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Flow Velocity in Common Carotid Artery

A. Rahman Rasyada and Azran Azhim

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Abstract

A significant blood flow disruption as seen in cardiovascular diseases and disorders is related to hemodynamic dysfunction. Gender influences the arterial hemodynamic functions. Understanding of gender-related differences in blood flow and pressure is crucial in the prevalence and burden of cardiovascular disease. This chapter presents about characteristic profile of carotid flow velocities to extend the fundamental understanding of arterial hemodynamic functions in gender differences. Comparison of both synchronized carotid blood flow velocity and blood pressures at normodynamics state are introduced to contribute to targeted therapeutic goal based on gender. Gender-related differences in body size has influenced on arterial hemodynamics in carotid artery. Body height has influenced on systolic blood pressure, pulse pressure, wave reflection, pulse wave velocity in carotid artery. Carotid blood flow velocities are largely accounted for not only body height but also body weight. The predictors for modulating blood flow velocities were not only limited to age, but also influenced by several body compositions that largely accounted for the gender-related differences including visceral fat, muscle mass and total body fat. These data may useful to effective prevention and management of cardiovascular disease by considering the gender-difference.

Keywords: flow velocity, common carotid artery, health, gender, body composition

1. Introduction

Hemodynamic is dealing with blood flow and forces concerned therein to circulate blood through the cardiovascular system. A significant blood flow disruption as seen in cardiovascular diseases and disorders is related to hemodynamic dysfunction. Doppler ultrasound has potential to serve as a non-invasive method for detecting and quantifying blood flow functions in cardiovascular diseases. However, the use of blood flow in clinical application is limited and development of blood flow is prevailing rather than blood flow [1].

Gender influences the arterial hemodynamic functions. Cardiovascular disease is a leading cause of death for both women and men, but there are crucial gender-related differences in the prevalence and burden of cardiovascular disease. An approach to understand this disparity is to evaluate the underlying changes in hemodynamic functions and discover the relationship between the gender differences and cardiovascular disease risk. Gender-related differences in systolic blood pressure (SBP) are reported in previous studies [2, 3]. It is widely reported that gender differences in blood pressures (i.e. SBP and pulse pressure) and arterial wave reflections are associated to smaller body height of women [4–6].

Azhim et al. have developed a Doppler measurement system to evaluate flow velocity functions in common carotid artery with synchronized monitoring of blood pressure (BP) and electrocardiogram (ECG) [6, 7]. Firstly, this chapter presents about characteristic profile of carotid flow velocities in an attempt to extend the fundamental understanding of arterial hemodynamic functions in gender differences. Secondly, comparison of carotid flow velocity and other parameters at resting posture in gender are introduced. The extent to which body size including body height and weight have influenced on blood velocities in carotid artery is described in Section 3. Furthermore, the blood flow velocity also useful for comparing the effect of fat compositions in gender differences as presented in Section 4.

2. Normohemodynamics in gender

In hemodynamics studies, abnormality of blood flow can be detected from Doppler waveforms, vascular structure and function may be identified through various quantitative measurements made [1, 8]. This section does not focus on hemodynamic disorders, aging, and response to exercise or during exercise. But, the findings do fill important literature gap in correlation between gender-related differences with hemodynamic variables. The normohemodynamics of carotid artery and other parameters are determined in healthy sedentary subjects to rule out the effects that exercise may have on the dependent variables. From a total of 85 sedentary subjects, 49 of them are men.

The Doppler frequency shift represents temporal changes in peak velocities of blood cells movement during particular cardiac cycle. Several analytic techniques have been proposed for analyzing the velocity waveform. Most of these techniques involve analysis of maximum velocity at particular points on Doppler waveforms described as peak velocity envelope. By using the developed measurement system by Azhim et al., carotid blood flow velocity was measured simultaneously with commercialized ECG by three-leads and brachial BP [6, 7]. Measurements of ECG and BP were used as reference data. To extract peak velocity values from its velocity spectra, a threshold method and computation using ensemble averaging technique was implemented in this study. As shown in **Figure 1**, 30 consecutive cardiac cycles were selected from 2 minutes spectral to characterize the feature points of peak velocity envelope and calculate its indices. In this study, flow velocities in carotid artery were characterized into five feature points [9, 10]. The first peak systolic velocity wave was peak velocity S1. It represents the maximum velocity during systole. Consequently it is usually used as an ejection parameter in cardiac systole [11]. An augmented velocity in late systole wave was the

