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Health-related quality of life of cancer patients undergoing chemotherapy*

Qualidade de vida relacionada à saúde de pacientes com câncer em quimioterapia

Calidad de vida relacionada con la salud de pacientes con cáncer en quimioterapia

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It is a cross-sectional study to evaluate the health-related quality of life in cancer patients undergoing chemotherapy, to identify the domains affected and associate them with sociodemographic and clinical-therapeutic features of the sample. It was performed with 152 patients between 2009 and 2011 in two centers of chemotherapy, in Ribeirão Preto, SP, Brazil. The instrument *Quality of Life Questionnaire Core-30* was used. The general Quality of Life was considered good, the domains affected were: emotional and role function, pain, fatigue, insomnia and loss of appetite. Female patients, between 40 and 60 years, economically active, with gastric, lung, neurological and skin cancer, with metastasis, and patients who underwentsurgery and/or radiotherapy showed concomitant deficitsin several areasand the presence of more symptoms. We concluded that the cancer and its treatment somehow affected patients, causing more symptoms and deficits of the performed functions, jeopardizing their health-related quality of life.

Descriptors: Quality of Life; Neoplasms; Drug Therapy; Oncologic Nursing.

Estudo transversal, com o objetivo de avaliar a Qualidade de Vida Relacionada à Saúdeem pacientes com câncer em quimioterapia, identificar domínios afetados e associá-los com características sociodemográficas e clínico-terapêuticas da amostra. Foi realizado com 152 pacientes entre 2009-2011 em duas centrais de quimioterapia, na cidade de Ribeirão Preto, SP, Brasil.Utilizou-se o instrumento *Quality of Life Questionnaire Core-30*. A Qualidade de Vida geral foi considerada boa, os domínios afetados foram: função emocional, desempenho de papel, dor, fadiga, insônia e perda de apetite. Pacientes do sexo feminino, entre 40-60 anos, economicamente ativos, com câncer gástrico, pulmão, neurológico e pele, os metastáticos e os pacientes que realizaram cirurgia e/ou radioterapia concomitantemente apresentaram déficits em vários domínios e presença de mais sintomas. Concluiu-se que o câncer e seu tratamento afetaram de algum modo os pacientes, causando déficits nas funções desempenhadas e presença de mais sintomas, prejudicando sua Qualidade de Vida Relacionada à Saúde.

Descritores: Qualidade de Vida; Neoplasias; Quimioterapia; Enfermagem Oncológica.

Estudio transversal,cuyo objetivo fue evaluar la Calidad de Vida relacionada con la Salud en pacientes con cáncer en quimioterapia, identificar dominios afectados y asociarlos con datos sociodemográficos, clínicos y terapéuticos de la amuestra. Llevado a cado con 152 pacientes entre 2009-2011 en dos centros de quimioterapia, en RibeirãoPreto, SP, Brasil. Se utilizó el instrumento *Quality of Life Questionnaire Core-30*. La Calidad de Vida general fue considerada buena,los dominios afectados fueran: función emocional, desarrollo de papel, dolor, fatiga, insomnio y pérdida de apetito. Pacientes del sexo femenino, entre 40-60 años, económicamente activos, con cáncer gástrico, pulmón, neurológico y piel, con metástasis y los pacientes que se sometieron a cirugía y/o radioterapia concomitante presentaran déficit en varias áreas y presencia de más síntomas. El cáncer y su tratamiento afectaran de alguna manera los pacientes, causando déficits en las funciones desarrolladas e más síntomas, perjudicando la Calidad de Vida Relacionada con la Salud.

Descriptores: Calidad de Vida; Neoplasias; Quimioterapia; Enfermería Oncológica.

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Introduction

In the last decades, cancer acquired a broader dimension, being converted in an evident world public health problem. The estimates of incidence of cancer in Brazil for the year 2013 is 518,510 new cases, including skin cancer of the non melanoma type. The most frequent are the following cancers: non melanoma skin, prostate, lung, colon, rectum and stomach for the male sex; and for the female sex: non melanoma skin, breast, uterine cervical, colon, rectum and thyroid glandule(1).

The objective of the treatment of cancer is the cure, to prolong life when there is no cure and to provide palliative care. When the treatment does not result in cure, it must lead to an improvement of the welfare and the quality of life(2).

