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Evaluation of Cardiovascular Risk and Its Correlation with Cardiac Autonomic FunctionTesting in Adults

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Abstract

In India, NCDs are responsible for 60% of deaths, with cardiovascular incidents being more prevalent in rural areas.[1] Advances in the understanding of cardiac autonomic functioning have led to more accessible and effective strategies for preventing and managing major adverse cardiac events (MACE), even with minimal setup. Hospital based prospective observational study of 150 sample size was carried out on adult subjects over the age 20 years reported to Departmentof Cardiology, Gandhi Medical College, Bhopal from August 2022 to December 2023. MACE risk was assessed by Framingham risk score in all subjects and correlated with Cardiac Autonomic function testing. Among 150 subjects, 40% were diagnosed with Early CAN, 21.33% with Definite CAN, and 2% with Severe CAN based on Ewing's criteria. Regarding MACE risk, 37.33% were at very high risk, 19.33% at high risk, 15.3% at moderate risk, and 28% at mild risk. Diabetic subjects had early and definite CAN at 40.63% each. Hypertensives primarily had early CAN (21.33%), while smokers had a high rate of Definite CAN (43.75%). A significant positive correlation (R=0.2959, p=0.000237) was found between Mean CAN scores and Mean FRS. Weak positive correlations were observed in some cardiac autonomic function tests (lying to standing up, Valsalva) with FRS, while others showed weak negative correlations. Significant correlations ($p<0.05$) were noted between CAN scores and FRS parameters like age, diabetes, and smoking. Individual FRS parameters also had a highly significant correlation with CAFTs ($P<0.0001$). Hence, we conclude that this prospective study, established a positive correlation between Cardiac Autonomic Function Testing (CAFT) and Cardiovascular Risk in adults. Thus, CAFT could be used as a cost-effective and accessible test for even healthcare centers with limited resources for early identification and screening of MACE.

Keywords: Cardiac Autonomic Function Testing, Autonomic Function Testing, Framingham Risk Score, Cardiovascular Risk, Major Adverse Cardiac Events, MACE.

Introduction

Cardiovascular diseases (CVD) are one of the leading causes of death and disability in the world. Among Indians its characterized by higher relative risk, earlier age of onset, higher mortality and premature mortality. [1] The prevalence of CVD is influenced by a mix of genetic predispositions and lifestyle factors, including diet, physical activity, and tobacco use, all compounded by the challenges of a transitioning healthcare landscape that struggles with both noncommunicable and infectious diseases. The effects of these risk factors can ruin the physiological homeostasis of our body and manifest as co morbidities like hypertension, hyperglycemia, obesity etc. The risks factors can be measured in primary care facilities and indicate an increased risk of heart attack, stroke, heart failure and other complications. [2] Alongwith these lifestyle changes, aging also plays a crucial role in wear and tear of the physiologicaldefensive mechanisms of our body to these complications. Hence, it is vital to establish a proactive approach to decrease the incidence of cardiovascular disease in today's world.

The physiological homeostasis of health and response to disease are maintained by the autonomic nervous system. Autonomic nervous system integrates functions and coordinate input from peripheral and visceral afferent nerves to orchestrate a dynamic balance among organ systems. Its adaptive processes respond instantly to the different types of stress the bodygoes through its parasympathetic and sympathetic components. [3]

Disorders affecting the autonomic nervous system may be manifested by failure or hyperactivity of one or many of the visceral effector organs. Autonomic neuropathies that disconnect central autonomic centers and autonomic ganglia from their peripheral effectors may result in deficits in autonomic function. [3]

Cardiac autonomic function testing is a non-invasive test used to assess the function of the autonomic nervous system, which controls the heart rate and blood pressure. Thus, by using Cardiac autonomic function testing we can try to identify early signs of heart disease.

