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The C-reactive protein and cardio-ankle vascular index of Mongolian and Japanese people

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Abstract: Mongolian people suffer from atherosclerotic diseases more than Japanese people, while both people are thought to share similar genetic background under different lifestyles and environments. Comparative studies using novel atherosclerotic parameters of Mongolian and Japanese people may demonstrate the atherosclerotic features of both populations. We have recently reported the findings regarding atherosclerosis of both populations using circulating high sensitivity C-reactive protein (CRP: as low-grade inflammatory parameter) and cardio-ankle vascular index (CAVI: as arterial stiffness parameter), herein summarizing the data. Our studies revealed that in comparison to the Japanese subjects, the Mongolian subjects had higher levels of CRP and CAVI, in addition to a higher percentage of current smoking and higher levels of body mass index, heart rate and blood pressure and insulin, even though there were not so higher levels of serum total cholesterol and glucose. These results were confirmed in healthy young subjects and patients with hypertension and diabetes mellitus. These comparative studies used recent parameters suggest that Mongolian people may be at higher risk for cardiovascular disease than Japanese people. The management strategies of atherosclerotic diseases are also expected in the near future.

Keywords: Atherosclerosis, Altitude, Ethnic, Cardio-Ankle Vascular Index, C-Reactive Protein

1. Introduction

Atherosclerosis is leading pathophysiologic basic pathway of cardiovascular disease (CVD) including cerebrovascular disease, coronary heart disease (CHD) and hypertension (HT) is nowadays a possible world-wide cause of premature death [1]. Recently, in a clinical practice arterial stiffness has been established blood pressure independent a novel atherosclerotic parameter cardio-ankle vascular index (CAVI). The increased level of CAVI is associated to risk of CVD and predictive to HT, CHD, chronic kidney disease and diabetes mellitus (DM) [2,3]. Vascular inflammation is one of the pathophysiologic processes of atherosclerotic lesion, investigated in serum high sensitive C-reactive protein (hsCRP) which induces adhesion molecule expression in human endothelial cells [4]. Small elevation in serum levels of hsCRP are associated to higher risk of atherosclerosis and ischemic heart disease in apparently healthy population[5,6]. Higher level of CAVI and CRP are established in Mongolian people than Japanese people are showed there have higher risk of CVD [7-9]. Morbidity and mortality rates of CVD, levels of CAVI and serum CRP are different in all of ethnical countries associated to their food intake, unhealthy lifestyle, genetic background and environmental risk factors (exp: altitude difference, oxidative stress…). Ethnical comparative studies significant for each country to detect a crucial features of lifestyle related diseases and important to select preventive suitable methods. There have been several ethnical comparative studies of Mongolian and Japanese population which are including in Asian country [7, 8, 10, 11]. Atherosclerosis related early preventive method is important to decline premature deaths of cardiovascular events.

2. Epidemiologic Features of Atherosclerotic Disease in Japan and Mongolia

Japanese people are the world highest life expectancy population and have been maintained over 20 years [12]. Global feature of CVD in Japan is high stroke and low CHD mortality rate among industrialized country however serum total cholesterol (TC) and smoking consumption rate was high [13]. In 1965, age-adjusted all-stroke mortality rate in Japan was highest in the world after then the mortality rate was gradually reduced until 1990 [14]. Mortality rate of CHD also reduced from 1970 recorded that diagnosis of heart failure has a higher proportion in Japan than in the United States [14]. According to the World Health Organization (WHO) data 2009 reported age-standardized death rate per 100 000 people stroke was 42.20, CHD was 32.14, DM was 4.53 and HT was 1.74 in Japan, respectively [15]. HT and smoking are the main reason to reduce stroke and CHD in Japan [12]. The prevalence of HT was decreased by 17% in 1990, prevalence of smoking is decreased by 43.2% in men and 17.5% in women compared to 1965, respectively. Current health global situation in Japan is a high level of serum TC however mortality rate of CVD is decreased related to CHD.

