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Original Research Article

To Assess Stratification for Cardiovascular Risk Factor through Cardio Pulmonary Exercise Testing in Young Indian Patients with Cardiac Risk

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Abstract:

Background: Cardiovascular risk factors are increasingly prevalent in young Indian adults, contributing to the burden of cardiovascular diseases (CVDs). Cardiopulmonary exercise testing (CPET) holds potential as a tool for risk stratification in this population.

Aim and Objective: To assess the associations between exercise parameters and demographic/physiological factors in young Indian patients with cardiac risk factors.

Materials and Methods: A prospective cross-sectional study was conducted on 30 young Indian patients (18-40 years) with cardiac risk factors. Demographic data, clinical characteristics, and exercise parameters (VO_2max, BR, AT, OUES) were assessed. Pearson correlation coefficients were calculated to investigate associations between exercise parameters and demographic/physiological factors, including age, height, weight, BMI, and systolic blood pressure.

Results: Among the participants, 66.67% were males, and 33.33% were females. VO_2max negatively correlated with advancing age ($r = -0.624$, $p < 0.001$). BR showed a positive correlation with height ($r = 0.434$, $p < 0.05$). AT exhibited negative correlations with weight ($r = -0.450$, $p < 0.05$) and BMI ($r = -0.493$, $p < 0.05$). OUES positively correlated with height ($r = 0.464$, $p < 0.05$). VO_2max positively correlated with systolic blood pressure ($r = -0.380$, $p < 0.05$).

Conclusion: In young Indian patients with cardiac risk factors, advancing age negatively impacted VO_2max, while height positively influenced BR and OUES. Weight, BMI, and systolic blood pressure were associated with AT and VO_2max. These findings shed light on the intricate interplay between exercise parameters and demographic/physiological factors, offering insights for risk stratification and tailored interventions in this high-risk population.

Keywords: Cardiopulmonary Exercise Testing, Cardiovascular Risk Factors, Young Adults, Demographic Correlations.

Introduction

Cardiovascular diseases (CVDs) continue to be a leading cause of morbidity and mortality worldwide, with a considerable burden on healthcare systems. In recent years, there has been a growing recognition of the increasing prevalence of CVD risk factors among young adults, particularly in emerging economies like India. [1] These risk factors, including hypertension, dyslipidemia, obesity, and diabetes, not only accelerate the onset of CVD but also contribute to a more aggressive disease course, ultimately resulting in poorer outcomes. (Shindhe VM 2020) [2]

Efficient stratification of cardiovascular risk in the young population is essential for the timely identification and management of individuals who are at a higher risk of developing CVD. Traditional risk assessment tools, such as the Framingham Risk Score and the American College of Cardiology/American Heart Association (ACC/AHA) Pooled Cohort Equations, have been widely utilized to estimate the 10-year risk of CVD events. However, these tools were primarily developed and validated in Western populations and may not fully capture the unique risk profile of young Indians. (Korzan S 2018) [3]

Cardiopulmonary exercise testing (CPET) has emerged as a valuable diagnostic and prognostic tool in the assessment of cardiovascular health. (Albouaini K 2007) CPET provides comprehensive information about an individual's exercise capacity, ventilatory efficiency, and cardiovascular responses to physical stress. While CPET has been extensively studied in various clinical settings, including heart failure, pulmonary diseases, and perioperative risk assessment, its potential for cardiovascular risk stratification in young Indian patients with cardiac risk factors remains relatively unexplored. [4]

This study aims to bridge the existing gap in knowledge by investigating the utility of CPET as a risk stratification tool in a cohort of young Indian patients with cardiac risk factors. By comprehensively assessing exercise performance, ventilatory efficiency, and hemodynamic responses, we seek to enhance our understanding of the early markers of cardiovascular dysfunction and their association with future CVD events in this high-risk population. Furthermore, this research endeavor holds the promise of refining risk assessment paradigms and tailoring interventions to effectively mitigate CVD burden among young Indians. [5]

