ORIGINAL ARTICLE

https://doi.org/10.1590/1806-9282.20230733

Effect of pulmonary embolism location on electrocardiological parameters

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SUMMARY

OBJECTIVE: Pulmonary thromboembolism is a disease with high morbidity and mortality. Various changes occur on the electrocardiogram secondary to pulmonary thromboembolism. The objective of this study was to investigate variations in QT dispersion, Tpeak-Tend duration, and Tpeak-Tend/QT ratio in relation to pulmonary thromboembolism localization and their impacts on 30-day mortality.

METHODS: This study was carried out in a tertiary emergency medicine clinic between December 1, 2019 and November 30, 2020. We evaluated correlations between radiological outcomes of patients, QT dispersions, T-wave dispersions, Tpeak-Tend durations, and Tpeak-Tend/QT ratios. We sought statistically significant disparities between these values, considering the presence or localization of pulmonary thromboembolism. The 30-day mortality in pulmonary thromboembolism-diagnosed patients was reassessed.

RESULTS: Electrocardiogramfindings revealed that T-wave dispersion (p<0.001), Tpeak-Tend duration (p=0.034), and Tpeak-Tend/corrected QT ratio (p=0.003) were lower in patients than controls. Conversely, QT dispersion (p=0.005) and corrected QT dispersion (p<0.001) were higher in patients.

CONCLUSION: Electrocardiogram findings such as T-wave dispersion, QT duration, Tpeak-Tend time, and Tpeak-Tend/corrected QT ratio can detect pulmonary thromboembolism. More studies with larger cohorts are required to further understand the role of QT and corrected QT dispersion in pulmonary thromboembolism patient mortality.

KEYWORDS: Pulmonary embolism. Electrocardiography. Morbidity. Radiography.

INTRODUCTION

Pulmonary thromboembolism (PTE), a condition that accounts for approximately 100,000 mortalities per year in the United States, leads to significant morbidity and mortality. It often requires high clinical suspicion for diagnosis due to its non-specific symptoms[1]. Multidetector computed tomographic pulmonary angiography (CTPA) is commonly used for diagnosis, though it cannot predict clinical severity[2].

Electrocardiogram (ECG) changes, such as QT dispersion (QTd), indicative of myocardial repolarization heterogeneity, can occur in PTE. Increased QTd is associated with severe ventricular arrhythmias and sudden cardiac death[3]. Moreover, recent studies have suggested that Tpeak-Tend (Tp-e), a marker of arrhythmogenicity, and Tp-e/QTc ratio increments may influence mortality[4,5]. Due to thrombus-induced pressure changes, especially in the right heart chambers, Tp-e, QTd, and Tp-e/QTc ratios may increase[3,4].

Investigating these changes based on PTE location (main pulmonary artery or other branches) and their impact on mortality may inform patient management, given ECG's accessibility and reproducibility. Thus, our study aims to explore the Tp-e, Tp-e/QT, and QTd variations depending on PTE location and their correlation with 30-day mortality.

METHODS

Our study, conducted in an emergency medicine clinic of a tertiary hospital, received approval from the local Ethics Committee on November 14, 2019. The investigation involved patients over the age of 18 years, who presented to the emergency department between December 1, 2019 and November 30, 2020 with suspected PTE and consequently underwent CTPA. However, patients with ECGs not suitable for examination or those diagnosed with left or right bundle branch block and atrial fibrillation were excluded from the study.

A total of 742 patients with suspected PTE underwent CTPA, of whom 97 were confirmed to have PTE. From this group, 44 patients were further excluded due to unsuitable ECGs, atrial

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Conflicts of interest: the authors declare there is no conflicts of interest. Funding: none.
Received on June 13, 2023. Accepted on August 26, 2023.

fibrillation, and left or right bundle branch block, resulting in a final cohort of 53 patients. To facilitate comparative analysis, we selected a control group of 54 individuals without PTE, matched based on age, gender, and comorbidities (Figure 1).

Upon presentation to the emergency department, written informed consent was obtained from all patients or their legal representatives. We meticulously recorded pertinent patient information, including names, contact information, medical history, and current medications. Standard 12-lead ECGs were obtained from patients presenting with suspected PTE. These ECGs were then digitally scanned, transferred to a computerized environment, and evaluated independently to maintain blindness in the study.

Using the "Windows Photo Viewer" software and the "PixelRuler program," a cardiologist measured the QT interval, T wave, and Tp-e duration for each ECG. In patients diagnosed with PTE, the localization of the thrombi in the right and left pulmonary arteries was individually determined and classified. The relationships between these radiological findings and ECG measurements were subsequently analyzed. Furthermore, the presence or absence of PTE, its localization, and the 30-day mortality of patients diagnosed with PTE were evaluated.

