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Influential factors for pressure pulse waveform in healthy young adults

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Abstract. The effects of gender and other contributory factors on pulse waveform are still under arguments. In view of different results caused by few considerations of possible influential factors and general agreement of gender relating to pulse waveform, this study aims to address the confounding factors interfering with the association between gender and pulse waveform characteristics. A novel method was proposed to noninvasively detect pressure pulse wave and assess the morphology of pulse wave. Forty healthy young subjects were included in the present research. Height, weight, systolic blood pressure (SBP), and diastolic blood pressure (DBP) were measured manually and body mass index (BMI), pulse blood pressure (PP) and heart rate (HR) were calculated automatically. Student's t test was used to analyze the gender difference and analysis of variance (ANOVA) to examine the effects of intrinsic factors. Univariate regression analysis was performed to assess the main factors on the waveform characteristics. Waveform features were found significantly different between genders. However this study indicates that the main factors for time-related and amplitude-related parameters are HR and SBP respectively. In conclusion, the impact of HR and SBP on pulse waveform features should not be underestimated, especially when analyzing the gender difference.

Keywords: Pressure pulse waveform, gender, heart rate, systolic blood pressure, pulse blood pressure

1. Introduction

The correlation between rhythm and morphology of pulse wave and cardiovascular disease has been reported by many researchers [1-3]. For healthy adults, upper-limb pulse wave usually has three main peaks: systolic peak, tidal wave and dicrotic wave, as described in Figure 1 [4, 5]. The discrepancy of pulse waveform between genders has been described by former studies [5-8], which, however, still remains a major bone of contention. Hayward, et al. [7] indicated that augmentation index (AI) had a higher value in men than that in women; while Katsuhiko's finding [9] was against the result.

Besides gender-related difference, recent studies have also investigated a couple of intrinsic factors that would influence pulse waveform, for instance, aging, obesity, smoking, blood pressure, and exercise [5, 8, 10-14]. However, most of these studies are concerned about insufficient variants of

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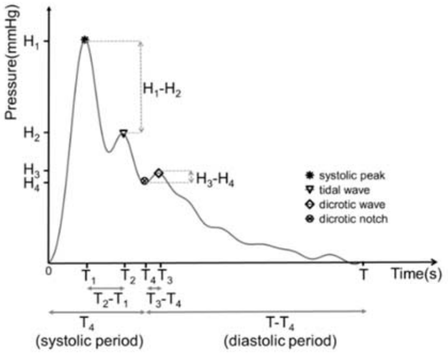

Fig. 1. Annotated brachial arterial pulse pressure waveform.

physical measurements associated with pulse waveform. Therefore, the aim of this research is to assess the effect of possible physical measurements, including height, weight, body mass index (BMI), systolic blood pressure (SBP), diastolic blood pressure (DBP), pulse blood pressure (PP) and heart rate (HR) on healthy young men and women, which may be the main cause of pressure pulse waveform and may lead to gender difference in healthy young adults.

2. Method

2.1. Subjects and clinical measurements

A total of 40 healthy young adults (20 men, 20 women) were recruited in this study after giving informed consent. None of the participants was smoker or alcoholic. Height and weight were measured before the experiment, and then BMI was calculated.

Before clinical measurements, subjects were asked to keep still for three minutes lying supine in a comfortable bed. Brachial SBP and DBP were obtained in the left brachial artery using a mercury sphygmomanometer (YUYUE medical equipment & supply Co., Ltd, Jiangsu, China). All the measurements were conducted in a quiet room by an experienced operator. PP was calculated by SBP minus DBP. Left and right brachial-ankle pulse wave velocities (baPWV) were measured using an automatic arteriosclerosis detector MB3000 (M&B Electronic Instruments Co., Ltd, Beijing, China). Four cuffs with a low pressure (under DBP) were wrapped around both upper arms and ankles to obtain pulse wave signals simultaneously for more than 30 seconds. Time delay between brachial artery and homolateral posterior tibial artery (T_{ba}) was averaged in successive 10 periods. The distance from brachial artery to homolateral posterior tibial artery and baPWV were calculated automatically by Eqs. (1) [15] and (2). Mean baPWV was depicted as the mean value of left and right baPWV. HR was determined from the trough of the pulse wave in successive 8 periods.

