

Arterial Stiffness is More Associated with Abdominal than Generalized Obesity in Adult Males of Western Rajasthan, India

Dr. Rajnish Kanojia¹, Dr. Raghuveer Chaudhary², Dr. Abhinav Purohit^{3*}, Dr. Rekha Singhvi⁴, Dr. N.D. Soni⁵, Dr. Raju Ram Dudi⁶

¹Resident, Department of Physiology, Dr S.N. Medical College, Jodhpur

²Prof. Deptt of Physiology, Dr S.N. Medical College, Jodhpur

³Sr. Demonstrator, Deptt of Physiology, Medical College, Pali

⁴Junior Specialist, Mahatma Gandhi District Hospital, Bhilwara

⁵Sr. Prof., Deptt of Physiology, Dr S.N. Medical College, Jodhpur

⁶Sr. Demonstrator, Medical College, Churu

Original Research Article

*Corresponding author

Dr. Abhinav Purohit

Article History

Received: 11.10.2017

Accepted: 16.10.2017

Published: 30.10.2017



Abstract: Studies suggested that obesity; arterial stiffness and cardiovascular diseases (CVD) are interrelated. Analyzing relation between arterial stiffness and type of obesity can be helpful in prediction of CVD in obese. We performed this study in western Rajasthan, India to assess type of obesity more related with arterial stiffness. 77 healthy non smoker, free of CVD, male participant, age 20 to 40 years, examined for Body Mass Index (BMI) and Waist Circumference (WC) as indices of obesity and Right and Left brachial ankle Pulse Wave Velocity (ba PWV), Carotid-Femoral (C-F) PWV and Augmentation Index at Heart Rate 75/min (AIx@HR75) as indices of arterial stiffness and measured non-invasively using an oscillometric device PeriScope. Result suggested Pearson's Correlation Coefficients (r) of WC with indices of stiffness are greater than as of BMI ($r = 0.482$ vs 0.356 , 0.396 vs 0.219 , 0.484 vs 0.316 and $r = 0.433$ vs 0.31 respectively for Right ba PWV, Left ba PWV, CF PWV and AIx@HR75). Simple linear regressions were significant ($p < 0.05$) except between BMI and Left ba PWV ($p > 0.05$). The present study concluded that vessel wall properties were well explained by central obesity as compare to generalized obesity. So for CV health, individual should be focused on reducing belly fat.

Keywords: Obesity, Arterial stiffness, Pulse wave velocity, Cardiovascular risk

INTRODUCTION

In the history of mankind, increase in weight has been considered as an indication of well-being and health. The cause of this increasing prevalence of weight gain is adoption of lack of regular physical exercise, sedentary lifestyle, and excessive intake of junk foods.

Obesity supervenes bringing with it increased risk of metabolic disturbance. Not only that, but the pattern of obesity, central obesity (abdominal accumulation of adipose tissue), contribute an added risk to some of the chronic non-communicable diseases. The contribution of excess generalized weight as measured by BMI and central obesity measured by WC to the prediction of cardiovascular (CV) risk has been the subject of long-standing debate.[1-5] Higher BMI is associated with Arterial stiffness[6,7], which is considered an independent risk factor of CVD, cerebrovascular accidents (CVA) [8], a marker of target organs lesion in hypertensive patients [9], such as Chronic kidney disease [10-12], besides being connected with the secondary development atherosclerosis, chronic

tissue inflammation and endothelial dysfunction.[13,14] measuring the arterial stiffness can help in quantify the CV risk with various type of adiposity. There are various indices of arterial stiffness such as elastic modulus, arterial distensibility, arterial compliance, Pulse wave velocity (PWV), Augmentation index(AIx), and Arterial Stiffness index(ASI) are available.[15] Out of these PWV, AIx and ASI are widely accepted and recommended markers for measure arterial stiffness and non-invasive easy methods have been developed for these. PWV is velocity of the systolic pressure wave within the arterial walls and an augmentation of arterial pulse pressure due to wave reflection is known as Augmentation Index (AIx). AIx is measure by pulse waveform analysis. Measurement of PWV and AIx

have now become recognized, important prognostic indicator than blood pressure to assess the cardiovascular risk [16].

