



## **Chinese Menopause Society Member Country Session**

**Date:** Monday 27 September 2010

**Time:** 07.30am – 08.30am

**Session Chair:** Professor Qi Yu

### **Session Topics:**

#### **Professor Xie Meiqing**

- The characteristics of cardio - vascular disease of women in mainland China.

#### **Professor Xiangyan Ruan**

- The characteristics of breast cancer in mainland China.

#### **Professor Ling Xu**

- Epidemiology of osteoporotic fracture in China.

#### **Professor Qi Yu**

- The characteristics of menopausal transition, treatment status and CME activities by the CMS in mainland China.

## ABSTRACTS

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### **Characteristics of Cardiovascular Disease of Women in Mainland China**

**Professor Xie Meiqing, M.D.<sup>1</sup>**

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The cardiovascular disease (CVD) has received increased attention since 1980s. Recently, a number of studies on the health of female in china demonstrate that CVD has become the principal cause of death in women. Cardiovascular mortality is low in women at the reproductive age, while the incidence increases rapidly following the onset of menopause.

#### 1. Epidemiological characteristics

The cohort study of Chinese Multi-Provincial cardiovascular disease risk factors displayed that, in mainland China, characteristics of cardiovascular disease were different from western countries, for the relatively low incidence of coronary heart disease, high stroke incidence. An observation survey conducted in several provinces recruited a total of 30,384 people without CVD with an average age of 46.19. During 1992-2002, 640 cardiovascular events occurred among these people, including 193 cases of acute coronary heart disease, 447 cases of acute stroke (314 cases of ischemic stroke, 128 cases of hemorrhagic stroke, 16 cases of non-typical events and 11 samples have two events).

In China, with a population of over 1.3 billion, the incidence of dyslipidemia and hypertension in 35-74 year-old- women was 53% and 25% respectively. There is apparent gender difference of CVD. Many studies have shown that CVD in different age groups of women are related to changes of estrogen level. From the point of age, the incidence of CVD in female prior to 45 years old is significantly lower than men, which is the result of normal ovarian function. However, with the estrogen deficiency in postmenopausal phase, the prevalence of CVD in female increases year by year. There is no significant difference between men and women in the prevalence of CVD since 64 years of age.

#### 2. The risk factors of coronary heart disease in female

According to the report of World Health Organization and World Hypertension League in 2007, in China, the totally risk of cardiovascular disease is generally lower in women than men. In the 60 to 69 age group, 72.7% of women have a less than 10% risk of suffering from cardiovascular events in the next 10 years; 13% of women have a 20% ~ 29.9% risk of suffering from cardiovascular events in the next 10 years, the rest have about 10% ~ 20% and 30% risk. However, men in the 60 to 69 age group, who have a less than 10% risk of suffering from cardiovascular events only account for 50%.

#### 2.1 Age

During the age of 20-30 years old, the ratio of coronary event between male and female is 7:1. Changing along with age, then, the ratio gradually decreases to 1 at the age of 60 ~ 70 years old. The risk of CVD is increasing by 2% in postmenopausal women annually. Xin Zheng revealed that the risk factors of CVD were relatively low under 45-year-old in female. A study in Ghangzhou of China showed that the average age of the onset of coronary heart disease was  $55.2 \pm 9.9$  years old in male and  $64.54 \pm 10.1$  years old in female. Male get coronary artery disease almost 9.3 years earlier than female.

## 2.2 Family History

With a family history of myocardial infarction (MI) in female relatives before 55 years old or in first grade relatives before 60, the risk of myocardial infarction in women is 2.8 times higher than other women without MI family history.

