Visceral Fat Accumulation influenced Blood Flow Velocity in Hypertensive Subjects

Hamdon Zulaika[1], Azran Azhim[1]*, A Rahman Rasyada[1], Masatake Akutagawa[2], Takahiro Emoto[2] and Yohsuke Kinouchi[3]

[1]Malaysia-Japan International Institute of Technology, Universiti Teknologi Malaysia, Kuala Lumpur, Malaysia
[2]Department of Life system, Institute of Technology and Science, Tokushima University, Tokushima, Japan
[3]Faculty of Engineering, Tokushima University, Tokushima, Japan
Phone: +603-2203 1295
Email: azhim.kl@utm.my

Abstract

Arterial function measurements are widely used as surrogate markers of cardiovascular disease. However, it is unknown whether non-pathological factor may influence these measurements in particularly blood velocity function. The aim of current study was to investigate the relationship between visceral fat (VF) accumulation and hypertension incidence. The study evaluated the changes of blood velocity waveforms among normotensive and hypertensive subjects. One hundred twenty six individuals were classified into three groups which are lower VF, middle VF and higher VF regarding on their VF level. Resistive index (RI), velocity reflection index (VRI) and vascular elastic recoil index (VEI) were calculated from the 3 minutes assemble average of envelope waveform. The VF accumulation was higher in hypertensive than normotensive subjects. Peak systolic (S1), peak diastolic (D), VRI and VEI modulated significantly ($P < 0.05$) in higher VF compared to lower VF groups. RI and VRI show significantly different in hypertensive compared to normotensive groups. In conclusion, increased VF influences hypertension incidence and blood velocity regulation.

1. Introduction

Adiposity has been linked to hypertension development and arterial stiffness [1-3]. Even though, obese patients have significant adiposity, many of them remain normotensive [4]. In a study by Chandra et al., it is suggested that hypertension is mainly influenced by visceral fat (VF) accumulation compared to subcutaneous adipose tissue and lower body fat [2]. Differences, in distribution of adipose tissue may influence occurrence of hypertension. High accumulations of VF contribute to greater aortic stiffness in older adult as measured by pulse wave velocity (PWV) [3]. Pulse pressure showed the strongest correlation with PWV compared to other blood pressure measurement in normotensive and hypertensive patients with medication [5]. Thus, the PWV provides important hemodynamics information for hypertension management. However, blood flow velocity waveform in untreated hypertensive subjects not well demonstrated.

Although, the VF could be an important factor of increased hypertension incidence, but the blood flow velocity among viscerally normotensive and hypertensive subjects is unclear. Therefore the aim of present study is to investigate the relationship between different viscerally hypertensive groups with flow velocity waveforms.

2. Materials and Methods

2.1 Subject

In this study, 126 subjects participated and classified into three groups with their visceral fat level VF < 4 as lower VF, 4 < VF < 7 as middle VF and VF > 7 as higher VF based on the ranking of visceral fat area [6]. Subjects were recruited through various forms of advertisement. All subjects gave their written informed consent to participate. This study was reviewed and approved by the Ethics Committee of Tokushima University Hospital.

2.2 Measurement System and Data Collection

To measure blood velocity, we used the developed portable measurement system; consisted of a probe, a Doppler signal discriminator (DSD), a transmitter, a receiver, an analog-digital converter and a laptop personal computer [7-11]. The miniaturization of the DSD enabled the blood flow velocity to be monitored during physical exercise and postural changes.

The velocity (Vd) could be estimated from its Doppler shift frequency (fd) using $Vd = c\, fd / (2f0 \cos\theta)$, where c is

the speed of acoustic waves in human tissue (=1540 m/s), f0 is the irradiated ultrasound frequency (=2.0 MHz) and θ is the Doppler insonation angle (=50°).

SBP and diastolic blood pressure (DBP) was measured for the left brachial artery using an automatic blood pressure monitor (Tango, SunTech Medical, US). The mean blood pressure (MBP) and pulse blood pressure (PP) were calculated using DBP+(SBP-DBP)/3 and SBP-DBP, respectively.

Body weight and visceral fat level were measured InnerScan body composition monitors (BC-610, Tanita, Japan). Height was measured to the nearest 0.5cm using a stadiometer (THP-DA, Ogawa Iriki, Japan). The body mass index (BMI) was obtained by dividing the body weight by the square of the height (kg/m2). Waist circumference was measured to the nearest 0.5cm using a 1-cm-wide measuring tape.

