51.49% of cancer patients (n = 52) did not report any familial history of cancer. Genetic heritage is a risk factor that affects the occurrence of some cancers, such as breast, ovary, gastric, non-polypoid, thyroid, prostate, and renal cancer (MORROW et al., 2018; ETTER et al., 2018; GINTHER et al., 2018).

Moreover, according to BMI categorization, two-thirds of our sample (66.33%; n= 67) were overweight or obese during data collection. Despite not being evaluated at present work, excessive body weight is a well-recognized risk to several cancer subtypes, and obese cancer patients have worse clinical outcomes compared with non-obese patients (AVGERINOS et al., 2019; HOROWITZ et al., 2015). In addition, obesity presence negatively affects the chemotherapy response in breast cancer (GOURGUE et al., 2021).

The FC of cancer patients evaluated by KPS score is shown in Figure 2. In the present study, most patients presented a KPS of 80%, indicating that they performed their activities with some effort but still with autonomy. Our findings corroborate a Brazilian study conducted in Minas Gerais with cancer patients receiving chemotherapy. In this study, the FC was analyzed by Palliative Performance Scale (PPSv2), and the score was considered stable (70%). Thus, most patients had little or no impairment in performing instrumental activities of daily living (SOUZA, 2011).

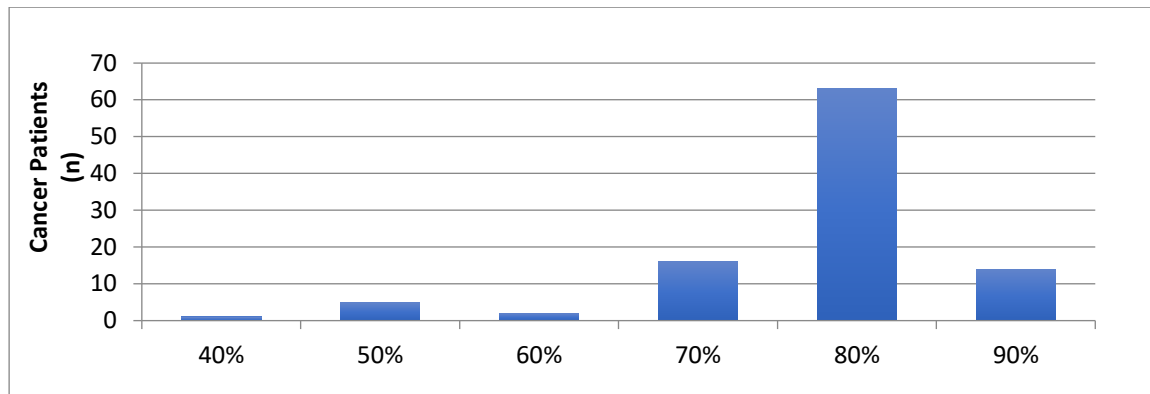


Figure 2 – FC assessment in cancer patients undergoing chemotherapy according to KPS.

We also found significant associations among the parameters evaluated by KPS, global health status, and disease features in our sample (Table 2). Significant positive associations of KPS with metastasis at diagnosis, active disease, and outcome were found, suggesting that this instrument can predict such features in cancer patients undergoing chemotherapy treatment. Moreover, the disease stage was negatively associated with KPS at present work. In accordance, Puiggròs et al. (2009) showed a relationship between KPS and mortality in cancer patients. In this study, 201 oncologic patients or those with neurological sequelae were accompanied for ten months. By the end of this period, 74 patients had died, of which 87.83% had initial KPS \leq 40%. No patient with initial KPS \geq 70% died in this period. According to these authors, the KPS is a valuable tool for predicting patient mortality (PUIGGRÒS et al., 2009).

Table 2 - Association between KPS, Global Health Status and Disease Status in cancer patients undergoing chemotherapy.

Predictor	KPS [§]			QoL ^{§§§}		
	R	p	Beta	R	p	Beta
Metastasis at diagnosis	0.327	0.000	0.327	-	>0.05	-
Staging	0.378	0.000	-0.378	-	>0.05	-
Active Disease or Late MTX ^{§§}	0.205	0.000	0.205	-	>0.05	-
Outcome	0.422	0.000	0.422	0.210	= 0.037	0.210

[§] KPS - Karnofsky Performance Scale ^{§§} Late MTX – Late metastasis ^{§§§} QoL - Quality of Life

Chi-square test (p<0.05).

The analysis of QoL, evaluated by the EORTC QLQ-C30, is shown in Table 3. Our study observed that cancer patients had a more significant global health status than 65%. Maisey et al. (2002) found similar results in a survey of cancer patients evaluated by the EORTC QLQ-C30. This study evaluated 501 patients diagnosed with advanced colorectal cancer and found a global health status of 67%. Another study developed in Brazil with cancer patients reported the general health status as 69.71% (SAWADA et al., 2009). Altogether, these data suggest that despite our small sample and regional particularities, the condition of QoL our patients with cancer is very similar to other regions of Brazil and worldwide.

Table 3 - Evaluation of quality of life in cancer patients undergoing chemotherapy.