## 2.3. Smoking

Female smokers have higher risks of myocardial infarction than men. Though less women are active to smoke, but the harm of smoking for coronary heart disease (CHD) is more severe in women than in men as second hand smoking raise the chance of CHD significantly in women. In 2002, it is estimated that some 33,800 people died of ischemic heart disease because of second hand smoking in China, and most of them are female. Another data from a survey in 2008 showed that 39.5% women are second hand smoker in china, and the incidence of CHD, ischemic stroke and peripheral vascular disease is obviously high among them (OR=1.6;1.56;1.47~1.87)

## 2.4. Obesity

The aggravation of CHD is highly related to overweight. CHD risk in women whose weight is 20kg above the normal level is 2.7 times higher than in whom with overweight of 4.9 kg. The obesity cooperating study group of China recruited a total of 239972 adults, with an age range of 20 to 70, in 21 provinces in mainland as well as Taiwan. It showed that body mass index (BMI)  $\geq 24$  happened in approximately 30% ~ 40% of the population and waist circus  $\geq 85$ cm happened in 35 % of total male population. Similarly waist circus  $\geq 80$ cm is accounted for approximate 35 % among women. Keeping BMI below 24, it may prevent people from 45 % ~ 50 % of risk factors of CHD. Keeping BMI below 28 with pills, it may decrease 15 % ~ 17 % of the risk factors for CVD, as well as for the risk of diabetes and cardiovascular disease. Waist circus below 85cm in male and 80cm in female can reduce 47 % ~ 58% of the risk factors crowded.

## 2.5 Hypertension

The risk of CHD is four times higher among hypertensive patients than healthy person. The research sponsored by the Cardiovascular Disease Research Institute of Beijing Epidemics Institute for 10 years (3,531 person recruited, 1992-2002) aimed to evaluate the trend of the changes of high risk factors of CVD. Systolic blood pressure (SBP) was risen by 3.2 mmHg and 3.6 mmHg in the male by two different age stage respectively, and 2.3 mmHg and 1.0 mmHg in female. The diastolic blood pressure (DBP) was risen by 4.0 mmHg above the normal level in male and 2.7mmHg in female. Among 55~64 years old cohort, the absolute value of DBP raised by 2.3 mmHg above the normal level in male, while there is no significant change in female. Hypertension is the one of most important risk factors for CVD, especially systolic blood pressure.

## 2.6 Abnormalities of lipid profile

In a study in China, within 5 years cardiovascular events in 971 patients with metabolic syndrom(MS) is 5.15 times higher than in whom without MS above 40 years old.

In our hospital in 2009, we recruited 536 women within different stages of menopause. The results showed that metabolic syndrome was taken part in 19.1% in premenopausal female with normal menses cycle, while the incidence was greatly higher in menopause transition and postmenopause. The average TC in all of the subjects was above 5.18 mmol/L (200mg/dl) and the TC, TG, LDL-C showed an increase trend with menopausal stage, while the HDL-C showed a reverse tendency.

The research in Epidemic Institute of Cardiovascular Disease in Beijing for 10 years (1992-2002) shows that the level of HDL-c was decreased and the level of TC increased within 10 years. Meanwhile, morbidity of ischemic cardiovascular disease was raised. About 51.9% of ischemic cardiovascular disease, 11.17% of acute coronary heart disease and 21.9 % of acute ischemic stroke could be attributable to high TC level.

## 2.7. Diabetes

Framingham research shows that the mortality in female with diabetes was twice as high as male with diabetes. This data was supported by a study in Beijing. Therefore, diabetes is an independent risk factor of coronary heart disease (CHD) in female. Female with CHD combined with diabetes mellitus or abnormal glucose tolerance account for bigger proportion than male. Diabetes has more significant influence in mortality of female with CHD.

## **2.8 Menopause**

Postmenopausal women have a higher risk of cardiovascular disease. Dongzi Yang, et,al recruited 1,090 women above 40 in Guangzhou, the results showed that the incidence of CVD among postmenopausal women (14.6%) were higher than premenopausal women (3.4%). Another study in Guangzhou also suggests that the prevalence of CHD in postmenopause women was 67.9% and it's significantly higher than premenopausal group.

### **3. The treatment and prevention of women's cardiovascular diseases**

Xiujuan Tian et al showed that, in postmenopausal women with hormone-replacement therapy (HRT), the level of E<sub>2</sub>, HDL-C, ApoA1 was significantly increased, while TC, LDL-C, TG, Apo B was decreased. One research in Rui Jin hospital in Shanghai shows that in joint treatment group (antihypertensive and sex hormones), a slight decrease of SBP and DBP was observed, which was better than antihypertensive therapy only. Sex hormones can reduce TC and Lp(a) level in postmenopausal women. HRT starting from "window of opportunity" may be beneficial in reducing the CHD risk.