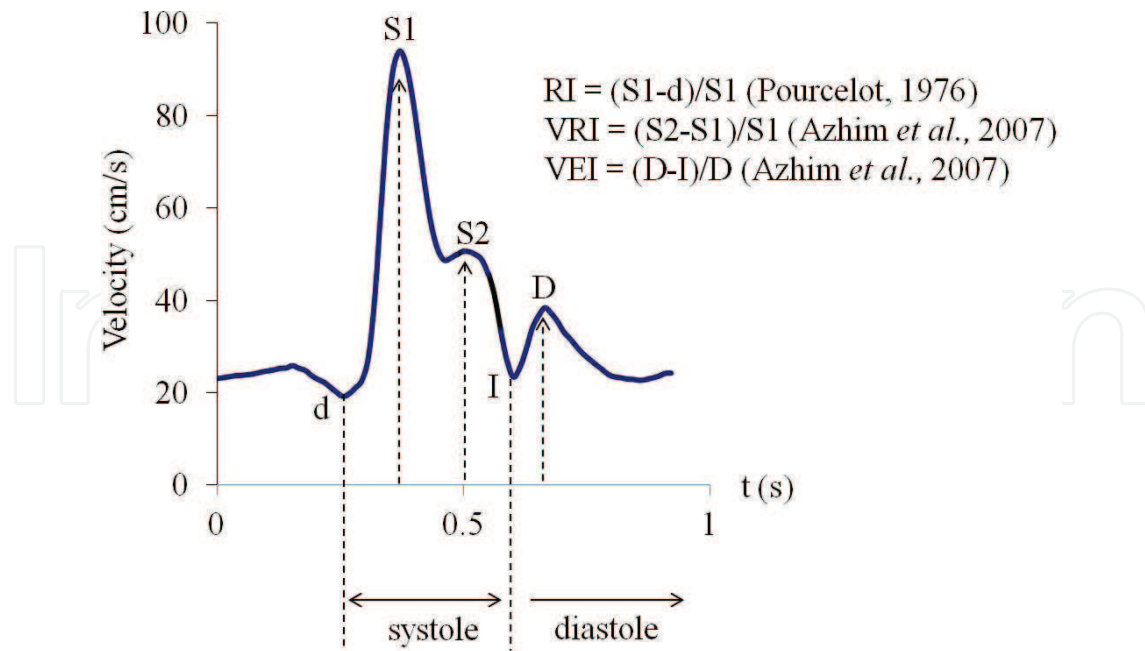


Figure 1. Doppler indices derived from peak systolic velocity (S1), second systolic (S2), insicura between systole and diastole (I), peak diastolic (D) and end-diastolic (d) velocities.

second systolic velocity S2. Augmentation of S2 was related to both reflection of pulse wave velocity at branching site and reflection of pressure wave [1, 9]. The peak diastolic velocity, D velocity was the maximum velocity which rises due vascular elastic recoil during cardiac diastole, insicura between systole and diastole (I) [9] and the end-diastolic velocity, d represents the minimum velocity during diastole [9, 11].

Usually blood velocity indices or ratios were derived from various combinations of the peak systolic velocity, end-diastolic velocity, and temporal mean values of the maximum Doppler frequency shift envelope [11, 12]. Of various indices, resistance index (RI) has been used extensively to measure the pulsatility that reflects the resistance to blood flow [12]. RI has defined range limit which is between value of 0–1.0. It was suggested to be used for analyzing waveforms with continuous forward flow throughout the diastole such as in carotid artery [8]. Unlike S1/d ratio as developed by Stuart and Drumm [13], RI shows Gaussian distribution and therefore can be analyzed through parametric statistical analyses. The RI data also reported to have better discriminatory performance compared to pulsatility index (PI) data [11]. Velocity reflection index (VRI) and velocity elastic index (VEI) were first proposed by [9] to evaluate aging and exercise effects. The VRI was a relation with S1 and S2 which calculated from $(S2 - S1)/S1$. The validation of VRI was analyzed using linear regression analysis. It increased with pressure reflection wave of augmentation index ($r^2 = 0.836$). The latter index was calculated from $(D - I)/D$. It corresponds to vascular elasticity properties during cardiac diastole [9] as shown in **Figure 1**. Because of the velocity features are obtained from same cardiac cycle, the indices are independent of insonation angle [11].

