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Original Article

Cardiovascular Involvement in Children with Type 1 Diabetes Mellitus: Insights from Cardiac Electrophysiological Balance and Electrocardiographic Parameters

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Abstract

Objective: We examined whether children with type 1 diabetes mellitus (T1DM) demonstrated early, subclinical electrical alterations on electrocardiography by evaluating dispersion indices, ventricular repolarization markers, and electrophysiological balance measures.

Methods: In this prospective case–control study, 20 children with T1DM and 20 age- and sex-matched healthy controls underwent transthoracic echocardiography and 12-lead electrocardiogram (ECG). We quantified P-wave, QTc, and Tp–e dispersion; Tp–e/QT and Tp–e/QTc ratios; and electrophysiological balance indices (QT/QRS and QTc/QRS). Relationships between ECG indices and clinical variables (diabetes duration and glycated hemoglobin [HbA1c]) were assessed.

Results: Conventional echocardiographic parameters were normal in both groups. Compared with controls, children with T1DM had higher P-wave dispersion, QTc dispersion, and Tp–e dispersion (all $p<0.001$), whereas Tp–e-based ratios and electrophysiological balance indices were similar between groups. Diabetes duration correlated positively with P-wave dispersion ($r=0.489$, $p=0.029$), and HbA1c correlated inversely with QT/QRS ($r=-0.475$, $p=0.034$).

Conclusion: Pediatric T1DM may be accompanied by subtle ECG abnormalities despite preserved conventional echocardiographic findings. Increased dispersion indices support early electrical heterogeneity, and the association between electrophysiological balance and glycemic control suggests an effect of metabolic burden on myocardial electrical stability.

Keywords: Cardiac electrophysiology; child; electrocardiography; type 1 diabetes mellitus; ventricular repolarization

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Tip 1 Diabetes Mellituslu Çocuklarda Kardiyovasküler Tutulum: Kardiyak Elektrofizyolojik Denge ve Elektrokardiyografik Parametreler

Özet

Amaç: Tip 1 diabetes mellituslu (T1DM) çocuklarda, yapisal kardiyak bulgu olmaksizin görülebilecek erken elektriksel değişiklikleri; EKG dispersiyon ölçütleri, ventriküler repolarizasyon belirteçleri ve kardiyak elektrofizyolojik denge indeksleri üzerinden araştirmayi amaçladik.

Yöntem: Bu prospektif olgu–kontrol çalişmasina 20 T1DM'li çocuk ve yaş/cinsiyet açisindan eşleştirilmiş 20 sağlikli kontrol dahil edildi. Tüm olgularda transtorasik ekokardiyografi ve 12 derivasyonlu EKG değerlendirildi.

P-dalga, QTc ve Tp–e dispersiyonu ile Tp–e/QT ve Tp–e/QTc oranlari ve QT/QRS ile QTc/QRS (elektrofizyolojik denge) indeksleri hesaplandi. EKG parametreleri ile diyabet süresi ve HbA1c arasindaki ilişkiler incelendi.

Bulgular: Her iki grupta konvansiyonel ekokardiyografi bulgulari normaldi. T1DM grubunda P-dalga dispersiyonu, QTc dispersiyonu ve Tp–e dispersiyonu kontrol grubuna göre daha yüksekti (tümü için p<0,001). Tp–e temelli oranlar ve QT/QRS ile QTc/QRS indeksleri açisindan gruplar arasinda anlamli fark saptanmadi. Diyabet süresi P-dalga dispersiyonu ile pozitif; HbA1c ise QT/QRS orani ile negatif yönde ilişkiliydi.

Sonuç: T1DM'li çocuklarda, ekokardiyografik bulgular normal olsa bile EKG'de subklinik elektriksel değişiklikler izlenebilir. Dispersiyon ölçütlerindeki artiş erken elektriksel heterojeniteyi desteklerken, elektrofizyolojik denge ile glisemik kontrol arasindaki ilişki metabolik yükün elektriksel stabilite üzerine etkisini düşündürmektedir.

Anahtar sözcükler: Kardiyak elektrofizyoloji; çocuk; elektrokardiyografi; tip 1 diabetes mellitus; ventriküler repolarizasyon.

