

The triglyceride-glucose index as a predictive marker for coronary slow flow phenomenon

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Abstract. – OBJECTIVE: The triglyceride-glucose index (TyG) has been proposed as a marker of insulin resistance (IR) and has shown associations with cardiovascular diseases. This study aimed to investigate the relationship between the TyG and the coronary slow flow phenomenon (CSFP) and explore the index's potential as a predictor of this condition.

PATIENTS AND METHODS: A total of 187 patients who underwent coronary angiography were included; of these, 91 patients were diagnosed with CSFP, and 96 patients with normal coronary flow served as a control group. The TyG was calculated using fasting triglyceride and glucose levels.

RESULTS: The results showed that the TyG was significantly higher in the CSFP group compared with the control group ($p < 0.001$). Additionally, the TyG exhibited a moderate positive correlation with the thrombolysis-in-myocardial-infarction frame count in coronary arteries ($p < 0.001$). A multivariate logistic regression analysis revealed that the TyG, along with gender, ejection fraction, and uric acid, remained significant predictors of CSFP ($p < 0.05$).

CONCLUSIONS: This study's findings suggest that the TyG may serve as a useful marker for identifying individuals at risk of CSFP and provide insights into the potential role of IR in its pathophysiology.

Key Words:

Coronary slow flow, Triglyceride-glucose index, Insulin resistance.

out occlusion of the epicardial coronary arteries. Despite its relatively benign nature, CSFP has been associated¹⁻³ with adverse cardiovascular outcomes, including recurrent angina, myocardial infarction, and cardiac arrhythmias. The etiopathogenesis of CSFP remains poorly understood, and there is a growing interest²⁻⁴ in identifying novel biomarkers and predictors of this condition.

Insulin resistance (IR), a key pathophysiological feature of metabolic syndrome and type 2 diabetes mellitus, has been implicated⁴ in the development and progression of various cardiovascular diseases (CVDs). The triglyceride-glucose index (TyG), a composite marker derived from fasting triglyceride and glucose levels, has emerged as a proxy measure of IR. Several studies⁵⁻⁷ have demonstrated the clinical utility of the TyG in predicting IR, metabolic syndrome, and cardiovascular risk.

To date, little research in literature has been done on the association between the TyG and CSFP. Understanding the potential link between IR and CSFP could provide valuable insights into the underlying mechanisms and aid in risk stratification and targeted management strategies for patients with CSFP⁸.

This study aimed to evaluate the TyG in patients with CSFP and investigate its predictive value for diagnosing the phenomenon.

Introduction

The coronary slow flow phenomenon (CSFP) is a microvascular disorder characterized by the slow progression of contrast media into distal vasculature during coronary angiography with-

Patients and Methods

This retrospective study included a total of 187 patients, of which 91 patients were diagnosed with coronary slow flow (CSF) and 96 patients with normal coronary flow (NCF), selected from

the medical records of a tertiary care center between October 2020 and September 2022. The indications for coronary angiography were determined in accordance with the European Society of Cardiology (ESC) guidelines, which consider various factors, such as symptoms, electrocardiographic findings, and the presence of significant risk factors. Treatment was administered to the patients according to the current ESC guidelines^{9,10}. Appropriate medications and interventions were prescribed based on each patient's condition and risk profile as determined by the attending physicians.

Exclusion Criteria

The study implemented a set of exclusion criteria to ensure the integrity of the research findings. Patients who met any of the following criteria were excluded from the study: (1) individuals who developed CSF as a result of percutaneous coronary angioplasty following myocardial infarction or coronary bypass surgery; (2) indi-

viduals with significant organic valvular heart disease, congestive heart failure, congenital heart disease, atrial fibrillation, hypo/hyperthyroidism, or any connective tissue disorder; (3) individuals diagnosed with hematological diseases; (4) individuals with autoimmune or neoplastic diseases; (5) individuals with severe chronic renal insufficiency; (6) individuals with severe hepatic insufficiency; and/or (7) individuals with active infections. A total of 1,246 patients were excluded from the study based on these criteria. Figure 1 presents the flow diagram of the study, depicting the inclusion and exclusion criteria, as well as the number of patients at each stage of the research process.

Ethical approval was obtained from the institutional review board. This study was approved by the ethics committee of Başakşehir Cam and Sakura City Hospital (date: 09/14/2023, decision No.: KAEK/13.09.2023.399).

