

# Prospective Analysis of Health-Related Quality of Life in Older Adults With Cancer

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## Abstract

**Objective:** The aim of the present study was to evaluate health-related quality of life (HRQoL) changes at 6 to 12 months after cancer diagnosis and to assess the impact of age in older adults with cancer. **Methods:** A cohort study using patients  $\geq 60$  years old diagnosed with cancer. Health-related quality of life scores were calculated according to the European Organisation for Research and Treatment of Cancer questionnaire. Student's *t* tests for paired samples and a binomial logistic regression were performed. **Results:** The study included 241 patients. At diagnosis, the affected HRQoL functions were physical and emotional functions, financial difficulties, pain, and insomnia. At follow-up, cognitive function ( $P < .001$ ) and dyspnea ( $P = .004$ ) worsened, while emotional function improved ( $P = .003$ ). **Discussion:** At the 6 to 12 months of follow-up, older adult cancer patients showed worsening cognitive function and dyspnea and improved emotional function. These HRQoL changes were not associated with age.

## Keywords

prospective analysis, quality of life, health, older adults, cancer

## Introduction

Cancer has a high incidence in the older adult population. It is estimated that 70% of all cancers will occur in individuals aged  $\geq 65$  years old in 2020, and this will have a significant impact on global public health (1,2). Longitudinal studies within this population are important to focus attention and care and to help determine the most appropriate cancer treatments and better health-care approaches (3,4).

The assessment of health-related quality of life (HRQoL) is one of the main clinical research outcomes in older adults with cancer. It is intended to help with the evaluation of treatment indication and response and also act as a prognostic marker (5,6). In older adults with cancer, HRQoL is investigated according to physical, emotional, social, cognitive, and economic functions; the perception of clinical symptoms; progression of the disease; family support; gender conditions; and access to health-care and education. The individual perception of quality of life (QoL) is a complex condition that is perceived adversely in social and economic

environments (7). In addition, the assessment of HRQoL and the clinical condition of older adults with cancer at diagnosis and after treatment allow changes in functions and symptoms to be evaluated to identify the best clinical approach (8). Both clinicians and patients may benefit from these assessments. First of all, the evidence delivered from clinical research can help to determine more appropriate cancer treatments and better health-care approaches. Additionally,

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the assessment of HRQoL in daily clinical practice may facilitate patient health-care professional communication, allow for the detection of physical or psychological problems, help to monitor the impact of treatment, and improve patient satisfaction and adherence to treatment (9). Moreover, HRQoL has been used to predict morbidity, mortality, and survival (10).

Health-related quality of life may be investigated by several validated instruments both at diagnosis and during the progress of the disease and treatment (11). The HRQoL questionnaire developed by the European Organisation for Research and Treatment of Cancer (EORTC QLQ-C30) (12) is the most widely used tool to assess HRQoL in patients with cancer (13). The reliability of the Brazilian EORTC QLQ-C30 version is shown by Cronbach's alpha values higher than 0.70 for 6 of the 9 scales. In the multi-trait scaling analysis, convergent and divergent validity were considered adequate with values higher than 90%. Furthermore, moderate to strong correlations were found between the subscales of the EORTC QLQ-C30 and its respective dimensions of other instruments proposed to measure the same constructs (14).

According to the World Health Organization, the classification of age has varied between countries and over time, which reflects the differences in social class and functional abilities. Most developed countries have accepted that 65 years should be used to define an elderly or older person (2). In Brazil,  $\geq 60$  years is used as the general definition of an older person, with those aged 60 to 70 years considered younger older adults, those aged 70 to 80 years considered moderately older adults, and those aged  $>80$  years considered very older adults (15). There is some evidence that age has an impact on HRQoL (16); however, to the best of the author's knowledge, no study has investigated the influence of age on perceived HRQoL in Brazilian cancer patients. Therefore, this study aimed to compare HRQoL changes at 6 to 12 months after a cancer diagnosis in 2 age groups: patients aged 60 to 75 years versus 75 years and older.

