



THE ROLE OF THE MACRUZ INDEX IN STROKE PATIENTS: PREDICTIVE VALUE AND ATRIAL REMODELING

İNME HASTALARINDA MACRUZ İNDEKSİNİN ROLÜ: TAHMİN DEĞERİ VE ATRİYAL REMODELİNG

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ABSTRACT

Introduction: Atrial fibrillation (AF) is the most common arrhythmia involved in the etiology of stroke. Even stroke patients without AF, who are in sinus rhythm, may exhibit atrial electrical abnormalities. The Macruz index, which is the focus of our study, is defined on electrocardiography (ECG) as the ratio of the P-wave duration to the PQ (PR) segment duration and is normally considered to be within the range of approximately 0.9–1.1. A value above 1.1 is associated with atrial conduction disturbance or left atrial enlargement, whereas a value below 0.9 suggests prolongation of the PQ segment or shortening of the P-wave. The Macruz index is a surface ECG marker that reflects atrial conduction delay and enlargement. Clinically, it is an important parameter used to predict the risk of atrial fibrillation development, to assess atrial enlargement, to determine the prognosis of cardiovascular diseases such as hypertension and stroke, and to detect atrial conduction disorders. This study aimed to investigate the clinical significance of the Macruz index in stroke patients with normal sinus rhythm.

Methods: Between April 15, 2025, and September 15, 2025, 89 stroke patients who were hospitalized in the neurology department of Gazi Yaşargil Training and Research Hospital, received cardiology consultations, and showed no AF on 24-hour Holter monitoring (sinus rhythm) were included in the study. For the control group, 106 patients who presented to the cardiology outpatient clinic during the same period with complaints of palpitations but had sinus rhythm on their admission ECGs were included. The ECGs of these patients were reviewed, and their Macruz indexes were calculated. Clinical, laboratory, and electrocardiographic data were compared. Regression analyses were performed to determine independent predictors.

Results: Stroke patients had a significantly higher Macruz index compared with the control group (1.9 ± 0.8 vs. 1.2 ± 0.5 , $p < 0.001$). In multivariable analysis, age ($\beta = 0.010$, $p = 0.040$) and neutrophil-to-lymphocyte ratio (NLR) ($\beta = 0.110$, $p = 0.002$) were independent predictors. HDL cholesterol showed a marginal inverse association ($p = 0.052$).

Conclusions: An elevated Macruz index may reflect atrial remodeling in stroke patients even in the absence of AF. This index may serve as an early indicator of atrial vulnerability and arrhythmogenic potential, suggesting the need for extended rhythm monitoring in this population.

Keywords: Stroke, Macruz Index, Atrial remodeling, Atrial fibrillation, Electrocardiogram, Inflammation

ÖZET

Giriş: Atrial fibrilasyon(AF) inme etyolojisinde yer alan en sık ritm bozukluğudur. AF olmayan inme hastaları, sinus ritminde olsa bile atriyal elektriksel anormallikler olabilmektedir. Çalışmamıza konu olan Macruz indeksi, elektrokardiyografide (EKG) P dalgası süresinin PQ (PR) segmenti süresine oranı olarak tanımlanır ve normalde yaklaşık 0,9-1,1 aralığında kabul edilir. Bu değer 1,1'in üzerinde olması atriyal iletim bozukluğu veya sol atriyum genişlemesi ile ilişkilendirilirken, 0,9'un altında olması PQ segmentinin uzadığını veya P dalgasının kısalacağını düşündürür. Macruz indeksi, atriyal iletim gecikmesini ve genişlemesini yansıtan bir yüzey EKG belirteçidir. Klinik olarak atriyal fibrilasyon gelişme riskinin öngörülmesinde, atriyal büyümenin değerlendirilmesinde, hipertansiyon ve inme gibi kardiyovasküler hastalıkların prognozunun belirlenmesinde ve atriyal iletim bozukluklarının saptanmasında kullanılan önemli bir parametredir. Bu çalışma, normal sinüs ritmine sahip inme hastalarında Macruz indeksinin klinik önemini araştırmayı amaçlamıştır.

