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ORIGINAL RESEARCH

# Effect of Remifentanil on the Tpeak-Tend Interval During Electroconvulsive Therapy

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## ABSTRACT

***Introduction***: QT interval dispersion, which reflects the regional heterogeneity of ventricular repolarization, increases during electroconvulsive therapy (ECT). Tpeak-Tend (TpTe) is considered a new marker of the transmural dispersion of ventricular repolarization (TDR). This study aimed to evaluate the effect of remifentanil on TpTe during ECT.

***Methods***: Forty-two patients who were scheduled to undergo ECT with American Society of Anesthesiologists physical status I or II randomly received 0.1 μg/kg remifentanil (group R: $n = 21$) or saline (group C: $n = 21$). After the induction of general anesthesia, we measured the TpTe, TpTe/QT, TpTe/QTc, TpTe/RR, TpTe/$\sqrt{RR}$ and TpTe/$\sqrt[3]{RR}$ every minute during ECT (QT: QT interval, QTc: corrected QT interval, RR: RR interval). Statistical analysis was performed using two-way analysis of variance (ANOVA).

***Results***: Immediately (T0) and 1 min (T1) after electrical stimulation, the RRs (group C: T0; 654.2 ± 145.9 ms, T1; 657.3 ± 114.8 ms, group R: T0; 849.6 ± 249.3 ms, T1; 885.4 ± 213.6 ms, $p < 0.05$) were significantly increased, while systolic (group C: T0; 177.1 ± 35 mmHg, group R: T0; 129 ± 27.2 mmHg, $p < 0.05$) and diastolic blood pressures (group C: T0; 107.1 ± 22.4 mmHg, T1; 101.3 ± 23.2 mmHg, group R: T0; 75.4 ± 19.3 mmHg, T1; 80.6 ± 18.3 mmHg, $p < 0.05$) were significantly decreased in group R compared to group C. The TpTe/RR was significantly lower at T1 in group R compared to group C (group C: 101.5 ± 28.2, group R: 76.8 ± 21.8, $p < 0.05$). However, there was no significant difference in TpTe, TpTe/QT, TpTe/QTc, TpTe/$\sqrt{RR}$ or TpTe/3$\sqrt{RR}$ between the two groups throughout the study.

***Conclusion***: Pretreatment with remifentanil suppressed the increase of TpTe/RR after electrical stimulation. Our results imply that remifentanil may lead to a decrease in TDR during ECT.

***Trial Registration***: This trial was registered with the University Hospital Medical Information Network (registration number: UMIN000051958).

**Keywords:** Electroconvulsive therapy; Remifentanil; Tpeak tend; Transmural dispersion of ventricular repolarization

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**Key Summary Points**

| |
|---|
| ***Why carry out this study?*** |
| Tpeak-Tend (TpTe) is considered a relatively new marker of the transmural dispersion of ventricular repolarization (TDR) |
| No studies have reported the effects of remifentanil on TpTe during electroconvulsive therapy (ECT) |
| To clarify the effect of remifentanil on TDR during ECT, we measured the TpTe in the present study |
| ***What was learned from the study?*** |
| Remifentanil suppressed the significant hemodynamic change during ECT |
| Remifentanil significantly attenuated the increase in TpTe/RR (RR: RR interval) |
| Our findings suggest that remifentanil likely reduces the TDR, a predictor of ventricular tachyarrhythmia |

## INTRODUCTION

Electroconvulsive therapy (ECT) is usually performed to treat various psychiatric disorders when other treatments are unsuccessful. In most cases, this procedure is conducted under general anesthesia. Previous studies have demonstrated that remarkable hemodynamic changes, such as hypertension or tachycardia, are observed immediately after electrical stimulation in ECT because of the activation of the sympathetic nervous system [1, 2]. Most ECT-related deaths are due to adverse cardiovascular events following electrical stimulation [3, 4].

