

Influence of clinical variables on the functional capacity of women undergoing chemotherapy

Influência de variáveis clínicas na capacidade funcional de mulheres em tratamento quimioterápico

Influencia de variables clínicas en la capacidad funcional de mujeres en tratamiento quimioterápico

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ABSTRACT

Objective: To evaluate how the chemotherapy protocol and tumor type influence the functional capacity of women diagnosed with gynecological cancer, breast cancer and gestational trophoblastic disease during chemotherapy. **Methods:** This was an observational and retrospective study with a quantitative approach and longitudinal design. The study included 438 women undergoing chemotherapy in a general hospital from January 2000 to December 2012. **Results:** The functional capacity of the study population had a mean score of 70 on the Karnofsky Performance Scale. A higher decline was noted in the functional capabilities of patients with gynecological cancer, and in women who used taxane chemotherapy protocols. **Conclusion:** It is germane to establish measures aimed at ensuring the prevention of side effects caused by chemotherapy, providing comprehensive and effective care for oncology patients.

Keywords: Karnofsky Performance Status; Activities of Daily Living; Drug Therapy; Women's Health.

RESUMO

Objetivo: Avaliar a influência do protocolo quimioterápico e tipo tumoral sobre a capacidade funcional de mulheres diagnosticadas com câncer ginecológico, câncer de mama e doença trofoblástica gestacional durante o tratamento quimioterápico. **Métodos:** Trata-se de um estudo observacional e retrospectivo com abordagem quantitativa e delineamento longitudinal. Participaram do estudo 438 mulheres em tratamento quimioterápico, em um hospital de clínicas no período de janeiro de 2000 a dezembro de 2012. **Resultados:** A capacidade funcional da população estudada apresentou um escore médio de 70,00 no índice de Karnofsky. Notou-se maior impacto pontual no declínio da capacidade funcional das pacientes com câncer ginecológico e nas mulheres que utilizaram protocolos baseados em quimioterápicos taxanos. **Conclusão:** É oportuno o estabelecimento de medidas capazes de garantir a prevenção dos efeitos colaterais causados pelo tratamento quimioterápico, proporcionando uma assistência integral e de qualidade às pacientes oncológicas.

Palavras-chave: Avaliação de Estado de Karnofsky; Atividades Cotidianas; Quimioterapia; Saúde da Mulher.

RESUMEN

Objetivo: Evaluar la influencia del protocolo quimioterápico y tipo tumoral en la capacidad funcional de mujeres diagnosticadas con cáncer ginecológico, cáncer de mama y enfermedad trofoblástica gestacional durante el tratamiento quimioterápico. **Métodos:** Se trata de estudio observacional y retrospectivo con abordaje cuantitativa y delineamiento longitudinal. Participaron del estudio 438 mujeres en tratamiento quimioterápico, en un hospital de clínicas en el período de enero de 2000 a diciembre de 2012. **Resultados:** La capacidad funcional de la población estudiada presentó un escore promedio de 70,00 en el índice de Karnofsky. Se notó mayor impacto puntual en el declino de la capacidad funcional de las pacientes con cáncer ginecológico y en mujeres que utilizaron protocolos embazados en quimioterápicos taxanos. **Conclusión:** Es oportuno el establecimiento de medidas capaces de garantizar la prevención de los efectos colaterales causados por el tratamiento quimioterápico, proporcionando una asistencia integral y de calidad a las pacientes oncológicas.

Palabras clave: Estado de Ejecución de Karnofsky; Actividades Cotidianas; Quimioterapia; Salud de la Mujer.

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INTRODUCTION

Due to the extended life expectancy enabled by technological advances in health, cancer has become a global public health problem, and its incidence is increasingly common among the populations¹.

Among the Brazilian female population, breast cancer present the highest incidence rate of neoplasia and mortality. In turn, gynecological cancer accounts for more than half the deaths by cancer among Brazilian women, and cervical cancer has the highest incidence rate among these types of cancer¹. Additionally to the malignant tumors that affect women, it is also important to observe that gestational trophoblastic disease (GTD) is included in this group, and this includes several pathologies. The non-malignant form of the disease includes the hydatidiform mole and the malignant form includes the gestational trophoblastic neoplasia. This is divided into invasive mole, choriocarcinoma and placental site trophoblastic tumors. The non-malignant forms are likely to become malignant^{2,3}.