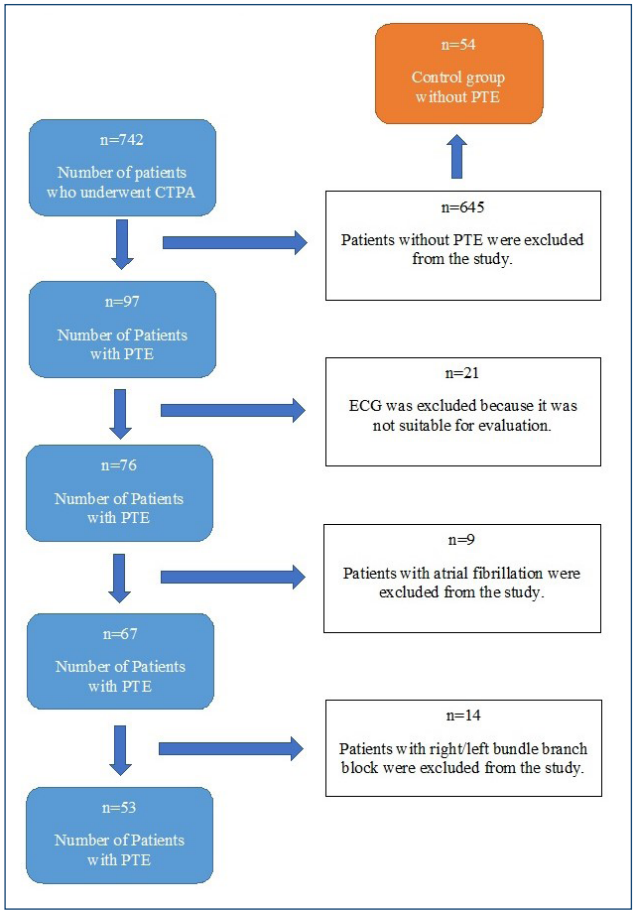

Figure 1. Flowchart of the study design.

By employing statistical analyses, we sought to investigate whether significant differences exist between T-wave dispersion, QTd, corrected QT dispersion (QTcd), Tp-e duration, Tp-e/QT, Tp-e/QTc ratios, and patient mortality. This comprehensive approach allowed us to deeply explore potential correlations between ECG measurements, thrombus localization, and patient outcomes.

Sample size analysis

When the difference between the alpha 0.05 and beta 0.02 groups was considered significant at 32.4%, the sample size was calculated as 54 for each group, with a total of 108 patients with the G Power program[6].

Statistical analysis

All statistical analyses were conducted using the SPSS v21 software (SPSS Inc., Chicago, IL, USA). The normality of quantitative data distribution was assessed using the Kolmogorov-Smirnov test. Quantitative variables were presented as mean±standard deviation or median (range), while categorical variables were presented as frequency (percentage). Quantitative variables following a normal distribution assumption were analyzed using independent samples t-test. For quantitative variables that did not meet the assumption of a normal distribution, the Mann-Whitney U test was used. Categorical variables were analyzed using the chi-square test or Fisher's exact test, as appropriate. The diagnostic performance of ECG findings in detecting PTE was evaluated using receiver operating characteristic (ROC) curve analysis. Performance measures such as sensitivity, specificity, accuracy, positive predictive value, and negative predictive value were calculated for various cutoff points. Statistical significance was set at a $p<0.05$.

RESULTS

A total of 107 individuals (53 patients and 54 controls) were included in the study. While there were 30 (56.60%) females in the patient group, there were 26 (48.15%) females in the control group (p=0.495). There was no statistically significant difference between the groups in terms of chronic disease. In total, 27 (50.94%) patients had main pulmonary artery involvement, while 26 (49.05%) patients had involvement in other branches. In the patient group, 4 (7.55%) cases were fatal (Table 1).

When the ECG findings were examined, T-wave dispersion, QT wave duration, Tp-e time, and Tp-e/QTc ratio were

Table 1. General characteristics of individuals by groups (qualitative data).

