North Clin Istanb 2026;13(5):551–557
doi: 10.14744/nci.2026.34793

Original Article INTERNAL MEDICINE

Evaluation of the relationship between the SCORE2-diabetes mellitus cardiovascular risk score, degree of obesity, and systemic inflammatory indices in patients with type 2 diabetes mellitus

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ABSTRACT

OBJECTIVE: This study evaluated the relationship between the SCORE2 diabetes mellitus (SCORE2-DM) cardiovascular risk score, obesity status, clinical and laboratory parameters, and hematologic systemic inflammatory indices in patients with type 2 diabetes mellitus (T2DM).

METHODS: This single-center, retrospective cross-sectional study included 100 patients with T2DM aged 40–69 years without established atherosclerotic cardiovascular disease. Patients with type 1 diabetes, active infection or inflammatory disease, malignancy, or hematologic disease were excluded from the study. Ten-year cardiovascular risk was calculated using the SCORE2-Diabetes algorithm. Patients were classified by body mass index (BMI) into normal weight, overweight, and obesity classes. Systemic immune-inflammation index, systemic inflammation response index, neutrophil-to-lymphocyte ratio, monocyte-to-lymphocyte ratio, and platelet-to-lymphocyte ratio were calculated from complete blood count (CBC) parameters. Obesity-class comparisons were performed using the Kruskal–Wallis test, the sex comparison using the Mann–Whitney U-test, and correlations using Spearman analysis.

RESULTS: The median age was 50 (40–67) years, and 50% of participants were women. Obesity class distribution was: Normal weight 13%, overweight 36%, class 1 obesity 35%, class 2 obesity 12%, and class 3 obesity 4%. SCORE2-DM did not differ significantly according to obesity class ($p=0.250$) or sex (Mann–Whitney $U=1289.5$, $p=0.788$). SCORE2-DM correlated significantly with variables directly incorporated into the algorithm, including age (rho=0.621, $p<0.001$), smoking status (rho=0.324, $p=0.001$), systolic blood pressure (rho=0.230, $p=0.021$), total cholesterol (rho=0.227, $p=0.023$), glycated hemoglobin (rho=0.338, $p<0.001$), age at diabetes diagnosis (rho=0.338, $p<0.001$), and estimated glomerular filtration rate (rho=-0.223, $p=0.026$); these associations are expected because of mathematical coupling. Diabetes duration also showed a positive correlation with SCORE2-DM (rho=0.291, $p=0.003$). BMI showed an exploratory weak inverse correlation with SCORE2-DM (rho=-0.214, $p=0.032$). None of the inflammatory indices were significantly correlated with SCORE2-DM.

CONCLUSION: In this retrospective cross-sectional T2DM cohort, SCORE2-DM did not differ significantly according to BMI-defined obesity class or sex, and CBC-derived inflammatory indices showed no significant cross-sectional association with the score. Correlations with variables incorporated into SCORE2-DM are expected because of mathematical coupling and should not be interpreted as independent validation findings. The weak inverse association between BMI and SCORE2-DM should be interpreted cautiously in view of multiple exploratory comparisons. Longitudinal studies with cardiovascular outcomes are required to evaluate the prognostic or predictive value of the inflammatory indices.

Keywords: Biomarkers; cardiovascular diseases; diabetes mellitus type 2; inflammation; obesity; risk assessment.

Cite this article as: *Tayfur M, Emir S. Evaluation of the relationship between the SCORE2-diabetes mellitus cardiovascular risk score, degree of obesity, and systemic inflammatory indices in patients with type 2 diabetes mellitus. North Clin Istanb 2026;13(5):551–557.*

Received: July 21, 2026 *Revised:* August 19, 2026 *Accepted:* September 09, 2026 *Online:* October 16, 2026

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Istanbul Provincial Directorate of Health - Available online at www.northclinist.com

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disease whose global prevalence is rising rapidly and which is recognized as one of the leading risk factors for cardiovascular disease (CVD) [1, 2].

The risk of cardiovascular events is markedly higher in individuals with diabetes than in those without diabetes, and CVD constitutes the leading cause of morbidity and mortality in patients with T2DM [3].