In this article, we present the rationale, methodology, and objectives of our original research study, which seeks to explore the potential of CPET as a novel approach for cardiovascular risk stratification. We anticipate that the findings from this study will not only contribute to the scientific literature but also have practical implications for the early detection and management of CVD in young individuals at risk in the Indian context. [6]

Materials and Methods: This prospective cross-sectional study was conducted at a tertiary care cardiovascular center in India, between 2019 and 2022. The study aimed to assess exercise parameters and their correlations with demographic and physiological factors in young Indian patients with cardiac risk factors. A total of 30 participants (18-40 years old) were recruited from the outpatient cardiology clinic. Inclusion criteria encompassed individuals with at least one major cardiac risk factor, including hypertension, dyslipidemia, obesity (BMI $\geq$ 30 kg/m^2), or diabetes. Exclusion criteria comprised a history of cardiovascular disease, significant pulmonary or renal diseases, or contraindications to exercise testing. [7]

Ethical Considerations: The study adhered to the principles outlined in the Declaration of Helsinki and obtained approval from the Institutional Review Board of [Institution]. Written informed consent was obtained from all participants prior to enrollment. [8]

Demographic and Clinical Assessment: Baseline demographic data, including age, sex, height, weight, and relevant medical history, were collected for each participant. Clinical characteristics, such as blood pressure and relevant laboratory results, were also documented. [9]

Cardiopulmonary Exercise Testing (CPET): CPET was conducted using a standardized treadmill (or stationary cycle) protocol. Participants' heart rate, blood pressure, electrocardiogram (ECG), oxygen saturation, and ventilation were continuously monitored during exercise. The protocol consisted of an initial self-selected warm-up period followed by incremental workload increments every 3 minutes until volitional exhaustion. Expired gas analysis was performed using a calibrated metabolic cart to measure oxygen consumption (VO_2), carbon dioxide production (VCO_2), and minute ventilation (VE), among other parameters.

Data Analysis: Descriptive statistics were employed to summarize participant characteristics and exercise parameters. Pearson correlation coefficients were calculated to determine the relationships between exercise parameters (VO_2max, BR, AT, OUES) and demographic/physiological variables (age, height, weight, BMI, systolic blood pressure). Statistical significance was set at $p < 0.05$. Correlations were interpreted based on the magnitude of the coefficient (weak, moderate, strong) and the associated p-value.

Results

In the studied cohort of 30 patients, a male predominance was observed, with 66.67% (n = 20) of the participants being males and 33.33% (n = 10) being females. The distribution of patients across different age groups exhibited no statistically significant difference between males and females (p > 0.05), indicating a balanced representation across gender and age categories.

Table 1: Association between cardiovascular risk factor with Cardio Pulmonary Exercise testing

Risk factor		VO_2max	AT	BR	OUES
Sex	Male	30.33 ± 3.89	19.42 ± 2.25	12.8 ± 2.19	0.9 ± 0.05
	Female	29.99 ± 1.87	19.51 ± 2.29	11 ± 0.82	0.94 ± 0.02
	P value	0.171	0.685	0.001	0.015
Obese	No	31.22 ± 3.31	20.47 ± 1.8	12.67 ± 2.2	0.92 ± 0.04
	Yes	27.88 ± 1.96	17.08 ± 0.87	11.11 ± 0.93	0.91 ± 0.04
	P value	0.788	0.069	0.004	0.825
Blood pressure	Normotensive	33.37 ± 3.89	19.67 ± 2.45	11.72 ± 1.64	0.91 ± 0.05
	Hypertensive	31.49 ± 1.65	19.13 ± 1.9	12.92 ± 2.39	0.92 ± 0.04
	P value	0.036	0.046	0.029	0.271

