Impact of Neoadjuvant Chemotherapy on Health-Related Quality of Life in Women with Breast Cancer

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Impacto da Quimioterapia Neoadjuvante na Qualidade de Vida Relacionada à Saúde em Mulheres com Câncer de Mama

Impacto de la Quimioterapia Neoadyuvante en la Calidad de Vida Relacionada con la Salud en Mujeres con Cáncer de Mama

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ABSTRACT

Introduction: Neoadjuvant chemotherapy (NACT), used in the treatment of breast cancer, may cause symptoms and impair functionality, with repercussions on health-related quality of life (HRQoL). **Objective**: To evaluate changes in HRQoL over the course of neoadjuvant chemotherapy in women with breast cancer. **Method:** Prospective cohort study included women diagnosed with breast cancer who were allocated to the control group of a prehabilitation program. HRQoL was assessed before initiation and after completion of NACT using the European Organization for Research and Treatment of Cancer questionnaires: Core 30 (EORTC QLQ-C30) and Breast Cancer Module (EORTC QLQ-BR23). Descriptive analyses were performed, and mean scores were compared using the paired t-test. **Results**: Fifty-one women participated in the study, with a mean age of 52 years. After NACT, significant declines were observed in physical (p=0.001) and sexual function (p=0.016), as well as worsening fatigue (p=0.042) and systemic therapy side effects (p=0.036). Conversely, improvements were found in insomnia (p=0.026), global health status (p=0.048), and breast symptoms (p=0.001). **Conclusion:** During neoadjuvant chemotherapy for breast cancer, women experienced relevant changes in HRQoL, characterized by functional decline and increased systemic symptoms, alongside improvement in breast-related symptoms and global health status, highlighting the importance of continuous HRQoL monitoring throughout treatment.

Key words: Breast Neoplasms/therapy; Neoadjuvant Therapy/adverse effects; Quality of Life; Women's Health.

RESUMO

Introdução: A quimioterapia neoadjuvante, utilizada no tratamento do câncer de mama, pode ocasionar sintomas e comprometer a funcionalidade, repercutindo na qualidade de vida relacionada à saúde (QVRS). **Objetivo:** Avaliar as alterações na QVRS ao longo da quimioterapia neoadjuvante em mulheres com câncer de mama. **Método:** Coorte prospectiva com mulheres diagnosticadas com câncer de mama, incluídas no grupo controle de um programa de pré-habilitação. A QVRS foi avaliada antes do início e após o término da quimioterapia neoadjuvante por meio dos questionários da *European Organization for Research and Treatment of Cancer: Core 30* (EORTC QLQ-C30) e da *Breast Cancer Module* (EORTC QLQ-BR23). Foram realizadas análises descritivas e comparação das médias pelo teste *t* pareado. **Resultados:** Participaram 51 mulheres, com média de idade de 52 anos. Após a quimioterapia neoadjuvante, observou-se declínio significativo nas funções física (p=0,001) e sexual (p=0,016), além de agravamento da fadiga (p=0,042) e dos efeitos da terapia sistêmica (p=0,036). Em contrapartida, houve melhora na insônia (p=0,026), no estado de saúde global (p=0,048) e nos sintomas mamários (p=0,001). **Conclusão:** Durante a quimioterapia neoadjuvante para o câncer de mama, mulheres apresentaram alterações relevantes na QVRS, caracterizadas por declínio funcional e intensificação de sintomas sistêmicos, concomitantes à melhora de sintomas mamários e do estado de saúde global, ressaltando a importância do monitoramento contínuo da QVRS ao longo do tratamento.

Palavras-chave: Neoplasias da Mama/terapia; Terapia Neoadjuvante/efeitos adversos; Qualidade de Vida; Saúde da Mulher.

