ORIGINAL ARTICLE

RISK ESTIMATION OF T WAVE ALTERNANS AND VENTRICULAR LATE POTENTIALS IN PATIENTS WITH CARDIOMYOPATHY

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Background: T wave alternans and ventricular late potentials represent repolarization heterogeneity and slowing of cardiac impulse which may lead to ventricular arrhythmias. Cardiomyopathy is a disorder which puts the patients on the risk of sudden arrhythmic death. Present study was designed to evaluate the risk of developing T wave alternans and ventricular late potentials in patients with cardiomyopathy. **Methods:** This cross-sectional comparative study was carried out at Armed Forces Institute of Cardiology, Rawalpindi from Feb to Aug 2016. Sixty cardiomyopathic patients and 60 healthy controls were recruited through convenience sampling. Ambulatory ECG was recorded by using DMS 300-4L Holters. T wave analysis was done by Cardioscan Premier 12 Lux software. Mortara ELI 350 Electrocardiograph was used to obtain Signal Averaged ECG for analysis of Ventricular Late Potentials. **Results:** T wave alternans was positive in 13 (21.66%) cardiomyopathic patients while in healthy controls only 4 (6.66%) participants demonstrated positive T wave alternans. Ventricular late potentials were present in 14 (23.33%) cases and 5 (8.33%) healthy controls. The relative risk of having positive T wave alternans and ventricular late potentials was 3.3 and 2.8 times greater respectively in patients with cardiomyopathies as compared to healthy controls. **Conclusion:** Patients with cardiomyopathy are at higher risk of developing positive T wave alternans and ventricular late potentials. Patients positive for both parameters constitute a high-risk subset for developing ventricular arrhythmias.

Keywords: T wave alternans, Ventricular late potentials, Cardiomyopathy

Pak J Physiol 2018;14(4):14–7

INTRODUCTION

T wave alternans (TWA) is a beat-to-beat alternation in the morphology and amplitude of T wave.[1] It represents an augmented heterogeneity of ventricular repolarization on a beat-to-beat basis which may offer a substrate for reentry.[2] The mechanisms intricating T wave alternans are instabilities in membrane voltage and disturbances in intracellular calcium cycling.[3] Unstable membrane voltage due to the vertical relationship between action potential duration and the previous diastolic interval[4] endorses noticeable gradients of repolarization and a substrate for re-entry leading to ventricular late potentials.[5]

Ventricular Late Potentials (VLPs) are high frequency signals of decreased amplitude located at the terminal part of QRS complex that may range up to a variable length in ST segment. They are considered as non-invasive markers of myocardial tissue damage.[6] A high resolution, non-invasive signal detecting technique identified as signal averaged ECG is used to detect VLPs.[7] Presence of ventricular late potentials on signal averaged electrocardiogram is considered as an indication of underlying anatomical and electrophysiological variations which can give rise to fatal ventricular arrhythmia.[8]

Cardiomyopathies are one of the common causes of sudden cardiac death in young population ostensibly due to ventricular arrhythmias.[9] It is associated with muscle or electrical abnormality of the heart often leading to heart failure.[10] Damaged myocardium in cardiomyopathy acts as an area of delayed conduction. It is detected on signal averaged electrocardiogram as ventricular late potentials.[11] The morphological modifications in the interstitial, vascular or muscular compartments due to any pathological condition provide a significant substrate for re-entry. These damaged portions of myocardium give rise to abating zones allowing sluggish or fragmented depolarization areas.[12] These segments act as seedbeds for the development of ventricular late potentials. These structural changes set a substrate for arrhythmias of diverse mechanisms[13] mostly ventricular tachycardia.[5] Many other studies have also highlighted the correlation of VLPs and cardiomyopathies.[14,15]