Yöntemler: Bu çalışmada 15 Nisan 2025 ve 15 Eylül 2025 tarihleri arasında Gazi Yaşargil Eğitim ve Araştırma Hastanesi'ne inme nedeniyle nöroloji servisine yatmış ve kardiyoloji konsültasyonu istenmiş, 24 saatlik holter monitorizasyonlarında ise AF saptanmamış, normal sinus ritminde 89 inme hastası dahil edilmiştir. Kontrol grubu için ise belirtilen tarihlerde kardiyoloji polikliniğine başvuru nedeniyle başvurmuş, gelişmiş ekg si normal sinus ritminde olan 106 hasta ise kontrol grubu olarak dahil edildi. Bu hastaların EKG leri tarandı ve Macruz indeksleri hesaplandı. Klinik, laboratuvar ve elektrokardiyografik veriler karşılaştırıldı. Bağımsız öngörücüleri belirlemek için regresyon analizleri yapıldı.

Bulgular: İnme hastaları, kontrol grubuyla karşılaştırıldığında önemli ölçüde daha yüksek bir Macruz indeksi saptandı ($1,9 \pm 0,8$ 'e karşı $1,2 \pm 0,5$, $p < 0,001$). Çok değişkenli analizde, yaş ($\beta = 0,010$, $p = 0,040$) ve nötrofil-lenfosit oranı (NLR) ($\beta = 0,110$, $p = 0,002$) bağımsız öngörücülerdi. HDL kolesterol marjinal bir ters ilişki gösterdi ($p = 0,052$).

Sonuç: Yükselen Macruz indeksi, AF yokluğunda bile inme hastalarında atriyal yeniden şekillenmeyi yansıtabilir. Bu indeks, atriyal kırılganlığın ve atriyal ritm bozukluğunun erken bir belirteci olarak kullanılabilir ve bu popülasyonda genişletilmiş ritm takibi ihtiyacını düşündürür.

Anahtar Kelimeler: İnme, Macruz İndeksi, Atrial remodelling, Atrial Fibrilasyon, Elektrokardiyogram, inflamasyon

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INTRODUCTION

Stroke is a major cause of morbidity and mortality worldwide, and AF is one of the most important risk factors for cardioembolic stroke(1).

Atrial fibrillation the most common sustained cardiac arrhythmia, is strongly associated with ischemic stroke through mechanisms involving both large emboli and small vessel pathology(2).

Traditionally linked to cardioembolic stroke due to thrombus formation in the left atrial appendage, AF has also been implicated in small vessel occlusion type stroke.

The association is thought to arise from atrial cardiopathy and microembolization leading to lacunar infarcts, systemic inflammation and endothelial dysfunction that damage cerebral microvascular and shared vascular risk factors such as hypertension, diabetes and aging. Furthermore, many patients initially diagnosed with cryptogenic or cardioembolic stroke are later found to have paroxysmal subclinical AF on prolonged monitoring, suggesting that part of the apparent stroke burden may in fact reflect covert atrial disease(3).

These observations underscore the importance of considering AF not only as a cause of overt cardioembolism but also as a contributor to cerebral small vessel disease, with implications for extended arrhythmia monitoring and anticoagulation strategies. However, even in stroke patients without AF, atrial electrical abnormalities may be present during sinus rhythm, such as atrial conduction delay and prolonged P-wave duration.

The Macruz index, calculated as the ratio of P-wave duration to PR segment duration on a surface EKG, is a simple and non-invasive parameter that reflects atrial conduction properties and structural remodeling. Normally, its value ranges between 0.9 and 1.1; values greater than 1.1 are associated with atrial conduction delay or left atrial enlargement, whereas values below 0.9 suggest prolongation of the PQ segment or shortening of the P-wave(4).

Previous studies have shown that the Macruz index is significantly increased in patients with mitral stenosis and tends to decrease after successful valvuloplasty, highlighting its role as a marker of atrial electrical and structural remodeling(5).

In addition, higher Macruz index values have been associated with an increased risk of atrial fibrillation, suggesting its potential as a prognostic marker beyond traditional echocardiographic measures. Recent evidence also indicates that electrocardiographic indices of atrial remodeling, including the Macruz index, can be integrated into risk prediction models for stroke and AF recurrence(6).

In this context, the present study was designed to evaluate the prognostic role of the Macruz index in stroke patients without documented atrial fibrillation. Specifically, we aimed to investigate the clinical significance of the Macruz index in patients with sinus rhythm and no AF detected on 24-hour Holter monitoring, assessing its potential as an early marker of atrial remodeling and subclinical atrial dysfunction.

