ORIGINAL ARTICLE

COMPARISON OF T-WAVE ALTERNANS IN PATIENTS WITH ISCHEMIC AND NON-ISCHEMIC CARDIOMYOPATHY

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Background: Early detection of T-wave alternans in patients with cardiomyopathy can help in risk stratification of ventricular arrhythmias leading to sudden cardiac death. The present study was designed to compare T-wave alternans in patients with ischemic and non-ischemic cardiomyopathy. **Methods:** This cross-sectional comparative study was carried out at Department of Cardiac Electrophysiology, Armed Forces Institute of Cardiology, Rawalpindi during 2019. Thirty patients with ischemic cardiomyopathy along with equal number of non-ischemic cardiomyopathy 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 anti-arrhythmic 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:** A total of 60 subjects were studied. The mean value of T-wave alternans was 52.73±30.76 µV and 57.47±36.54 µV for patients with ischemic and non-ischemic cardiomyopathy respectively. The difference between mean values was statistically insignificant (p=0.59). T-wave alternans was present in 8 (26.7%) patients with ischemic cardiomyopathy, while 5 (16.7%) patients with non-ischemic cardiomyopathy showed positive T-wave alternans and the difference was statistically insignificant (p=0.35). **Conclusion:** The mean value of T-wave alternans and frequency of patients with positive T-wave alternans is not significantly different in ischemic and non-ischemic cardiomyopathy.

Keywords: T-Wave Alternans, Ischemia, Ischemic cardiomyopathy, Non-ischemic cardiomyopathy

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INTRODUCTION

T-wave alternans refers to a change in the shape and amplitude of T-wave on alternate 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 duration of action potential.[3] The alternation in the duration of action potential 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. Cardiomyopathy can be classified into ischemic and non-ischemic type. Ischemic cardiomyopathy describes significantly impaired left ventricular function that results from coronary artery disease. Ischemic cardiomyopathy is the most common cause of heart failure.[5] Non-Ischemic cardiomyopathy includes all causes of decreased heart function other than those caused by coronary artery disease. The most common causes of non-ischemic cardiomyopathy are viral myocarditis, drug reactions, inflammation or autoimmune reactions, amyloid and sarcoid infiltration. Ventricular arrhythmias are common in patients with cardiomyopathy, ranging from asymptomatic ventricular premature beats to sustained ventricular tachycardia or ventricular fibrillation, which can lead to sudden cardiac death.[6,7]

Almost all cardiomyopathies have a genetic basis that causes myofibrillar disarray. This disarrangement results in histological changes providing an ideal substrate for re-entry and arrhythmias.[8] Many studies have been carried out to discover the relationship between cardiomyopathy and T-wave alternans.[9,10] Early detection of T-wave alternans in patients with cardiomyopathy can help in risk stratification of ventricular arrhythmias leading to sudden cardiac death.[11] There is a lot of concern in the field of cardiac electrophysiology to find out non-invasive markers for 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.[12,13]

Unfortunately, because of lack of awareness and resources, no local study has been conducted to our knowledge. Present study was planned to evaluate T-wave alternans in patients with two different types of cardiomyopathy. The objective of this study was to compare T-wave alternans in patients of ischemic and non-ischemic cardiomyopathy. 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 Raosoft sample size calculator using 95% confidence interval. Thirty patients with ischemic cardiomyopathy along with thirty patients with non-ischemic cardiomyopathy were recruited through non-probability purposive sampling. Cases diagnosed as both types of cardiomyopathy by the cardiologist at outpatient department of AFIC were selected for the study. 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 anti-arrhythmic therapy were also excluded.

All sixty patients were Holtered with DMS 300-4L from DM Systems Company Ltd. at Electrophysiology Department of AFIC for monitoring in order to detect T-wave alternans. Ambulatory ECG data was transferred to the computer and edited for 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 channels. It was defined as the highest T-wave alternans value in any channel. T-wave alternans ≥60 μV was considered positive.[3]

Data were analysed on SPSS-23. Independent samples *t*-test was used to compare mean values of T-wave alternans between ischemic and non-ischemic cardiomyopathic patients. Chi-square test was used to compare the frequency of individuals with positive and negative T-wave alternans between the groups keeping alpha at 0.05 and confidence level at 95%.

RESULTS

Among the patients with ischemic cardiomyopathy, there were 23 (76.7%) males and 7 (23.3%) females with mean age of 51.27±12.65 years. There were 20 (66.7%) male and 10 (33.3%) female patients with non-ischemic cardiomyopathy with the mean age of 51.23±16.28 years.

The mean values of T-wave alternans was 52.73±30.76 μV and 57.47±36.54 μV for patients with ischemic and non-ischemic cardiomyopathy respectively and the difference was statistically insignificant (p=0.59) (Table-1).

