

Effect of Cytisine on Ventricular Repolarization Parameters in Healthy Smokers

Sağlıklı Sigara İçicilerinde Sitizinin Ventriküler Repolarizasyon Parametreleri Üzerine Etkisi

ABSTRACT

Objective: Cytisine is a pharmacological agent widely used for smoking cessation, acting as a partial agonist of the $\alpha 4\beta 2$ nicotinic acetylcholine receptor. While varenicline, a drug with a similar mechanism of action, has been associated with electrocardiographic (ECG) alterations, to our knowledge, the effect of cytisine on ECGs has not yet been studied. This study aimed to evaluate the effects of cytisine use on electrocardiographic parameters, particularly QT, QTc, Tp-e, and the Tp-e/QTc ratio.

Method: A retrospective analysis was conducted on 110 patients who completed a 25-day cytisine regimen for smoking cessation. Patients with known cardiovascular disease, clinically significant arrhythmias, use of QT-prolonging medications, electrolyte abnormalities, or incomplete follow-up data were excluded from the analysis. Standard 12-lead ECGs and serum biochemistry were assessed before treatment and at the one-month follow-up. Statistical analyses included paired tests and correlation analysis.

Results: No statistically significant changes were observed in QT, QTc, Tp-e intervals, or the Tp-e/QTc ratio following cytisine treatment (all $P > 0.05$). A modest increase in potassium and a decrease in calcium levels were noted, though both remained within normal limits. No correlation was found between smoking exposure (pack-years) and baseline Tp-e/QTc.

Conclusion: In healthy smokers, approximately one month of cytisine treatment was not associated with statistically significant changes in QT, QTc, Tp-e, or Tp-e/QTc. These results suggest that there is no detectable short-term effect on ventricular repolarization in this population. However, further prospective, randomized, and long-term studies are warranted to confirm these findings, particularly in patients with pre-existing cardiovascular conditions.

Keywords: Arrhythmias, cytisine, electrocardiography, ventricular repolarization, ventricular tachycardia

ÖZET

Amaç: Sitizin, sigara bırakma tedavisinde yaygın olarak kullanılan ve $\alpha 4\beta 2$ nikotinik asetilkolin reseptörüne parsiyel agonist olarak etki eden farmakolojik bir ajandır. Benzer etki mekanizmasına sahip vareniklinin elektrokardiyografik (EKG) değişikliklerle ilişkili olduğu bildirilmiştir. Ancak, bildiğimiz kadarıyla sitizinin EKG üzerine etkisi daha önce incelenmemiştir. Bu çalışmanın amacı, sitizin kullanımının elektrokardiyografik parametreler üzerindeki etkilerini, özellikle QT, QTc, Tp-e ve Tp-e/QTc oranını değerlendirmektir.

Yöntem: Sigara bırakma amacıyla 25 günlük sitizin tedavisini tamamlayan 110 hasta retrospektif olarak incelendi. Bilinen kardiyovasküler hastalığı, klinik olarak anlamlı aritmisi, QT'yi uzatan ilaç kullanımı, elektrolit bozukluğu veya eksik takip verisi olan hastalar analize dâhil edilmedi. Tedavi öncesinde ve 1. ay kontrolünde tüm hastaların standart 12 derivasyonlu EKG ve serum biyokimyası değerlendirildi. İstatistiksel analizlerde eşleştirilmiş testler ve korelasyon analizi kullanıldı.

Bulgular: Sitizin tedavisi sonrasında QT, QTc, Tp-e aralıkları ve Tp-e/QTc oranında istatistiksel olarak anlamlı bir değişiklik gözlenmedi (tüm $P > 0.05$). Serum potasyumunda hafif artış ve kalsiyumda azalma saptandı, ancak bu değişiklikler normal sınırlar içinde kaldı. Sigara içme yükü (paket-yıl) ile başlangıç Tp-e/QTc arasında anlamlı bir ilişki bulunmadı.