The antineoplastic chemotherapy has become one of the most important and promising manners to combat cancer, and can be used both for healing, as well as palliative purposes. Its indication implies in a series of factors which must be considered in its planning, as well the age of the patient, his nutritional condition the renal hepatic and lung functions, presence of infections, the type of tumor, presence of metastasis and its extension and the condition of life of the patient(3).

Cancer can produce many different symptoms, some are subtle others not so much. They occur according to the type and stage of the cancer and some types of cancer do not present any symptoms until they are in advanced stages. The time from the diagnosis, the acceptance of the patient the intensity of the disease and the level of psychic suffering experienced by the caregivers can affect the Quality of Life (QL) of the patients with cancer(4).

The technological advancement, in the scope of medical science, has provided a greater optimism in the treatment of cancer and an increase of the rate of surviving patients; therefore, it is necessary to evaluate the quality of life of these patients, while this is an important indicator of welfare(3).

Health-related quality of life (HRQL) and its evaluation have become each time more important in health care, especially in the area of chronic diseases. Normally, the evaluations in the health area were focused in the rates of survival, of local control, of complication and under the point of view of the doctor. These evaluations did not have knowledge and understanding of the mental and emotional welfare of the patients. Currently, the HRQL has been evaluated as the perception of the patient, of the effects of the disease and of impact on his daily life. It has two fundamental characteristics: it is considered multidimensional, once it incorporates the physical, psychological, social, emotional and functional domains; and it is subjective, that is, according to the experiences of the patient(5).

Determining how to measure and quantify the subjective experience of HRQL is a challenging question. There is a variety of validated instruments available for use in the field of oncology. They are classified in three types: generic, which evaluates QL/HRQL independently of the presence of some pathology; the specific one for patients with cancer in general and the specific for the type of cancer, like for example, instruments that evaluate the breast cancer, the head and neck cancer, etc.(5).

In this sense, the present study has as objectives: evaluate the HRQL with patients with cancer undergoing chemotherapy treatment, identify the domains affected, using the instrument *Quality of Life Questionnaire-Core30* (QLQ-C30)(6) and associate these domains with the social demographic and the clinical therapeutical characteristics of the sample.

Method

This is a descriptive, exploratory and cross-sectional study. An intentional sampling was made, in which the researcher selects the subjects considered typical of population under analysis(7); once it was composed by patients diagnosed with cancer from

May 2009 to December 2011, a sample of 152 patients.

The venues for study were the Specialized Center on Oncology (ECO) of the Hospital Sociedade Portuguesa de Beneficência and the Chemotherapy Center of the Hospital das Clínicas da Faculdade de Medicina de RibeirãoPreto of the Universidade de São Paulo (HC-FMRP-USP).

The criteria of inclusion were: patients over 18 years of age, both sexes, diagnosed with cancer beginning chemotherapy treatment at ECO and in the Chemotherapy Center of HC, assisted by the Unified Health System (UHS) and that accepted to participate in the research signing the Free Consent Form. The patient who had some difficulty to understand the research and/or the participation in the study and in the interviews were excluded.

A weekly survey of the patients who were begging chemotherapy treatment was made in both venues, by the main researcher, a monthly average for the sample was calculated and those who complied with the criteria of inclusion and exclusion were invited to participate in the research.

For the characterization of the data of the patients, a questionnaire of identification was used for the socio-demographic data collection, such as: sex, age, marital status, precedence, profession/ occupation, schooling and religion; and the clinical and therapeutical data such as: diagnosis, making and type of the surgery; radiotherapy; protocol, session and side effects of chemotherapy.

For the evaluation of HRQL and of the affected domains (scales and items) the following instrument was used: *Quality of Life Questionnaire Core-30* (QLQ-C30) of the *European Organization for Research and Treatment of Cancer* (EORTC) to evaluate the HRQL(6).

The QLQ-C30 is specific instrument of quality of life for patients with cancer, dully validated for the Brazilian population(8). The instrument has 30 questions which make a scale of the General Condition of Health/ quality of life; five functional scales: physical, cognitive, emotional, social and role functions; three scales of symptoms: fatigue, pain and nausea and vomit; five items of symptoms; dyspnea, loss of appetite, insomnia, constipation and diarrhea, and one item of evaluation of the financial impact of the treatment and of the disease(6). The instrument requires that the patients choose the answers according to the last week experienced, therefore, the instrument was applied one week after the beginning of the chemotherapy treatment.

