Original Article

Prediction of Head-Up Tilt Test outcomes through Heart Rate Variability Using Receiver Operating Characteristic Curve (ROC)

Heart Rate Variability as a Predictor of Head-Up Tilt Test

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ABSTRACT

Objective: To determine the cut-off values of heart rate variability (HRV) as a predictor of head-up tilt test (HUTT) outcomes using receiver operating characteristic (ROC) curve.

Study Design: Diagnostic accuracy study

Place and Duration of Study: This study was conducted at the Department of Cardiac Electrophysiology, Armed Forces Institute of Cardiology, Rawalpindi from January 2016 to October 2016.

Materials and Methods: Ninety- three adult patients both male and female with complaint of repeated unexplained syncope were registered. Head-up tilt test was performed, during the test patients were Holtered for getting ambulant ECG records using DMS 300-4L Holters. Cardio Scan premier 12 lux software was used to analyze frequency domain parameters of HRV. Heart Rate Variability cut-off values were determined by using Receiver operating characteristic (ROC) curve.

Results: Out of a total of 93 patients, 77 (82.8%) responded positively and 16 (17.2%) responded negatively to HUTT. The receiver operating characteristic (ROC) curve was utilized to find out the cut-off values of heart rate variability frequency domain parameters. ROC analysis of total power (TP) parameter measured during initial and terminal 5 minutes of stage -I of head-up tilt test was statistically significant.

Conclusion: Determination of cut-off values of total power (TP) parameters of heart rate variability by using the receiver operating characteristic (ROC) curve could predict the outcome of head-up tilt test results. This initial estimation can change the administration of nitroglycerine and shorten the duration of head-up tilt test.

Key Words: Heart rate variability (HRV), Head-up tilt test (HUTT), Receiver operating characteristic (ROC) curve

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INTRODUCTION

Head-up tilt table test is an accepted modality for investigating an individual's predisposition to syncope related to orthostatic stress[1]. It is a provocation test that is recommended in the diagnosis of syncope[2]. The test examines the tendency of an individual to experience syncope when subjected to orthostatic stress, improving the understanding and management of patients[3]. Syncope is temporary loss of consciousness due to transient diminution of blood flow to the brain[4]. The most common form of syncope in all age groups is neurally mediated syncope[5]. Syncope is characterized by brief loss of consciousness occurring because of profound systemic hypotension due to reflex vasodilatation, or vagally driven bradycardia, or both[6]. After prolonged standings, inability of the underlying autonomic nervous system to maintain hemodynamics of the body in upright posture causes cerebral hypoperfusion resulting in syncope[7].

Head up tilt table test is a major progress in the evaluation of patients presenting with syncope[8]. Two main responses are observed when a patient is subjected to Head up tilt table test[9]. The first response is the positive response, characterized by reappearance of symptoms of syncope and the second response is the negative response which shows slight variations in the blood pressure but no other abnormality[10].

Heart rate variability is a physiological phenomenon defined as temporal fluctuations of beat to beat intervals

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during normal sinus rhythm[11]. Heart rate variability analysis gives an assessment of state of autonomic nervous system responsible for regulating heart rate and rhythm[12]. Anomalies of autonomic nervous system (ANS) play a main role in the beginning of syncope[13]. Analyzing Heart rate variability is a good tool for the evaluation of syncope due to malfunction of autonomic system analysis[14].

The sympathetic and parasympathetic divisions are affected by the variations occurring during the course of test in subjects of syncope[15]. This study was planned to predict the outcomes of Head up tilt test by determining cut-off readings of frequency domain parameters of Heart rate variability using Receiver operating characteristic curve[16].

MATERIALS AND METHODS

Our study was a cross-sectional comparative study and carried out at Cardiac Electrophysiology Department, Armed Forces Institute of Cardiology in collaboration with Army Medical College (AMC), Rawalpindi. AMC, Ethical review committee and AFIC Institutional Review Board granted permission to conduct the study.