T wave alternans is one of the recently emerged parameters for arrhythmias risk stratification in patients with cardiomyopathy.[16,17] The probable mechanism of T wave alternans in cardiomyopathy is the myofibril disarray and fibrosis. The anatomic remodelling has also been implicated as a paramount mechanism responsible for heterogeneity of repolarization leading to T wave alternans. Stern histological changes are associated with greater electrical instability in the ventricular myocardium.[5] Electronic uncoupling of myocytes leading to repolarization aberration is a characteristic feature of dilated cardiomyopathy. It is demonstrated in secluded myocytes and increased dispersion of repolarization may make the heart vulnerable to non-excitable gap re-entry. These repolarization abnormalities most

commonly demonstrated as T wave alternans. In cardiomyopathy it increases the probability of after depolarization leading to arrhythmias.[12,13] Estimation of arrhythmia risk is hallmark in increasing the life expectancy of patients with cardiomyopathy.[18,19]

Early diagnosis and timely interventions can delay occurrence of ventricular arrhythmias and sudden cardiac death in these patients.[20] By assessing the risk of development of T wave alternans and ventricular late potentials the arrhythmia prone patients can be highlighted and appropriate measures can be taken for better prophylaxis.[21] With this backdrop, present study was designed to evaluate the risk of developing T wave alternans and ventricular late potentials in patients with cardiomyopathy.

MATERIAL AND METHODS

This cross-sectional comparative study was carried out at the Department of Cardiac Electrophysiology, Armed Forces Institute of Cardiology (AFIC) in association with Physiology Department, Army Medical College, Rawalpindi. An official approval was obtained prior to commencement of the study from Institutional Review Board of AFIC and Ethical Review Committee of Army Medical College, Rawalpindi.

Sample size was calculated using WHO sample size calculator considering hypothesis test for two population means. 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. We used sample size of 120 in current study.

Sixty diagnosed cases of cardiomyopathy attending outpatient department of AFIC along with sixty age and gender matched healthy controls were enrolled through non-probability convenience sampling. Written and informed consent was obtained from all the participants before starting 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. Standard ECG and echocardiography were performed for all selected participants to rule out bundle branch block, heart failure, hypertension and any other structural heart disease. Patients with ongoing antiarrhythmic therapy were also omitted.

Selected participants were requested to visit Electrophysiology Department of AFIC for Holter monitoring to detect T wave alternans. DMS 300-4L Holters from DM System Company Ltd were applied on patients and controls to record T wave alternans. Ambulatory ECG data were shifted to the computer and amended for all the improper beats (ectopic and artefacts) with the help of DMS Cardioscan Premier 12 Lux version. T wave alternans was analyzed by time domain analysis 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.

Signal Averaged ECG (SAECG) of every participant was recorded by using commercially available Mortara ELI 350 ECG Machine by Mortara Instruments available at AFIC. It records 12 or 15-lead resting electrocardiogram. It is a portable battery-operated signal acquisition device allowing for Signal averaged ECG testing at bedside. Total 500 beats were recorded in approximately 12–15 minutes. All the three bipolar leads were recorded, averaged, filtered and combined into a QRS vector magnitude called 'filtered QRS' (fQRS) complex. This fQRS complex was analyzed for the detection of ventricular late potentials. Signal Averaged ECG was considered positive for presence of VLPs when at least two out of the following three criteria were fulfilled:

1. Filtered QRS duration (fQRS) greater than 114ms
2. Low amplitude signals (LAS) under 40 μV in the terminal QRS complex greater than 38 ms
3. Root mean square (RMS) voltage in the terminal 40ms less than 20 μV

Data were analyzed using SPSS-23. T wave alternans and SAECG parameters (VLPs) were compared between patients and controls. Relative risk was determined to measure the effect of association of TWA and VLPs with cardiomyopathy. 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.

Table-1 shows the frequency comparison of individuals with and without TWA between cases and controls along with p-value and relative risk. Table-2 shows cross tabulation between VLPs and cases/ controls displaying frequency comparison, p-values and relative risk.