## Materials and Methods

A cohort study was performed using patients  $\geq 60$  years old who were diagnosed with cancer at the Oncogeriatrics Clinic at the Instituto de Medicina Integral Professor (IMIP) between February 2015 and November 2016. Patients were followed up for 6 to 12 months from the time they were included in the study. Patients were excluded if they did not undergo cancer treatment at the institution, they died during follow-up, or they failed to answer the HRQoL questionnaire at the end of the follow-up. All participants signed an informed consent form. This study was approved by the IMIP Ethics Committee on November 09, 2014 under protocol number 4412-14.

Data regarding sociodemographic characteristics (e.g. age, gender, education, race, ethnicity, marital status, smoking, alcohol consumption, functional status, and income),

nutritional risk (assessed using the Mini-Nutritional Assessment; Vellas et al., 1999 (17)), Charlson Comorbidity Index (18), Karnofsky Performance Scale (19), body mass index, polypharmacy, and physical activity (assessed using the International Physical Activity Questionnaire (20,21)) were all collected through interviews. Clinical characteristics (eg, tumor stage and tumor site according to the 10th revision of the International Classification of Diseases) and therapy use (eg, chemotherapy, radiotherapy, or hormone therapy) were collected from the patient's medical records. Patients were categorized into 2 groups depending on their age at the time of diagnosis:  $<75$  years and  $\geq 75$  years.

The EORTC QLQ-C30 questionnaire was used for HRQoL evaluation (dependent variable). This questionnaire covers overall QoL and contains 5 functional subscales (physical, role, emotional, cognitive, and social), 3 symptom scales (fatigue, nausea/vomiting, and pain) and 6 single-item symptoms (dyspnea, insomnia, appetite loss, constipation, diarrhea, and financial difficulties). Scores can range from 0 to 100 and are calculated according to the protocol proposed by the EORTC QLQ-C30. Higher scores for the functional scales and global health status indicate a better QoL, while lower scores for the symptom scales indicate a worse QoL (22,23). The questionnaire was translated into Portuguese and validated for the Brazilian population (24). During the follow-up, patients who lived in the countryside or the metropolitan region were required to answer the HRQoL questionnaire over the phone due to their limited mobility. The primary outcome was a clinically relevant change in the HRQoL score, analyzed as a binary variable (yes/no). Changes  $\geq 10$  points in the score between baseline and 6 to 12 months of follow-up were considered clinically relevant (8).

Calculation for the necessary sample size showed that the inclusion of 236 patients would give a power of 80%, with a significance level of 0.05, to detect a difference of 10 points in the HRQoL domains between age groups.

Descriptive analyses were performed. Quantitative variables are presented as mean  $\pm$  standard deviation and median (minimum–maximum), while qualitative variables are presented as absolute and relative frequency. Student's *t* tests for paired samples were used to compare the HRQoL at diagnosis and after 6 to 12 months. Binomial logistic regression was performed to evaluate the association between age groups ( $<75$  years and  $\geq 75$  years) and the dichotomous outcome, a  $\geq 10$  points change in each HRQoL domain from baseline to follow-up. Odds ratios and 95% confidence intervals were calculated. All assumptions for binomial logistic regression were met. Differences were considered significant at  $P < .05$ . There were no missing data for the analyzed variables. The Statistical Package for Social Sciences (version 23.0) was used for data analysis.

## Results

A total of 241 older adult patients undergoing treatment for cancer were included in the study. The patients were aged

**Table 1.** Demographic and Behavioral Variables (n = 241).

Variables	n (%)
Mean age, years (range)	71 (61-94)
Age group	
<75 years	167 (69.3)
≥75 years	74 (30.7)
Sex	
Male	125 (51.9)
Female	116 (48.1)
Education	
<4 years	112 (46.5)
≥4 years	129 (53.5)
Race/ethnicity	
White	60 (24.9)
Nonwhite	181 (75.1)
Marital status	
Living without a partner	102 (42.3)
Living with a partner	139 (57.7)
Work outside the home	
No	210 (87.1)
Yes	31 (12.9)
Income	
≤1 minimum wage	65 (27.0)
>1 and ≤2 minimum wages	75 (31.1)
>2 minimum wages	101 (41.9)
Smoking	
Smoker and former smoker	134 (55.6)
Never smoked	107 (44.4)
Consumption of alcohol	
Consumers and ex-consumers	131 (54.4)
Nonconsumers	110 (45.6)
Physical activity	
Very active and active	70 (29.0)
Irregularly active	86 (35.7)
Sedentary	85 (35.3)

between 61 and 94 years, although most (69.3%) were <75 years old. All patients were native Portuguese speakers. With regard to their demographic characteristics, 51.9% of patients were men, 53.5% had ≥4 years of education, 75.1% were nonwhite, 57.7% were living with a partner, 87.1% did not work outside the home, and 58.1% had income from 2 minimum wages or less. With regard to their behavior, 55.6% were smokers or former smokers and 54.4% consumed alcohol (Table 1).

