

IMPACT OF PHYSICAL ACTIVITY ON FATIGUE AND QUALITY OF LIFE OF CANCER PATIENTS



ORIGINAL ARTICLE
ARTIGO ORIGINAL
ARTÍCULO ORIGINAL

IMPACTO DA ATIVIDADE FÍSICA NA FADIGA E QUALIDADE DE VIDA DE PACIENTES COM CÂNCER

IMPACTO DE LA ACTIVIDAD FÍSICA EN LA FATIGA Y CALIDAD DE VIDA DE PACIENTES CON CÁNCER

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ABSTRACT

Introduction: Physical exercise has been considered an important non-pharmacological treatment for reducing tiredness, pain, low self-esteem and increases in body mass in individuals diagnosed with cancer. **Objective:** To verify the relationship between fatigue, quality of life and levels of physical activity in cancer patients undergoing chemotherapy. **Methods:** Observational, cross-sectional study. The sample consisted of 85 adult patients undergoing cancer treatment at a university hospital. Physical activity was assessed by the IPAQ, and fatigue and quality of life by the PFS and EORTC QLQ-C30 questionnaires, respectively. Student's t and the Fisher's Exact tests were used to identify differences between active and physically inactive patients for the variables fatigue and quality. Additionally, covariance analysis (ANCOVA) was used, in which simple (outcome and exposure) and adjusted models (age, time of diagnosis and type of cancer) were tested. **Results:** The study included 85 cancer patients, with a mean of 51.78 years of age (± 11.72). Most were female and not physically active. Patients classified as physically inactive had higher scores for "total fatigue" ($p=0.01$), "behavioral" ($p=0.01$), "affective" ($p=0.02$) and psychological/sensory fatigue ($p=0.04$), compared to the physically active patients ($p=0.01$). Patients classified as physically not very active presented poorer quality of life in the dimensions: "overall" quality of life ($p=0.05$) and "functional" ($p=0.04$), "appetite" ($p=0.02$), "insomnia" ($p=0.02$), "diarrhea" ($p=0.04$), "fatigue" ($p=0.01$), "pain" ($p=0.01$) and "nausea" ($p=0.03$), when compared to the physically active patients in both analyses; simple and adjusted. **Conclusion:** The practice of physical activity during treatment can be a determining factor for increasing quality of life and reducing fatigue in cancer patients, minimizing the adverse effects of chemotherapy. **Level of evidence II; retrospective study.**

Keywords: Motor activity; Fatigue; Quality of Life; Neoplasms.

RESUMO

Introdução: O exercício físico tem sido considerado um importante tratamento não farmacológico para diminuir a sensação de cansaço, as dores, a baixa autoestima e o aumento da massa corporal em indivíduos com diagnóstico de câncer. **Objetivo:** Verificar a relação entre fadiga, qualidade de vida e níveis de atividade física em pacientes oncológicos submetidos à quimioterapia. **Métodos:** Estudo observacional, transversal. A amostra foi composta por 85 pacientes adultos em tratamento oncológico em hospital universitário. A atividade física foi avaliada pelo IPAQ, a fadiga e a qualidade de vida, pelos questionários PFS e EORTC QLQ-C30, respectivamente. Foram empregados os testes t de Student e Exato de Fisher para identificar diferenças entre os pacientes fisicamente ativos e pouco ativos para as variáveis de fadiga e qualidade de vida. Adicionalmente, foi empregada a análise de covariância (ANCOVA) em que foram testados modelos simples (desfecho e exposição) e ajustados (idade, tempo de diagnóstico e tipo de câncer). **Resultados:** Participaram do estudo 85 pacientes com câncer e média de 51,78 anos de idade ($\pm 11,72$). A maioria era do sexo feminino e pouco ativa fisicamente. Pacientes classificados como fisicamente pouco ativos apresentaram maiores escores de "fadiga total" ($p = 0,01$), "comportamental" ($p = 0,01$), "afetiva" ($p = 0,02$) e fadiga psicológica/sensorial ($p = 0,04$), em comparação com pacientes fisicamente ativos ($p=0,01$). Os pacientes classificados como fisicamente pouco ativos tinham pior qualidade de vida nas dimensões: qualidade de vida "geral" ($p = 0,05$) e "funcional" ($p = 0,04$), "apetite" ($p = 0,02$), "insônia" ($p = 0,02$), "diarreia" ($p = 0,04$), "fadiga" ($p = 0,01$), "dor" ($p = 0,01$) e "náuseas" ($p = 0,03$) quando comparados com os pacientes fisicamente ativos, em ambas as análises, simples e ajustada. **Conclusão:** A prática da atividade física durante o tratamento pode ser um fator determinante para aumentar a qualidade de vida e reduzir a fadiga em pacientes com câncer, minimizando os efeitos adversos da quimioterapia. **Nível de Evidência II; Estudo retrospectivo.**