Some study suggested the central obesity is best correlated with CVD and mortality [17-25] in contrast, some concluded that measure of central obesity such as WC is not superior than BMI in predicting CVD. [26-33] According to National Family Health Survey (NFHS) 2015-16 in Rajasthan 23.7% urban women, 10.7% rural women (total 14.1%), 19.7% urban men, 10.6% rural men (total 13.2%) have BMI more than or equal to 25kg/m². And it is almost doubled as compare to NFHS 2005-2006 [34] BMI is most accepted and studied measure of obesity attributed to CVD and other non-communicable diseases. Researchers are also been focused on central obesity. There are very few studies available that comparing type of obesity associated with arterial stiffness in western Rajasthan. So to fill the gap in scientific knowledge we performed this present study.

MATERIAL & METHOD

Study Design

In present cross sectional study all 77 participants gave a written informed consent to participate in this study. Institutional ethical committee clearance was obtained. Age 20 to 40 years adult male, native and resident of Western Rajasthan, BMI not more 30 kg/m², apparently healthy for at least one week are included in this study. Smokers, history of Cardiovascular attacks, medical conditions influencing degree of obesity such as thyroid disease, Cushing syndrome, chronic medications and medication or regime for weight reduction were excluded.

Anthropometric measures

BMI was calculated by dividing the participant’s weight in kilograms by the square of his height in meters. Weight and Height of participants were measured by calibrated electrical weighing Scale and Calibrated Stadiometer respectively. Waist circumference was measured using a measuring tape in standing position at the level midway between the lower rib margin and the iliac crest in a horizontal plane. It is an approximate index of central obesity.

Measurement of arterial stiffness

Indices of Arterial Stiffness is measured by PeriScope (developed by Genesis Medical Systems, Hyderabad, India) based on Oscillometric Method in morning in fasting condition with 8 to 10 hours over night sound sleep. PeriScope records arterial Blood pressure (BP), arterial pressure Waveform non-invasively through Cuffs Wrapped on all four limbs. Simultaneously it records Electrocardiogram (ECG) by 4 leads applied to four limbs. Time taken by pressure

wave to reach limbs is calculated by time point recording of R Wave of ECG and foot of arterial pressure Waveform. The system software of this device supports sophisticated digital signal-processing algorithm to calculate all the results. It calculates right and left brachial ankle PWV (Right Br Ank PWV & Light Br Ank PWV), carotid to femoral PWV (C-F PWV), Arterial Stiffness Index (ASI), Ankle Brachial Index (ABI) & Augmentation Index (AIx) and estimated AIx at Heart Rate (HR) of 75 beats/min (AIx@HR75). Participants were asked to refrain from drinking caffeine containing beverages 12 hrs before the test. They were also informed not to speak or sleep during the procedure. All subjects were explained about the procedure to be undertaken and written consent was obtained from all the subjects prior to the study. Br Ank PWV and cf PWV were measure of central arterial stiffness. Brachial and ankle ASI were measure of peripheral local arterial stiffness. [16]

STATISTICS

Results were statistically analyzed using Data Analysis ToolPak in Microsoft Excel. Pearson’s Correlation Coefficients are analysed between parameters and performed simple linear regression. “t” test is applied to test the correlations. Effect size with 95% confidence interval (CI) measured with help of result of simple linear regression.

RESULTS

Table 1 is showing the descriptive statistics of studied population. Fig 1 and Fig 2 are showing the unadjusted simple linear regression of BMI and WC (in cm) respectively on various indices of arterial indices. Figures also showing the R squared (R²), correlation coefficient (r) and p value derived by t test for regression for simple linear regression.

Table-1: Descriptive Statistics of Studied Participants*

Numbers of Participants	77
Age(in Yrs)	31.17 ± 5.54
Weight (in Kg)	69.00 ± 10.02
Height (in Cm)	169.99 ± 5.92
BMI (In Kg/m2)	23.83 ± 2.83
BMI < 22.9 Kg/m2	28
BMI 23 to 24.9 Kg/m2	23
BMI 25to 30 Kg/m2	26
Waist Circumference (Cm)	90.08 ± 9.74
Right baPWV (cm/sec)	1316.53 ± 162.77
Left baPWV (cm/sec)	1256.72 ± 171.60
C-F PWV(cm/sec)	838.82 ± 125.82
AIx (%)	15.71 ± 6.68
AIx@HR75 (%)	15.56 ± 7.40

