DOI: 10.7860/JCDR/2021/47899.14521

Original Article

Physiology Section

Association of Obesity with Peripheral Vascular Disease- A Case-control Study

SADHASIVA BHAVADEEP KUMAR REDDY[1], KOTHAREDDY DILEEP[2], RAJA REDDY RAMYA[3], SHRIPAD B DESHPANDE[4]

ABSTRACT

Introduction: Peripheral Vascular Disease (PVD) is an important public health problem, due to its insidious course and the associated co-morbidities. Obesity has been implicated as one of the risk factor besides others. However, the reports on obesity are not consistent.

Aim: To assess the association between central obesity and PVD along with other risk factors and the present study is undertaken to examine the correlation of central obesity as a risk factor for PVD. Further, the association between other risk factors and PVD was also ascertained.

Materials and Methods: A total of 124 subjects were recruited in this case-control study. Ankle Brachial Index (ABI) was measured using peripheral Doppler studies. Patients with ABI <0.9 were taken as cases and with ABI >0.9 were taken as controls. Blood pressure was measured in the sitting position and the authors obtained anthropometric and demographic data. Chi-square test was used as the test of significance and p-value <0.05 to be considered as level of significance.

Results: Of the total 124 participants in the study, 62 participants were the cases and 62 participants were controls. Body Mass Index (BMI) was higher in cases with PVD but Waist Circumference (WC) and hip circumference were significantly lower (p-value=0.003 and <0.001 respectively) and Waist-Hip Ratio (WHR) did not show any significant difference between cases and controls. Thus, fat mass is located elsewhere in these individuals, possibly it may be accumulated in the extremities. Other risk factors like history of smoking, history of alcoholism and history of diabetes mellitus had a positively significant association with PVD with p-values <0.001, 0.023 and <0.001 respectively.

Conclusion: The results obtained from this data suggests that PVD is not associated with central obesity, instead it provides evidence that PVD correlates with peripheral fat mass. Subsequent studies separating central and peripheral obesity are required to get more clarity on the relationship between obesity and PVD.

Keywords: Ankle brachial index, Central obesity, Peripheral vessels

INTRODUCTION

Peripheral vascular disease is a condition affecting the peripheral vessels (extremities), sparing the cardiac and cerebral arteries. This is often due to atherosclerosis, that leads to partial obstruction of the peripheral arteries, reducing perfusion to the tissues supplied by these arteries [1]. PVD is usually asymptomatic in many patients. But over the time, it can lead to severe tissue damage due to ischaemia, gangrene and necrosis and eventually amputation of the limb. There are many known risk factors for PVD such as diabetes, hypertension, smoking, hyperlipidaemia, etc. However, there are conflicting results with regard to obesity. Obesity has become a major public health problem in many countries. The role of BMI in defining the severity of obesity of different grades has been well-established in numerous epidemiological studies [2,3]. Some studies show that inflammatory markers are elevated in patients of PVD with an abnormal WHR [2].

Vascular dysfunction resulting from adipocyte-mediated cytokine release has been implicated in triggering hypertension and dyslipidaemia [3]. Cardiovascular outcomes are not altered as expected in obese individuals. Despite the strong evidence between elevated BMI and cardiovascular risk factors, favorable cardiovascular outcomes have been observed in obese patients as compared to those with normal BMI, which is otherwise referred to as the 'obesity paradox' [4]. Different theories, such as body composition, and improved cardiorespiratory fitness have been postulated to explain the improved prognosis in such individuals. Similar results were noted in patients with PVD [5]. Identification of obesity apart from other risk factors assumes importance because PVD is associated with reduction in functional work capacity and quality of life [6]. In addition, PVD is also associated with personal, social and economic burden [7]. Therefore, this study was undertaken to correlate the central and peripheral fat mass as a risk factor for PVD along with other risk factors.

MATERIALS AND METHODS

Recruitment of subjects: The study was conducted on the patients attending the OPD of Apollo Institute of Medical Sciences and Research, Chittoor, Andhra Pradesh. Ethical clearance was obtained from the Institutional Ethical Committee (Number: IEC12/AIMSR/05/2019). Informed consent was taken from each of the participants. A total of 124 participants were recruited for the study.