Clinical, demographic, and biochemical data were collected from the medical records of the in-

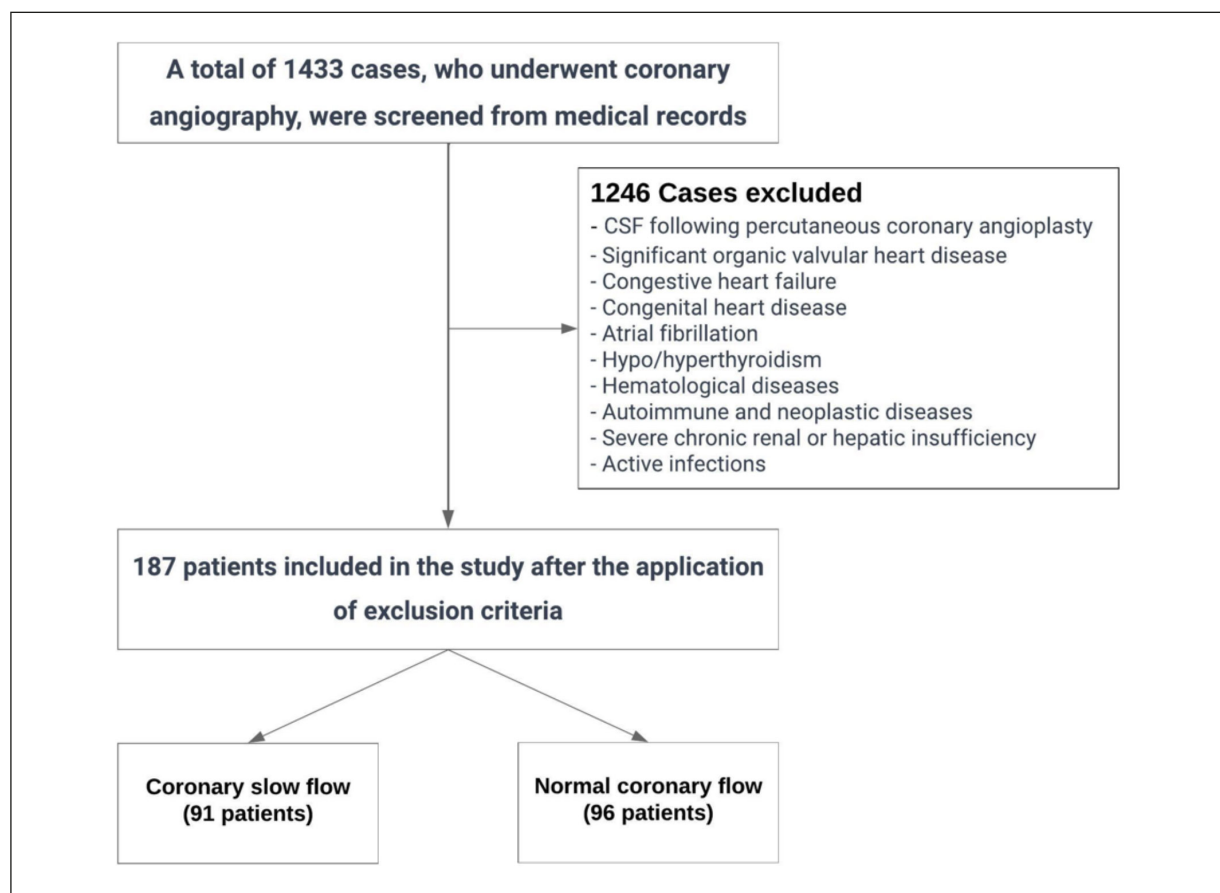


Figure 1. The flow diagram of the study.

cluded patients. Fasting glucose and triglyceride levels were measured using standard laboratory techniques. The TyG was calculated using the following formula: $TyG = \ln [\text{fasting triglycerides (mg/dL)} \times \text{fasting glucose (mg/dL)} / 2]$.