In this context, chemotherapy is a chemical and systemic treatment that has been widely used for cancer control and treatment. However, the general aggression to the cells eventually leads to the occurrence of several toxicities⁴⁻⁶ that, as a result, may adversely affect functional capacity (FC), which is directly related to the quality of life of patients submitted to this therapeutics⁷.

In the perspective of managing the functional state, a growing use and development of assessment tools that may measure the aspects pertinent to FC⁴ is observed. The Karnofsky's tool, developed by David A. Karnofsky and Joseph H. Burchenal in 1948 in order to assess the physical performance of patients undergoing chemotherapy treatment from the perception of the professional, contributes to a safer administration of the chemotherapy^{6,8}. This tool has a 0-100 scale, where 0 represents death and 100 represents preservation of FC. This is the most commonly used tool to assess cancer patients, representing a guiding element for care and an evaluator for the response to the treatment. It is essential for assessing the capacity to perform activities of daily living, the symptoms of the disease, and the required level of care. Also, it indicates the tolerance and the response to the treatment, thus contributing to the selected therapy⁴.

Nursing has been actively participating in all initiatives for cancer control and FC management presented by patients during the therapy, consistently managing care actions in the administration of the various modalities of treatment of the disease^{5,6}.

The present study aimed at assessing factors that affected the functional capacity of women diagnosed with gynecological cancer, breast cancer and GTD during chemotherapy treatment in the oncogynecology department of a public hospital.

METHODS

This observational, retrospective study with a quantitative approach and longitudinal design was developed in the Center of Chemotherapy of the Clinical Hospital of the Federal University of Triângulo Mineiro (CQT/HC/UFTM) in the city of Uberaba, state of Minas Gerais. The study had the participation of women undergoing treatment against gynecological cancer, breast cancer and GTD in the CQT/HC/UFTM within the period from January 2000 to December 2012. Patients who did not complete at least three cycles of the chemotherapy treatment were excluded due to the analytical impossibility of data. The period of compilation and analysis of data was from January to April 2014.

Initially, the patients were identified by means of a follow-up form of patients submitted to antineoplastic chemotherapy containing sociodemographic and clinical characterization, information related to the identification of the patient, and a database about the disease and the proposed treatment.

The tool proposed by Karnofsky was used to assess the impact of the treatment in the FC presented by such patients during the antineoplastic therapy. The assessment of FC of patients was performed continuously during the chemotherapy cycles, being concluded at the end of the treatment or due to death of the patient^{4,5}. The utilized form and tools were filled by the same professional during the entire period, as this professional monitored the patients in the oncologic service between 2000 and 2012, thus ensuring the quality of the study.

The Karnofsky's tool consists of three major areas, each one covering the scores related to the FC presented by the patient. In this context and in relation to the ability to perform daily activities, the first area is related to patients that require minimum assistance, corresponding to the scores between 80 and 100. The second condition is related to patients that sometimes require some kind of assistance, corresponding to scores between 50 and 70. The third condition is related to patients that require a higher level of support, being unable to self-care and requiring hospital care, corresponding to the scores between 0 and 40. Score 0 indicates death⁵.

The software Statistical Package for the Social Sciences (SPSS) version 16.0 was used to store and codify the data. The univariate descriptive analysis of the qualitative variables was performed through absolute and relative frequencies analysis. Measures of central tendency (mean and median) and measures of dispersion (standard deviation) were used for the quantitative variables. The development of the functional capacity for the different cycles included the analysis of variance (ANOVA) with repeated measures. The multiple linear regression model was used to statistically analyze the impact of some variables in the progress of the scores related to FC. The level of significance for all inferential procedures was 5%.

The present study was submitted to analysis by the Human Research Ethics Committee of the Federal University of Triângulo

Mineiro and approved in 2010 according to statement 1698/2010. Confidentiality of data of the individuals was guaranteed according to Resolutions 1196/1996 and 466/2012⁹. A Free and Informed Consent Form was not required from patients as this was a retrospective study, that is, data were collected from the files of the service.

RESULTS

This study had the participation of 438 women; 273 (62.3%) were from the city of Uberaba. Their mean age was 50.62 years, ranging between 16 and 84 years old and with a standard deviation of 13.70. The most prevalent type of tumor was breast cancer, with a total of 224 (51.1%) cases of the disease, followed by 194 (44.3%) cases of gynecological cancer and 20 cases of GTD (4.57%). The patients of the present study underwent a minimum of three and a maximum of twelve chemotherapy cycles (Table 1).

A higher number of patients was between the first and sixth chemotherapy cycle; thus, after the sixth cycle a significant reduction of the population undergoing this treatment was observed. Therefore, only the period between the first and sixth chemotherapy cycle was considered in the present research (Table 2).