The history of hypertension, diabetes, coronary artery disease, smoking and alcohol intake was taken. Anthropometric measurements included height and weight measurements and BMI was determined according to kilogram per meter square. Waist and hip circumference were measured using standard techniques and the WHR was calculated [8]. The blood pressure was recorded using a mercury sphygmomanometer in sitting posture [9]. They were categorised into cases and controls on the basis of Ankle Brachial Pressure Index (ABPI) [10]. Doppler studies were performed on both upper and lower limbs and the ABI was calculated.

Inclusion criteria: All adults residing in Chittoor town with age 18 years and above attending the OPD and the subjects having ABI value of <0.9 were considered as cases of PVD. An ABI value of 0.9 to 1.14 was taken as the cut-off value for controls and were included in the study.

Exclusion criteria: Bilateral upper/lower limb amputees/absence of limbs, critically-ill patients, pregnant and lactating women and the patients with history of cerebrovascular accidents were excluded from the study.

STATISTICAL ANALYSIS

Data was entered in MS excel and analysed using SPSS version 22.0 software. Chi-square test was used as the test of significance. A p-value <0.05 was considered as statistically significant.

RESULTS

A total of 124 participants were included in the study, among which 62 participants were cases having PVD identified by ABI less than 0.9, and 62 participants were controls having ABI ≥0.9. Comparison of demographic factors between cases and controls are presented in [Table/Fig-1]. The mean age of the subjects among cases was 59.94 years and among controls, it was 61.29 years. Individuals of both the groups were of the same demographic frequency.

Variables	Cases (62) n (%)	Controls (62) n (%)	p-value
Age categories			
≤50 years	16 (25.8%)	12 (19.4%)	χ^2=2.406 (df=3) p=0.493
51-60 years	19 (30.6%)	15 (24.2%)	
61-70 years	15 (24.2%)	22 (35.5%)	
>70 years	12 (19.4%)	13 (20.9%)	
Gender			
Male	39 (58.5%)	35 (56.5%)	χ^2=0.00 (df=1) p=1.000
Female	23 (41.5%)	27 (43.5%)	

[Table/Fig-1]: Demographic factors of the study subjects.
df: Demographic frequency; p-value <0.05 considered significant

The mean systolic blood pressure was higher in cases (140.4±8.04 mm of Hg) compared to controls (137.7±8.12 mm of Hg), but the difference was not significant statistically. However the mean diastolic blood pressure was significantly higher in cases (85.0±7.44 mm of Hg) than controls (81.5±6.73 mm of Hg). A significantly higher number of cases (54.8%) were smokers as compared to controls (17.7%). Similarly, a higher number of cases (33.9%) were consuming alcohol compared to controls (16.1%). A significantly higher number of cases were having diabetes mellitus and hypertension compared to controls [Table/Fig-2].

Clinical history and signs	Cases	Controls	p-value
Blood pressure (mm of Hg) (mean±SD)			
Systolic blood pressure	140.4±8.04	137.7±8.12	0.065
Diastolic blood pressure	85.0±7.44	81.5±6.73	0.007
History of smoking n (%)			
Yes	34 (54.8%)	11 (17.7%)	χ^2=18.45 (df=1) p<0.001
No	28 (45.2%)	51 (82.3%)	
History of alcoholism			
Yes	21 (33.9%)	10 (16.1%)	χ^2=5.20 (df=1) p=0.023
No	41 (66.1%)	52 (83.9%)	
History of diabetes mellitus			
Yes	57 (91.9%)	19 (30.6%)	χ^2=49.1 (df=1) p<0.001
No	5 (8.1%)	43 (69.4%)	

[Table/Fig-2]: Personal and lifestyle factors of the study subjects. History of coronary artery disease was reported in one patient.
p-value <0.05 considered significant

In both cases and controls, a greater number of participants were in obesity grade I (45.2% cases and 58.1% controls). The number of participants with grade II obesity is more in cases (38.7%) compared to controls (8.1%). A significantly higher number of cases were in higher BMI categories (obesity grade I and grade II) compared to controls. Mean waist circumference, hip circumference was significantly higher in controls compared to cases. But, WHR did not show any significant difference between cases and controls as the majority of the subjects were within the normal cut-off values of WHR in both cases and controls [Table/Fig-3].