Sonuç: Sağlıklı sigara içicilerinde yaklaşık bir aylık sitizin tedavisi, QT, QTc, Tp-e veya Tp-e/QTc'de istatistiksel olarak anlamlı değişikliklerle ilişkili bulunmamıştır. Bu sonuçlar, bu popülasyonda ventriküler repolarizasyon üzerinde saptanabilir kısa dönem bir etkinin olmadığını düşündürülebilir. Bununla birlikte, özellikle kardiyovasküler hastalığı bulunan bireylerde prospektif, randomize ve uzun dönemli çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: Aritmiler, sitisin, elektrokardiyografi, ventriküler repolarizasyon, ventriküler taşikardi

ORIGINAL ARTICLE KLİNİK ÇALIŞMA

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Globally, cigarette smoking is still recognized as a predominant cause of avoidable morbidity and mortality.¹ Various pharmacological agents have been proven effective in smoking cessation therapy, and their use is recommended for all patients without contraindications.² Cytisine is a plant-based alkaloid with potent efficacy in smoking cessation treatment that exerts its effect via partial agonism at the $\alpha 4\beta 2$ nicotinic acetylcholine receptor.³ Cytisine's agonist activity is determined by both receptor activation and receptor desensitization. It binds to $\alpha 4\beta 2$ receptors with higher affinity than nicotine, thereby attenuating nicotine withdrawal. It also has a competitive antagonistic effect on these receptors and partially blocks the activity of nicotine.⁴ Large-scale trials have reported smoking cessation rates of around 30–50% after one month and 18–23% after six months with cytisine.^{4,5} Furthermore, recent randomized controlled trials and meta-analyses have demonstrated that cytisine is more effective than placebo and nicotine replacement therapy (NRT).^{6,7} In addition to its strong efficacy, cytisine has been shown to have good tolerability.⁶

Electrocardiography (ECG) is widely used in cardiology practice as a rapid and cost-effective diagnostic tool. On ECG, the QT interval, corrected QT interval (QTc), Tpeak-Tend (Tp-e), and Tp-e/QTc ratio are ventricular repolarization markers used to predict the risk of arrhythmia.⁸ Changes in these parameters have been closely linked to the development of ventricular arrhythmias and the occurrence of sudden cardiac death.⁹ Varenicline, which shares a similar mechanism of action with cytisine, has been reported to cause alterations in ventricular repolarization parameters and may potentially increase the risk of cardiac arrhythmias.¹⁰

To the best of our knowledge, the impact of cytisine on electrocardiographic parameters has not previously been investigated. Therefore, the aim of our study is to evaluate the effects of cytisine use on electrocardiographic parameters, particularly QT, QTc, Tp-e, and the Tp-e/QTc ratio.

Materials and Methods

This study was designed to retrospectively evaluate changes in the QT interval, QTc, Tp-e duration, and Tp-e/QTc ratio before and after cytisine treatment in individuals who were initiated on cytisine therapy for smoking cessation. Between January 2024 and April 2025, 315 patients who presented to the smoking cessation clinic and were prescribed cytisine were screened. The following patients were excluded based on prespecified criteria:

- known cardiovascular disease (coronary artery disease, heart failure/cardiomyopathy, congenital heart disease, or moderate-to-severe valvular disease);
- history of clinically significant arrhythmia (including atrial fibrillation, supraventricular tachycardia, or ventricular tachycardia);
- concomitant use of medications known to influence ventricular repolarization (e.g., antiarrhythmics, antipsychotics, macrolides/fluoroquinolones);
- known chronic kidney disease;
- known thyroid disease;
- electrolyte imbalance at baseline and at one-month; and

ABBREVIATIONS

CI	Confidence interval
ECG	Electrocardiography
ICC	Intraclass correlation coefficients
NRT	Nicotine replacement therapy
QTc	QT interval
Tp-e	Tpeak-Tend

