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Quality of life in hematopoietic stem cell transplantation during the Covid-19 pandemic: case series

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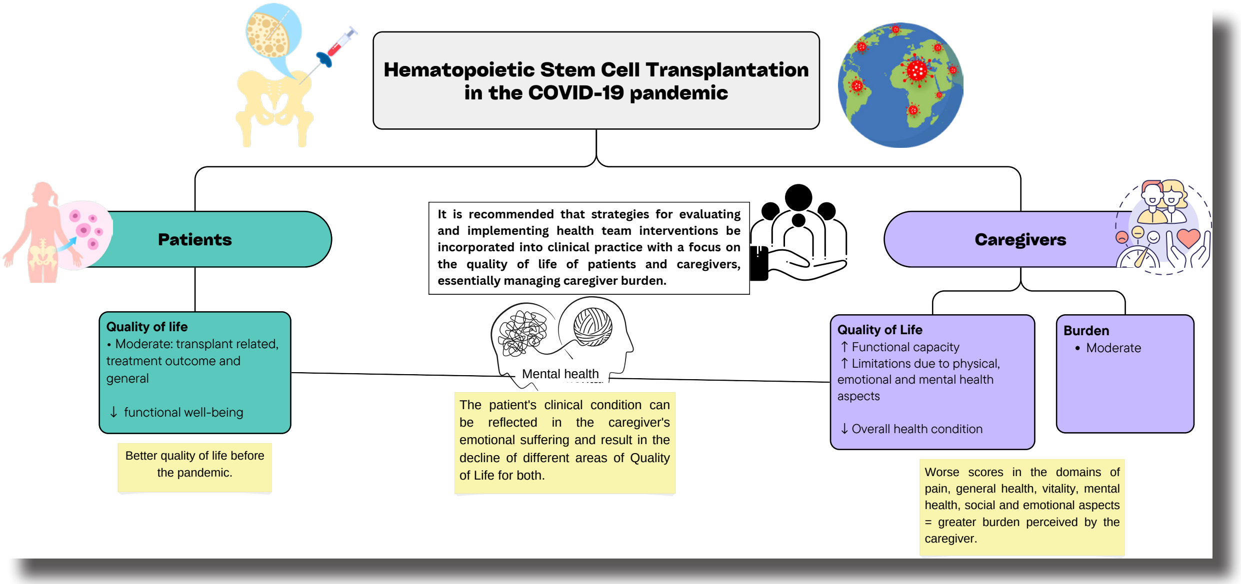
Graphical Abstract



Hematopoietic Stem Cell Transplantation in the COVID-19 pandemic

Patients

Quality of life
- Moderate: transplant related, treatment outcome and general

↓ functional well-being

Better quality of life before the pandemic.

It is recommended that strategies for evaluating and implementing health team interventions be incorporated into clinical practice with a focus on the quality of life of patients and caregivers, essentially managing caregiver burden.

The patient's clinical condition can be reflected in the caregiver's emotional suffering and result in the decline of different areas of Quality of Life for both.

Caregivers

Quality of Life
↑ Functional capacity
↑ Limitations due to physical, emotional and mental health aspects

↓ Overall health condition

Burden
- Moderate

Worse scores in the domains of pain, general health, vitality, mental health, social and emotional aspects = greater burden perceived by the caregiver.

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Abstract

Hematopoietic Stem Cell Transplantation is a complex treatment, aimed at curing malignant and benign diseases, which directly affects the quality of life of patients and caregivers. Studies prior to the pandemic period presented aspects of caregiver burden and quality of life for both; this current research contributes to this gap on the topic during the pandemic. To evaluate and correlate the quality of life of hematopoietic stem cell transplant recipients with the quality of life and caregiver burden during the COVID-19 pandemic. Case series with 16 dyads, carried out in a public hospital in Brazil, a reference in Latin America. The quality of life of transplant recipients was assessed with the Functional Assessment Cancer Therapy-Bone Marrow Transplantation, caregivers with the Medical Outcomes Studt 36-Item Short Form Health Survey, burden with the Zarit Burden Interview. There was a lower perception of the functional well-being of transplant recipients and a worse general health status of caregivers; the caregiver's mental health interfered in different domains of quality of life; there was a negative correlation between quality of life and caregiver burden. The pandemic impacted the dyads' quality of life; there is a need for additional support for both the patient and the caregiver.

