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The role of Geriatric Nutritional Risk Index in sepsis-related mortality in intensive care

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ABSTRACT

Aims: This study explores the link between nutritional status and sepsis outcomes, focusing on Geriatric Nutritional Risk Index (GNRI) scores and clinical endpoints such as mortality, intensive care unit (ICU) stay duration, and functional recovery.

Methods: The study was a retrospective, observational investigation of 250 older patients with sepsis in the intensive care unit. GNRI was calculated based on admission albumin level and ratio of actual body weight to ideal body weight. Groups were defined as major risk (GNRI <82), moderate risk (GNRI 82 to <92), low risk (GNRI 92 to ≤98), and no risk (GNRI >98). The primary outcome measured was 28-day hospital mortality. Additionally, the relationship between the GNRI score and the SOFA and APACHE II scores was assessed.

Results: In the univariate analysis comparing median values between survivor and non-survivor groups, significant differences were found in body-mass index, albumin levels, C-reactive protein levels, SOFA score, APACHE II score, and GNRI score. The 28-day hospital mortality rates for each GNRI group were: 5.7% in the very low risk group (GNRI >98), 9.8% in the low risk group (GNRI 92-98), 8.5% in the moderate risk group (GNRI 82-92), and 35.8% in the very high risk group (GNRI <82). The optimal cutoff for predicting outcomes was identified as GNRI <85. In a comparison of area under the curve (AUC) values, GNRI demonstrated superior predictive ability compared to APACHE II and SOFA scores, with AUC values of 0.629 (95% CI 0.543-0.715) for GNRI, 0.579 (95% CI 0.493-0.664) for SOFA, and 0.550 (95% CI 0.455-0.646) for APACHE II.

Conclusion: This study demonstrates that GNRI is a significant predictor of mortality and prolonged length of stay in patients with sepsis in the ICU. These findings underscore the importance of assessing and improving nutritional status in the management of sepsis.

Keywords: Geriatric Nutritional Risk Index, sepsis, malnutrition, mortality

INTRODUCTION

Sepsis is a critical condition that arises from the body's overactive response to an infection, resulting in widespread inflammation, organ failure, and potentially fatal outcomes. This condition predominantly affects older adults and remains one of the leading causes of mortality in influencing sepsis outcomes in the elderly, and understanding this risk factor is crucial for improving patient prognoses.[1,2]

In older adults, sepsis can exacerbate or initiate nutritional deficiencies due to increased catabolic processes and insufficient oral intake. These patients face a higher risk of sepsis attributable to weakened immune function, multiple chronic diseases, and existing nutritional deficiencies. The progression of sepsis in this population can rapidly worsen, resulting in higher mortality rates compared to younger individuals. Therefore, it is crucial to assess the nutritional status of the elderly using comprehensive nutritional screening tools. Implementing early nutritional interventions based on reliable assessments can help mitigate the severity of illness and expedite recovery.[3] Among the available tools, the Geriatric Nutritional Risk Index (GNRI) has proven to be an essential predictor of sepsis-related mortality. The GNRI is a straightforward yet effective metric that incorporates body weight, height, and serum albumin levels. Lower GNRI scores are indicative of a higher risk of malnutrition and are associated with poorer clinical outcomes.[4]

One critical advantage of the GNRI is its ability to identify patients at risk of malnutrition before overt clinical symptoms manifest. Timely detection of at-risk patients can significantly inform clinical decision-making. The GNRI serves as a practical and swift screening tool, enabling healthcare providers to stratify patients based on nutritional risk and allocate resources effectively.[5] The nutritional risk screening 2002 (NRS-2002), another malnutrition screening tool, demands a more comprehensive assessment. In contrast, the

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malnutrition universal screening tool (MUST) primarily addresses the general population, rather than specifically targeting older intensive care unit (ICU) patients. This specificity makes the GNRI more practical and relevant for assessing nutritional risk in the elderly ICU demographic.[6]