*Values are in Mean ±SD or Numbers, Abbreviations are same as in text

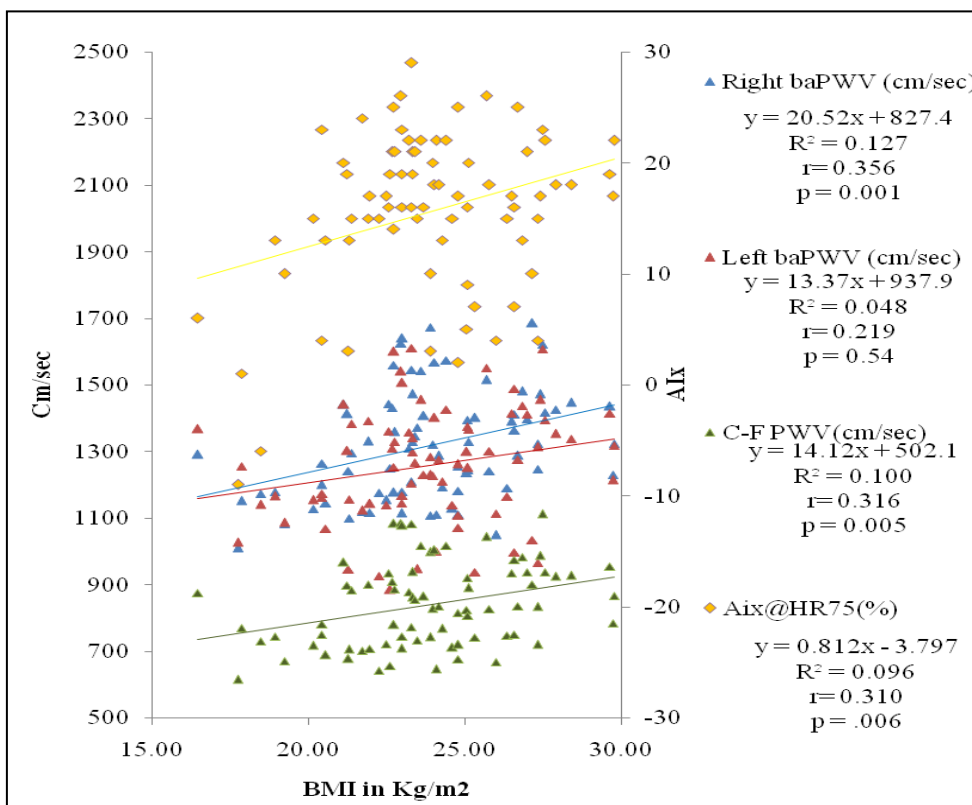


Fig-1: Linear Regression of BMI on PWVs and AIX. Abbreviations are same as in text