Rough reference of gender-related differences in hemodynamic characteristics is summarized in **Table 1**. As previously we have reported that carotid flow velocities have influenced by multiple effects including regular exercise, aging and visceral fat accumulation [7, 14–16], the

Variable	Women (n = 36)	Men (n = 49)	p-value
Age (years)	35.2 ± 1.9	38.4 ± 2.2	NS
Height (cm)	157.9 ± 0.9	168.8 ± 0.9	<0.01
Blood pressure data			
SBP (mmHg)	118.5 ± 2.4	129.2 ± 2.1	<0.01
DBP (mmHg)	73.7 ± 1.8	80.5 ± 1.8	<0.05
MBP (mmHg)	89.0 ± 2.0	96.7 ± 1.9	<0.01
HR (bpm)	73.8 ± 2.1	73.6 ± 1.6	NS
Flow velocity data			
d (cm/s)	23.7 ± 0.8	18.9 ± 0.7	<0.01
S1 (cm/s)	96.9 ± 3.2	91.2 ± 3.1	NS
S2 (cm/s)	64.3 ± 2.0	50.0 ± 1.8	<0.01
I (cm/s)	35.6 ± 1.3	27.5 ± 0.9	<0.01
D (cm/s)	45.6 ± 1.2	39.1 ± 1.0	<0.01
RI	0.750 ± 0.010	0.785 ± 0.009	<0.05
VRI	-0.318 ± 0.026	-0.423 ± 0.028	<0.05
VEI	0.223 ± 0.016	0.298 ± 0.017	<0.01

Data are presented as mean ± standard error of mean. The *p*-value indicates significance difference versus women. NS indicates not significant. d: end-diastolic velocity; S1: peak systolic velocity; S2: second systolic velocity; I: incisura between systole and diastole; D: peak diastolic velocity; RI: resistive index; VRI: velocity reflection index; VEI: vascular elasticity index.

Table 1. Differences in hemodynamic characteristics in women and men.

presented data of hemodynamics differences in gender are also considering the influenced effects of that. The age differences is taken into account by matching the age variable with keeping not significant mean and low standard error. The range subjects' age for men and women are 20–58 years (38.4 ± 2.2) and 20–64 years (35.2 ± 1.9) respectively. Generally men are taller than women.

Study of blood pressure to explain gender-related differences in arterial hemodynamic functions is prevailing than blood flow velocity. It has been reported that hemodynamic dysfunction increases with SBP [17]. Women have a lower SBP when measured in both brachial and ankle-arm and pressure index than age-matched men [2]. Gender-related differences in body height has influenced to arterial hemodynamics such as SBP, pulse pressure, wave reflection and pulse wave velocity in carotid artery [4, 5]. We found that the gender differences in arterial hemodynamics in carotid flow velocities are largely accounted for body height and weight [6, 7].

With increases of blood pressure in men, all velocity waveforms were homeostatically lower. Men and women have different envelope velocity waveforms in carotid artery shown in **Figure 2**. In this study, we found that women have a lower brachial SBP than men, but higher