Variables	Cases n (%)	Controls n (%)	p-value
Body Mass Index (BMI)			
<18.5 kg/m² (Underweight)	2 (3.2%)	1 (1.6%)	χ^2=20.365 (df=4) p=0.002
18.5-22.9 kg/m² (Normal)	5 (8.1%)	7 (11.3%)	
23.0-24.9 kg/m² (Overweight)	3 (4.8%)	13 (20.9%)	
25.0-29.9 kg/m² (Obesity I)	28 (45.2%)	36 (58.1%)	
≥30 kg/m² (Obesity II)	24 (38.7%)	5 (8.1%)	
Waist Circumference (WC)	82.2±8.16	86.3±6.48	0.003
Hip circumference	103.2±6.75	111.2±8.83	<0.001
Waist-Hip Ratio (WHR)			
Normal	54 (87.1%)	57 (91.9%)	χ^2=0.77 (df=1) p=0.379
Increased	8 (12.9%)	5 (8.1%)	

[Table/Fig-3]: Anthropometric variables of the study subjects.
p-value <0.05 considered significant

DISCUSSION

It was derived from observations of this study that PVDs are correlated positively with BMI. Further, there is evidence that it is the peripheral fat mass that is positively correlated with PVD and not the central obesity or abdominal obesity [11]. Patients with PVD had lower waist circumference values as compared to controls but higher BMI. This finding possibly indicates a reduction in abdominal fat in PVD cases due to various reasons or accumulation of fat in the lower extremities. The causes of greater distribution of fat in lower extremities may be due to the functional impairment (disuse) caused by the disease [9]. Similar findings were observed in some studies. In a study done by Jayanthy AK, et al., it was found that BMI is directly related to ABI in PVD patients which is in agreement with the present study [10]. Lu B et al., showed that WHR increases the risk of PVD in men and higher WC increases the risk of PVD in women [12]. However, some studies have reported BMI as a protective factor for PVD [13] while many others reported that the association between obesity and PVD was not significant [14].

In cases of PVD, over a period of time leg muscle is replaced by adipose tissue due to physical inactivity, genetic factors, associated neuropathy and other co-morbid conditions. These observations are in agreement with earlier studies which show that PVD patients with significant ABI discrepancies have lower calf muscle area and higher calf muscle percent fat in the leg with severe ischaemia [9]. In the same study it was found that PVD participants had lower calf muscle density, lower calf muscle area, and higher calf fat and were associated with decreased mobility at two year follow-up. In a study done by Golledge J et al., it has been reported that obese patients with PVD were associated with reduced mortality as compared to underweight patients with PVD [15]. In a study done by Anusruti A et al., it was found that reactive oxygen metabolites (determinant of high oxidative stress in obese individuals) were independent of the participant's weight [16].

Despite this, several studies have shown the obesity survival paradox, showing the association between higher BMI and survival. The role of obesity in PVD outcomes is also not well-established, but some studies have shown clear survival benefits [10]. Some of the possible explanations are that obese patients are more likely to seek medical care at an earlier stage because of other co-morbid conditions which potentially influence long-term outcomes. More aggressive treatment and medication in this population may lead to a reduction in unfavourable outcomes. High level of suspicion and better screening have reduced the time of diagnosis drastically and hence they tend to take better precautionary measures. The other well known risk factors like diabetes, hypertension and smoking were associated directly with PVD.

In a study done by Criqui MH et al., it was shown that diabetes was significantly associated with PVD [17]. American Diabetes Association reported diabetes mellitus as the strongest risk factor of PVD [18]. Dyslipidaemia also has been identified as a significant risk factor for PVD in many studies. Ridker PM et al., reported dyslipidaemia as an independent risk factor [19]. Some studies have reported hypertension as a significant risk factor of PVD [20-22]. Smoking is a well known risk factor for PVD. It showed significant relation with PVD in the present study. Among cases in the age group of 61-70 years, there was a significant correlation with history and duration of smoking. A similar finding was observed with the controls. In both these instances, they had a lower ABI. This clearly indicates smoking as a very important risk factor which plays a key role in the pathogenesis of PVD. Many studies have identified smoking as a potent risk factor of PVD with consistent dose response relationship. In a study done by He Y et al., it was reported that both current smoking and former smoking was a significant risk factor of PVD [22]. A systematic review done by Willigendael EM et al., found that the prevalence of PVD had increased by two-three folds among current smokers compared to non-smokers and a clear dose-response relationship was seen [23]. Similar findings have been reported in previous studies also [24]. A higher number of cases were consuming alcohol in the present study, however Fabsitz RR et al., showed that current alcohol consumption is negatively associated with PVD [25].

