Med & Health 2016; 11(2): 218-231 https://doi.org/10.17576/MH.2016.1102.11

ORIGINAL ARTICLE

The Assessment of Finger Photoplethysmography Fitness Index (PPGF) among Young Men with Cardiovascular Disease Risk Factors: A Cross Sectional Study

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ABSTRAK

Dua petanda kesihatan salur darah baru yang dihasilkan daripada gelombang fotopletismografi jari (PPG) telah diperkenalkan berdasarkan populasi rakyat Malaysia iaitu indeks kecergasan PPG (PPGF) dan indeks jangkaan risiko salur darah (VRPI). Antara objektif kajian ini adalah untuk mengkaji hubungan antara PPGF dengan petanda penyakit jantung (CVD) yang lain seperti halaju gelombang denyutan karotid femoral (PWVCF), untuk membandingkan PPGF antara mereka yang sihat dan mempunyai faktor risiko CVD dan untuk menentukan sensitiviti VRPI dalam mengenalpasti mereka yang mempunyai faktor risiko CVD. Seramai 114 lelaki berumur antara 20 hingga 40 tahun yang sihat atau mempunyai mempunyai faktor risiko CVD telah diambil. Faktor risiko CVD termasuk hipertensi, merokok, dislipidemia, obesiti abdomen dan sejarah keluarga berpenyakit CVD pramatang. Subjek dibahagikan kepada kumpulan sihat, mereka yang mempunyai satu faktor risiko dan mereka yang mempunyai dua atau lebih faktor risiko. Berat, tinggi, tekanan darah (BP) periferi dan pusat, PWVCF dan PPGF mereka diukur dan sensitiviti VRPI dalam mengenal pasti mereka yang berisiko CVD dikira. Data dianalisis dengan menggunakan SPSS versi 15 dan nilai $P<0.05$ adalah signifikan. Purata umur subjek adalah 28.94 ± 4.86 tahun. Tiada perbezaan pada PPGF didapati antara kumpulan-kumpulan ($p > 0.05$). Pembolehubah tidak bersandar untuk PPGF adalah tekanan hadapan (Beta = 0.35, $p < 0.01$), PWVCF (Beta = -0.26, $p < 0.01$), BP sistolik (Beta = -0.26, $p = 0.04$) dan ketinggian (Beta = 0.24, $p < 0.01$). Sensitiviti VRPI adalah 82.02%. Kesimpulannya, PPGF adalah berkait dengan PWVCF dan berpotensi untuk menjadi petanda kekenyalan arteri. Tambahan lagi,

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VRPI adalah sensitif untuk digunakan sebagai petanda untuk saringan awal faktor risiko CVD.

Kata kunci: fotopletismografi, kardiovaskular, orang muda

ABSTRACT

Two new vascular health markers which are derived from finger photoplethysmography (PPG) waveform have been introduced based on Malaysian population, namely PPG fitness index (PPGF) and vascular risk prediction index (VRPI). The objectives of this study were to investigate the associations between PPGF and other cardiovascular disease (CVD) markers such as carotid femoral pulse wave velocity (PWV_{CF}), to compare PPGF between those with and without CVD risk factors and to determine the sensitivity of VRPI in identifying young subjects with CVD risk factors. A total of 114 men age 20 to 40 yrs with and without CVD risk factors were recruited. Risk factors included hypertension, smoking, dyslipidemia, abdominal obesity and family history of premature CVD. Subjects were divided into healthy, those with one risk factor and those with at least two risk factors. Their weight, height, peripheral and central blood pressure (BP), PWV_{CF} and PPGF were measured and the sensitivity of VRPI in predicting subjects with CVD risk factor was calculated. Data was analyzed via SPSS version 15 and $p < 0.05$ was considered significant. The mean age of the subjects was 28.94 ± 4.86 yrs. No differences in PPGF was observed between groups ($p > 0.05$). The independent variables for PPGF were forward pressure (Beta = 0.35, $p < 0.01$), PWV_{CF} (Beta = -0.26, $p < 0.01$), systolic BP (Beta = -0.26, $p = 0.04$) and height (Beta = 0.24, $p < 0.01$). The sensitivity of VRPI was 82.02%. In conclusion, PPGF was correlated to PWV_{CF} and may be a potential marker of arterial stiffness. In addition, VRPI is sensitive to be used as an early screening of CVD risk factors.