Accurate cardiovascular risk estimation is important for planning preventive treatment strategies. The SCORE2 algorithm, developed by the European Society of Cardiology (ESC), is widely used to estimate 10-year cardiovascular risk in the general population [4]. Because the original SCORE2 model does not incorporate diabetes-specific risk information, the SCORE2-diabetes mellitus (SCORE2-DM) algorithm was developed by adding diabetes-specific variables – age at diabetes diagnosis, glycated hemoglobin (HbA1c), and estimated glomerular filtration rate (eGFR) – to conventional risk factors such as age, smoking, systolic blood pressure, and total and high-density lipoprotein (HDL) cholesterol, and it has been validated in European populations [5].

Obesity plays an important role in the pathogenesis of T2DM and in the development of cardiovascular complications, and is traditionally associated with increased cardiovascular risk [6]. Nevertheless, conflicting findings referred to in the literature as the "obesity paradox" have also been reported, indicating that patients with mild-to-moderate obesity in certain chronic disease groups (such as heart failure, diabetes, and acute coronary syndrome) may show better clinical outcomes than normal-weight patients [7, 8]. The validity of this paradox in the T2DM population, and the mechanisms underlying it, remain a subject of ongoing debate.

In recent years, a growing number of publications have suggested that low-cost, readily accessible systemic inflammation markers derived from the routine complete blood count – such as the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), monocyte-to-lymphocyte ratio (MLR), systemic immune-inflammation index (SII), and systemic inflammation response index (SIRI) – may be associated with cardiovascular risk and mortality [9–11]. However, studies evaluating the relationship between these indices and SCORE2-DM, a current and diabetes-specific risk score, remain limited.

In this study, we aimed to evaluate the relationship between the SCORE2-DM cardiovascular risk score and sex, degree of obesity, demographic, clinical, and laboratory parameters, and hematologic inflammatory indices (SII, SIRI, NLR, MLR, and PLR) in patients with T2DM. We hypothesized that the degree of glycemic control and accompanying metabolic parameters would be more strongly associated with SCORE2-DM than conventional obesity measures, whereas simple hematologic inflammatory indices would not show a significant cross-sectional association with the score in this population.

Highlight key points

- Correlations between SCORE2-DM and variables incorporated into its algorithm were expected because of mathematical coupling.
- SCORE2-DM did not differ significantly according to BMI-defined obesity class or sex in this sample.
- BMI showed an exploratory weak inverse correlation with SCORE2-DM; this marginal finding requires cautious interpretation because no multiplicity adjustment was applied.
- CBC-derived inflammatory indices, including SII, SIRI, NLR, MLR, and PLR, showed no significant cross-sectional correlations with SCORE2-DM.

MATERIALS AND METHODS

Study Design, Setting, and Ethical Approval

This study was designed as a single-center, retrospective cross-sectional study based on existing medical records of patients attending the outpatient internal medicine clinic of a tertiary training and research hospital. Demographic, clinical, anthropometric, and laboratory data used in the analyses corresponded to the same outpatient encounter, and no additional intervention or sample collection was performed. The protocol was approved by the local Scientific Research Ethics Committee as a non-pharmaceutical clinical study on December 18, 2025 (decision no. 472; reference no. B.10.1.TKH.4.34.H.GP.0.01/478). Study-specific written informed consent was not obtained; the retrospective protocol and submitted study documentation were reviewed and approved by the ethics committee. The study followed the principles of the Declaration of Helsinki.

Patient Selection

Inclusion criteria: Patients aged 40–69 years with a diagnosis of T2DM and no established atherosclerotic CVD (ASCVD) were included in the study. This age range and the requirement of being free of ASCVD were chosen

to match the target population, in which the SCORE2-DM algorithm was developed and validated.

Exclusion criteria: Patients with type 1 diabetes, established ASCVD, active infection or inflammatory disease, a history of malignancy, or hematologic disease were excluded from the study.

Eligible patient records were screened according to the inclusion and exclusion criteria. A sex-balanced analytical sample was intentionally constructed, comprising 50 women and 50 men who met the eligibility criteria; therefore, the final sample was not a consecutive sample.

Data Collection

Demographic data (age, sex, and smoking history), anthropometric and clinical data (systolic and diastolic blood pressure, waist circumference, height, weight, and body mass index [BMI]), and age at diabetes diagnosis were recorded from the outpatient evaluation. Laboratory data (total cholesterol, HDL cholesterol, HbA1c, eGFR, and albuminuria) and the neutrophil, lymphocyte, monocyte, and platelet counts used to calculate the inflammatory indices were obtained from laboratory testing performed as part of the same outpatient visit as the clinical and anthropometric assessment.