Sample size of 93 was estimated utilizing WHO sample size calculator, where confidence interval was kept at 95%, predicted population proportion at 0.4 and absolute precision (d) at 0.1.

A total number of Ninety-three individuals having a history of un explained syncope were included in the study using convenience sampling. For exclusion of patients with a history of any cardiac illness, arrhythmias and ischemic heart disease, Electrocardiography and echocardiography were done. The selected patients reported with a four hour fast on the day of the test. All subjects gave a detailed history and written consent.

DMS 300-4L Holters from DM Systems Company was applied to each subject while lying in supine position on the tilt table and Heart rate variability was measured in frequency domain for first 5 minutes, while at the same time baseline blood pressure, heart rate and ECG were also recorded. Using Italian protocol, during the first 20 minutes of Stage-I the subjects were kept at a tilt of 70 degrees for 20 minutes whilst recording heart rate variability frequency domain parameters for initial 5 and terminal 5 minutes. Stage-II comprised of keeping the patients in the same tilted position and giving 400 µgm of nitroglycerine. Once the subject developes syncope test was concluded by bringing them back to the initial lying down position. Positive responders were the subjects developing syncope or near-syncope and the rest were labelled as negative responders. Ambulatory ECG data was screened for ectopic and artefact beats using DMS Cardioscan software premier 12 lux version. Heart rate variability frequency domain parameters (low frequency, high frequency (HF) and LF/HF ratio and total power (TP) was assessed.

IBM SPSS version 23 was used for Data analysis. Numerical variables for example age and frequency domain parameters were represented as Mean and standard deviation and categorical variables like gender and positive and negative responders of head up tilt test was represented as frequency and percentage. Independent samples t test was applied for comparing mean values of frequency domain parameters of heart rate variability. Frequency of positive and negative responders to active phase of head-up tilt test was compared using Chi Square test. Alpha value of 0.05 was considered statistically significant.

RESULTS

Among 93 patients, there were 77 (82.8%) positive responders and 16 (17.2%) negative responders to head-up tilt test. Cut-off values of heart rate variability frequency domain parameters were calculated using the receiver operating characteristic (ROC) Curve. Values of frequency domain parameters of HRV (HF, TP) measured for 5 minutes in supine position and then for beginning 5 minutes and end 5 minutes of passive phase of three phases of head-up tilt test were plotted against the reference line in the receiver operating characteristic (ROC) curve. Figure I show the ROC curve analysis of high frequency parameters, and total power parameters in three phases.

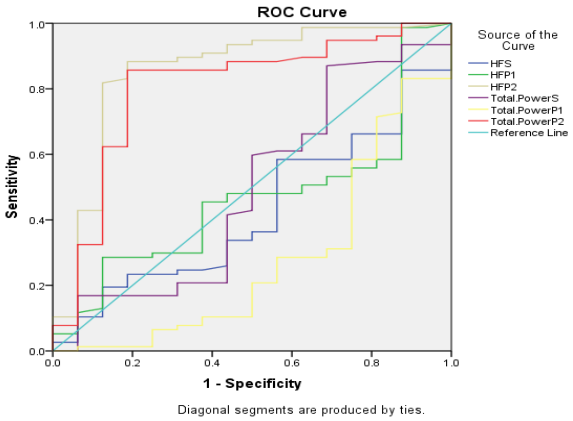

Figure No.1: Receiver Operating Characteristic (ROC) Curve for Diagnostic Accuracy of Heart Rate Variability

Table No.1: Area under curve for different HRV parameters

Heart Rate Variability Parameters	Area Under Curve	P-Value
HF (Supine)	0.43	0.34
HF (Passive Phase 1)	0.46	0.64
HF (Passive Phase 2)	0.421	0.610
TP (Supine)	0.49	0.94
TP (Passive Phase 1)	0.278	0.005*
TP (Passive Phase 2)	0.804	<0.001*

* p-value significant (<0.05)

Analysis of total power (TP) using ROC curve measured during first 5 minutes and last 5 minutes of passive phase has an area under curve of 0.278 and 0.804 and are significant (p=0.005) and (p<0.001). The cut-off value of TP measured during first 5 minutes is 1485.5500 (sensitivity of 58.4% and specificity of 25%) and the cut-off value measured during last 5 minutes is 1131.0500 (sensitivity of 85.7% and specificity of 81.2%). These are shown in table 1 and 2.