	Patient group (n=53)	Control group (n=54)	p-value
Sex			
Women	30 (56.60%)	26 (48.15%)	0.495[1]
Men	23 (43.40%)	28 (51.85%)	
Hypertension	16 (30.19%)	20 (37.04%)	0.586[1]
Asthma/COPD	11 (20.75%)	6 (11.11%)	0.271[1]
Diabetes mellitus	7 (13.21%)	14 (25.93%)	0.158[1]
History of pulmonary embolism	9 (16.98%)	2 (3.70%)	0.052[1]
Chronic kidney disease	3 (5.66%)	3 (5.56%)	1.000[2]
Chronic arterial disease	9 (16.98%)	15 (27.78%)	0.268[1]
Left pulmonary artery involvement	33 (62.26%)	–	
Subsegmental pulmonary artery	1 (1.89%)	–	N/A
Segmental pulmonary artery	8 (15.09%)	–	
Lobar pulmonary artery	7 (13.21%)	–	
Main pulmonary artery	17 (32.08%)	–	
Right pulmonary artery involvement	43 (81.13%)	–	
Subsegmental pulmonary artery	1 (1.89%)	–	N/A
Segmental pulmonary artery	2 (3.77%)	–	
Lobar pulmonary artery	15 (28.30%)	–	
Main pulmonary artery	25 (47.17%)	–	
Total main pulmonary artery involvement	27(50.94%)	–	N/A
Mortality	**4 (7.55%)**	–	**N/A**

The data are summarized as frequency (percentage). (1) Chi-square test; (2) Fisher's exact test; N/A: test not applicable; COPD: chronic obstructive pulmonary disease. Bold indicates the number of patients with a fatal outcome in the patient group of n=4.

lower in the patient group than in the control group (p<0.001, p=0.001, p=0.034, and p=0.003, respectively). QT and corrected QTd (QTcd) were higher in the patient group than in the control group (p=0.005 and p<0.001, respectively). When ECG findings were analyzed according to pulmonary artery involvement, no statistically significant difference was found between patients with main pulmonary involvement and other patients. When the relationship between ECG findings and mortality was examined, no statistically significant difference was found between patients with mortality and other patients (Table 2).

The performance of ECG findings in the diagnosis of pulmonary embolism was examined. For the T-wave dispersion of 71 cutoff point (values less than this indicate the presence of pulmonary embolism), the sensitivity was 66.04%, the specificity was 79.63%, the correct classification rate was 72.90%, the positive predictive value was 76.09%, and the negative predictive value was 70.49% (AUC=0.733; 95%CI 0.635–0.832; p<0.001). QTd for 58 cutoff point (values above and below this indicate the presence of pulmonary embolism) has a sensitivity of 66.04%, a specificity of 59.26%, a correct classification rate of 62.62%, a positive predictive value of 61.40%, and a negative predictive value of 64.00% (AUC=0.643; 95%CI 0.539–0.747; p=0.011). Corrected QTd was found to have a sensitivity of 64.15%, a specificity of 74.07%, a correct classification rate of 69.16%, a positive predictive value of 70.83%, and a negative predictive value of 67.80% for 75 cutoff point (this or greater values indicate the presence of pulmonary embolism) (AUC=0.744; 95%CI 0.652–0.837; p<0.001). The Tp-e/QTc ratio for 0.20 cutoff point (values less than this indicate the presence of pulmonary embolism) has a sensitivity of 64.15%, a specificity of 61.11%, a correct classification rate of 62.62%, a positive predictive value of 61.82%, and a negative cutoff value of 63.46% (AUC=0.656; 95%CI 0.553–0.759; p=0.005). The performance of corrected QT duration, Tp-e duration, Tp-e/QT ratio, and S1Q3T3 finding in the diagnosis of pulmonary embolism was statistically insignificant.

Table 2. Electrocardiographic findings according to groups, pulmonary artery involvement, and presence of mortality.