Descritores: Atividade motora; Fadiga; Qualidade de vida; Neoplasias.

RESUMEN

Introducción: El ejercicio físico ha sido considerado un importante tratamiento no farmacológico para disminuir la sensación de cansancio, los dolores, la baja autoestima y el aumento de la masa corporal en individuos con diagnóstico de cáncer. **Objetivo:** Verificar la relación entre fatiga, calidad de vida y niveles de actividad física en pacientes oncológicos sometidos a quimioterapia. **Métodos:** Estudio observacional, transversal. La muestra fue compuesta por 85 pacientes adultos en tratamiento oncológico en hospital universitario. La actividad física fue evaluada a través de IPAQ, la fatiga y la calidad de vida, por los cuestionarios PFS y EORTC QLQ-C30, respectivamente. Fueron empleados los tests t de Student y Exacto de Fisher para identificar diferencias entre pacientes fisicamente activos y poco activos para las variables de fatiga y calidad de vida. Adicionalmente, fue empleado el análisis de covariancia (ANCOVA) en el que fueron testeados modelos simples (resultado y exposición) y ajustados (edad, tiempo de diagnóstico y tipo de cáncer). **Resultados:** Participaron en el estudio 85 pacientes con



cáncer y promedio de 51,78 años de edad ($\pm 11,72$). La mayoría era del sexo femenino y poco activa físicamente. Los pacientes clasificados como físicamente poco activos presentaron mayor puntuación de "fatiga total" ($p = 0,01$), "comportamental" ($p = 0,01$), "afectiva" ($p = 0,02$) y fatiga psicológica/sensorial ($p = 0,04$), en comparación con pacientes físicamente activos ($p = 0,01$). Los pacientes clasificados como físicamente poco activos tenían peor calidad de vida en las dimensiones: calidad de vida "general" ($p = 0,05$) y "funcional" ($p = 0,04$), "apetito" ($p = 0,02$), "insomnio" ($p = 0,02$), "diarrea" ($p = 0,04$), "fatiga" ($p = 0,01$), "dolor" ($p = 0,01$) y "náuseas" ($p = 0,03$), cuando comparados con los pacientes físicamente activos en ambos análisis, simples y ajustados. Conclusión: La práctica de actividad física durante el tratamiento puede ser un factor determinante para aumentar la calidad de vida y reducir la fatiga en pacientes con cáncer, minimizando los efectos adversos de la quimioterapia.

Nivel de Evidencia II; Estudio retrospectivo.

Descriptor: Actividad motora; Fatiga; Calidad de Vida; Neoplasias.

DOI: http://dx.doi.org/10.1590/1517-8692202026062019_0045

Article received on 11/02/2019 accepted on 07/17/2020

INTRODUCTION

Cancer is considered the first or second leading cause of premature death in almost 100 countries worldwide, including Brazil, where 600,000 new cases are estimated per year.¹ In 2017, the World Health Assembly passed a resolution on cancer prevention through an integrated approach, directing governments to accelerate actions to reduce mortality.²

According to the Pan American Health Organization (PAHO), about one-third of cancer deaths are due to the five leading behavioral risks, including physical inactivity.³ The conventional therapeutic approach involves surgery, chemotherapy, radiation therapy, and hormone therapy, which may cause several biological and behavioral changes, such as the reduction in physical activity levels.⁴

The low daily energy expenditure and the effects of treatment increase fatigue levels (in any type of neoplasms), which are reported by up to 91% of patients, and may last for up to ten years.⁵ Professionals from various fields indicate physical exercises as an important non-pharmacological treatment for reducing tiredness, pain, low self-esteem, and increased body mass resulting from the fatigue.⁶