Keywords: cardiovascular, photoplethysmography, young adults

INTRODUCTION

Cardiovascular disease (CVD) is still the most common cause of mortality worldwide (Santulli 2013). This may be attributed to the increase in the prevalence of CVD risk factors such as hypertension, dyslipidemia, smoking and obesity (Berry et al. 2012; Santulli 2013). Among the young population, lack of health screening may also predispose to increase CVD prevalence and they may present with advanced stage of the disease (Kuklina et al. 2010). Thus, there is a requirement to develop a screening method that is simple, non-invasive, reproducible and less time consuming.

The assessment of vascular function via finger photoplethysmography (PPG) has gained popularity since this method has the characteristics mentioned above at significantly lower cost. PPG detects blood volume changes of the

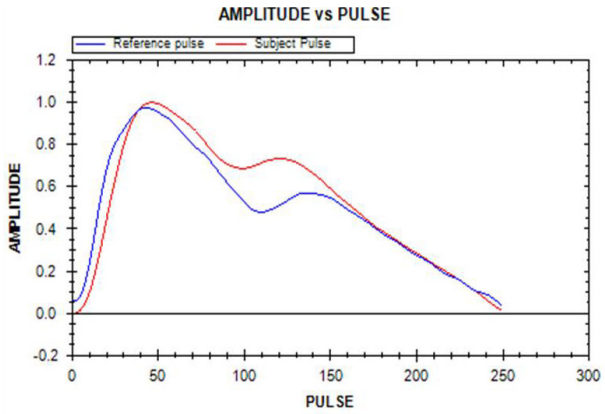

Figure 1: Single PPGF Plot (Blue: 19 year old healthy reference pulse; Red: target subject).

finger arterial bed and is influenced by several factors such as ventricular ejection, aortic and peripheral arterial stiffness (AS), peripheral arterial resistance and blood viscosity (Elgendi 2012; Millasseau et al. 2002). Several common parameters that were derived from finger PPG are stiffness index (SI), reflection index (RI), crest time and a, b, c, d and e waves, and all were proposed to be indices of vascular function and vascular ageing (Millasseau et al. 2002; Brillante et al. 2008; Baek et al. 2007; Hashimoto et al. 2005; Takazawa et al. 1998; Tsai et al. 2007).

Recently, Chellappan et al. (2008) has introduced another parameter designated as PPG fitness index (PPGF). PPGF was derived from AC component of PPG morphological changes against a healthy 19-yr-old reference (gender specific) identified from study population as seen in Figure 1 (Chellappan et al. 2008). PPGF also has a good reproducibility record (Chellappan 2010). Compared to the previous PPG waveforms parameters, PPGF was derived by analyzing the entire waveforms and not concentrating on a specific part; e.g. systolic or diastolic component. The potential of derived PPGF was further improved through empirical modeling to produce a vascular health indicator named vascular risk prediction index (VRPI) (Chellappan 2009). An aged based empirical model was established among Malaysian population, which has been named as Model 1 for age group between 19 to 44 and Model 2 for 45 to 66 yrs. Hypertension, diabetes mellitus, hypercholesterolemia, obesity and smoking are the CVD risk factors considered in this model development and were compared with the healthy subjects. VRPI classified the subject into very low risk, low risk, moderate risk or high risk to have CVD risk factor (Chellappan 2009). VPRI was derived from the regression analysis, the difference between the observed PPGF value and the predicted PPGF value which is called the residual [risk score (e)]. In this study, we have selected Model 1 to be tested among young men with CVD risk factor from Malaysian population (Chellappan 2009) (Table 1).

CVD is closely related with atherosclerosis. Atherosclerosis involves inflammatory reactions in

Table 1: Vascular risk prediction index for Model 1 (19 to 44 yrs)

	Risk Score
Very low risk	Risk score 6
Low risk	6 < Risk score 16
Moderate risk	16 < Risk score 22
High risk	Risk score > 22

every step (Stoger et al. 2012; Drechsler et al. 2010). In advanced lesion, there is development of fibrous tissue and calcification and these structural changes may lead to functional disability which can be measured as arterial stiffness (Crowther 2005; Zieman et al. 2005). Based on this knowledge, several established markers of CVD were found such as C-reactive protein (CRP), carotid intima media thickness (CIMT), pulse wave velocity (PWV) and augmentation index (AI) (Anderson et al. 2009; Polak et al. 2011; Kaptoge et al. 2010). CRP is an inflammatory marker, PWV and AI are markers of arterial stiffness/vascular function and CIMT is an atherosclerotic marker. However, all these markers either need an invasive procedure (needle prick), experience technician (CIMT, PWV) or expensive device (CIMT, PWV, AI). These factors may limit the screening process among the subjects especially in an open and large scale setting.