While the GNRI is a valuable tool for identifying malnutrition, it has limitations, particularly its reliance on serum albumin levels. Albumin levels can be influenced by factors unrelated to nutritional status, such as inflammation, infection (e.g., sepsis), fluid imbalances (e.g., hypervolemia or dehydration), liver function abnormalities, and renal insufficiency. These conditions can significantly alter serum albumin concentrations, leading to potential misinterpretations of a patient's nutritional status. Consequently, the GNRI may not always accurately reflect the true nutritional health of individuals, especially in populations with high rates of comorbid conditions.[3]

To address these limitations, it is essential to use the GNRI alongside other clinical and nutritional assessments. Integrating comprehensive clinical evaluations, dietary intake records, anthropometric measurements, and other biochemical markers can provide a more holistic and accurate assessment of a patient's nutritional status. This multifaceted approach ensures that clinicians can identify and address malnutrition more effectively, thereby improving patient care and outcomes in vulnerable populations.

Few studies have examined the relationship between the GNRI and short-term mortality in acutely hospitalized older patients. This study aims to evaluate the predictive value of GNRI for outcomes in older ICU patients with sepsis. By analyzing the association between GNRI scores and various clinical endpoints, including mortality, length of ICU stay, and functional recovery, we aim to gain a deeper understanding of the impact of nutritional status on sepsis outcomes in this frail group.

METHODS

Ethics

The study protocol was approved by the KTO Karatay University Faculty of Medicine Non-drug and Medical Device Researches Ethics Committee (Date: 31.10.2024, Decision No: 2024/024) (Document Date and Number: 01.11.2024-96819). The study was conducted in accordance with the 1975 Declaration of Helsinki, as revised in 2013.

Study Setting and Patients

This retrospective, descriptive, observational study focuses on patients with sepsis in ICUs. Conducted between January 1, 2022, and September 30, 2024, the study included 250 patients over the age of 65 who were followed for sepsis in the third step ICU (internal medicine 1-2-3) of Konya City Hospital, which has a total of 45 beds. Demographic, physiological, and laboratory data were collected. The GNRI score was classified into four categories according to Bouillanne et al.'s[4] study: major risk (GNRI <82), moderate risk (GNRI 82 to <92), low risk (GNRI 92 to ≤98), and no risk (GNRI >98).

Definition

Sepsis was diagnosed based on confirmed ICU admission for sepsis or infection, with accompanying organ dysfunction. This was identified using a Sequential Organ Failure Assessment (SOFA) score of 2 or above, in line with the third International consensus definitions for sepsis and septic shock (sepsis-3).[7] Severe sepsis is defined as sepsis in conjunction with one of the following conditions: cardiovascular organ dysfunction, acute respiratory distress syndrome, or dysfunction in two or more other organs. Septic shock is characterized by severe sepsis with persistent hypotension, necessitating vasopressor therapy despite adequate fluid resuscitation (20-30 ml of crystalloid per kilogram of body weight).[7]

Data Collection

We retrospectively gathered clinical and laboratory data from the hospital information system. For each patient, age, sex, height, body mass index, co-morbidities, sites of infection, vital signs, APACHE II score, Glasgow Coma Scale, and SOFA score were recorded. Both SOFA and APACHE II scores were utilized as mortality risk factors.

The GNRI score was calculated using the equation described by Bouillanne et al.[4] Ideal body weight (IBW) was determined according to the Lorentz formula, and the GNRI score was derived from the ratio of the admission albumin level and actual body weight to the IBW.

The Lorentz formula was used to calculate the IBW;

- For men: IBW=(height-100)-[(height-150)/4]
- For women: IBW=(height-100)-[(height-150)/2]

The GNRI score was calculated using the following formula:

- GNRI=[1.489×albumin (g/L)]+[41.7×(weight/IBW)]

Risk categories based on GNRI were defined as follows: very low risk (GNRI >98), low risk (GNRI 92-98), moderate risk (GNRI 82-92), and very high risk (GNRI <82).

Outcome Measures

The primary outcome measured was 28-day hospital mortality. Additionally, the relationship between the GNRI score and the SOFA and APACHE II scores was assessed.

Statistical Analysis

The data analyses were conducted using SPSS statistical software (version 21.0; SPSS, Chicago, IL, USA). Continuous variables were expressed as means with standard deviation (SD) for parametric data, or medians with interquartile range (IQR) for non-parametric data. Categorical variables were presented as numbers and percentages. Univariate analyses were performed using student's T test or the Mann-Whitney U test for continuous variables, and the chi-square test or Fisher's exact test for categorical variables.