In the field of cardiovascular diseases, studies using the epidemiological method have led to findings of considerable practical importance for prevention and treatment**.** [4]

Multiple studies were conducted regarding the assessment of cardiovascular risk assessment. The Framingham Heart Study is one of the studies of similar kind of in 1948 with 5,209 adultsubjects from Framingham, and is now on its third generation of participants. [5]

The complex interplay between widespread traditional risk factors at the population level and inherent biological variances places Indians at an increased risk for cardiovascular disease (CVD). So there is a need for a multifaceted approach to prevention that includes intersectoral, public health and health-service level interventions at all - primordial, primary, secondary aswell as tertiary levels. Several interventions have already been tested in various low to middleincome countries and have shown to improve the CVD burden in a cost-effective manner.[2]The most appropriate way forward would be to address the gaps based on our presentknowledge and develop robust targeted solutions. Hence with this study we are aiming assesswhether cardiac autonomic function testing can be a useful tool for evaluation and earlyindicator for major adverse cardiac events.

Methodology

This is a hospital based prospective observational study on adult subjects over the age 20 years reporting to Department of Cardiology, Gandhi Medical College, Bhopal for cardiac evaluationfrom August 2022 to December 2023.

After taking approval from the Institution Ethics Committee of Gandhi Medical College, Bhopal, Madhya Pradesh and informed consent from patient, the study was conducted which included a total 150 participants of either sex (113 males and 37 females) who satisfied the inclusion and exclusion criteria.

Inclusion Criteria: Subjects of age 20 years and above undergoing cardiac evaluation in Department of Cardiology, Gandhi Medical College, Bhopal, Madhya Pradesh.

Exclusion Criteria: Subjects who are not giving consent. Patient suffering from asthma/epilepsy/COVID-19, patients with history of chronic diseases, history of hernia or any recent surgery.

Protocol

After collecting demographic details and history of the study subjects, generalphysical examination was done. Cardiovascular risk assessment was done using Framingham Cardiovascular risk score [6] followed by CAFTs. Ewings score was used to assess Cardiac autonomic neuropathy.
The Framingham risk score was categorized as per level of risk into mild risk, moderate risk, high risk and very high risk for Major adverse cardiac events as given below.

MACE RISK CALCULATION USING FRAMINGHAM RISK SCORE

FRAMINGHAM RISK SCORE CALCULATION FOR MEN							
SCORE	PARAMETERS						
	AGE	HDL	TOTAL CHOLESTEROL	SBP NOT TREATED	SBP TREATED	SMOKER	DIABETIC
-2		60+		<120			
-1		50-59					
0	30-34	45-49	<160	120-129	<120	No	No
1		35-44	160-199	130-139			
2	35-39	<35	200-239	140-159	120-129		
3			240-279	160+	130-139		Yes
4			280+		140-159	Yes	
5	40-44				160+		

6	45-49						
7							
8	50-54						
9							
10	55-59						
11	60-64						
12	65-69						
13							
14	70-74						
15	75+						

MACE RISK AS PER FRS POINTS FOR MEN					
SCORE	**MACE RISK**	**SCORE**	**MACE RISK**	**SCORE**	**MACE RISK**
-3 or less	Below 1%	5	3.9%	13	15.6%
-2	1.1%	6	4.7%	14	18.4%
-1	1.4%	7	5.6%	15	21.6%
0	1.6%	8	6.7%	16	25.3%
1	1.9%	9	7.9%	17	29.4%
2	2.3%	10	9.4%	18+	Above 30%
3	2.8%	11	11.2%		
4	3.3%	12	13.2%		

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FRAMINGHAM RISK SCORE CALCULATION FOR WOMEN							
SCORE	PARAMETERS						
	AGE	HDL	TOTAL CHOLESTEROL	SBP NOT TREATED	SBP TREATED	SMOKER	DIABETIC
<-3				<120			
-2		60+					
-1		50-59			<120		
0	30-34	45-49	<160	120-129		No	No
1		35-44	160-199	130-139			
2	35-39	<35		140-149	120-129		
3			200-239		130-139	Yes	
4	40-44		240-279	150-159			Yes
5	45-49		280+	160+	140-159		
6					160+		
7	50-54						
8	55-59						
9	60-64						
10	65-69						
11	70-74						
12	75+						

