COMPARISON OF T WAVE ALTERNANS IN PATIENTS WITH CARDIOMYOPATHY AND HEALTHY CONTROLS

Hira Ashraf, Azmat Hayat*, Muhammad Alamgir Khan, Madiha Sarwar**

Army Medical College/National University of Medical Sciences (NUMS) Rawalpindi Pakistan, *Armed Forces Institute of Cardiology (AFIC)/National University of Medical Sciences (NUMS) Rawalpindi Pakistan, **Foundation University Medical College (FUMC) Rawalpindi Pakistan

ABSTRACT

Objective: To compare T wave alternans in patients with cardiomyopathy and healthy controls.
Study Design: Cross-sectional comparative study.
Place and Duration of Study: Department of Cardiac Electrophysiology, Armed Forces Institute of Cardiology Rawalpindi, from Feb 2016 to Aug 2016.
Material and Methods: Sixty patients with cardiomyopathy (any type) along with sixty healthy controls of matched age and gender were recruited through non-probability purposive sampling. Patients with diabetes mellitus, cerebrovascular accident, heart failure, bundle branch block, systemic arterial hypertension and ongoing antiarrhythmic therapy were excluded from the study. DMS 300-4L Holters were used to obtain ambulatory ECG recordings. Cardio Scan premier 12 lux software was used for analysis of T wave alternans.
Results: Total one twenty subjects were enrolled in the study. Cardiomyopathic patients with positive T wave alternans were 13 (21.7 %) out of 60, while only 4 (6.7%) out of 60 healthy controls demonstrated positive T wave alternans. There was significant variation in frequency of patients with positive T wave alternans as compared to healthy controls with *p*-value of 0.02. In cases the mean value of T wave alternans was 55.10 µv ± 33.58 while 39.45 µv ± 13.53 in controls. The difference in mean value of T wave alternans between cases and controls was significant with *p*-value of 0.001.
Conclusion: The frequency of patients with cardiomyopathy having positive T wave alternans was significantly higher as compared to the healthy controls.

Keywords: Cardiomyopathy, T wave alternans.

INTRODUCTION

T wave alternans refers to a change in the contour and amplitude of T wave on every other beat[1]. It represents an increased heterogeneity of ventricular repolarization on a beat-to-beat basis which may provide a substrate for re-entry. T wave alternans has emerged as a robust tool for arrhythmia risk stratification in patients with cardiac diseases. It gives an insight about the mechanism of arrhythmogenesis leading to sudden cardiac death[2]. The mechanisms involved in T wave alternans are instabilities in membrane voltage and disruptions in intracellular calcium cycling. They affect a number of ionic currents in ventricular myocytes and action potential duration[3]. The alternation in the action potential duration reflected by T wave alternans occurs at two distinct sites and at opposite phases of action potential. This, in turn promotes marked gradients of repolarization and a substrate for re-entry leading to ventricular arrhythmias[4].

Cardiomyopathy is an anatomic and pathologic diagnosis related with structural or electrical dysfunction of the heart. It is the disease of myocardium, usually with disproportionate ventricular hypertrophy or dilatation. The most common complication of cardiomyopathy is ventricular arrhythmias which may escort to sudden cardiac death[5].

Almost all cardiomyopathies have a genetic basis that causes myofibrillar disarray. This disarrangement results in histological changes

Correspondence: Dr Hira Ashraf, Dept of Physiology Army Medical College Rawalpindi Pakistan
Email: hiraawan@hotmail.com
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providing an ideal substrate for re-entry and arrhythmias[6]. Many studies have been carried out to discover the relationship between cardiomyopathy and T wave alternans[7,8]. Early detection of T wave alternans in patients with cardiomyopathy can help in risk stratification of ventricular arrhythmias leading to sudden cardiac death[9]. There is a lot of concern in the field of cardiac electrophysiology to find out non-invasive markers for the detection of arrhythmogenic sudden cardiac death. T wave alternans is a relatively newer marker which has been investigated for its association with the genesis of ventricular arrhythmias[10,11].

The present study was planned to evaluate T wave alternans in patients with cardiomyopathy. The objective of the study was to compare T wave alternans in patients of cardiomyopathy with healthy controls in terms of mean values and frequency of individuals with positive and negative T wave alternans. Results of the study will not only identify patients at high risk of developing ventricular arrhythmias but will also provide an understanding about the probable pathophysiologic mechanism of disrupted electrical activity within the myocardium of these patients. The patients so identified at high risk of ventricular arrhythmias can be subjected to additional investigations for further refinement of arrhythmia risk and appropriate therapeutic measures to avoid sudden cardiac death.

PATIENTS AND METHODS

This cross sectional comparative study was conducted at the Department of Cardiac Electrophysiology, Armed Forces Institute of Cardiology (AFIC) in collaboration with Army Medical College (AMC), Rawalpindi. An official approval was obtained prior to commencement of the study from Institutional Review Board of AFIC and Ethical review committee of AMC, Rawalpindi.

Sample size was calculated using WHO sample size calculator considering hypothesis test for two population means (two-sided test). By keeping the values of alpha as 5%, power as 80%, population standard deviation as 22 and mean difference as 8, sample size was calculated as 119. However we used sample size of 120 in present study.

Sixty patients with cardiomyopathy along with sixty healthy controls were recruited through non-probability purposive sampling. Cases diagnosed as cardiomyopathy by the cardiologist at outpatient department of AFIC were selected for the study. Controls were healthy individuals without cardiomyopathy. Written informed consent was taken from all the patients included in the study. History and general physical examination of all the cases and controls were carried out and the individuals having known cardiac diseases or diabetes mellitus were excluded. The selected participants were subjected to standard ECG and echocardiography to rule out bundle branch block, heart failure, hypertension and any other structural heart disease. Patients with ongoing antiarrhythmic therapy were also excluded.