RESUMEN

Introducción: La quimioterapia neoadyuvante, utilizada en el tratamiento del cáncer de mama, puede provocar síntomas y comprometer la funcionalidad, con repercusiones en la calidad de vida relacionada con la salud (CVRS). **Objetivo:** Evaluar los cambios en la CVRS a lo largo de la quimioterapia neoadyuvante en mujeres con cáncer de mama. **Método:** Cohorte prospectiva con mujeres diagnosticadas con cáncer de mama, incluidas en el grupo control de un programa de prehabilitación. La CVRS se evaluó antes del inicio y después de la finalización de la quimioterapia neoadyuvante mediante los cuestionarios de la *European Organization for Research and Treatment of Cancer: Core 30* (EORTC QLQ-C30) y *Breast Cancer Module* (EORTC QLQ-BR23). Se realizaron análisis descriptivos y la comparación de medias se efectuó mediante la prueba *t* pareada. **Resultados:** Participaron 51 mujeres, con una edad promedio de 52 años. Tras la quimioterapia neoadyuvante, se observó descensos significativos en las funciones física (p=0,001) y sexual (p=0,016), así como un empeoramiento de la fatiga (p=0,042) y de los efectos de la terapia sistémica (p=0,036). Por otro lado, se identificó mejoría del insomnio (p=0,026), del estado de salud global (p=0,048) y de los síntomas mamarios (p=0,001). **Conclusión:** Durante la quimioterapia neoadyuvante para el cáncer de mama, las mujeres presentaron cambios relevantes en la CVRS, caracterizados por un declive funcional e intensificación de síntomas sistémicos, concomitantes con la mejoría de los síntomas mamarios y del estado de salud global, lo que refuerza la importancia del seguimiento continuo de la CVRS a lo largo del tratamiento.

Palabras clave: Neoplasias de la Mama/terapia; Terapia Neoadyuvante/efectos adversos; Calidad de Vida; Salud de la Mujer.

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INTRODUCTION

Breast cancer is the most common malignant neoplasm among women in Brazil, being the main cause of death from cancer in this population, considering that, for each year of the 2026-2028 triennium, a total of 518 thousand new cancer cases have been estimated in the country, excluding non-melanoma skin cancer[1,2]. The therapeutic strategies vary according to clinical staging and the tumor's biological characteristics, involving locoregional modalities, such as surgery and radiotherapy, and systemic modalities, like chemotherapy, hormone therapy, and immunotherapy[3,4].

Neoadjuvant chemotherapy, administered before surgical treatment, is widely employed with the objective of reducing tumoral volume, enabling more conservative surgeries, and contributing to better prognostic outcomes[5-7]. However, the adverse effects associated with this therapeutic modality may compromise functionality and have a negative repercussion on health-related quality of life (HRQoL), manifesting through symptoms like fatigue, nausea, altered sexual function, and breast symptoms[8,9].

HRQoL is defined as the individual's perception of their physical, emotional, and social condition in the face of cancer diagnosis and treatment, being acknowledged as an important indicator of health and response to oncological care. The systematic assessment of this outcome has taken a key role in the clinical follow-up of people with cancer, allowing a broader understanding of the treatment impacts beyond the traditional clinical outcomes[10].

In this context, validated instruments, such as the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire: Core 30 (EORTC QLQ-C30) and its specific Breast Cancer Module (EORTC QLQ-BR23), enable tracking functional and symptomatic alterations throughout the treatment, supporting planning and adjustment of clinical interventions[10].

Despite the consolidation of validated questionnaires that assess quality of life, the literature indicates that the incorporation of these patient-reported measures is done heterogeneously in healthcare services and, often, limited to the context of clinical research, due to the methodological heterogeneity and lack of professionals' familiarity with the interpretation of these instruments[11]. It is also worth mentioning that there is still no global consensus as to the best way to assess quality of life, which contributes to how diversely this outcome is measured[12].

In the Brazilian context, studies have pointed to the negative influence of chemotherapy on the HRQoL of women with breast cancer[12]. Among the national analyses with a prospective design, an observational study conducted with 140 women in the Brazilian Northeast stands out. They were assessed in the intermediate cycle and at the end of chemotherapy, showing a significant decline in several quality of life domains throughout the oncological treatment[13]. Similarly, a national cohort with 33 women submitted to adjuvant chemotherapy observed reduced general health status at multiple functional scales, in addition to increased treatment-related symptoms[14].

Thus, the present study aims to assess the impact of neoadjuvant chemotherapy on the HRQoL of women with breast cancer.