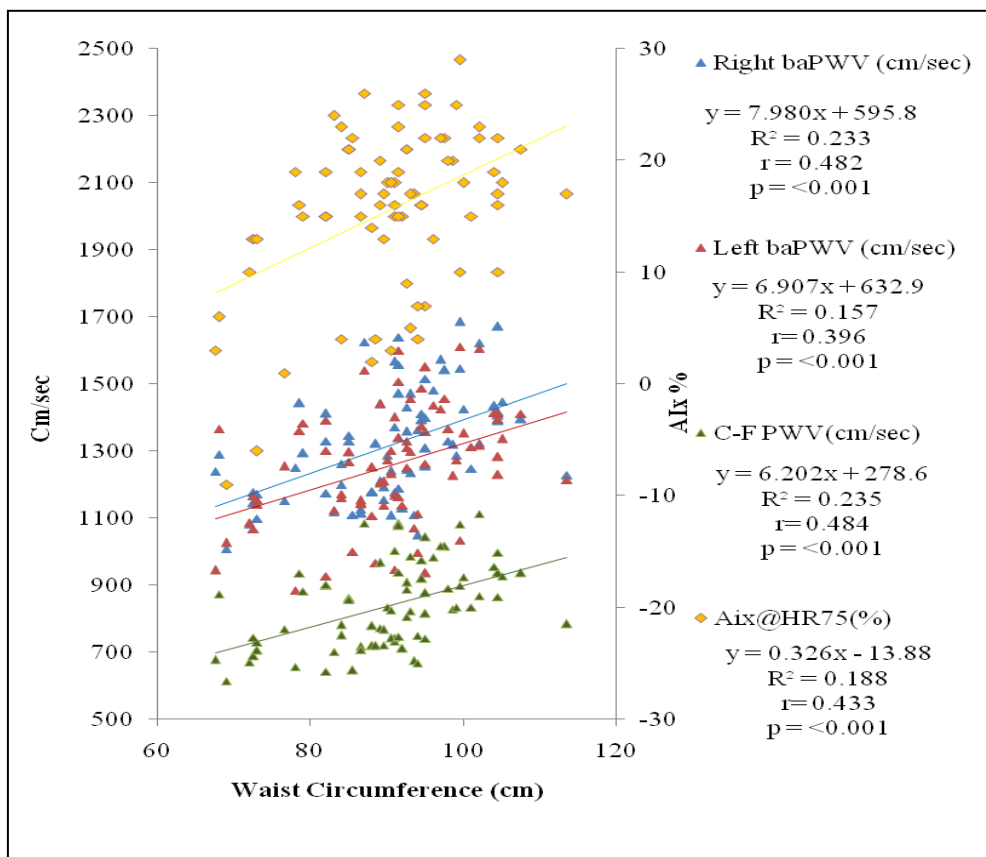


Fig-2: Linear Regression of WC of PWVs and AIX. Abbreviations are same as in text

Table-2: Change in value of Indices of arterial stiffness associated with 1 SD increase in BMI and WC

Indices	Associated with BMI*	Associated with WC*
Right baPWV (cm/sec)	39.9 (23.09 - 93.14)	60 (45.58 - 110.84)
Left baPWV (cm/sec)	58.07 (-0.71 - 76.38)	77.7 (31.56- 103.73)
C-F PWV(cm/sec)	37.83 (12.48 - 67.44)	67.27 (35.65 - 86.00)
AIx@HR75 (%)	2.29 (0.68 - 3.91)	3.17 (1.66 - 4.68)

*effect size (95% Confidence Interval), Abbreviations are same as in text

It is observed in results that BMI explained cf PWV of 10% of cases ($p = .005$) whereas WC explained 23.5% of cases of cf PWV ($p = <0.001$). WC explained Indices of arterial stiffness in more number of cases as compare to BMI ($r = 0.482$ vs $.356$, 0.396 vs $.219$, 0.484 vs 0.316 and $r = 0.433$ vs 0.31 respectively for relation with Right ba PWV, Left ba PWV, CF PWV and AIx@HR75). Tables 2 provided the predicted effect size which is associated with increase in BMI by 2.83 kg/m^2 and in WC by 9.74 cm (1 standard deviation (SD)) in the participants. Left ba PWV is increases more than other PWV with BMI whereas all PWV increases in consistent manner with WC. Overall WC is greater associated with increase in PWVs and AIx@HR75 than BMI.

DISCUSSION

Our study suggested that BMI and WC both have mild positive linear relation with arterial stiffness. But WC is greater associated with increase in Arterial stiffness than BMI. It indicates central obesity affect characteristics of central arteries more as compare to generalized obesity. Both type of obesity is inter-related and increases simultaneously but increasing in fat deposition on thighs, arm and chest may not be as harmful as deposition of intra-abdominal fat for risk of arteriosclerosis. Increasing in arterial stiffness also predicts plaque development [35]. This decrease in elasticity of large arteries is earliest sign of atherosclerosis [36] arterial stiffness is nothing but a measure of tunica intima-medica thickening. Intima-media thickening and plaque development is more prevalent in Cardio-Vascular Diseases [37]. The Rotterdam Study found no association between mild plaque score and Pulse wave velocity (PWV). However, in the presence of severe plaque score, as determined by ultrasound or abdominal calcification determined by X-ray, PWV was significantly increased [38]. Some studies support our findings that measures of abdominal obesity such as waist circumference is to be the parameters best correlated with cardiovascular disease and mortality [17-25]. In contrast, some conclude that measure of central obesity is not superior to BMI in predicting CVD [26-33]. Weight gain leads to expansion of extracellular volume, cardiac output and regional blood flow to tissues [39, 40]. The mechanisms responsible for the increased regional blood flow still to be explained, but must involve the system-wide increased metabolic rate, local accumulation of vasoactive metabolites [41]. These hemodynamic

changes, Sheer stress, BP, elevated sympathetic nerve activity, hormonal mechanism such as of leptin, adipokines, prothrombin activator inhibitor and norepinephrine etc. in obese can explain the functional association between arterial stiffness and obesity, which in the long run may lead to structural adaptations in the arteries [39, 42-45].