		T-wave dispersion (ms)	QT wave duration (ms)	Corrected QT duration (ms)	QT dispersion (ms)	Corrected QT dispersion (ms)	Tpeak-Tend duration (ms)	Tp-e/QT ratio	Tp-e/QTc ratio
Electrocardiographic findings by groups									
mean±std. deviation	Patient (n=53)	71.64±22.78	348.91±34.84	441.36±31.77	66.55±18.15	86.17±25.48	83.17±16.66	0.24±0.05	0.19±0.04
	Control (n=54)	85.31±18.54	376.24±47.24	429.52±31.64	57.70±13.52	67.15±16.92	90.85±20.02	0.24±0.05	0.21±0.04
median (min–max)	Patient (n=53)	64.7 (38.1–139.2)	348.5 (283.3–458)	441 (373–507)	62.2 (38.9–123.5)	82 (45–192)	83.3 (44.4–120.9)	0.24 (0.16–0.34)	0.19 (0.11–0.27)
	Control (n=54)	83.4 (50–130.3)	371.35 (272.7–483,7)	431 (368–490)	55.05 (34.1–88.4)	65 (40–115)	90.55 (51–138)	0.24 (0.12–0.39)	0.21 (0.11–0.30)
p		<0.001 (2)	0.001 (1)	0.056 (1)	0.005 (1)	<0.001 (1)	0.034 (1)	0.714 (1)	0.003 (1)
Electrocardiographic findings according to pulmonary artery involvement									
mean±std. deviation	Main pulmonary artery (n=27)	69.06±17.43	340.28±27.14	439.30±32.78	66.88±20.70	87.89±30.29	79.68±15.68	0.23±0.04	0.18±0.04
	Others (n=26)	74.33±27.36	357.87±39.94	443.50±31.18	66.22±15.48	84.38±19.75	86.80±17.17	0.24±0.05	0.20±0.04
Median (min–max)	Main pulmonary artery (n=27)	64.7 (44.5–106,6)	340 (283.3–391.8)	437 (377–507)	60.9 (40.9–123.5)	80 (52–192)	80 (44.4–111.7)	0.24 (0.16–0.32)	0.19 (0.11–0.25)
	Others (n=26)	69.8 (38.1–139.2)	360.9 (295–458)	445 (373–504)	64.9 (38.9–103.4)	84.5 (45–123)	88.15 (50–120.9)	0.24 (0.16–0.34)	0.20 (0.13–0.27)
p		0.669 (2)	0.066 (1)	0.635 (1)	0.896 (1)	0.621 (1)	0.121 (1)	0.413 (1)	0.177 (1)
Electrocardiographic findings according to the presence of mortality									
mean±std. deviation	Mortality (no) (n=49)	72.20±23.56	349.02±34.86	440.00±29.83	65.73±16.67	84.98±24.37	82.62±15.85	0.24±0.04	0.19±0.04
	Mortality (yes) (n=4)	64.78±6.77	347.63±39.92	458.00±53.37	76.70±33.42	100.75±38.09	89.95±26.97	0.26±0.07	0.19±0.04
Median (min–max)	Mortality (no) (n=49)	64.8 (38.1–139.2)	343.5 (283.3–458)	438 (373–507)	62.2 (38.9–123.5)	82 (45–192)	83.3 (44.4–111.7)	0.23 (0.16–0.34)	0.19 (0.11–0.27)
	Mortality (yes) (n=4)	62.6 (59.4–74.5)	364.35 (288.8–373)	469.5 (389–504)	67.75 (48.7–122.6)	95.5 (63–149)	89.75 (59.4–120.9)	0.27 (0.17–0.33)	0.20 (0.13–0.24)
p(2)		0.661	0.833	0.369	0.661	0.444	0.615	0.405	0.569

(1) Independent samples t-test; (2) Mann-Whitney U test; QTc: corrected QT.

DISCUSSION

Various changes in the ECG are observed in correlation with the severity of PTE[3]. One of the ECG parameters that reflects ventricular repolarization heterogeneity is QTd, which can be affected by several factors[6]. Studies have demonstrated that patients with acute PTE have significantly higher QTd and QTcd compared to control groups, with higher values observed in high-risk PTE patients[7]. This suggests that increased QTd and QTcd may indicate right ventricular failure due to elevated pulmonary artery pressure in acute PTE[8]. Consistent with these findings, our study also revealed significantly higher QTd and QTcd values in PTE patients compared to the control group ($p=0.05$ and $p<0.001$, respectively). Furthermore, we evaluated the sensitivity and specificity of various cutoff points for QTd, indicating its potential as a diagnostic marker. Patient groups were not categorized based on the risk levels in our study, as clinical severity does not always align with CTPA findings[8]. Therefore, we adopted a radiological classification based on PTE involvement sites to ensure an objective evaluation.

To assess the impact of PTE location on ECG parameters, we considered the possibility that involvement of the main pulmonary artery may lead to increased right ventricular workload, resulting in heightened right ventricular tension, heterogeneity, and subsequent elevation of QTd and QTcd. However, no significant difference was observed when comparing major branch involvement with other branch involvement. Several factors could explain this finding. Most patients with major branch involvement in our study had a clinically stable course, suggesting that severe right ventricular afterload may not have been present, thus exerting a limited effect on QTd and QTcd compared to other patients. Additionally, the limited sample size in our study might have affected the statistical

power, potentially influencing the results. In contrast, previous studies have shown a significant association between high QTcd and increased mortality in patients diagnosed with PTE[4]. It has been suggested that a QTcd threshold above 71.5 ms could predict mortality in acute PTE patients, with a sensitivity of 73% and a specificity of 71%[9]. However, our study did not find a significant correlation between QTd, QTcd, and 30-day mortality, likely due to the relatively low number of patients with fatal outcomes compared to the overall study population.