Obesity Classification

Patients were classified into five categories according to World Health Organization BMI cut-off points [12]: Normal Weight (18.5–24.9 kg/m^2), overweight (25.0–29.9 kg/m^2), Class 1 obesity (30.0–34.9 kg/m^2), Class 2 obesity (35.0–39.9 kg/m^2), and Class 3 obesity (≥40.0 kg/m^2).

Calculation of the SCORE2-DM Cardiovascular Risk Score

Ten-year CVD risk was calculated using the SCORE2-Diabetes algorithm [5], which is recommended for clinical use in the 2023 ESC Guidelines on the management of CVD in patients with diabetes. In addition to conventional risk factors (age, sex, smoking status, systolic blood pressure, and total and HDL cholesterol), this algorithm incorporates diabetes-specific variables, namely, age at diabetes diagnosis, HbA1c, and eGFR, the latter reflecting the well-established independent contribution of impaired renal function to cardiovascular risk [13]. Risk calculation was performed with all patients assigned to the "high-risk" European risk region. Total cholesterol and HDL-C values were entered into the calculator (MDCalc) in mg/dL, and HbA1c values recorded as percentages (%) were converted to mmol/mol before SCORE2-DM calculation. In the descriptive tables, HbA1c is presented as a percentage (%) for clinical readability.

Calculation of Inflammatory Indices

Systemic inflammatory indices were calculated from complete blood count parameters using the following formulas:

NLR = Neutrophil count/Lymphocyte count

PLR = Platelet count/Lymphocyte count

MLR = Monocyte count/Lymphocyte count

SII = (Platelet count × Neutrophil count)/Lymphocyte count

SIRI = (Neutrophil count × Monocyte count)/Lymphocyte count.

Statistical Analysis

Statistical analyses were performed using Jamovi (v2.7) [14] and R (v4.5) [15]. Normality of continuous variables was assessed using the Shapiro–Wilk test. Normally distributed variables were expressed as mean±standard deviation (mean ± standard deviation), non-normally distributed variables as median (minimum-maximum), and categorical variables as number (%). The Kruskal–Wallis test was used to compare SCORE2-DM scores across the five obesity classes; when the omnibus test was significant, the Dwass-Steel-Critchlow-Fligner test was planned for pairwise *post hoc* comparisons. The Mann–Whitney U-test was used for the two-group comparison between sexes, with rank-biserial correlation reported as the effect-size estimate. Relationships between SCORE2-DM and demographic, clinical, laboratory, and inflammatory index parameters were assessed using Spearman correlation analysis. These correlation analyses were exploratory, and no formal adjustment for multiple comparisons was applied; marginal p-values were therefore interpreted cautiously. No formal a priori sample-size calculation was performed. A sensitivity analysis based on the available sample (n=100), a two-sided $\alpha=0.05$, and 80% power indicated that correlation magnitudes of approximately $|r|\geq 0.28$ could be detected under standard correlation-test assumptions; smaller associations may therefore have remained undetected. A two-sided $p<0.05$ was considered statistically significant for the exploratory analyses.

Table 1. Distribution of patients according to obesity class (n=100)

Obesity class	Percentage
Normal weight	13.0
Overweight	36.0
Class 1 obesity	35.0
Class 2 obesity	12.0
Class 3 obesity	4.0

RESULTS

Descriptive Statistics

A total of 100 participants were included in the study. Of these, 50 (50%) were men and 50 (50%) were women. Active smoking was present in 33% (n=33) of the participants. All patients were classified within the "high-risk" SCORE2 risk region. The distribution of participants according to obesity classification is presented in Table 1.

Baseline demographic, clinical, laboratory, and inflammatory index characteristics are summarized in Table 2.

Comparison of the SCORE2-DM Score between Groups

SCORE2-DM scores did not differ significantly across obesity classes (Normal Weight, Overweight, Class 1, Class 2, and Class 3 Obesity) (χ^2=5.39, df=4, p=0.250, ε^2=0.054). As the omnibus test was not significant, *post hoc* pairwise comparisons were not performed. Similarly, the Mann–Whitney U-test showed no significant difference in SCORE2-DM scores between men and women (U=1289.5, p=0.788), with a negligible rank-biserial effect size (r_rb=0.032).