The dispersion of QT interval (QTD), defined as the difference between the maximum and minimum QT interval on 12-lead surface electrocardiography (ECG), is known to reflect the regional heterogeneity of ventricular repolarization of the myocardium. This marker has been proposed as a predictor of ventricular arrhythmia, which may lead to sudden cardiac death [5]. Our previous reports have suggested that QTD significantly increased after electrical stimulation [6, 7].

The interval from the peak to the end of the T wave (TpTe) on 12-lead electrocardiogram (ECG) is a comparatively novel parameter which reflects the transmural dispersion of ventricular repolarization (TDR). The TDR is strongly associated with the incidence of ventricular tachyarrhythmia [8], and its evaluation is beneficial for predicting the lethal arrhythmias in patients with coronary artery disease, Brugada syndrome, short QT and long QT syndromes [9]. Similar to QTD, TpTe is suggested to be a predictor of lethal ventricular arrhythmias, which may cause sudden death [10, 11]. The TpTe/QT ratio is also considered a marker of TDR and a noninvasive arrhythmogenic index of sudden cardiac death [12]. In addition, patients who developed ventricular tachycardia (VT) displayed prolonged TpTe/$\sqrt{}$RR (collected by RR interval) compared to patients who did not develop VT [13].

Remifentanil, an ultra-short-acting μ-opioid receptor agonist, is approved for general anesthesia and achieves predictable recovery because it allows fast emergence from anesthesia. Our previous study clarified that pretreatment with remifentanil significantly suppressed the increase of hemodynamic change and QTD during ECT [14]. The effectiveness of remifentanil against QTD, a marker of myocardial ventricular repolarization, during ECT has been demonstrated, but its effect on TpTe, a novel marker of TDR, has not been established. The purpose of this study is to investigate the change of TpTe during ECT and the effect of remifentanil on TpTp during ECT.

## METHODS

We included 44 patients with American Society of Anesthesiologists (ASA) physical status I or II, aged 20–65 years, who were scheduled to undergo modified electroconvulsive therapy (mECT). The study was approved by the ethics

committee of Dokkyo Medical University (R-32-1) and registered with the University Hospital Medical Information Network (UMIN, registration number: UMIN000051958). We received written informed consent from all patients. All procedures were performed in accordance with the ethical standards of the Institutional and National Research Committee and the principles of the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. We excluded patients with cardiovascular, respiratory, metabolic or cerebrovascular diseases, and preoperative electrocardiogram (ECG) abnormalities. None of the patients had received premedication. The participants were randomly assigned to two groups: patients in group R ($n$ = 22) received IV remifentanil (1 μg/kg) before the induction of general anesthesia, while those in group C ($n$ = 22) received IV saline. In the operating room, standard monitoring of three-lead ECG signals, noninvasive measurement of arterial blood pressure and pulse oximetry were performed (DS-7780W; FUKUDA DENSHI Co., Ltd., Tokyo, Japan). After adequate preoxygenation, pretreatment with 1 μg/kg remifentanil or placebo (saline), intravenously injected, and anesthesia was induced with 1 mg/kg IV propofol. After confirming loss of consciousness, 1 mg/kg succinylcholine was intravenously administered. Subsequently, we performed assisted mask ventilation with 100% oxygen. An electrical stimulus was delivered via bitemporal electrodes using an ECT stimulator (Thymatron System; Somatics LLC, Lake Bluff, IL.). The magnitude of the energy setting for the ECT stimulus was predetermined according to age. We determined the efficacy of ECT using the tourniquet technique, which is based on the observation of convulsive movements of the distal leg. The seizures were detected using an electroencephalogram (EEG) monitor set in the electrical stimulator.

We measured the RR interval (RR), systolic blood pressure (sBP), diastolic blood pressure (dBP), TpTe, TpTe/QT (QT: QT interval), TpTe/QTc (QTc: corrected QT interval), TpTe/RR, TpTe/$\sqrt{}$RR or TpTe/3$\sqrt{}$RR before the induction of general anesthesia, after loss of consciousness (baseline), immediately after electrical stimulus (T0), and every 1 min to 7 min after electrical stimulus (T1–T7). Three-lead ECG signals were recorded using LRR-03 (GMS, Tokyo, Japan).