Limitation(s)

Firstly, the other measures of obesity like waist-to-height ratio and waist-to-thigh ratio were not measured. Secondly, a larger study population would have given more consistent results. Thirdly, the data regarding the physical activity levels of the subjects were not obtained.

CONCLUSION(S)

The findings obtained from this study suggest that PVD is not associated with central obesity instead it is associated with peripheral fat mass. Further, BMI, diabetes, hypertension and smoking were significant risk factors for PVD. Though the WC was lower among the cases of PVD, the accumulation of fat in the lower extremities could have possibly contributed to higher BMI in these individuals. Further studies in relation to the pathophysiology of PVD and the correlation of these results with other obesity indices are needed to come to a proper conclusion.

REFERENCES

[1] Kullo IJ, Rooke TW. Clinical Practice. Peripheral artery disease. N Engl J Med. 2016;374(9):861-71.
[2] Almahameed A. Peripheral arterial disease: Recognition and medical management. Cleve Clin J Med. 2006;73(7):621-38.
[3] Redinger RN. The pathophysiology of obesity and its clinical manifestations. Gastroenterol Hepatol (N Y). 2007;3(11):856-63.
[4] Elagizi A, Kachur S, Lavie CJ, Carbone S, Pandey A, Ortegad FB, et al. An overview and update on obesity and the obesity paradox in cardiovascular diseases. Prog Cardiovasc Dis. 2018;61(2):142-50.
[5] Wael Galal, Yvette R B M van Gestel, Sanne E Hoeks, Don D Sin, Tamara A Winkel, Jeroen J Bax. The obesity paradox in patients with peripheral arterial disease. Chest. 2008;134(5):925-30. 10.1378/chest.08-0418.
[6] John RB, Jeffrey WO. Pathophysiology of peripheral arterial disease and risk factors for its development. Cleve Clin J Med. 2006;73:S08-14. doi: 10.3949/ccjm.73.suppl_4.s8.
[7] Marso SP, Hiatt WR. Peripheral arterial disease in patients with diabetes. J Am Coll Cardiol. 2006;47(5):921-29.
[8] Waist circumference and waist-hip ratio: Report of a WHO expert consultation, Geneva, 8-11 December 2008.
[9] McDermott MM, Hoff F, Ferrucci L, Pearce WH, Guralnik JM, Tian L, et al. Lower extremity ischemia, calf skeletal muscle characteristics, and functional impairment in peripheral arterial disease. J Am Geriatr Soc. 2007;55(3):400-06. doi: 10.1111/j.1532-5415.2007.01092.x [PubMed: 17341243].
[10] Jayanthy AK, Balaji N, Balasubramanyam M, Krishnan A, Rhaphaela AMR. Assessment of ankle brachial index in subjects and its relationship with age and body mass index- A pilot study AIP Conference Proceedings 2112, 020054 (2019); https://doi.org/10.1063/1.5112239.
[11] Tankó LB, Bagger YZ, Alexandersen P, Larsen PJ, Christiansen C for the PERF study group. Central and peripheral fat mass have contrasting effect on the progression of aortic calcification in postmenopausal women. European Heart Journal. 2003;24(16):1531-37.
[12] Lu B, Zhou J, Waring ME, Parker DR, Eaton CB. Abdominal obesity and peripheral vascular disease in men and women: A comparison of waist-to-thigh ratio and waist circumference as measures of abdominal obesity. Atherosclerosis. 2010;208(1):253-57.
[13] Tseng CH. Prevalence and risk factors of peripheral arterial obstructive disease in Taiwanese type 2 diabetic patients. Angiology. 2003;54(3):331-38.
[14] Selvin E, Erlinger TP. Prevalence of and risk factors for peripheral arterial disease in the United States results from the national health and nutrition examination survey, 1999-2000. Circulation. 2004;110(6):738-43.