The WHO statistical data in 2008 reports Mongolian people to have a 15-years shorter life expectancy than Japanese people however their genetic backgrounds are similar [16-18]. Mongolian statistical data in 2008 investigated, non-communicable diseases (NCD) such as diseases of the respiratory system, digestive system, genitor-urinary system, circularity system and injury, poisoning is leading five causes of morbidity and increased 25-40% compared to 2001 [16]. Since 1991, mortality rate of circularity system has been increasing and become global first health issue in Mongolia [16]. The statistical data showed morbidity and mortality rates of NCD such as CVD had been rapidly increasing in Mongolia. The data WHO 2009 reported age-standardized death rate per 100 000 people stroke was 185.60, CHD was 92.82, DM was 2.05 and HT was 50.98 in Mongolia, respectively [15]. This data was showed mortality rate of stroke, CHD and HT is 3-5 folds higher in Mongolia than Japan. Ischemic heart disease morbidity rate of inpatients accounted for 19.2% diseases of the circularity system in 2000, 25.7% in 2004, 30.1% in 2008 [17]. Mortality rate caused by NCD such as stroke, CHD and HT had been Mongolian health global issue however the concentration of TC is lower than Korean people and Japanese people [10]. Therefore comparative study is helpful to clarify required ethnical health feature issue and predict premature deaths.

Therefore, there are required country special new preventive methods to decrease premature deaths, mortality and morbidity rates of CVD in both countries.

3. New Markers of Atherosclerotic Diseases: Cardio-Ankle Vascular Index (CAVI) and C-Reactive Protein (CRP)

CAVI is arterial stiffness measurement blood pressure independent new marker. This index is measured VaSera VS-1000 made by Fukuda Denshi Co., Ltd in Japan. Formulation of CAVI is basic of the stiffness parameter-β theory and the values are calculated by: a $\{(2\rho/\Delta P)xIn(Ps/Pd)\ xPWV^2\}+b$ (ρ: blood density, Ps: systolic blood pressure, Pd: diastolic blood pressure, ΔP: Ps-Pd, a and b: constant). Measurement method of CAVI is non-invasive and superior of brachial-ankle pulse wave velocity which had been currently using in a clinical practice [19]. CAVI is able to investigate whole body vascular stiffness including from aorta to ankle. There have several clinical studies regarding CAVI and their relation to CVD [8.19-22]. In fact, CAVI is associated with atherosclerotic risk factors and predict the future of CVD [23]. In patients with HT or CHD, CAVI is positively correlated to carotid intima-media thickness (IMT) and helpful to menage anti-hypertensive medication [21.22]. Furthermore, increased CAVI level is associated to diabetic micro-vascular complication such as neuropathy and nephropathy patients with type II DM [24,25]. The clinical significance of the CAVI for CVD has been established recently [7,8, 19-22].

Recent studies investigated that inflammation plays a role in the pathogenesis of CVD associated to the initiation and progression of atherosclerosis. CRP is an acute-phase inflammatory protein primary synthesized and released from hepatocytes [25]. Several studies found CRP may be occurring other sites such as macrophages and smooth cells which play pathogenesis of vascular atherosclerosis. Torzewski J et al also noted CRP found early atherosclerotic lesion of human coronary arteries such around foam cells [26]. High concentration of serum CRP may be related to accumulation of CRP in early atherosclerotic vascular wall lesion and thought to be predictive of CVD [26 27].