Variables		Score (%)
Global Health Status/Quality of Life		67.50
Domains	Physical Function	60.73
	Labour Function	52.83
	Emotional Function	71.50
	Cognitive Function	57.50
	Social Function	70.83
Symptom Scale	Fatigue	47.00
	Nausea/Vomiting	32.00
	Pain	33.50
Individual Symptoms	Dyspnea	16.00
	Insomnia	39.00
	Constipation	36.66
	Diarrhea	13.33
	Financial Difficulty	29.33

It was observed that the labor function was the functional scale most affected in the sample. The work function was evaluated by analyzing two factors: the difficulty in working or carrying out activities of daily living and the difficulty in practicing the patient's preferred hobby or participation in leisure activities. In this analysis, 37.4% of the sample reported having moderate to high difficulty performing leisure or hobby activities, and 50.4% had moderate to increased difficulty working or performing activities of daily living. Corroborating, Sawada et al. (2009) report that the EORTC QLQ-C30 showed the mean physical, cognitive, and social functions score, and paper performance demonstrated a satisfactory level. However, for emotional function, the mean was low (55.46%). Chemotherapy causes well-established toxic physiologic effects, such as

nausea, pain, fatigue, and insomnia. In our study, symptom scales pointed to the predominance of insomnia, followed by pain and fatigue. A study performed in the south of Brazil with breast cancer patients during adjuvant chemotherapy showed that cognitive dysfunction, depressive symptoms, and poor sleep quality evaluated by EORTC QLQ-C30 might be improved by melatonin treatment (PALMER et al., 2020). Our analysis also demonstrated that scores of QoL were satisfactory in all domains except for the emotional function, which was low in our sample. In this regard, a significant proportion of Greek patients with cancer experienced intense anxiety and depression throughout chemotherapy, confirming the importance of depression as a strong predictor of global QoL (ICONOMOU et al., 2004). Brazilian study also found higher average scores for distress in cancer patients with advanced stage and receiving palliative chemotherapy (BRAGA MENDONÇA et al., 2022).

Finally, we also investigated possible associations among parameters related to the global health status and QoL obtained by EORTC QLQ-C30 with the FC evaluated by KPS (Table 4). In this sense, in our cancer patients, a significant association was found between QoL and FC, as measured by labor function, physical function, fatigue symptoms, pain, dyspnea, and nausea and vomiting, among others. Moreover, regarding patients' global health status, it was observed that labor functions and the scales of individual symptoms were highly associated.

Table 4 - KPS profile in cancer patients undergoing chemotherapy.

		QoL			Total
		Bad	Average	Good	
KPS	Unable (n; %)	1; 100	0; 0	0; 0	1; 100
	Partially Capable (n; %)	1; 4.3	18; 78.3	4; 17.4	23; 100
	Capable (n; %)	0; 0	31; 40.3	46; 59.7	77; 100
Total (n; %)		2; 2	49; 48.5	50; 49.5	101; 100

When comparing the specific factors that interfere with the QoL and the patient's FC, it was observed that the labor function had the most significant influence on the KPS. On the other hand, emotional and social functions showed the most remarkable association with global health status. Costa and colleagues (2017a) evaluated 400 women who survived breast cancer and, like our study, observed a positive correlation between KPS and overall QoL scores (ZIMMERMAN et al., 2011). Therefore, when KPS scores increase, patients' symptoms decrease, and functional scales improve, as reported by other studies (GUZELANT et al., 2004). Costa et al. (2017b) found a significant relationship between metastasis and decreased FC, affecting the QoL. We also

observed that metastasis reduced FC, limiting daily activities and lessening patients' QoL. Thus, this lack of functionality leads to physical inactivity and worsens health status and the quality of patient care (COSTA et al., 2017a). Zimmerman et al. (2011) also confirmed that performance status is an essential determinant of QoL in patients with advanced cancer. Several recent reports have stated that better performance scores are directly associated with survival in oncological patients (ZIMMERMAN et al., 2011; EFFICACE et al., 2004; GOTAY et al., 2008). In a large prospective cohort of early-stage breast cancer survivors, the Life After Cancer Epidemiology (LACE) cohort showed that 39% of the sample had at least one physical limitation nine years after diagnosis, regardless of clinical factors, lifestyle, and sociodemographic. The author emphasized that functional limitations affected the patients' QoL (ALFANO et al., 2007). Understanding the multiple functional limitations associated with cancer and improving rehabilitation and coping care is essential.

In conclusion, our study is the first to demonstrate a statistically positive correlation between the FC assessed using the KPS score and the QoL using the EORTC QLQ-C30 instrument in cancer patients living in the southern region of Brazil and undergoing chemotherapy, independent of the disease topography. Furthermore, it is essential to note that, in addition to significantly affecting overall health scores in these patients, the number of symptoms increases in proportion to the worsening of their FC. Thus, establishing FC and its correlation with the QoL in cancer patients is an important aspect to be evaluated by the health professionals involved in the care of these individuals. It could provide a tool to predict the subjective QoL conditions and favors the targeting of care interventions to improve the patient's well-being and provide a safe, comprehensive, and humanized treatment.

However, this study has limitations related to the regionalization of patients (only one oncology service that serves only one health region in the state of Paraná), as well as the offer of facilitated access for patients suspected of having neoplasms to the oncology service. It makes patients access diagnosis and treatment in advance, arriving at the service with better performance and shorter staging.

In addition, we still need to reflect on this patient's needs and desires, as these go far beyond physical needs. It is up to us, professionals, to know the individual's reality and the changes that occur due to the disease so that we can offer all the care and support necessary to redirect life after cancer.

Anyway, we need to keep in mind that our main objective as health professionals is to increase the life in the patients' days and not simply to increase days in their lives.

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