Chellappan et al. (2008) proposed that PPGF and VRPI can be used as assessment of vascular health to detect vascular dysfunction. However, further validation is important before PPGF and VRPI can be incorporated as vascular health screening tools. Therefore, this study assessed the correlations between PPGF and other CVD risk markers namely CRP, CIMT, PWV and AI. This study also aimed to investigate the independent variables of PPGF which are still unknown, but theoretically related to ventricular ejection and aortic stiffness. Lastly, this study compared the PPGF among subjects with and without CVD risk factors and assessed the sensitivity of VRPI in predicting subjects with CVD risk factors.

MATERIALS AND METHODS

Ethical approval was obtained from the Ethics Committee of Universiti Kebangsaan Malaysia Medical Centre (Project Code: FF-262-2011). Subjects were recruited around Klang Valley which is an urban and the most densely populated area in Malaysia. The recruitments were made through public health screening. Subjects were men aged between 20 to 40 yrs, who were healthy or had any CVD risk factor. CVD risk factors include systolic or diastolic blood pressure (BP) 140/90 mmHg or on antihypertensive medication, abdominal obesity (waist circumference > 90 cm), smoker, dyslipidemia (Total cholesterol > 6.2 mmol/L or low density lipoprotein > 4.1 mmol/L or triglyceride > 1.7 mmol/L or high density lipoprotein < 1.02 mmol/L) or family history of premature CVD (Aminuddin et al. 2014). These risk factors may affect peripheral and central vascular functions and cause vascular damage, that may be detected by PPGF. Exclusion criteria were: CVD, diabetes mellitus and any chronic inflammatory diseases. These factors were excluded since they are associated with advanced vascular

damage and contradict with the focus of this study which was screening for early vascular lesion. Sample size was 24 subjects per group as calculated by using a published formula based on previous paper on PPGF (Eng 2003; Chellappan et al. 2008). Subjects were divided into three groups, healthy subjects (HG), subjects with one risk factor (G1) and subjects with at least two risk factors (G2) and this was done to determine whether PPGF has the ability to differentiate these groups.

ETHICS, CONSENT AND PERMISSIONS

All the subjects gave written informed consent for their participation.

MEASUREMENT OF BODY WEIGHT, HEIGHT AND WAIST CIRCUMFERENCE

On the day of the procedure, the subjects were asked to fast and to avoid smoking for at least six hrs. Weight was measured by using digital scale (SECA, German). Height was measured by using a wall-mounted stadiometer (SECA, German) with the subjects not wearing shoes. Body mass index (BMI) was then calculated by dividing weight with height (kg/m^2). Waist circumference (WC) was measured by using a measuring tape over the bare midriff midway between the lowest rib and iliac crest at the end of normal expiration.

MEASUREMENT OF BLOOD PARAMETERS

Blood was taken from the antecubital vein after fasting for at least eight hrs. Samples were sent to Gribbles Pathology Laboratory, Petaling Jaya for estimation of total cholesterol (TC), low density lipoprotein (LDL), high density lipoprotein (HDL), triglyceride (TG), high sensitivity C reactive protein (hs-CRP) and fasting blood sugar (FBS). The details of the method for the blood test was published earlier (Aminuddin et al. 2014).

MEASUREMENT OF CENTRAL BLOOD PRESSURE (BP), AUGMENTATION PRESSURE, AUGMENTATION INDEX AND FORWARD PRESSURE

Subjects were asked to lay supine. A blood pressure cuff (Vicorder system, SMT Medical, Wuerzburg, Germany) was put on the right arm of the subject for measurements of the brachial systolic and diastolic BP (bSBP/bDBP) via oscillometric method. The system also recorded the brachial pressure waveforms which were then transformed to the aortic pressure waveforms by using a brachial-to-aortic generalized transfer function and calibrated to brachial mean BP and DBP for the estimation of central SBP (cSBP), DBP (cDBP) and central pulse pressure (cPP). The estimated aortic pressure waveform was also used to measure augmentation pressure (AP) and forward wave pressure (P1) (Figure 2) (Aminuddin 2015). AI was measured as [(augmentation pressure (AP) /pulse pressure x 100] (Laurent et al. 2007).