The primary outcome of the present study was the effect of remifentanil on TDR during ECT. Therefore, the primary endpoints of TDR were defined as TpTe, TpTe/QT, TpTe/QTc, TpTe/RR, TpTe/$\sqrt{}$RR or TpTe/3$\sqrt{}$RR in ECG during ECT. The secondary endpoints of our study were RR interval, sBP or dBP.

## Statistical analysis

Statistical analyses were performed using Prism 6 software (GraphPad, La Jolla, CA, USA). Data were expressed as mean ± standard deviation (SD). Patient characteristics were analyzed using Student's t-test and Fisher's exact test. Changes in RR interval, sBP, dBP, TpTe, TpTe/QT, TpTe/QTc, TpTe/RR, TpTe/$\sqrt{}$RR (corrected by Bazzet formula) and TpTe/3$\sqrt{}$RR (corrected by Fridericia formula) were analyzed using two-way analysis of variance. When a significant overall effect was detected, Bonferroni's post hoc test was conducted. In all analyses, the probability of detecting a significant difference was set at 5% ($p < 0.05$). A sample size of 18 subjects in each group was considered adequate, based on a previous study [15], to detect a difference of 10 and SD of 20 in the TpTe between the two groups at a power of 80%, with $\alpha = 0.05$.

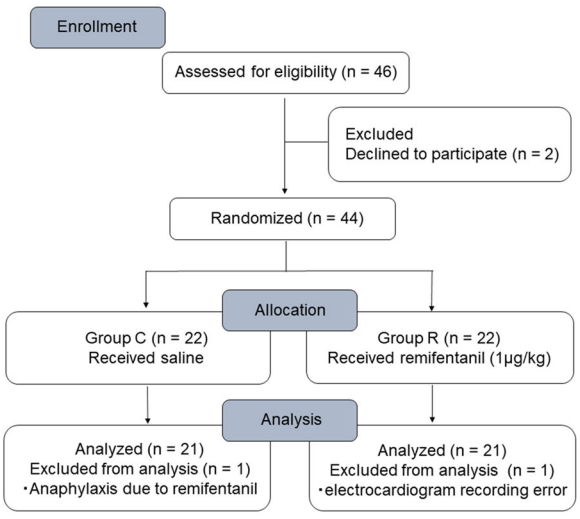


**Fig. 1** Flow diagram of the study

## RESULTS

Two patients were excluded from this study. A patient in group C was excluded because of ECG recording error, and one patient in group R was excluded because of remifentanil-induced anaphylaxis. Finally, we enrolled 42 patients (Fig. 1). There were no significant differences in age, sex, ASA physical status or body mass index (BMI) between the two groups (Table 1). Neither complications nor lethal arrhythmias were observed in this study. All patients received psychiatric medications (Table 2) .

Table 3 shows the values of the RR interval, systolic (sBP) and diastolic blood pressures (dBP) during the present measurement. The RR interval was significantly increased at T0 and T1 in group R compared with that in group C (group C: T0; 654.2 ± 144.9 ms, T1; 657.3 ± 114.8 ms, group R: T0; 849.6 ± 249.3 ms, T1; 885.4 ± 213.6 ms, $p < 0.05$). The sBP at T0 in group C was significantly increased compared with that in group R (group C: 177.1 ± 35 mmHg, group R:

**Table 1** Patient characteristics

| | **Group C (*n* = 21)** | **Group R (*n* = 21)** |
|---|---|---|
| Age (years) | 48 ± 11 | 49 ± 12 |
| Gender (male/female) | 9/12 | 11/10 |
| BMI (kg/m$^2$) | 24 ± 6 | 23 ± 6 |
| ASA physical status (I/II) | 13/8 | 10/11 |
| Diagnosis (depression/schizophrenia) | 4/17 | 6/15 |
| Medications | | |
| Hypertension | 4 | 5 |
| Diabetes mellitus | 3 | 2 |
| Gastritis | 1 | 0 |
| Asthma | 0 | 1 |