Nutritional risk and malnutrition were observed in 27.8% of patients, and at least one comorbidity listed on the Charlson comorbidity index was present in 46.5% of patients. With regard to the tumor characteristics, 46.5% were classified as clinical stages III and IV. The highest incidences were seen in male genital organs (39.0%), female breasts (20.7%), and the digestive tract (16.6%). A total of 58.9% of patients did not receive chemotherapy, 61.8% did not receive radiotherapy, and 64.7% did not receive hormone therapy (Table 2).

The HRQoL scores at diagnosis and follow-up are presented in Table 3. At diagnosis, the worst scores were observed for emotional and physical functions, financial

**Table 2.** Clinical and Tumor Variables (n = 241).

Variables	n (%)
Mini Nutritional Assessment (MNA)	
Normal	174 (72.2)
At risk of malnutrition/undernutrition	67 (27.8)
Comorbidities (Charlson)	
0	129 (53.5)
I or +	112 (46.5)
Karnofsky Performance Scale (KPS)	
50/60	22 (9.0)
70/80	39 (16.2)
90/100	180 (74.7)
Body mass index (BMI)	
<23 kg/m <sup>2</sup>	65 (27.0)
≥23 kg/m <sup>2</sup>	176 (73.0)
Polypharmacy	
<5 medications	193 (80.1)
≥5 medications	48 (19.9)
Clinical stage	
I	29 (12.0)
II	100 (41.5)
III	72 (29.9)
IV	40 (16.6)
Tumor site	
Male genital organs	94 (39.0)
Female breast	50 (20.7)
Digestive organs	40 (16.6)
Female genitals	32 (13.3)
Urinary tract	12 (5.0)
Others	13 (5.3)
Chemotherapy	
No	142 (58.9)
Yes	99 (41.1)
Radiotherapy	
No	149 (61.8)
Yes	92 (38.2)
Hormone therapy	
No	156 (64.7)
Yes	85 (35.3)

difficulties, pain, and insomnia. When comparing the HRQoL scores between diagnosis and follow-up, the patients presented worse HRQoL scores for cognitive function ( $P < .001$ ) and improved scores for emotional function ( $P = .003$ ). With regard to their symptoms, patients presented a worsening score for dyspnea ( $P = .004$ ). There was no significant change for any other function or symptom in the follow-up period.

A clinically relevant change in HRQoL (difference of ≥10 points between diagnosis and follow-up scores) was seen for cognitive function (41.5%), physical function (29.9%), and overall QoL (24.5%). With regard to the symptoms, a clinically relevant change was reported for fatigue (27.8%), pain (27.8%), financial difficulties (25.3%), and insomnia (23.2%). There was no association between age and a worsening HRQoL between baseline and follow-up in any domain of HRQoL (Table 4).