Selected participants were requested to visit electrophysiology department of AFIC for Holter monitoring in order to detect T wave alternans. Patients and controls were Holtered with DMS 300-4L from DM Systems Company Ltd. Ambulatory ECG data was transferred to the computer and edited for all the improper beats (ectopic and artefacts) with the help of DMS Cardioscan software premier 12 lux version. Time domain analysis was used for T wave alternans analysis. T wave alternans values were analyzed in all the channels. It was defined as the highest T wave alternans value in any channel. T wave alternans ≥ 60 µV was considered positive.

Data Analysis

Data were analyzed using computer software IBM SPSS version 23. Mean and standard deviation were calculated for numerical variables like age and T wave alternans whereas frequency and percentage was calculated for categorical variables like gender and status of T wave alternans (positive/negative). Independent samples t test was used to compare mean values

of T wave alternans between cases and controls. Chi Square test was used to compare the frequency of individuals with positive and negative T wave alternans between cases and controls. Alpha value was kept at 0.05 at confidence level of 95%.

RESULTS

There were 89 (74.16%) male and 31 (25.83%) female participants (N=120) with the mean age of 45.01 ± 15.75 years. Among cases, there were 43 (71.66%) male and 17 (28.33%) female patients with mean age of 51.25 ± 14.45 years whereas among controls there were 46 (76.66%) male and 14 (23.33%) female participants with mean age of 38.77 ± 14.56 years.

The mean values of T wave alternans in cases and controls along with standard deviation are shown in table-I. The difference of T wave alternans between cases and controls is significant at *p*-value of 0.001.

Table-I: Comparison of mean values of T wave alternans between cases and controls.

Group	T wave alternans (μv)	*p*-value
Cases	55.10 ± 33.58	0.001*
Controls	39.45 ± 13.53	

**p*-value significant (less than 0.05).

Table-II: Frequency comparison of individuals with positive and negatives T wave alternans between cases and controls.

Group	T wave alternans		*p*-value
	Positive	Negative	
Cases	13 (21.7%)	47 (78.3%)	0.02*
Controls	4 (6.7%)	56 (93.3)	

**p*-value significant (less than 0.05).

Frequency and percentage of cases and controls with positive and negative T wave alternans is shown in table-II. Difference in frequency of individuals with positive as well as negative T wave alternans between cases and controls (13 versus 4 and 47 versus 56) was significant at *p*-value of 0.02. This reflects the dependency (association) of the two variables with each other.

DISCUSSION

The results of our study demonstrated high frequency of patients with cardiomyopathy having positive T wave alternans as compared to healthy controls. Cases with positive T wave alternans were 13 (21.7 %) out of 60, while only 4 (6.7%) out of 60 healthy controls exhibited positive T wave alternans. This difference was significant with *p*-value of 0.02. The results of our study helped in identification of patients with cardiomyopathies that are at risk of fatal arrhythmias. The probable cause of increased frequency of patients with positive T wave alternans is the structural disarrangement in the fibrillar compartment of myocardium. The disarray leads to electrotonic uncoupling of the myocytes resulting in alternation in repolarization and T wave alternans. Myofibrillar disarray is the characteristic feature of cardiomyopathy raising the susceptibility of ventricular arrhythmias. The results of our study are comparable to the study conducted by Hennersdorf et al. They enrolled 60 patients with cardiomyopathy and found positive T wave alternans in 12 (20%) of them. Grimm et al recruited 110 healthy individuals and found positive T wave alternans in 5 (4.5%) of them which is comparable to our results[12]. Another study conducted by Adachi et al found 23 (39.6%) patients with cardiomyopathy having positive T wave alternans out of 58 total cases[13]. The increased frequency could be due to the difference in analysis method. We used the latest modified moving average method which has high sensitivity as compared to the spectral method applied by them.

The mean values of T wave alternans were significantly different among cases and controls. In cases the mean value was 55.10 μv ± 33.58 while in controls it was 39.45 μv ± 13.53. The mean value in cases of our study is less than the cut off value for positive T wave alternans with high standard deviation. Small number of cases (21.7%) having positive T wave alternans out of total recruited cases may be the reason of raised standard deviation. Results of Mollo et al are comparable to our study in which the mean value was 59.4 ± 25. In there study the mean value of T wave alternans in healthy controls was 44.6 ± 21[14]. The scant difference between the mean values is may be due to the different technique for detection of T wave alternans. They used exercise stress test while we detected T wave alternans on ambulatory ECG.

T wave alternans is closely related to arrhythmia events as observed by numerous studies[15,16]. Bloomfield et al detected 29 positive T wave alternans cases out of 290 and after five years follow up 20 of them had ventricular tachycardia events[17]. Similar findings were observed by Gold and his colleagues as their 22 out of 31 cases with positive T wave alternans experienced ventricular fibrillation/sudden cardiac death[18]. We were unable to follow the cases with positive T wave alternans for arrhythmic events due to time restriction, but with ample confidence from literature, can relate the presence of positive T wave alternans with vulnerability to fatal arrhythmias.

Cardiomyopathy mostly occurs in old age patients. Preferably, age matched controls must have been taken in the study but due to limited duration it was arduous to find age matched controls. This is the limitation of our study.

CONCLUSION

Frequency of patients with cardiomyopathy having positive T wave alternans was significantly higher as compared to healthy controls.

The concernment of T wave alternans with cardiomyopathy identifies the vulnerability of these patients to ventricular arrhythmias and sudden cardiac death. T wave alternans assessment can be used as a noninvasive tool for stratification of high risk patients. These patients must be placed on appropriate prophylactic therapies for deferment of fatal outcomes.

CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

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