METHOD

Prospective cohort study within the project titled *"Programa de pré-habilitação para mulheres indicadas ao tratamento cirúrgico do câncer de mama"* (Prehabilitation program for women referred to surgical breast cancer treatment). The study was conducted at the Physiotherapy Service of the National Cancer Hospital's (INCA) *Hospital do Câncer III*, a national reference unit for breast cancer treatment, located in Rio de Janeiro (RJ), from January 2022 through March 2025.

The study included randomized women for the control group of the original project, who met the following eligibility criteria: aged between 18 and 80 years, breast cancer diagnosis, and referral to oncological treatment with healing intention. The study excluded patients with clinical staging IV or with dysfunctions that prevented them from doing physical exercise.

The sociodemographic (age, race/skin color, marital status, and education), clinical (weight and height to calculate body mass index – BMI – and clinical staging), and treatment-related variables (chemotherapy type, number of cycles undergone) were obtained from reviewing the physical and electronic patient records.

HRQoL was assessed using EORTC QLQ-C30 questionnaires and its specific breast cancer model, EORTC QLQ-BR23, both translated and validated for Portuguese. EORTC QLQ-C30 is composed of 30 items distributed across five functional scales (physical, role functioning, cognitive, emotional, and social), three symptom scales (fatigue, pain, and nausea/vomiting), six single items (dyspnea, insomnia, appetite loss, constipation, diarrhea, and financial difficulties), and a global health status. The QLQ-BR23 module contains 23 items, organized in functional scales (body image, sexual functioning, sexual enjoyment, and future perspective) and symptom scales (systemic therapy side effects, breast symptoms, arm symptoms, and hair loss).

The reference period of the HRQoL questionnaires corresponds to the experiences of participants in the seven days before the application, except for the sexual enjoyment domain, whose time frame refers to the previous four weeks. The items in the functional and symptoms scales are classified on a Likert[15] four-point scale, ranging from 1 ("not at all") to 4 ("very much"), while the global health status scale uses a Likert[15] seven-point scale, ranging from 1 ("much worse") to 7 ("much better"). The subscales' scores were standardized on a scale of 0 to 100, where higher values in the functional scales and global health status indicate better quality of life, while higher scores in the symptoms scales reflect more symptomatologic intensity[16].

The questionnaires were applied at two separate times: before initiating neoadjuvant chemotherapy (inclusion assessment) and after the last chemotherapy cycle treatment (post-CT assessment), conducted during institutional follow-up consultation. The descriptive analysis of the study population was performed using measures of central tendency and dispersion for continuous variables and frequency distributions for categorical variables. The paired *t*[17] test was used to compare the mean HRQoL scores between the two assessment moments, adopting the statistical significance level of $p<0.05$.

The study was developed according to the ethical precepts that rule research involving human beings, set forth by Resolution N. 466, of December 12, 2012, by the National Health Council[18]. This project has been approved by the INCA Research Ethics Committee, report number 4,576,731 (CAAE (submission for ethical review): 42627521,6,0000,5274) and recorded on the ClinicalTrials.gov platform (identifier NCT04861220). All the participants signed a Free and Informed Consent Form (FICF) and were assured the right to drop out at any time, with no prejudice to the oncological treatment performed at the institution.

RESULTS

A total of 71 women met the eligibility criteria; of those, 20 were considered lost-to-follow-up: 13 for not undergoing the post-chemotherapy assessment, 4 due to changes in the therapeutic proposal, and 3 evolved to stage IV during follow-up. The loss-to-follow-up rate was 28.2%, a figure that must be considered in interpreting the findings, since changes in the therapeutic course and clinical evolution may have influenced the profile of participants who did not complete follow-up, introducing a potential attrition bias. Therefore, the final analysis contemplated 51 women, with a mean age of 52.1 years (standard deviation 12.6).

Regarding sociodemographic characteristics, 78.4% of participants have self-declared themselves as black or brown, 52.9% had no spouse, and 82.4% had incomplete elementary school. As to clinical characteristics, 80.4% of women presented advanced clinical staging (≥IIB) and 64.7% had a BMI over 25 kg/m², with 43.1% being classified as obese. Regarding treatment, 66.7% of patients have undergone a full chemotherapy scheme, composed of four doxorubicin and cyclophosphamide (AC) cycles, followed by four cycles of one taxane (either paclitaxel or docetaxel). The total number of chemotherapy cycles varied from 3 to 16, with a median of 8 cycles (Table 1).