$$D_{\mathrm{ba}} = 0.593 \times Height\ (\mathrm{cm}) + 14.37 \tag{1}$$

$$\mathrm{baPWV} = D_{\mathrm{ba}}/T_{\mathrm{ba}} \tag{2}$$

Before the examination, exercise, alcohol and caffeine-containing beverages were forbidden. The demographic characteristic and general clinical data were displayed in Table 1. No significant difference in age, BMI, HR or mean baPWV between genders were found. However, height, weight,

Table 1

Demographic Characteristics

	Gender Men (mean ± SD)	Women (mean ± SD)	p-Value
Number of Subjects	20	20	NS
Age (years)	24.3±1.6	24.2±1.2	0.739
Height (cm)	175.6±6.7	161.1±3.3	0.000
Weight (kg)	67.5±10.5	54.0±6.8	0.000
BMI (kg/m^2)	22.2±2.3	20.8±2.5	0.069
Brachial SBP (mmHg)	114.0±8.1	97.4±7.4	0.000
Brachial DBP (mmHg)	69.4±6.5	60.7±6.3	0.000
Brachial PP (mmHg)	44.6±10.1	36.7±7.0	0.007
HR(beats/min)	65.6±7.9	66.9±9.6	0.642
Mean baPWV(cm/s)	949.9±89.2	899.5±80.0	0.067

SBP, DBP and PP in young men were significantly higher than those in young women.

2.2. Supra-systolic blood pressure pulse wave and preprocessing

The participants were asked to stay calm and quiet breathing before and during the testing. After taking five minutes rest, the brachial pressure pulse wave was measured in a supine position and recorded with MB3000, which applied a cuff to the left upper arm with a cuff pressure of 35 mmHg higher than brachial SBP [16]. The cuff pressure pulse wave was stored in a computer at a sampling rate of 1000 Hz for more than 1 minute, and then de-noised by a low-pass filter with the cut-off frequency at 10 Hz. Baseline wander mainly caused by the slight leak of cuff was removed.

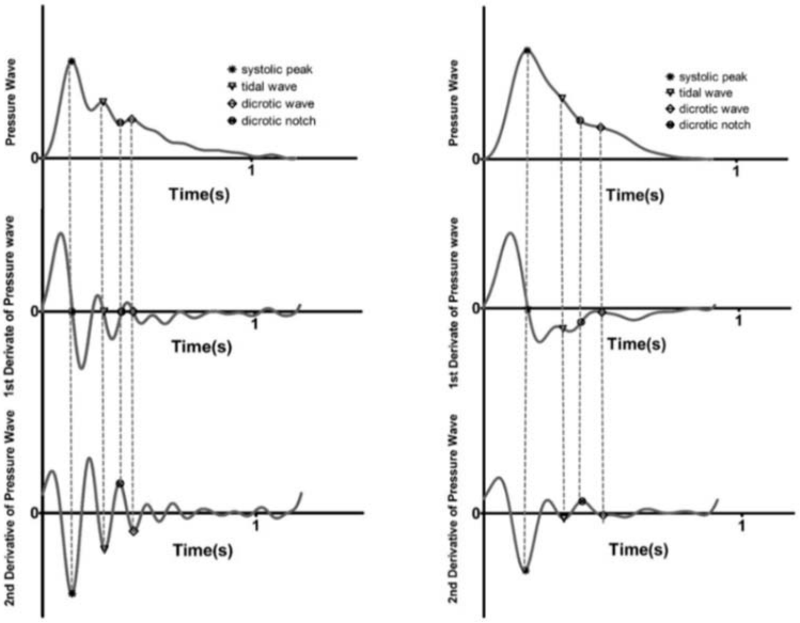

Fig. 2. Illustration of two types of feature extraction on pulse waveform. The left panel shows the waveform with pronounced tidal wave, dicrotic wave, and dicrotic notch, which was mainly identified by the first derivative of pulse waveform; the right panel demonstrates the situation that tidal wave and dicrotic wave are extracted from the second derivative of pulse waveform.