Data are presented as the mean ± standard deviation
*BMI*: body mass index, *ASA*: American Society of Anesthesiologists physical status

**Table 2** Psychiatric medications of all patients in this study

| | ***n*** | | ***n*** |
|---|---|---|---|
| Benzodiazepines | | Antipsychotics | |
| Flunitrazepam | 13 | Olanzapine | 8 |
| Nitrazepam | 7 | Levomepromazine | 2 |
| Lorazepam | 4 | Zotepine | 1 |
| Brotizolam | 2 | Risperidone | 15 |
| Clonazepam | 3 | Quetiapine | 13 |
| Estazolam | 3 | Paliperidone | 4 |
| Diazepam | 1 | Haloperidol | 4 |
| Alprazolam | 4 | Brexpiprazole | 5 |
| Suvorexant | 2 | Aripiprazole | 3 |
| Ethyl loflazepate | 1 | Lithium carbonate | 1 |
| | | Asenapine | 1 |
| Non-benzodiazepines | | Perospirone | 1 |
| Zolpidem | 7 | Chlorpromazine | 3 |
| Eszopiclone | 5 | Sulpiride | 2 |
| | | Lurasidone | 1 |
| Orexin antagonists | | Blonanserin | 2 |
| Suvorexant | 1 | | |
| Lemborexant | 2 | Antidepressants | |
| | | Paroxetine | 3 |
| Melatonin agonist | | Escitalopram | 3 |
| Ramelteon | 2 | Mirtazapine | 4 |
| | | Nortriptyline | 1 |
| Anticonvulsants | | Duloxetine | 1 |
| Carbamazepine | 2 | Amitriptyline | 1 |
| Levetiracetam | 1 | Amoxapine | 1 |
| Valproate | 2 | Trazodone | 3 |
| | | Vortioxetine | 1 |
| Anticholinergic | | Venlafaxine | 2 |
| Biperiden | 11 | Sertraline | 1 |

**Table 3** Measurement of hemodynamic values during electroconvulsive therapy

| | Group | Baseline | T0 | T1 | T2 | T3 | T4 | T5 | T6 | T7 |
|---|---|---|---|---|---|---|---|---|---|---|
| RR (ms) | Group C | 865.9 ± 223.5 | 654.2 ± 144.9* | 657.3 ± 114.8* | 700.1 ± 126 | 728.4 ± 151.4 | 717.4 ± 136.3 | 727.3 ± 156.6 | 755.4 ± 133.6 | 752.2 ± 129.7 |
| | Group R | 944.7 ± 225.1 | 849.6 ± 249.3 | 885.4 ± 213.6 | 826.5 ± 195.1 | 805.4 ± 177.7 | 816.2 ± 141.4 | 852.1 ± 182.5 | 852.8 ± 174.9 | 854.6 ± 150.3 |
| sBP (mmHg) | Group C | 128.5 ± 16.2 | 177.1 ± 35* | 165.3 ± 33.4 | 156.1 ± 36 | 146.5 ± 30.3 | 140.4 ± 28.8 | 136.2 ± 25.7 | 145.3 ± 31.1 | 136.6 ± 26.4 |
| | Group R | 117 ± 14.1 | 129 ± 27.2 | 140.5 ± 29.2 | 139.5 ± 30.4 | 134.1 ± 23.3 | 132.9 ± 23 | 130.3 ± 22.8 | 129.6 ± 21.3 | 130.5 ± 23 |
| dBP (mmHg) | Group C | 77.7 ± 11.8 | 107.1 ± 22.4* | 101.3 ± 23.2* | 95.1 ± 21.3 | 88.2 ± 18.3 | 84.2 ± 19.5 | 81.9 ± 16 | 88.4 ± 18.7 | 84.8 ± 20.2 |
| | Group R | 73.5 ± 10.6 | 75.4 ± 19.3 | 80.6 ± 18.3 | 81.9 ± 19.9 | 77.1 ± 13.9 | 74.6 ± 14 | 73.8 ± 15.5 | 77.5 ± 14.3 | 74 ± 15.7 |