For multivariate analysis, a logistic regression model with a stepwise variable selection method was employed. Variables that remained significant ($p<0.05$) in the multivariate model were considered independent predictors for 28-day hospital mortality. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated for each predictor.

To compare the discriminative ability of the GNRI, APACHE II, and SOFA scores, receiver operating characteristic (ROC) curve analysis with area under the curve (AUC) calculations was utilized. The cutoff points for mortality risk for each score were determined from the highest sensitivity and (1-specificity) values on the ROC curve.

RESULTS

Between January 1, 2022, and September 30, 2024, a total of 3,456 patients were admitted to the 45-bed internal medicine intensive care unit. Among these, 1,876 patients received intensive care for infection-related reasons. During this period, 876 patients were diagnosed with sepsis, and from this group, 250 patients aged 65 and older were included in our study. The overall 28-day hospital mortality rate was 28.9% (95% CI, 22.8%-33.0%). The characteristics of survivors and non-survivors are detailed in Table 1.

Table 1. General characteristics of the patients

Variable[a]	Total (n: 250)	Survivors (n: 178)	Non-survivors (n: 72)	p-value[b]
Age (years-mean±SD)	77±10.1	76±9.6	79±9.5	0.156
Male sex, n (%)	116 (46.4)	90 (50.5)	35 (48.6)	0.265
BMI, kg/m²-median (IQR)	23.4 (22.4-25.2)	22.7 (21.5-23.6)	20.9 (19.8-22.3)	<0.003
Sepsis severity, n (%)				
Severe sepsis	61 (24.4)	33 (19)	28 (38.8)	<0.012
Septic shock	27 (10.8)	17 (9.6)	10 (13.8)	<0.011
Co-morbidity, n (%)				
Hypertension	197 (78.8)	142(80)	55(79)	0.242
Diabetes mellitus	161 (64.4)	115(65)	46(64)	0.453
Cerebrovascular disease	73 (29.2)	53(30.1)	20(29.8)	0.324
Cancer	22 (8.8)	5 (2.80)	8 (11.1)	0.001
COPD	141 (56.4)	101(56.7)	40 (55.2)	0.165
Chronic kidney disease	17 (6.8)	12(6.7)	5 (6.1)	0.231
Congestive heart failure	116 (46.4)	82 (46)	34 (47)	0.435
Dementia	49 (19.6)	34 (19.1)	15 (20.1)	0.276
Site of infection, n (%)				
Lower respiratory	163 (65.2)	102 (57.3)	61 (84.7)	<0.001
Genitourinary	102 (40.8)	73 (41)	29 (40.1)	0.158
Hepatobiliary	35 (14)	24 (13.4)	11 (15.1)	0.276
Gastrointestinal	40 (16)	28 (15.7)	12 (16.2)	0.119
Laboratory parameter-median (IQR)				
Hemoglobin, g/dl	12 (10.6-13.4)	11.9 (10.8-13.2)	12.2 (9.6-12.4)	0.082
Platelet count, x1000 cells/mm³	225 (165-342)	221 (166-365)	217 (163-348)	0.584
Albumin, g/dl	3.8 (3.3-4.0)	3.6 (3.2-3.8)	2.9 (2.6-3.6)	<0.001
C-reactive protein, g/dl	101 (67-221)	106 (72-198)	110 (78-278)	<0.002
Mortality prediction model				
SOFA score-median (IQR)	2 (2-5)	2 (1-4)	4 (2-7)	<0.001
APACHE II-median (IQR)	19 (14-25)	18 (13-21)	27 (18-32)	<0.001
GNRI score-median(IQR)	94.3 (86.3-98.8)	95.1 (85.3-99.1)	84.3 (77.1-93.2)	<0.001
LOS in ICU (day)	12 (5-18)	13 (6-19)	18 (12-27)	<0.001