2.3. Feature extraction and pulse waveform parameters

The first and second derivatives of pulse wave were calculated to extract critical features [3-5, 17]. The foot point and systolic peak were detected as a pair of zero-crossing points in the first derivative of pressure wave in each period [3, 18]. When cuff pressure was raised to a supra-systolic level, a tidal wave after the first systolic peak would appear in the late systole (see Figure 2) [16, 19], which had been used to assess aortic stiffness [19, 20]. If the tidal wave was notable, it would be defined as the second point that crosses zero in the first derivative; or it was recorded as the minimal value of the second derivative after systolic peak. Dicrotic notch and dicrotic wave were portrayed as the paired maximum and minimum value of second derivative after tidal wave, respectively [21]. All algorithms used to process the signal were realized under Matlab platform (MATHWORKS INC, Natic, USA).

The following 13 parameters extracted from pressure pulse waveform were calculated for statistical analysis (see Table 2). (1) Time-related parameters: T_1/T, T_2/T, T_3/T, T_4/T, $(T_1- T_2)/T$, $(T_3- T_4)/T$, $(T-T_4)/T$ and $T_4/(T-T_4)$. (2) Amplitude-related parameters: H_2/H_1, H_3/H_1, H_4/H_1, $(H_1-H_2)/H_1$ and $(H_3-H_4)/H_1$. All thirteen indices were calculated by averaging the results from the 8 successive periods.

2.4. Statistical analysis

All statistical tests were performed with SPSS (IBM corp., USA). All of the data were presented as number or mean ± standard deviation. Differences of pulse waveform characteristics between genders

Table 2

Definition and physiological significance of pulse waveform feature parameters

Parameters	Definition	Physiological significance
T_1/T	Normalized time interval between trough and peak	Systolic wave transit time associated with heart ejection capability[3, 22]
T_2/T	Normalized time interval between trough and tidal wave	Arrival time of tidal wave associated with peripheral vascular resistance
T_3/T	Normalized time interval between trough and dicrotic wave	Arrival time of dicrotic wave associated with peripheral vascular resistance
T_4/T	Normalized time interval between trough and dicrotic notch	Systole [8, 13]
H_2/H_1	Ratio of amplitude tidal wave to amplitude peak	Reflection index (RI), associated with peripheral vascular resistance [8]
H_3/H_1	Ratio of amplitude dicrotic wave to amplitude peak	Another definition of RI [12]
H_4/H_1	Ratio of amplitude dicrotic notch to amplitude peak	Amplitude of dicrotic notch[13]
$(T_2-T_1)/T$	Normalized time interval between peak and tidal wave	Pulse transit time[16, 23]
$(T_3-T_4)/T$	Normalized time interval between dicrotic wave and dicrotic notch	Unknown
$(T-T_4)/T$	Normalized time interval between dicrotic notch and trough in next period	Diastole [8, 13]
$T_4/(T-T_4)$	Ratio of time interval between trough and dicrotic notch and time interval between dicrotic notch and trough in next period	Ratio of systole to diastole [13]
$(H_1-H_2)/H_1$	Normalized amplitude difference between peak and tidal wave	Augmentation index (AI), associated with aortic stiffness [12,16,22]
$(H_3-H_4)/H_1$	Normalized amplitude difference between dicrotic wave and dicrotic notch	Another definition of AI [24]