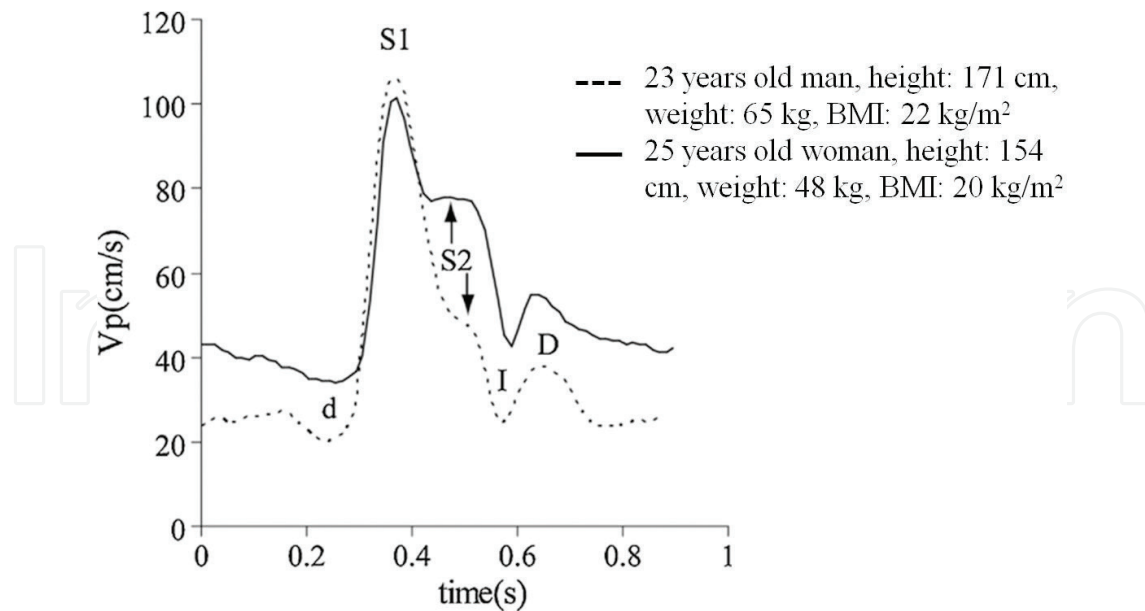


Figure 2. Comparison of typical envelope velocity waveforms in carotid artery for age-matched man (dashed line) and woman (solid line). d: end-diastolic velocity; S1: peak systolic velocity; S2: second systolic velocity; I: insicura between systole and diastole; D: peak diastolic velocity. Adapted from Azhim et al. [7].

d, S2, I and D velocities. Therefore, women have lower RI and VEI, and had higher VRI than men. Consistent with previous studies, pressure wave reflection and propagation are known to be correlated with body height [2, 3, 18], Azhim et al. also suggests that the reflected wave in flow components was higher in women and is significantly correlated with body height [7]. Men have been reported to have more elastic arterial trees than women [2, 7].

3. Arterial hemodynamic changes: role of body size

Effective regulation of blood flow and blood pressure in order to maintain homeostasis is a primary aspect of cardiovascular health. In general young women have lower resting blood pressure [19–21] and in response to physiological changing [22]. The systolic and diastolic BP increased in response to the graded, incremental tilt and the difference observed between men and women is reflective of differences in body size (i.e. in particular height) as shown in **Figure 3** [22]. Epidemiological studies based on brachial artery pressure indicate that blood pressures were lower in young women than in age-matched men [2, 6]. Generally, SBP and pulse pressure increased as a pulse travels from aorta towards the peripheral, the increase being all the more pronounced as the distance of pulse propagation [2].

Changes in velocity envelope waveforms at peak systolic velocity, augmented velocity in late systole wave (i.e. S2) and end-diastolic velocity are focused on their relationship with aging and carotid diseases [23]. Addition to S1, d velocities and its index (i.e., RI) decreasing with age, S2, D velocities and its indices (i.e., VRI and VEI) decrease continuously with age that may increase the complication in cardiovascular disease risk [7]. Only few studies have considered the latter velocities and indices in association with gender or disease [22, 24]. To the best of our knowledge, no other studies have characterized the correlations of these velocities with