Keywords: Quality of Life. Hematopoietic Stem Cell Transplantation. COVID-19. Caregivers. Adult Health.

INTRODUCTION

Hematopoietic Stem Cell Transplantation (HSCT) consists of replacing defective hematopoietic progenitor cells with healthy cells from the donor, after conditioning with chemotherapy (which may be associated with radiotherapy), to eliminate the defective cells, enabling the patient to receive the graft. It is an effective alternative in the absence of a good prognosis of primary therapy, despite being a complex and long-lasting treatment. It is considered curative for various disorders, malignant or not, hereditary or acquired. Among its indications are: lymphomas, multiple myeloma, leukemias, myeloproliferative and hemophagocytic syndromes, immunodeficiencies, among others[1].

The therapeutic itinerary begins with diagnosis and, subsequently, the search for a compatible donor, followed by stem cell collection, conditioning, aplasia, graft, immediate and late complications, until the recovery of hematopoietic functions[2]. During this process, the patient's Quality of Life (QoL) is compromised, with negative psychological, physiological and behavioral effects[3]. These conditions significantly impact the family nucleus, since care demands are almost always carried out by the primary caregiver, a family member, who may also suffer losses due to burden and changes in their QoL[4].

The primary caregiver is understood as the one who assumes constant and permanent responsibility for the patient, committing to the task of caring, even without technique, preparation or remuneration to carry out this activity[4]. It is considered a powerful facilitator of the clinical evolution and social reintegration of this patient after HSCT. Due to physical vulnerability and the potential for adverse events, the patient needs to have a caregiver to assist them with hospital discharge, at least in the first 100 days after transplantation[5].

Primary caregivers play a crucial role in the recovery of patients undergoing HSCT. Their active participation contributes to the patient's physical, emotional, social and mental well-being, promoting an environment of hope, comfort and determination throughout the treatment and recovery process[4]. Patients and their caregivers must navigate this complex care together, whether in the hospital, outpatient or home environment, in simple or complex tasks, until the patient recovers[5].

Although these caregivers feel satisfied in caring for and contributing significantly to the recovery and success of their family member's treatment, it is common that, along the way, due to the continuous support, they feel overwhelmed with tasks added to their daily routine. Thus, burden can cause changes in their social and professional environment, compromising other areas of their lives and compromising their QoL[4.]

In a Chinese multicenter study, approximately a quarter of caregivers of patients with different neoplasms had depression. This prevalence varied with age, the marital relationship between caregivers and the patient, the stage of the disease, complications related to treatment and psychotherapeutic support measures[6].

In the COVID-19 pandemic, patients and caregivers faced additional challenges, such as fear of contagion, restrictions on access to health services, work overload and financial concerns[7]. Patients undergoing HSCT were more vulnerable to SARS-CoV-2 infection, due to the development of complications and more severe evolution, due to systemic immunosuppression, the development of graft-versus-host disease (GVHD) and other factors arising from the therapies to which they are subjected[8]. Furthermore, social distancing and isolation led to the cancellation of medical appointments and other abrupt changes in the routine of the patient and their caregiver, with an impact on the QoL of both[3].

Therefore, this study is justified by addressing the QoL of patients undergoing HSCT and their primary caregiver during the COVID-19 pandemic, as well as awakening the need for a closer look by health professionals, especially the nursing team, considering that changes in care flows and care provided by health services and family members directly or indirectly influenced the health-disease process of this population.

Thus, the following research questions emerged: what was the quality of life of hematopoietic stem cell transplant recipients and their primary caregivers during the COVID-19 pandemic? Is there a correlation between the QoL of patients and caregivers and care burden? To answer them, the objective was to evaluate and correlate the quality of life of hematopoietic stem cell transplant recipients with the quality of life and caregiver burden during COVID-19.

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METHOD

This is a series of cases, which had prospective data collection, based on the method (of case series studies) developed by Mohammad Hassan Murad[9], with the following steps: establishment of inclusion criteria, sampling definition, selection of variables of interest, systematic collection and robust data analysis.