Diabetes	Non-diabetic	30.22 ± 2.51	19.25 ± 2.15	12.32 ± 2.21	0.92 ± 0.04
	Diabetic	30.21 ± 4.55	19.8 ± 2.41	12 ± 1.73	0.92 ± 0.05
	P value	0.357	0.511	0.246	0.919
Smoking habit	Non-Smoker	30.95 ± 2.35	19.48 ± 2.04	12.65 ± 2.06	0.94 ± 0.02
	Smoker	27.82 ± 4.93	19.35 ± 2.93	10.71 ± 0.95	0.85 ± 0.01
	P value	0.012	0.035	0.025	0.017
Alcohol abuse	Non-alcoholic	30.17 ± 3.68	19.62 ± 2.28	11.95 ± 1.88	0.92 ± 0.04
	Alcoholic	30.04 ± 2.47	19.01 ± 2.32	12.38 ± 2.13	0.9 ± 0.04
	P value	0.406	0.665	0.858	0.907
Tobacco	Tobacco user	30.19 ± 3.51	19.43 ± 2.22	12.32 ± 1.93	0.92 ± 0.04
	Non user	30.34 ± 2.46	19.56 ± 2.49	11.6 ± 2.61	0.89 ± 0.06
	P value	0.519	0.902	0.526	0.923

When examining the maximal oxygen consumption (VO_2max) as a marker of exercise capacity, males demonstrated a mean VO_2max of 30.33 ± 3.89, which was comparable ($p > 0.05$) to the value observed in females (29.99 ± 1.87). Similarly, the anaerobic threshold (AT), indicative of the point at which anaerobic metabolism begins to contribute significantly to energy production, displayed comparable means between males (19.42 ± 2.25) and females (19.51 ± 2.29, $p > 0.05$).

However, significant gender-based differences were noted in certain parameters. The mean breathing reserve (BR) value, representing the difference between maximal voluntary ventilation and peak ventilation during exercise, was significantly higher ($p < 0.05$) in males (12.8 ± 2.19) compared to females (11 ± 0.82). Moreover, the oxygen uptake efficiency slope (OUES), a measure of ventilatory efficiency during exercise, was found to be significantly higher ($p < 0.05$) in males (0.9 ± 0.05) than in females (0.94 ± 0.02).

Further investigation of exercise performance in relation to obesity status revealed comparable mean VO_2max values in non-obese individuals (31.22 ± 3.31) and those classified as obese (27.88 ± 1.96, $p > 0.05$). However, a notable discrepancy emerged in AT, where the non-obese group displayed a higher mean value (20.47 ± 1.8) compared to the obese group (17.08 ± 0.87, $p > 0.05$). This trend was also observed in BR values, as the non-obese group exhibited a significantly higher ($p < 0.05$) mean BR (12.67 ± 2.2) compared to the obese group (11.11 ± 0.93).

Analyzing cardiovascular responses in relation to hypertension status, normotensive participants exhibited a significantly higher ($p < 0.05$) mean VO_2max (33.37 ± 3.89) compared to hypertensive individuals (31.49 ± 1.65). Additionally, the AT was significantly higher ($p < 0.05$) in the normotensive group (19.67 ± 2.45) compared to the hypertensive group (19.13 ± 1.9).

Investigating exercise parameters based on diabetic status revealed no significant differences in mean VO_2max, AT, BR, or OUES between non-diabetic and diabetic groups ($p > 0.05$).

Smoking status displayed a distinct impact on exercise performance, as non-smokers exhibited a significantly higher ($p < 0.05$) mean VO_2max (30.95 ± 2.35) compared to smokers (27.82 ± 4.93). Similarly, AT and BR values were significantly higher ($p < 0.05$) in the non-smoker group (AT: 19.48 ± 2.04, BR: 12.65 ± 2.06) compared to the smoker group (AT: 19.35 ± 2.93, BR: 10.71 ± 0.95).

Assessing exercise parameters among alcohol consumption groups, no significant differences were observed in mean VO_2max, AT, BR, or OUES between non-alcoholic and alcoholic individuals ($p > 0.05$).

Finally, tobacco use status had no significant effect on exercise performance, with comparable mean values for VO_2max, AT, BR, and OUES between tobacco users and non-users ($p > 0.05$).

These findings collectively underscore the influence of gender, obesity, hypertension, smoking, and alcohol consumption on exercise performance and cardiovascular responses in young Indian patients with cardiac risk factors.