Correlation Analyses

Exploratory relationships between the SCORE2-DM score and demographic, clinical, laboratory, and inflammatory index findings were assessed using Spearman correlation analysis. The results are summarized in Table 3. Because no formal multiplicity adjustment was applied, marginal p-values should be interpreted cautiously.

Regarding demographic parameters and algorithm components, SCORE2-DM showed a strong positive correlation with age (rho=0.621, p<0.001) and positive correlations with smoking status (rho=0.324, p=0.001) and systolic blood pressure (rho=0.230, p=0.021). These associations are expected because age, smoking status, and systolic blood pressure are direct inputs to the SCORE2-DM algorithm and, therefore, represent mathematical coupling rather than independent validation findings. A positive correlation was also observed with age at diabetes diagnosis (rho=0.338, p<0.001), another direct algorithm input. Diabetes duration,

Table 2. Demographic, clinical, laboratory, and inflammatory index characteristics of the participants (n=100)

Variable	Mean±SD / Median (min–max)
Age (years)†	50 (40–67)
Smoking, n (%)	33 (33.0)
Systolic BP (mmHg)†	130 (90–180)
Diastolic BP (mmHg)†	80 (65–110)
Waist circumference (cm)	104.2±8.8
Height (cm)	165.2±10.1
Weight (kg)	82.5±13.3
BMI (kg/m²)†	30.0 (21.8–45.0)
Diabetes duration (years)†	7 (1–20)
Age at diabetes diagnosis (years)	44.4±7.0
Total cholesterol (mg/dL)†	199 (96–453)
HDL-C (mg/dL)†	42 (20–76)
HbA1c (%)†	7.9 (6.2–14.9)
eGFR (mL/min/1.73 m²)†	97 (47–139)
Albuminuria (mg/g)†	17 (2–278)
Neutrophil (10³/µL)†	4.69 (2.20–10.70)
Platelet (10³/µL)†	262.5 (148.0–726.0)
Lymphocyte (10³/µL)†	2.66 (1.40–5.20)
Monocyte (10³/µL)†	0.48 (0.22–1.05)
SII†	499.2 (196.0–1908.3)
SIRI†	0.84 (0.33–2.24)
NLR†	1.78 (0.62–4.50)
MLR†	0.18 (0.10–0.37)
PLR†	102.6 (40.0-251.0)
SCORE2-DM (%)†	12.1 (2.8–40.2)

†Median (minimum-maximum) values are presented for variables that did not follow a normal distribution according to the Shapiro–Wilk test. BP: Blood pressure; BMI: Body mass index; HDL-C: High-density lipoprotein cholesterol; eGFR: Estimated glomerular filtration rate; SII: Systemic immune-inflammation index; SIRI: Systemic inflammation response index; NLR: Neutrophil-to-lymphocyte ratio; MLR: Monocyte-to-lymphocyte ratio; PLR: Platelet-to-lymphocyte ratio; SD: Standard deviation; SCORE2-DM: SCORE2-Diabetes mellitus; HbA1c: Glycated hemoglobin.

TABLE 3. Spearman correlation results between the SCORE2-DM score and the parameters examined

Parameter	rho	p
Age	0.621	<0.001*
Smoking	0.324	0.001*
Systolic blood pressure	0.230	0.021*
Diastolic blood pressure	0.089	0.381
Diabetes duration	0.291	0.003*
Age at diabetes diagnosis	0.338	<0.001*
Waist circumference	-0.042	0.679
BMI	-0.214	0.032*
Total cholesterol	0.227	0.023*
HDL-C	-0.174	0.083
HbA1c	0.338	<0.001*
eGFR	-0.223	0.026*
Albuminuria	0.088	0.384
Neutrophil	-0.100	0.322
Platelet	-0.171	0.089
Lymphocyte	-0.017	0.865
Monocyte	-0.028	0.780
SII	-0.109	0.279
SIRI	-0.041	0.684
NLR	-0.051	0.616
MLR	0.020	0.844
PLR	-0.031	0.756