MACE RISK AS PER FRS POINTS FOR WOMEN					
SCORE	MACE RISK	SCORE	MACE RISK	SCORE	RISK
-2 or less	Below 1%	6	3.3%	14	11.7%
-1	1.0%	7	3.9%	15	13.7%
0	1.2%	8	4.5%	16	15.9%
1	1.5%	9	5.3%	17	18.5%
2	1.7%	10	6.3%	18	21.5%
3	2.0%	11	7.3%	19	24.8%
4	2.4%	12	8.6%	20	28.5%
5	2.8%	13	10.0%	21+	Above 30%

MACE RISK STRATIFICATION

MACE RISK	FRS (%)
Mild	<10
Moderate	10-15
High	15-20
Very high	>20

This risk categorization was correlated with Cardiac autonomic neuropathy then after performing Autonomic function tests in the given subject.

Under Autonomic function tests both sympathetic and parasympathetic assessment was done.[8]

For Sympathetic assessment - Sustained hand grip test (HGT) and BP changes response to lying to standing test

For Parasympathetic assessment:

- Deep breathing test (E/I test)
- Heart rate response to Lying to standing test (30:15)
- Valsalva maneuver test

EWINGS BATTERY OF TEST SCORE

The Ewing score is a composite of scores from a battery of five autonomic tests. Individual Test scores are calculated as per Ewings Reactivity score as given in the below table: [7,8,9]

Scoring of Cardiac Autonomic Function Tests

TEST	PARAMETER	CRITERIA	CATEGORY	SCORE
Deep Breathing Test	E/I	>1.03	Normal	0
		1.01-1.03	Borderline	1
		<1.01	Abnormal	2
Valsalva Maneuver	VR	>1.20	Normal	0
		1.11-.20	Borderline	1
		<1.11	Abnormal	2

Hand grip test	ΔDBP	>15	Normal	0
		11-15	Borderline	1
		<10	Abnormal	2
Lying to standing	Fall in SBP	<10	Normal	0
		10-20	Borderline	1
		>20	Abnormal	2
	30:15	>1.03	Normal	0
		1.01-1.03	Borderline	1
		<1.01	Abnormal	2

The Ewing score is marked as normal (0 points), borderline (0.5 points), or positive (1 point). The Ewing test score ranges from 0–5.

Ewing's test Scoring table

DIAGNOSIS	**EWING'S PARASYMPATHETIC SCORE**	**EWING'S SYMPATHETIC SCORE**
NORMAL STUDY	0 TO 2	0
EARLY CAN	2 TO 4	1
DEFINITE CAN	≥ 4	≥ 2
SEVERE CAN	PARASYMPATHETIC SCORE ≥ 4 + SYMPATHETIC SCORE ≥1	

On completion of the assessment of Cardiac Autonomic neuropathy by Ewings Battery score the subjects were labelled under Normal Autonomic function /Normal study, Early CAN, Definite CAN and Severe CAN as mentioned above. The CAN analysis results were then compared with Framingham risk score for determining the correlation between Cardiac Autonomic function and cardiovascular risk in the study sample.

Data Analysis Plan:

Data was collected on individual basis, which were recorded and compiled using Microsoft excel data sheet. Statistical analysis of data was done using Epi info- software, Social Science Statistics, GraphPad and wherever appropriate descriptive analysis were applied using statistical tests (Oblique Anova test, Pearson Correlation Calculator). P<0.05 will be considered as significant.