Non-invasive measurement of vascular wall elasticity as PWV and analysis of arterial waveforms is an important diagnostic tool which allows one to collect information on the functional status of the arteries [46]. Some studies support the present study. R. Niruba *et al.* performed a study in Tamilnadu, India on 50 male subjects with mean value of age = 38 ± 2 years and BMI = 26 ± 3 . They concluded BMI is associated with Stiffness Index (an analogous parameter to CF PWV) and AIx ($r = 0.564$ and 0.437 ($p < .05$)). [7] 146 adults of both genders of mean age of 50 ± 6 years analyzed for relation between BMI and CF PWV ($r = 0.203$, $p < .05$) and WC and CF PWV ($r = 0.369$, $p < 0.001$) in USA by Strasser B. *et al.* [47] 92 non hypertension healthy and 113 Hypertension subjects were examined for the same by Recio-Rodriguez J *et al* (2012). They found a very weak relation with BMI in non-hypertensive ($r = 0.078$) but mild in hypertensive ($r = 0.232$ ($p < .05$)). But with WC CF PWV is stronger related in both cases ($r = 0.209$ and 0.267 respectively) [48] Pandit DS. *Et al.* performed study on healthy adolescent subjects of India and observed $r = 0.5$ ($p < 0.05$) between BMI and CF PWV as well as WC and CF PWV [49]. Wildman R. *et al.* concluded $r = 0.370$ ($p < 0.01$) between BMI and CF PWV and $r = 0.380$ ($p < 0.01$) between WC and CF PWV in 186 young adults of pennsylvania [50].

Some studies did not support present study. In a large study by Oren A *et al.* the relationship between pulse wave velocity and BMI did not reach statistical significance [51]. No differences in PWV were observed in relation to adiposity by Ryder JR *et al.* in a study in children [52].

The present study has been interpreted within the context of its limitations. We did not assess body fat but used anthropometric measures to estimate adiposity. We did not exclude the effect of age and hypertension on arterial stiffness. These two are primary predictor of arterial stiffness. Blood pressure and distensibility of arterial system are inversely proportional and influences each other. Our sample size was not large enough too

stratified in age groups. We did not collect the information about sleep apnea which is common in obese and may affect the cardiac function and arterial properties [53]. Age, hypertension and sleep apnea confounded our results. But comparing the relationship of arterial stiffness with generalized and central obesity these confounders are almost ineffective.

CONCLUSION

Central obesity measured as WC is more associated with vessel wall properties stiffness as compare to generalized obesity. People should give more emphasis on reducing belly fat, than just losing weight for better cardio vascular health.