4. Comparative Studies Findings of Japanese and Mongolian People

Regarding to the comparative study, Mongolian healthy young (age 18-25) subjects had significantly higher percentage of meat intake and current smoking (47.0% vs. 19.0%) compared with that Japanese subjects (13% vs. 2.6%), respectively [7]. Other lifestyle factors including vegetable intake, salt intake and physical activity were not significant differences. It may be related the study participators were young and the data questionnaire was a general. The study, who participated residents of Murun (prefecture) in Mongolia showed a daily calorie intake is 1.3 fold higher in Mongolian people and their have

association with lifestyle related diseases than Japanese people [28]. Salt intake is one of the lifestyle related risk factor to increase blood pressure associated to cardiovascular function [23]. Nutritional data 2000 reported a total daily salt intake is 16.7g in Mongolian population and 12.3g in Japanese population, respectively [29,30]. Additionally, Mongolian people have higher level of oxidative stress markers including malondialdegyde-modified low density lipoprotein cholesterol (LDLc), urinary 8-hydroxy-2'-deoxyguanosine and serum reactive oxygen metabolism compared to Japanese people [28]. Several researchers found lower level of plasma n-3 polyunsaturated fatty acid (n-3 PUFA) in Mongolian people which related to higher risk of CVD [21,25]. N-3 PUFA includes in a fish which have high consumption Japanese people. The lower level of n-3 PUFA negatively related to triglyceride (TG) in Mongolian people, higher n-3 PUFA associated to HDL-c and TG in Japanese people while it was associated systolic blood pressure in Korean people[31]. Recently, collision between traditional and westernized lifestyles has been seen in the urban areas of Mongolia. The previous studies showed Mongolian people may be having higher risk of cardiovascular events related to their lifestyles.

One of the health crucial issues to prevent CVD is the detection of atherosclerotic alterations among asymptomatic subjects. There have been a few comparative studies which including healthy young aged 18-25 years subjects. This study was first time used a new atherosclerotic parameters, CAVI and ABI in Mongolian subjects. Modern high quality techniques may help to find new important scientific detailed information which did not detected last years. The data investigated that body mass index (BMI), heart rate (HR), diastolic blood pressure (DBP), CAVI and ABI levels were significantly higher and TC and glucose levels were significantly lower in Mongolian subjects than those in Japanese subjects. Similar results, in Mongolian over age (age 30-60) subjects than that of Japanese subjects and Korean subjects was found in early survey [10]. Furthermore, interestingly Mongolian healthy young subjects have significantly higher level of CAVI and ABI than that of Japanese subjects. Researchers explained the higher level of CAVI and ABI in Mongolian subjects may be related to their hematocrit, oxidative stress and peripheral resistance which are including hypoxia-related factors at higher altitude level [20, 32]. Mongolia is landlocked country located 1580 m above sea level which is higher than Japan (Tochigi prefecture; 50 m). The highest altitude in Mongolia is 2180 m above sea level (Gobi-Altai) and lowest is 625 m above sea level (Selenge). CVD such as blood pressure and hematocrit are increased with altitude level which was reported in previous study [32].

Although, rising level of CAVI is showing vascular elasticity changing but the Mongolian subjects were young. Therefore future study needs to clarify higher level of CAVI in Mongolian young subjects which is including normal level. Additionally, this study determined correlation patterns of CAVI and ABI with other atherosclerotic parameters between the Mongolian and Japanese subjects was different [7]. In 1965, serum lower level of TC in Mongolian healthy young subjects was first time found compared to Czechoslovak people (age 19-23) [10, 33]. This result is confirmed other further studies including Japan and Korean population [10]. Some of the data showed low density lipoprotein cholesterol (LDL-c) level is lower in Mongolian people than Asian ethnic countries however physiologic pathway is not yet explained clearly. Carotid atherosclerosis is assessed by carotid IMT with non-invasive high frequency ultrasound which is widely useful in clinical practice. Carotid IMT is surrogate marker for CVD and preventive cardiological fields. Carotid IMT in Mongolian subjects was (median [interquartile range]; 0.63[0.49-0.86]) greater and strongly associated to age when indirectly compared other ethnic studies results [11]. Furthermore, carotid IMT related parameters were different in Mongolian people compared other Asian country [34, 35].