The treatments for cancerous tumors activate pro-inflammatory cytokines, causing exhaustion and other disruptive side effects, such as pain, nausea, vomiting, anxiety, depression, and low self-esteem, besides influencing social and emotional aspects,⁷ decreasing thus the quality of life of these patients. According to the literature, practicing physical activity may lessen the severity of these issues, besides providing greater incentive and adherence to physical exercise programs.⁸

Given the favorable evidence of the positive impact of physical exercises on the physical and mental state of patients receiving cancer treatment⁹, university hospitals are promising institutions to investigate fatigue levels and quality of life of this subgroup, due to their multidisciplinary features, through an integrated approach with other university courses linked to the hospital, such as Physical Education.

The main purpose of this study was to verify the association between exhaustion, quality of life, and physical activity levels in cancer patients undergoing chemotherapy at a University Hospital of a Federal Public University.

MATERIALS AND METHODS

Type of study

This is a cross-sectional, observational, and analytical study.

Population and Sample

The population consisted of adult individuals receiving cancer treatment at the High-Complexity Cancer Care Center (CACON) of the Hospital Universitário Prof. Alberto Antunes (HUPAA), in the city of Maceió, Alagoas, Brazil.

According to CACON-HUPAA records, during the first half of 2018, the department of chemotherapy treated, on average, 256 cancer per

month. We used information from the study conducted by Kummer et al.¹⁰, based on correlation coefficients of investigated variables, to estimate the required sample size. Considering an 80% power (β) and a 5% alpha, a sample size of 85 patients was reached.

Inclusion criteria were: presenting clinical diagnosis of malignant neoplasia, in any location, recurrent or not; having received at least two chemotherapy sessions, regardless of any other treatment associated with chemotherapy. Patients who had some clinical condition that could interfere with the practice of physical activity were excluded from the study.

Instruments

We selected sociodemographic and clinical variables from previous studies that addressed the same topic as ours.¹¹⁻¹²

Quality of life was assessed by applying the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire C30 (EORTC QLQ-C30), specific for cancer patients, and validated for the Portuguese language.¹³ The questionnaire contains 30 questions divided into three scales: global health, functional, and symptoms. Scores range from 0 to 100 and are calculated separately for each scale. In the global and functional health scales, the higher the score, the better the quality of life. Conversely, for the symptom scale, the higher the score, the worse the quality of life.

Fatigue was investigated with the Piper Fatigue Scale (PFS), applied in patients after cancer diagnosis and validated for the Brazilian population.¹⁴ The scale contains 22 questions divided into three dimensions: behavioral, affective, and cognitive/mood. Each dimension, as well as the total score, receives a score that corresponds to each item mean score, ranging from zero to ten; the closer to 10, the greater the fatigue.

Physical activity was assessed using a short version of the International Physical Activity Questionnaire (IPAQ), validated for Brazil.¹⁵ The questionnaire contains six questions that analyze the amount of time (at least 10 continuous minutes) spent by the individual with walking and moderate/vigorous physical activity in the last week. Individuals who accumulated 150 minutes or more moderate to vigorous physical activity during the week were considered physically active.

The same researcher applied all questionnaires in the form of an interview to include illiterate patients. All patients were interviewed in the waiting room for chemotherapy before the beginning of the usual session. This study was approved by the Human Research Ethics Committee of the Federal University of Alagoas, under opinion no. 3.455.770, and all participants signed the informed consent form.

Statistical analysis

First, descriptive data analysis (median and interquartile interval) was carried out, and missing data were excluded. Kurtosis and asymmetry were used to verify data normality (interval between -2 and $+2$), and histogram analysis to test normal distribution. We also used the Fisher's Exact test and Student's t-test to identify differences between physically

active and inactive patients regarding fatigue and quality of life, and the Analysis of covariance (ANCOVA) to test simple (outcome and exposure) and adjusted models (age, diagnosis time, and cancer type).

Then, simple and multiple linear regression analysis was performed to estimate the regression coefficients (β), 95% confidence interval (95% CI), and coefficient of determination (R^2) for each model analyzed. For this analysis, the outcomes were each fatigue indicator and quality of life domain; that is, a simple and multiple model was constructed for each of these variables. Exposure was the physical activity level, where “physically active” was deemed as the reference and coefficients were estimated for the category “physically inactive”. All analyses were made using the Statistical Package for the Social Sciences (IBM SPSS Statistics, Chicago, United States) software, version 22.0, with significance level set at 5%.