Data are presented as mean ± standard deviation

*Group C* patients received IV saline, *Group R* patients received IV remifentanil (1 μg/kg), *T0* immediately after electrical convulsion, *T1–T7* 1–7 min after electrical stimulus, *RR* RR interval, *sBP* systolic arterial pressure, *dBP* diastolic arterial pressure

*$p < 0.05$ versus remifentanil group

129 ± 27.2 mmHg, $p < 0.05$). The dBP at T0 and T1 in group C significantly increased compared to that in group R (group C: T0; 107.1 ± 22.4 mmHg, T1; 101.3 ± 23.2 mmHg, group R: T0; 75.4 ± 19.3 mmHg, T1; 80.6 ± 18.3 mmHg, $p < 0.05$).

Table 4 shows the measurement values of TpTe, TpTe/QT, TpTe/QTc, TpTe/RR, TpTe/$\sqrt{}$RR and TpTe/3$\sqrt{}$RR during the ECT. The TpTe/RR at T1 in group R was significantly lower than that in group C (group C: T1; 101.5 ± 28.2, group R: T1; 76.8 ± 21.8). However, there were no significant differences in the TpTe, TpTe/QT, TpTe/QTc, TpTe/$\sqrt{}$RR and TpTe/3$\sqrt{}$RR values between the two groups during ECT.

## DISCUSSION

The present study demonstrated the effect of remifentanil on TpTe/RR, a maker of TDR and predictor of lethal ventricular arrhythmia during ECT.

### TpTe as an index of TDR

The T peak represents complete repolarization of the epicardium and T end represents complete repolarization of the M cell action potential (mid-myocardium). Thus, the action potential duration of the longest M cell determines the TpTe interval and serves as a parameter of transmural dispersion of the whole ventricular repolarization [16, 17].

The efficacy of remifentanil on TDR using TpTe, TpTe/QT, TpTe/RR, TpTe/$\sqrt{}$RR and TpTe/3$\sqrt{}$RR during ECT has not been reported. Several studies have reported that TpTe has been established as a reliable parameter to determine the risk of ventricular arrythmia and sudden death [11, 18, 19]. The prolongation of TpTe leads to lethal arrhythmias such as ventricular tachycardia (VT) or ventricular fibrillation (VF) [13]. Similar to TpTe, TpTe/QT ratio is also considered a useful marker to evaluate TDR. Gupta et al. demonstrated that TpTe/QT ratio is independent of RR interval and more accurate compared to TpTe, especially under the conditions of long QT, short QT, Brugada syndrome and acute ST segment elevation [12].