Introduction

Type 1 diabetes mellitus (T1DM) is a chronic endocrine disease that usually manifests in pediatric and adolescent populations. Although the disease manifests early in life, its cardiovascular consequences are often considered long-term complications. Large-scale follow-up studies in adult populations have consistently demonstrated a markedly increased risk of cardiovascular morbidity and mortality in individuals with T1DM.[1,2] In contrast, clinically overt cardiovascular disease is rarely observed during childhood. Nevertheless, accumulating evidence suggests that subtle cardiovascular alterations may emerge during pediatric life and remain clinically silent for years before becoming apparent in adulthood.

In recent years, increasing attention has been directed toward cardiac electrophysiological abnormalities as an early component of cardiovascular involvement in T1DM. Alterations in atrial conduction and ventricular repolarization – commonly reflected by parameters such as P-wave dispersion, QT/QTc dispersion, prolonged Tp–e interval, and Tp–e-based ratios – have been associated with heightened susceptibility to both atrial and ventricular arrhythmias.[3–5] These electrocardiographic indices are thought to reflect increased myocardial electrical heterogeneity and may serve as sensitive markers of subclinical cardiac involvement, even in the absence of detectable structural heart disease. While such electrophysiological changes have been extensively described in adults with T1DM, data in pediatric populations remain limited and are largely derived from a small number of studies.[6]

Beyond conventional dispersion parameters, cardiac electrophysiological balance has gained attention as a framework for characterizing the interplay between ventricular depolarization and repolarization. This balance is quantified by the QT-to-QRS ratio, referred to as the index of cardiac electrophysiological balance (ICEB), as well as its corrected form incorporating the QTc interval (ICEBc).[7] In adult populations, these indices have been linked to ventricular arrhythmias and unfavorable cardiovascular outcomes.[8] In contrast, evidence supporting the applicability and clinical relevance of ICEB and ICEBc in pediatric patients with T1DM remains scarce, with only a limited number of studies available to date.[9]

This study was designed to provide a comprehensive assessment of cardiac electrophysiological alterations in children with T1DM, integrating conventional electrocardiographic dispersion parameters with ventricular repolarization markers, including the Tp–e interval and Tp–e-based ratios (Tp–e/QT and Tp–e/QTc), as well as indices of cardiac electrophysiological balance (ICEB and ICEBc). By comparing these parameters with those obtained from age- and sex-matched healthy controls, the study sought to elucidate potential subclinical electrophysiological changes and to explore their associations with key clinical characteristics such as disease duration and glycemic control.

Materials and Methods

Study Design and Study Population

Between June 2024 and January 2025, a total of 40 children were prospectively evaluated as part of a case–control study. The study population included 20 children diagnosed with T1DM who were followed in the pediatric endocrinology clinic and referred for cardiovascular assessment, along with 20 age- and sex-matched healthy controls. Cardiac evaluations were performed in the pediatric cardiology outpatient clinic. Control participants had no known systemic disease and demonstrated normal clinical, echocardiographic, and electrocardiographic findings. All participants underwent transthoracic echocardiography and standard 12-lead electrocardiography, and the collected data were analyzed prospectively.

Clinical and Laboratory Data Collection

Clinical and laboratory variables were recorded prospectively during cardiovascular assessment. Collected data included demographic characteristics (age and sex), duration of T1DM, and glycated hemoglobin (HbA1c) levels. Anthropometric evaluation comprised measurements of body weight and height obtained using standard procedures, and body mass index (BMI) was calculated as weight divided by height squared (kg/m^2). Standard deviation scores (SDS) for weight, height, and BMI were derived using age- and sex-specific reference data for Turkish children based on the Neyzi growth charts.[10] HbA1c measurements were obtained as part of routine clinical follow-up, and all clinical, laboratory, echocardiographic, and electrocardiographic assessments were completed within the same week.

Echocardiographic Evaluation

Transthoracic echocardiographic examinations were performed in all participants by the same pediatric cardiologist using a Philips EPIQ 7 ultrasound system. Standard two-dimensional, M-mode, Doppler, and tissue Doppler imaging (TDI) were obtained in accordance with the recommendations of the American Society of Echocardiography.