METHODS

This retrospective case-control study was conducted at Gazi Yaşargil Training and Research Hospital between April 15 2025, and September 15, 2025. A total of 89 consecutive patients with confirmed ischemic stroke who were hospitalized in the neurology clinic and evaluated with a cardiology consultation were included in the stroke group. All stroke patients were documented to be in sinus rhythm and

had no atrial fibrillation detected on 24-hour Holter monitoring. The control group consisted of 106 patients who presented to the cardiology outpatient clinic with the complaint of palpitations during the same period, also in sinus rhythm and without atrial fibrillation on Holter monitoring.

Inclusion and Exclusion Criteria

Patients aged 18 years or older who had a confirmed diagnosis of ischemic stroke based on imaging findings were included in the stroke group. No formal age- or sex-matching was performed between the stroke and control cohorts; given the older age of the stroke group, multivariable analyses adjusted for age to mitigate confounding. All participants were required to be in sinus rhythm on ECG and to have no evidence of atrial fibrillation on 24-hour Holter monitoring. Only those with complete clinical, laboratory, and electrocardiographic data were eligible for inclusion in the study.

Patients were excluded if they had a prior history of atrial fibrillation or atrial flutter, a previous stroke or transient ischemic attack (TIA), or known heart failure. Those with significant valvular heart disease or left atrial enlargement greater than 45 mm on echocardiography were also excluded. Additional exclusion criteria included severe uncontrolled hypertension, significant carotid or vertebral artery stenosis, malignancy, or the presence of a chronic systemic inflammatory disease.

Data collection and ECG analysis

Demographic, clinical, and laboratory data were obtained from hospital records, including comorbidities such as hypertension, diabetes mellitus, chronic obstructive pulmonary disease (COPD), chronic kidney disease (CKD), and coronary artery disease (CAD). Standard 12-lead ECGs were analyzed by two independent cardiologists blinded to patient data. The P-wave duration and PR segment duration were measured manually, and the Macruz index was calculated as P-wave duration divided by PQ segment duration. All calculations were performed by experienced cardiologist researchers.

Statistical analysis

All statistical analyses were performed using IBM SPSS Statistics, Version 28.0. The distribution of continuous variables was assessed using the Shapiro-Wilk test. Results were expressed as mean $\pm$ standard deviation (SD) for normally distributed data, or median (interquartile range, IQR) for non-normally distributed data.

Categorical variables were presented as counts (percentages). Group comparisons were made using independent samples t-tests or Mann-Whitney U tests for continuous variables, and chi-square or Fisher's exact tests for categorical variables. Univariable linear regression was used to identify factors associated with the Macruz index. Variables with a significance level of $p < 0.10$ were entered into a multivariable linear regression model (backward elimination method) to determine independent predictors. Collinearity was assessed using variance inflation factors (VIF < 5). A two-tailed p -value < 0.05 was considered statistically significant. For the multivariable linear regression, a backward elimination strategy was applied. Multicollinearity was assessed using variance inflation factors (VIF), with all retained variables meeting the criterion of VIF < 5 . Given the retrospective design, no a priori power analysis was performed; however, a post-hoc power calculation indicated 86% power ($\alpha = 0.05$) to detect the

