CHAPTER V

DISCUSSION AND CONCLUSIONS

Discussion

We measured serum hs-CRP twice and used an averaging results, according to a previous study recommendation to ensure the reproducibility of this test, in view of biological variation (Thomas, A. Pearson, 2003; Andreas Pfützner, 2010). Any recent illness, tissue injury, infection, autoimmune diseases, cancer, general inflammation, chronic inflammation, such as arthritis, could raise the amount of CRP and falsely elevate estimations of risk. In contrast, antithrombotic medications (e.g. aspirin, cholesterol-lowering statin drugs, and ACE inhibitors) may reduce CRP. Therefore, subjects related to illnesses and medications used above were excluded from the study. The hs-CRP results were excluded if the concentration was higher than 10 mg/L (Rinkoo Dalan, 2010). The hs-CRP concentrations in healthy blood samples obtained from the automated Olympus were correlated to other 8 automated analyzers having imprecision less than 10%, except for the concentrations of hs-CRP lower than 0.15 found in only 2% of in this study (Robert, WL, 2001).

hs-CRP concentration in this study (1.33 mg/L) was different than previous reports. Navapun Charuruks, et al. (Navapun Charuruks, 2005) investigated the reference value of hs-CRP in healthy volunteers from 4 center regions of Thailand (1.9 mg/L, 0.2-8.1 mg/L) which was higher than Asian women (1.12 mg/L) in the United States study (Albert, M.A., 2004). There were no significant differences in the hs-CRP concentration because of region, time, and gender of age. Therefore, the determination of hs-CRP for medical purpose can be performed at any time without concerns (Albert, M.A., 2004) and we can use 0.2-8.1 mg/L as the reference value for hs-CRP in healthy Thai adults (Navapun Charuruks, 2005) .

Peripheral vascular in healthy subjects were assessed using the non-invasive analyzer at Ban Krang Primary Care Unit as the point of care testing. To operate the instrument for ABI and PWV measurement, skilled operators are still required for consistent and accurate results. These issues have rendered ABI unpopular in primary

care, due to the perceived difficulties and time taken (Hirsch, A.T., 2001). However, an advanced technology of the VP-1000 analyzer allows for the oscillometric to simultaneously calculate ABI by readings of blood pressure at the levels of the ankle and upper arm using specially calibrated oscillometric modules. This allows the measurement of ABI to be standardized and makes it accessible to the point of need. Most people with PAD have a higher risk of death from heart attack and stroke (Criqui, M.H., 1991; Leng, G.C., 1996; Criqui, M.H., 1998).

PWV and ABI are widely used for assessing vascular stiffness and occlusion. Brachial-ankle PWV was measured using a volume plethysmographic apparatus form ABI. The VP-1000 Analyzer provided PWV and ABI along with interpretations using the individual information of subject such as age, gender, and disease status. The ABI below 0.9 at rest is generally considered abnormal. The validation of ABI obtained from this method has been reported previously; the inter-observer coefficient of variation (CV) was 8.4% and the intra-observer CV was 10.0% (Yamashina, A., 2002).

Increasing of WC was associated with increased hs-CRP concentrations. This association may be due to increasing WC as in central obesity has been associated with visceral adipose mass and a group of metabolic risk factors, such as hyperinsulinemia, dyslipidemia, and an expression of the pro-inflammatory gene tumor necrosis factor-α (Hotamisligil, G., 1993; Hak, A.E., 1999; Visser, M., 1999; Festa, A., 2000; Chambers, J.C., 2001; Dehnavi, R.A., 2008). Several studies have shown that hs-CRP is correlated with BMI and visceral adiposity (Hak, A.E., 1999; Visser, M., 1999; Festa, A., 2000; Chambers, J.C., 2001; Dehnavi, R.A., 2008). However, this study shows that hs-CRP was associated with PWV, ABI, WC and TG in healthy people and was not associated with BMI and other variables such as SBP, DBP, GLU, TC, LDL, and HDL. BMI of all subjects in this study ranged from 17-30 kg/m^2. WC is one component involved in metabolic syndrome classifications such as the NCEP, International Diabetes Federation (IDF), and World Health Organization (WHO) (Florez, H., 2006; Rahim, M.A., 2007).

Peripheral vascular stiffness and occlusion are indications of blocked peripheral blood vessels. Non-disease subjects having peripheral vascular stiffness and occlusion are at risk of PVD.

PVD leads to structural changes in the blood vessels resulting in inflammation and tissue damage. Previous study showed subjects with PAD often have fatty buildup in the arteries of the heart and brain. Because of this association, most people with PAD have a higher risk of death from heart attack and stroke (Criqui, M.H., 1991; Leng, G.C., 1996; Criqui, M.H., 1998). This study shows that hs-CRP concentration in abnormal vascular with stiffness and occlusion was higher than those of normal vascular. This may due to CRP enhancing foam cell formation in arteries and activating complementary factors in atherosclerotic plaque, potentially leading to plaque rupture (Yasojima, K., 2001).