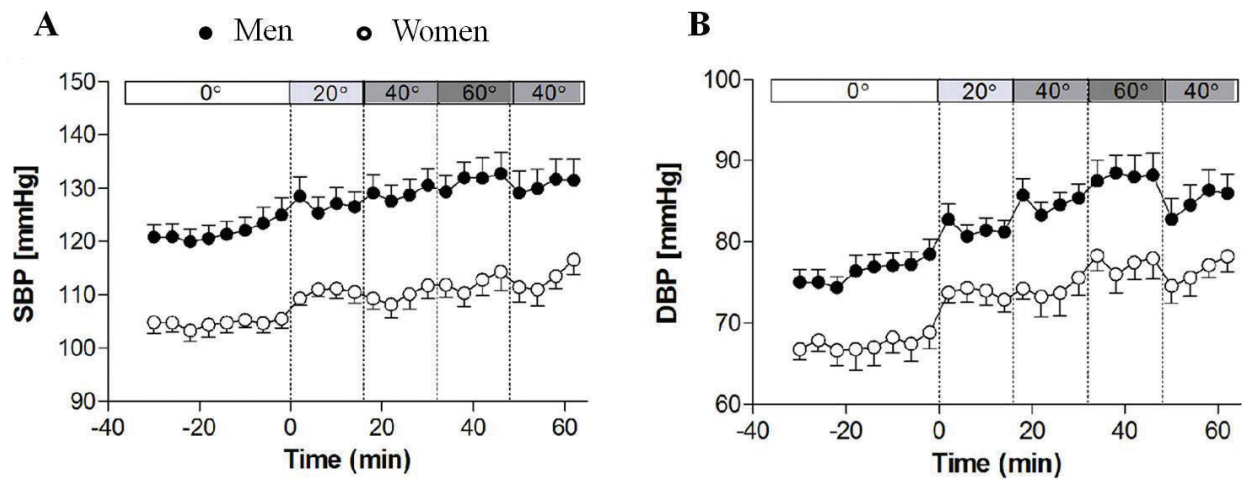


Figure 3. Blood pressure variability in response to graded, incremental tilt in healthy young men ($n = 13$) and women ($n = 10$). (A) Systolic blood pressure and (B) diastolic blood pressure. Tilt angle is indicated in the bar above each panel (i.e., 0° (resting posture), 20° , 40° , 60° , and back to 40°). Adapted from Sarafian and Miles-Chan [22].

gender, age, visceral fat accumulation and exercise [7, 16]. In this study, we found significant differences in the carotid velocity waveforms of age-matched men and women to contribute to clinical evaluations and healthcare monitoring [6].

Women had larger reflected waves than men, in part due to shorter body height and closer physical proximity between heart and reflecting sites. However, body height was not sufficient to fully explain higher reflected wave flow and pressure in women. In the study we indicated that the reflected wave had higher in women and was significantly correlated to body height and weight as described in **Figures 4** and **5** [6]. In addition to knowledge that pressure wave reflection and propagation are known to correlate with body height [2, 3], we also found that increased reflected flow wave was partially influenced by decreased body