The QLQ-C30 creates scores in the functional scales, in the scales of symptoms and in the other evaluated items. Each score is transformed into a scale from 0 to 100, according to guidelines of the EORTC in which zero shows the worst functioning and 100, the best functioning in the scale of General Condition of Health/ Quality of Life (GCH/QL); whereas in the scale and items of symptoms and the item of financial difficulty, 100 indicates more symptoms (or difficulties) present, and 0, no symptom (or difficulty)(6).

For the data analysis the *Statistical Package for Social Science* version 17.0 (SPSS for Windows) was used. Cronbach´s Alpha coefficient of internal consistence test was used to test the reliability of the instrument. The average and the standard deviation were calculated for the descriptive analysis of the data; and the Analysis of variance (ANOVA) parametric test to compare the domains of the instruments of HRQL with the socio-demographical clinical and therapeutic data in which the level of significance established was 0.05.

The project was approved by the Committee of Ethics of the Nursing School of Ribeirão Preto – USP – São Paulo – Brasil, under protocol no. 1002/2009, complying with Resolution 196/96 of Health National Council (HNC)(9).

Result

The sample was composed of 152 patients with cancer. As to the socio-demographic characteristic, 85 (55.9%) were female and 67 (44.1%) male. Regarding age range: between 18 and 39 years old, 9 (5.9%) patients were found, between 40 and 59 years old, 83 (54.6%) patients, between 60 and 79 years old, 58 (38.2%), and over 80 years old, 2 (1.3 %) patients.

Regarding marital status, 87 (57.2%) patients were married, 23 (15.1%) single, 25 (16.5%) divorced and/or had lovers and 17 (11.2%) widows. As to the origin, 80 (52.6%) lived in Ribeirão Preto, 68 (44.7%) were from the Ribeirão Preto region and (2.7%) from other regions.

As to the profession, 35 (23.0%) were retired; 36 (23.7%) housewives; 21 (13.8%) had as occupation: painter, bricklayer, driver, porter; 21 (13.8%) worked in the commerce and the remaining 39 (25.7%) were professionals from several other areas.

As to schooling, 100 (65.8%) had grade school, 26 (17.1%) had high school and 26 (17.1%) had university degree. As to the religion, the majority, 107 (70.4%), were catholic, 35 (23.0%) were evangelics, 6 (3.9%) spiritualists, 1 (0.7%) was Buddhist and 3 (2.0%) atheists.

Regarding the clinical and therapeutical data, the most frequent types of cancer were: breast (23.7%), intestinal (21.7%) and gastric (12.5%); as to the presence of metastasis, 117 (77.0%) had primary cancer and 35 (23.0%) had metastasis.

As to the types of treatment, 117 (77.0%) had undergone surgery. Of this 117, 38(32.5%) patients had a surgery for a partial removal of the affected organ and adjacencies, 25 (21.4%) biopsy, and 24 (20.5%) had a total removal of the affect organ and adjacencies, 15 (12.8%) patients had tumorectomy, 5 (4.2%) surgeries were palliative, and there was 1 (0.8%) with a bone marrow transplant and 9 (7.8%) patients did not know how to inform the surgery made. Only 42 (27.6%) patients underwent radiotherapy.

Regarding the protocol of chemotherapy (CT), 46 different medication schemes were found, the most used were: 5-Fluorouracil (5-FU) + Leucovorin (LV) in 19 (12,5%) patients; Cisplatin in 18 (11,8%); Paclitaxel + Carboplatin in 17 (11,2%); Oxaliplatin + Capecitabine (endovenous and/or oral) in 12 (7,9%); and Epirubicin + Cyclophosphamide + Docetaxel in 11 (7,2%) patients.

The side effects presented by the patients regarding chemotherapy were also evaluated and 35 (23.0%) were asymptomatic, 85 (55.9%) with physical symptoms such as: heat, sweating, malaise, weakness and dizziness, among others associated to gastro-intestinal uncomfortable, such as: nauseas and vomit, constipation and/or diarrhea; 22 (14.5%) only gastro-intestinal symptoms; 9 (5.9%) only physical symptoms; and 1(0.7%) complained of physical and gastro-intestinal symptoms, and also referred to emotional symptoms such as: depression, anguish and or/irritability.