Results & Observations

150 subjects over the age 20 years reporting to Department of Cardiology, Gandhi Medical College, Bhopal for cardiac evaluation who met with the inclusion and exclusion criteria were taken for study. In the study of 150 subjects,113(75.3%) were males and 37(24.67%) were females. The malefemale ratio being 3.05:1 with a mean age was 54.85 Years

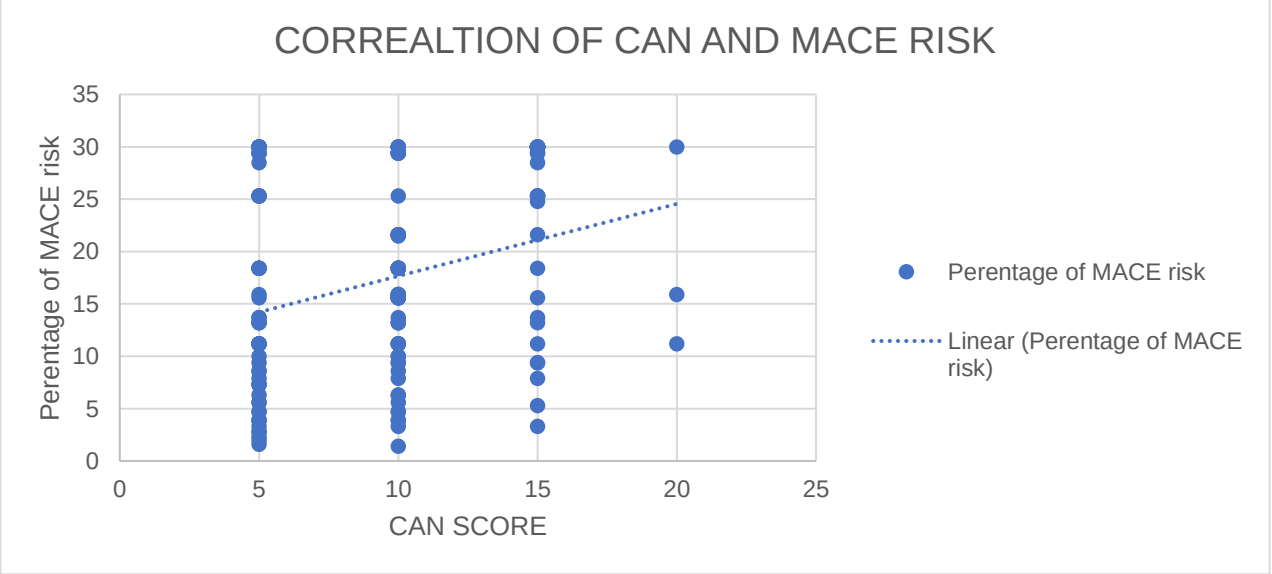
Among the study sample ,55 (36.67%) subjects were with Normal study, 60 (40%) subjects were diagnosed with Early CAN, 32 (21.33%) subjects were diagnosed with Definite CAN and 3(2%) subjects werediagnosed with Severe CAN.

Among the subjects 28% are at mild MACE risk, 15.3% at moderate MACE risk, 19.33% at high MACE risk, and 37.33% at very high MACE risk; i.e., the majority of subjects (37.33%) are in the very high-risk category, while only 15.3% are in the moderate-risk category.

The correlation analysis of CAN and MACE risk in the study sample was done on the basis ofMean ± SD of CAN score and FRS respectively, which was found to have statistically highly significant relationship and a weak positive correlation with each other (R=0.2959).

Figure No:1

Correlation of CAN and MACE risk in the study sample(N=150)



CORRELATION BETWEEN INDIVIDUAL CAFT AND FRAMINGHAM RISK SCORE (FRS) IN THE STUDY SAMPLE

Individual cardiac autonomic function tests (CAFTs) and Framingham risk score (FRS) in the study sample were analyzed, which was found to have statistically non-significant relationship with p value >0.05, but weak positive correlation was observed in Lying to standing test and Valsalva test (VR). Weak Negative correlation was observed in 30:15 test, Deep breathing test (E/I test) and Hand grip test (HGT).