Coronary Angiography and Thrombolysis-In-Myocardial-Infarction Frame Count

Coronary angiography was performed according to the current guidelines^{9,10}. Coronary slow flow is defined angiographically as the presence of thrombolysis-in-myocardial-infarction (TIMI)-2 flow in at least one major epicardial artery in the absence of ischemic provocative maneuvers, such as angioplasty, in coronary arteries that are normal or near normal¹¹. The TIMI frame count (TFC), which represents the number of frames required for a contrast agent to reach the distal end of the left anterior descending (LAD) coronary artery, was adopted as a numerical variable for the more objective evaluation of coronary blood flow. The frame in which the contrast agent entered the coronary artery was considered the first frame, and the frame in which the contrast agent reached the distal end of the LAD coronary artery was considered the last frame. The difference between the last and first frames was calculated to determine the TFC. The distal bifurcation of the LAD, known as the “mustache” of the LAD, the distal bifurcation of the responsible longest branch for the left circumflex artery (LCx), and the point where the first lateral branch of the posterolateral artery emerged from the right coronary artery (RCA) were identified. From the measurements, it was observed that the LAD was, on average, 1.7 times longer than the RCA and the LCx. To account for this difference, the calculated LAD frame count (FC) was divided by 1.7, resulting in a corrected LAD TFC¹².

Statistical Analysis

Statistical analyses were performed using Statistical Package for the Social Sciences 25.0 for Windows (IBM Corp., Armonk, NY, USA) software. The normality of the data was assessed using the Kolmogorov-Smirnov test. Normally distributed variables were reported as the mean \pm standard deviation, while non-normally distributed variables were reported as the median and the interquartile range. Categorical variables were presented as percentages. Differences in categorical variables between groups were evaluated using the Chi-squared test. Unpaired samples

were compared using either Student's *t*-test or the Mann-Whitney U test as appropriate. Pearson's or Spearman's correlation analysis was used to assess the relationships among variables based on the normality of the data. Univariate and multivariate logistic regression analyses were conducted to identify independent variables associated with CSF. Variables that showed significance in the univariate analysis were included in the multivariate logistic regression analysis using the stepwise method. The results of the univariate and multivariate regression analyses were reported as odds ratios with a 95% confidence interval (CI). Receiver operating characteristic curves were generated, and the optimal cutoff values with the highest combined sensitivity and specificity for predicting slow coronary flow were determined. Statistical significance was considered at a two-sided *p*-value < 0.05 .

Results

The results of this study revealed significant differences between the demographic and clinical characteristics of patients with CSF and those with NCF (Table I). The mean age of the CSF group was 51.5 ± 9.6 years, while it was 50.6 ± 9.9 years in the NCF group. The difference in age between the two groups was not statistically significant ($p = 0.514$). The patients with CSF had a higher prevalence of being male (79.1% vs. 40.6%, $p < 0.001$) and a smoker (64.8% vs. 39.6%, $p = 0.001$) compared with those with NCF. Additionally, the patients with CSF exhibited lower ejection fraction (EF) values ($57.0 \pm 5.0\%$ vs. $62.0 \pm 5.4\%$, $p < 0.001$) compared with the patients with NCF. Regarding medical history, there were no significant differences in the prevalence of diabetes mellitus and hypertension between the two groups. However, hyperlipidemia was more common in the patients with CSF compared with those with NCF (65.9% vs. 42.7%, $p = 0.001$).

In terms of treatment, the use of beta-blockers (16.5% vs. 5.2%, $p = 0.017$) and acetylsalicylic acid (24.2% vs. 11.5%, $p = 0.023$) was significantly higher in the patients with CSF compared with those with NCF. However, there was no significant difference in the use of angiotensin-converting enzyme inhibitors/angiotensin-receptor blockers between the two groups.

The laboratory findings revealed significantly higher fasting glucose levels (113.0 ± 43.8 mg/dL

Table I. Demographic and clinical characteristics of the study population.