REFERANCES

1. Haffner S, Taegtmeyer H. Epidemic obesity and the metabolic syndrome. *Circulation*. 2003 Sep 30;108(13):1541-5.
2. Hubert HB, Feinleib M, McNamara PM, Castelli WP. Obesity as an independent risk factor for cardiovascular disease: a 26-year follow-up of participants in the Framingham Heart Study. *Circulation*. 1983 May 1;67(5):968-77.
3. Sorof J, Daniels S. Obesity hypertension in children. *Hypertension*. 2002 Oct 1;40(4):441-7.
4. Stamler R, Stamler J, Riedlinger WF, Algera G, Roberts RH: Weight and blood pressure. Findings in hypertension screening of 1 million Americans. *JAMA* 1978; 240: 1607–1610.
5. Stamler R, Ford CE, Stamler J: Why do lean hypertensives have higher mortality rates than other hypertensives? Findings of the Hypertension Detection and Follow-up Program. *Hypertension* 1991; 17: 553–564.
6. Pantelis E, Zebekakis, Tim Nawrot, LutgardeThijs, Elisabeth J. Balkestein, Janneke van der Heijden-Spek, Luc M. Van Bortel , Harry A. Struijker-Boudier , Michel E. Safar and Jan A. Staessen. Obesity is associated with increased arterial stiffness from adolescence until old age. *Journal of Hypertension* 2005, 23:1839–1846.
7. Niruba R, Kannan KT, Subha KC, and Vijiyalakshmi. Correlation between BMI and arterial stiffness in middle aged subjects. *International Journal of Current Research and Review* 2016, 8 (6), 14-17.
8. Lee SW, Youm Y, Kim CO, Lee WJ, Choi W, Chu SH, Park YR, Kim HC. Association between skeletal muscle mass and radial augmentation index in an elderly Korean population. *Archives of gerontology and geriatrics*. 2014 Aug 31;59(1):49-55.
9. Bianchini E, Giannarelli C, Maria Bruno R, Armenia S, Landini L, Faita F, Gemignani V, Taddei S, Ghiadoni L. Functional and structural alterations of large arteries: methodological issues. *Current pharmaceutical design*. 2013 Apr 1;19(13):2390-400.
10. Aroor AR, Demarco VG, Jia G, Sun Z, Nistala R, Meininger GA, Sowers JR. The role of tissue ReninAngiotensinaldosteronesystem in the development of endothelial dysfunction and arterial stiffness. *Front Endocrinol (Lausanne)* 2013; 4, 161.
11. Cavalcante JL, Lima JA, Redheuil A, Al-Mallah MH. Aortic stiffness: current understanding and future directions. *J Am Coll Cardiol*. 2011;57:1511–1522.
12. Shirai K, Hiruta N, Song M, Kurosu T, Suzuki J, Tomaru T, Miyashita Y, Saiki A, Takahashi M, Suzuki K, Takata M. Cardio-ankle vascular index (CAVI) as a novel indicator of arterial stiffness: theory, evidence and perspectives. *Journal of atherosclerosis and thrombosis*. 2011;18(11):924-38.
13. Castellon X, Bogdanova V. Screening for subclinical atherosclerosis by noninvasive methods in asymptomatic patients with risk factors. *Clin Interv Aging*. 2013; 8: 573-580.
14. Lim JH, Kim Y-K, Kim Y-S, Na S-H, Rhee M-Y, Lee M-M. Relationship Between Serum Uric Acid Levels, Metabolic Syndrome, and Arterial Stiffness in Korean. *Korean Circulation Journal*. 2010;40(7):314-320.
15. IS Mackenzie, IB Wilkinson and JR Cockcroft. Assessment of arterial stiffness in clinical practice. *Q J Med* 2002; 95:67–74.
16. Laurent S, Cockcroft J, Van Bortel L, Boutouyrie P, Giannattasio C, Hayoz D, Pannier B, Vlachopoulos C, Wilkinson I, Struijker-Boudier H. Expert consensus document on arterial stiffness: methodological issues and clinical applications. *European heart journal*. 2006 Sep 25;27(21):2588-605.
17. De Koning L, Merchant AT, Pogue J, Anand SS. Waist circumference and waist-to-hip ratio as predictors of cardiovascular events: meta-regression analysis of prospective studies. *European heart journal*. 2007 Apr 1;28(7):850-6.
18. Coutinho T, Goel K, Correa de Sa D, Kragelund C, Kanaya AM, Zeller M, Park JS, Kober L, Torp-Pedersen C, Cottin Y, Lorgis L, Lee SH, Kim YJ, Thomas R, Roger VL, Somers VK, Lopez-Jimenez F: Central obesity and survival in subjects with coronary artery disease: a systematic review of the literature and collaborative analysis with individual subject data. *J Am Coll Cardiol* 2011, 57:1877-1886.
19. Schneider HJ, Klotsche J, Silber S, Stalla GK, Wittchen HU: Measuring abdominal obesity: effects of height on distribution of cardiometabolic risk factors risk using waist circumference and waist-to-height ratio. *Diabetes Care* 2011, 34:e7.