2.3 Data Analysis and Characterization of Velocity Features

The envelope waveform of the flow velocity was extracted the spectrogram using a threshold method, was computed using ensemble averaging technique [7, 8]. Blood velocities in CCA were characterized to 5 components waveforms: peak systolic (S1), second systolic (S2), insicura between systole and diastole (I), peak diastolic (D) and end-diastolic (d) velocities [9-11]. Then, these values were used to calculate the following velocity indices: the resistive index (RI) (=1-d/S1), the velocity reflection index (VRI) (=S2/S1-1) and the vascular elastic recoil (VEI) (=1-I/D).

2.4 Statistical Analysis

Data were expressed as means ± standard errors (SE). The differences between VF or hypertensive groups were analysed by one-way ANOVA. Correlation analysis (*r*-value) was performed to examine the relationship between visceral fat and age. A *P*-value less than 0.05 were considered statistically significant. Statistical analyses were performed using SPSS for Windows software (version 21.0; SPSS, Chicago, II, USA)

3. Results

The subjects were classified into three groups based on their VF levels (**Table 1**). Age and height between lower and higher VF groups showed significantly different ($p < 0.05$). The result showed that VF has positive correlation with age ($r = 0.669$). The average weight significantly different across the VF groups where the highest average weight (71.4 ± 10.1 kg) observed in higher VF followed by middle and then lower VF groups. The same pattern also observed in the average WC, where the high VF group had the highest WC (87.24 ± 6.9 cm). Additionally, increased of VF contributed to have higher BMI ($P < 0.05$). As the BMI increased, SBP, DBP and MBP also increased significantly ($P = 0.0001$).

Significant differences of visceral fat in the hypertensive subjects were observed in the present study (**Fig. 1**). The hypertensive subjects the subjects were classified into three groups which are normotensive, prehypertension and hypertension based on their BP status. Increased of VF contributed the higher blood pressure measurements including SBP, DBP and MBP.

Fig. 2 shows hemodynamics data for blood flow velocity in different groups of hypertension. There were significant differences ($P < 0.05$) in the indices RI and VRI between normotensive and hypertensive groups. The S1 and D were decrease significantly ($P < 0.05$) from nomortensive to hypertension groups.

4. Discussions and conclusion

The remarkable finding of the present study is increased visceral fat accumulation influences hypertension incidence and blood flow velocity in common carotid artery. We found that increased VF raise blood pressure measurements including SBP, DBP and MBP with significantly different ($P< 0.05$) between the VF groups (**Table 1**). In previous studies, increased VF result in high SBP, DBP [2, 13], MBP and PP [13]. It is widely known these blood pressure measurements were used in hypertension assessment. Chandra et al. observed the relationship between fat distributions with hypertension incidence. It is suggested that VF was independent fat parameter associated with hypertension

Table 1: Subject Characteristics

	Lower VF	Middle VF	Higher VF
Age (years)	27 ± 9	29±11‡	43±12*
Body mass data			
Height (cm)	161.9±8.5	163.0±6.8‡	169.5±5.5*
Weight (kg)	51.1±5.9	60.4±4.9*‡	71.4±10.1*†
BMI (kg/m^2)	19.4±1.4	22.6±1.5*‡	24.7±2.8*†
WC (cm)	69.6±4.6	78.2±4.4*‡	87.24±6.9*†
BP data (mmHg)			
SBP	109.8±5.8	128.9±5.6*‡	147.6±8.9*†
DBP	68.0±9.1	74.7±9.1*‡	85.3±11.5*†
MBP	109.8±5.8	128.9±5.6*‡	147.6±8.9*†

Data are means ± SD. deviation. Tukey significances: *P<0.05 versus Lower VF, †P<0.05 versus Middle VF and ‡P<0.05 versus Higher VF.