**Table 4** Measurement of electrocardiogram parameter during electroconvulsive therapy

| | Group | Baseline | T0 | T1 | T2 | T3 | T4 | T5 | T6 | T7 |
|---|---|---|---|---|---|---|---|---|---|---|
| TpTe (ms) | Group C | 65 ± 18 | 58.7 ± 12.8 | 62.1 ± 12.4 | 63.6 ± 8.3 | 62.5 ± 14.8 | 66 ± 13.1 | 65.5 ± 16.7 | 67.6 ± 15.4 | 63.6 ± 16.4 |
| | Group R | 64.8 ± 11 | 63.8 ± 10.7 | 64.7 ± 9.7 | 67.5 ± 12.1 | 67.4 ± 14.2 | 66.5 ± 17.2 | 66.2 ± 19.1 | 67 ± 13.3 | 68.3 ± 12.7 |
| TpTe/QT | Group C | 0.18 ± 0.04 | 0.18 ± 0.04 | 0.2 ± 0.05 | 0.2 ± 0.03 | 0.19 ± 0.04 | 0.19 ± 0.04 | 0.19 ± 0.04 | 0.19 ± 0.03 | 0.18 ± 0.03 |
| | Group R | 0.17 ± 0.03 | 0.18 ± 0.04 | 0.18 ± 0.03 | 0.19 ± 0.03 | 0.19 ± 0.04 | 0.19 ± 0.04 | 0.19 ± 0.05 | 0.19 ± 0.04 | 0.19 ± 0.04 |
| TpTe/QTc | Group C | 0.17 ± 0.04 | 0.15 ± 0.04 | 0.16 ± 0.04 | 0.16 ± 0.02 | 0.15 ± 0.03 | 0.15 ± 0.03 | 0.15 ± 0.04 | 0.15 ± 0.04 | 0.15 ± 0.04 |
| | Group R | 0.17 ± 0.04 | 0.16 ± 0.04 | 0.17 ± 0.04 | 0.17 ± 0.04 | 0.18 ± 0.04 | 0.17 ± 0.05 | 0.18 ± 0.05 | 0.17 ± 0.05 | 0.17 ± 0.04 |
| TpTe/RR | Group C | 78.5 ± 22.4 | 98.2 ± 28.8 | 101.5 ± 28.2* | 95.6 ± 20 | 89.9 ± 23.4 | 95.4 ± 18.5 | 94.4 ± 16.7 | 94.2 ± 16 | 87.4 ± 18.2 |
| | Group R | 71.9 ± 19.3 | 81.5 ± 27.2 | 76.8 ± 21.8 | 85.6 ± 24.8 | 86.3 ± 22.9 | 83 ± 18.6 | 82.1 ± 24.1 | 82.2 ± 19.1 | 83.6 ± 18 |
| TpTe/$2\sqrt{}$RR | Group C | 69.9 ± 17.3 | 76.8 ± 19.8 | 77.7 ± 19.2 | 76.5 ± 10.8 | 74.7 ± 12.8 | 74.1 ± 14.6 | 73.5 ± 16.1 | 73.7 ± 19.3 | 73.3 ± 16.6 |
| | Group R | 68.9 ± 12.1 | 70.4 ± 13.6 | 71.3 ± 21.5 | 74.2 ± 15.4 | 79.2 ± 18 | 77.2 ± 17.3 | 74.4 ± 23.1 | 76.2 ± 20.2 | 75.5 ± 17.7 |
| TpTe/$3\sqrt{}$RR | Group C | 68.2 ± 17.1 | 70.7 ± 16.7 | 72.3 ± 16.7 | 71.9 ± 9.7 | 70.7 ± 12.2 | 69.8 ± 13.8 | 69.1 ± 15 | 69.9 ± 18.5 | 68.1 ± 16.8 |
| | Group R | 67.9 ± 11.2 | 68 ± 12 | 69.4 ± 18.8 | 71.5 ± 13.7 | 76 ± 15.9 | 74.6 ± 17 | 71.8 ± 21.8 | 74 ± 19.1 | 73.6 ± 16.8 |

Data are presented as mean ± standard deviation

*TpTe* T peak-T end, *QT* QT interval, *QTc* corrected QT Interval, *RR* RR interval, *Group C* patients received IV saline, *Group R* patients received IV remifentanil (1 μg/kg), *T0* immediately after electrical convulsion, *T1–T7* 1–7 min after electrical stimulus

*$p < 0.05$ versus control group

A previous study suggested that TpTe/$\sqrt{}$RR corrected using the Bazzet formula or TpTe/$3\sqrt{}$RR corrected using the Fridericia formula is the preferred marker for sudden cardiac arrest risk [20]. However, significant efficacy of remifentanil on TpTe/$\sqrt{}$RR and TpTe/$3\sqrt{}$RR was not observed in the present study.