Recent studies have highlighted the importance of Tp-e duration, Tp-e/QT ratio, and Tp-e/QTc ratio as noninvasive indicators of myocardial transmural repolarization[10]. Unlike QTd and QTcd, Tp-e measurements are less influenced by heart rate variations, providing a potentially more accurate assessment of repolarization[10]. In patients with acute PTE, increased Tp-e duration has been associated with adverse outcomes, including higher 30-day mortality[5]. Furthermore, a decrease in Tp-e duration, Tp-e/QT, and Tp-e/QTc ratios has been observed following the thrombolytic therapy in hemodynamically unstable acute PTE patients, indicating improved cardiac function[11].

Contrary to previous studies, our study demonstrated a decrease in Tp-e duration (p=0.034) and Tp-e/QTc ratio (p=0.03) in patients with acute PTE compared to the control group[11]. This unexpected finding may be attributed to differences in the composition of our control group compared to previous studies. Nonetheless, the reported Tp-e duration and Tp-e/QTc ratio values in our study were within a similar range as those in the literature, providing consistency in these measurements. We identified a sensitivity of 64.15% and a specificity of 61.11% for a Tp-e/QTc ratio cutoff point of 0.20, indicating its potential as a diagnostic marker. However, similar to the QTd and QTcd analyses, no significant differences were found in Tp-e duration, Tp-e/QT, and Tp-e/QTc ratios between patients with major branch involvement and those with embolism in other branches. This suggests that the presence of major branch involvement alone may not impose a significant right ventricular load, leading to clinical instability. Nevertheless, due to the limited sample size in our study, further investigations with larger populations are needed to confirm these findings.

Regarding the association between Tp-e duration, Tp-e/QT, and Tp-e/QTc ratios with mortality, our study did not find a significant correlation. This lack of significance can be attributed to the relatively low number of patients who experienced fatal outcomes compared to the overall study population. It is reasonable to assume that with a larger sample size, the relationship between these ECG parameters and mortality could become more apparent.

Finally, our study evaluated T-wave dispersion as an indicator of ventricular heterogeneity within the QT interval. We found a significant difference in T-wave dispersion (p=0.001) between patients diagnosed with acute PTE and the control group. This observation suggests that right ventricular heterogeneity induced by increased right ventricular loading contributes to altered T-wave dispersion in PTE patients. However, no significant differences in T-wave dispersion were found when comparing major branch involvement with other involvements or when considering mortality. Further studies investigating T-wave dispersion in conjunction with clinical severity and PTE involvement sites may yield more comprehensive results. Given the limited literature on T-wave dispersion in PTE, additional studies focusing on this parameter in PTE patients can provide valuable insights.

Limitations

Our study has certain limitations that need to be acknowledged. First, it was conducted at a single center, which may limit the generalizability of our findings to other populations or settings. Additionally, the sample size was relatively small, partly due to the challenges posed by the COVID-19 pandemic, which restricted the study duration and patient recruitment. Consequently, the limited number of patients with fatal outcomes may impact the statistical power of our analysis.

Another potential limitation is the selection of the control group, consisting of patients who underwent CTPA but did not show any evidence of embolism. This approach may introduce selection bias and influence the comparability of the control and PTE groups.

Furthermore, the measurement of QT duration remains a subject of ongoing debate in the scientific community. There are discrepancies and variability in the techniques used to determine the precise end point of the T wave, leading to inconsistent results. Despite utilizing digital measurement methods to improve accuracy, concerns persist regarding the reliability and reproducibility of these techniques, which may influence the interpretation of our study findings[12].

CONCLUSSION

Our study revealed significant alterations in ECG parameters, including QTd, QTcd, Tp-e duration, Tp-e/QT, and Tp-e/QTc ratios, in patients with acute PTE compared to the control group. However, the impact of PTE location on these parameters and their association with mortality was not significant in our study, possibly due to the limited sample size. Future studies with larger populations are warranted to validate

these findings and further elucidate the clinical significance of ECG changes in PTE.

ETHICAL APPROVAL

Our study was approved by the Health Sciences University, Kocaeli Derince Training and Research Hospital Clinical Research Ethics Committee on November 14, 2019 (Decision Number: 2019-117).

AUTHORS' CONTRIBUTIONS

SG: Conceptualization, Data curation, Investigation, Methodology, Supervision, Writing – original draft. **EŞ:** Conceptualization, Formal Analysis, Resources. AES: Data curation, Visualization. **SAG:** Data curation, Visualization. **DKÖ:** Data curation, Validation. **HCH:** Conceptualization, Methodology, Project administration, Supervision, Writing – review & editing.

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