Health-related quality of life

Regarding the psychometric characteristics of the instrument for the sample studied, Cronbach´s Alpha coefficient was 0.84, showing reliability of the instrument for this sample.

Table 1 presents the average and the standard deviation of the scales of instrument QLQ-C30. The average of the General Condition of Health/ Quality of Life (GCH/QL) found was 74.91 and of the scores for the physical, cognitive and social functions varied from 72.92 to 77.11 considered good scores for being close to 100 (maximum); for role and emotional function, they varied from 57.75 to 63.26, representing a satisfactory result (results between 50.0 and 70.0). The scores of the scales and items of symptoms showed these symptoms as the most frequent: pain, fatigue, insomnia and loss of appetite, besides, the patients reported that their physical or treatment condition had brought some financial difficulty, according to the score of the item that evaluates financial difficulty.

Table 1 - Average and standard deviation of the scales in items of the QLQ-C30 instrument of the sample

Scalesanditems	Average	Standard Deviation
General and functional scales		
General condition of health (GCH/QL)	74.91	23.36
Physical function (PF)	72.92	23.34
Role function (RF)	57.75	39.08
Emotional function (EF)	63.26	29.00
Cognitive function (CF)	76.82	28.84
Social function (SF)	77.11	31.87
Scales and items of symptoms		
Fatigue (FAT)	32.44	29.80
Nauseasandvomit (NAV)	9.45	20.00
Pain (Pain)	38.28	36.60
Dyspnea (DIS)	10.88	24.66
Insomnia (INS)	32.28	37.67
Lossofappetite (LAP)	23.19	39.08
Constipation (CON)	16,14	29,88
Diarrhea (DIA)	7,18	19,42
Item		
Financial difficulties (FDI)	27,74	38,94

Association of the socio-demographic variables were made: sex, age, marital status, profession/occupation and religion with each scale of the QLQ-C30 and the following statistically significant associations were found (p≤0,05): the female sex presented a worse score for the cognitive function than the male one; patients in the age range of 40 and 60 years old obtained higher scores meaning they presented more diarrhea and more financial difficulties than those of the other age ranges; retired and housewives presented a better (GCH/QL) and fewer symptoms of nausea and vomit than the economically active patients, as shown in Table 2.

Table 2 - Average, standard deviation and statistical significance of the application of the QLQ-C30 instrument with the socio-demographic data of the sample

Scales and items of QLQ-C30	Sociodemographic data	Average	Standard-deviation	p-value
Cognitivefunction	Sex			0.039
	Female	72.54	29.46	
	Male	82.26	27.30	
Diarrhea	Age range (years)			0.023
	20 |— 40	0.00	0.00	
	40 |— 60	11.56	24.54	
	60 |— 80	2.27	8.43	
	≥ 80	0.00	0.00	
Financial difficulties	Age range (years)			0.056
	20 |— 40	25.77	36.32	
	40 |— 60	35.21	42.01	
	60 |— 80	18.31	33.06	
	≥ 80	0.00	0.00	
GCH/QL	Profession			0.026
	Retired	82.59	20.35	
	Housewives	79.37	26.68	
	Business man	74.57	20.83	
	Mechanic, painter, electrician	70.20	22.14	
	Otherprofessions	66.64	22.37	
NauseaandVomit	Profession			0.026
	Retired	6.66	15.22	
	Housewives	3.23	9.60	
	Business man	17.44	24.97	
	Mechanic, painter, electrician	17.45	25.53	
	Otherprofessions	9.11	22.62	

Associations of the clinical data were also made: diagnosis (location of the cancer) and presence of metastasis with each scale of the QLQ-C30. Table 3 shows the associations with statistically significant clinical data (p≤0,05): patients with gastric, lung, neurological and skin cancer had higher scores for fatigue and the ones with neurological and lung cancer for dyspnea showing a greater presence of the symptom; the metastatic patients presented a lower physical function than those non metastatic patients.