Left ventricular systolic function was assessed by measuring the left ventricular ejection fraction using M-mode echocardiography from the parasternal long-axis view. Left ventricular diastolic function was evaluated using TDI, including mitral septal and lateral early diastolic myocardial velocities (E′). Right ventricular systolic function was assessed by measuring tricuspid annular systolic velocity (S′) using TDI and tricuspid annular plane systolic excursion (TAPSE) using M-mode echocardiography. All measurements were performed during quiet respiration and averaged over three consecutive cardiac cycles.

Electrocardiographic Analysis and Cardiac Electrophysiological Balance (ICEB) Calculation

After a brief rest, a standard 12-lead electrocardiogram (ECG) was recorded in the supine position at 25 mm/s and 10 mm/mV. All ECG tracings were scanned and transferred to a personal computer. For accurate measurements and to reduce intraobserver variability, the digitized ECG images were enlarged up to 400% using Adobe Photoshop software.

Using the enlarged digital ECG recordings, a single investigator manually assessed P-wave duration, QT interval, QRS duration, and Tp–e interval. Heart rate correction of the QT interval was performed using Bazett's formula. Dispersion indices for the P wave, QTc, and Tp–e were defined as the numerical difference between the maximum and minimum measurements obtained across leads.

Cardiac electrophysiological balance was defined as the QT-to-QRS ratio (ICEB), and its corrected form (ICEBc) was calculated using the QTc interval divided by QRS duration.

Ethical Approval

Ethical approval was obtained from the Kartal Dr. Lütfi Kırdar City Hospital (Date: 27.05.2024, Decision no: 2024/010.99/4/6). The study was carried out in compliance with the principles of the Declaration of Helsinki, and written informed consent was obtained from parents or legal guardians before participation.

Statistical Analysis

Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) software for Windows, version 15.0 (SPSS Inc., Chicago, IL, USA). Descriptive statistics were presented as numbers and percentages for categorical variables and as mean±standard deviation for continuous variables. Group comparisons of categorical variables were performed with the Chi-square test.

Comparisons between two independent groups were conducted using the Student's t-test when the assumption of normal distribution was met and the Mann–Whitney U test when normality was not satisfied. Relationships between continuous variables were analyzed using Spearman correlation analysis, as the assumptions for parametric correlation analysis were not met.

Statistical significance was defined as $p<0.05$.

Table 1. Demographic characteristics of the study population

Variable	T1DM group (n=20)	Control group (n=20)	p
Age, years			
Mean±SD	12.4±2.8	11.7±2.9	0.461*
Min–max (median)	6.7–16.1 (12.8)	7–17 (11.5)	
Sex, n (%)			
Male	13 (65)	13 (65)	1.000∅
Female	7 (35)	7 (35)	

*: Student's t-test; ∅: Chi-square test.T1DM: Type 1 diabetes mellitus; SD: Standard deviation.

Table 2. Clinical and anthropometric characteristics of the T1DM group

Variable	T1DM group (n=20)	
	Mean±SD	Min–max (median)
Duration of diabetes (years)	4.2±2.7	2.0–10.7 (3.1)
Weight (kg)	44.7±14.1	23.6–73 (43.6)
Weight SDS	-0.13±1.12	-2.49–1.91 (0.23)
Height (cm)	149.1±16.1	121.5–173.5 (149.1)
Height SDS	-0.38±0.86	-2.31–1.30 (-0.26)
BMI (kg/m^2)	19.6±2.7	14.4–25 (19.0)
BMI SDS	0.13±1.04	-2.45–1.43 (0.50)
HbA1c	9.4±2.0	6.6–14.3 (8.95)

T1DM: Type 1 diabetes mellitus; SD: Standard deviation; SDS: Standard deviation score; BMI: Body mass index; HbA1c: Glycated hemoglobin.

Results

Study Population and Demographic Characteristics

A total of 40 children were included in the study, comprising 20 patients diagnosed with T1DM and 20 age- and sex-matched healthy controls. The mean age of the T1DM group was 12.4±2.8 years (range: 6.7–16.1), while the control group had a mean age of 11.7±2.9 years (range: 7.0–17.0). There was no statistically significant difference in age between the groups ($p=0.461$).

Sex distribution was identical in both groups, with 13 males (65.0%) and 7 females (35.0%) in each group ($p=1.000$) (Table 1).