*: P<0.05 (unadjusted). Correlation analyses were exploratory, and no formal correction for multiple comparisons was applied. BMI: Body mass index; HDL-C: High-density lipoprotein cholesterol; eGFR: Estimated glomerular filtration rate; SII: Systemic immune-inflammation index; SIRI: Systemic inflammation response index; NLR: Neutrophil-to-lymphocyte ratio; MLR: Monocyte-to-lymphocyte ratio; PLR: Platelet-to-lymphocyte ratio; SCORE2-DM: SCORE2-Diabetes mellitus; eGFR: Estimated glomerular filtration rate; HbA1c: Glycated hemoglobin.

which is not entered separately into SCORE2-DM, was positively correlated with the score (rho=0.291, p=0.003); however, this should be interpreted cautiously because diabetes duration is mathematically related to current age and age at diabetes diagnosis. BMI showed an exploratory weak inverse correlation with SCORE2-DM (rho=-0.214, p=0.032). eGFR was inversely correlated with SCORE2-DM (rho=-0.223, p=0.026), as expected because eGFR is a direct component of the algorithm. No significant relationship was found with diastolic blood pressure (p=0.381) or waist circumference (p=0.679).

Regarding laboratory findings, SCORE2-DM was positively correlated with total cholesterol (rho=0.227, p=0.023) and HbA1c (rho=0.338, p<0.001). Because both variables are directly incorporated into the SCORE2-DM algorithm, these correlations are expected and should not be interpreted as independent validation findings. No statistically significant correlation was found between SCORE2-DM and HDL-C, albuminuria, neutrophil, platelet, lymphocyte, or monocyte values (p>0.05 for all parameters).

Regarding inflammatory indices, no statistically significant correlation was found between the SCORE2-DM score and any of the inflammatory indices studied (SII, SIRI, NLR, MLR, PLR) (p=0.279, p=0.684, p=0.616, p=0.844, and p=0.756, respectively).

DISCUSSION

In this retrospective cross-sectional study of 100 patients with T2DM aged 40–69 years and free of established ASCVD, we evaluated the relationship between the SCORE2-DM cardiovascular risk score and degree of obesity, sex, clinical and laboratory parameters, and hematologic systemic inflammatory indices. The main findings were that SCORE2-DM did not differ significantly according to BMI-defined obesity class or sex; correlations with variables directly incorporated into SCORE2-DM were observed as expected because of mathematical coupling; diabetes duration was positively associated with the score but is mathematically related to age and age at diagnosis; BMI showed an exploratory weak inverse correlation with SCORE2-DM; and none of the inflammatory indices studied showed a significant cross-sectional association with SCORE2-DM.

The absence of statistically significant differences in SCORE2-DM scores between sexes or across BMI-defined obesity classes should not be interpreted as statistical independence. SCORE2-DM is a composite algorithm that incorporates sex, age, smoking status, systolic blood pressure, total and HDL cholesterol, age at diabetes diagnosis, HbA1c, and eGFR [5]; consequently, group-level score distributions reflect the combined distribution of these inputs. A recent retrospective study of 203 individuals with obesity reported that Framingham cardiovascular risk scores were correlated with several anthropometric and metabolic variables, including waist circumference, blood pressure, glycemic measures, and lipid parameters, further illustrating the multifactorial nature of cardiovascular risk estimation in obesity [16].

The observed correlations between SCORE2-DM and HbA1c, total cholesterol, systolic blood pressure, age, smoking status, age at diabetes diagnosis, and eGFR are expected because these variables are direct inputs to the SCORE2-DM calculation [5]. Although these variables are well-established cardiovascular risk factors in T2DM [17–21], their correlations with a score that mathematically incorporates them do not constitute independent validation findings and should not be interpreted as demonstrating independent effects within the present dataset. This distinction is particularly important when interpreting the associations with HbA1c, total cholesterol, and systolic blood pressure.

An exploratory weak inverse correlation was observed between BMI and SCORE2-DM (rho=−0.214, unadjusted p=0.032). This finding requires substantial caution because 22 correlation tests were examined without formal adjustment for multiple comparisons and no cardiovascular outcome data were available. Although inverse associations between BMI and outcomes, often termed the "obesity paradox," have been reported in some chronic disease populations [7, 8], the present cross-sectional association with a calculated risk score does not constitute evidence of an obesity paradox. The result may instead reflect confounding by the distribution of age, age at diabetes diagnosis, smoking status, or other SCORE2-DM inputs, as well as the limitations of BMI as a measure of adiposity [22, 23]. Accordingly, this marginal finding should be regarded as hypothesis-generating and requires confirmation in larger longitudinal cohorts with actual cardiovascular outcomes.