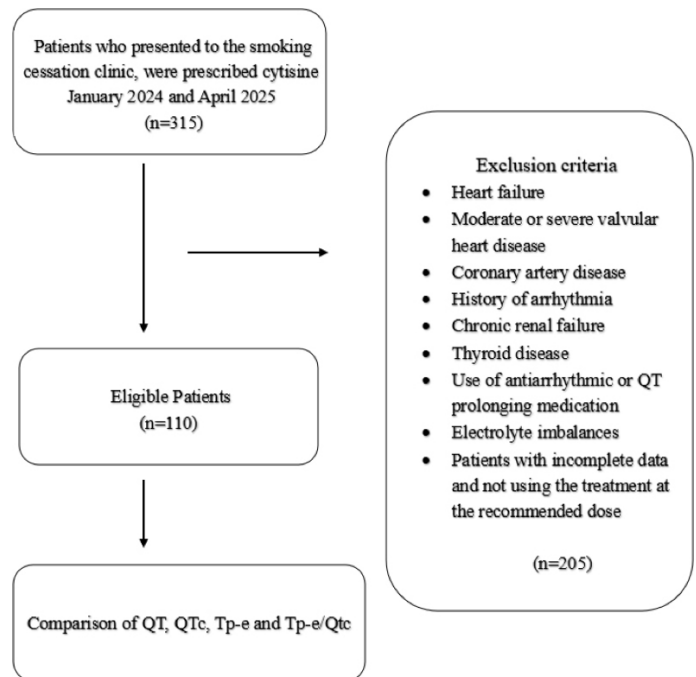


Figure 1. Flowchart of patient selection and inclusion process.

- incomplete data, defined as absence of either the baseline or one-month 12-lead ECG, or ECG quality insufficient for interval measurements.

Patients who followed the manufacturer's recommended 25-day dosing schedule were included in the study.^{3,11} The regimen began with one tablet every 2 hours (up to 6 tablets per day) on days 1–3, then gradually decreased: every 2.5 hours (up to 5 tablets) on days 4–12, every 3 hours (up to 4 tablets) on days 13–16, every 4–5 hours (up to 3 tablets) on days 17–20, and finally every 6 hours (up to 2 tablets) on days 21–25.

A total of 205 individuals did not meet the criteria and were excluded from the analysis, which ultimately included 110 patients. A summarized flow of the study design is presented in Figure 1.

The demographic characteristics (age, height, weight, etc.) and clinical data of the patients at the time of their initial visit to the smoking cessation clinic were obtained from the hospital's electronic medical records. We reviewed venous blood samples and standard 12-lead ECGs acquired at the initial visit and at the one-month follow-up (filter 150 Hz; paper speed 25 mm/s; amplitude 10 mm/mV). ECG measurements were performed manually on digitally archived images at a magnification of at least 400%; no automated software was used.

QT intervals were assessed from the onset of the Q wave to the termination of the T wave. QTc was derived using the Fridericia correction formula to account for heart rate variability.¹² The Tp-e interval was determined as the duration between the peak and the end of the T wave, with any U wave excluded. Tp-e intervals were measured in the precordial leads, and the Tp-e/QTc ratio was calculated accordingly. Electrocardiographic assessments were carried out by two cardiologists working independently. To assess inter- and intra-observer variability, a random sample of 40 ECGs was re-evaluated. Two cardiologists measured QTc and Tp-e independently in separate, blinded sessions. Inter-observer agreement was derived from the readings obtained in the first session, and intra-observer agreement from a repeat reading by one of the cardiologists.

Ethical Considerations

The study was approved by the Manisa Celal Bayar University Ethics Committee (Approval Number: 20.478.486/3142, Date: 11.06.2025). Written informed consent was waived due to the retrospective nature of this study. No artificial intelligence-assisted technologies, including chatbots, image generators, or large language models (LLMs), were used in this study.

Statistical Analysis

All statistical analyses were performed using SPSS software version 22.0 (SPSS Inc., Chicago, IL, USA). The distribution of continuous variables was assessed visually using histograms and statistically with the Kolmogorov-Smirnov and Shapiro-Wilk tests. Variables with normal distribution were reported as mean $\pm$ standard deviation, whereas those not normally distributed were expressed as median with interquartile ranges. Between-group comparisons for continuous variables were conducted using the Independent Samples t-test for parametric data and the Mann-Whitney U test for non-parametric data. Categorical variables were presented as frequencies and percentages and analyzed using the chi-square or Fisher's exact test, as appropriate. For variables with normal distribution, temporal comparisons were made using the paired t-test, whereas the Wilcoxon signed-rank test was applied to non-normally distributed variables. Correlation between smoking burden (pack-years) and baseline Tp-e/QTc was analyzed using Spearman's method. Variability was evaluated in a subset using intraclass correlation coefficients (ICC): ICC (2,1) for inter-observer variability (two-way random-effects, absolute agreement, single measures) and ICC (3,1) for intra-observer variability (two-way mixed-effects, absolute agreement, single measures). Ninety-five percent confidence intervals (CI) for ICCs were reported. Statistical significance was defined as $P < 0.05$.