Table 1. Baseline Characteristics of the Study Population

Variable	SVO Patients (n=89)	Non-SVO Controls (n=10)	Total Cohort (n=195)	p-value
Age (years)	68.5 ± 12.3	55.2 ± 10.8	61.9 ± 12.6	<0.001
Sex (Female), n (%)	45 (50.6%)	62 (58.5%)	107 (54.9%)	0.27
Creatinine (mg/dL)	1.2 ± 0.5	0.8 ± 0.3	1.0 ± 0.5	<0.001
Total Cholesterol (mg/dL)	185.4 ± 42.1	195.2 ± 48.3	190.3 ± 45.2	0.12
LDL (mg/dL)	112.7 ± 38.5	120.4 ± 41.2	116.5 ± 39.8	0.18
HDL (mg/dL)	42.3 ± 12.6	47.8 ± 14.2	45.0 ± 13.5	0.003
Triglycerides (mg/dL)	145.2 ± 78.3	158.6 ± 85.4	151.9 ± 82.0	0.22
Hemoglobin (g/dL)	12.1 ± 1.8	13.4 ± 1.6	12.8 ± 1.8	<0.001
NLR	2.8 ± 1.5	1.6 ± 0.9	2.2 ± 1.4	<0.001
Platelets (×10 ³ /μL)	245.6 ± 85.2	238.4 ± 76.5	242.0 ± 81.0	0.55
Diabetes, n (%)	38 (42.7%)	25 (23.6%)	63 (32.3%)	0.006
Hypertension, n (%)	65 (73.0%)	48 (45.3%)	113 (57.9%)	<0.001
COPD, n (%)	18 (20.2%)	10 (9.4%)	28 (14.4%)	0.03
Smoking, n (%)	32 (36.0%)	40 (37.7%)	72 (36.9%)	0.81
Malignancy, n (%)	9 (10.1%)	5 (4.7%)	14 (7.2%)	0.14
CKD, n (%)	22 (24.7%)	8 (7.5%)	30 (15.4%)	0.001
CAD, n (%)	40 (44.9%)	15 (14.2%)	55 (28.2%)	<0.001
PAH, n (%)	7 (7.9%)	4 (3.8%)	11 (5.6%)	0.22
Macruz Index	1.9 ± 0.8	1.2 ± 0.5	1.5 ± 0.7	<0.001

Data are expressed as mean ± SD, median (IQR), or n (%).

Abbreviations: NLR, neutrophil-to-lymphocyte ratio; COPD, chronic obstructive pulmonary disease; CKD, chronic kidney disease; CAD, coronary artery disease; PAH, pulmonary arterial hypertension

observed between-group difference in the Macruz index.

For regression analyses, 95% confidence intervals (CIs) were calculated for all β coefficients, though only p-values are presented in Tables 2 and 3 for clarity.

“The study protocol was approved by the Gazi Yaşargil Training and Research Hospital Ethics Committee on 11.04.25, with approval number 434. All procedures were conducted in accordance with the Declaration of Helsinki.”

RESULTS

In univariable analysis, age, HDL, NLR, hypertension, COPD, and CAD were found to be significantly associated with the macruz index. However, in the multivariable model, only age and NLR remained as independent predictors, suggesting their predominant role in influencing this index. The inverse trend between HDL and the Macruz index may reflect a protective effect, though this association was marginally significant and warrants further investigation. Patients with stroke exhibited a significantly higher mean age and a higher prevalence of hypertension, diabetes mellitus, COPD, CKD, and coronary artery disease when compared to the control group.

Laboratory findings revealed higher creatinine levels, lower HDL cholesterol, lower hemoglobin, and a significantly elevated neutrophil-lymphocyte ratio (NLR) in stroke patients. The Macruz index demonstrated a significant increase in stroke patients (1.9 ± 0.8) in comparison to the control group (1.2 ± 0.5), with a p-value of less than 0.001.

Baseline Characteristics

The study included 195 participants (89 SVO patients, 106 controls). Stroke patients were significantly older ($68.5 \pm$

12.3 vs. 55.2 ± 10.8 years, $p < 0.001$) and had higher prevalences of hypertension (73.0% vs. 45.3%, $p < 0.001$), diabetes (42.7% vs. 23.6%, $p = 0.006$), COPD (20.2% vs. 9.4%, $p = 0.03$), CKD (24.7% vs. 7.5%, $p = 0.001$), and CAD (44.9% vs. 14.2%, $p < 0.001$) compared to controls.

Laboratory results revealed stroke patients had higher creatinine (1.2 ± 0.5 vs. 0.8 ± 0.3 mg/dL, $p < 0.001$), lower HDL (42.3 ± 12.6 vs. 47.8 ± 14.2 mg/dL, $p = 0.003$), lower hemoglobin (12.1 ± 1.8 vs. 13.4 ± 1.6 g/dL, $p < 0.001$), and elevated NLR (2.8 ± 1.5 vs. 1.6 ± 0.9 , $p < 0.001$). The Macruz index was significantly higher in stroke patients (1.9 ± 0.8 vs. 1.2 ± 0.5 , $p < 0.001$) (Table 1)

Regression Analyses

Univariable linear regression identified age ($\beta = 0.012$, $p = 0.002$), HDL ($\beta = -0.008$, $p = 0.010$), NLR ($\beta = 0.120$, $p < 0.001$), hypertension ($\beta = 0.180$, $p = 0.016$), COPD ($\beta = 0.210$, $p = 0.028$), and CAD ($\beta = 0.140$, $p = 0.045$) as significant predictors of the Macruz index (Table 2).