Table 3 - Average, standard-deviation and statistic significance of the application of the QLQ-C30 instrument with the clinical data of the sample

Scales and items of QLQ-C30	Clinical data	Average	Standard-deviation	P value
Fatigue	Location of the cancer			
	Breast	24.97	25.08	0.019
	Gastric	54.34	33.49	
	Intestinal	24.28	26.06	
	Female reproductive system	27.38	21.74	
	Lung/mediastinal	43.88	31.01	
	Reproductive/genital male	22.20	19.22	
	Head and neck	29.88	30.86	
	Neurological	42.18	31.78	
	Leukemia/lymphoma	34.68	30.50	
	Skinand e melanomas	41.65	49.98	
Dyspnea	Location of the cancer			
	Breast	9.19	21.88	0.057
	Gastric	3.47	10.40	
	Intestinal	7.25	21.88	
	Female reproductive system	6.66	25.81	
	Lung/mediastinal	28.66	32.83	
	Reproductive/genital male	0.00	0.00	
	Head and neck	12.69	25.34	
	Neurological	33.20	47.02	
	Leukemia/lymphoma	12.37	24.55	
	Skinand e melanomas	16.50	33.00	
Physical-function	Metastasis			
	Yes	65.68	27.98	0.036
	No	75.09	21.42	

Other statistically significant associations were made with the therapeutic data, were the following types of surgery caused different deficits in the functions and the presence of more symptoms, for example, patients who had tumorectomy presented lower scores for GCH/QL and physical, emotional, cognitive and social functions, and higher scores meaning more symptoms present such as: nausea and vomits, dyspnea, insomnia, loss of appetite and constipation. The patients who had palliative surgeries reported worse scores for GCH/QL and physical, emotional and cognitive functions, and also reported more symptoms of fatigue, nausea, dyspnea, insomnia and loss of appetite. But the patient who had transplant of bone marrow obtained worse scores for the emotional, cognitive and social functions, besides the symptoms of fatigue and constipation. The patients who underwent radiotherapy had more symptoms of pain than the ones who did not undergo such therapy.

Discussion

The average of 74.91 for the GCH/QL showed that the patient with cancer undergoing chemotherapy, despite facing the diverse modifications in their lives due to the disease and the treatment, considered that their HRQL was good. They also reported as good their physical, cognitive and social functions and obtained a satisfactory result for the role and emotional functions; but still were attacked with symptoms of pain, fatigue, insomnia and loss of appetite and they also reported some financial difficulty.

The HRQL was analyzed in women with breast cancer undergone chemotherapy and average of 71.43 for the GCH/QL was found, which was also considered good, as well as the physical and social functions and they also presented deficits in the emotional function and more symptoms of nausea and vomit, fatigue, constipation and pain, besides reporting financial difficulties(3). Another evaluation of HRQL of patients with cancer undergoing chemotherapy, also found a relatively good HRQL in the beginning of chemotherapy, however, after three to six months of treatment, it was observed that it was significantly worse and impairment in the sexual and physical functions was detected(2).

This research found that the women had the worse scores for the cognitive function. Literature shows that the highest impacts perceived by the women were in the sexual and emotional function, financial difficulties, besides the emerging of pain, fatigue, nausea and vomits(3); women with colorectal cancer presented the worse scores for the emotional and cognitive functions and with more symptoms of pain, insomnia, fatigue, constipation and loss of appetite than men(10). Falta a referência 9Women with depression and fatigue after one year or more of chemotherapy and radiotherapy showed jeopardizing in their QL, with lower scores for sexual function and satisfaction and future perspectives(11).

Regarding the age range, significant differences were found among the groups of age(3), in the scale GCH/QL the group of women of 30 years old evaluated the HRQL in a more positive way than the group of 60 years old. When compared to this research, patients who were between 40 and 60 years old reported more diarrhea (Average= 11.56) and greater financial difficulties (Average= 35.21). The study found diarrhea as the most frequent in the groups of 30 (Average=49.99) and 50 years old (Average=28.52) and the financial difficulties were more important in the groups between 30 and 40 years old (Averages= 61.90 e 49.99, respectively)(3). Another study that analyzes the HRQL of patients with cancer of head and neck found that the financial difficulties, the loss of appetite and nausea and vomit caused the greatest negative impact in the age range 40 to 60 years old, especially in the women(12).

In the present study, the patients with gastric, lung, neurological and skin cancer presented more fatigue and the ones with neurological and lung cancer had more dyspnea. In another research made with oncological patients, the gastrointestinal cancer was the most common and the patients presented problems related to fear concerning the future, thought about the disease and its consequences, impatience and depression; HRQL was favorable in most patients and this study also found relation between fatigue and HRQL in the patients with chemotherapy treatment, that is, the more intense the fatigue was, the worse the HRQL was reported by the patients (4). In another study which evaluated the HRQL of patients with the gliomas shows that this patients presented deficits in five functions of QLQ-C30 (emotional, social, cognitive, physical and functional), besides the presence of the symptoms of fatigue, pain, loss of appetite, insomnia and nausea and vomit(13).