The HRQoL scores before and after neoadjuvant chemotherapy are presented in Table 2. In EORTC QLQ-C30, the functional scales with higher scores were social function, global function, and physical function. However, there was a decline of 8.6 points in physical function after chemotherapy ($p=0.001$), indicating statistically relevant functional worsening. Regarding the symptom scale, there was an average increase of 7.2 points in fatigue ($p=0.042$), suggesting symptom intensification after neoadjuvant chemotherapy, becoming one of the most expressive symptoms in that period. On the other hand, insomnia, which presented a higher score in the initial assessment, presented an average reduction of 13.0 points after the treatment ($p=0.026$), configuring a clinically relevant improvement. Additionally, an average increase of 7.2 points in the global health status ($p=0.048$) was observed.

In the specific module EORTC QLQ-BR23, an average reduction of 9.4 points in sexual function after neoadjuvant chemotherapy was observed ($p=0.016$), as well as an average increase of 5.7 points in the effects of systemic therapy ($p=0.036$). In contrast, an average decline of 22.2 points in breast symptoms ($p<0.001$), indicating expressive clinical improvement in this domain. The sexual enjoyment and hair loss scales were not included in the comparative analysis due to the reduced number of responses (n=4 and n=1, respectively).

DISCUSSION

In the present study, the HRQoL assessment using EORTC QLQ-C30 showed a significant decline in physical function throughout neoadjuvant chemotherapy ($p=0.001$). This finding is consistent with that observed in a French prospective cohort composed of 100 women with breast cancer, in which physical function presented a significant reduction between the assessments conducted before chemotherapy and after the treatment, going from 89 (±14) to 79 (±19) points[19]. Similarly, a study conducted in Poland with 211 women identified an important commitment of physical function after chemotherapy, with a reduction of the average overall score from 81.3

Table 1. Sociodemographic, clinical, and treatment characteristics of patients (n=51)

Variable	n (%)
Age (years), mean (SD)	52.1 (12.6)
Race/skin color	
White	11 (21.6)
Black and Brown	40 (78.4)
Marital status	
Has a spouse	24 (47.1)
No spouse	27 (52.9)
Education	
Complete elementary school	42 (82.4)
Incomplete elementary school	9 (17.6)
Staging	
I and IIA	10 (19.6)
IIB and IIIA	23 (45.1)
IIIB and IIIC	18 (35.3)
Body mass index (BMI)	
Normal (18.5 to 24.9 kg/m²)	18 (35.3)
Overweight (25 to 29.9 kg/m²)	11 (21.6)
Obesity (≥30 kg/m²)	22 (43.1)
Chemotherapy type	
Complete scheme (4 AC + 4 T)	34 (66.7)
Other schemes	17 (33.3)
Number of cycles, median (min.–max.)	8 (3-16)

Captions: n = absolute number; SD = standard deviation; min. = minimum; max. = maximum; AC = doxorubicin + cyclophosphamide.

(confidence interval – 95% CI: 78.5–84.1) to 57.2 (95% CI: 54.2–60.2), also with statistical significance (p<0.001)[20]. These findings corroborate the results from the present study and reinforce a negative association between chemotherapy and functional performance. Although essential for disease control, chemotherapy can cause adverse effects that impact physical function and quality of life, highlighting the relevance of continuous monitoring of this domain and planning specific interventions throughout the treatment.

Regarding the QLQ-C30 symptom scale, there was a significant increase in fatigue after neoadjuvant chemotherapy (p=0.042), a result aligned with the previously mentioned French prospective study, in which fatigue intensified at the end of the treatment, with an increase in the average score from 27.0 (±21.0) to 50.0 (±26.0)[19]. Cancer-related fatigue is a frequent and multifactorial symptom, characterized by a persistent feeling of tiredness that is not completely relieved by rest[21]. This condition can trigger a reduction of the functional level and muscle deconditioning, establishing a cycle that perpetuates intolerance to exercise and compromised HRQoL[22].