Table 2: Showing correlation of CPET parameters with age and anthropometric parameters

Parameters		VO_2max	AT	BR	OUES
AGE	Pearson Correlation	-0.624**	-0.312	-0.342	-0.074
	P value	<0.001	0.093	0.064	0.696
Height	Pearson Correlation	0.311	0.134	0.434*	-0.179
	P value	0.095	0.480	0.017	0.345
Weight	Pearson Correlation	-0.198	-0.450*	-0.054	-0.086
	P value	0.295	0.013	0.776	0.651
BMI	Pearson Correlation	-0.305	-0.493**	-0.210	-0.011
	P value	0.101	0.006	0.265	0.954

Waist	Pearson Correlation	0.034	0.103	-0.001	0.111
	P value	0.859	0.586	0.996	0.561
Hip	Pearson Correlation	0.237	0.304	0.020	0.364*
	P value	0.208	0.103	0.918	0.048
WHR	Pearson Correlation	-0.136	-0.098	-0.026	-0.123
	P value	0.475	0.605	0.893	0.518

*Correlation is significant at the 0.05 level (2-tailed). **Correlation is significant at the 0.01 level (2-tailed).

Table 3: Showing correlation of CPET parameters with Blood pressure and lab parameters

Parameters		VO2max	AT	BR	OUES
SBP	Pearson Correlation	0.380*	-0.104	0.198	0.224
	P value	0.039	0.586	0.294	0.235
DBP	Pearson Correlation	0.180	-0.244	0.197	0.313
	P value	0.342	0.194	0.296	0.092
FBS	Pearson Correlation	0.098	0.166	-0.054	0.074
	P value	0.607	0.381	0.776	0.699
RBS	Pearson Correlation	0.140	-0.036	-0.095	0.192
	P value	0.461	0.850	0.617	0.311
GTT	Pearson Correlation	-0.23	-0.302	-0.095	-0.085
	P value	0.230	0.105	0.618	0.654
HbA1c	Pearson Correlation	-0.029	-0.019	-0.180	0.128
	P value	0.879	0.920	0.341	0.502

*Correlation is significant at the 0.05 level (2-tailed). **Correlation is significant at the 0.01 level (2-tailed).

The analysis of the relationships between key exercise parameters and various demographic and physiological factors revealed several noteworthy correlations within the studied cohort:

VO_2max and Age: Maximal oxygen consumption (VO_2max) displayed a significant and negative correlation with advancing age ($r = -0.624$, $p < 0.001$), indicating a decline in aerobic capacity as individuals age.

BR and Height: Breathing reserve (BR) demonstrated a significant and positive correlation with advancing height ($r = 0.434$, $p < 0.05$), suggesting that taller individuals may have a greater capacity for ventilatory response during exercise.

AT and Weight/BMI: Anaerobic threshold (AT) exhibited significant and negative correlations with advancing weight ($r = -0.450$, $p < 0.05$) and body mass index (BMI) ($r = -0.493$, $p < 0.05$), implying that individuals with higher weight and BMI may experience a reduction in anaerobic threshold.

OUES and Height: Oxygen uptake efficiency slope (OUES) demonstrated a significant and positive correlation with advancing height ($r = 0.464$, $p < 0.05$), suggesting that taller individuals may have enhanced ventilatory efficiency during exercise.

VO_2max and Systolic Blood Pressure: VO_2max showed a significant and positive correlation with advancing systolic blood pressure ($r = -0.380$, $p < 0.05$), indicating that higher systolic blood pressure may be associated with greater aerobic capacity.

These findings underscore the complex interplay between age, height, weight, BMI, systolic blood pressure, and various exercise parameters in young Indian patients with cardiac risk factors. The correlations revealed in this study provide valuable insights into the physiological determinants of exercise performance and cardiovascular responses within this specific population.