Studies evaluated that the HRQL of the patients with colorectal cancer undergoing chemotherapy found significant changes in the course of the treatment, with deficits in the cognitive, dyspnea, insomnia, constipation and diarrhea functions(14), emotional, pain, insomnia and fatigue functions and the general QL as satisfactory (average = 79.13)(10).

Factors which contributed for the decrease of HRQL were evaluated in women with gynecological cancer and they were divided into four subgroups (quartiles) according to the result of HRQL, it was found that, for the women whose total QL was in the inferior quartile (Q1), the result showed that the falls are due to the considerable differences in specific questions, including nauseas, pains sensation of malaise and being bothered by the side effects of the treatment. they believe that the fact that practically there are no differences in the welfare among those subgroups of women, confirms the main hypothesis that harms in HRQL are specific for the disease and the treatment and they do not reflect a generalized deficiency of QL and that simple interventions that improve the physical symptoms can have great effects, thus improving other aspects of physical and functional welfar (15).

The HRQL was evaluated in patients with non small cells lung cancer undergoing adjunctive chemotherapy and the alterations in the HRQL during chemotherapy were relatively small, with the worsening of the symptoms of fatigue, nausea and vomit, however there was a reduction in the pain and no change in the general HRQL. These results indicated that the negative effects of adjunctive chemotherapy in HRQL seem to be temporary and that the improvement is common in most patients(16).

Women with neurological cancer undergoing antineoplastic chemotherapy has the physical and environmental domains more jeopardized, and the social, the most preserved, and the average of general QL was 68.6. All the domains are significantly correlated with the general QL. They showed that the HRQL is satisfactory and suggest that the domains with lower scores should be target of more accurate observations, during the multiprofessional intervention, in order to provide better HRQL during the chemotherapy treatment(17).

Chemotherapy itself, caused symptoms in the patients of this study, as pain, fatigue, insomnia and loss of appetite and when associated to other treatments, such as surgery and radiotherapy also caused damage in the functions and symptoms scales.

The surgeries with healing and palliative purposes caused deficits in the functions and the presence of more symptoms, the patient who underwent palliative surgeries reported worse scores for GCH/QL and the physical, emotional and cognitive functions, and reported more symptoms of fatigue, nausea e vomits, dyspnea, insomnia and loss of appetite. Patients who underwent palliative surgery presented a decrease in the general QL and in the cognitive function in the first six months after the surgery(18). Women with mastectomy, together with their control group, presented worse punctuation in limitation due to physical aspects dimension and better punctuation for functional capacity, and once combined with the presence of comorbidities, they presented lower levels of QL in the functional capacity, pain and GCH/QL dimensions(19).

Patients with cancer of head and neck who underwent radiotherapy treatment were affected with symptoms as fatigue and insomnia, besides reporting financial difficulties(5). Women with cervical uterine cancer presented sexual disorder after radiotherapy(20). In this research, the patients who underwent radiotherapy reported more pain than the others.

Conclusion

This study provided the evaluation of the health-related quality of life of patients with cancer undergoing chemotherapy treatments. The average of GCH/QL measured by the instrument QLQ-C30 for the sample of 74.91 was considered good for these patients. The main domains of HRQL affected, were: emotional functional, role function, pain, fatigue, insomnia and loss of appetite.

The cancer and its treatment affected somehow the patients causing deficits in the functions and presence of more symptoms, jeopardizing their HRQL. The improvement in the HRQL of the patients can occur in as much as the side effects of the treatment can be avoided and controlled, and also in the adhesion of complementary effective treatments which could help the patients to better face the disease and the treatment received.

Researches of longitudinal section are suggested so that the nurse can better understand and evaluate the HRQL of patients with cancer, to better evaluate the changes occurred in the HRQL in the course of time, and also to modify the factors associated to these changes and the possible interventions which face their reduction or control.

Collaborations

Nicolussi AC participated in the elaboration, collection and analysis of the data, writing and critical analysis of the article. Sawada NO participated in the analysis of the data and critical analysis of the article. Cardozo FMC, Andrade V and Paula JM participated in the data collection.

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