Table No:1

Correlation between individual CAFT and FRS in the study sample

SL No	CAFTs (N=150)	CAN Score	FRS	P value	R value	Correlation of CAN score with FRS
		Mean ± SD	Mean ± SD			
1	BP RESPONSE TO LYING TO STANDING TEST	0.53±0.499	17.26 ± 9.40	.077487	0.1446	Weak Positive correlation
2	30:15 TEST	0.41±0.77		.980621	0.0022.	Weak Negative correlation
3	E/I TEST	0.19±0.55		.055025	-0.1579	Weak Negative correlation
4	VR	0.81±0.86		.084572	0.1413	Weak Positive correlation
5	HGT	1.83±0.37		.394661	-0.0739	Weak Negative correlation

*P value < .05 is considered statistically significant.

CORRELATION ANALYSIS BETWEEN CAN AND INDIVIDUAL PARAMAETERS OF FRS IN THE STUDY SAMPLE:

Each individual parameters of FRS were correlated with CAN score and statistically significant relationship was observed with Age, history of DM, Smoking parameters with p value <0.05. Parameters like age, HDL, DM, Smoking showed weak positive correlation and SBP, Total cholesterol showed weak negative correlation.

Table No:2

Correlation analysis between CAN and individual parameters of FRS in the study sample

FRS PARAMETER		CAN SCORE	P VALUE	R VALUE	REMARKS
(N=150)	**MEAN ± SD**	**MEAN ± SD**			
AGE SCORE	8.233±3.79	9.433 ± 4.036	**0.022599**	0.1861.	Weak Positive correlation
SBP	1.89±2.44		.903332	-0.01	Weak Negative correlation
S CHOLESTROL	0.99±0.86		0.480808	-0.0589	Weak Negative correlation
HDL	0.92±0.61		0.051814	0.1591	Weak Positive correlation
DM	0.73±1.41		**.000026**	0.3362	Weak Positive correlation
SMOKING	0.85±1.64		**0.001609**	0.2554	Weak Positive correlation

CORRELATION ANALYSIS BETWEEN INDIVIDUAL CAFT AND INDIVIDUAL PARAMETERS OF FRS IN THE STUDY SAMPLE

Individual cardiac autonomic function tests and FRS parameters (Age, DM, Smoking and HDL) were correlated using Analysis of Variance (ANOVA)test and a statically positive correlation was found. The means of different parameters and each test were observed to be statistically highly significantly different from each other with a p value of <0.00001 rejectingthe null hypothesis and F value of 3027.35.

Table No:3

Correlation analysis between individual CAFT and individual parameters of FRS (Age,DM, Smoking, HDL) in the study sample

FRS PARAMETER		CAFTs (N=150)									
	MEAN ± SD	BP response to lying to standing test		30:15 Test		E/I Test		VR Test		HGT	
		MEAN±SD		MEAN±SD		MEAN±SD		MEAN±SD		MEAN±SD	
		0.53±0.499		0.41±0.77		0.19±0.55		0.81±0.86		1.83±0.37	
		P Value	F value	P value	F value	P value	F value	P value	F Value	P value	F Value
AGE SCORE	8.23±3.79	<0.05	349.90	<0.05	413.5	<0.05	409.7	<0.05	410.5	<0.05	407.5
DM	0.73±1.41										
SMOKING	0.85±1.64										
HDL	0.92±0.61										
OVERALL		P VALUE = <0.00001				F VALUE =	3027.35				

CATEGORIZATION OF SUBJECTS IN THE STUDY SAMPLE BASED ON HISTORY OF DIABETES MELLITUS, HYPERTENSION AND SMOKING IN THESTUDY SAMPLE

In addition to above details, a further analysis was done on the subjects who were known case of Diabetes mellitus type II, Hypertensives and smokers. Among study subjects 32 were Diabetics, 90 subjects were Hypertensives and 90 subjects were smokers. On analyzing CAFT results in the study sample, among diabetics' majority were having Early CAN (40.63%) or Definite CAN (40.63%); 21.33% hypertensives were having Early CAN and 43.75% smokers were having Definite CAN. On analyzing MACE risk in the study sample,50% diabetics ,44.4% Hypertensives and 75%smokers were having very high MACE risk.