Parameters	Patients with coronary slow flow (n = 91)	Patients with normal coronary flow (n = 96)	p-value
Age (years)	51.5 ± 9.6	50.6 ± 9.9	0.514
Male, n (%)	72 (79.1)	39 (40.6)	< 0.001
Smoker, n (%)	59 (64.8)	38 (39.6)	0.001
Ejection fraction, %	57.0 ± 5.0	62.0 ± 5.4	< 0.001
Medical history, n (%)			
Diabetes mellitus	7 (7.7)	5 (5.2)	0.488
Hypertension	14 (15.6)	13 (13.5)	0.697
Hyperlipidemia	60 (65.9)	41 (42.7)	0.001
Treatment, n (%)			
Beta blocker	15 (16.5)	5 (5.2)	0.017
ACE-I/ARB	10 (11)	14 (14.6)	0.463
Acetylsalicylic acid	22 (24.2)	11 (11.5)	0.023
Laboratory findings			
Fasting glucose (mg/dl)	113.0 ± 43.8	93.0 ± 23.6	< 0.001
Triglyceride/glucose index	5.0 ± 0.2	4.3 ± 0.6	< 0.001
Triglyceride (mg/dl)	210.4 ± 90.1	110.1 ± 30.3	< 0.001
AST (IU/L)	24.8 ± 9.2	24.4 ± 10.3	0.754
ALT (IU/L)	26.0 ± 9.9	23.8 ± 11.1	0.186
Uric acid (mg/dl)	5.8 ± 0.8	4.2 ± 0.7	< 0.001
Creatinine (mg/dL)	0.8 ± 0.1	0.8 ± 0.2	0.443
Sodium (mEq/L)	139.5 ± 2.7	138.8 ± 2.9	0.125
Potassium (mEq/L)	4.4 ± 0.4	4.3 ± 0.4	0.357
Total cholesterol (mg/dl)	208.0 ± 40.7	191.7 ± 46.5	0.016
LDL cholesterol (mg/dl)	124.9 ± 34.3	110.0 ± 37.8	0.008
HDL cholesterol (mg/dl)	34.5 ± 5.5	43.5 ± 10.8	< 0.001
Hemoglobin (g/dL)	14.6 ± 1.6	13.7 ± 1.9	0.001
Angiographic data			
LAD FC	43.5 ± 5.8	31.2 ± 2.0	< 0.001
LCX FC	29.3 ± 4.1	21.4 ± 1.6	< 0.001
RCA FC	30.0 ± 7.4	19.5 ± 1.8	< 0.001

LAD, left anterior descending; CX, CX circumflex artery; RCA, right coronary, ACE-I, angiotensin-converting enzyme inhibitor; ARB, angiotensin-receptor blockers; AST, aspartate aminotransferase; ALT, alanine aminotransferase; LDL, low-density lipoprotein; HDL, High-density lipoprotein; LAD, left anterior descending artery; LCX, circumflex artery; RCA, right coronary artery; FC, corrected TIMI frame count.

vs. 93.0 ± 23.6 mg/dL, $p < 0.001$), TGIs (5.0 ± 0.2 vs. 4.3 ± 0.6, $p < 0.001$), triglyceride levels (210.4 ± 90.1 mg/dL vs. 110.1 ± 30.3 mg/dL, $p < 0.001$), and uric acid levels (5.8 ± 0.8 mg/dL vs. 4.2 ± 0.7 mg/dL, $p < 0.001$) in the patients with CSF compared with those with NCF. However, there were no significant differences in AST, ALT, creatinine, sodium, and potassium levels between the two groups.

Furthermore, the patients with CSF had higher levels of total cholesterol (208.0 ± 40.7 mg/dL vs. 191.7 ± 46.5 mg/dL, $p = 0.016$) and low-density lipoprotein (LDL) cholesterol (124.9 ± 34.3 mg/dL vs. 110.0 ± 37.8 mg/dL, $p = 0.008$) compared with the patients with NCF. In contrast, the patients with NCF had higher levels of high-density lipoprotein (HDL) cholesterol (43.5 ± 10.8 mg/dL vs. 34.5 ± 5.5 mg/dL, $p < 0.001$)

and hemoglobin (13.7 ± 1.9 g/dL vs. 14.6 ± 1.6 g/dL, $p = 0.001$) compared with the patients with CSF.

The angiographic data showed significantly higher corrected TFC values in the LAD (43.5 ± 5.8 vs. 31.2 ± 2.0, $p < 0.001$), LCx (29.3 ± 4.1 vs. 21.4 ± 1.6, $p < 0.001$), and RCA (30.0 ± 7.4 vs. 19.5 ± 1.8, $p < 0.001$) in the patients with CSF compared with those with NCF.

The predictors of slow coronary flow were identified through logistic regression using both univariate and multivariate analyses. The results of the logistic regression analyses for the predictors of slow coronary flow are presented in Table II. The variables examined included age, gender, smoking status, EF, TyG, uric acid, and hemoglobin. The univariate analysis showed significant associations between slow coronary flow

Table II. Univariate and multivariate logistic regression analyses of predictors of slow coronary flow.