RESULTS

The study included 85 cancer patients with mean age of 51.78 years (± 11.72). Most were female and physically inactive. Among them, 55.3% were married, 8.2% completed higher education, and 38.8% presented comorbidity. Over 40% of the sample had been diagnosed with cancer more than three years ago, and the most frequent cancer was breast cancer (Table 1).

The analysis adjusted for age, cancer type, and time since diagnosis found patients classified as physically inactive those who had higher scores of “total fatigue” ($p=0.01$), “behavioral” ($p=0.01$), “affective” ($p=0.02$) and “cognitive/mood fatigue” ($p=0.04$) than physically active patients ($p=0.01$) (Table 2).

The analysis adjusted for age, cancer type, and time since diagnosis found patients classified as poorly active to reach lower scores on the “global” ($p=0.05$) and “functional” ($p=0.04$) quality of life scales than physically active patients, indicating that poorly active patients have a worse quality of life. In the scales “appetite” ($p=0.02$), “insomnia” ($p=0.02$), “diarrhea” ($p=0.04$), “fatigue” ($p=0.01$), “pain” ($p=0.01$), and “nausea” ($p=0.03$), physically inactive patients reached higher scores than those physically active in both simple and adjusted analyses, indicating a worse quality of life (Table 3).

Table 1. Sample characterization according to the regular practice of physical activity.

	Total (n=85)	Physically active (n=21)	Poorly active (n=64)	p-value
Chronological age (mean \pm sd)	51.7 \pm 11.7	50.6 \pm 10.8	52.1 \pm 12.0	0.601
Gender (n, %)				0.847
Female	70 (64.8)	17 (24.3)	53 (75.7)	
Male	15 (13.9)	04 (26.7)	11 (73.3)	
Marital status (n, %)				
Single	25 (29.4)	08 (32.0)	17 (68.0)	0.392
Married	47 (55.3)	09 (19.1)	38 (80.9)	
Divorced/Widowed	13 (15.3)	04 (30.8)	09 (69.2)	
Education level (n, %)				
Illiterate	11 (12.9)	01 (9.1)	10 (90.9)	0.088
Elementary school	44 (51.8)	08 (18.2)	36 (81.8)	
High school	23 (27.1)	09 (39.1)	14 (60.9)	
Higher education	07 (8.2)	03 (42.9)	04 (57.1)	
Comorbidities (n, %)				
Yes	33 (38.8)	11 (33.3)	22 (66.7)	0.142
No	52 (61.2)	10 (19.2)	42 (80.8)	
Time since cancer diagnosis (n, %)				
\leq 1 year	23 (27.1)	07 (30.4)	16 (69.6)	0.589
1 – 2 years	23 (27.1)	04 (17.4)	19 (82.6)	
3 – 4 years	17 (20.0)	03 (17.6)	14 (82.4)	
> 4 years	22 (25.8)	07 (31.8)	15 (68.2)	
Cancer type (n, %)				0.067
Breast cancer	43 (39.8)	12 (27.9)	31 (72.1)	
Endometrial-ovarian cancer	09 (8.3)	00 (0.0)	09 (100.0)	
Colon cancer	07 (6.5)	03 (42.9)	04 (57.1)	
Lung Cancer	04 (3.7)	01 (25.0)	03 (75.0)	
Leukemia	05 (4.6)	03 (60.0)	02 (40.0)	
Other	17 (15.7)	02 (11.8)	15 (88.2)	

Table 2. Comparison of fatigue indicators among physically active and poorly active cancer patients (n=85).

	Physically active (n=21)		Poorly active (n=64)	
	M (SEE**)	M (SEE)	p	R ²
Total				
Simple	2.30 (0.73)	3.89 (0.42)	0.06	0.02
Adjusted	2.10 (0.65)	3.96 (0.37)	0.01*	0.33
Behavioral				
Simple	1.98 (0.66)	3.35 (0.37)	0.07	0.02
Adjusted	1.79 (0.58)	3.41 (0.33)	0.01*	0.31
Affective				
Simple	3.00 (0.95)	4.95 (0.54)	0.08	0.02
Adjusted	2.77 (0.87)	5.02 (0.50)	0.02*	0.30
Cognitive/Mood				
Simple	2.04 (0.66)	3.23 (0.38)	0.12	0.01
Adjusted	1.86 (0.60)	3.29 (0.34)	0.04*	0.30

*p<0.05; 95% CI: 95% confidence interval. ** standard error of the estimate.