The study was carried out at the day hospital of the Bone Marrow Transplant Service (STMO), a tertiary institution in southern Brazil, a reference in HSCT in Latin America, where outpatient post-transplant follow-up is carried out, with clinical, therapeutic and care in the different demands of the patient and caregivers.

The research was approved by the institution's Human Research Ethics Committee under opinion number 4,894,397. As it was a prospective collection, it was authorized by the participants (patients and caregivers) with the application of a free and informed consent form, signed after the explanation and agreement with the research procedures.

To compose the sample, all patients undergoing HSCT from July 2021 to November 2022 (n=49) were identified. Of these, 11 died, 20 remained without a companion due to institutional recommendations (same caregiver during hospitalization up to 100 days post-transplant) due to the pandemic, and two were hired caregivers. Thus, 16 dyads (patients and primary caregivers) were included, totaling 32 participants. This sample consisted of all hospitalized patients, as during the pandemic the number of beds was reduced due to the additional isolation measures recommended.

The inclusion criteria for both were: age equal to or greater than 18 years, with preserved cognitive and verbal capacity, patients undergoing HSCT within 100 days post-transplant (D+100) and primary caregivers who lived or provided direct care at the patient, from diagnosis to 100 days after HSCT. The exclusion criteria were caregivers hired to work on a shift basis.

The instruments used were: For Patients: 1) sociodemographic and clinical data developed by the researchers; and 2) Functional Assessment Cancer Therapy– Bone Marrow transplantation (FACT-BMT) – version 4.0, to measure QoL that comprises a general scale (FACT-G) and a specific one, divided into five domains: emotional well-being (0 and 24 points), physical well-being, social/family well-being, functional well-being (0 and 28 points) and the specific domain that evaluates the effects of HSCT, entitled additional concerns (0 and 40 points). The subscores are calculated to evaluate general QoL (FACT-G: 0 and 108 points, sum of the scores from the physical, social/family, emotional and functional domains), specific QoL (FACT-BMT: 0 and 148 points) and related to symptoms (Trial Outcome Index-TOI: 0 and 96 points, sum of the five domains and reflects the evaluation index of the treatment result), higher scores represent better QoL[10].

For Caregivers: 1) sociodemographic data to identify the characteristics of the primary caregivers; 2) Medical Outcomes Study 36 (SF-36) - Short Item - Form Health Survey - is a generic instrument for multidimensional assessment of the QoL of healthy people with eight scales: functional capacity, physical aspects, pain, general health status, vitality, social, emotional and mental health aspects; the final score from 0 (worst) to 100 (best general condition)[11] and, 3) Zarit Burden Interview (ZBI) Scale, to assess the impact perceived by the primary caregiver on their physical and emotional health, social activities and financial conditions arising from the practice of caring[12], the total score varies between 0 and 88 points, indicating the burden perceived by the primary caregiver as mild (0 and 20), moderate (21 and 40), moderate to severe (41 to 60) and severe (61 and 88 points).

All data collected was double entered and inconsistencies were identified electronically, a third reviewer made the necessary corrections based on the answers to the questionnaires. Regarding the data obtained with the sociodemographic and clinical questionnaires, they were tabulated in Microsoft Excel® 2020 with the results expressed as simple and absolute frequencies. The QoL (FACT-BMT and SF-36) and burden (ZBI) scores followed the developers' recommendations, expressed as mean (M) and standard deviation (SD). For the different QoL scales, equivalences adjusted to the percentage of domain and general scores were considered, such as high (≥ 70) and low (≤ 55)[13]. For statistical analysis, the Statistical Package for the Social Sciences (SPSS)®, version 19, was used: between the FACT-BMT and SF-36 domains, the Spearman correlation and a significance test (p-value) were calculated; for the SF-36 and ZBI, the scatter diagram, Spearman correlation and a significance test (p-value) were used, considered very weak (0.00 to 0.19), weak (0.20 and 0 .39), moderate (0.40 and 0.69), strong (0.70 and 0.89) and very strong (0.90 and 1.00)[14].