Parameters	Univariate			Multivariate		
	OR	95% CI	p	OR	95% CI	p
Age	1.009	0.980-1.039	0.552			
Gender	5.538	2.894-10.600	< 0.001	0.451	0.206-0.782	0.005
Smoke	2.814	1.554-5.095	0.001	1.500	0.188-11.949	0.702
EF	0.834	0.781-0.889	< 0.001	0.769	0.626-0.946	0.013
TG/glucose index	9.956	3.459-18.868	< 0.001	11.219	2.387-20.290	< 0.001
Uric acid	9.361	5.043-17.376	< 0.001	7.767	2.776-19.755	0.001
Hemoglobin	1.323	1.111-1.575	0.002	0.851	0.369-1.960	0.704

EF, ejection fraction; TG, triglyceride.

Table III. Demographic and clinical characteristics of the study population.

	Spearman	LAD-FC	LCX-FC	RCA-FC
TG/G index	<i>r</i>	0.448	0.437	0.437
	<i>p</i>	< 0.001	< 0.001	< 0.001

TG/G, triglyceride/glucose index; LAD, left anterior descending artery; LCX, circumflex artery; RCA, right coronary artery; FC, corrected TIMI frame count.

and gender, smoking, EF, TyG, uric acid, and hemoglobin. In the multivariate analysis, gender, EF, TyG, and uric acid remained significant predictors of slow coronary flow (Table II).

As shown in Table III, Pearson’s correlation indicated a moderate positive correlation between the TyG and the LAD-FC, LCx-FC, and RCA-FC.

The area under the curve for the TyG variable in predicting CSF was 0.951 ($p < 0.001$, 95% CI: 0.923-0.980). The sensitivity and specificity values of the TyG cutoff value at 4.76 were 88% and 89%, respectively (Figure 2).

Discussion

This study aimed to evaluate the importance of the TyG in patients with CSFP. The main findings of the study are as follows: i) the TyG was significantly higher in patients with CSF compared with those with NCF (5.0 ± 0.2 vs. 4.3 ± 0.6 , $p < 0.001$); ii) there was a moderate positive correlation observed between the TyG and the TFC in the coronary arteries; iii) the multivariate analysis revealed that gender, EF, TyG, and uric acid were significant predictors of slow coronary flow.

Increasing evidence supports the significant contribution of IR to the pathogenesis of CVDs, with the TyG emerging as a valuable tool for assessing IR. Several studies¹³⁻¹⁶ have investigated

the relationship between the TyG and outcomes such as coronary artery disease, myocardial infarction, hypertension, and metabolic syndrome. These studies¹³⁻¹⁶ have consistently demonstrated

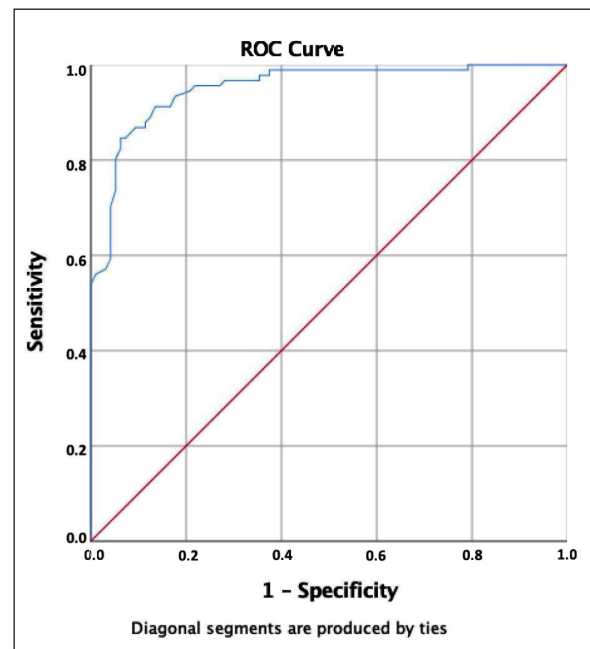


Figure 2. Receiver Operating Characteristic (ROC) curves illustrating the predictive ability of the TG/G index variable for coronary slow flow.

that elevated TyG levels are associated with an increased risk of cardiovascular events and adverse cardiac outcomes.