MEASUREMENT OF PWV_{CF}

This measurement was done using Vicorder system (SMT Medical, Wuerzburg, Germany). The subjects

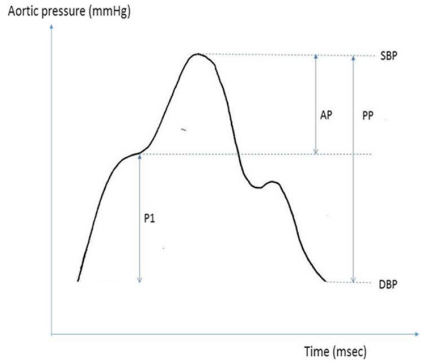

Figure 2: Aortic blood pressure waveform (AP=augmentation pressure, PP=pulse pressure, SBP=systolic blood pressure, DBP=diastolic blood pressure, P1=forward pressure).

were asked to lie supine with head propped up at 45°. A neck cuff was placed around the neck at the level of common carotid area, while a thigh cuff was placed at the upper thigh. The distance between the suprasternal notch and mid-thigh cuff was determined by using a measuring tape (D). The time taken for the pressure wave to travel from the aorta to the femoral artery was measured from the foot to foot of the pressure wave (T) by the system. PWV_{CF} was then calculated by the system as D over T (m/s).

MEASUREMENT OF PPGF

The measurement was done in a room with controlled temperature between 20-25°C. The subject was in supine position. After resting for five mins, the PPG probe was attached to the left index finger of the subject and measurement was done for 120 secs. The signals were acquired through the serial port of pulse-oximeter modules (NiVaRiX 1.0, Universiti Kebangsaan Malaysia). The system was connected to a personal computer running the application developed by the manufacturer of the NiVaRiX 1.0. The sampling rate was 100 Hz and the resolution was 16 bits. PPGF was derived by using real-time PPG signal with age as a confounding factor since age is a non-modifiable risk factor of CVD. The application also provided an estimation of VRPI. VRPI consisted of very low risk, low risk, moderate risk and high risk, which refer to the risk of having any risk factor of CVD (Chellappan 2009).

MEASUREMENT OF CIMT

Measurement was done with subjects lying supine with head supported with one pillow in a dimmed-light room. CIMT was defined as the distance between lumen-intima interface and media-adventitia interface. A guideline for measurement of CIMT published by American Society of Echocardiography was adopted (Stein et al. 2008). Intima-media thickness of the right and left common carotid arteries (CCA) were measured using B mode ultrasound (Vivid-I) via linear array probe (10 MHz). The CIMT measurement was done with

Table 2: Subjects' classification based on clinical characteristic and VRPI results for sensitivity and specificity analysis.

Subjects' characteristic	VRPI results	Classification
Have any CVD risk factor	positive	TP
No CVD risk factor	negative	TN
No CVD risk factor	positive	FP
Have any CVD risk factor	negative	FN

Positive= Low/moderate/high risk, negative= very low risk
TP= true positive, TN=true negative, FP=false positive, FN=false negative

the subject's head lifted upwards and turned slightly to the contralateral side. CIMT measurement was done on the smallest vessel diameter (diastole) by using a caliper on the far wall of the CCA. Three measurements were taken within one cm proximal to the carotid bulb in the right (RCIMT) and left CCA (LCIMT) and the average were calculated on each side. All measurements were done by a single trained technician.

STATISTICAL ANALYSIS

The normality of the data was checked using Kolmogorov-Smirnov test. All the data were presented as mean SD, except for hs-CRP which was in median interquartile range as it was not normally distributed. Hs-CRP value was also log transformed and was used in further analysis. Data were analyzed via SPSS version 15. The differences between groups were compared by ANOVA, and when adjustment for confounders were needed then ANCOVA was used. Age and race were important confounders for all the vascular properties. In addition, based on previous studies, heart rate was important confounder for PWV and AI (Tomiyama et al. 2010; Laurent et al. 2007) and height was important confounder for AI (Laurent et al. 2007). Post-hoc Gabriel analysis was done for parameters that were significant between groups ($p<0.05$). Associations between the markers were determined by Pearson correlation *r*. Multiple linear regression was used to determine the independent variables of PPGF.

