Prognostic Value of T wave Positivity in Lead aVR in COVID-19 Pneumonia

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Abstract

Background:T wave positivity in the lead aVR is a marker of ventricular repolarization abnormality and provides information on short and long-term cardiovascular mortality in patients who have heart failure, anterior myocardial infarction, and receive hemodialysis for various reasons. The aim of this study was to investigate the relationship between T wave positivity in the lead aVR on superficial ECG and mortality from COVID-19 pneumonia. Methods: This study retrospectively included 130 patients who were diagnosed with COVID-19 and treated as an outpatient or in the thoracic diseases ward in a single center between January 2021 and June 2021. All patients included in the study had clinical and radiological features and signs of COVID-19 pneumonia. The COVID-19 diagnosis of all patients was confirmed by polymerase chain reaction (PCR) studied from an oropharyngeal swab Results: A total of 130 patients were included in this study. Patients were divided into 2 groups: survived and deceased. There were 55 patients (with a mean age of 64.76-14.93 years, 58.18% male, 41.12% female) in the survived group, while there were 75 patients (with a mean age of 65-15 years, 58.67% male, 41.33% female) in the deceased group. The univariate and multivariate regression analyses showed that positive TAVR (OR: 5.151, 95% CI: 1.001-26.504, p: 0.0012), lactate dehydrogenase (LDH) (OR: 1.006, 95% CI: 1.001-1.010, p: 0.012) and D-dimer (OR:1.436, 95% CI: 1.115-1.848, p: 0.005) were independent risk factors for mortality Conclusions: positive TAaVR is useful in risk stratification for COVID-19 pneumonia mortality. KEY WORLD:Electrocardıographıa, positive TAaVR, COVID-19 pneumonia, mortality

INTRODUCTION

Although COVID-19 infection primarily affects the lungs and causes pneumonia, acute respiratory distress syndrome, and death, various cardiovascular complications are among the leading causes of mortality. (1) Numerous studies and case series have shown that COVID-19 causes myocarditis, (2-3-4) tamponade (5), acute heart failure (6), arrhythmia (tachycardia or bradycardia) (7), Brugada-like ECG pattern (8), transient ST elevation, and sudden cardiac death. (9-10)

Cardiac involvement is associated with a poor prognostic outcome, independent of other causes, with an incidence of 22-44% in cases of advanced and severe COVID-19 infection. (11-12) Cardiovascular damage can occur through a diverse range of pathways. In addition to the direct cardiotoxic effect, cardiovascular damage may be caused by inhibition of ACE-2 receptors, cytokine storm, coronary plaque rupture, coronary spasm, and microthromboembolism. (13-14)

On a superficial ECG, the lead aVR is usually neglected. However, it provides prognostic information on many cardiovascular diseases. A positive T wave amplitude in thelead aVR gives prognostic information onrepolarization abnormality and provides diagnostic and prognostic information on many cardiovascular

diseases as in heart failure. (15-16) However, there is no information regarding its relationship with COVID-19 pneumonia. The aim of this study was to investigate the relationship between T wave positivity in the lead aVR on superficial ECG and mortality from COVID-19 pneumonia.

MATERIALS and METHODS

This study retrospectively included 130 patients who were diagnosed with COVID-19 and treated as an outpatient or in the thoracic diseases ward in a single center between January 2021 and June 2021 after the approval of the local ethics committee and the Ministry of Health of the Republic of Turkey. The study was conducted in accordance with the principles of the Declaration of Helsinki.

All patients included in the study had clinical and radiological features and signs of COVID-19 pneumonia. The COVID-19 diagnosis of all patients was confirmed by polymerase chain reaction (PCR) studied from an oropharyngeal swab. All patients were treated with hydroxychloroquine, azithromycin, and favipiravir. Patients with chronic kidney or liver failure, use of anti-arrhythmic drugs, pacemaker rhythm, atrial fibrillation, coronary artery disease, heart failure (with preserved systolic function or systolic heart failure), abnormal serum electrolyte values were not included in the study.

All patients were questioned in detail for hypertension, hyperlipidemia, diabetes mellitus, tobacco use, asthma, COPD (Chronic Obstructive Pulmonary Disease), and the drugs used. Hematological, biochemical, and serological values were obtained from the peripheral blood samples taken following 12 hours of fasting and recorded. A troponin value above the 99th percentile upper reference limit value or newly developed electrocardiographic and echocardiographic change was considered myocardial damage. Chronic renal failure was defined as a glomerular filtration rate less than 60 mL/min per 1.73 square meters, persisting for 3 months. The diagnosis of hypertension was defined as receiving antihypertensive therapy or having a systolic blood pressure above160 mmHg and diastolic blood pressure above90 mmHg in at least 3 measurements. Diabetes was defined as the use of antidiabetic drugs and having at least 2 postprandial blood glucose measurements above 126 mg/dL or an HbA1c level >6.5. The diagnosis of hyperlipidemia was considered as having a low-density lipoprotein (LDL) level >160mg/dL or the use of statins.