Results

A total of 110 patients who met the inclusion criteria and completed a 25-day course of cytosine therapy were included in the study. The mean age of the participants was 43 ± 11 years, and 17 patients (15.4%) were female. The demographic characteristics of the study population are presented in Table 1. Laboratory and electrocardiographic parameters obtained before treatment and at the one-month follow-up were compared and summarized in Table 2. No statistically significant changes were observed in hemogram parameters, serum creatinine, or liver function tests.

Table 1. Demographic characteristics of the study population

Variables	Value
Age (years)	43 ± 11
Female sex (n, %)	17 (15.4)
BMI (kg/m ²)	24.1 ± 4.9
Smoking (pack-years)	23.4 ± 12.0

BMI, Body mass index.

Table 2. Comparison of laboratory and electrocardiographic parameters before and after cytosine treatment

	Initial	Follow-up	p
Leukocyte ($\times 10^3/\mu\text{L}$)	8.49 ± 2.31	8.46 ± 3.03	0.84
Hemoglobin (g/dL)	14.92 ± 1.60	14.86 ± 1.85	0.64
Platelet ($\times 10^3/\mu\text{L}$)	232 ± 43	243 ± 33	0.65
Creatinine (mg/dL)	0.92 ± 0.34	0.96 ± 0.43	0.67
AST (IU/L)	22.1 ± 6.2	22.5 ± 6.1	0.48
ALT (IU/L)	26.3 ± 7.8	26.1 ± 8.0	0.51
Na (mEq/L)	138.85 ± 15.89	136.52 ± 22.79	0.89
K (mEq/L)	4.14 ± 0.30	4.2 ± 0.41	0.03
Ca (mg/dL)	9.10 ± 0.40	8.8 ± 0.44	0.02
Mg (mg/dL)	1.97 ± 0.22	1.87 ± 0.22	0.16
Systolic BP (mmHg)	128 ± 18	130 ± 20	0.06
Diastolic BP (mmHg)	75 ± 11	76 ± 13	0.09
Heart rate	76 ± 11	77 ± 12	0.10
QT, ms	363.4 ± 25.6	364.1 ± 26.6	0.45
QTc, ms (Fridericia)	$392 (21.5)$	$390 (29.5)$	0.36
QRS, ms	94 ± 10	95 ± 9	0.52
Tp-e, ms	$80 (14)$	$80 (15.5)$	0.07
Tp-e/QTc	0.20 ± 0.03	0.20 ± 0.03	0.26

ALT, Alanine aminotransferase; AST, Aspartate aminotransferase; BP, Blood pressure; Ca, Calcium; K, Potassium; Mg, Magnesium; Na, Sodium; QTc, Corrected QT interval; Tp-e, Tpeak-Tend.

Among the electrolyte parameters, potassium levels showed a statistically significant increase after treatment (4.14 ± 0.30 vs. 4.20 ± 0.41 mmol/L; $P = 0.03$), while calcium levels significantly decreased (9.10 ± 0.40 vs. 8.80 ± 0.44 mg/dL; $P = 0.02$). Although systolic and diastolic blood pressure, as well as heart rate, were slightly higher at the one-month follow-up, these changes did not reach statistical significance.

Regarding electrocardiographic parameters, there were no statistically significant differences in QT, QTc, Tp-e, and Tp-e/QTc values before and after treatment (all $P > 0.05$).

Inter-observer variability was (ICC (2,1) 0.837, 95% CI: 0.686–0.918) for QTc and (ICC (2,1) 0.909, 95% CI: 0.869–0.959) for Tp-e. Intra-observer variability was (ICC (3,1) 0.859, 95% CI: 0.704–0.924) for QTc and (ICC (3,1) 0.917, 95% CI: 0.856–0.961) for Tp-e.

No significant correlation was observed between cumulative smoking exposure (pack-years) and baseline Tp-e/QTc ratio (Spearman's $\rho = -0.03$, $P = 0.80$). The correlation plot is presented in Figure 2.