Frequency of individuals with and without T-wave alternans was also compared between patients of ischemic and non-ischemic cardiomyopathy (Table-2). T-wave alternans was present in 8 (26.7%) patients with ischemic cardiomyopathy. While 5 (16.7%) patients with non-ischemic cardiomyopathy showed positive T-wave alternans and the difference was statistically insignificant (p=0.35).

Table-1: Comparison of mean values of T-wave alternans between ischemic and non-ischemic cardiomyopathy

Group	T-wave alternans (μV)	*p*
Ischemic Cardiomyopathy	52.73±30.76	0.59
Non-ischemic Cardiomyopathy	57.47±36.54	

Table-2: comparison of individuals with and without T-wave alternans between ischemic and non-ischemic cardiomyopathy

Group	T-wave alternans		*p*
	Present	Absent	
Ischemic Cardiomyopathy	8 (26.7%)	22 (73.3%)	0.35
Non-ischemic Cardiomyopathy	5 (16.7%)	25 (83.3%)	

DISCUSSION

Cardiomyopathy is a disease of vast aetiology including genetic factors, secondary to effects of ischemia, and other cardiovascular diseases. Most common types of cardiomyopathies are ischemic and non-ischemic cardiomyopathy.[14] In our study the patients were divided into these two categories and T-wave alternans were recorded in both the groups. Mean values and frequency of patients with positive T-wave alternans were slightly higher in patients with ischemic than non-ischemic cardiomyopathy but the difference was statistically insignificant (p=0.59, p=0.35). Our results suggest the probable cause of development of T-wave alternans in both types of cardiomyopathy. The cause

may be present in the primal but not the ischemia affected infracted myocardium of patients with cardiomyopathy thereby suggesting that ischemia has little effect on development of T-wave alternans in patients with cardiomyopathy. Gold *et al*[15] studied T-wave alternans and other non-invasive tools in patients with ischemic and non-ischemic cardiovascular diseases and suggested that ischemia plays diminutive role in pathophysiology of T-wave alternans in some diseases. This may highlight the importance of evaluation of T-wave alternans as arrhythmia risk stratifier in both types of cardiomyopathy.

Klingenheben *et al*[16] conducted a study in Germany recruiting 204 patients with ischemic and non-ischemic cardiomyopathy and quantitatively assessed T-wave alternans. In their study the mean value of T-wave alternans was significantly higher in patients with non-ischemic cardiomyopathy as compared to ischemic cardiomyopathy. Our results are in contrary to their findings which may be due to a smaller number of subjects involved in our study or due to difference in recording and analysis methods. They recruited 204 patients while we checked T-wave alternans in 60 patients only. We used modified moving average method for recording T-wave alternans while they analyzed T-wave alternans using spectral method. Another difference may be due to dissimilarity in aetiology of non-ischemic cardiomyopathy in European countries. There, some of the common causes of non-ischemic cardiomyopathy are substance abuse (i.e., cocaine or alcohol), connective tissue disorders, and infection with the human immunodeficiency virus (HIV)[17], these being less common among our population. Difference in aetiology may have affected the mean values, possibly reflecting more extensive myocardial damage and a higher arrhythmia propensity in non-ischemic cardiomyopathy patients.

Many studies endorse the findings of our study emphasizing the significance of T-wave alternans as a promising arrhythmia risk assessment tool in both types of cardiomyopathies.[18] Chow *et al*[19] conducted a study evaluating 768 patients with ischemic cardiomyopathy and found significantly higher prevalence of arrhythmias in patients with ischemic cardiomyopathy. Four hundred and forty-six patients with non-ischemic cardiomyopathy were recruited in a study conducted by Salerno *et al*[20] in Italy assessing T-wave alternans. A fourfold increased risk of arrhythmia was calculated in non-ischemic cardiomyopathic patients with positive T-wave alternans as compared to patients with negative T-wave alternans.

T-wave alternans is closely related to arrhythmia events as observed by some studies.[21,22] Bloomfield *et al*[23] detected 29 positive T-wave alternans cases out of 290 and after five years follow up 20 of them had ventricular tachycardia events. Similar findings were reported by Gold *et al*[15] as their 22 out of 31 cases with positive T-wave alternans experienced ventricular fibrillation/sudden cardiac death. We were unable to follow the patients with positive T-wave alternans for arrhythmic events, but with ample evidence from literature, can relate the presence of positive T-wave alternans with vulnerability to fatal arrhythmias.

Cardiomyopathy mostly occurs in old age patients.[15] Preferably, age-matched participants must have been taken in the study but due to limited duration it was arduous to find age matched patients.

CONCLUSION

There was no significant difference in mean values and frequency of T-wave alternans in patients with ischemic and non-ischemic cardiomyopathy. It can therefore be concluded that the development of T-wave and vulnerability of these cardiomyopathic patients to ventricular arrhythmias is not related to ischemia as it is equally exhibited in non-ischemic cardiomyopathic patients as well.

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