

## ORIGINAL RESEARCH

# The effect of upper endoscopic procedures under sedation on ventricular repolarization: retrospective study

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**Abstract**

**Background:** Over the past twenty-five years, endoscopic procedures have played a substantial role in diagnosing and treating gastrointestinal system diseases. This study aimed to analyze the impact of balanced propofol sedation on myocardial repolarization parameters during endoscopy. **Methods:** Our study comprised 58 patients who underwent elective upper endoscopic (UE) procedures. A 12-lead electrocardiography was conducted on all patients at various time points, including before the procedure, after sedation, during the first and fifth minutes of UE, and post-procedure. Calculations of the QT interval, corrected QT (QTc) interval, Tpeak-Tend (Tp-e) interval, Tp-e/QT and Tp-e/QTc were performed using the 12-lead electrocardiograms. **Results:** Among 58 patients (46.6% female and 53.4% male) who underwent elective endoscopy, a statistically significant prolongation of QRS and Tp-e/QT intervals was observed after administration of sedation, during the endoscopy procedure and post-procedure in comparison to the pre-procedure measurements ( $p^1 = 0.018$ ,  $p^2 = 0.005$ ,  $p^3 = 0.003$ ,  $p^4 = 0.007$  and  $p^1 < 0.001$ ,  $p^2 < 0.001$ ,  $p^3 < 0.001$ ,  $p^4 = 0.017$  respectively). A marked reduction in the Tp-e/QTc ratio was observed following sedation, throughout the endoscopy procedure, and in the post-procedure phase, relative to the pre-procedure baseline ( $p^1 < 0.001$ ,  $p^2 < 0.001$ ,  $p^3 < 0.001$ ,  $p^4 < 0.001$ ). **Conclusions:** The findings of this study indicate that propofol sedation with a balanced approach resulted in a significant prolongation of QRS, QT and Tp-e/QT duration, along with a decrease in the Tp-e/QTc ratio. The impact of such sedation on ventricular repolarization necessitates acknowledgment and calls for caution regarding potential arrhythmias.

**Keywords**

Balanced propofol sedation; Endoscopy; Electrocardiography; Tp-e interval; QT interval; Tp-e/QT ratio

## 1. Introduction

The utilization of endoscopy as a diagnostic, screening and therapeutic measure for gastrointestinal tract diseases has become increasingly prevalent. The use of sedation has experienced a growing trend in its utilization to assist patients in tolerating distressing endoscopic procedures, as it alleviates anxiety, discomfort and pain. Hence, the preference lies in utilizing drugs that have a brief duration of action and limited side effects. Despite being widely used as an anesthetic drug in outpatient settings like endoscopy, propofol lacks adequate analgesic properties. The development of Balanced Propofol Sedation (BPS) aimed to decrease the overall amount of propofol used by incorporating small amounts of benzodiazepines and opioids. The method involves the controlled administration of minute doses of a blend of various neuronal depressants to maximize the therapeutic effects and minimize

the probability of dose-dependent adverse reactions from any specific drug [1].

Anesthetic agents can potentially display arrhythmogenic properties due to their impact on cardiac electrical activity. The detection of ventricular repolarization can be achieved through measurements of the QT interval, QT dispersion and T wave. In actuality, QT dispersion serves as a general and approximate gauge of the overall abnormality in repolarization. Findings from recent studies have demonstrated that the Tpeak-Tend interval (Tp-e) is a simple and accessible measure that can be used to evaluate the transmural distribution of repolarization and its relationship with arrhythmogenesis. In addition, Tp-e/QT and Tp-e/QTc ratios have also been employed as indicators of arrhythmogenesis. Numerous studies have indicated that an Tp-e, Tp-e/QT and Tp-e/QTc interval predicts both ventricular arrhythmias and mortality [2–5].

This study aimed to assess the influence of sedation during

endoscopy on myocardial depolarization and repolarization parameters.

## 2. Material and methods

### 2.1 Study population

Following the approval granted by the clinical research ethics committee of Bursa City Hospital (E-13012450-514.99-230162044), a cohort of 58 patients, aged 18–65 years, with (American Society of Anesthesiologists) ASA I–II classification, who were undergoing elective upper endoscopy were included. Informed consent was obtained from all subjects. Exclusion criteria included patients with any form of cardiac disease, drug-induced QT prolongation, or electrolyte disturbances. Furthermore, a patient was excluded due to atrial fibrillation with rapid ventricular response.