Table No2: Cut-Off Values of Total Power (TP)

Heart Rate Variability Parameters	Cut-Off Value	Sensitivity (Percentage)	Specificity (Percentage)
TP (Passive Phase 1)	1485.5500	58.4	25
TP (Passive Phase 2)	1131.0500	85	81.2

ROC analysis of TP during first and last 5 minutes of passive phase are statistically significant being helpful in discriminating amongst positive and negative responders to head-up tilt test. However, TP measured during terminal 5 minutes of stage – I can differentiate better amongst the two.

DISCUSSION

The results of current study helped us to detect the patients that would develop syncope at the end of head-up tilt test, before the administration of nitroglycerine. The results of our study showed that Receiver operating characteristic (ROC) curve analysis of heart rate variability frequency domain parameters (HF, LF, LF/HF, TP) parameters done in the first 5 minutes and last 5 minutes of passive phase of head-up tilt test was helpful in determining the cut- off values of these parameters for predicting the results of head-up tilt test. The parameter that turned out to be the most significant for determining the cut- off values were total power (TP) measured in the first and last 5 minutes of passive phase of head-up tilt test. Receiver operating characteristic (ROC) curve analysis of total power (TP) parameter done in the first 5 minutes of passive phase of head-up tilt test revealed an area under the curve (AUC) of 0.278 being statistically significant (P =0.005). At an optimal sensitivity of 58.4% and specificity of 25% the established cut-off value of total power (TP) was 1485.5500. Receiver operating characteristic (ROC) curve analysis of total power (TP) parameter done in last 5 minutes of passive phase of head-up tilt test revealed an area under the curve (AUC) of 0.804 being statistically significant (P <0.001) and hence a cut-off of 1131.05 was established at an optimal sensitivity of 85.7% and specificity of 81.2%.

The results of our study are comparable to the study conducted by M.A.P Ciliberti and his colleagues who carried out a study in 2018 to assess the capacity of the frequency domain parameters of heart rate variability at rest to foresee syncope among patients with syncope using receiver operating characteristic curve[17]. Virag et al. conducted a study presenting an algorithm using dynamics of heart rate variability to predict the occurrence of syncope at a substantial time before the event[18]. They enrolled 1,155 subjects with history of fainting who underwent tilt test, 759 patients had syncope during the tilt test after the drug was administered, while the other 396 patients did not develop syncope. Receiver operating characteristic analysis was done that defined the diagnostic accuracy by determining the cut-off values of parameters supporting the results of our study[19]. In a recent study carried out by QY kong and his colleagues, it was documented that LF at rest foretold the occurrence of syncope during test[20]. A value of LF > 2048 ms^2 was the optimal cut-off to predict syncope during head-up tilt test using receiver operating characteristic (ROC) curve[21].

CONCLUSION

Receiver operating characteristic (ROC) curve analysis can determine the cut-off values of heart rate variability frequency domain parameter for the prediction of head-up tilt test outcomes. Total power (TP) component of heart rate variability measured in the last 5 minutes of passive phase of head-up tilt test has maximum power to predict the result of test without giving the drug.

Author's Contribution:

Concept & Design of Study:	Sara Naeem
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Revisiting Critically:	Sara Naeem, Saima Mukhtar
Final Approval of version:	Sara Naeem

Conflict of Interest: The study has no conflict of interest to declare by any author.

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