Table-1: Association of T wave alternans with Cardiomyopathy

	TWA [n (%)]		*p*	Relative Risk	95% CI
	Present	Absent			
Cases	13 (21.66)	47 (78.33)	0.01*	3.3	1.12–9.4
Controls	4 (6.66)	56 (93.33)			

*Significant

Table-2: Association of ventricular late potentials with Cardiomyopathy

	VLPs		*p*	Relative Risk	95% CI
Groups	**Present**	**Absent**			
Cases	14 (23.33)	46 (76.66)	0.02*	2.8	1.1–7.28
Controls	5 (8.33)	55 (91.66)			

*Significant

DISCUSSION

The present study aimed to find out the risk for development of T wave alternans and ventricular late potentials in patients with cardiomyopathy. Results showed that the risk was significantly higher in cases as compared to controls for both the variables under consideration. Results also showed that the percentage of patients with T wave alternans and ventricular late alternans was greater as compared to controls.

The increased risk of developing T wave alternans and ventricular late potentials in cardiomyopathic patients may be due to pathophysiological mechanisms capable of causing delayed conduction in myocardium of cardiomyopathic patients leading to evolution of ventricular arrhythmias.[12] Mozoş *et al* suggested that, in patients with dilated cardiomyopathy, patchy interstitial fibrosis adjacent to viable myocardium causes fibrosis thus decreasing electrical coupling. It slows down the propagation of cardiac impulses between myocytes leading to T wave alternans and ventricular late potentials. These anatomical abnormalities later serve as substrate for re-entrant ventricular tachycardia.[18]

Relative risk of T wave alternans and ventricular late potentials in our study group was 3.3 and 2.8 times respectively in patients with cardiomyopathy as compared to healthy controls. These results are synchronous with the study conducted by Garcia *et al*[22]. They found significantly higher frequency of T wave alternans in patients with cardiomyopathy. Mollo *et al*[23] checked T wave alternans in patients with cardiomyopathy and healthy controls and found significantly higher risk of developing T wave alternans in cardiomyopathic patients.

Our findings of increased frequency of ventricular late potentials on signal averaged ECG in cardiomyopathic patients are comparable to the study conducted by Adachi *et al*. They studied 58 cardiomyopathy patients, and found relatively high frequency (20.6%) of ventricular late potentials in their study group.[24] Zimmermann and his colleagues also demonstrated high risk of developing ventricular late potentials in patients of cardiomyopathy.[25] Both studies endorsed the findings of our study highlighting the augmented risk of developing ventricular late potentials in cardiomyopathic patients.

The findings of current study were further strengthened by Towbin *et al*[26], who conducted a study on electrical dysfunction caused by the ion channels in patients with cardiomyopathy. They concluded that the gene defects in myocardium lead to mechanical instability causing myocardial dysfunction and ventricular dilation. These instabilities lead to increased risk of developing depolarization and repolarization abnormalities depicted as T wave alternans and ventricular late potentials on SAECG.[26–28]

Literature strongly supports that patients who develop T wave alternans and ventricular late potentials are at increased risk of having ventricular arrhythmias mostly ventricular tachycardia.[14,29,30] Bloomfield and Gold followed the cases with positive T wave alternans and observed a high frequency of ventricular fibrillation or sudden cardiac death later in their life.[31,32] Studies conducted by Poll *et al*[33] and Manaci *et al*[34] on cardiomyopathic patients evaluating ventricular late potentials revealed ventricular arrhythmias in patients presenting with ventricular late potentials. All these studies strengthen the findings of our study and provide evidence of strong association of T wave alternans and ventricular late potentials with ventricular arrhythmias in patients with cardiomyopathy.

Due to constraints of time and resources, we were unable to follow these patients for any arrhythmic events. However, being the first study of its type, it can serve as an important risk assessment tool to set local guidelines for prophylaxis against fatal arrhythmias and sudden cardiac death. Future studies may be planned whereby association of arrhythmic outcomes may be determined with T wave alternans and ventricular late potentials in patients suffering from cardiomyopathy.

CONCLUSION

Risk of developing T wave alternans and ventricular late potentials is significantly higher in patients with cardiomyopathy as compared to healthy controls. T wave alternans and ventricular late potentials may be employed as risk stratification tools in these patients to possibly avoid the fatal arrhythmic outcomes.

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Received: 17 Mar 2018 Reviewed: 24 Aug 2018 Accepted: 13 Sep 2018