### 2.2 Anesthesia

The monitoring of all patients included continuous electrocardiography (ECG) and pulse oximetry. Noninvasive blood pressure monitoring was conducted through the application of oscillometry. The patients were provided with a 12-channel GE MAC 2000 ECG device (Milwaukee, WI, USA) for monitoring. The standard procedure involved positioning patients in the left lateral position for endoscopy. Before the initiation of anesthesia, nasal oxygen was commenced at a flow rate of 2–3 liters per minute and maintained throughout the procedure. The administration of anesthesia commenced with the intravenous (IV) injection of 1–2 mg of midazolam, 50 mcg of fentanyl, and a bolus of 20–30 mg of propofol.

Further administration of propofol was carried out as required until the Ramsey sedation scale (RSS) score achieved a value of 5. Patients exhibiting a Ramsey sedation scale (RSS) score of 5 were eligible for endoscopic intervention. Measurements of oxygen saturation (SaO<sub>2</sub>), heart rate, systolic arterial pressure (SAP), mean arterial pressure (MAP), and diastolic arterial pressure (DAP), were taken at five specific time points, at pre-procedure, at 1 and 5 minutes post-sedation during the endoscopic procedure when the RSS score was 5, and at 3 minutes post-procedure.

### 2.3 Electrocardiographic measurements

Electrocardiograms (ECGs) were acquired from all patients using a GE MAC 2000 ECG device, with measurements taken in 12 leads at a 25 mm/sec speed and an amplitude of 1 mV. 12-lead ECG were taken at five specific time points, at pre-procedure, at 1 and 5 minutes post-sedation during the endoscopic procedure when the RSS score was 5, and at 3 minutes post-procedure. The ECGs were converted to portable document format (PDF) format using a scanner and subsequently magnified to ×400% using Adobe Photoshop software (Adobe Photoshop, version 20.0.0, Adobe Inc., San Jose, CA, USA). ECG measurements of QT and Tp-e intervals were conducted by two cardiologists blinded to patient data. The determination of the QT interval involved the assessment of the span commencing at the initiation of the QRS complex and concluding at the termination of the T wave, and this

computation was conducted independently for every lead. The corrected QT (QTc) was determined using the Bazett formula:  $QTc = QT/\sqrt{(RR \text{ interval})}$ . QTc dispersion was defined as the discrepancy between the longest and shortest QTc measurements. The difference between the T wave's peak and its end was referred to as the Tp-e interval. The U wave was omitted from the Tp-e interval. The evaluation of Tp-e interval measurements was conducted from precordial leads. The calculated TP-e and the calculated QT and QTc were noted by finding the Tp-e/QT and Tp-e/QTc ratios, which were calculated separately with Tp-e.

### 2.4 Statistical analysis

The statistical analysis was conducted utilizing SPSS 22.0, developed by SPSS Inc (Chicago, IL, USA). The Kolmogorov-Smirnov test was employed to assess the normal distribution of continuous variables. Mean ± (Standard deviation) SD was used to express continuous variables, while numbers and percentages were used to express categorical variables. The pre-procedure and post-procedure variables were compared using the paired *t*-test. A *p*-value below 0.05 was deemed statistically significant.

## 3. Results

Table 1 offers a comprehensive overview of the patient characteristics. The patients' mean age was determined to be 52.62 ± 13.64 years. The female patients accounted for 46.6% of the total, while the male patients accounted for 53.4%.

The duration of QRS and Tp-e/QT ratio observed during and after sedation, endoscopy, and post-procedure showed significant increases compared to the intervals before the procedure ( $p^1 = 0.018$ ,  $p^2 = 0.005$ ,  $p^3 = 0.003$ ,  $p^4 = 0.007$  and  $p^1 < 0.001$ ,  $p^2 < 0.001$ ,  $p^3 < 0.001$ ,  $p^4 = 0.017$ , respectively). Significant reductions in the Tp-e/QTc ratio were observed following sedation, during the endoscopy procedure, and post-procedure, as compared to the pre-procedure phase ( $p^1 < 0.001$ ,  $p^2 < 0.001$ ,  $p^3 < 0.001$ ,  $p^4 < 0.001$ ). Furthermore, the pre-procedure QT value was notably more prolonged than the post-procedure value ( $p < 0.001$ ), with no disparity observed between the values recorded during sedation and the procedure. Although not statistically significant, it was observed that the duration of Tp-e intervals observed after sedation, endoscopy and procedure decreased compared to before the procedure ( $p^1 = 0.085$ ,  $p^2 = 0.548$ ,  $p^3 = 0.996$ ,  $p^4 = 0.092$ ). No significant changes were observed in QT dispersion, QTc and QTc dispersion compared to baseline values (Table 2). Figs. 1,2 depict the changes in Tp-e/QTc and Tp-e/QT during sedated upper endoscopy.