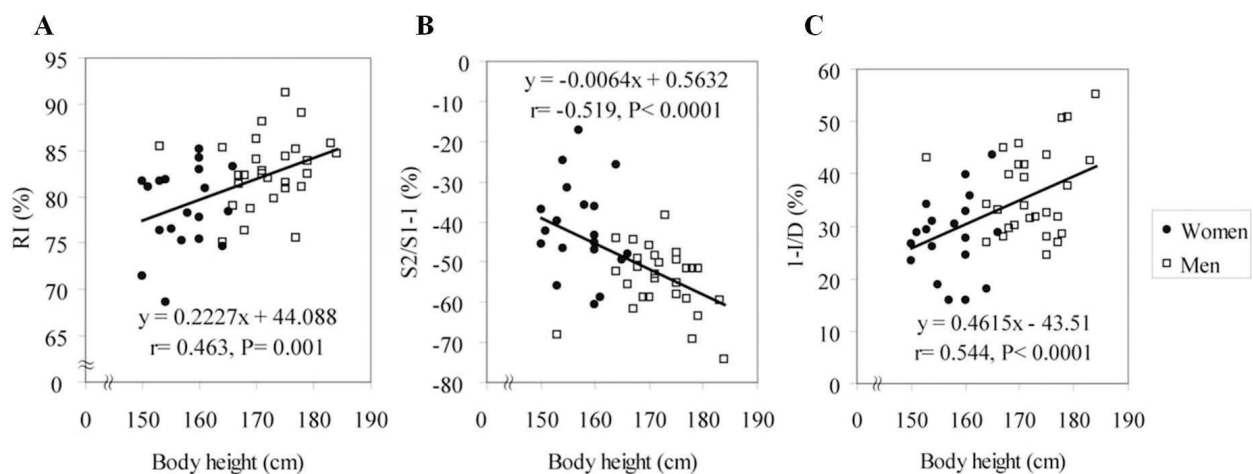


Figure 4. The velocity indices correlated with height. (A) RI: resistive index ($1 - d/S1$); (B) VRI: velocity reflection index ($S2/S1 - 1$); (C) VEI: vascular elasticity index ($1 - I/D$). Men ($n = 30$) are represented by open circles and women ($n = 20$) represented by closed circles. Adapted from Azhim et al. [6].

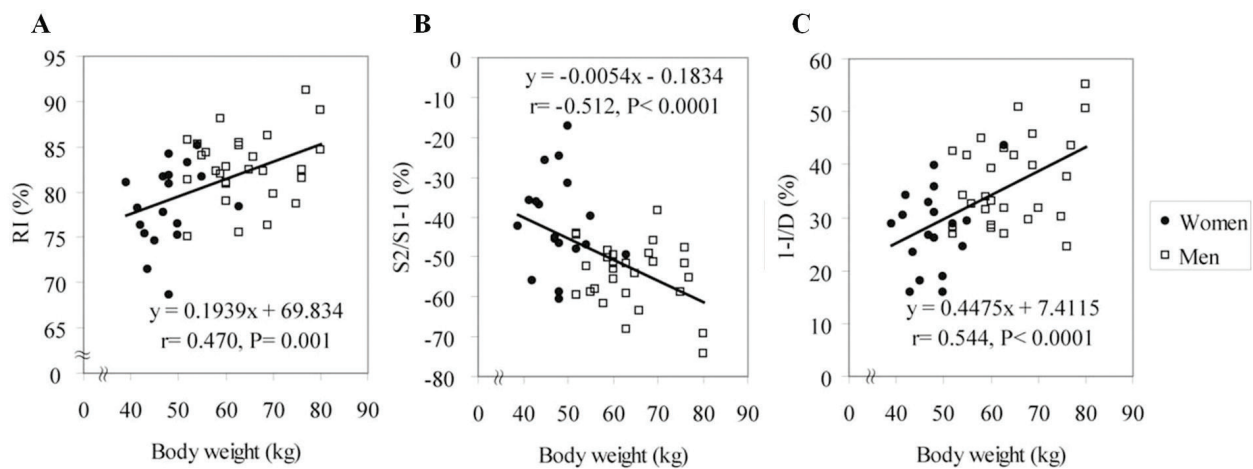


Figure 5. The velocity indices correlated with weight. (A) RI: resistive index ($1 - d/S1$); (B) VRI: velocity reflection index ($S2/S1 - 1$); (C) VEI: vascular elasticity index ($1 - I/D$). Men ($n = 30$) are represented by open circles and women ($n = 20$) represented by closed circles. Adapted from Azhim et al. [6].

weight and increased heart rate level [6]. It had been reported that women had lower carotid artery distensibility compared with men [25]. From the proposed velocity indices (i.e. VEI), we agreed that women had lower arterial elasticity [6, 7]. The difference in the velocities and its indices were related to smaller body size in women that largely accounted for the gender differences. The difference in velocity indices may also contributed by concentrations of estrogen in women hormone status of women [26].

4. Arterial hemodynamic changes: role of body compositions

Although the risk for cardiovascular disease increases with age, occurrence and burden of cardiovascular disease may possibly higher in men as described by differences in blood flow velocities and blood pressures [2, 7]. Furthermore body fat composition in the specific body region could explain underlying relationship between the gender-related differences and cardiovascular disease risk such as hypertension [15, 27]. Men tend to accumulate upper body fat which mainly around the abdominal area in the form visceral fat (VF), whereas women tend to have fat deposited in the gluteofemoral region [28, 29]. In the Framingham Heart Study indicated that small differences in VF among three different body mass index classifications; normal-weight, overweight or obese groups can significantly change health risk profile including hypertension [30]. It also widely known that VF increase with aging and associated with clinical features of metabolic variables including elevated triglyceride, glucose and reduced high density lipoprotein [31, 32]. The presented data in **Table 2** is to demonstrate a rough reference of gender-related differences in body compositions in sedentary healthy subjects. Men showed a greater body mass index, weight and muscle mass. An alternative to general indication of abdominal VF is waist circumference measurement. The prevalence of having higher VF and waist circumference in men was dominant. But, women showed higher total body fat.