**Table 3.** Quality of Life at Diagnosis and After 6 to 12 Months of Follow-Up (n = 241).<sup>a</sup>

Domains	EORTC C-30			P Value
	At Diagnosis, Mean (SD)	At Follow-Up, Mean (SD)	Change Difference (95% CI)	
Global health status	79.72 (20.36)	77.39 (20.60)	-2.33 (-5.32 to 0.66)	.126
Functional scales <sup>b</sup>				
Physical functioning	74.61 (23.44)	74.26 (24.79)	-0.34 (-3.55 to 2.86)	.833
Role functioning	77.52 (28.84)	81.74 (30.31)	4.21 (-0.19 to 8.62)	.061
Cognitive functioning	90.04 (26.04)	81.88 (25.55)	-8.16 (-11.62 to -4.69)	<b>&lt;.001</b>
Emotional functioning	75.66 (28.23)	80.68 (23.68)	5.03 (1.67 to 8.38)	<b>.003</b>
Social functioning	84.02 (26.17)	86.79 (26.93)	2.77 (6.74 to 1.21)	.172
Symptom scales/items <sup>c</sup>				
Fatigue	18.72 (23.66)	16.16 (23.12)	-2.56 (-5.55 to 0.42)	.092
Pain	23.37 (30.43)	22.36 (30.52)	-1.02 (-5.67 to 3.63)	.667
Dyspnea	2.63 (11.69)	7.05 (21.77)	4.43 (1.46 to 7.39)	<b>.004</b>
Insomnia	22.27 (33.15)	21.41 (33.30)	-0.86 (-5.78 to 4.05)	.730
Appetite loss	16.18 (29.04)	12.70 (27.95)	-3.48 (-7.82 to 0.85)	.115
Nausea and vomiting	5.95 (15.26)	5.34 (14.52)	-0.61 (-3.03 to 1.80)	.619
Constipation	15.77 (32.35)	16.45 (32.38)	0.68 (-3.99 to 5.35)	.775
Diarrhea	7.19 (21.38)	6.47 (18.71)	-0.72 (-4.16 to 2.72)	.681
Financial difficulties	30.98 (37.99)	31.39 (40.12)	0.41 (-5.41 to 6.24)	.889

Abbreviations: CI, confidence interval; EORTC C-30, European Organization for Research and Treatment of Cancer; HRQoL, health-related quality of life; SD, standard deviation.

<sup>a</sup>Statistically significant differences are in bold.

<sup>b</sup>For the global quality of life and the functional scales, a higher score represents a better HRQoL.

<sup>c</sup>For a symptom scale, a higher score represents greater symptom severity.

**Table 4.** Number and Percent of Patients With a Clinically Relevant Change in HRQoL (≥10 points) From Baseline to Follow-Up According to Age Groups (n = 241).

Domains	Age Groups						OR (95% CI)	P Value
	Total		<75 years		≥75 years			
	No, n (%)	Yes, n (%)	No, n (%)	Yes, n (%)	No, n (%)	Yes, n (%)		
Global QoL	175 (72.9)	65 (27.1)	122 (73.1)	45 (26.9)	53 (72.6)	20 (27.4)	1.02 (0.55-1.90)	.942
Functional scales								
Physical functioning	169 (70.1)	72 (29.9)	123 (73.7)	44 (26.3)	46 (62.2)	28 (37.8)	1.70 (0.95-3.05)	.074
Role functioning	182 (75.5)	59 (24.5)	130 (77.8)	37 (22.2)	52 (70.3)	22 (29.7)	1.49 (0.80-2.76)	.209
Cognitive functioning	141 (58.5)	100 (41.5)	94 (56.3)	73 (43.7)	47 (63.5)	27 (36.5)	0.74 (0.42-1.30)	.294
Emotional functioning	198 (82.2)	43 (17.8)	137 (82.0)	30 (18.0)	61 (82.4)	13 (17.6)	0.97 (0.47-1.99)	.941
Social functioning	196 (81.3)	45 (18.7)	136 (81.4)	31 (18.6)	60 (81.1)	14 (18.9)	1.02 (0.51-2.06)	.948
Symptom scales/items								
Fatigue	174 (72.2)	67 (27.8)	126 (75.4)	41 (24.6)	48 (64.9)	26 (35.1)	1.66 (0.92-3.01)	.092
Pain	174 (72.2)	67 (27.8)	123 (73.7)	44 (26.3)	51 (68.9)	23 (31.1)	1.26 (0.69-2.30)	.450
Dyspnea	216 (89.6)	25 (10.4)	150 (89.8)	17 (10.2)	66 (89.2)	08 (10.8)	1.07 (0.44-2.60)	.882
Insomnia	185 (76.8)	56 (23.2)	125 (74.9)	42 (25.1)	60 (81.1)	14 (18.9)	0.69 (0.35-1.37)	.292
Appetite loss	211 (87.6)	30 (12.4)	148 (88.6)	19 (11.4)	63 (85.1)	11 (14.9)	1.36 (0.61-3.04)	.451
Nausea and vomiting	212 (88.0)	29 (12.0)	149 (89.2)	18 (10.8)	63 (85.1)	11 (14.9)	1.44 (0.65-3.24)	.370
Constipation	204 (84.6)	37 (15.4)	144 (86.2)	23 (13.8)	60 (81.1)	14 (18.9)	1.46 (0.70-3.03)	.308
Diarrhea	213 (88.4)	28 (11.6)	146 (87.4)	21 (12.6)	67 (90.5)	07 (9.5)	0.73 (0.29-1.79)	.488
Financial difficulties	180 (74.7)	61 (25.3)	128 (76.6)	39 (23.4)	52 (70.3)	22 (29.7)	1.39 (0.75-2.57)	.295