Analysis of multiple comparisons using Bonferroni method presents the cycles in which the comparisons of means of FC were statistically significant, showing that the last two cycles presented a higher decline in the evolution of FC. In addition, the differences were found to be more important between the extremes; therefore, the use of mean scores of the three first and the three last chemotherapy cycles is pertinent considering the similarity between the three first and three last mean scores of FC.

The patients were divided into two groups for the assessment of the influence of the number of therapeutic modalities on FC: the first group included those who underwent chemotherapy exclusively; the second group included those who underwent chemotherapy associated with other treatment methods. In general, four treatments were performed during the present study: chemotherapy, radiotherapy, surgery and curettage.

In relation to the chemotherapeutics corresponding to the utilized protocol, groupings of protocols were made according to the similarity with the main base of treatment. These measures were adopted for a better analysis of the adopted protocols, which were allocated into four groups: Anthracycline group: corresponding to fluorouracil, doxorubicin or epirubicin and cyclophosphamide (FAC); doxorubicin or epirubicin and cyclophosphamide (AC); platinum group: related to cisplatin, doxorubicin or epirubicin and cyclophosphamide (PAC); cisplatin and cyclophosphamide; cisplatin and etoposide; carboplatin and etoposide; cisplatin and doxorubicin (PA); cisplatin, etoposide and bleomycin (PEB); cisplatin and fluorouracil (PLA-FLU); cisplatin and vincristine; cisplatin; taxanes group: paclitaxel and carboplatin; docetaxel and carboplatin; doxorubicin and paclitaxel; paclitaxel; 'others' group: with the drugs melphalan; cyclophosphamide, vincristine and epirubicin; cisplatin, topotecan and cytarabine; vinorelbine, actinomycin and cyclophosphamide; cisplatin and vinorelbine; topotecan and cytarabine; cyclophosphamide, methotrexate and fluorouracil (CMF); methotrexate (MTX); etoposide, methotrexate, actinomycin-D, cyclophosphamide and vincristine (EMA-CO).

The diagnoses were divided into three groups: the group of patients with breast cancer corresponding to women

Table 1. Measures of position and variability of functional capacity scores of women with gestational trophoblastic disease, breast cancer and gynecological cancer according to the Karnofsky's tool between chemotherapy cycles. Uberaba, Minas Gerais, Brazil, 2014

Scores	N	Mean	Median	Standard deviation	Minimum	Maximum
Score corresponding to Cycle 1	438	78.22	80.00	11.482	30	100
Score corresponding to Cycle 2	438	78.11	80.00	9.980	30	100
Score corresponding to Cycle 3	438	77.67	80.00	9.642	40	100
Score corresponding to Cycle 4	390	77.28	80.00	9.556	40	100
Score corresponding to Cycle 5	339	77.02	80.00	9.372	40	100
Score corresponding to Cycle 6	316	76.09	80.00	9.008	40	100
Score corresponding to Cycle 7	57	75.26	80.00	11.512	40	90
Score corresponding to Cycle 8	45	75.78	80.00	11.380	40	90
Score corresponding to Cycle 9	21	75.71	80.00	13.256	40	90
Score corresponding to Cycle 10	14	73.57	80.00	12.774	40	90
Score corresponding to Cycle 11	8	76.25	80.00	11.877	50	90
Score corresponding to Cycle 12	4	77.50	80.00	5.000	70	80

Source: Data collected by the authors between 2000 and 2012.

Table 2. ANOVA test with repeated measures for comparison between the mean scores of functional capacity of women with gestational trophoblastic disease, breast cancer and gynecological cancer according to the Karnofsky's tool in the six first chemotherapy cycles. Uberaba, Minas Gerais, Brazil, 2014

Variable	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Cycle 5	Cycle 6
Cycle 1	_____	$p = 0.63$	$p = 0.812$	$p = 0.211$	$p = 0.004$	$p \leq 0.001$
Cycle 2	$p = 0.63$	_____	$p = 1.000$	$p = 1.000$	$p = 0.016$	$p \leq 0.001$
Cycle 3	$p = 0.812$	$p = 1.000$	_____	$p = 1.000$	$p = 0.001$	$p \leq 0.001$
Cycle 4	$p = 0.211$	$p = 1.000$	$p = 1.000$	_____	$p = 0.005$	$p \leq 0.001$
Cycle 5	$p = 0.004$	$p = 0.016$	$p = 0.001$	$p = 0.005$	_____	$p \leq 0.001$
Cycle 6	$p \leq 0.001$	_____				

Source: Data collected by the authors between 2000 and 2012.

diagnosed with this type of cancer; the GTD group, involving patients with MH and choriocarcinoma; and the group of patients with gynecological cancer, including patients with ovarian cancer, uterine cancer, cervical cancer, vaginal cancer, fallopian tubes cancer and vulvar cancer (Table 3).