The study participants did not exhibit any noteworthy ventricular or supraventricular arrhythmias, and no instances of mortality or morbidity were recorded.

## 4. Discussion

This study investigated the effects of endoscopy under sedation on myocardial repolarization parameters. During the process of sedated endoscopy, we discovered a significant prolongation

**TABLE 1. Characteristics of the study population.**

	n (%)*
Age (yr), Mean $\pm$ SD	52.62 $\pm$ 13.64
<b>Gender</b>	
Female	27 (46.6)
Male	31 (53.4)
Body weight (kg), Mean $\pm$ SD	74.81 $\pm$ 15.97
<b>ASA</b>	
ASA I	13 (22.5)
ASA II	45 (77.5)
<b>DM</b>	
Absent	18 (31.0)
Present	40 (69.0)
<b>HT</b>	
Absent	48 (82.7)
Present	10 (17.3)
<b>CRF</b>	
Absent	58 (100.0)
Present	0 (0.0)
<b>CVE</b>	
Absent	58 (100.0)
Present	0 (0.0)
<b>CAD</b>	
Absent	57 (98.3)
Present	1 (1.7)

\*Categorical data were summarized as n (%).

ASA: American Society of Anesthesiologists; DM: Diabetes mellitus; HT: Hypertension; CRF: Chronic renal failure; CVE: Cerebrovascular event; CAD: Coronary artery disease; SD: Standard deviation.

**TABLE 2. Electrocardiographic features.**

	Pre-procedure	Sedation	During endoscopy		Post-procedure	p
			1st min	5th min		
Heart rate	88.38 $\pm$ 14.88	87.72 $\pm$ 16.27	87.17 $\pm$ 16.94	84.53 $\pm$ 16.09	80.81 $\pm$ 14.82	$p^1 = 0.156^*$ $p^2 = 0.460^*$ $p^3 = 0.024^*$ $p^4 < 0.001^*$
QRS	79.84 $\pm$ 13.22	83.70 $\pm$ 14.29	84.68 $\pm$ 13.95	84.45 $\pm$ 13.68	84.10 $\pm$ 14.93	$p^1 = 0.018^*$ $p^2 = 0.005^*$ $p^3 = 0.003^*$ $p^4 = 0.007^*$
QT	364.10 $\pm$ 32.92	359.91 $\pm$ 39.83	364.56 $\pm$ 40.98	368.59 $\pm$ 34.35	378.41 $\pm$ 32.96	$p^1 = 0.256^*$ $p^2 = 0.645^{**}$ $p^3 = 0.207^*$ $p^4 < 0.001^{**}$
QT disp	48.12 $\pm$ 34.94	44.35 $\pm$ 26.82	45.19 $\pm$ 53.00	40.91 $\pm$ 25.55	41.76 $\pm$ 30.87	$p^1 = 0.713^*$ $p^2 = 0.358^*$ $p^3 = 0.152^*$ $p^4 = 0.240^*$

TABLE 2. Continued.

	Pre-procedure	Sedation	During endoscopy		Post-procedure	p
			1st min	5th min		
QTc	435.48 ± 26.47	430.05 ± 33.12	431.79 ± 36.61	432.76 ± 30.33	434.74 ± 27.09	$p^1 = 0.093^*$ $p^2 = 0.379^{**}$ $p^3 = 0.489^{**}$ $p^4 = 0.849^{**}$
QTc disp	50.82 ± 32.91	44.35 ± 26.82	46.56 ± 33.35	46.86 ± 33.89	54.07 ± 47.25	$p^1 = 0.789^*$ $p^2 = 0.236^*$ $p^3 = 0.211^*$ $p^4 = 0.743^*$
Tp-e	81.07 ± 18.80	77.40 ± 18.54	79.89 ± 18.17	80.81 ± 18.30	77.62 ± 19.51	$p^1 = 0.085^*$ $p^2 = 0.548^*$ $p^3 = 0.996^*$ $p^4 = 0.092^*$
Tp-e/QT	0.187 ± 0.04	0.218 ± 0.06	0.222 ± 0.05	0.220 ± 0.05	0.207 ± 0.05	$p^1 < 0.001^*$ $p^2 < 0.001^*$ $p^3 < 0.001^*$ $p^4 = 0.017^{**}$
Tp-e/QTc	0.225 ± 0.05	0.181 ± 0.04	0.186 ± 0.04	0.187 ± 0.04	0.179 ± 0.04	$p^1 < 0.001^*$ $p^2 < 0.001^{**}$ $p^3 < 0.001^{**}$ $p^4 < 0.001^*$

$p^1$  value between pre-procedure and sedation.