In china, the people have very poor knowledge of menopause. An investigation showed that about 90% of women eager to know the information of preventative measures from doctors, but only 30% accomplish their wishes. A lot of people do not understand that menopause is caused by the dysfunction of the ovaries, and the menopause related problems is caused by estrogen deficiency, and this may in turn cause anomalies of lipid profile and cardiovascular disease. Therefore, it is particularly important for postmenopausal women to develop medical knowledge vigorously and enhance the whole nation's health consciousness, which makes people willingly adopt healthy behaviors, reduce the risk factors and thus the incidence of CVD, improve the quality of life.

## The characteristics of breast cancer incidence in mainland China

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Breast cancer is the commonest cancer among women worldwide, with the lower incidence being reported from China. Over the last two decades, breast cancer incidence has increased threefold throughout all parts of the mainland in China. In Shanghai, Beijing and Guangzhou cities, the incidence of female breast cancer has become the highest amongst female malignancies.

The tendency of the increase of breast cancer incidence:

The increasing incidence rate was due to the change of risk factors rather than the change of population structure and size.

The breast cancer used to occur in women aged 40-65. But in recent years, it has been reported that the age of peak occurrence rate became younger. That means the increase was more dominant in the younger age group than in the older age group.

More than 50% of breast cancer cases are premenopausal women. The highest breast cancer incidence was observed in 40-59 years of age. The peak occurrence rate is in 40-50 years of age. The incidence declines after the age of 60. This is quite different from the data observed in Caucasian, among them the incidence of breast cancer increased significantly after 75 years.

The distribution of the breast cancer:

Breast cancer incidence is significantly higher in big cities than that in small cities, significantly higher in the laborers than that in the teachers, civil servants and technical staff, significantly higher in lower-educated people than that in high-educated ones, significantly higher in townfolk than that in the country dwellers.

There is accumulating evidence that breast cancer in younger women is biologically more aggressive than that in their older counterparts, and most of them are ER-negative.

The risk factors of breast cancer:

There are probably many factors that explain the incidence characteristic of breast cancer in mainland China. Genetic difference is probably occupies the dominant part. But other factors, such as environment pollution and life style change (diet and exercise), can also play an important role in breast cancer risk in different places.

The use of HRT is very rare in mainland China. The recent investigation revealed that there are only approximately 1% HRT users in postmenopausal women. So there will be almost no influence of HRT to the breast cancer incidence.

Conclusions:

Among younger women, the rising incidence of breast cancer probably reflects the lifestyle changes observed in younger generations. The hormone replacement rate in postmenopausal women in mainland China is only about 1%, which has no contribution for the increased incidence of female breast cancer

## Epidemiology of osteoporotic fracture in China

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Osteoporosis is one of major health problems related aging. Recent decades, life expectancy is getting longer, and population is getting aging rapidly in China. It is estimated that in 2050, more than half hip fractures all over the world will happen in Asia, of course, mostly will be Chinese, because of the big population in China.

Many changes may influence the incidence of hip fracture in China. The Life expectancy is getting longer, population is getting aging, the economic is getting developed, and life style is changing a lot. In order to explore the changing trends of incidence of hip fracture in China during the last decade, an epidemiological study on the changing of hip fracture rates in Beijing was conducted.