20. Dhaliwal SS, Welborn TA. Central obesity and multivariable cardiovascular risk as assessed by the Framingham prediction scores. *The American journal of cardiology*. 2009 May 15;103(10):1403-7.
21. Czernichow S, Kengne AP, Stamatakis E, Hamer M, Batty GD: Body mass index, waist circumference and waist-hip ratio: which is the better discriminator of cardiovascular disease mortality risk? Evidence from an individual-participant meta-analysis of 82 864 participants from nine cohort studies. *Obes Rev* 2011.
22. Sehested TS, Hansen TW, Olsen MH, Abildstrom SZ, Rasmussen S, Ibsen H, Torp-Pedersen C, Madsbad S, Jeppesen J: Measures of overweight and obesity and risk of cardiovascular disease: a population-based study. *Eur J Cardiovasc Prev Rehabil* 2010, 17:486-490.
23. Schneider HJ, Friedrich N, Klotsche J, Pieper L, Nauck M, John U, Dorr M, Felix S, Lehnert H, Pittrow D, Silber S, Volzke H, Stalla GK, Wallaschofski H, Wittchen HU: The predictive value of different measures of obesity for incident cardiovascular events and mortality. *J Clin Endocrinol Metab* 2010, 95:1777-1785.
24. Park SH, Choi SJ, Lee KS, Park HY: Waist circumference and waist-to-height ratio as predictors of cardiovascular disease risk in Korean adults. *Circ J* 2009, 73:1643-1650.
25. Lee CM, Huxley RR, Wildman RP, Woodward M: Indices of abdominal obesity are better discriminators of cardiovascular risk factors than BMI: a meta-analysis. *J Clin Epidemiol* 2008, 61:646-653.
26. Liu Y, Tong G, Tong W, Lu L, Qin X. Can body mass index, waist circumference, waist-hip ratio and waist-height ratio predict the presence of multiple metabolic risk factors in Chinese subjects? *BMC Public Health*. 2011;11:35.
27. Qiao Q, Nyamdorj R. Is the association of type II diabetes with waist circumference or waist-to-hip ratio stronger than that with body mass index? *Eur J Clin Nutr*. 2010;64:30-34.
28. Tuan NT, Adair LS, Stevens J, Popkin BM. Prediction of hypertension by different anthropometric indices in adults: the change in estimate approach. *Public Health Nutr*. 2010;13:639-646.
29. Taylor AE, Ebrahim S, Ben-Shlomo Y, Martin RM, Whincup PH, Yarnell JW, Wannamethee SG, Lawlor DA. Comparison of the associations of body mass index and measures of central adiposity and fat mass with coronary heart disease, diabetes, and all-cause mortality: a study using data from 4 UK cohorts. *Am J Clin Nutr*. 2010;91:547-556.
30. Freiberg MS, Pencina MJ, D'Agostino RB, Lanier K, Wilson PW, Vasan RS. BMI vs. waist circumference for identifying vascular risk. *Obesity (Silver Spring)* 2008;16:463-469.
31. Wang F, Wu S, Song Y, Tang X, Marshall R, Liang M, Wu Y, Qin X, Chen D, Hu Y. Waist circumference, body mass index and waist to hip ratio for prediction of the metabolic syndrome in Chinese. *Nutr Metab Cardiovasc Dis*. 2009;19:542-547.
32. Palacios C, Perez CM, Guzman M, Ortiz AP, Ayala A, Suarez E. Association between adiposity indices and cardiometabolic risk factors among adults living in Puerto Rico. *Public Health Nutr*. 2011. pp. 1-10.
33. Boffetta P, McLerran D, Chen Y, Inoue M, Sinha R, He J, Gupta PC, Tsugane S, Irie F, Tamakoshi A, Gao YT, Shu XO, Wang R, Tsuji I, Kuriyama S, Matsuo K, Satoh H, Chen CJ, Yuan JM, Yoo KY, Ahsan H, Pan WH, Gu D, Pednekar MS, Sasazuki S, Sairenchi T, Yang G, Xiang YB, Nagai M, Tanaka H. Body Mass Index and Diabetes in Asia: A Cross-Sectional Pooled Analysis of 900,000 Individuals in the Asia Cohort Consortium. *PLoS One*. 2011;6:e19930.
34. Kumar S, Kaushik A, Kansal S. FACTORS INFLUENCING THE WORK PERFORMANCE OF ASHA UNDER NRHM A CROSS SECTIONAL STUDY FROM EASTERN UTTAR PRADESH. *Indian Journal of Community Health*. 2013 Jan 31;24(4):325-31.
35. Hopkins KD, Lehmann ED, Gosling RG. Aortic compliance measurements: a non-invasive indicator of atherosclerosis? *Lancet* 1994;343:1447.
36. Stary HC, Blankenhorn DH, Chandler AB, Glagov S, Insull W, Richardson M, Rosenfeld ME, Schaffer SA, Schwartz CJ, Wagner WD. A definition of the intima of human arteries and of its atherosclerosis-prone regions. A report from the Committee on Vascular Lesions of the Council on Arteriosclerosis, American Heart Association. *Circulation*. 1992 Jan 1;85(1):391-405.
37. Ebrahim S, Papacosta O, Whincup P, Wannamethee G, Walker M, Nicolaides AN, Dhanjil S, Griffin M, Belcaro G, Rumley A, Lowe GD. Carotid plaque, intima media thickness, cardiovascular risk factors, and prevalent cardiovascular disease in men and women. *Stroke*. 1999 Apr 1;30(4):841-50.
38. von Popele NM. Association between arterial stiffness and atherosclerosis. *The Rotterdam Study*. *Stroke*. 2001;32:454-60.
39. Hall JE. The kidney, hypertension, and obesity. *Hypertension* 2003;41:625-633.
40. Oren S, Grossman E, Frohlich ED. Arterial and venous compliance in obese and nonobese subjects. *Am J Cardiol* 1996; 77:665-667.
41. Ardilouze JL, Fielding BA, Currie JM, Frayn KN, Karpe F. Nitric oxide and b-adrenergic stimulation