It is worth underscoring that, in the studied sample, 64.7% of women presented BMI above the recommended, with 43.1% classified as obese. This data deserves attention since obesity is associated with inflammatory and metabolic mechanisms that may favor both tumoral progression and symptom intensification during treatment[13]. Evidence from a prospective study with 565 women with breast cancer showed that patients with obesity reported significantly higher levels of fatigue at the end of chemotherapy (p=0.002)[23], which may have contributed to the findings observed in the present study.

Consistent with these results, the Polish study with 211 women undergoing neoadjuvant chemotherapy identified impairment of all functions and overall worsening of symptoms as assessed by the QLQ-C30 (p<0.001), highlighting physical function as the most affected domain and fatigue as the predominant symptom after treatment[20]. This pattern reinforces the findings of the present study, which also showed functional decline and fatigue intensification through neoadjuvant chemotherapy.

Insomnia, defined as difficulty initiating or maintaining sleep, is a frequent complaint in the oncological population, affecting around 30% to 50% of patients[22]. In the present study, this symptom presented the highest score in the initial assessment, highlighting its early impact. This finding is in line with national cross-sectional studies, in which insomnia was highly prevalent in the pre-treatment period, with averages of 36.1 (±41.1) in a study with 302 women[24] and 37.6 (±41.8) in a study with 961 participants[25]. The significant insomnia reduction after chemotherapy observed in this study may be related to reduced breast symptoms and adaptation to the treatment, although this finding must be interpreted with caution, considering that insomnia may negatively influence other outcomes, like fatigue, pain, cognition, and HRQoL[21].

The patients followed up in this study reported improvement in the global health status item (p=0.048), a result that diverges from those frequently reported in the literature[19,20], which identified loss on this scale (p=0.013 and p<0.001, respectively). This divergence may be related to sociocultural, ethnic, and contextual differences among the studied population, in addition to variations in post-treatment assessment. While the French cohort made the assessment two weeks after finishing chemotherapy[19], the Polish study adopted a three-week interval[20], which may influence subjective perception of global health status. Additionally, it is possible that this finding reflects a psychological adaptation process to the oncological treatment, which, even in the presence of persistent symptoms, the patients perceive global

Table 2. HRQoL assessment using the QLQ C30 and QLQ BR23 questionnaire at the time of inclusion and post neoCT assessment (n=51)

EORTC-QLQ C30	Inclusion	Post CT	Difference between neoCT start and finish	*p*
Functional Scales	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**	
Physical function	82.2 (20.6)	73.6 (21.5)	-8.6 (18.1)	**0.001***
Role function	82.7 (24.7)	74.8 (31.2)	-7.9 (29.5)	0.063
Cognitive function	73.5 (30.9)	74.5 (26.7)	1.0 (24.4)	0.775
Emotional function	56.5 (29.5)	60.9 (31.0)	4.4 (30.4)	0.305
Social function	83.7 (25.5)	85.6 (25.6)	1.9 (31.6)	0.659
Symptom/items scales				
Fatigue	30.9 (27.6)	38.1 (25.0)	7.2 (24.6)	**0.042***
Pain	36.6 (32.5)	37.3 (30.5)	0.7 (40.5)	0.909
Dyspnea	18.3 (30.1)	18.3 (30.8)	0 (38.3)	1.000
Insomnia	43.1 (39.6)	30.1 (37.9)	-13.0 (40.6)	**0.026***
Appetite loss	13.1 (23.2)	20.9 (35.3)	7.8 (36.9)	0.135
Nausea and vomiting	7.5 (16.4)	9.2 (18.7)	1.7 (22.7)	0.609
Constipation	15.0 (31.5)	15.7 (27.8)	0.7 (33.7)	0.890
Diarrhea	5.9 (20.8)	13.1 (25.0)	7.2 (29.3)	0.086
Financial concerns	26.1 (39.1)	24.2 (35.3)	-1.9 (45.4)	0.759
Global health status	65.5 (22.8)	72.7 (18.6)	7.2 (25.4)	**0.048***
EORTC-QLQ BR23				*p*
Functional Scales	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**	
Body image	84.2 (22.4)	76.3 (28.4)	-7.9 (32.5)	0.091
Sexual function	29.7 (30.6)	20.3 (25.2)	-9.4 (27.1)	**0.016***
Future perspectives	38.6 (39.1)	49.0 (36.7)	10.4 (42.9)	0.088
Symptom/items scales				
Systemic therapy effects	22.5 (17.0)	28.2 (18.4)	5.7 (18.8)	**0.036***
Breast symptoms	37.4 (31.0)	15.2 (19.8)	-22.2 (27.7)	**<0.001****
Arm symptoms	15.7 (20.3)	17.2 (19.8)	1.5 (24.2)	0.655