The hospital discharge data of hip fracture cases coded with 72.0, S72.1 and T93.1 in ICD-10 and 820 and 821 in ICD-9 from 143 hospitals in Beijing 2002-2006 were collected. The validation of the data was assessed through stratified sampling. The data of 2003 were not included because SARS spread in Beijing this year. The completeness and accuracy of data were confirmed by examining the discharge records and/or operating room logs. Medical records were reviewed to check the diagnosis and permanent residence. After the above steps of validation, the total number of Beijing hip fractures during 4 years was defined of 17939. Based on 2004 Beijing census, during this 4 years period, the hip fracture incidence rate for men was 103 per 100,000, and for women was 150 per 100,000. After standardized by the 2004 American population, the rates were 129 per 100,000 and 229 per 100,000 for men and women respectively. The corresponding rates during 1990-1992 were 80 per 100,000 and 83 per 100,000, after standardized by the same American population. From 2002 to 2006, the hip fracture incidence rates for men and women increased 50% and 59% respectively. In conclusion, the hip fracture rate in Beijing area increased significantly during the recent 12 years. This changing trend is coincident with those in other countries or regions in Asia. It means that hip fracture will be one of the major society and health problems during the aging process of Chinese population.

# The characteristics of menopausal transition, treatment status and CME activities by CMS in mainland China

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Menopause, a physiologic phenomenon in women's natural life span, is caused by the decline of ovarian function and thus the insufficiency of estrogen, which may in turn result in the termination of reproductive function, climacteric symptoms (hot flash, anxiety and restlessness, depression and so on), as well as the tendency of various kinds of chronic diseases in the old age, such as osteoporosis, CHD and AD. Nevertheless, menopause is a physiologic course affected by heredity, environmental factors, diet and life style. The symptoms vary with ethnicity, culture background and menopause age.

## **1. Demographic characteristic**

### **1.1 Data from demography**

Chinese population census in 2005 showed that the population in the mainland of China has reached 1.3 billion. And 12.88% were aged 50 years or older, accounting for 167,440,000 perimenopausal or postmenopausal women in China. It was estimated that the population of women older than 50 would have exceeded 2.8 billion by 2030.

### **1.2 Key age point during menopausal transition**

In the 1990s, it was reported that the average age of natural menopause was 48.4±3.8 for Chinese women. The onset of menopausal symptoms was at 46.1 years old on average, and mostly at 1~3 years before menopause. An investigation for the prevalence of climacteric symptoms in perimenopausal women in Beijing city by random sampling and a series of questionnaires, involving 1278 women (mean age 51.8) were conducted by Li et al. in 2006. The results showed that the mean age of natural menopause was 49.4±3.4. A national survey conducted by Chinese Menopause Society (CMS) in 1850 perimenopausal and postmenopausal women (including 599 natural menopausal women) in 2008. The results suggested that the mean age of menopause was 49.6±2.7. The mean age for the first menstrual cycle alteration more than 7 days (representing the beginning of perimenopausal period) was 46.22, and the mean age for the second alteration 46.8. The menopausal symptoms emerged at age 46.28 on average.

## **2. Prevalence of menopause related problem symptoms**

The common complaints in perimenopausal and early postmenopausal women may include abnormal uterine bleeding, vasomotor symptoms (eg, hot flash and sweating), abnormal skin sensation, insomnia, anxiety, depression, headaches, arthralgia and myalgia, dryness of vagina and dyspareunia, urinary incontinence, and so on. However, late postmenopausal women may develop some severe consequences, such as osteoporotic fracture, cardiovascular disease and senile dementia.

As early as in the 1990s, Xu Ling and colleagues from the Peking Union Medical College Hospital had conducted an epidemiologic survey among perimenopausal women aged 40 to 46 in Dongcheng district in Beijing. They found that the most common symptoms were irritability (46.6%), sweating (37.2%) and hot flash (36.8%). In menopausal women, 72.7% had menopause symptoms, among which 61.6% had at least one kind of symptoms. The survey in 2006 investigated the climacteric symptoms in perimenopausal women in urban area of Beijing city. The result demonstrated that 51.3% women had 5 symptoms or more, 16.7% women had Kupperman menopausal index score over 17. The prevalence of different symptoms ranged between 15.6% and 59.7%. The first 5 prevalent symptoms were arthralgia and myalgia (n=763, 59.7%), fatigue (n=732, 57.3%), insomnia (n=673, 52.7%), vasomotor symptoms (n=615, 48.1%), high irritability (n=615, 48.1%). Meanwhile, the prevalence of depression reached 23.8%. While the national study involving 1850 perimenopausal women in different regions of China, suggested that the first 5 prevalent menopause symptoms were

insomnia (n=1124, 60.80%), vasomotor symptoms (n=956, 51.7%), abnormal skin sensation or tinnitus (n=836, 45.20%), arthralgia and myalgia (n=338, 18.30%) and fatigue (n=311, 16.80%).