Variable	Women (n = 36)	Men (n = 49)	p-Value
VF (level)	3.1 ± 0.3	8.0 ± 0.7	<0.01
Weight (kg)	52.0 ± 1.1	65.2 ± 1.5	<0.01
BMI (kg/m ²)	20.8 ± 0.4	22.8 ± 3.2	<0.01
WC (cm)	72.5 ± 1.2	81.0 ± 1.3	<0.01
Total body fat (kg)	28.2 ± 0.7	19.2 ± 0.8	<0.01
Muscle mass (kg)	34.0 ± 1.1	49.7 ± 0.8	<0.01
TCho (mmol/L)	191.4 ± 6.8	194.3 ± 5.6	NS
LDL (mmol/L)	97.2 ± 7.6	109.8 ± 5.3	<0.01

Data are presented as mean ± standard error of mean. The *p*-value indicates significance difference versus women. NS indicates not significant. VF: visceral fat; BMI: body mass index; WC: waist circumference; TCho: total cholesterol; LDL: low-density lipoprotein cholesterol.

Table 2. Differences in body compositions in women and men.

Extensive research in obesity when elucidating hypertension showed that site-specific fat accumulation is more important rather than total body fat [27]. Chandra et al. demonstrated that hypertension is mainly influenced by VF accumulation compared to lower body fat and subcutaneous fat [27]. The VF is also associated to coronary heart disease and systemic arteriosclerosis [33, 34]. Consequently, VF accumulation contributed to greater aortic stiffness in older adult as measured by pulse wave velocity [35]. Comparison data of gender difference is essential to provide rough indication risk of developing health problems related to fat composition.

It is widely known from literature that rising blood pressure is associated with increased cardiovascular disease risk. Women has lower blood pressures, homeostatically higher velocity waveforms with the heart rate did not comparable different than men. The VF and age were two important determinants for increase in blood pressures in our study as shown in **Table 3**.

Variable	Predictor	β	<i>p</i>	<i>r</i> ²
SBP (mmHg)	Constant	107.35	<0.001	0.304
	VF (level)	1.30	0.002	
	Age (years)	0.26	0.045	
DBP (mmHg)	Constant	60.64	<0.001	0.354
	Age (years)	0.34	0.002	
	VF (level)	0.78	0.017	
MBP (mmHg)	Constant	76.21	<0.001	0.359
	Age (years)	0.31	0.005	
	VF (level)	0.95	0.005	

Beta (β) value indicates regression coefficient. The *p*-value less than 0.05 indicates predictor variable has significant association with hemodynamic variable. SBP: systolic blood pressure; DBP: diastolic blood pressure; MBP: mean blood pressure.

Table 3. Stepwise linear regression analysis of blood pressure measurements.

Similar to this study, association between VF and blood pressures is found consistently in some studies [16, 27]. Using multiple regression analysis, VF becomes superior predictor to hypertension compared to lower body fat and subcutaneous fat in other study [27]. Aging is associated with a significant increase in the prevalence of hypertension and especially of systolic hypertension in elderly [36]. Elevation of blood pressure with aging is mostly associated with structural and functional changes in the arteries like large artery stiffness [9, 37]. However, the predictors for modulating blood flow velocities were not only limited on age, but also influenced by several body compositions that largely accounted for the gender differences as presented in **Table 4**.

