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ABNORMAL T-WAVE ALTERNANS IN CORONARY ARTERY DISEASE LEFT VENTRICLE EJECTION FRACTION >40% WITH MYOCARDIAL INFARCTION

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Abstract

Coronary artery disease (CAD) may present with or without myocardial infarction, with the left ventricle ejection fraction (LVEF) <40% or >40%. Myocardial infarction with LVEF <40% has been reported to cause abnormal T-wave alternans (TWA) value. The data about abnormal TWA value in myocardial infarction with LVEF >40% is still limited. A case-control analytic study was held at Dr. Sardjito general hospital Since March 2021 until April 2022 on adult CAD subjects with LVEF >40%. The TWA value was obtained from treadmill test which was then divided into the case group if the TWA value was abnormal and into the control group if the TWA value was normal. The data about myocardial infarction was retrospectively evaluated afterwards. Hypothesis testing was performed by Chi-Square test. Multivariate analysis using logistic regression test was conducted to determine the effect of confounding variables on TWA value. A total of 124 subjects were included in this study (62 subjects in the case group with abnormal TWA value, and 62 subjects in the control group with normal TWA value) with the mean age of 55,48 ± 8,6 years old and 83,8% were male subjects The proportion of subjects with abnormal TWA value with myocardial infarction and without myocardial infarction were 74,6% and 16,7% respectively. The Chi-Square test showed an association between PAH and abnormal TWA with OR 14,395 (CI 95%: 5,88-35,21; p<0,001). After multivariate analysis, myocardial infarction was the only remaining variable independently associated with abnormal TWA values. Abnormal TWA value occurred more frequently in subjects with myocardial infarction compared to subjects without myocardial infarction, in population of CAD LVEF >40%, with the possibility of 14,395 times more frequent.

Keywords: T-wave Alternans, Coronary Artery Disease, Myocardial Infarction, LVEF>40%

INTRODUCTION

The dynamic natural history of CAD may present in different clinical presentation, such as acute coronary syndrome or chronic coronary syndrome

(Knuuti et al., 2020). The difference in clinical presentation is based on the burden of the atherosclerosis and coronary blood flow, it may be divided into three levels, such as ischemia (myocardial hypoxia <20 minutes and reversible), injury (myocardial hypoxia >20 minutes and reversible, and infarction (myocardial hypoxia >2 hours and irreversible)(Wagner et al., 2009). Patients with CAD may also be divided based on the LVEF into <40% and >40%(Janusek et al., 2015).

Myocardial ischemia and infarction cause slowed repolarization and manifest as changes of the ST-segment and T-wave in the electrocardiogram (ECG)(Li et al., 2021). One of the most potential ECG parameter is the TWA, which detects beat to beat morphological and amplitude changes of the T wave(Janusek et al., 2015; Puljevic et al., 2019; Verrier & Nieminen, 2010). TWA has a one-year negative predictive value (near 95%) for ventricular arrhythmia(Narayan, 2006).

Patients with CAD, especially with myocardial infarction, has been reported to have a higher TWA value(Mollo et al., 2012). Low LVEF has also been reported to cause a higher TWA value. Patients with myocardial infarction LVEF <40% has a higher TWA value than patient with myocardial infarction LVEF >40%. Somehow, the sudden cardiac deaths happen more often in population with LVEF>40%(Janusek et al., 2015).

The study and profile of TWA in CAD patients with myocardial infarction and LVEF>40% has not been well understood. In this study, the number of abnormal TWA values in CAD patients with myocardial infarction and LVEF>40% has been investigated. Furthermore, the association of myocardial infarction and abnormal TWA value in CAD patients with LVEF >40% has been evaluated.

RESEARCH METHODS

The research design was a case-control study. The subjects of this research were CAD patients with LVEF >40% at Dr. Sardjito general hospital Yogyakarta, Indonesia, until April 2022. Previous data from the treadmill test examination and data record were extracted and analyzed for this research. The inclusion criteria were (1) the age of the subjects were >18 years old, (2) subjects diagnosed with CAD, (3) subjects LVEF >40%, and (4) subjects with sinus rhythm. The exclusion criteria were (1) acute myocardial infarction event with onset <10 weeks from TWA examination, and (2) incomplete data record.

The diagnosis of CAD was based on percutaneous coroangiography or multislice computed tomography (MSCT) angiography examination. The burden of CAD was categorized based on the number of coronary vessel with stenosis ≥50% into 1 vessel disease (VD), 2VD, or 3 VD which was then simplified into single-VD and multi-VD(Ibanez et al., 2018; Neumann et al., 2020; PERKI, 2016; Villa et al., 2018). To determine whether there was a myocardial infarction or not was based on the medical record of acute myocardial infarction event and evidence of loss of viable myocardium in a pattern consistent with an ischemic etiology(PERKI, 2018; Thygesen et al., 2019; Wagner et al., 2009). The evidence of loss of viable myocardium was obtained by echocardiography examination. The TWA value was obtained from treadmill test using General Electric T2100 with it's modified moving average (MMA) method. The result of TWA examination was then categorized into normal if the value was <47 μV and categorized as abnormal if the value was ≥47 μV(Aro et al., 2016; Verrier et al., 2011).

Data of confounding variables such as history of hypertension (HT), diabetes mellitus (DM), diastolic dysfunction, and use of pharmacological agents were obtained from the case report form. The diagnosis of HT was based on the systolic (≥140 mmHg) and diastolic (≥90 mmHg) blood pressure examination and history of previous examination and HT treatment(Piepoli et al., 2016). The diagnosis of DM was based on Indonesian DM consensus(Soebagijo et al., 2015). The assessment of systolic and diastolic function was based on the echocardiography guidelines(McDonagh et al., 2021; McMurray et al., 2013; Nagueh et al., 2016; Sharma & Klein, 2018).