Table 3

Mean values of parameters derived from pulse waveform by gender

Parameters	Gender		p-Value
	Men	Women	
T_1/T	0.16±0.02	0.17±0.02	0.123
T_2/T	0.32±0.04	0.33±0.04	0.780
T_3/T	0.48±0.05	0.51±0.05	0.125
T_4/T	0.40±0.04	0.41±0.05	0.367
H_2/H_1	0.44±0.13	0.56±0.13	**0.008**
H_3/H_1	0.37±0.07	0.38±0.08	0.603
H_4/H_1	0.32±0.09	0.37±0.08	0.112
$(T_2\text{-}T_1)/T$	0.16±0.02	0.16±0.02	0.366
$(T_3\text{-}T_4)/T$	0.09±0.01	0.10±0.01	**0.001**
$(T\text{-}T_4)/T$	0.60±0.04	0.60±0.05	0.363
$T_4/(T\text{-}T_4)$	0.66±0.11	0.70±0.13	0.335
$(H_1\text{-}H_2)/H_1$	0.56±0.13	0.44±0.13	**0.008**
$(H_3\text{-}H_4)/H_1$	0.04±0.04	0.01±0.04	**0.016**

Note: Bold values denote significant differences between genders ($p<0.05$).

were analyzed using the student's t test. Two-way ANOVA was used to assess the effects of clinical factors (height, weight, BMI, SBP, DBP, PP and HR) on all the extracted feature waveform characteristics. Univariate regression analysis was performed to assess the main factor for the waveform parameters associated with multiple clinical measurements. The p-value of <0.05 was considered statistically significant.

3. Result

Gender difference in pulse waveform was validated in our study. When examining the difference of indices derived from pulse waveform between genders, H_2/H_1 and $(T_3\text{-}T_4)/T$ were significantly lower in men than those in women ($p<0.05$), respectively. Notable gender difference was also found in $(H_1\text{-}H_2)/H_1$ and $(H_3\text{-}H_4)/H_1$, which were higher in men than that in women ($p<0.05$, respectively). The mean values of feature parameters by genders were listed in Table 3.

Table 4

ANOVA analysis for time-related and amplitude-related parameters

Parameters	Height	Weight	BMI	SBP	DBP	PP	HR
T_1/T	NS	NS	NS	NS	NS	NS	**0.000**
T_2/T	NS	NS	NS	NS	NS	NS	**0.000**
T_3/T	NS	NS	NS	NS	NS	NS	**0.000**
T_4/T	NS	NS	NS	NS	NS	NS	**0.000**
H_2/H_1	**0.007**	NS	NS	**0.043**	NS	NS	NS
H_3/H_1	NS	NS	NS	**0.016**	NS	**0.012**	NS
H_4/H_1	**0.046**	NS	NS	**0.017**	NS	NS	NS
$(T_2\text{-}T_1)/T$	NS	NS	NS	NS	NS	NS	**0.000**
$(T_3\text{-}T_4)/T$	**0.035**	**0.008**	NS	**0.003**	NS	**0.014**	**0.002**
$(T\text{-}T_4)/T$	NS	NS	NS	NS	NS	NS	**0.000**
$T_4/(T\text{-}T_4)$	NS	NS	NS	NS	NS	NS	**0.000**
$(H_1\text{-}H_2)/H_1$	**0.007**	NS	NS	**0.043**	NS	NS	NS
$(H_3\text{-}H_4)/H_1$	**0.019**	NS	NS	NS	NS	NS	NS

Note: Bold values denote significant differences between genders ($p<0.05$).

This result indicated that gender was not the only cause of pulse waveform variation; HR, SBP, height, and PP may also have influence on the waveform parameters. Table 4 listed the ANOVA analysis results, indicating the influence of clinical measurements (including height, weight, BMI, SBP, DBP, PP and HR) on the waveform features. Indices T_1/T, T_2/T, T_3/T, T_4/T, $(T_2-T_1)/T$, $(T-T_4)/T$, $(T_3-T_4)/T$ and $T_4/(T-T_4)$ were mostly susceptible to HR. Indices H_2/H_1, H_3/H_1, H_4/H_1, $(T_3-T_4)/T$ and $(H_1-H_2)/H_1$ were influenced by SBP. Height has impact on H_2/H_1, H_4/H_1, $(T_3-T_4)/T$, $(H_1-H_2)/H_1$ and $(H_3-H_4)/H_1$. Besides, H_3/H_1 and $(T_3-T_4)/T$ were also influenced by PP.