Recently, three studies^{8,17,18} have examined the relationship between the TyG and CSF. Yuksel and Yildiz¹⁷ conducted a study to evaluate the TyG in patients with CSFP. They compared the TyG values of patients with CSFP with those of patients with normal coronary arteries. The study found that the TyG was higher in patients with CSFP compared with those with NCF. Additionally, the TyG showed a positive correlation with the TFC and various biochemical variables. The authors concluded that IR may play a role in CSFP.

Kaplangoray et al¹⁸ conducted a retrospective case-control study to investigate the relationship between the TyG and CSF. They compared the TyG values of patients with CSF with those of patients with NCF. The study found that the TyG, LDL, body mass index (BMI), and neutrophil-to-lymphocyte ratio (NLR) were higher in the CSF group, although HDL levels were significantly lower. A correlation analysis showed a strong correlation between CSF and the TyG. The study also identified the TyG, BMI, NLR, and male gender as independent predictors for CSF. The authors concluded that there is a significant relationship between CSF and the TyG.

Buber et al⁸ aimed to assess the TyG with respect to CSF. The study retrospectively evaluated patients who underwent coronary angiography and detected 72 patients with CSF. Compared with the control group, the CSF group showed significantly higher glucose levels, TyG, and triglyceride levels. However, there was no statistically significant correlation between the TyG and the TFC of specific coronary arteries. A multiple logistic model analysis indicated that the TyG was statistically significant for the risk of CSF. The authors concluded that the TyG was higher in the CSF group but did not predict the severity of slow coronary flow.

The present study's findings revealed that the TyG was significantly higher in the CSFP group compared with the NCF group. In the multivariate analysis, gender, EF, TyG, and uric acid were identified as significant predictors of slow coronary flow. Additionally, a positive correlation was observed between the TyG and the TFC.

The TyG has been implicated in the pathophysiology of CSFP through potential mechanisms involving IR and endothelial dysfunction^{19,20}. Insulin resistance, characterized by impaired insulin signaling and increased insulin levels, leads to the

dysregulation of glucose and lipid metabolism. Elevated triglyceride levels and impaired glucose utilization contribute to systemic inflammation, oxidative stress, and endothelial dysfunction^{21,22}. These processes can result in abnormal vascular tone, reduced nitric oxide bioavailability, and increased vascular resistance, ultimately leading to impaired coronary microcirculation and the development of CSFP. Furthermore, an elevated TyG has been associated with increased levels of inflammatory markers and prothrombotic factors, further exacerbating the pathological processes in CSFP. However, further research is needed to fully elucidate the complex pathophysiological mechanisms underlying the association between TyG and CSFP.

The present study has significantly contributed to advancing understanding in this field by highlighting a strong association between the TyG and CSF. An elevated TyG index, along with a positive correlation with the TFC, indicates a potential link to IR in the pathophysiology of CSF. Moreover, this study enhances the current literature, building upon the works of Yuksel and Yildiz¹⁷, Kaplangoray et al¹⁸, and Buber et al⁸. While these studies have explored the association between TyG and CSFP, the present study goes further by identifying gender, left ventricular EF, TyG, and uric acid as key predictors of CSF via multivariate analysis. This nuanced approach improves risk stratification and offers valuable insights for targeted management in patients with CSF.

Limitations

The limitations of this study include its retrospective design, single-center nature, and reliance on medical records for data collection. Additionally, the study's findings may not be generalizable to the broader population, and further prospective studies are required to validate the results.

Conclusions

This study identified a significant association between the TyG and CSFP. The TyG may serve as a marker or predictor of CSFP and could be linked to IR. These findings suggest a possible role of the TyG in the pathophysiology of CSFP and highlight its potential as a valuable tool in the evaluation of CVDs. Further research is needed to better understand the relationship between the TyG and CSFP and determine the clinical utility of this index in practice.

Conflict of Interest

All the authors declare no conflict of interest.

Informed Consent

Not applicable due to the retrospective design of the study.

Ethics Approval

The study was approved by the Ethics Committee of Başakşehir Cam and Sakura City Hospital (date: 09/14/2023, decision No.: KAEK/13.09.2023.399), and conducted following the Helsinki Declaration and its latest amendments.

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Availability of Data and Materials

The datasets of the current study are available upon reasonable request.

Authors' Contributions

All authors contributed to one or more of the following steps: the design of the study, data acquisition, analysis and interpretation of data, drafting or revising the article, and final approval of the manuscript to be published.

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