Clinical and Anthropometric Characteristics of the T1DM Group

In the T1DM group, the mean duration of diabetes was 4.2±2.7 years (range: 2.0–10.7). The mean HbA1c level was 9.4±2.0% (range: 6.6–14.3). Anthropometric measurements, including weight, height, BMI, and their corresponding SDS, were within the expected ranges for age (Table 2).

Echocardiographic Findings

Conventional two-dimensional, Doppler, and tissue Doppler echocardiographic evaluations revealed no pathological findings in the T1DM group. Left ventricular systolic function was preserved in all patients, and no abnormalities were detected in chamber dimensions or wall motion.

Table 3. Conventional and tissue Doppler echocardiographic findings of the T1DM group

Parameter	T1DM Group (n=20)	
	Mean±SD	Min–max (median)
Left ventricular ejection fraction (%)	69.3±4.4	61–75 (70)
Mitral septal E′ (cm/s)	12.7±2.2	9–17 (12.4)
Mitral lateral E′ (cm/s)	20.9±6.0	12–35.9 (20)
Tricuspid annular S′ (cm/s)	14.9±2.3	10.9–18.6 (15)
TAPSE (mm)	23.9±3.3	18.5–30.2 (23.4)

T1DM: Type 1 diabetes mellitus; SD: Standard deviation; TAPSE: Tricuspid annular plane systolic excursion.

Left ventricular diastolic function parameters, including mitral septal and lateral early diastolic velocities (E′), were within normal limits. Right ventricular systolic function, assessed by tricuspid annular systolic velocity (S′) and TAPSE, was also normal across the study population (Table 3).

Electrocardiographic Findings

Comparative electrocardiographic analysis demonstrated significant differences between the T1DM and control groups. Heart rate, P-wave axis, and QRS axis were similar between groups.

In contrast, dispersion-based electrophysiological parameters were significantly increased in the T1DM group. P-wave dispersion, QTc dispersion, and Tp–e dispersion were all markedly higher in patients with T1DM compared with controls (all p<0.001) (Table 4).

No statistically significant differences were observed between groups with respect to Tp–e/QT, Tp–e/QTc, QT/QRS (ICEB), or QTc/QRS (ICEBc) ratios.

Correlation Analysis

Correlation analysis revealed a significant positive correlation between diabetes duration and P-wave dispersion (r=0.489, p=0.029). In addition, a significant negative correlation was identified between HbA1c levels and the QT/QRS ratio, an ICEB (r=–0.475, p=0.034).

No significant correlations were observed between diabetes duration or HbA1c levels and other ventricular repolarization dispersion parameters, including QTc dispersion and Tp–e dispersion, nor with derived ratios such as Tp–e/QT, Tp–e/QTc, or QTc/QRS. Furthermore, no statistically significant correlations were identified between diabetes duration or HbA1c levels and echocardiographic parameters (Table 5).

Discussion

In the present study, children with T1DM demonstrated significant alterations in cardiac electrophysiological parameters despite the absence of clinically evident cardiovascular disease. When compared with healthy peers, patients with T1DM exhibited marked increases in atrial and ventricular dispersion indices, including P-wave dispersion, QTc dispersion, and Tp–e dispersion, indicating enhanced electrical heterogeneity. In contrast, standard echocardiographic assessment revealed preserved

Table 4. Electrocardiographic dispersion parameters and cardiac electrophysiological balance indices in T1DM and control groups

Parameter	T1DM group (n=20)	Control group (n=20)	p
	Mean±SD Min–Max (median)	Mean±SD Min–Max (median)	
Heart rate (bpm)	85.9±13.6 60–112 (86.5)	87.1±12.2 60–108 (87.5)	0.771*
P-wave axis (°)	42.7±8.9 20.6–63.4 (45)	47.5±15.1 16–71 (49)	0.231*
QRS axis (°)	61.6±26.3 11–130 (66)	63.1±19.2 27–87 (69.1)	0.478**
P-wave dispersion (ms)	44.7±13.2 26.7–85.7 (42.9)	28.9±8.1 11.1–42.1 (33.3)	<0.001**
QTc dispersion (ms)	64.0±24.3 28.6–111.8 (56.8)	39.3±12.1 19.2–63 (38.8)	<0.001**
Tp–e dispersion (ms)	55.0±9.7 40–85.7 (53.1)	30.4±10.6 11.8–63.2 (33.3)	<0.001**
Tp-e/QT	0.22±0.03 0.17–0.27 (0.22)	0.23±0.03 0.18–0.27 (0.24)	0.056**
Tp-e/QTc	0.18±0.03 0.14–0.24 (0.18)	0.19±0.02 0.15–0.22 (0.20)	0.065*
QT/QRS (ICEB)	4.55±0.89 3–7 (4)	4.20±0.70 3–5 (4)	0.327**
QTc/QRS (ICEBc)	5.45±0.94 4–8 (5)	5.05±0.83 4–6 (5)	0.341**