ECHOCARDIOGRAPHIC EVALUATION

All patients included in the study underwent echocardiographic examination with an iE33 cardiac ultrasound system (Phillips Healthcare, Best, The Netherlands) and 2.5–5-MHz probes system, and ejection fraction was measured with the modified Simpson method.

ELECTROCARDIOGRAPHIC EVALUATION

Superficial 12-lead ECGs of all patients (Nihon Kohden Cardiofix V Model ECG-1550K Device 25 mm/s and standard 1 mv/10mm) were recorded before the treatment of COVID-19 infection and were evaluated by two independent cardiologists who were blinded to the characteristics of the patients. Heart rate, P-R interval, QT and QTc intervals, and QRS duration were recorded. The P-R interval was measured as the time from the beginning of the P wave to the beginning of the QRS complex in milliseconds. The QRS duration was measured from the beginning of the Q or R wave to the end of the R or S wave in milliseconds. The QT interval was measured from the beginning of the QRS complex to the end of the T wave in milliseconds. The QT corrected distance was measured using Bazett's formula. The depression or elevation of the ST segment in the lead aVR from the isovolumetric line was measured numerically (STaVR). According to the T wave amplitude in the lead aVR, patients with a positive peak (>0mv) from the isovolumetric line were recorded as positive (positive TAVR), while patients with a negative peak (<0mv) from the isovolumetric line were recorded as negative (negative TAVR). The amplitude of the T wave (TPAVR) was recorded by calculating its negative or positive deflection from the isoelectric line. The TPAVR/STAVR ratio was obtained by dividing whichever value is greater by the other (large value/small value).

STATISTICAL ANALYSIS

The study data were evaluated using SPSS 21.0 statistical software. Normality distribution of contin-

uous variables was investigated using visual (histogram and probability charts) and analytical methods (Kolmogorov-Smirnov/Shapiro-Wilk tests). The descriptive statistics of the study were presented as mean and standard deviation for normally distributed data and as median, minimum and maximum for non-normally distributed data. The Chi-square test was used to show whether there was a difference between categorical variables. The Student's t-test was used to compare the continuous variables with parametric properties in independent groups, while the Mann-Whitney U test was used to compare continuous variables with non-parametric properties in independent groups. The level of statistical significance was set at a p-value less than 0.05.

RESULTS

A total of 130 patients were included in this study. Patients were divided into 2 groups: survived and deceased. There were 55 patients (with a mean age of 64.76-14.93 years, 58.18% male, 41.12% female) in the survived group, while there were 75 patients (with a mean age of 65-15 years, 58.67% male, 41.33% female) in the deceased group. There was no difference between the groups in terms of age and gender. While there was no difference between the groups in terms of hypertension, diabetes mellitus, and cerebrovascular disease, the number of patients in the deceased group was statistically higher in terms of asthma (p:0.030) and COPD (p:0.003). The baseline clinical and laboratory characteristics of the groups are shown in Tables 1 and 2.

The comparison of laboratory characteristics showed that the deceased group had higher CK-MB (60.88-46.99 vs. 30.55-21.77, p: 0.000), troponin (106-64.02 vs. 39.87+-14.36, p: 0.000), LDH (554.61-209.22 vs. 365.24+-155.47 p: 0.000), CRP (127-75.32 vs. 87.4-68.24, p: 0.001), leukocyte (13.01- 4.87 vs. 8.82-4.84, p: 0.000) and D-dimer values (25.29+-23.09 vs. 1.18+-1.06, p: 0.000).

The electrocardiographic and echocardiographic characteristics are shown in Table 3. There was no difference between the groups in terms of heart rate (83.21-19.16 vs. 86.51-17.06, p: 0.290), TPAVR (-0.07+0.26 vs. 0.12+-0.8, p: 0.65), P-R interval (107.51+-7.30 vs. 109+-23.52, p: 0.173), QRS interval (110.52+- 5.71 vs. 112.15+- 9.42, p: 0.333), QT (393.73+-42.85 vs. 382.22+-27.63, p: 0.11) and QTc intervals (393.73+-42.85 vs. 382.22+-27.63, p: 0.388), and STAVR/TPAVR ratio (1.58+-0.79 vs. 1.62+-0.62, p: 0.739). Positive TaVR (28 patients in the deceased group, 5 patients in the survived group, p:0.000) and STAVR (0.15+-0.6 vs. 0.19+-0.12, p: 0.002) were statistically significant in the deceased group. There was no difference between the groups in terms of left ventricular ejection fraction (p: 0.05). The univariate and multivariate regression analyses showed that positive TAVR (OR: 5.151, 95% CI: 1.001-26.504, p: 0.0012), lactate dehydrogenase (LDH) (OR: 1.006, 95% CI: 1.001-1.010, p: 0.012) and D-dimer (OR:1.436, 95% CI: 1.115-1.848, p: 0.005) were independent risk factors for mortality. (Table 4)

DISCUSSION

Our study is the first study to examine the findings of lead aVR on superficial ECG in patients with Sars-Cov-2 infection. The primary result found in this study is that the positive T wave in lead aVR is an independent risk factor for mortality. The secondary result is that D-dimer and LDH values are independent risk factors, which has also been shown in previous studies.