Abbreviations: CI, confidence interval; OR, odds ratio; QoL, quality of life.

### Discussion

This study reports the HRQoL in 241 older adults at the time of cancer diagnosis and after 6 to 12 months. At the follow-up, a worse HRQoL was observed in association with

cognitive function and dyspnea, while an improved HRQoL was observed in association with emotional function.

Most patients in the study were receiving a low income, had a low education level, had nonwhite skin color, and did

not undertake professional activity outside the home. With regard to the topography, most tumors were in the male genitals or female breasts. This reflects the incidence of these cancers in the Brazilian population (25). Less than half of the older adult patients received chemotherapy (41.1%), radiotherapy (38.2%), or hormone therapy (35.3%). These results agree with a study that evaluated the effects of pain, fatigue, and insomnia on the HRQoL in older adults with cancer, where less than half of participants received chemotherapy, radiotherapy, or chemoradiotherapy (26). A study in 40 000 Brazilian patients with lung cancer showed that adults >70 years old received 39% less chemotherapy, 31% less surgery, and 14% less radiotherapy (27).

Cancer can cause clinical complications that manifest themselves in a number of metabolic disorders such as nutritional balance deficiency and immune system dysfunction. The most common metabolic disorders are weight loss, malnutrition, and cachexia as these occur as a result of decreased food intake, the convergence of nutrients to tumor cells, and basal energy expenditure. Nevertheless, the older adults included in this study presented a mostly good clinical condition and proper nutrition. It is important to highlight that only patients who survived for 6 to 12 months after their cancer diagnosis were interviewed and included in the study.

A total of 46.5% of the older adults included in this study had 1 or more comorbidities at the time of diagnosis. In a Chinese cohort of 598 survivors of gynecological cancer, approximately 75% of patients reported at least 1 comorbidity. Individuals with comorbidities had lower scores on most scales of the EORTC QLQ-C30 in comparison to individuals without comorbidities. This was especially evident for patients suffering from cardiovascular diseases, respiratory diseases, digestive diseases, and musculoskeletal disorders (28). Another Chinese study evaluated the HRQoL in 120 cancer patients and reported that the prevalence of hypertension, diabetes, and heart disease was 58.2%, 20.0% and 6.4%, respectively (26). Unfortunately, the study reported here did not evaluate hypertension as this does not form part of the Charlson Comorbidity Index.

Most of the older adults included in this study were sedentary or irregularly active. In a study that compared women who survived cancer with healthy controls, 42.7% and 49.5% were sedentary, respectively. The same authors observed that sedentary individuals, in either group, had a worse HRQoL when compared to those who were physically active (29).

In this study, a worsening of cognitive function was observed between diagnosis and follow-up in the older adult participants. This may be due to the influence of cancer progression and aggressive treatments on the cognition of the patient (30). However, contrary to these results, a prospective study of 139 patients undergoing chemotherapy for lung cancer found no difference in HRQoL related to cognitive function after treatment (4).

The older adult patients evaluated in this study also showed improved emotional function after the follow-up.

In the hospital where the patients were recruited, patients receive a multidisciplinary approach that focuses on humanized care. This may justify the improved emotional condition during the treatment period. In opposition to these results, a study comparing the HRQoL at 3 and 6 months after diagnosis showed no improvement in emotional function and decreased symptoms of nausea and vomiting (31). A systematic review of HRQoL in Brazilian women undergoing breast cancer treatment revealed that the most affected areas were those associated with functionality, emotional issues, financial difficulties, sexuality, and general symptoms (32).