SENSITIVITY AND SPECIFICITY ANALYSIS

The sensitivity of VRPI to detect those with CVD risk factor was calculated as [true positive (TP)/ (TP + false negative)] x 100% and the specificity was calculated as [true negative (TN)/ (TN + false positive)] x 100%. In the present study, positive result refers to those having VRPI at either low risk, moderate risk or high risk and negative result refers to those having VRPI at very low risk. As this study is focused on young subjects, low risk is also considered as a positive result. True positive were those with CVD risk factor and VRPI results were low/moderate/high risk. True negative refers to those without CVD risk factor and VRPI result was very low risk. False positive refers to those without CVD risk factor but VRPI results were low risk/moderate risk/ high risk. False positive refers to those with CVD risk factor but VRPI results were very low risk (Table 2).

Table 3: General characteristics of the subjects.

	şHG (25)	G1 (27)	G2 (62)	P
Age (years)	27.00 4.97	28.75 4.90	29.84 4.62[a]	0.04
HR (bpm)	67.50 10.68	67.07 13.01	69.67 8.19	0.45
bSBP (mmHg)	122.96 9.37	126.74 10.03	130.11 10.63[a]	0.01
bDBP (mmHg)	71.15 7.93	72.67 7.51	75.65 7.62[a]	0.03
bMAP (mmHg)	91.65 8.00	94.19 7.80	98.19 8.27[a]	<0.001
cSBP (mmHg)	113.27 8.78	116.37 8.43	121.21 9.50[a]	0.001
cDBP (mmHg)	71.15 7.93	72.67 7.51	75.65 7.62[a]	0.03
WC (cm)	79.81 5.83	85.27 6.20	96.17 12.86[a,b]	0.001
BMI (kg/m^2)	22.12 2.52	24.18 2.61	28.98 5.12[a,b]	0.001
TC (mmol/L)	5.03 0.50	5.09 0.69	5.52 0.91[a,b]	<0.01
TG (mmol/L)	0.93 0.29	1.15 0.57	1.64 0.80[a,b]	0.001
HDL (mmol/L)	1.33 0.25	1.13 0.26[c]	1.04 0.22[a]	0.001
LDL (mmol/L)	3.27 0.38	3.43 0.64	3.73 0.86[a]	0.02
FBS (mmol/L)	4.77 0.39	4.72 0.41	4.61 0.34	0.13
Hs-CRP (mg/L)	0.40 (2.00)	0.60 (2.00)	1.40 (3.20)[a]	<0.01

Data are mean SD except for hs-CRP which are median interquartile range (IQR). [a] P<0.05 vs. HG, [b]P<0.05 vs. G1, [c]P<0.05 vs. HG

b=brachial, c=central, SBP= Systolic blood pressure, DBP= Diastolic blood pressure, MAP= mean arterial pressure, PP=pulse pressure, HR=heart rate, WC= waist circumference, BMI=body mass index, TC=total cholesterol, TG=triglyceride, HDL=high density lipoprotein, LDL=low density lipoprotein, FBS=fasting blood sugar, hs-CRP=high sensitivity C-reactive protein.

RESULTS

Table 3 summarized the general characteristics of the subjects. A total of 114 subjects were involved. The mean age of all the subjects was 28.94 ± 4.86 yrs. There were significant increasing trends for age, bSBP, bDBP, brachial mean arterial pressure (bMAP), cSBP, cDBP, WC, BMI, hs-CRP and lipid profiles (except for HDL which had significant reducing trend) as the number of risk factors increased (P<0.05 for all).

Table 4 summarized the vascular properties of the groups. Post-hoc analysis revealed that the level of AI was significantly increased in G2 when compared to G1 and HG, which remained significant after adjustment for the age, race, HR and height. No differences were observed in terms of PWV_{CF}, AP, P1, RCIMT, LCIMT and PPGF between groups.

Table 5 showed the correlations between PPGF with other vascular properties and risk factors. PPGF was significantly correlated with height, DBP, MAP and PWV_{CF}. In multiple linear regression, the independent variables of PPGF were P1 (Beta = 0.35, $p < 0.01$), PWV_{CF} (Beta = -0.26, $p < 0.01$), SBP (Beta = -0.26, $p = 0.04$) and height (Beta = 0.24, $p < 0.01$).

For sensitivity study, the analysis showed that the sensitivity of VRPI to identify young subjects with CVD risk factor was 82.02% and the specificity was 15.38%. This indicated that VRPI

Table 4: Vascular properties of the subjects.