RESULTS

The patients (n=16) were adults, with an average of 32 years old, n=10 (62%) male; n=11 (69%) married or in a stable relationship; nine (56%) had completed high school; nine (56%) allogeneic HSCT and two had treatment postponed due to the COVID-19 pandemic. Regarding the underlying disease, six had leukemia (37%), four (25%) lymphoma, three (18%) aplastic anemia and three (18%) multiple myeloma. The following comorbidities stand out in n=10 (63%): SAH, DM, neurofibromatosis, dyslipidemia, HIV, COVID-19 and hypothyroidism. Regarding QoL data, a moderate score was observed in the scales related to HSCT (FACT-BMT), in the treatment outcome assessment index (TOI) and general (FACT-G), considered to have a lower value in the domain functional well-being (Table 1).

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Table 1 - Quality of Life of patients (n=16). Curitiba/PR, Brazil, jul 2021-nov 2022.

Domains	Mean	Minimum	Maximum	Standard Deviation
Physical well-being	17.81	2	28	6.83
Social well-being	18.13	10	28	5.73
Emotional well-being	17.50	4	24	4.87
Functional well-being	14.73	1	26	5.91
Additional concerns	22.94	9	35	7.20
TOI†	55.48	12	59	17.86
FACT-G‡	68.17	31	106	16.36
FACT-BMT*	91.10	40	141	22.86

*FACT-BMT = QoL related to HSCT; †TOI = treatment outcome assessment index (sum of the five domains); ‡FACT-G = overall QoL (scores for the physical, social/family, emotional and functional domains).↑

Of the primary caregivers, n=10 (62%) were women, with an average of 43 years old, n=10 (62%) were spouses, n=12 (75%) were economically active and nine (56%) had completed high school. The average caregiver burden score was considered moderate (26.69 points and standard deviation of 12.80) and in QoL (SF-36), it was considered high in the domains of functional capacity, limitations due to physical, emotional and mental health aspects (Table 2). However, the perception of general health status (55.19/100) was classified as low, a fact that may suggest a decline in health perception.

Table 2 - Quality of Life of patients (n=16). Curitiba/PR, Brazil, jul 2021-nov 2022.

Domains	Mean	Minimum	Maximum	Standard Deviation
Functional capacity	84.69	60	100	13.84
Limitation due to physical aspects	76.56	0	100	34.72
Pain	67.38	31	100	21.39
Overall health condition	55.19	32	100	17.98
Vitality	64.38	35	90	14.93
Social aspects	68.75	25	100	22.82
Limitation due to emotional aspects	81.25	0	100	40.31
Mental health	70.50	32	96	18.98

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When correlating the QoL domains of caregivers (SF-36) with those of patients (FACT-BMT), statistical significance was observed between the caregiver's mental health and functional well-being, general QoL (FACT-G), specific to HSCT and treatment outcome (FACT-TOI) (Table 3). This result shows the caregiver's mental health with potential influence on the different domains of the patient's QoL.

Table 3 - Correlation between the SF-36 and FACT-BMT domains. Curitiba/PR, Brazil, jul 2021-nov 2022

SF-36	X	FACT-BMT*	Spearman R	p-value
Mental health	x	Functional well-being	0.629	0.009
		TOI†	0.518	0.040
		FACT-G‡	0.617	0.011
		FACT-BMT*	0.621	0.010

*FACT-BMT = QoL related to HSCT; †TOI = treatment outcome assessment index (sum of the five domains); ‡FACT-G = overall QoL (scores for the physical, social/family, emotional and functional domains).).

When analyzing the domains of QoL (SF-36) and care burden (ZBI), negative correlations were observed for the domains of pain, general health, vitality, mental health, social and emotional aspects (Table 4). This data reveals that the lower the score in these domains, the greater the burden perceived by the caregiver.

Table 4 - Teste de significância entre QV (SF-36) e sobrecarga (ZBI) dos cuidadores (n=16). Curitiba/PR, Brasil, jul 2021-nov 2022.