Regarding the symptoms, dyspnea, which was reported in approximately half of the older adult cancer patients, worsened by the follow-up. The etiology of dyspnea is related to cardiorespiratory diseases, anemia, ascites, and psychogenic disease (33). Contrary to these results, a study in a similar population found that pain, fatigue, and insomnia were associated with a worsening HRQoL (26). This discrepancy may have been produced by the different cancer topographies analyzed in this study.

When comparing the <75 and  $\geq 75$  age groups, no statistically significant differences were found between the functional and symptom scales. Conversely, a randomized study of 619 cancer patients found a worse HRQoL in patients >70 years old in relation to physical, emotional, and social domains as well as to financial difficulties (34). Another study found a worse HRQoL in patients  $\geq 70$  years old in relation to physical and cognitive functions and symptoms of fatigue and dyspnea (35). The different demographic, tumor, and clinical characteristics of the study populations may justify the divergences in the literature.

The main advantages of this study are its prospective design, the inclusion of older adults with different topographies, and the follow-up at 6 to 12 months after diagnosis. Moreover, the fact that the study was carried out in a single referral institution enabled the standardization of data collection instruments, which minimized possible bias and increased internal validity. However, there were some limitations, such as the difference in population size with those aged <75 years accounting for almost 70% of the study population. Another potential limitation was the short follow-up time (6-12 months), which did not allow comprehensive evaluation of the treatment effects on HRQoL.

In clinical practice, specific attention should be directed to the vulnerable group of older adults with cancer. More specifically, HRQoL assessment should be performed at diagnosis and during treatment to contribute to the best indication of antineoplastic therapies and to understand the individual needs of each patient with a view to enhancing the prognosis, well-being, and HRQoL in older adults with cancer.

## Conclusion

This study provides new information on the relationship between age and HRQoL in older adults with cancer. At the

time of diagnosis, the worst HRQoL was observed in emotional and physical function, financial difficulties, pain, and insomnia. When analyzing the change in HRQoL between diagnosis and follow-up, the patients presented worsening cognitive function and dyspnea and improving emotional function. As there was no clinically relevant change ( $\geq 10$  points) between baseline and follow-up in either age group ( $< 75$  years and  $\geq 75$  years) for any of the HRQoL domains studied, from a public health perspective, the results support the notion that, in Brazil, all patients 60 years old and older should be considered similar with regard to the impact of cancer and its treatment on their HRQoL.

### Authors' Note

Wigna Rayssa Pereira Lima is now affiliated with Federal University of Pernambuco (UFPE), Recife, Brazil.

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**Jurema Telles de Oliveira Lima** is a medical oncologist and head of oncology service with interfaces with geriatric and palliative care. She started monitoring a cohort of old patients with cancer since 2015 with almost 2100 patients enrolled until December 2019. Her expertise includes quality of life and research studies focus on epidemiology, diagnosis, and prognostic of cancer.

**Wigna Rayssa Pereira Lima** is a speech, language, and hearing therapist with the formation in the analysis of human behavior and quality of life. Nowadays she develops research studies with children within autistic spectrum.

**Murilo Carlos de Britto** is a pediatric pulmonologist working at Instituto de Medicina Integral Prof. Fernando Figueira – IMIP since 1985 with academic and clinical activities and is a senior lecturer in epidemiologic studies at post-graduation service. His research focuses on respiratory diseases, especially cystic fibrosis, with attention to screening and early detection.

**Maria Júlia Goncalves de Mello** is a pediatrician working at Instituto de Medicina Integral Prof. Fernando Figueira – IMIP since 1987 with academic and clinical activities and is a senior lecturer in epidemiologic studies at post-graduation service. His expertise includes the analysis of cohort studies.

**Luiz Claudio Santos Thuler** is a physical doctor currently working since 1998 at INCA – Instituto Nacional do Cancer in research, academic, and clinical activities. He is a senior lecturer at Clinical Research Center in Epidemiology and his research studies focus on epidemiology, diagnosis, and prognostic cancer especially in women as well as lung cancer. His expertise includes analysis of Brazilian cancer databases.