	HG (N=25)	G1 (N=27)	G2 (N=62)	P
PWV_{CF} (m/s)	7.31 ± 0.96	7.31 ± 0.77	7.41 ± 0.72	0.80§
				0.93*
				0.95**
				0.96†
AI (%)	7.75 ± 4.01	7.85 ± 4.82	10.92 ± 5.53[a]	<0.008§
				0.03*
				0.04**
				0.004†
				0.002††
AP (mmHg)	3.92 ± 2.62	3.88 ± 2.82	5.18 ± 2.71	0.05§
				0.13*
P1 (mmHg)	37.96 ± 4.64	39.73 ± 5.37	40.07 ± 5.80	0.29
				0.08*
RCIMT (mm)	0.5234 ± 0.08	0.5497 ± 0.11	0.5748 ± 0.11	0.11§
				0.32*
				0.32**
LCIMT (mm)	0.5077 ± 0.10	0.5360 ± 0.10	0.5495 ± 0.09	0.19§
				0.26*
				0.28**
PPGF (%)	61.20 ± 8.64	59.69 ± 6.89	60.10 ± 8.81	0.79§
				0.88*

Data are mean ± SD. § unadjusted, *after adjustment for the age, **after adjustment for the age and race, †after adjustment for the age, race and HR, ††after adjustment for the age, race, HR and height. [a]P<0.01 when compared to HG and G1 after adjustment for age, race, HR and height. PWV_{CF}=carotid femoral pulse wave velocity, AI=augmentation index, AP=augmentation pressure, RCIMT=right common carotid intima media thickness, LCIMT=left common carotid artery intima media thickness, PPGF= Finger photophlethysmography fitness index.

had high sensitivity but low specificity in detecting those with CVD risk factors.

DISCUSSION

The use of peripheral vascular signal such as via PPG has gained a lot of focus since this method is easy, reproducible, non-invasive and cost-friendly. PPGF is developed by comparing PPG signal of a subject with a healthy young subject. The value of PPGF is in percentage and the higher value indicates better vascular health. In the present study, the relationship between PPGF and other CVD biomarkers were studied. This study found that PPGF correlated independently with PWV_{CF}, a gold standard measurement of aortic stiffness (AS). This suggests that AS is one of the determinants of PPGF and PPGF may be a potential marker of AS.

Past research that studied the correlations between other PPG waveforms such as stiffness index (SI) digital volume pulse (SI_{DVP}) and B/A ratio with aortic stiffness indices also found similar finding, but at different strengths

Table 5: Correlations between PPGF with other vascular properties and risk factors

	PPGF
Age	0.10
Height	0.22*
BMI	0.06
SBP	-0.05
DBP	-0.24*
MAP	-0.22*
AI	-0.16
P1	0.16
PWV_{CF}	-0.27**
RCIMT	-0.00
LCIMT	-0.07
TC	-0.09
TG	-0.05
HDL	0.06
LDL	-0.10
Log CRP	-0.04

Values are Pearson correlation *r.*
*P<0.05
**P<0.01

of correlation. Study by Salvi et al. (2008) found that among subjects with risk factors and CVD, SI_{DVP} correlated to PWV (*r*=0.55). Among the healthy subjects, Millasseau et al. (2002) found that SI_{DVP} correlated to PWV (*r*=0.65). Another study by Chen et al. (2005) observed that among hypertensive subjects, SI_{DVP} correlated to aortic SI (*r*=0.31) and distensibility (*r*=-0.34) measured via echocardiogram. Study by Woodman et al. (2003) found that SI_{DVP} correlated to PWV (*r*=0.54). Hashimoto et al. (2002) observed that among hypertensive subjects, PWV correlated to B/A (b/a) ratio obtained by analyzing the second derivative PPG, which is a proposed index of AS. However, this correlation became insignificant after adjustment for the age and MAP (*r*=0.16). A study by von Wowern et al. (2015) found that b/a ratio was correlated significantly with PWV (*r*=0.56). Compared to above studies, PPGF correlation with PWV was weak (*r*=-0.27) which suggest that PWV may not be the only marker that influence PPGF. We found that forward pressure (P1), SBP and height also influenced PPGF. Again, all these factors contributed only about 18% variability of PPGF. Other factors that affected PPGF were still unknown and should be investigated further.