Descriptively, the most commonly used protocols by patients were FAC and AC, both classified as anthracyclines, and the group of patients using taxanes, which presented the worst score of FC.

Gynecological tumor was the type responsible for the worst FC presented by the patients, followed by breast cancer and GTD. In turn, the latter presented the best mean scores of FC.

Regarding the adopted therapeutics, patients that used chemotherapy associated with other therapies presented the worst FC.

Using the multiple linear regression analysis to assess the factors that may affect the decline of FC, the variables with better mean scores of FC were selected as a reference category for the analysis of influence of higher impact factors on FC (Table 4). In the regression, each predictor was adjusted in Table 4 for the following variables: medical diagnosis, chemotherapy protocol, and therapeutic modality.

In the group that received the taxane-based protocol it was evidenced that the taxane chemotherapy only caused a significant impact on the decline of FC of women between the first and third treatment cycle.

Regarding the variable related to tumor type, it is possible to affirm that the FC presented by patients with breast cancer, gynecological cancer and GTD presented no similarity between them, thus indicating that patients with gynecological cancer presented worst mean scores of FC throughout the treatment. In addition, given the similarity presented between the protocols, the use or non-use of chemotherapy associated with other types of treatment showed no significant impact on the decline of FC.

DISCUSSION

In general, the women presented mean scores of FC of 70, indicating that the patients showed incapacity to perform

activities of daily living, although their capacity for self-care remained preserved⁵. Furthermore, reduced FC was observed in the first cycles of treatment. This event may be certainly related to the presence of side effects caused by the use of chemotherapy. A study showed that early in the beginning of the treatment there is a loss of FC that may reach approximately 30% of its totality, making the patient vulnerable during the treatment¹⁰.

Data analysis of multiple linear regression showed that the group that received the taxane-based protocol showed that the taxane chemotherapeutic agents caused a significant impact on the decline of FC in women only between the first and third treatment cycles. Thus, the use of taxanes by women in this study was directly associated with the worst FC, possibly due to its toxicity potential⁴.

In this perspective, a cross-sectional study conducted with 21 women diagnosed with breast cancer concluded that patients using paclitaxel presented higher levels of symptoms when compared to those using FAC and CMF protocols, respectively, in the groups' anthracycline and others¹¹. The study also pointed out that fatigue¹¹ was the most recurrent symptom presented by women using taxane-based chemotherapy. It is important to emphasize that fatigue is directly associated with reduced FC¹².

In addition, descriptive analysis of the group of women that received taxane- and platinum-based protocols indicated similarity between the mean scores, but the analysis of their influence on the FC showed that only the use of taxanes significantly affected functional impairment. Thus, although platinum chemotherapeutic agents are nephrotoxic¹³, they present lower functional impact when compared to the taxanes.

Regarding the variable related to tumor type, it is possible to affirm that there was a significant difference between the mean scores of FC during both analyzed moments. It showed that the FC presented by patients with breast cancer, gynecological cancer and GTD had no similarity between them, and indicating that patients with gynecological cancer presented the worst mean scores of FC throughout the treatment. Therefore,

Table 3. Clinical characterization and functional capacity of women with gestational trophoblastic disease, breast cancer and gynecological cancer according to the Karnofsky's tool in relation to the chemotherapy protocol, type of tumor and therapeutic modality. Uberaba, Minas Gerais, Brazil, 2014

Variable	N	%	Mean (Karnofsky)
Chemotherapy protocol			
Anthracyclines	206	47.03	81.29
Platinum	163	37.21	73.90
Taxanes	30	6.85	71.88
Others	39	8.9	82.39
Total	438	100	77.99
Tumor type			
Breast cancer	224	51.14	81.38
Gynecological cancer	194	44.29	73.50
GTD	20	4.6	83.66
Total	438	100	77.99
Therapeutic modality			
Exclusive chemotherapy	41	9.4	74.31
Chemotherapy associated with other therapies	397	90.63	78.38
Total	438	100	76.34
Mean scores of FC between the fourth and sixth chemotherapy cycle			
Chemotherapy protocol			
Anthracyclines	204	52.3	79.43
Platinum	125	32.05	72.36
Taxanes	28	7.18	72.02
Others	33	3.55	81.21
Total	390	100	76.78
Tumor type			
Breast cancer	220	56.41	79.65
Gynecological cancer	153	39.23	71.77
GTD	17	4.36	84.70
Total	390	100	76.78
Therapeutic modality			
Exclusively chemotherapy	34	9.4	74.07
Chemotherapy associated with other therapies	356	90.63	77.05
Total	390	100	75.56