In the multivariable model, only age ($\beta = 0.010$, $p = 0.040$) and NLR ($\beta = 0.110$, $p = 0.002$) remained independent predictors, explaining 25% of the variance ($R^2 = 0.25$, adjusted $R^2 = 0.22$, $p < 0.001$). HDL showed a marginal inverse association ($\beta = -0.006$, $p = 0.052$) (Table 3). These multivariable results were derived from a backward elimination model with acceptable multicollinearity (all VIF < 5).

Our findings support the hypothesis that the Macruz index may serve as a simple and inexpensive tool for assessing atrial conduction abnormalities in stroke patients without previously documented AF. The observation that higher

Table 2. Univariable Linear Regression Analysis of Factors Associated with the Macruz Index

Variable	Beta Coefficient	Standard Error	p value
Age	0.012	0.004	0.002
Sex (Female)	-0.105	0.078	0.180
Creatinine (KRE)	-0.032	0.040	0.420
Total Cholesterol	0.001	0.001	0.320
LDL	0.002	0.001	0.150
HDL	-0.008	0.003	0.010
Triglycerides (TG)	0.000	0.000	0.950
Hemoglobin (HB)	-0.025	0.015	0.090
NLR	0.120	0.030	<0.001
Platelets	0.000	0.000	0.760
DM	0.150	0.080	0.060
HT	0.180	0.075	0.016
COPD	0.210	0.095	0.028
Smoking	0.090	0.082	0.270
Malignancy	0.130	0.110	0.240
CKD	0.160	0.085	0.058
CAD	0.140	0.070	0.045
PAH	0.095	0.100	0.340

Abbreviations: NLR, neutrophil-to-lymphocyte ratio; DM, diabetes mellitus; HT, hypertension; COPD, chronic obstructive pulmonary disease; CKD, chronic kidney disease; CAD, coronary artery disease; PAH, pulmonary arterial hypertension

Notes: Bold indicates statistical significance ($p < 0.05$).

Table 3. Multivariable Linear Regression Analysis of Factors Independently Associated with the Macruz Index

Variable	Beta Coefficient	Standard Error	p-value
Age	0.010	0.005	0.040
HDL	-0.006	0.003	0.052
NLR	0.110	0.035	0.002
HT (Yes)	0.130	0.080	0.110
COPD (Yes)	0.180	0.100	0.070
CAD (Yes)	0.120	0.075	0.110

Model Summary:

R^2 : 0.25 (The model explains 25% of the variance in the Macruz index.)

Adjusted R^2 : 0.22

Overall model significance (F-test): $p < 0.001$

Age and **NLR** were independently associated with higher Macruz index values ($p < 0.05$).

HDL showed a marginal inverse association ($p = 0.052$).

HT, COPD, and CAD lost significance after adjustment for covariates.

Macruz index values were associated with atrial dysfunction is consistent with earlier reports. These findings collectively suggest that the Macruz index could complement conventional risk scores and echocardiographic parameters, offering clinicians an easily applicable method for early identification of patients at risk. Nevertheless, prospective multicenter studies with larger sample sizes and long-term follow-up are needed to validate its prognostic role and to explore whether integrating this parameter into clinical practice improves outcomes.

In conclusion, our study contributes to the growing body of evidence supporting the Macruz index as a potential marker of atrial remodeling and arrhythmic risk, reinforcing its relevance for stroke survivors without documented AF.

DISCUSSION

The present study demonstrated that stroke patients in sinus rhythm, without atrial fibrillation detected on Holter monitoring, exhibited significantly elevated Macruz index values compared with the control group. This finding indicates the presence of underlying atrial electrical remodeling, even in the absence of documented AF. Our results also support the hypothesis that processes such as aging and systemic inflammation contribute to atrial conduction delay, as shown by the independent associations of age and neutrophil-to-lymphocyte ratio (NLR) with the Macruz index.