Fig.No.2

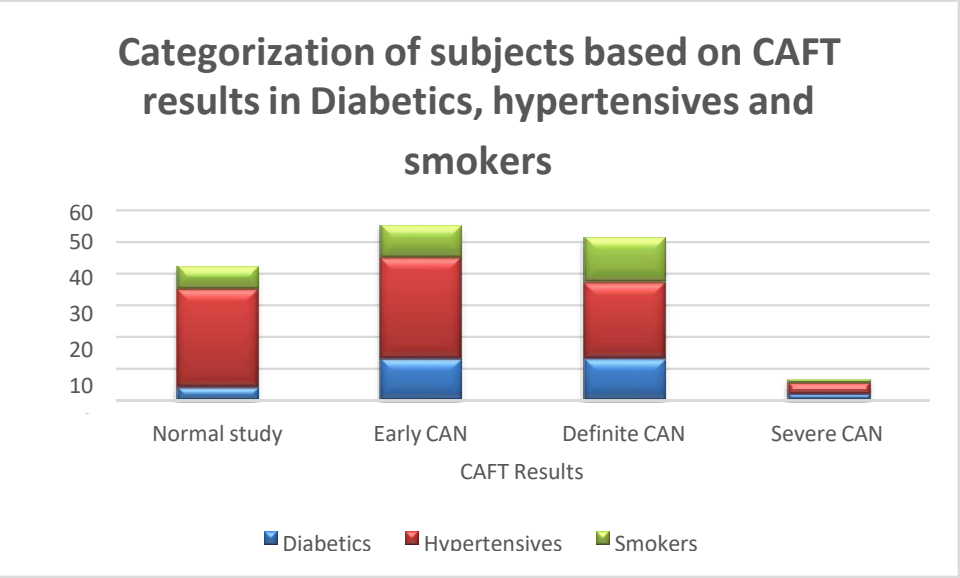
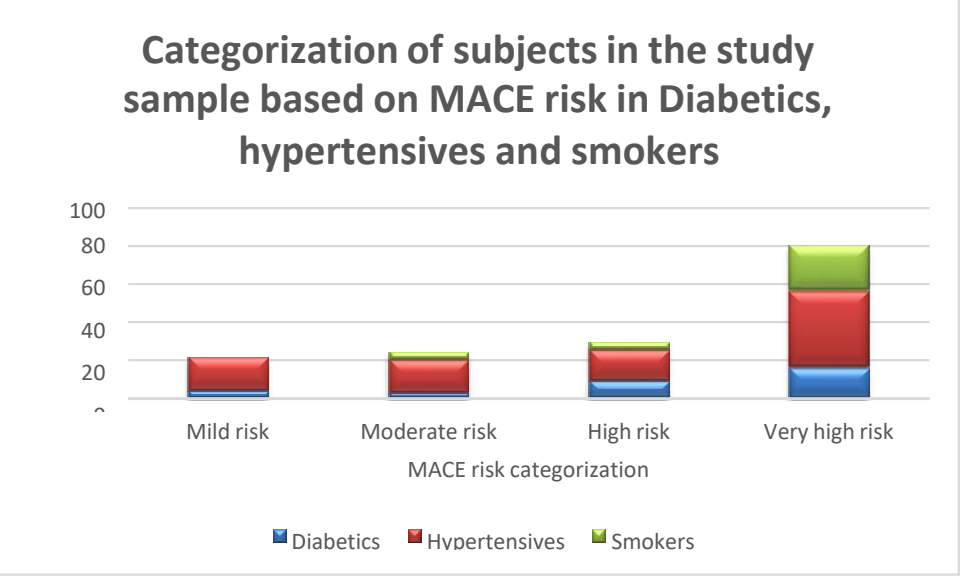