Table 3. Comparison of quality of life scales among physically active and poorly active cancer patients (n=85).

	Physically active (n=21)		Poorly active (n=64)	
	M (SEE)	M (SEE)	P	R ²
Global				
Simple	66.76 (5.19)	55.15 (2.97)	0.05	0.03
Adjusted	66.80 (5.18)	55.14 (2.96)	0.05	0.17
Functional				
Simple	71.47 (4.60)	62.07 (2.63)	0.08	0.02
Adjusted	72.15 (4.47)	61.85 (2.55)	0.04	0.08
Physical				
Simple	5.23 (2.82)	11.09 (1.62)	0.07	0.02
Adjusted	5.14 (2.85)	11.12 (1.63)	0.07	0.01
Role				
Simple	11.09 (5.15)	15.95 (2.95)	0.41	0.01
Adjusted	10.87 (5.17)	16.02 (2.96)	0.39	0.02
Cognitive				
Simple	10.19 (3.85)	11.29 (2.20)	0.80	0.01
Adjusted	10.06 (3.90)	11.33 (2.23)	0.77	0.03
Social				
Simple	10.76 (2.67)	6.37 (5.37)	0.23	0.01
Adjusted	16.70 (4.64)	10.90 (2.65)	0.28	0.02
Emotional				
Simple	23.85 (5.51)	23.21 (3.40)	0.92	0.01
Adjusted	22.66 (5.65)	23.61 (3.23)	0.88	0.08
Dyspnea				
Simple	11.04 (6.89)	24.32 (3.95)	0.09	0.02
Adjusted	10,10 (6.78)	24.63 (3.88)	0.06	0.05
Appetite				
Simple	14.23 (7.80)	34.70 (4.47)	0.02	0.04
Adjusted	14.20 (7.84)	34.71 (4.48)	0.02	0.04
Insomnia				
Simple	25.28 (9.42)	58.75 (5.39)	<0.01	0.09
Adjusted	24.10 (9.24)	59.13 (5.28)	0.02	0.23
Constipation				
Simple	17.33 (6.70)	17.07 (3.84)	0.97	0.01
Adjusted	17.28 (6.74)	17.09 (3.88)	0.98	0.03
Diarrhea				
Simple	4.71 (3.96)	21.28 (3.96)	0.04	0.03
Adjusted	4.62 (6.98)	21.31 (3.99)	0.04	0.02
Financial				
Simple	39.57 (9.07)	41.53 (5.19)	0.85	0.01
Adjusted	38.05 (8.79)	42.03 (5.02)	0.69	0.05
Fatigue				
Simple	22.04 (8.73)	46.71 (5.00)	0.01	0.05
Adjusted	21.63 (8.79)	46.85 (5.03)	0.01	0.11
Pain				
Simple	33.09 (8.40)	53.93 (4.81)	0.03	0.04
Adjusted	31.60 (8.01)	54.42 (4.58)	0.01	0.25
Nausea				
Simple	17.38 (8.42)	38.39 (4.82)	0.03	0.04
Adjusted	16.97 (8.51)	38.52 (4.87)	0.03	0.05

M: Mean; SEE: standard error of the estimate; R²: coefficient of determination. Simple model: outcome and exposition; Adjusted model: age, cancer type, and time since diagnosis.