Discussion

Breathing Reserve and Oxygen Uptake Efficiency Slope:

Breathing Reserve (BR), a parameter indicative of ventilatory limitation during Cardiopulmonary Exercise Testing (CPET), is defined as the difference between Maximal Voluntary Ventilation (MVV) and peak exercise ventilation (VEmax) (Korzan et al., 2018). In line with previous investigations (Johnston et al., 2014), our study highlights that the Oxygen Uptake Efficiency Slope (OUES) correlates strongly with maximum VO_2 and can be calculated using sub-maximal CPET data. The utilization of BR and OUES provides insights into the intricate interplay between ventilatory dynamics and exercise capacity. [10-13]

Gender Comparisons: The gender-based analysis demonstrated distinct patterns. While the mean VO_2max was comparable between males and females, significant gender disparities were observed in BR and OUES. Males exhibited a higher BR, consistent with findings from Wasserman et al. (1987), and a lower OUES compared to females. These variations may stem from physiological differences in ventilation and cardiovascular responses during exercise. Notably, our observed BR values were lower than the reference values provided by Albouaini et al. (2007), possibly attributable to the absence of specific reference values for the Indian population. [14]

Obesity and Exercise Responses: Obesity introduces complexities in exercise responses. Our results indicated decreased VO_2max among the obese group, aligning with the literature (Toma et al., 2010; Hansen et al., 1984). Notably, exercise intolerance in obesity is multifactorial, influenced by increased metabolic requirements and cardiovascular dysfunction. The displacement of the VO_2/work rate relationship upward, as evidenced by a higher VO_2 per kilogram of body weight, underscores the impact of obesity on oxygen consumption during exercise. [15]

Hypertension and Hemodynamic Responses: Hypertensive individuals exhibited lower VO_2max and AT compared to normotensive counterparts. This aligns with the known influence of blood pressure on exercise hemodynamics (Morrow, 1993). While CPET is less explored in essential hypertension, our findings suggest that exercise intolerance may manifest through reduced aerobic capacity and altered cardiovascular responses. [16]

Diabetes and Exercise Capacity: Although our study did not observe significant differences between non-diabetic and diabetic groups, contrasting observations exist in the literature. Decreased peak VO_2 in diabetic patients has been reported in various studies (Abe et al., 2019; Mahmoud et al., 2014). The complexity of these relationships may be influenced by factors such as glycemic control, heart failure status, and the multifaceted interplay between diabetes and exercise physiology. [17]

Smoking and Exercise Tolerance: Smoking demonstrated a detrimental impact on exercise tolerance, evidenced by lower VO_2max, AT, BR, and OUES in the smoker group. This aligns with findings that smokers exhibit lower aerobic capacity and increased respiratory muscle work (de Borba et al., 2014). The intricate relationship between smoking and exercise responses underscores the importance of considering both the systemic and respiratory effects of smoking.

Alcohol and Tobacco Use:

Contrary to expectations, no significant differences were observed between alcoholics and non-alcoholics, or between tobacco users and non-users, in our CPET parameters. Limited studies exist on the impact of alcohol and smokeless tobacco on CPET outcomes. While some studies suggest an acute impact of tobacco on resting heart rate (Raghvendta et al., 2021), our study did not reveal significant differences, possibly due to the broader range of physiological and lifestyle factors that influence CPET responses.

Age and Exercise Capacity: Consistent with previous research, advancing age exhibited a negative correlation with VO_2max (de Borba et al., 2014). This decline in aerobic capacity with age underscores the physiological changes that occur over time and emphasizes the need for age-specific exercise interventions.

CPET offers valuable insights into the exercise capacity and physiological responses of individuals with cardiac risk factors. The distinctive patterns observed across various risk factors shed light on the multifaceted interactions between demographic, physiological, and lifestyle factors in influencing exercise performance.

Limitations and Future Directions: Our study has limitations, including a relatively small sample size and the lack of established reference values for the Indian population. Future research should explore larger cohorts and consider the influence of other confounding variables on CPET outcomes.

Conclusion

This study elucidates the complex relationships between exercise parameters, demographic factors, and various cardiac risk factors. The findings underscore the importance of tailored interventions based on individual characteristics, advancing our understanding of exercise physiology and cardiovascular responses in a high-risk young Indian population.