$p^2$  value between pre-procedure and 1st min.

$p^3$  value between pre-procedure and 5th min.

$p^4$  value between pre-procedure and post-procedure.

\*Non-parametric test; \*\*Parametric test.

disp: dispersion; QTc: corrected QT; Tp-e: Tpeak-Tend.

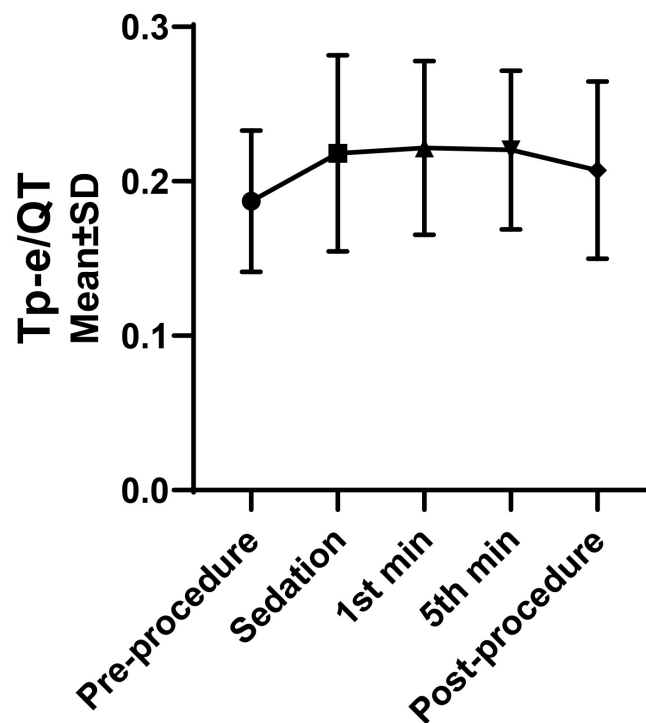
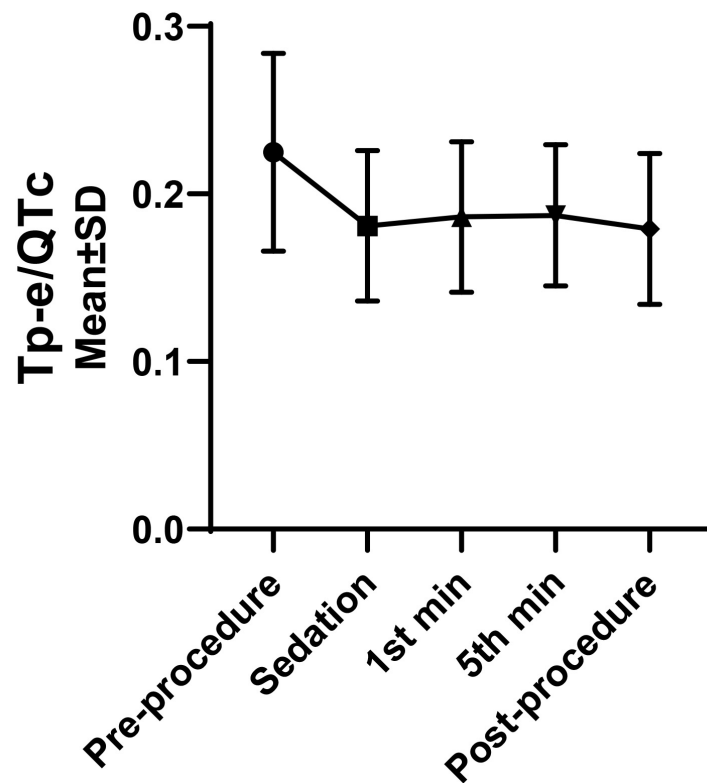


FIGURE 1. Tp-e/QT changes due to upper endoscopy under sedation. Tp-e: Tpeak-Tend; SD: Standard deviation.



**FIGURE 2. Tp-e/QTc changes due to upper endoscopy under sedation.** Tp-e: Tpeak-Tend; QTc: corrected QT; SD: Standard deviation.

of QRS and Tp-e/QT intervals, as well as a decrease in the Tp-e/QTc ratio. To our knowledge, this study represents the initial evidence of the link between balanced propofol sedation and Tp-e/QTc duration and Tp-e/QT ratio in asymptomatic patients without arrhythmia.