The Sars-Cov-2 virus, which first emerged in December 2019, has spread all over the world in a short time and caused a pandemic. There is currently no prophylactic treatment for this disease. Although Sars-Cov-2 infection primarily affects the lungs and causes pneumonia and/or acute respiratory distress syndrome, it leads to complications such as myocarditis, cardiac tamponade, transit ST elevation, acute heart failure, arrhythmia (tachycardia or bradycardia), and sudden cardiac death. (17) Cardiac damage can occur through a diverse range of pathways. While it may be directly related to cardiac damage, it may cause myocardial inflammation and edema by inhibiting ACE-2 receptors and impairing the cellular defense mechanism. Another mechanism of action is the cytokine storm, which results from excessive cytokine release from type1-2 T helper cells and leads to immunopathological events. These factors may cause direct myocyte damage as well as coronary spasm, plaque rupture, microthromboembolism by leading to vascular inflammation and hypercoagulopathy. (18-19-20) A recently published study showed that the SARS-CoV-2

virus causes cell necrosis by activating CD40, caspase recruitment domain family member 8 (CARD8), and serine/threonine kinase 4 (STK4) in human bile duct epithelial cells. A similar mechanism is thought to occur within the myocardial tissue. As a result, irregular cell death and fibrosis may occur in the myocardial tissue. (21) In the clinical study of WANG et al., acute heart damage, shock, and arrhythmia complications were observed in 7.2% and 8.7%, 16.7% of the patients, respectively. (22)

Although the lead aVR is often neglected on a superficial 12-lead ECG, it provides diagnostic and prognostic information for many cardiovascular diseases. Since the lead aVR is a unipolar right extremity lead, represents the cavity of the heart, and is the opposite of the main cardiac vector, all positive deflection waves are negative in the lead aVR. (23) A positive T wave in the lead aVR is usually an uncommon finding. Although the exact mechanism is unknown, there are various hypotheses. According to the most common and valid hypothesis, the T wave is thought to be positive after vectorial deviation caused by damage to the left ventricular apical, inferior and inferior lateral wall due to various reasons. (24-25) Recent studies have shown that the T wave positivity in the lead aVR is a marker of ventricular repolarization abnormality and provides information on short and long-term cardiovascular mortality in patients who have heart failure, anterior myocardial infarction, and receive hemodialysis for various reasons .(15-16) In their long-term follow-up study of male individuals, Tan et al. showed the T wave positivity as an independent risk factor for cardiovascular events.(26) The 33-month follow-up study of 93 patients with heart failure and narrow QRS ECG by Okuda et al. showed that the T wave positivity provided long-term prognostic information independent of other causes. (27) The 31-month follow-up study of 93 patients with ICD (implantable cardioverter defibrillation) and ischemic and non-ischemic cardiomyopathy by Tanaka et al. showed that a positive T wave in the lead aVR was an independent risk factor for long-term mortality. (28) The study of 86 cases by Donmez et al. showed that the occurrence of the T wave positivity in the lead aVR after transaortic valve implantation (TAVI) procedure was an independent risk factor for postoperative short and long-term mortality. (29) The NHAES (National Health And Nutrition Examination Survey) study of 7,928 cases showed that the T wave positivity in the lead aVR was an independent risk factor for cardiovascular events. Moreover, the addition of this factor to the Framingham risk score may improve the distinction of patients with moderate risk factors. (30) Ekizler et al. showed that positive TAVR was an independent risk factor for cardiovascular events in patients with peripartum cardiomyopathy. In our study, the examination of the electrocardiographic findings of the lead aVR in patients with COVID-19 infection revealed that positive TAVR alone was an independent indicator for mortality. (31) This suggests that a positive TAVR wave provides information on the entire myocardial tissue rather than the apical, inferior, and inferior lateral wall.

Limitations of the study

This study has several limitations. First of all, the sample size was small, and the study had a retrospective design. In addition, values such as CRP and troponin, which are associated with subclinical myocardial damage, were not followed up serially. The ECGs of the patients at initial diagnosis were examined, while positive or negative T wave changes on ECGs were not examined. The medical treatments of the patients were not questioned in detail and their post-treatment ECG changes were not investigated. A prospective study with a large number of patients is needed to validate the results of this study.

CONCLUSION

This study demonstrated that positive T aVR wave in the lead aVR was a significant and independent risk factor for mortality from COVID-19 infection. This unique ECG parameter, which is often overlooked, provides information on the mortality of patients even when other ECG parameters are normal. We recommend that a positive TAVR wave not be neglected when evaluating high-risk patients.

FIGURE LEGEND

Table 1 Baseline Characteristics, Electrocardiographic Findings

Table 2 Basıc Laboratory Parameters Of Patients

Table 3 Comparison of The Electrocardiographic Findings To deceased and living group

Table 4 Effects Of Various Variables On COVID-19 Mortality İn Univariate And Multivariate Logistic Regression Analyses

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