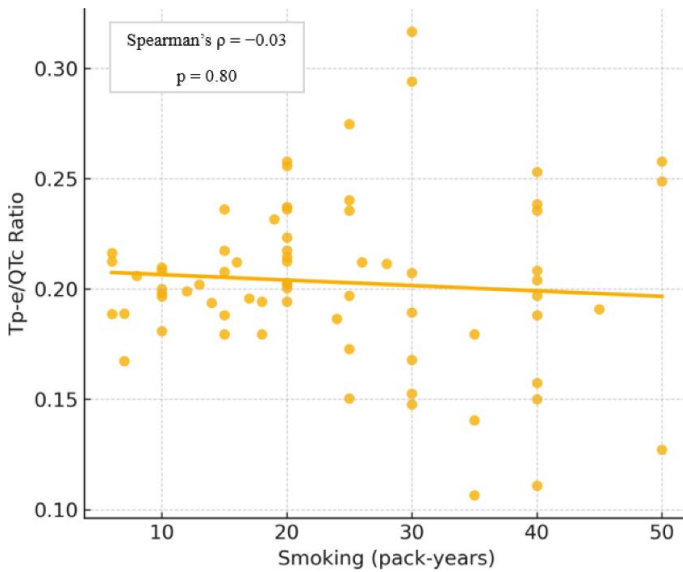


Figure 2. Correlation between cumulative smoking exposure (pack-years) and baseline Tp-e/QTc ratio.

Discussion

The main finding of our study was that no changes were observed in QT, QTc, Tp-e, and Tp-e/QTc parameters, which are important indicators of arrhythmia risk, after 25 days of cytisine treatment used for smoking cessation.

Most patients who begin smoking cessation treatment are individuals at high risk of atherosclerotic cardiovascular disease.¹⁰ Therefore, the risk of arrhythmic side effects from a drug prescribed for this purpose is of particular importance. Varenicline, NRT, and bupropion are first-line agents in current guidelines, but there is strong evidence that varenicline is more effective than bupropion or NRT.¹³ Although varenicline, which acts on the same $\alpha 4\beta 2$ nicotinic acetylcholine receptors as cytisine, has been shown in several studies to influence ventricular repolarization parameters (particularly by prolonging QTc and Tp-e intervals), our findings did not demonstrate a similar effect with cytisine. For instance, in a randomized crossover trial, varenicline significantly prolonged Tp e, QTc, and Tp e/QTc ($P = 0.02$, $P = 0.02$, and $P = 0.01$, respectively), suggesting a potential arrhythmogenic effect.¹⁴

Although varenicline and cytisine have similar pharmacodynamic properties, their electrophysiological effects may differ. Both drugs reduce nicotine dependence by binding with high affinity to $\alpha 4\beta 2$ nicotinic acetylcholine receptors; however, the longer half-life (approximately 24 hours) and higher receptor affinity of varenicline may lead to more pronounced effects on the central nervous system and autonomic cardiac control.¹⁵ This may affect the vagal and sympathetic balance, causing changes in the repolarization process. Additionally, due to the renal elimination of varenicline, the potential for accumulation, especially in patients with impaired renal function, may predispose to electrocardiographic changes such as QTc prolongation.¹⁶ Cytisine, on the other hand, exerts a more limited effect on the cardiac autonomic system due to its shorter half-life (~4.8 hours) and relatively weaker partial agonistic effect, which may explain the preservation of repolarization parameters. The mechanisms

underlying the difference in arrhythmogenic safety observed in our study may therefore be attributed to these pharmacokinetic and pharmacodynamic properties.

The Tp-e interval and Tp-e/QTc ratio are recognized as sensitive indicators of transmural dispersion of repolarization and predictors of malignant ventricular arrhythmias.^{17,18} Gupta et al.⁹ reported that patients at increased risk of arrhythmia, including those with long or short QT syndrome and individuals with organic cardiac disease or a history of myocardial infarction, exhibited significantly higher Tp-e/QT ratios. Therefore, the stability of these markers in our study supports the cardiac safety of cytisine during early-phase smoking cessation treatment. In 2023, Livingstone-Banks et al.⁵ conducted a review of 75 trials, which included data on whether there were any significant cardiac side effects associated with cytisine and varenicline. In this review, although it is very valuable that the authors stated no serious cardiac side effects were observed after cytisine, ECG parameters were not evaluated. In our study, unlike others, ECG parameters were evaluated primarily.