Subjects in this study were divided into the case group if the TWA value was abnormal, and into the control group if the TWA value was normal. The two groups were matched using the group matching method. After classifying the case and control group, the history and status of myocardial infarction of each subject was assessed retrospectively. The comparison of continuous data among groups were analyzed with independent T-test (normally distributed data/parametric) or Mann Whitney-U test (not normally distributed data/non parametric). The comparison of categorical data among groups were analyzed with chi-square test. Multivariate analysis using logistic regression test was conducted to determine the effect of confounding variables on TWA value. A p value <0.05 is considered as statistically significant limit.

RESULT AND DISCUSSION

In this study, there were 124 subjects, 62 of which were in the case group with abnormal TWA value, and the other 62 were in the control group with normal TWA value. The male gender comprised of 83,8% and predominant in both subgroups of case and control groups. The mean age was 55,48 ± 8,6 years old. There was no significant difference in comorbid parameters (HT and DM), in pharmacologic treatment (beta blockers and calcium channel blockers), in echocardiographic parameters (diastolic function and LVEF), and in CAD burden between the case and control group. However, the frequency of each parameter was found to be slightly higher in the case group. The frequency and value of characteristics of subjects are presented in Table 1.

There were 53 subjects (74,6%) with abnormal TWA values that had myocardial infarction, compared with only 9 subjects (16,7%) with abnormal TWA values that did not have myocardial infarction. The *Chi-square* analysis of myocardial infarction condition and TWA value (Table 2) shows that a myocardial infarction condition had a significant effect on abnormal TWA value with the odds ratio of 14,395 (CI 95%: 5,88-35,21; p<0,001). After multivariate analysis, myocardial infarction was the only the remaining variable independently associated with abnormal TWA values (Table 3).

The results of this study show that male gender was dominant in CAD with 83,8% of all subjects. This result was similar with previous studies reporting that male gender was dominant in CAD with 77,4%. This phenomenon is related with the risk factors of CAD such as smoking, HT, DM, and dyslipidemia which are more frequently found in male(Hosseini et al., 2021; Jamee et al., 2013). The gender percentage between the group with abnormal and normal TWA values were almost similar, meaning that gender did not have significant effect on TWA value as reported by Hashimoto et al. in 2018(Hashimoto et al., 2019). The mean age of the

subjects in this study (55,48 ± 8,6 years old) was similar with the results in other studies where the mean age of CAD subjects were 50-60 years old(Hosseini et al., 2021; Okunrintemi et al., 2020). Age did not have any significant effect on TWA value, especially in the age <60 years old(Hashimoto et al., 2019, 2020), the result of which were similar with the result of this study where the mean age in the case and control group is almost similar.

There was no significant difference in comorbid parameters (HT and DM) between the group with abnormal TWA value and the group with normal TWA value. Nevertheless, the number of subjects with the comorbid was higher in the group with abnormal TWA value. These results were in accordance with result of studies by Hennersdorf et al. in 2001 reporting that a higher number of abnormal TWA value in patients with HT(Hennersdorf et al., 2001), and the study that mentioned a higher number of abnormal TWA value in patients with DM(Bonapace et al., 2011; Molon et al., 2007). The number of subjects receiving beta blockers in the case and control group were exactly the same, and the number of subjects receiving calcium channel blockers in the case and control group were almost the same. This resembles the treatment in these groups are almost equal.

There were 33 subjects with diastolic dysfunction, 17 of which had abnormal TWA value, and the other 16 had normal TWA value. Previous studies mentioned that diastolic dysfunction may cause abnormal TWA values if there was a myocardial fibrosis(Bonapace et al., 2011). The similar number of subjects with diastolic dysfunction within both groups was most likely due to the profile of the subjects with LVEF >40% and less likely to have fibrosis that may lead to significant difference between the groups. The mean LVEF in the case and control group were 61,9% (±8,5) and 63,9% (±8,2) respectively, which were almost equal. The TWA value was reported to be significantly higher in subjects with LVEF <40%(Bloomfield et al., 2006; Janusek et al., 2015). The similar LVEF profile of subjects was most likely because of the inclusion criteria LVEF >40% in this study design. The number of subjects with multi-VD in the abnormal TWA value group was higher than the number in the other group, 44 subjects vs 35 subjects respectively. Eventhough it was not statistically significant, the result is similar with the study that mentioned there will be higher TWA value if there is more vessels with significant stenosis(Puljevic et al., 2019).

In this study, there were 53 subjects (74,6%) with abnormal TWA values that had myocardial infarction, compared with only 9 subjects (16,7%) with abnormal TWA values that did not have myocardial infarction. Myocardial infarction condition had a significant effect on abnormal TWA value with the odds ratio of 14,395 (CI 95%: 5,88-35,21; p<0,001). These results elaborate the fact on the effect of myocardial infarction on TWA value, thus supporting the theory of impaired calcium handling and repolarization heterogenicity in myocardial infarction may cause abnormal TWA value(Cutler & Rosenbaum, 2009). The multivariate analysis shows that myocardial infarction was the only the variable independently associated with abnormal TWA values. The study by Hasan et al. (2016) and Puljevic et al. (2018) also stated that myocardial infarction will have a higher TWA value(Hasan et al., 2016; Puljevic et al., 2019). This study only included subjects with LVEF >40%, so the possibility for other confounders such as low LVEF as the cause of abnormal TWA value is very small, and the cause of abnormal TWA value is more likely due to the myocardial infarction.

CONCLUSION

In population of CAD patients with LVEF>40%, the number of abnormal TWA value was significantly higher in patients with myocardial infarction compared to patients without myocardial infarction. Myocardial infarction was the only variable with significant independent association with abnormal TWA value.

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