Domains	Spearman R	p-value
Functional capacity	-0.424	0.102
Limitation due to physical aspects	-0.047	0.864
Pain	-0.711	0.002
Overall health condition	-0.557	0.025
Vitality	-0.766	0.001
Social aspects	-0.583	0.018
Limitation due to emotional aspects	-0.435	0.092
Mental health	-0.850	0.000

DISCUSSION

This study evaluated and correlated the quality of life of hematopoietic stem cell transplant recipients with the quality of life and burden of caregivers. The patients were mostly male, young adults and underwent allogeneic HSCT, characteristics similar to those found in a study carried out in Boston, in the United States[15], and in the Chinese multicenter study that showed greater physical and psychological suffering in this population, with significant rates of anxiety and depression, due to the process of diagnosis and treatment of leukemia[16], as well as being in the productive phase of life.

Regarding patients' QoL, it was moderate on the general (FACT-G) and transplant-related (FACT-BMT) scales. These same scores, if compared with a study carried out in the same institution, service and stage of HSCT with the present research, in the period before the pandemic (2013-2016), the participants (n=55) presented better QoL (9.33 and 13.9 points respectively)[17]. It is worth highlighting that a difference of 10 points in QoL can be considered clinically valid due to better symptom control; an average change of two to three points on the FACT-BMT is associated with changes in the performance status classification and can be considered clinically significant[11].

An American cross-sectional analysis of patients (n=205) undergoing HSCT with similar demographic data and clinical conditions found no differences in distress, fatigue or QoL before or during the COVID-19 pandemic (FACT-BMT score of 108 and 107.5, respectively) despite reporting the negative (isolation) and positive (focus on meaningful activities) implications of the pandemic[15].

The scores identified in the QoL scale referring to the physical, social, emotional and functional well-being domains, the patients in this research presented scores close to the study carried out before the pandemic in the same institution[3], with a maximum variation of approximately three points. These data are corroborated by an Indian study conducted during the pandemic period (2021-2022), which evaluated the effect of a meditative practice with patients (n=72) during HSCT, with no significant difference in the groups[18]. However, a decline in emotional and social well-being in HSCT is expected during the pandemic, resulting from uncertainty about the future, concerns about the results of treatment or worsening of the disease, anguish about postponing the transplant, consultations or exams if they test positive for SARS-CoV-2 and social isolation[6,19].

A secondary analysis of data with transplant recipients (n=250), carried out in Massachusetts, prior to the pandemic period, showed that formal (example: professionals) or informal (example: family caregivers and friends) social support is crucial for a successful patient recovery. Greater pre-HSCT social well-being was associated with better quality of life, lower psychological distress, and lower post-traumatic stress symptoms. This is a modifiable target, an intervention that can be constructed and implemented in services to systematically cultivate formal sources of social support, mediated by formal caregivers and family members in this population[16].

The lower perception of QoL in patients can be explained by biobehavioral processes: they are immunocompromised and psychologically vulnerable, they have a worse immune-mediated response to infection and psychosocial stressors due to the greater risk of infectiousness and mortality from COVID-19; present dysregulation of neuroendocrine function and the central nervous system in the presence of inflammatory processes; higher prevalence of depression, anxiety, fatigue, sleep changes, social isolation, loneliness, and neurocognitive impairment overlapping with HSCT and social distancing[20]. Therefore, this diversity of psychological and immunological responses must be rethought, as well as preparation for future pandemics, in addition to considering their impacts on clinical practice and the QoL of patients and caregivers.

In relation to caregivers, similar characteristics were identified in the Canadian study, with the participation of 849 dyads, during HSCT, female caregivers and patients' spouses, although the average age (62 years) was different from the present research. Some characteristics influenced the QoL of both: female caregiver and

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higher education, the patient's QoL, relapse after HSCT and period of immunosuppression. Furthermore, there is a higher prevalence of depression and sleep disorders in caregivers, and, in clinical practice, in these services, interventions for problem solving, communication and cognitive-behavioral therapy are promising for improving QoL and minimizing the burden on caregivers[19].

Given the complexity of HSCT, after discharge, assisting the patient is one of the caregiver's tasks, as patients' wives and spouses enable better adherence to the therapeutic regimen and the prevention of adverse clinical outcomes. Therefore, the predictors of worse adherence are indicated in the presence of depression in the caregiver, fragile relationship between the dyad, having a non-spouse caregiver and other comorbidities, it is recommended to consider the factors of both post-HSCT[4].