In the present study, no correlation was found between PPGF and age. This can be due to low sample size and narrow range of age. Furthermore, the influence of aging on the PWV_{CF} as the determinant of PPGF may not be apparent among the young subjects (Aminuddin et al. 2014, McEniery et al. 2005). In contrast, study by Chellappan et al. (2008) found significant decrease in PPGF as the age increased. In her study, the age range was wider which was from 19 to 68 yrs.

In the present study, no correlation was found between PPGF and CIMT. Previous study by Wykretowicz et al. (2009) found that SI_{DVP} was not correlated to CIMT. Another study found that among Japanese subjects there was a significant correlation between b/a ratio with CIMT but this correlation was weak (β=0.069) (Tabara et al. 2016). This suggests that CIMT and PPGF reflects different vascular characteristic and should be used complimentary with each other and not interchangeably. This study also found no correlation between PPGF and hs-

CRP. Similar finding was observed in a study by Kawada & Otsuka (2013) which found no correlation between b/a ratio and CRP. In contrast, study by Tsai et al. (2007) observed that SI_{DVP} was correlated with CRP but weak (*r*=-0.17). Their subjects' was much older (mean age=41 yrs) and only involved hypertensive subjects, which may account for the discrepancy in the results.

The results showed that there was no significant difference in PPGF among the study groups. This was unexpected since previous study found that PPGF was significantly reduced among young and old subjects with CVD risk factors (Chellappan 2009). There are several reasons for this. Firstly, previous study involved subjects who had more severe clinical characteristic compared to the current study and the cut-off point to be in the risk factors groups were much higher (Chellappan 2009). For example, hypertension was diagnosed if DBP> 100 mmHg compare to the current study which was >140/90 mmHg. Low HDL was diagnosed as HDL<0.85 mmol/L compare to the current study which was <1.02 mmol/L. They also involved diabetic subjects, which usually had vascular damage by the time of diagnosis but in the current study diabetic subjects were excluded. Thus, their subjects may have had significant vascular damage that can be detected as low PPGF. In addition, the mean value of physical and biochemical status (SBP, DBP, TC, TG, LDL) of the subjects with at least two risk factors in the present study were still within normal range. Secondly, PPGF was influenced by PWV. No difference in PWV between the groups in the current study might also explain the insignificant difference for PPGF between the groups. No difference observed for AS measured by PWV_{CF} between the groups were in line with previous studies in young subjects (Dart et al. 1991; Ferreira et al. 2007; Toikka et al. 1999). This can be due to the fact that our subjects were still young and aortic stiffening may not be significant at the early stage of the occurrence of the risk factor (Aminuddin et al. 2014).

The significantly increased AI among those with risk factors was in line with previous studies (Jatoi et al. 2007; Kyvelou et al. 2010; Urbina et al. 2012; Wilkinson et al. 2000). Previous studies also suggested that AI may be a sensitive index of vascular dysfunction among the young subjects (Aminuddin et al. 2014; McEniery et al. 2005; McEniery et al. 2010). Increased AI may be due to increased ventricular ejection, aortic stiffness or total peripheral resistance (Casey et al. 2012). The present finding suggests that AI can be used as an early marker of vascular damage due to CVD risk factor.

The novel finding of the present study was that the sensitivity of VRPI to identify young subjects with CVD risk factor was nearly 82%, which was quite high. However, the specificity was low (nearly 15%). High sensitivity result means that the test rarely misdiagnosed those with positive test, and those with negative test can be said as having high probability to not have the disease. In other words, high sensitivity test is beneficial to exclude a disease. Thus, for VRPI, it can be said that those with negative result (very low risk) is safe and

they can repeat the measurement after one year for continuous assessment of vascular health. It is also suggested that those with positive result (low risk, moderate risk and high risk) should be referred for further evaluation of CVD risk factor such as measurement of BP and lipid profiles. In this context, VRPI can be used as a first hand screening for CVD risk factor. VRPI can be also used to assess the changes in vascular health due to lifestyle intervention such as dietary modification and exercise program.

CONCLUSION

In conclusion, PPGF is independently associated with PWV and may be a potential marker of AS, which may need further validation. VRPI can also be used as early screening of CVD risk factors since the method is sensitive.

ACKNOWLEDGEMENT

The present study was supported by Pusat Perubatan Universiti Kebangsaan Malaysia (PPUKM) Fundamental Grant (FF-262-2011) and Universiti Kebangsaan Malaysia grant (GGPM-2011-078).

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