For the waveform parameters influenced by multiple factors, the main factor was analyzed by univariate regression (Table 5). SBP was the main factor for all amplitude-related parameters except H_3/H_1. PP was superior to SBP as the main factor for H_3/H_1. Time-dependent parameter $(T_3-T_4)/T$ was mainly related to HR. However, no significant main factor was found in $(H_3-H_4)/H1$, indicating that it might be mainly influenced by other unknown factors or co-effects. In general, the main factors for waveform characteristics were inclined to SBP or HR, other than gender.

4. Discussion and conclusion

This research demonstrated the confounding factors that could cause the differences on brachial pulse waveform between genders in young adults and verified that the main causes of time-related and amplitude-related parameters are HR and SBP respectively. The pressure pulse waveform was acquired by a cuff with supra-systolic pressure. As a new noninvasive method to detect pulse morphology, supra-systolic pulse wave was validated to resemble the blood pressure wave in brachial artery by Fuyou Liang on modeling study [16, 23]. The pulse waveform derived in this study showed the same morphology with Fuyou Liang's modeling study and experiment signals on healthy young adults.

No difference of arrival time of dicrotic wave between genders was found in this study, which was

Table 5

Main factors for parameters

Parameters	Clinical Influences	P-Value
H_2/H_1	Height	0.330
	Gender	0.126
	SBP	**0.014**
H_3/H_1	SBP	0.003
	PP	**0.002**
H_4/H_1	Height	0.024
	SBP	**0.009**
$(T_3-T_4)/T$	Height	0.070
	Gender	0.024
	Weight	0.485
	SBP	0.088
	PP	0.040
	HR	**0.000**
$(H_1-H_2)/H1$	Height	0.330
	Gender	0.131
	SBP	**0.015**
$(H_3-H_4)/H1$	Height	0.335
	Gender	0.837

Note: Bold values denote the main factors to each parameter.

different from the results in Park's work that the value of this parameter was higher in women than that in men [5]. Previous studies generally accepted the difference of pulse waveform between genders and analyzed the waveform separately [5], while this research focused on the main cause of pulse waveform and figured out the impact of gender is inferior to HR or SBP on time-related and amplitude-related parameters. Unlike the population in Yim's work [8], no significant difference of HR was discovered between young men and young women in this demography. Present study confirmed that the gender difference of time-dependent parameter, manifested by time lag between dicrotic notch and dicrotic wave, actually is more susceptible to HR, other than gender. It is widely accepted that the change in systole and diastole caused by HR change is non-uniform. Furthermore, time-related parameters are still related to HR significantly after normalization as demonstrated in this research. Present work also supported Hayward's research that men have a higher value in AI ($(H_1\text{-}H_2)/H_1$ in this study) than women [7], which can be ascribed to the inequality of SBP between genders. SBP is associated with mechanical properties of the arterial wall and is related to the reflection wave. For example, it is verified that a higher SBP will lead to an increase of AI [25]. This finding will benefit future studies on cardiovascular diseases which may lead to the change of HR or SBP. For instance, inflammation is verified to be the risk factor of arterial stiffness [26] and is always combined with an increase of HR. In this state, time-related parameters may change as the disease progresses.

Nevertheless, this study has potential limitations. Firstly, the participants of this experiment are aged in their 20s. Studies on elder groups are also needed to assess the gender difference with a wider age distribution. Secondly, only healthy subjects are recruited for the sake of controlling variables. A more comprehensive research on pathological subjects is also needed for the application of pulse wave features to cardiovascular disease. Further studies with a larger demographic sample are essential to verifying the main factors for pulse waveform.

In conclusion, this study demonstrates that gender difference exists in some parameters that indicate cardiovascular diseases, however, physical measurements, especially HR and SBP, are the disruptive factors when analyzing gender difference of pulse waveform in young adults. The impact of HR and SBP on pulse waveform should not be underestimated when analyzing the characteristics of pulse wave in both healthy subjects and cardiovascular patients. Awareness of the effects of intrinsic factors on pulse waveform is helpful to understanding the changes of cardiac cycle and mechanism of pulse wave propagation, and may contribute to cardiovascular modeling and pathological diagnosis in future studies.

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