In the occurrence of post-HSCT complications, the complexity of care is aggravated, so much so that an American multicenter study evaluated the impact of GVHD on dyads (n=165), with adaptations in employment, leave, reduction of working hours, financial toxicity, patient perception of receiving regular care due to caregiver burden[4]. Although women and wives are culturally linked to caring, in addition to their multiple tasks, they go through intense role changes and suffer from different care adjustments, a fact that results in overload and impacts on QoL.

In relation to caregivers, quality of life (SF-36) was considered moderate to high in almost all domains and low in the perception of general health status. Divergent data were identified in Canada, with the participation of (n=849) dyads. Caregivers of post-HTCT patients reported a lower perception of quality of life in all domains; the maximum score identified (52.8) was in mental health[19]. The pandemic impacted the quality of life of caregivers with the closure of non-essential services, increasing the burden of care in situations where they were responsible for domestic care, remote schooling for children or other family members, remote work and other abrupt changes in routine related to measures such as social isolation[18].

In this research, a negative correlation was identified between the caregiver's mental health and the different domains of the patient's QoL. This fact can be explained by the challenges that family caregivers of post-HSCT patients face on a daily basis, which range from positive emotions to hiding negative emotions. Feelings of care can reflect the patient's state, just as the patient's clinical condition can be mirrored in the emotional suffering of the caregiver and result in a decline in different domains of QoL for both[21].

Caregivers also had to deal with isolation and the various feelings that permeated their routines, including: fear, anxiety, economic uncertainty, as many of them had their family income compromised due to social isolation. All of these issues can negatively influence the family context and impact the mental health of caregivers[22]. It is noteworthy that in cases of HSCT, isolation measures are frequently adopted for patients, due to the high risk of infections, a fact that can impact QoL and caregiver burden and can be exacerbated by the pandemic.

Adequately preparing the family caregiver for the tasks and demands of their role before HSCT can prevent potential negative consequences (symptoms of depression) greater competence, self-efficacy and better overall QoL. It is necessary for the team to identify those with insufficient preparation to provide psychoeducational support, with the aim of obtaining better results for the dyads[23]. Furthermore, regardless of the pandemic period, it is presumed that the majority of caregivers were not adequately prepared to care for their family members, much less face the pandemic, a fact that justifies the negative correlation in QoL and caregiver burden.

In addition to preparation, it is recommended to pay attention to the support needs of patients' family caregivers. A Brazilian longitudinal study pointed out that the main needs were: “knowing what to expect in the future” and “how to deal with your own feelings”, these and other support needs remained before and up to four months after HSCT, a fact that demands greater attention to the needs of caregivers during treatment[24].

The existence of a negative correlation between domains of caregivers' QoL and the burden of care highlighted in this study is justified, as this is responsible for 30% of the variance in QoL. Often, these caregivers assist their family members with functional deterioration, in addition, care provided to hospitalized patients negatively affects the caregiver's QoL. Therefore, it is highly recommended to assess care burden, especially in complex treatment contexts, and refer caregivers to supportive care[25].

Knowing the characteristics of the quality of life of patients and their caregivers during transplantation and post-transplantation can support the implementation of interventions with the purpose of improving the experience of patients and caregivers; better prepare the patient/caregiver during all phases of treatment, especially after hospital discharge; and identify patients at higher risk of post-transplant complications due to difficulties in home care.

As it was a single-center study with a limited number of participants, it was a limiting factor. This is possibly due to the reduced number of beds available for HSCT in the hospital where the research was carried out, due to institutional changes caused by the pandemic.

CONCLUSION

This study correlated the quality of life of dyads and the burden of care during HSCT in the context of the COVID-19 pandemic. The results highlight that, in addition to the decline in some domains of QoL of dyadic couples, there was a potential influence of mental health and caregiver burden on the QoL of both, especially at the time of the study.

It is recommended that strategies for evaluating and implementing interventions with the healthcare team be incorporated into clinical practice with a focus on the QoL of dyads and caregiver burden. It is important that centers providing care to this patient profile can identify the scalable impact on the long-term QoL of patients and caregivers, as well as develop intervention research and care guidelines to better support patients and their primary caregivers.

CREdiT author statement

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All authors have read and agreed to the published version of the manuscript.

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