[15] Golledge J, Cronin O, Iyer V, Bradshaw B, Moxon JV, Cunningham MA. Body mass index is inversely associated with mortality in patients with peripheral vascular disease. Atherosclerosis. 2013, 229:549-55. 10.1016/j.atherosclerosis.2013.04.030.
[16] Anusruti A, Eugène HJM Jansen, Xīn Gào, Yang Xuan, Hermann Brenner, Ben Schöttkera. Longitudinal Associations of Body Mass Index, Waist Circumference, and Waist-to-Hip Ratio with Biomarkers of Oxidative Stress in Older Adults: Results of a Large Cohort Study. Obes Facts. 2020;13(1):66-76.
[17] Criqui MH, Vargas V, Denenberg JO, Ho E, Allison M, Langer RD, et al. Ethnicity and peripheral arterial disease: The San Diego Population Study. Circulation. 2005;112(17):2703-07.
[18] American Diabetes Association. Peripheral Arterial Disease in People With diabetes. Diabetes Care. 2003;26:3333-41.
[19] Ridker PM, Stampfer MJ, Rifai N. Novel risk factors for systemic atherosclerosis a comparison of C-reactive protein, fibrinogen, homocysteine, lipoprotein(a), and standard cholesterol screening as predictors of peripheral arterial disease. JAMA. 2001;285(19):2481-85.
[20] Korhonen PE, Syvänenb KT, Vesalainenc RK, Kantolad IM, Kautiainene H, Järvenpa AFP, et al. Ankle-brachial index is lower in hypertensive than in normotensive individuals in a cardiovascular risk population. J Hypertens. 2009;27(10):2036-43.
[21] Meijer WT, Grobbee DE, Hunink MM, Hofman A, Hoes AW. Determinants of peripheral arterial disease in the elderly: The Rotterdam study. Arch Intern Med. 2000;160(19):2934-8.
[22] He Y, Jiang Y, Wang J, Fan L, Li XY, Hu FB. Prevalence of peripheral arterial disease and its association with smoking in a population-based study in Beijing, China. J Vasc Surg. 2006;44:333-38.
[23] Willigendael EM, Teijink JAW, Bartelink ML, Kuiken BW, Boiten J, Moll FL, et al. Influence of smoking on incidence and prevalence peripheral arterial disease. J Vasc Surg. 2004;40(6):1158-65.
[24] Murabito JM, Evans JC, Nieto K, Larson MG, Levy D, Wilson PW. Prevalence and clinical correlates of peripheral arterial disease in the Framingham Offspring Study. Am Heart J. 2002;143(6):961-65.
[25] Fabsitz RR, Sidawy AN, Go O, Lee ET, Welty TK, Devereux RB, et al. Prevalence of peripheral arterial disease and associated risk factors in American Indians: The Strong Heart Study. Am J Epidemiol. 1999;149:330-38. doi: 10.1093/oxfordjournals.aje.a009817.

PARTICULARS OF CONTRIBUTORS:
1. Assistant Professor, Department of Pathology, Apollo Institute of Medical Sciences and Research, Chittoor, Andhra Pradesh, India.
2. Senior Resident, Department of Radiology, Apollo Institute of Medical Sciences and Research, Chittoor, Andhra Pradesh, India.
3. Assistant Professor, Department of Physiology, Apollo Institute of Medical Sciences and Research, Chittoor, Andhra Pradesh, India.
4. Professor and Head, Department of Physiology, Apollo Institute of Medical Sciences and Research, Chittoor, Andhra Pradesh, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
R Ramya,
Assistant Professor, Department of Physiology, Apollo Institute of Medical Sciences and Research, Chittoor-517127, Andhra Pradesh, India.
E-mail: ramyamayudhar@gmail.com

PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Nov 29, 2020
- Manual Googling: Dec 19, 2020
- iThenticate Software: Dec 29, 2020 (11%)

ETYMOLOGY: Author Origin

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Nov 26, 2020**
Date of Peer Review: **Dec 30, 2020**
Date of Acceptance: **Jan 15, 2021**
Date of Publishing: **Feb 01, 2021**