*: Student's t-test; **: Mann–Whitney U test. T1DM: Type 1 diabetes mellitus; SD: Standard deviation; QTc: Corrected QT interval; ICEB: Index of cardiac electrophysiological balance.

Table 5. Correlation analysis between clinical variables and echocardiographic and electrocardiographic parameters in patients with T1DM

	Diabetes duration (years)		HbA1c (%)	
	r	p	r	p
Echocardiographic parameters				
Left ventricular ejection fraction (%)	-0.045	0.852[£]	-0.240	0.308[£]
Mitral septal E′ (cm/s)	-0.297	0.217[£]	-0.371	0.118[#]
Mitral lateral E′ (cm/s)	-0.263	0.276[£]	-0.088	0.721[#]
Tricuspid annular S′ (cm/s)	0.175	0.474[£]	0.149	0.542[#]
TAPSE (mm)	-0.207	0.411[£]	0.109	0.665[£]
Electrocardiographic parameters				
P-wave dispersion (ms)	0.489	**0.029**[£]	0.297	0.204[£]
QTc dispersion (ms)	0.126	0.596[£]	0.327	0.160[#]
Tp–e dispersion (ms)	0.009	0.970[£]	-0.069	0.772[£]
Tp-e/QT	0.199	0.400[£]	-0.364	0.114[#]
Tp-e/QTc	-0.209	0.376[£]	-0.396	0.084[#]
QT/QRS (ICEB)	-0.344	0.137[£]	-0.475	**0.034**[£]
QTc/QRS (ICEBc)	-0.165	0.488[£]	-0.264	0.260[£]

[#]: Pearson correlation analysis; [£]: Spearman correlation analysis. HbA1c: Glycated hemoglobin; E′: Early diastolic myocardial velocity; S′: Systolic myocardial velocity; TAPSE: Tricuspid annular plane systolic excursion; ICEB: Index of cardiac electrophysiological balance; ICEBc: Corrected index of cardiac electrophysiological balance.

cardiac structure and function across the study population, suggesting that these electrophysiological abnormalities may represent early and subclinical manifestations of cardiovascular involvement. Although indices of cardiac electrophysiological balance (ICEB and ICEBc) were not significantly different between groups, the observed associations between selected electrophysiological parameters and clinical variables – particularly diabetes duration and glycemic control – highlight the potential clinical relevance of electrical alterations in pediatric T1DM.

Findings from the current study parallel observations previously reported in adult cohorts with diabetes mellitus. Investigations in adult populations have consistently documented elevations in atrial and ventricular dispersion measures, including prolongation of the Tp–e interval and increases in Tp–e-based ratios, which are thought to indicate greater ventricular repolarization heterogeneity and heightened arrhythmogenic susceptibility.[3,4] By comparison, evidence addressing electrophysiological alterations in pediatric patients with T1DM remains scarce. Existing pediatric studies have mainly examined traditional electrocardiographic indices, such as P-wave dispersion and QTc dispersion, and have identified modest yet statistically meaningful differences relative to healthy control groups.[5,6]

With respect to indices of cardiac electrophysiological balance, Ertaş et al. recently evaluated ICEB parameters in children with T1DM and reported alterations suggestive of early electrophysiological involvement.[9] In the present study, although ICEB and ICEBc values did not differ significantly between groups, the observed association between ICEB and glycemic control suggests that these indices may be more sensitive to metabolic status than to fixed group-related differences. Variations in study design, patient characteristics, diabetes duration, and glycemic control may account for discrepancies between studies, underscoring the heterogeneous nature of electrophysiological manifestations in pediatric T1DM.