### **3. Status quo of treatment**

Estrogen therapy could improve climacteric syndrome, prevent and treat postmenopausal osteoporosis. Hormone replacement therapy (HRT) is widely used in the USA and Europe. Nevertheless, Chinese women still know little about HRT. Doctor Xu conducted an epidemiologic survey in women aged 40~46 in Beijing. She found that merely 0.14% of postmenopausal women had ever used HRT for more than half a year. Another study in 2002 from Beijing showed that 7.9% of middle and old aged women were aware of HRT and 4.4% of postmenopausal women had ever used. In the survey in 2006, Li Y et al found that 19.1% of perimenopausal women knew about HRT and less than 1.4% of them had ever used in the past half a year. But we can do better in this field. Doctor Ge conducted a survey in female staff over 40 years old in PUMCH in 2003. The result showed that 35.7% of them had ever used HRT, much higher than that in ordinary population under the same condition.

Doctors should take the responsibility. A survey by Professor Xu showed that 55% of women were bothered by menopausal symptoms. 79% of women thought severe menopausal symptoms should be treated, but most women (80%) didn't receive any treatment. 61% of women held a negative understanding about HRT. The main reasons for them to reject HRT were concern about weight gain and breast cancer. Doctors' advice was the only reason for women taking hormone replacement therapy. 93% of non-HRT users had never been advised by their doctors. If advised by doctors, 40% of women would take HRT.

Chinese Menopause Society, therefore, we should take the responsibility and obligation to communicate with patients, to provide them with more information, to teach them more knowledge, and to give them better advice and help.

Continuing Medical Education (CME) on menopause in People's Republic of China has a relatively short history which can be roughly divided into three stages.

#### **1, Stage I: Starting (1999-2002)**

Nationwide CME on menopause in People's Republic of China started around 1999, basing on the cooperation of Ministry of Health of PR China with Wyeth. Teaching materials and books were prepared at that time. Educational courses and programs about menopause were given and a lot of students at that time later became specialists focusing on menopause. Chinese Menopause Society (CMS) was founded in 2001 in Beijing and at the same time the 1st National Menopause Congress was held. Professor Shouqing Lin was the first chairman of CMS.

#### **2, Stage II: Development in a difficult environment (2003-2007)**

In 2003, an important turning point of menopause management after the first data of Women's Health Initiative trial were released, Chinese Menopause Management Guidelines (2003) was published. In 2004-2005 seminars about menopause management were provided irregularly, mainly in major cities. In 2006 the revised Chinese Menopause Management Guidelines (2006) was issued. In 2006-2007 large circuiting CME was given nationwide, in total 51 times lectures were given and more than 4300 doctors attended but CME at that time was still in big cities, In 2006 2nd National Menopause Congress was held in Kunming and more than 400 doctors attended. Since then Professor Qi Yu has been the chairman of CMS.

#### **3, Stage III: Rapid development period (2008-)**

In this period CME has made a very rapid progress. In 2009 CMS started the cooperation with International Menopause Society (IMS). In the initiation congress of 2009 CME, both the current chairman and the former chairman of IMS came and gave lectures, more than 1000 doctors attended in 20 sub-meeting by internet.

CME provides suitable forms of education programs at different levels, including city congresses and teleconferences, primary education program for gynecologist and general practitioners and advanced education program for gynecological endocrinologist. Training courses for lecturers were offered in the spring of every year since 2008 and those lecturers would give lectures in subsequent nationwide seminars using the same powerpoint slides provided by CMS which were revised yearly. CME was given not only in big cities but also

in small cities. In 2008 more than 5,000 doctors got continuing educations about menopause. In 2009 this figure increased to 10,000 and in 2010 it should be more than 20,000. In 2009 Chinese Menopause Management Guidelines were updated.