Fig.No.3



Discussion

In this study of 150 subjects were sample with mean age of 54.85 years,113(75.3%) were males and 37(24.67%) were females. The study subjects underwent cardiac autonomic function testing (CAFT) which involved a battery of tests for both sympathetic and parasympathetic system, to assess the cardiac autonomic neuropathy (CAN) in them if any.
As per Ewings Scoring ,55 subjects had Normal study, 60 subjects were diagnosed with Early CAN, 32subjects were diagnosed with Definite CAN and 3 subjects were diagnosedwith Severe CAN, indicating a substantial prevalence of autonomic dysfunction. This aligns with previous studies that underscore the importance of early detection and management of CAN in preventing further cardiovascular complications. [7]

Major adverse cardiovascular event (MACE) risk was assessed in the study subjects using Framingham risk score (FRS).37.33% subjects were under very high MACE risk ,19.33% were under high MACE risk, 15.3% were under moderate MACE risk and 28% were under mild risk of MACE. , hence further emphasizing the critical need for targeted interventions in this group.[7]

The positive correlation between mean CAN scores and mean FRS (R=0.2959, p=0.000237) suggests that higher autonomic dysfunction is associated with increased cardiovascular risk, consistent with existing literature on the subject.

Notably, the study identified a high prevalence of comorbid conditions such as diabetes (21.33%), hypertension (60%), and smoking (28.3%) among the subjects. Diabetic subjects exhibited early and definite CAN of 40.63% respectively.Majority of hypertensives had early CAN (21.33%) and while smokers had Definite CAN (43.75%). Very high MACE risk was observed in Diabetics, hypertensives and smokers. These findings highlight the multifactorial nature of CAN and its association with common cardiovascular risk factors.[8]

Furthermore, the study observed significant correlations between CAN scores and individual FRS parameters, including age, diabetes history, and smoking status ($p<0.05$). The highly significant correlations between individual FRS parameters and CAFTs ($P<0.0001$, $F=3027.35$) reinforce the intricate relationship between cardiovascular risk factors and autonomic dysfunction. [8]

Thus, study underscores the importance of comprehensive cardiovascular risk assessment in individuals with CAN, particularly those with diabetes, hypertension, and smoking history. The findings advocate for early detection and management of CAN to mitigate the risk of major adverse cardiovascular events and improve overall cardiovascular outcomes. Further research is warranted to explore the underlying mechanisms and potential therapeutic interventions for CAN in diverse populations. [9]

Limitations of study

Even though study could establish a positive correlation between CAFT and Cardiovascular risk, its strength was weak which might be mostly due to smaller sample size. So, to generalize the result similar study can be done in a more diverse and wider population.

Advancing age having higher risk points felt so behave like a compounding factor for assessment.

Influence of regular antihypertensive /antidiabetic medications and impact of effect of smoking with its chronicity could have been incorporated for better risk assessment.

Conclusion

Cardiovascular disease is a major cause of disability and premature death throughout the world, and contributes substantially to the escalating costs of health care. Cardiovascular disease is influenced by genetic, environmental, and lifestyle factors, with modifiable risk factors like hypertension, diabetes, smoking, obesity, and physical inactivity. Modificationof risk factors has been shown to reduce mortality and morbidity in people with diagnosedor undiagnosed cardiovascular disease. [10] Despite significant advancements in the management of cardiovascular disease, early detection and intervention are paramount in improving patient outcomes. Since with this study a weak positive correlation was observed between cardiac autonomic function testing and cardiovascular risk ,to generalize the result similar study can be done in a more diverse and wider population. Additionally, integrating these tests into routine health check-ups enhances screening processes and allows healthcare workers to allocate resources more efficiently. This approach also provides an opportunity to educate patients about cardiovascular health, promoting proactive health behaviors and improving overall community health. By training healthcare workers to perform and interpret these tests, the quality of care in these areas is enhanced, contributing to better cardiovascular health outcomes at the rural centers. So, in conclusion, this can be considered as a pilot study promising preliminary evidence supporting the feasibility and potential efficacy of the Cardiac autonomic function testing as a prognostic tool for detecting cardiovascular risk aligning with the World health day 2024 motto -My Health, My Right, contributing to the realization of health as a universal human right. [11]

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