[a]Data are reported as mean±SD or percentages n (%) or the median IQR (inter quartile range), [b]Continuous and categorical variables were compared between groups with Mann-Whitney U test or the Fisher's exact test, respectively, p<0.05 was considered statistically significant in all analyses, SOFA: Sepsis-related organ failure assessment, APACHE II: Acute physiology and chronic health evaluation II, GNRI: Geriatric Nutritional Risk Index, COPD: Chronic obstructive pulmonary disease, LOS in ICU: Lenght of stay in intensive care unit, BMI: Body-mass index, N: Number, SD: Standard deviation, IQR: Inter-quartile range

In the univariate analysis comparing median values between survivor and non-survivor groups, significant differences were observed in body-mass index, albumin, C-reactive protein, SOFA score, APACHE II score, and GNRI score. Similarly, sepsis, septic shock, cancer, lower respiratory infection, and ICU length of stay also showed significant differences between survivors and non-survivors (Table 1).

The 28-day hospital mortality rates for each GNRI group were as follows: 5.7% in the very low-risk group (GNRI >98) (OR, 2.378; 95% CI, 0.981-7.527), 9.8% in the low-risk group (GNRI 92-98) (OR, 2.874; 95% CI, 1.023-7.872), 8.5% in the moderate-risk group (GNRI 82-92) (OR, 3.125; 95% CI, 1.745-8.683), and 35.8% in the very high-risk group (GNRI <82) (OR, 16.341; 95% CI, 7.215-32.143).

The optimal cutoffs for the indicators were GNRI <85, with a sensitivity of 61.9%, specificity of 78.8%, positive predictive value (PPV) of 32.3%, and negative predictive value (NPV) of 91.2%.

The ROC curves for GNRI, APACHE II, and SOFA are presented in Figure. When comparing the AUCs, GNRI demonstrated superior predictive ability over both APACHE II and SOFA scores. The AUC values were as follows: GNRI 0.629 (95% CI, 0.543-0.715); SOFA 0.579 (95% CI, 0.493-0.664); APACHE II 0.550 (95% CI, 0.455-0.646).

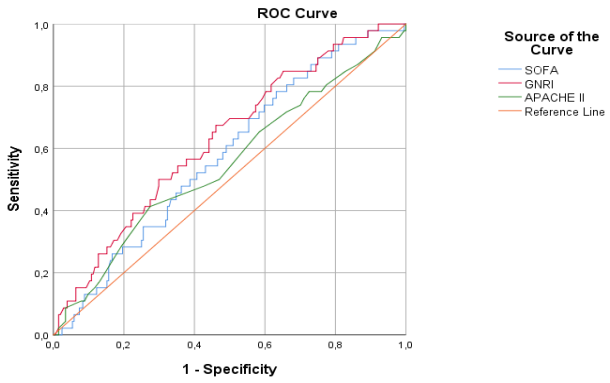

Figure. Receiver operating characteristic curves of the Geriatric Nutritional Risk Index, APACHE II, and the sepsis-related organ failure assessment for in-ICU mortality. Area under the ROC curve (AUC) (95% CI) values are also given: GNRI 0.629 (0.543-0.715), SOFA 0.579 (0.493-0.664), APACHE II 0.550 (0.455-0.646)

APACHE II: Acute physiology and chronic health evaluation II, ICU: Intensive care unit, ROC: Receiver operating characteristic, AUC: Area under the curve, CI: Confidence interval, GNRI: Geriatric Nutritional Risk Index

There was no statistically significant difference in CRP levels between the GNRI groups. CRP levels for each GNRI group were as follows: 88±12 in the very low-risk group (GNRI >98), 92±14 in the low-risk group (GNRI 92-98), 87±16 in the moderate-risk group (GNRI 82-92), and 98±21 in the very high-risk group (GNRI <82) (p=0.119).

The results of the multivariate logistic regression analysis are shown in Table 2. Specifically, lower albumin levels (OR=0.89, 95% CI: 0.77-1.03, p<0.001) were significantly associated with an increased risk of short-term mortality. The presence of septic shock (OR=1.53, 95% CI: 1.41-1.65, p<0.001) also markedly increased the risk. Additionally, older age (OR=1.06, 95% CI: 1.01-1.12, p=0.028) was associated with greater short-term mortality. Lower GNRI scores (OR=0.94, 95% CI: 0.83-1.05, p<0.001) and higher SOFA scores (OR=0.91, 95% CI: 0.82-1.10, p<0.001) were also significant predictors. Lastly,

elevated APACHE II scores (OR=0.88, 95% CI: 0.79-0.99, p<0.001) indicated a higher risk of short-term mortality.