To evaluate the predisposing factors for flow velocity in common carotid artery, stepwise regression analysis was performed with the following parameters: age, muscle mass, VF and

Variable	Predictor	β	p	r^2
d (cm/s)	Constant	30.45	<0.001	0.168
	Muscle mass (kg)	-0.22	<0.001	
S1 (cm/s)	Constant	125.93	<0.001	0.355
	Age (years)	-0.87	<0.001	
S2 (cm/s)	Constant	95.36	<0.001	0.308
	Muscle mass (kg)	-0.79	<0.001	
I (cm/s)	Constant	46.55	<0.001	0.193
	Muscle mass (kg)	-0.36	<0.001	
D (cm/s)	Constant	46.98	<0.001	0.251
	VF (level)	-0.86	<0.001	
RI	Constant	0.76	<0.001	0.341
	Age (years)	-0.002	<0.001	
	Muscle mass (kg)	0.002	<0.001	
VRI	Constant	-0.58	<0.001	0.667
	Age (years)	0.01	<0.001	
	Muscle mass (kg)	-0.01	<0.001	
	Total body fat (kg)	0.004	0.045	
VEI	Constant	0.24	<0.001	0.344
	Age (years)	-0.004	<0.001	
	Muscle mass (kg)	0.004	<0.001	

Beta (β) value indicates regression coefficient. The p -value less than 0.05 indicates predictor variable has significant association with hemodynamic variable. d: end-diastolic velocity; S1: peak systolic velocity; S2: second systolic velocity; I: insicura between systole and diastole; D: peak diastolic velocity; RI: resistive index; VRI: velocity reflection index; VEI: vascular elasticity index.

Table 4. Stepwise linear regression analysis of blood flow velocity measurements.

total body fat. This study found that VF is an important predictor that inversely related to carotid peak diastolic velocity waveform. Using the proposed index by Azhim et al., peak diastolic velocity, D is an important feature waveform to determine arterial elasticity [7]. Consequently poor arterial elasticity is attributed by accumulation of VF [16, 32] and lower arterial elasticity through its index, VEI is observed in women compared to men. Vaidya et al. also reported the same results where postmenopausal women had lower carotid elasticity compared to matched-age men based on its carotid distensibility [38]. This study can only speculate that the difference in this index could also be influenced by the sex hormone stimulation [38].

Women had greater vascular reflection wave using the proposed index (i.e. VRI) and second systolic velocity compared with men (see **Table 1**). The augmentation of second systolic flow velocity in carotid artery was related to wave reflection arriving from the lower body or thoracic aorta [39]. The wave reflection in women was related to shorter body height that reflects shorter distance to reflecting site [2, 3]. However, body height was not fully explaining the higher VRI. Significant correlations were observed between body composition variables and VRI, with age, muscle mass and total body fat also contributing to stepwise model for VRI.

Muscle mass found to be correlated with all blood flow velocities and blood pressures, but not with S1 velocity, likely due to a greater range of muscle mass among men. Interestingly, muscle mass was a stronger predictor for the most correlated blood flow velocities and indices, except for D velocity and all blood pressures. In agreement with the findings, study of healthy adults was shown an inversely correlation between thigh muscle mass and aortic pressure from wave reflections when characterized by augmentation pressure and its index [40]. By physiology and anatomy studies, left ventricular hypertrophy was observed in women via ventricular remodeling [41, 42] and had higher systolic left ventricular chamber function compared to men [43]. These factors might contribute consistent increase in the first velocity wave during systole in women. Furthermore RI was significantly lower due to increase of S1 velocity in women ($RI = 1 - d/S1$).

5. Conclusion

In conclusion, monitoring of blood flow velocity and blood pressure synchronized measurements may be potential to support the assessment of some main hemodynamic functions in gender difference. A fundamental understanding of gender-related differences in arterial hemodynamics is required for effective prevention and detection of cardiovascular disease at the early stage. Women have lower brachial blood pressure components than men, but higher d, S2, I and D velocities. Therefore, women have lower resistive and vascular elastic indices and had higher velocity reflection than men. Gender difference in arterial hemodynamics in carotid velocity waveforms is largely accounted for body size in particular height and weight. Furthermore unlike blood pressures, the predictors for modulating blood flow velocity not limited on age and VF factors, but also influenced by muscle mass and total body fat. Improvable screening of health problem can be achieved by monitoring the blood flow velocity together with blood pressure measurements and considering its gender-difference to fully assessing hemodynamics function in circulatory system.

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Conflict of interest

The authors do not have any conflict of interest.

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