DISCUSSION

For being one of the most common side effects during treatment, identifying and treating cancer-related fatigue is fundamental for the social reintegration of cancer patients.¹⁶ By investigating the association between this fatigue and physical activity levels throughout a multidisciplinary oncologic rehabilitation program of patients under treatment, we verified a substantial reduction in cancer-related exhaustion with the increase in energy expenditure, regardless of the treatment.⁶

Fatigue alone may preclude patients from becoming (more) active. Physical exercises do not increase treatment-related exhaustion, but exercise programs should be careful in incorporating high-intensity activities to not interfere with patients' adherence to treatment.¹⁷ Evidence indicates that moderate-intensity aerobic activity is more effective in combating this issue, besides improving treatment adherence.¹⁸⁻¹⁹

Cancer-related exhaustion is a multidimensional indicator: being physically active may bring positive effects in all dimensions of life. (Table 2) The impact of physical activity in these aspects may be explained by an improvement in fitness, especially cardiorespiratory strength and resistance, and indirectly by its effects on mood or immune function.²⁰

The National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology recommends physical activity as an important non-pharmacological strategy for managing fatigue, being considered a standard to be adopted in the therapy during and after treatment.²¹

Instruments assessing health-related quality of life include, among their investigated dimensions, functional aspects and a global quality of life scale.²² In the specific case of cancer patients, this concern is justified by the weaknesses caused by radiotherapy or chemotherapy cytotoxicity, reducing cardiorespiratory capacity, muscle strength and mass, and physical activity levels, and affecting activities of daily life.²³

Considering that demographic and clinical data of the population with cancer may interfere in the differences among physically active groups,²⁴ we found a significant contrast in the quality of life scores regarding general and functional status between physically active and poorly active individuals after adjusting sample data for cancer type and age.

Another essential characteristic of our sample was that all patients were in active treatment, which may imply greater deterioration of health-related quality of life components. The literature on systematic reviews and meta-analyses, with over 4,000 cancer patients, found that physical exercise significantly increases global and functional quality of life scales, specially regarding functional components, when compared to control groups.²⁵⁻²⁶

The most common side effects of chemotherapy are nausea, vomiting, pain, and fatigue, affecting not only patients' physical aspects, but also their emotional and cognitive aspects²⁷. Practicing exercises may mitigate the severity of these side effects, resulting in a positive impact

on the quality of life of cancer patients.²⁴ In our sample, physically active individuals reached better scores than poorly active individuals in several indicators of the investigated symptoms (Table 3), improving sleep, pain, and fatigue, and corroborating findings reported in the literature.²⁸

In the USA alone, the number of cancer survivors is expected to increase from 14 million in 2014 to 19 million in 2024²⁶, arising the need for developing strategies to relieve the side effects in the subgroup under treatment. The literature indicates that moderate-intensity exercise programs with mixed components (resistance and aerobic) reduce fatigue and improve quality of life scores.²⁹

A study conducted in a Brazilian northeastern city with women with breast cancer in various stages and treatments found a positive correlation between exercises, exhaustion, and quality of life. The authors concluded that physical activity is an essential behavior to enhance wellbeing in cancer patients.¹²

Regardless of the type of treatment or age, increased levels of daily physical activity were associated with improvements in quality of life and fatigue.¹⁴ Patients satisfaction with their functionality levels and increased muscle strength and cardiorespiratory resistance were some mechanisms mentioned by the authors, directly interfering in the perceived exhaustion and consequently in quality of life.^{12, 29}

A limitation of our study was its cross-sectional design, as it does not allow us to establish temporality relationships among the investigated variables. Another limitation was the inclusion of different types of cancer, because there is not enough evidence on whether physical activity is a protective factor for all types of cancer. However, we observed differences between the investigated groups, indicating that these limitations did not fully affect the study validity. Moreover, a single researcher collected all data.

As a positive aspect, this study was conducted at a teaching hospital, where developing actions involving physical exercise protocols and/or other strategies focused on this purpose is a real possibility.

CONCLUSIONS

Physical activity during treatment may be a determining factor for increasing the quality of life and reducing fatigue of cancer patients, minimizing chemotherapy side effects. In this study, we verified that patients who do at least 150 minutes of moderate to vigorous weekly physical activities experienced less fatigue in all dimensions and presented better scores in terms of quality of life.

Health professionals working with cancer patients must necessarily recommend the practice of physical activity from diagnosis to treatment, especially in supervised programs, where patients adherence is higher.

All authors declare no potential conflict of interest related to this article

AUTHORS' CONTRIBUTIONS: Each author made significant individual contributions to this manuscript. AFPC and JJOT: were the main contributors in the writing of the manuscript and performed the data collection at Hospital Universitário Prof. Alberto Antunes. DASS and PCM: evaluated the data from the statistical analysis. All authors performed the bibliographic review and revision of the manuscript, and contributed to the intellectual concept of the study.

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