In our study, 12-lead ECGs obtained at baseline and at one month were evaluated. As the one-month follow-up coincides with completion of the manufacturer-recommended 25-day cytisine regimen, we consider this a clinically appropriate time point to assess ventricular repolarization at the target dose. However, this interval may not capture delayed repolarization changes, which remains a limitation.

Non-adherence to medication is one of the reasons for failure in smoking cessation treatment.¹⁹ Insufficient knowledge of adverse effects has been linked to lower adherence rates.²⁰ We believe that our study may help bridge this knowledge gap, thereby improving clinician and patient confidence and supporting the design of future prospective studies.

Interestingly, we noted a statistically significant increase in serum potassium and a decrease in calcium levels after treatment. These changes remained within physiological limits, but their potential impact on cardiac electrophysiology cannot be completely ruled out. Hypocalcemia is known to prolong the QT interval by delaying phase 2 of the cardiac action potential, while hyperkalemia, depending on its severity, may cause various ECG alterations.^{21,22} Despite these biochemical changes, the absence of QT or Tp-e interval prolongation suggests that the electrolyte changes observed during cytisine therapy are not clinically significant in this population.

Our study is strengthened by stringent exclusion criteria and paired ECG-laboratory analyses, which minimized bias and improved validity. Still, the retrospective design, short duration of follow-up, and possible inter-observer variability in ECG interpretation represent limitations. Another limitation is that, given the limited sample size, our study may not have had sufficient power to detect subtle but clinically relevant changes in repolarization parameters; therefore, such minor differences may have remained undetected. Furthermore, the study design intentionally focused on individuals without known cardiovascular disease; consequently, the applicability of our results is confined to relatively healthy smokers. Future investigations are needed to delineate cytisine's electrophysiological safety profile in higher-

risk settings characterized by structural heart disease, impaired renal function, pre-existing arrhythmias, or polypharmacy with QT-prolonging agents.

Conclusion

Treatment with cytosine for smoking cessation did not significantly affect the QT, QTc, Tp-e, or Tp-e/QTc parameters, which may indicate a favorable short-term electrophysiological outcome. To our knowledge, this is the first study evaluating the effects of cytosine on ventricular repolarization. These findings support the use of cytosine as a safe option in smoking cessation therapy. Nevertheless, larger prospective and long-term studies are required to confirm these results and to further assess its cardiovascular safety, particularly in patients with established heart disease.

Ethics Committee Approval: Ethics committee approval was obtained from Manisa Celal Bayar University Ethics Committee (Approval Number: 20.478.486/3142, Date: 11.06.2025).

Informed Consent: Written informed consent was waived due to the retrospective nature of this study.

Conflict of Interest: The authors have no conflicts of interest to declare.