Table 2. Multivariate logistic regression analysis predicting short-term mortality

Variables	OR	95% CI	p-value
Albumin level	0.89	0.77-1.03	<0.001
Septic shock	1.53	1.41-1.65	<0.001
Weight	1.03	0.88-1.18	<0.001
Age	1.06	1.01-1.12	0.028
GNRI scores	0.94	0.83-1.05	<0.001
SOFA scores	0.91	0.82-1.10	<0.001
APACHE II scores	0.88	0.79-0.99	<0.001

GNRI: Geriatric Nutritional Risk Index, SOFA: Sequential organ failure assessment, APACHE II: Acute physiologic assessment and chronic health evaluation, OR: Odds ratio, CI: Confidence interval, p-value less than 0.05 was considered statistically signifcant

DISCUSSION

This study explored the role of the GNRI in sepsis-related mortality and ICU length of stay, demonstrating that low GNRI values were linked to a higher risk of malnutrition, increased mortality rates, and prolonged ICU stays. Additionally, significant correlations were identified between low GNRI values and advanced age, elevated CRP levels, as well as higher SOFA and APACHE II scores. These results support the hypothesis that a low GNRI not only heightens susceptibility to sepsis but also adversely impacts the clinical trajectory. We propose that a GNRI score below 85 serves as an independent predictor of mortality, particularly in older sepsis patients admitted to the ICU.

The observation that low GNRI values correlate with malnutrition aligns with existing literature, which underscores the adverse effects of malnutrition on the development of sepsis and mortality among older patients.[7]

While energy and protein requirements escalate in sepsis, inadequate fulfillment of these needs in the elderly can compromise the immune system, heightening infection susceptibility. Additionally, malnutrition has been linked to organ dysfunction in sepsis patients, leading to elevated SOFA and APACHE II scores. Nutritional assessment is very important in intensive care patients. As stated in the surviving sepsis campaign guidelines, nutritional support supports the healing process of patients.[2] Appropriate and adequate protein and carbohydrate support, having scores to define malnutrition in the early period, reduces complications that may develop during the intensive care period without muscle loss in patients. The GNRI seems to be a simple scoring system and a good marker for nutritional support at intensive care admission. Consequently, this study proposes that a low GNRI may serve as an indicator of malnutrition and a predictor of sepsis prognosis.

The findings of our study are consistent with the existing literature. For example, Durán Alert, et al.[8] have identified GNRI as a significant prognostic marker in critically ill patients, with lower GNRI values being associated with higher mortality rates. Similarly, Bouillanne, et al.[4] indicated that GNRI is an effective measure for assessing malnutrition risk in the elderly, noting that lower GNRI scores correlate with poorer clinical outcomes. These studies affirm the potential of GNRI as a valuable tool for predicting prognosis in older sepsis patients.

In this study, there was no statistically significant difference in CRP levels between the GNRI groups (p=0.119). The similar CRP levels across categories in our study demonstrate that the GNRI is a reliable nutritional assessment tool that is not influenced by the severity of inflammation. This finding suggests that the GNRI can independently evaluate nutritional status without the confounding effects of inflammation, making it a trustworthy tool for clinical practice. Consequently, these features of the GNRI can be highlighted as one of the strengths of our study and underscore its significant role in assessing the nutritional status of critically ill patients.

Furthermore, recent research has investigated the relevance of GNRI to mortality and length of hospital stay across various disease groups, particularly those with nutritional impairments and frequent malnutrition comorbidities. Markus Haas et al.[9] identified GNRI as an independent survival risk factor in patients with metastatic head and neck cancers. In addition, Xie et al.[10] demonstrated a correlation between GNRI and overall survival in a meta-analysis of patients with gastrointestinal malignancies.