ABI compares the systolic ankle blood pressure with the systolic brachial blood pressure at the same site of body part for investigating how well the blood flows. ABI lower than 0.9 shows the association with occlusion in peripheral arteries. Falling down of ABI is related with severe occlusion and it has shown to be associated with CVD risk factors (Yuanxi, X.U., 2007) . Previous studies found those with lower extremity arterial disease are 1.5 to 2 times more likely to experience a clinical CVD event (Albert, W. Tsai, 2001).

PWV is based on simultaneous measuring the difference sites of blood pressure velocity of the pulse wave traveling a given distance between 2 sites of arterial system. Several studies have shown that the non-invasive PWV and ABI are reliable with high sensitivity and specificity to assess peripheral vascular atherosclerosis (Albert, W. Tsai, 2001). However, some previous studies had shown variations and limitations of ABI (American Diabetes Association, 2003; Allison, M.A., 2008). Age and gender were influenced to PWV (Tomiyama, H., 2003). Therefore, the VP-1000 analyzer uses age, gender, and disease of individual to correct PWV calculation before providing each interpretation.

Limitations of this study are using non-invasive instrument to provide PWV and ABI to assess the vascular stiffness and occlusion, while the standard procedure is to assess the vascular stenosis is angiography or magnetic resonance imaging.

This study enrolled healthy adults with no history of any diseases or denied current active diseases. BMI of all subjects in this study ranged from 17-39 kg/m^2. BMI over than 30 kg/m^2 indicated the severity of obesity and may associate with hs-CRP and peripheral vascular atherosclerosis.

Because of hs-CRP test is measuring a marker of inflammation, any recent illness, tissue injury, infection, autoimmune disease, cancer, general inflammation, and chronic inflammation, such as arthritis, will raise the amount of CRP and give a falsely elevated estimate of risk, on the contrary antithrombotic medications (e.g. aspirin, cholesterol-lowering statin drugs, and ACE inhibitors) may also reduce CRP. Therefore, these subjects were excluded from the study. The hs-CRP results were excluded from the study. The hs-CRP results were excluded if the concentration was higher than 10 mg/L.

Relationships between waist circumference and anthropometrics were shown in Table 2. Waist circumference was significantly correlated with BMI, SBP, DBP, TG, HDL-C, LDL-C, and hs-CRP ($p < 0.05$) with correlation coefficient (r) 0.722, 0.166, 0.142, 0.133, -0.125, 0.101, and 0.189 respectively.

Table 8 showed the comparison data of biochemical analytes between central obesity and non-central obesity (normal waist circumference) participants. Means of HDL-C, LDL-C, and hs-CRP were significantly differed from control group ($p < 0.05$).

Classification of hs-CRP by CDC and AHA in central obesity and normal waist circumference were shown in Table 10. The concentration of serum hs-CRP > 3 mg/L was found in central obesity 21 % higher than those found in normal waist circumference when the Chi square statistical methods was applied for data analysis. This may due to central obesity had been associated with adipose mass and expression of the proinflammatory gene tumor necrosis factor-α (Hotamisligil, G.S., 1993).

Limitations of this study

The VP-1000 is a noninvasive device that simultaneously measures the ABI and baPWV by using the waveform analysis and vascular evaluation technology to generate diagnostic information. The device's capacity to evaluate patients highly correlates with classic Doppler measurement, performed within 5 to 10 minutes that is shorter than with classic Doppler measurements, which usually require 15 to 20 minutes.

Further investigations

To obtain the basic data of glucose, cholesterol, triglyceride, high density lipoprotein cholesterol, low density lipoprotein cholesterol, and high sensitivity C-reactive protein concentrations, blood pressure, and vascular indexes in central obesity adults.

To know the associations among blood chemistry testing, blood pressure, and vascular indexes in central obesity adults and the differences of those among central obesity and normal waist circumference adults. The data is valuable for cardiovascular disease prevention in central obesity adults.

Conclusion

This study concludes that risk factors of CVDs such as central obesity, dyslipidemia, hyperglycemia, and hypertension still occurred in healthy adults that without active diseases.

High sensitivity CRP was associated with increased WC, PWV, and triglyceride, but was associated with decreased ABI. Healthy adults with central obesity and having vascular atherosclerosis were at higher risk of CVD than those without having vascular atherosclerosis.

Reduction in WC in non-disease adults could predict in decrease hs-CRP and prevent of CVD. WC and serum hs-CRP may help guide preventive interventions to reduce future CVD in non-disease Thai adults.