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References

- Prochaska JJ, Benowitz NL. Smoking cessation and the cardiovascular patient. *Curr Opin Cardiol*. 2015;30(5):506–511. [CrossRef]
- Tobacco Use and Dependence Guideline Panel. Treating Tobacco Use and Dependence: 2008 Update. Rockville (MD): US Department of Health and Human Services. Accessed October 18, 2025. <https://www.ncbi.nlm.nih.gov/books/NBK63952/>
- Walker N, Howe C, Glover M, et al. Cytisine versus nicotine for smoking cessation. *N Engl J Med*. 2014;371(25):2353–2362. [CrossRef]
- Tutka P, Vinnikov D, Courtney RJ, Benowitz NL. Cytisine for nicotine addiction treatment: a review of pharmacology, therapeutics and an update of clinical trial evidence for smoking cessation. *Addiction*. 2019;114(11):1951–1969. [CrossRef]
- Livingstone-Banks J, Fanshawe TR, Thomas KH, et al. Nicotine receptor partial agonists for smoking cessation. *Cochrane Database Syst Rev*. 2023;5(5):CD006103. [CrossRef]
- Rigotti NA, Benowitz NL, Prochaska J, et al. Cytisinicline for Smoking Cessation: A Randomized Clinical Trial. *JAMA*. 2023;330(2):152–160. [CrossRef]
- De Santi O, Orellana M, Di Niro CA, Greco V. Evaluation of the effectiveness of cytosine for the treatment of smoking cessation: A systematic review and meta-analysis. *Addiction*. 2024;119(4):649–663. [CrossRef]
- Göçer K, Öztürk B, Kaniyolu M, Tekinalp M. Effect of Smokeless Tobacco (Maras Powder) on the Epicardial Fat Thickness and Ventricular Repolarization Parameters. *Medicina (Kaunas)*. 2023;59(6):1127. [CrossRef]
- Gupta P, Patel C, Patel H, et al. T(p-e)/QT ratio as an index of arrhythmogenesis. *J Electrocardiol*. 2008;41(6):567–574. [CrossRef]
- Yıldırım DI, Hayiroğlu Mİ, Ünal N, Eryılmaz MA. Evaluation of varenicline usage on ventricular repolarization after smoking cessation. *Ann Noninvasive Electrocardiol*. 2019;24(2):e12609. [CrossRef]
- Nides M, Rigotti NA, Benowitz N, Clarke A, Jacobs C. A Multicenter, Double-Blind, Randomized, Placebo-Controlled Phase 2b Trial of Cytisinicline in Adult Smokers (The ORCA-1 Trial). *Nicotine Tob Res*. 2021;23(10):1656–1663. [CrossRef]
- Richardson DR, Parish PC, Tan X, et al. Association of QTc Formula with the Clinical Management of Patients with Cancer. *JAMA Oncol*. 2022;8(11):1616–1623. [CrossRef]
- World Health Organization (WHO). WHO clinical treatment guideline for tobacco cessation in adults. Accessed October 17, 2025. <https://www.ncbi.nlm.nih.gov/books/NBK604664/>
- Ari H, Ari S, Coşar S, Celiloğlu N, et al. The effect of varenicline on Tp-e interval, Tp-e/QT ratio and Tp-e/QTc ratio in healthy smokers and nonsmokers. *Cardiol J*. 2015;22(5):551–556. [CrossRef]
- Rollema H, Shrikhande A, Ward KM, et al. Pre-clinical properties of the alpha4beta2 nicotinic acetylcholine receptor partial agonists varenicline, cytosine and dianicline translate to clinical efficacy for nicotine dependence. *Br J Pharmacol*. 2010;160(2):334–345. [CrossRef]
- Dobrinas M, Cornuz J, Oneda B, Kohler Serra M, Puhl M, Eap CB. Impact of smoking, smoking cessation, and genetic polymorphisms on CYP1A2 activity and inducibility. *Clin Pharmacol Ther*. 2011;90(1):117–125. [CrossRef]
- Akboğa MK, Gülcihan Balci K, Yılmaz S, et al. Tp-e interval and Tp-e/QTc ratio as novel surrogate markers for prediction of ventricular arrhythmic events in hypertrophic cardiomyopathy. *Anatol J Cardiol*. 2017;18(1):48–53. [CrossRef]
- Baytugan NZ, Mağden K. Evaluation of QTc Interval, Tp-e Interval, Tp-e/QT Ratio and Tp-e/QTc Ratio in Patients with Autosomal Dominant Polycystic Kidney Disease. *Turk Kardiyol Dern Ars*. 2025;53(5):328–335. [CrossRef]
- Pacek LR, McClernon FJ, Bosworth HB. Adherence to Pharmacological Smoking Cessation Interventions: A Literature Review and Synthesis of Correlates and Barriers. *Nicotine Tob Res*. 2018;20(10):1163–1172. [CrossRef]
- Kushnir V, Sproule BA, Cunningham JA. Mailed distribution of free nicotine patches without behavioral support: Predictors of use and cessation. *Addict Behav*. 2017;67:73–78. [CrossRef]
- Tang JKK, Rabkin SW. Hypocalcemia-Induced QT Interval Prolongation. *Cardiology*. 2022;147(2):191–195. [CrossRef]
- El-Sherif N, Turitto G. Electrolyte disorders and arrhythmogenesis. *Cardiol J*. 2011;18(3):233–245.