Ethnical diseased group study was attempted to compare atherosclerotic parameters between hospital-based of Mongolian and Japanese population with hypertensive and/or DM [8]. There have a few comparative studies on atherosclerotic parameters between Japanese and Mongolian patients. Significantly higher BMI, HR, DBP and CAVI, significantly lower TC and glucose in Mongolian patients than that of Japanese patients was consistent with the previous study results which were indicated in healthy and young Mongolian subjects. Additionally, systolic blood pressure, CRP, carotid IMT and insulin were significantly higher in Mongolian patients than that of Japanese patients. Higher serum CRP levels were seen with increased metabolic syndrome risk factors in both Japanese people and Mongolian people [9]. These higher atherosclerotic parameters in Mongolian patients may be showing the patients have more vascular stiffness.

CVD risk factors such as higher percentage of current smoking and higher BMI in Mongolian population (apparently healthy subjects, young subjects and patients) are detected in all of comparative studies. Smoking such as nicotine is one of the accelerator factors of atherosclerosis which have pathophysiologic affect to endothelial cell injury, inhibitor of prostacyclin and to increase LDLc level. Furthermore, interestingly Mongolian patients have similar level of insulin resistance while higher insulin and lower glucose than Japanese patients. Schindler et al reported that body weight is increasing with insulin resistance, chronic inflammation and is related to impairment of endothelial dependent coronary vasomotion in overweight individuals [36]. One possible conjecture explanation is affect existence of differences in environmental factors. The lowered effect of high altitude on plasma glucose has also been reported in previous study [37].

Researchers confirmed atherosclerotic parameters such as higher CAVI and CRP in Mongolian patients not associated to blood pressure[8]. There have several studies in

Mongolia which blood pressure is increasing with altitude level between different regions in Mongolia 32]. Additionally, different and unknown some genetic polymorphism may be played roles on atherosclerosis however genetic background in Japanese and Mongolian people is generally similar. These factors are thought to merit further investigation to elucidate such differences between Japanese and Mongolian people, while more unmeasured factors might remain hidden.

5. Perspective Strategy of Atherosclerosis in Mongolian People

The previous studies showed the level of CAVI is different in ethnical countries. The higher level of CAVI is not suspected Mongolian young subject's artery is stiffer than Japanese subjects. Adequate reference range of CAVI is required to Mongolian people to get down to back-rock of artery stiffness. In the previous study was suggested the level of CAVI is may be dependent on environment factors such altitude difference. The highest altitude is 2180 m above sea level (Gobi-Altai) and lowest is 625m above sea level (Selenge) in Mongolia. The CAVI level is may be different among Mongolian residents who are living at different altitude. Additionally, atherosclerotic parameters including hemoglobulin, oxidative stress and elasticity of peripheral artery and their associations are needed in future study. Peripheral vascular (radial and brachial artery) elasticity will measure transcutaneous ultrasonography by phased tracing method. Further study need specific comparative atherosclerotic study between Japanese and Mongolian people including lifestyle differences, meat intake, fruit intake, vegetable intake, salt intake and physical activity. Comparative studies such as arterial stiffness related study is required to understand pathophysiologic essence and feature of higher level of CAVI and CRP in ethnic countries.

6. Summary

The higher level of CAVI and atherosclerotic risk factors were detected in Mongolian young healthy population and diseased population. In the previous comparative study such as young healthy subjects data showed CAVI is may be different in ethnical country. This suggests future study need to indicate normal range of CAVI. Higher level of atherosclerotic parameters in Mongolian young healthy people and patients with HT and DM showed Mongolian people have high risk to increase morbidity and mortality rate of CVD in future. Therefore Mongolian people need to clarify the essence of atherosclerotic parameters and arterial wall stiffness , and their association of environment risk factors including lifespan, altitude level and weather features in the further study. These results may be a science basic key of the why CAVI is higher in Mongolian people than Japanese people.

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