Source: Data collected by the authors between 2000 and 2012.

gynecological cancer was found to significantly affect the FC of these patients in both analyzed moments.

It is appropriate to point out that the group of patients with gynecological cancer included aggressive types of cancer, many of which present difficult diagnosis or high incidence, and together with late diagnosis this eventually leads to a worse prognosis. In this context, a study pointed out that the high incidence rate and the late diagnosis of cervical cancer remain real¹⁴. In addition, through the analysis of national secondary databases, a cross-sectional study showed that between 2000 and 2009, respectively, 70.6% of the women with cervical cancer were diagnosed at an advanced stage of the disease¹⁵, thus contributing to the functional impairment caused by the advance of the neoplasia itself. Therefore, these findings certainly collaborated to the influence of the variable gynecological cancer in the decline of FC of patients diagnosed with this neoplasia. In this study, the therapeutic modality was not found to significantly affect the FC.

It is appropriate to mention that the choice of chemotherapy protocol and the tumor type are not the exclusive factors responsible for the presented score. Other factors include previous FC, tumor stage, number of chemotherapeutic cycles, prescribed dosage, and other individual aspects that, combined with the chosen protocol and the tumor type, represent the score of FC.

Understanding the aspects of functional capacity of oncologic patients undergoing chemotherapeutic treatment enables nurses and other nursing professionals to plan and schedule the care, thus enabling patients to improve their capacity to deal with the health-disease process¹⁶.

CONCLUSION

The studied population maintained a linear FC throughout the therapy; therefore, the population presented similar progress. In addition, in general and according to the mean FC scores presented by the Karnofsky's tool, the patients were not found to be able to perform activities of daily living and active tasks; they were able to self-care only.

In addition, punctual evaluation of the impact caused by the variables, chemotherapy protocols, tumor type, and oncologic treatment on FC showed that patients who suffered a greater impact were, in order of importance, those diagnosed with gynecological cancer and those who used taxane-based chemotherapy protocols. Therefore, it was observed that the type of cancer was the main influencing factor for the reduction of FC in these patients.

Therefore, it is necessary to provide appropriate care to the needs of each patient, aiming at a comprehensive and individual view as well as respecting the individuality of the patient undergoing anticancer treatment.

Limitations of this study include the approach, which was restricted to physical examination. Psychological, social, economic, and spiritual contexts of the patients were not

Table 4. Multiple linear regression test for the analysis of influence of clinical variables on the functional capacity of women with gestational trophoblastic disease. breast cancer. and gynecological cancer according to the Karnofsky's tool. Uberaba, Minas Gerais, Brazil, 2014

	Variables	β	<i>p</i>
Mean scores of FC between the first and third chemotherapy cycles in relation to sociodemographic and clinical variables	Tumor type		
	Breast cancer	-0.002	0.992
	Gynecological cancer	-3.382	0.028
	*GTD	_____	_____
	Chemotherapy protocol		
	Anthracyclines	-0.12	0.298
	Platinum	-0.102	0.462
	Taxanes	-0.146	0.049
	*Others	_____	_____
	Therapeutic modality		
	Exclusively chemotherapy	0.056	0.232
	*Chemotherapy associated with other therapies	_____	_____
Mean scores of FC between the fourth and sixth chemotherapy cycles in relation to sociodemographic and clinical variables	Tumor type		
	Breast cancer	-0.159	0.315
	Gynecological cancer	-0.732	< 0.001
	*GTD	_____	_____
	Chemotherapy protocol		
	Anthracyclines	-0.093	0.437
	Platinum	0.112	0.439
	Taxanes	-0.037	0.627
	*Others	_____	_____
	Therapeutic modality		
	Exclusively chemotherapy	-0.081	0.232
	*Chemotherapy associated with other therapies	_____	_____

Source: Data collected by the authors between 2000 and 2012. * Reference category.

taken into account. Although essential, it is clear that quality of life is not associated exclusively with physical functions.

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