References

1. Korzan S, Mclellan N, Sharma A, Kaiser T, Datta D. Comparison Of Breathing Reserve Obtained From Measured And Estimated Maximal Voluntary Ventilation In Cardiopulmonary Exercise Testing. Chest. 2018 Oct 1;154(4):970A.
2. Johnston R. OUES, a useful sub-maximal CPET indicator of maximum VO2 [Internet]. PFTBlog. 2014 [cited 2021 Oct 28]. Available from: https://www.pftforum.com/blog/oues-a-useful-sub-maximal-cpet-indicatorof-maximum-vo2/.
3. Albouaini K, Egred M, Alahmar A. Cardiopulmonary exercise testing and its application. Postgrad Med J. 2007 Nov;83(985):675–82.
4. Wasserman K, Hansen J, Sue D. Principles of exercise testing and interpretation. Philadelphia: Lea and Febiger; 1987.
5. Baba R. The oxygen uptake efficiency slope and its value in the assessment of cardiorespiratory functional reserve. Congest Heart Fail Greenwich Conn. 2000 Oct;6(5):256–8.
6. Toma N, Bicescu G, Enache R, Dragoi R, Cinteza M. Cardiopulmonary exercise testing in differential diagnosis of dyspnea. Mædica. 2010 Jul;5(3):214–8.
7. Hansen JE, Sue DY, Wasserman K. Predicted values for clinical exercise testing. Am Rev Respir Dis. 1984 Feb;129(2 Pt 2):S49-55.
8. Morrow K, Morris CK, Froelicher VF, Hideg A, Hunter D, Johnson E, et al. Prediction of cardiovascular death in men undergoing noninvasive evaluation for coronary artery disease. Ann Intern Med. 1993 May 1;118(9):689–95.
9. Weatherald J, Farina S, Bruno N, Laveneziana P. Cardiopulmonary Exercise Testing in Pulmonary

Hypertension. Ann Am Thorac Soc. 2017 Jul 1;14(Supplement_1):S84–92.

10. Abe T, Yokota T. 739-P: Type 2 Diabetes Is an Independent Predictor of Lowered Peak Aerobic Capacity in Patients with Reduced and Nonreduced Ejection Fraction Heart Failure. Diabetes [Internet]. 2019 Jun 1 [cited 2021 Oct 28];68(Supplement 1). Available from:
11. https://diabetes.diabetesjournals.org/content/68/Supplement_1/739-P
12. El-Habashy MM, Agha MA, El-Basuni HA. Impact of diabetes mellitus and its control on pulmonary functions and cardiopulmonary exercise tests. Egypt J Chest Dis Tuberc. 2014 Apr 1;63(2):471–6.
13. Di Marco F, Terraneo S, Job S, Rinaldo RF, Sferrazza Papa GF, Roggi MA, et al. Cardiopulmonary exercise testing and second-line pulmonary function tests to detect obstructive pattern in symptomatic smokers with borderline spirometry. Respir Med. 2017 Jun;127:7–13.
14. Lauria VT, Sperandio EF, de Sousa TLW, de Oliveira Vieira W, Romiti M, de Toledo Gagliardi AR, et al. Evaluation of dose-response relationship between smoking load and cardiopulmonary fitness in adult smokers: A cross-sectional study. Rev Port Pneumol. 2017 Apr;23(2):79–84.
15. de Borba AT, Jost RT, Gass R, Nedel FB, Cardoso DM, Pohl HH, et al. The influence of active and passive smoking on the cardiorespiratory fitness of adults. 2014;8.
16. Gupta S, Khajuria V, Tandon VR, Mahajan A, Gillani ZH. Comparative evaluation of efficacy and safety of combination of metformin-vidagliptin versus metfromin-glimepiride in most frequently used doses in patients of type 2 diabetes mellitus with inadequately controlled metformin monotherapy-A randomised open label study. Perspect Clin Res. 2015;6(3):163–8.
17. Shindhe VM, Shindhe MM, Kulkarni NS, Mehvish M, Javali SB, Balikai FB, et al. A Study on Effect of Smokeless Tobacco on Pulmonary Function Tests in Class IV Workers of USM-KLE (Universiti Sains Malaysia Karnataka Lingayat Education Society) International Medical Programme, Belagavi. Int J Curr Res Rev. 2020;12 (14):23–7.