The positive correlation between age at diabetes diagnosis and SCORE2-DM (rho=0.338, p<0.001) is expected because age at diagnosis is a direct input to the SCORE2-DM algorithm [5]. It therefore reflects mathematical coupling rather than an independent discovery. Diabetes duration is not entered as a separate variable in SCORE2-DM; however, it is mathematically related to current age and age at diabetes diagnosis (diabetes duration = current age − age at diagnosis). Thus, although diabetes duration was positively correlated with the score (rho=0.291, p=0.003), this association may partly reflect the mathematical structure of the algorithm and should not be interpreted as an independent validation finding.

Previous studies have suggested that hematologic indices such as NLR, SII, SIRI, MLR, and PLR may be associated with cardiovascular events or mortality in populations with diabetes [9–11]. In the present study, none of these indices showed a significant cross-sectional association with SCORE2-DM. This apparent difference in findings likely reflects the different outcome constructs: Previous studies primarily evaluated actual clinical outcomes, whereas our analysis examined association with a calculated risk score. Importantly, the absence of a cross-sectional association with SCORE2-DM does not establish that these inflammatory indices lack prognostic or predictive value, nor does it determine whether they provide incremental prognostic information beyond SCORE2-DM. Such questions require longitudinal studies incorporating cardiovascular events or mortality. The limited sample size may also have reduced the ability to detect associations of small magnitude.

The strengths of our study include the evaluation of a current, diabetes-specific risk score (SCORE2-DM) together with a comprehensive set of parameters in a clearly defined T2DM population. The study also has several limitations. Its single-center, retrospective cross-sectional design precludes causal or prognostic inference, and actual cardiovascular events or mortality were not assessed. The sample size was relatively limited (n=100), no formal a priori sample-size calculation was performed, and the sensitivity analysis indicates that smaller correlations may have remained undetected. The intentionally sex-balanced sample (50 women and 50 men) does not reflect the natural sex distribution of the source outpatient population and may limit representativeness. In addition, the Class 3 obesity subgroup included only four participants, which substantially limits the power and stability of comparisons across the five BMI categories. All patients were assigned to a single European risk region ("high risk"), and the exploratory correlation analyses were conducted without formal correction for multiple comparisons. Finally, BMI-based obesity classification provides limited information about visceral fat distribution and body composition; although waist circumference was available, more sensitive anthropometric or imaging-based measures of adiposity were not included.

Conclusion

In this retrospective cross-sectional T2DM cohort, SCORE2-DM did not differ significantly according to BMI-defined obesity class or sex, and the CBC-derived inflammatory indices studied (SII, SIRI, NLR, MLR, and PLR) showed no significant cross-sectional association with the score. Correlations between SCORE2-DM and variables incorporated into its calculation are expected because of mathematical coupling and should

not be interpreted as independent validation findings. The exploratory weak inverse association between BMI and SCORE2-DM should be interpreted cautiously because multiple correlations were examined without formal multiplicity adjustment and the smallest obesity subgroup was limited. Because actual cardiovascular outcomes were not assessed, no conclusions can be drawn regarding the prognostic, predictive, or incremental value of the inflammatory indices beyond SCORE2-DM. Larger longitudinal studies incorporating cardiovascular events and mortality are needed to address these questions.

Ethics Committee Approval: This study was approved by The Scientific Research Ethics Committee of the University of Health Sciences, Umraniye Training and Research Hospital, Republic of Turkiye Ministry of Health (Date: 18.12.2025; Decision no. 472).

Informed Consent: Study-specific written informed consent was not obtained because this was a retrospective study based on existing medical records. The study protocol was reviewed and approved by the institutional ethics committe.

Conflict of Interest: The authors declare that there is no conflict of interest.

Financial Disclosure: The authors declared that this study received no financial support.

Use of AI for Writing Assistance: During the preparation of this manuscript, the authors used ChatGPT for language editing and academic phrasing support.

Authorship Contributions: Concept – SE; Design – MT, SE; Supervision – MT; Materials – SE; Data Collection and/or Processing – MT; Analysis and/or Interpretation – SE; Literature Search – MT; Writing – MT; Critical Reviews – MT.

Peer-review: Externally peer-reviewed.

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