Captions: SD = standard deviation; CT = chemotherapy; neoCT = neoadjuvant chemotherapy; *p<0.05; **p<0.001; EORTC-QLQ C30 = European Organization for Research and Treatment of Cancer Quality of Life Questionnaire: Core 30; EORTC-QLQ BR23 = EORTC-QLQ Breast Cancer Module 23.

improvement associated with the feeling of concluding a therapeutic step.

In the specific QLQ-BR23 module, sexual function was the most compromised functional domain, with significant decline after neoadjuvant chemotherapy (p=0.016), underscoring the treatment's impact on the female sexual sphere. This finding is consistent with national and international studies[20,26,27]. In a Brazilian prospective study conducted with 80 women in chemotherapy treatment, a significant reduction was found in the sexual function scores (p<0.001)[28]. Similar results were described in a Portuguese study, in which there was a decline of sexual function throughout the first year after diagnosis, with slight recovery across three years, maintaining statistical significance (p=0.042)[27].

The "systemic therapy effects" domain of QLQ-BR23, which covers symptoms related to treatment toxicity, such as changes in taste, nausea, and hair loss, presented a significant increase in the scores of the present study (p=0.016). This finding is in line with national evidence that demonstrates expressive worsening of these symptoms during neoadjuvant chemotherapy (p<0.001)[15,26], reflecting the negative impact of systemic toxicity on HRQoL and the importance of proper management of these complaints during oncological treatment.

Most participants (66.7%) underwent the full chemotherapy scheme composed of four doxorubicin and cyclophosphamide cycles associated with four cycles of one taxane (paclitaxel or docetaxel), a widely used combination to improve survival. However, this regime is not free of the risks of systemic adverse effects, which may partly explain the observed results[13].

Regarding breast symptoms, there was a significant reduction in scores after neoadjuvant chemotherapy

(p<0.001), a result consistent with a national study conducted in the Brazilian Northeast with 140 women, in which self-reported clinical improvement was also identified during treatment (p<0.001)[13]. The agreement between the findings reinforces the potential benefit of neoadjuvant chemotherapy in reducing local symptoms, with a positive repercussion on quality of life.

Despite the relevance of findings, some limitations must be considered in the interpretation of results. The absence of a comparative group prevents inferring causal relations between neoadjuvant chemotherapy and the observed changes in HRQoL, restricting the analysis to the description of variations throughout the treatment. Moreover, the relatively reduced sample size and the unicentric character of the study limit generalization of results to other populations. Yet, the longitudinal assessment conducted in a real assistance setting allowed us to consistently identify functional domains and more change-sensitive symptoms during neoadjuvant chemotherapy. These findings reinforce the importance of systematic monitoring of quality of life during oncological treatment and may support planning of timely clinical interventions, especially in fatigue, physical, and sexual function management, contributing to a more integral patient-centered approach. The importance of including physical rehabilitation programs, nutritional monitoring, and psychological support is highlighted, with a multidisciplinary approach focused on preventing and reducing functional decline.

CONCLUSION

During breast cancer neoadjuvant chemotherapy, women presented a significant decline in physical and sexual function, as well as self-reported improvement of insomnia, global health status, and breast symptoms, concomitantly with fatigue worsening and systemic therapy effects. These findings show the complexity of changes experienced throughout the treatment and reinforce the importance of continuous follow-up of quality of life to promote integrity of care.

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CONTRIBUTIONS

All the authors have substantially contributed to the study design, data acquisition, analysis, and interpretation, wording, and critical review. They approved the final version for publication.

DECLARATION OF CONFLICT OF INTERESTS

The author Anke Bergmann declares a potential conflict of interests due to her being the scientific editor of INCA's *Revista Brasileira de Cancerologia*. The other authors do not have any conflict of interests.

DATA AVAILABILITY STATEMENT

All the contents associated with the article are included in the manuscript.

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