The mechanisms underlying the observed electrophysiological alterations in children with T1DM are likely multifactorial. Chronic hyperglycemia is closely linked to the development of cardiac autonomic neuropathy and autonomic imbalance, which may increase atrial and ventricular electrical heterogeneity and thereby contribute to dispersion-based ECG abnormalities.[11,12] In parallel, hyperglycemia-related oxidative stress, low-grade inflammation, and diabetes-associated electrophysiological remodeling – potentially involving altered ion channel function – have been proposed as contributors to repolarization disturbances, including Tp–e prolongation and increased Tp–e-based ratios.[13,14] Importantly, our finding of a significant association between ICEB and HbA1c suggests that cardiac electrophysiological balance may be sensitive to metabolic burden and glycemic status, even when between-group differences are not detectable in early-stage pediatric disease.

From a clinical perspective, the present findings align with existing evidence indicating that cardiovascular involvement in T1DM may begin at a subclinical stage, even during childhood. Large population-based studies have demonstrated that individuals with childhood-onset T1DM carry an increased long-term cardiovascular risk, underscoring the importance of early identification of cardiovascular alterations.[15] In parallel, scientific statements from major cardiovascular and diabetes societies emphasize that traditional imaging modalities may fail to detect early myocardial involvement in young patients with T1DM.[16]

In this context, non-invasive electrocardiographic markers, including dispersion-based indices and ventricular repolarization parameters, have gained interest as potential indicators of early electrical instability. Pediatric studies evaluating electrophysiological balance indices in T1DM have suggested that such parameters may reveal subtle abnormalities not captured by conventional echocardiography.[9] Our findings of increased dispersion parameters, together with a significant association between ICEB and glycemic control, support the concept that electrophysiological alterations may precede overt structural cardiac changes. Although these electrocardiographic markers cannot currently be recommended for routine clinical use or arrhythmia prediction, they may serve as adjunctive tools in longitudinal follow-up and comprehensive cardiovascular assessment, particularly in pediatric patients with suboptimal metabolic control.

Several limitations of the present study should be acknowledged. First, the relatively small sample size and single-center design may limit the generalizability of the findings. Second, the cross-sectional nature of the analysis precludes causal inferences regarding the relationship between metabolic control and electrophysiological parameters. In addition, although none of the participants exhibited clinical arrhythmias, the absence of long-term rhythm monitoring limits conclusions regarding the prognostic implications of the observed electrocardiographic abnormalities.

Despite these limitations, this study provides a comprehensive evaluation of cardiac electrophysiological alterations in children with T1DM by integrating conventional dispersion parameters, ventricular repolarization markers, and indices of cardiac electrophysiological balance. The findings suggest that subclinical electrophysiological changes may be present even in the absence of overt cardiac involvement and may be influenced by metabolic control. Future longitudinal studies with larger cohorts are warranted to clarify the clinical significance of these findings and to determine whether such electrocardiographic markers may contribute to long-term cardiovascular risk stratification in pediatric T1DM.

Conclusion

Subclinical cardiac electrophysiological alterations may be present in children with T1DM even in the absence of overt cardiovascular disease or conventional echocardiographic abnormalities. This study demonstrates increased atrial and ventricular dispersion parameters and altered ventricular repolarization indices in pediatric T1DM, suggesting early electrical heterogeneity that may precede structural cardiac involvement. Although indices of cardiac electrophysiological balance did not differ significantly between groups, their association with glycemic control highlights the potential influence of metabolic status on myocardial electrical stability.

These findings emphasize the importance of considering subclinical electrical changes as part of a comprehensive cardiovascular assessment in children with T1DM, particularly in those with suboptimal metabolic control. While the electrocardiographic markers evaluated in this study cannot currently be recommended for routine clinical use or arrhythmia prediction, they may provide complementary information during longitudinal follow-up. Further large-scale, prospective studies incorporating long-term rhythm monitoring are warranted to clarify the clinical and prognostic significance of these electrophysiological alterations and to determine their potential role in cardiovascular risk stratification in pediatric T1DM.

Disclosures

Ethics Committee Approval: The study was approved by the Kartal Dr. Lütfi Kırdar City Hospital Ethics Committee (no: 2024/010.99/4/6, date: 27/05/2024).

Informed Consent: Written informed consent was obtained.

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