The crucial aspect of preventing sudden cardiac death lies in the identification of high-risk patients. Thus, numerous parameters have been studied for performing risk analysis using resting ECG and identifying these at-risk patients. The research conducted by Xie *et al.* [6] revealed a heightened risk of ventricular arrhythmia in patients decreased Tp-e duration and Tp-e/QT ratio. Furthermore, studies have demonstrated that an extended Tp-e duration is linked to the occurrence of life-threatening arrhythmias in individuals diagnosed with long QT syndrome, ischemic heart disease, and hypertrophic cardiomyopathy [7–9].

Sedation is typically administered during gastrointestinal endoscopy to guarantee both the procedure's completion and the patient's comfort. It is common practice to administer anesthetic and analgesic medications in combination to mitigate potential adverse effects. Due to its rapid onset of action, ease of titration, and short half-life, Propofol is the preferred anesthetic agent in outpatient procedures such as endoscopy, dental procedures, catheter ablation and diagnostic laparoscopy. The utilization of propofol sedation in conjunction with benzodiazepine, as opposed to propofol alone, yields a quicker recovery time after endoscopy [1]. However, the use of this combination does not produce any analgesic effects. Hence, the combination with fentanyl is employed owing to its robust analgesic effects. Despite the safety of combination

therapy for endoscopic sedation, it is essential to note that anesthetic agents can exhibit arrhythmogenic properties due to their influence on cardiac electrical activity.

The QT interval denotes the period encompassing both the depolarization and repolarization of the left ventricle. The occurrence of prolongations within this specific interval presents a significant risk for the emergence of polymorphic ventricular tachycardia and ventricular fibrillation. Due to its dependence on heart rate, the corrected QT distance (QTc distance) is more commonly utilized in clinical practice [10]. The ventricular myocardium consists of three distinct types of cells with varying electrophysiologic properties: endocardial, epicardial and subendocardial. Among these, the M cells exhibit the highest sensitivity to action potential prolongation. Due to the transmural distribution of ventricular repolarization, the Tp-e interval is observed in the ECG, indicating the time frame when the myocardial epicardium is completely repolarized while the M cells are still undergoing repolarization. The occurrence of early repolarizations during this process renders the myocardium susceptible to fatal arrhythmias, such as ventricular tachycardia and fibrillation, through the reentry mechanism [11, 12]. There is ongoing controversy regarding the influence of propofol on myocardial repolarization. Various myocardial repolarization studies evaluated with QT interval have revealed that it does not either affect the QT distance or prolong/shorten the QT interval [13–16]. Additionally, it has been observed in several studies that propofol tends to prolong Tp-e [14, 17]. Nonetheless, studies have failed to demonstrate any noteworthy impact of fentanyl and midazolam on myocardial repolarization [18–21].

Our study's limitation was evaluating the relationship between ventricular arrhythmias and the myocardial repolarization parameters. Hence, the prognostic implications of Tp-e/QTc and Tp-e/QT ratio in our patients remained uncertain. Nonetheless, the Tp-e/QTc ratio and Tp-e/QT ratio hold significant prognostic value in numerous cohorts of patients. Furthermore, the study was significantly limited by its small patient sample size. Multicenter studies involving a larger cohort of patients are required. Since no control group was planned in the study, data regarding the endoscopy itself and the procedure time could not be evaluated.

## 5. Conclusions

According to our study, the use of propofol, fentanyl and midazolam in a balanced anesthesia combination during endoscopy of the upper gastrointestinal tract led to the following outcomes: prolongation in QRS duration, increase in QT distance, prolongation of Tp-e/QT, and decrease in Tp-e/QTc ratio. Hence, this outcome implies that using this commonly employed combination in clinical settings to mitigate adverse effects may potentially elevate the likelihood of arrhythmia in patients. However, it is essential to note that we did not observe any cases of arrhythmia in our study. This finding can be attributed to employing a relatively modest dose of propofol. Previous studies have reported that the effect of propofol on myocardial repolarization is dose-dependent [22–24]. Therefore, balanced propofol sedation is safe for endoscopy. However, it is essential to exercise caution regarding the impact of these sedatives on ventricular repolarization and the potential occurrence of arrhythmias.

## AVAILABILITY OF DATA AND MATERIALS

The data presented in this study are available on reasonable request from the corresponding author.

## AUTHOR CONTRIBUTIONS

SG, FG—designed the research study; wrote the manuscript. FG, SÇÖ, ST—performed the research. SG, SÇ, CUY and DY—analyzed the data. All authors read and approved the final manuscript.

## ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study was approved by the clinical research ethics committee of Bursa City Hospital (E-13012450-514.99-230162044). Informed consent was obtained from all subjects.

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## CONFLICT OF INTEREST

The authors declare no conflict of interest.

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