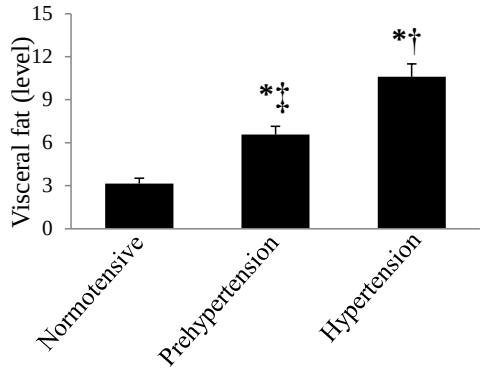

Fig. 1: The visceral fat accumulation influenced in hypertensive subject. *P<0.01 versus normal, †P<0.01 versus prehypertension and ‡P<0.01 versus hypertension. Data are mean ± SE.

incidence while BMI, subcutaneous fat and lower body fat not significantly associated with development of hypertension in multiple regression model [2]. The presence of excess visceral fat may result in dysregulated production of adipocytokines [14]. Lee et al. reported that adipocytokines, lipocalin-2 and MCP-1 were showed a positive correlation with VF with r = 0.288 and r = 0.313 respectively [15]. Both adipocytokines were reported to be associated with incidence of coronary artery disease [16, 17]. This suggesting that higher VF may increased secretion of pro-atherogenic adipocytokines.

Furthermore, we found that hypertensive subjects have strong correlation with the blood flow velocity waveforms. Previous study reveals that VRI had significant different when comparing between control subjects and diseased hypertension [13]. Surprisingly, in the present study VRI and RI showed significantly differences in untreated hypertensive subjects. This is might due to strict selection of subject characteristics by excluding patients with medical history of hypertension and under medication. Frequent intakes of medicine influence the arterial blood flow and blood vessel itself [18]. Yoshihisa et al. reported that cholesterol-lowering pravastatin improved forearm blood flow reserve as early as 4 to 8 weeks after starting the therapy [18]. The effect of oral anti-hypertensive drug, Nifedipine on cerebral blood flow velocity was noted in elderly hypertensive patients using transcranial Doppler [19]. The finding of the currents study shows that the increase in VF affected on the blood flow velocity change. Although the subject number is small, our findings showed significant when dividing the subjects based on VF and hypertension. In conclusion, increased VF influences hypertension incidence, blood flow velocity waveforms and its indices

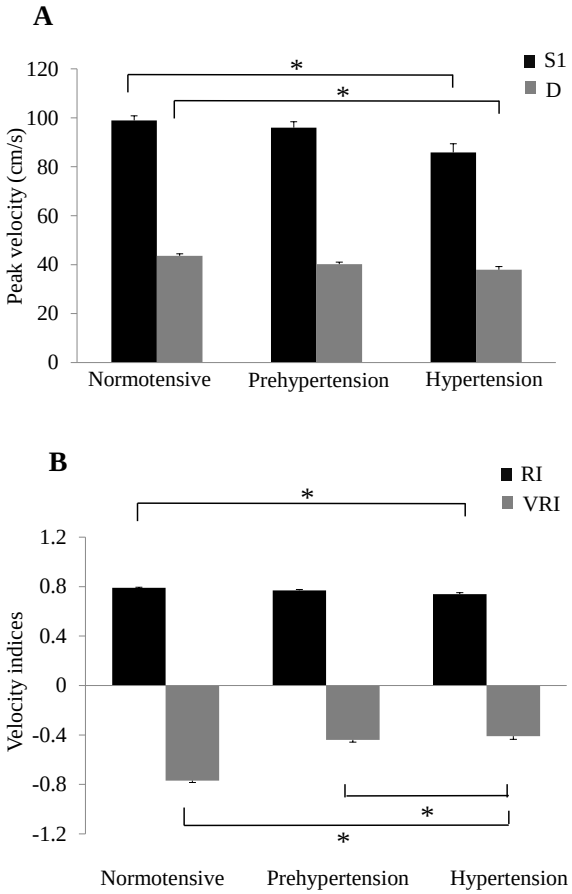

Fig. 2: Differences in blood flow velocity waveforms (A) and its indices (B) between normotensive, prehypertension and hypertension groups.

Acknowledgement

The authors are grateful to the Tokushima University Hospital and Malaysia-Japan International Institute of Technology, UTM, Malaysia for its financial supports.

References

[1] L. R. Krafoff (2014) Adiposity and Risk for Hypertension. J. of American Collage Cardiology. 64:10:1003-1004

[2] A. Chandra, I. J Neeland, J. D. Berry, C. R. Ayers, A. Rohatgi, S. R. Das, A. Khera, D. K. McGuire, J. A. de Lemos, A. T. Turer (2014) The Relationship of Body Mass and Fat Distribution With Incident Hypertension; Observations From the Dallas Heart Study, J. of The American College of Cardiology, 64:10: 997-1002.