We measured the TpTe/RR (not using a 24-h Holter electrocardiogram) as an index of TDR, and the prolongation of this marker was significantly suppressed by remifentanil. It has been reported that the TpTe/RR slope measured from 24-h Holter electrocardiogram may be a predictor for sudden cardiac death [21]. Although the reliability of TpTe/RR (but not TpTe/RR slope) as a predictor for lethal arrhythmia has not been established, our result implied that TpTe/RR may reflect the TDR during ECT and may be suppressed by remifentanil. This contradiction between TpTe/RR and other parameters such as TpTe, TpTe/QT, TpTe/$\sqrt{}$RR and TpTe/$3\sqrt{}$RR remains uncertain. However, the difference of the drug for general anesthesia might affect the TDR in our observation. Further studies using other anesthetic agents such as pentobarbital are required to determine the reliability of TpTe/RR.

### Efficacy of Remifentanil on Cardiovascular Systems

Our previous study demonstrated that QTD and QT interval was significantly increased during ECT [6]. Similar to TpTe, QTD has been considered as an index of ventricular arrhythmia, which may lead to sudden cardiac death [5]. In addition, we reported that remifentanil was effective in the suppression of QTD [14]. Thus, remifentanil might improve the TDR during ECT. Moreover, it is known that adding remifentanil reduced the consumption of propofol without adverse hemodynamic effects [22]. Generally, the benefits of adding remifentanil during ECT are as follows: (1) adequate seizure duration for convulsion therapy due to the reduction of propofol [23] and (2) attenuation of acute hemodynamic changes. In the present study, pretreatment with remifentanil attenuated the changes in RR interval, sBP and dBP after electrical stimulus. These results emphasize the efficacy of remifentanil for treating hemodynamic change during ECT.

### Limitations

There are several limitations in our study. We observed the effect of remifentanil on the TpTe/RR but not TpTe/RR slope. Essentially, the TpTe/RR slope is evaluated using a 24-h Holter electrocardiogram. The TpTe/RR was measured just during the ECT in this protocol. Further verification over an extended period is required to assess the reliability of the TpTe/RR.

In several studies, the QT interval and QTD were significantly increased during ECT [6, 24]. In contrast, it has been reported that there was no significant change in QTD and TpTe during ECT [25]. In our results, TpTe, TpTe/QT, TpTe/$\sqrt{}$RR and TpTe/$3\sqrt{}$RR were not changed during ECT. This discrepancy might be attributed to differences in the anesthetic agents. We conducted the induction of general anesthesia using propofol for all patients. Kleinsasser et al. demonstrated that hemodynamic change and QT interval were more stable under propofol anesthesia compared to sevoflurane anesthesia [26]. Propofol was likely to suppress the changes in TDR during ECT. Further studies should be conducted using other anesthetic agents, such as barbiturates.

In many cases, the relationship between TpTe and lethal ventricular arrhythmia is assessed using a receiver-operating characteristic (ROC) curve. However, no lethal ventricular arrhythmia was observed in the present study. In addition, the sample size of our trial was inadequate to conduct a ROC curve. Hence, a ROC curve could not be constructed. Further studies to evaluate the cutoff value of TpTe associated with lethal ventricular arrhythmia is needed.

## CONCLUSION

The current results suggest that pretreatment with remifentanil suppressed the prominent hemodynamic changes during ECT without any adverse effects. Moreover, remifentanil

prevented the increase in TpTe/RR after the electrical stimulus. These results imply that remifentanil is beneficial for attenuating TDR caused by electrical stimuli. However, further verification of TDR during ECT is essential.

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***Author Contributions.*** Shigeki Yamaguchi: made substantial contributions to the conception, design of the work and revision of the manuscript drafts. Toshifumi Takasusuki: made substantial contributions to the data analysis and manuscript drafting. Kazuya Akutsu and Kozue Eda: made substantial contributions to data acquisition. All the authors have approved the submitted version of the manuscript and agreed to be accountable for any part of the work.

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***Data Availability.*** The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

***Declarations***

***Conflict of Interest.*** Kozue Eda, Kazuya Akutsu, Toshifumi Takasusuki and Shigeki Yamaguchi declare that they have no conflicts of interest.

***Ethical Approval.*** The study was approved by the ethics committee of Dokkyo Medical University (R-32-1) and registered with the University Hospital Medical Information Network (UMIN, registration number: UMIN000051958). All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and national research committee and the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.

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