Previous studies have linked elevated Macruz index values with atrial conduction abnormalities and an increased risk of atrial arrhythmias. Balci et al. demonstrated that elevated Macruz index was linked to impaired atrial conduction and increased risk of AF onset (7). Cay et al. further showed its predictive utility in patients with mitral stenosis, highlighting its role in structural heart disease-related arrhythmias (8). Moreover, Wang et al. emphasized the use of electrocardiographic indices, including the Macruz index, in risk prediction algorithms for AF recurrence and stroke prevention (9). However, most of these investigations have focused on patients with valvular heart disease or structural abnormalities, whereas our study specifically evaluated stroke patients in sinus rhythm with no evidence of AF on 24-hour Holter monitoring. Mechanistically,

systemic inflammation may promote atrial fibroblast activation, extracellular matrix deposition, and interstitial fibrosis, all of which can slow intra-atrial conduction and manifest as a higher Macruz index. In parallel, autonomic imbalance characterized by heightened sympathetic tone and reduced vagal modulation may further prolong atrial conduction times and increase electrical heterogeneity, providing a plausible substrate for the elevated index observed in stroke patients without documented AF. This distinction is clinically relevant, as it suggests that the Macruz index may reveal subclinical atrial remodeling in patients who would otherwise be considered at lower arrhythmic risk.

The findings emphasize the potential role of surface ECG markers, such as the Macruz index, in identifying patients with hidden atrial vulnerability. The simplicity, cost-effectiveness, and wide availability of the ECG make this index a practical tool for routine use in stroke populations. Importantly, the elevated Macruz index observed in our study, despite the absence of AF, could indicate a pre-fibrillatory state, warranting closer cardiac monitoring and possibly extended rhythm surveillance.

Our findings also align with contemporary literature on atrial cardiopathy and stroke recurrence, wherein surface ECG markers such as prolonged P-wave duration/dispersion and abnormal P-wave terminal force in V1, as well as imaging-based atrial strain abnormalities, have been associated with recurrent stroke risk and atrial remodeling. Within this framework, the Macruz index emerges as a pragmatic ECG-derived metric that complements these markers and may be integrated into risk stratification algorithms to identify patients with subclinical atrial vulnerability.

The novelty of our study lies in highlighting the prognostic value of the Macruz index in a stroke population without previously documented AF. While conventional risk factors and imaging markers are widely used in clinical practice, incorporating an easily measurable ECG-derived index may improve risk stratification and provide additional insights into atrial remodeling. Future large-scale, prospective studies are required to confirm these findings and to explore whether early identification of patients with elevated Macruz

index values can guide preventive strategies, reduce the incidence of AF, and ultimately lower the risk of recurrent stroke.

Limitations

First of all, our study was a retrospective with a relatively small sample size. Secondly, prolonged rhythm monitoring (such as 7-days, 1 month Holter monitoring and loop recorder) wasn't performed, which may have led to missed episodes of subclinical atrial fibrillation. We need large size and prospective study associated with Macruz index and atrial electrical abnormalities in patients with stroke. The modest sample size may increase the risk of type II error for some associations; therefore, larger multicenter cohorts with longitudinal follow-up are warranted to validate these findings.

CONCLUSION

Patients with a history of stroke but without AF, and in sinus rhythm, demonstrated significantly elevated Macruz index values. This finding indicates the potential for atrial remodeling. The present study found that age and systemic inflammation were each independently associated with these elevations. The Macruz index has been proposed as potential non-invasive marker of atrial vulnerability and a predictor of subclinical atrial dysfunction. It is recommended that clinicians consider incorporation this simple ECG derived index into the risk stratification process of stroke patients. It may be useful to follow up the patients by using a long-term loop recorder, even if atrial fibrillation cannot be detected by ECG and rhythm Holter.

From a clinical perspective, an elevated Macruz index may justify prolonged rhythm surveillance (e.g., extended Holter or implantable loop recorder) to unmask subclinical AF and could inform secondary stroke prevention strategies in selected patients.

Ethics Committee Approval: The study protocol was approved by the Gazi Yaşargil Training and Research Hospital Ethics Committee on 11.04.25, with approval number 434. All procedures were conducted in accordance with the Declaration of Helsinki.

Informed Consent: It was not required as the study was conducted retrospectively.

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