[3] K. Sutton-Tyrrell, A. Newman, E. M. Simonsick, R. Havlik, M. Pahor, E. Lakatta, H. Spurgeon, P. Vaitkevicius (2001), Aortic Stiffness Is Associated with Visceral Adiposity in Older Adults Enrolled in the Stuidy of Health, Aging and Body Composition. American Heart Association, 38:429-433.

[4] N. Richard (2009), Obesity-Related Hypertension. The Ochsner Journal. 9:3:133-136.

[5] E. J. Kim, C. G. Park, J. S. Park, S. Y. Suh, C. U. Choi, J. W. Kim, S. H. Kim, H. E. Lim, S. W. Rha (2007), Relationship Between Blood Pressure Parameters and Pulse Wave Velocity in Normotensive and Hypertensive Subjects: Invasive Study. J. of Huamn Hypertension. 21: 141-148.

[6] The North American Association for the Study of Obesity (NAASO), 2004

[7] A. Azhim, A. Ueno, M. Tanaka, A. Masatake and Y. Kinouchi (2011). Evaluation of blood flow velocity envelope in common carotid artery for reference data. Biomed. Signal Process. Control, vol. 6, 2, pp. 209-215.

[8] A. Azhim, M. Akutagawa, Y. Hirao (2008) Measurement of Blood Flow Velocity Waveforms in the Carotid, Brachial and Femoral Arteries during Head-Up Tilt. J of Biomed & Pharm Eng. 2:1-6

[9] A. Azhim, M. Katai, M. Akutagawa, Y. Hirao, K. Yoshizaki, S. Obara, M. Nomura, H. Tanaka, H. Yamaguchi and Y. Kinouchi, "Exercise improved age-associated changes in the carotid blood velocity waveforms, "J. Biomed. Pharm. Eng., vol. 1-1, pp. 17-26, 2007

[10] A. Azhim, Y. Utsunomiya, K.Akioka (2008) Influence of aging and gender on blood velocity in the human common carotid artery: accounted for body size. J. of Aging and Physical Activity 16:30

[11] A. Azhim, M. Akutagawa, Y. Hirao (2007) Exercise Improved Age-associated Changes in the Carotid Blood Velocity Waveforms. Journal of Biomedical & Pharmaceutical Eng. 1:17 – 26

[12] W.W Nichols and M.F. O'Rourke, (2005) McDonald's Blood Flow in Arteries: Theoretic Experimental and Clinical Principles, 5th ed, Hodder Arnold, London.

[13] A. Azhim, K. Sakagami, A. Ueno, Y. Kinouchi and Y. Fukui (2013). Independent Factors of Flow Velocity Indices in common carotid Artery. World Congress on Medical Physics and Biomedical Engineering. 39:445-448.

[14] A. Hiuge-Shimizu, K. Kishida, T. Funahashi, M. Okutsu, R. Kametani,H. Kobayashi, Y. Nozaki, A. Nomura, H. Yokoi7, T. Yoshizumi, T. Ohira, T. Nakamura, Y. Matsuzawa, S. Sumitsujiand Iichiro Shimomura (2012) Coexistence of Visceral Fat and Multiple Risk Factor Accumulations is Strongly Associated with Coronary Artery Disease in Japanese (The VACATION-J Study). J. of Atherosclerosis and Thrombosis 19:657-663.

[15] Y. Lee, S. Lee, E. S. Jung, J. Kim, C. Y. Shim, Y. Ko, D. Choi, Y. Jang, N. Chung and J. Ha (2010) Visceral Adiposity and the severity of Coronary Artery Disease in Middle-aged Subjects with Normal Waist Circumference and Its Relation with Lipocalin-2 and MCP-1. J. of Atherosclerosis. 213:592-597.

[16] A.L Hemdahl, A. Gabrielsen, C. Zhu (2006) Expression of Neutrophil Gelatinase Associates Lipocalin in Atherosclerosis and Myocardial Infarction. J. of Arteriosclerosis. 26: 136-178

[17] C. Herder, J. Baumert, B. Thorand (2002) Chemokines and Incident Coronary Heart Disease. J. of Atherosclerosis. 26: 2147-2150

[18] Y. Matsuzawa, T. Funahashi and T. Nakamura.(2011) The Concept of Metabolic Syndrome: Contribution of Visceral Fat Accumulation and Its Molecular Mechanism. 18:8:629-639

[19] A.Yoshihisa (2007). Difference in early effect of statin therapy on coronary and forearm flow reverse in postmenopausal hypercholesterolemia women, Cir. J.,71:6:954-61