GNRI has also been evaluated as a prognostic factor in older patients with cardiac and renal conditions. A comprehensive meta-analysis by Hengdon, et al.[11] involving 10,589 patients revealed that a one-unit decrease in GNRI was associated with a 6% increase in all-cause mortality. In the context of hemodialysis patients, GNRI frequently correlates with the creatinine index, which is used to monitor nutritional status.[12] Additionally, a retrospective study involving 12,058 intensive care patients with acute kidney injury underscored the GNRI's utility as a critical nutritional assessment tool in this population.[13]

Collectively, these studies, along with our findings, underscore the crucial role of nutritional monitoring and its significant association with overall mortality rates, especially among vulnerable and critically ill patients.

However, there are also conflicting findings regarding the prognostic value of GNRI. Some studies suggest that GNRI may not be robust enough as an independent marker, particularly in critically ill patients. Plauth et al.[14] highlighted the importance of using more objective measurements to assess malnutrition and its clinical impacts, particularly in vulnerable groups such as critically ill patients. In addition, in our study, although the AUC value of GNRI was better than the other scoring systems, it was not sufficiently strong in all three. This may be explained by the retrospective nature of the study and the inadequacy of the study population. This indicates that GNRI can be used as a complementary tool in certain situations, but it may not be a powerful diagnostic tool alone.

The influence of GNRI on nutritional status and sepsis prognosis can be affected by various factors, including underlying comorbidities, the severity of the disease, and

the patient's overall clinical condition. Therefore, it may be more beneficial to use GNRI in conjunction with other clinical scores and biomarkers rather than relying on it alone. Combining GNRI with other nutritional assessment tools such as the mini nutritional assessment (MNA), subjective global assessment (SGA), or nutritional risk screening 2002 (NRS-2002) may provide a more comprehensive evaluation of nutritional status.[15]

The development of the GNRI within the older population brings into question its applicability to younger sepsis patients. This highlights the need to investigate the validity and reliability of the GNRI across different age groups.

This study demonstrates that the GNRI is a significant predictor of mortality and prolonged ICU stays in sepsis patients. Lower GNRI scores are linked to advanced age and higher disease severity scores. These findings underscore the critical importance of assessing and improving nutritional status in the management of sepsis.

Incorporating the GNRI into routine clinical practice may aid in the early identification of high-risk patients and the development of appropriate nutritional interventions. Future research should focus on comparing the GNRI with other nutritional assessment tools, validating it across different age groups, and assessing the impact of nutritional interventions on sepsis outcomes.

Randomized controlled trials could be designed to evaluate the effect of early and intensive nutritional support on clinical outcomes in high-risk patients identified using the GNRI.

The findings of this study highlight the critical importance of early nutritional assessment and intervention in the management of sepsis patients in the ICU. Regular use of nutritional risk assessment tools, such as the GNRI, can aid in the early identification and management of malnutrition in sepsis patients, thereby contributing to reduced mortality rates and shorter hospital stays. In conclusion, it is recommended to adopt a holistic approach to sepsis treatment, incorporating the optimization of nutritional status as an integral component of treatment protocols.

Limitations

Our study has certain limitations, including its single-center design and relatively small sample size. These factors may restrict the generalizability of the findings and highlight the need for larger, multicenter studies. Future research conducted in different geographical regions and diverse patient populations could offer a better understanding of the GNRI's impact on sepsis prognosis. Additionally, our study did not track the dynamic changes in GNRI, limiting our ability to assess how shifts in nutritional status affect prognosis. In acute and rapidly progressing conditions like sepsis, temporal changes in nutritional status may be crucial.

Future studies should consider measuring GNRI at regular intervals and exploring the relationship between these changes and clinical outcomes to better evaluate the effectiveness of nutritional interventions.

CONCLUSION

Low GNRI values are linked to an increased risk of malnutrition, higher mortality, and extended ICU stays in older sepsis patients. Additionally, significant correlations exist between GNRI and factors such as age, CRP levels, SOFA, and APACHE II scores. GNRI shows promise as a tool for assessing prognosis in older sepsis patients in clinical practice. However, its prognostic value should be evaluated in conjunction with other clinical parameters and validated through further research.

ETHICAL DECLARATIONS

Ethics Committee Approval

This study was conducted in the KTO Karatay University Faculty of Medicine Non-drug and Medical Device Researches Ethics Committee (Date: 31.10.2024, Decision No: 2024/024).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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