- are major regulators of preprandial and postprandial subcutaneous adipose tissue blood flow in humans. *Circulation* 2004; 109:47–52.
42. Visser M, Bouter LM, McQuillan GM, Wener MH, Harris TB: Elevated C-reactive protein levels in overweight and obese adults. *JAMA*. 1999;282: 2131–2135.
 43. Singhal A, Farooqi IS, Cole TJ, O’Rahilly S, Fewtrell M, Kattahorn M, Lucas A, Deanfield J: Influence of leptin on arterial distensibility: A novel link between obesity and cardiovascular disease? *Circulation*. 2002;106:1919-1924.
 44. Seals DR, Gates PE. Stiffening our resolve against adult weight gain. *Hypertension* 2005;45:175- 177.
 45. Juhan-Vague I, Alessi MC, Mavri A, Morange PE. Plasminogen activator inhibitor-1, inflammation, obesity, insulin resistance and vascular risk. *J ThrombHaemost*. 2003; 1: 1575–1579.
 46. Oliver JJ, Webb DJ. Noninvasive assessment of arterial stiffness and risk of atherosclerotic events. *Arterioscler. Thromb. Vasc. Biol*. 2003; 23: 554–566.
 47. Strasser B, Arvandi M, Pasha EP, Haley AP, Stanforth P, Tanaka H. Abdominal obesity is associated with arterial stiffness in middle-aged adults. *Nutrition, Metabolism and Cardiovascular Diseases* 2015; 25(5): 495-502.
 48. Recio-Rodriguez J, Gomez-Marcos M, Patino-Alonso M, Agudo-Conde C, Rodriguez-Sanchez E, Garcia-Ortiz L. Abdominal obesity vs general obesity for identifying arterial stiffness, subclinical atherosclerosis and wave reflection in healthy, diabetics and hypertensive. *BMC Cardiovascular Disorders*. 2012;12(1).
 49. Pandit DS, Khadilkar AV, Chiplonkar SA, Khadilkar VV, Kinare AS. Arterial stiffness in obese children: Role of adiposity and physical activity. *Indian J Endocr Metab* 2014;18:70-76.
 50. Wildman R, Mackey R, Bostom A, Thompson T, Sutton-Tyrrell K. Measures of Obesity Are Associated With Vascular Stiffness in Young and Older Adults. *Hypertension*. 2003;42(4):468-473.
 51. Oren A, Vos LE, Uiterwaal CSPM, Grobbee DE, Bots ML. Aortic stiffness and carotid intima-media thickness: two independent markers of subclinical vascular damage in young adults? *Eur J Clin Invest* 2003; 33:949 – 954.
 52. Ryder JR, Dengel DR, Jacobs DR, Sinaiko A, Kelly AS, Steinberger J. Relations among Adiposity and Insulin Resistance with Flow-Mediated Dilation, Carotid Intima-Media Thickness, and Arterial Stiffness in Children. *The Journal of pediatrics*. 2016;168:205-211. doi:10.1016/j.jpeds.2015.08.034.
 53. Jelic S, Bartels MN, Mateika JH, Ngai P, DeMeersman RE, Basner RC. Arterial stiffness increases during obstructive sleep apneas. *Sleep* 2002;25:850–855.