METABOLIC SYNDROME: MENOPAUSAL WOMEN AND THE HEALTH CARE CHALLENGE

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Menopause is defined as the cessation of ovarian function or of menstrual cycles. It is confirmed after 12 consecutive months without menses, or if the ovaries are removed or damaged. It can also be confirmed by hormone tests in women who have undergone hysterectomy. The mean age at menopause is 49.3 years in Taiwanese women [1]. The expected life span of Taiwanese women is 78 years, and one-third of a woman's life, therefore, occurs after the menopause.

The number of women aged ≥ 50 years has increased markedly in recent years, with an 87% increase over 16 years, from 1.74 million in 1992 to 3.25 million in 2008 (Figure) [2]. Although no accurate figure for the number of menopausal women in Taiwan is available, it was estimated to be around 3.25 million in 2008, with the mean age of menopause close to 50 years. The registered population in Taiwan in 2008 was 23.04 million. Women aged ≥ 50 years, therefore, accounted for 14.0% of the total population, or 28.4% of the total female population.

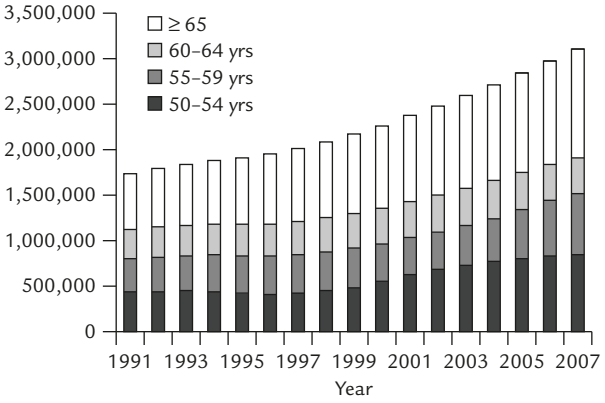

Figure. Number of women aged > 50 years in Taiwan.

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The incidence of chronic diseases and comorbidities increases markedly in menopausal women, and menopausal status, as well as the aging process, plays an important role in their development. It has been well documented that reduced hormone levels accelerate bone loss in postmenopausal women and, therefore, increase the incidence of osteoporosis and bony fractures [1]. The incidence of cardiovascular disease (CVD) in younger women is much lower than that in men of the same age, but the prevalence of hypertension and coronary heart disease (CHD) in women aged ≥ 50 years is higher than that in men [1].

Cerebrovascular accident, CHD and diabetes were the second, third and fourth leading causes of death in Taiwanese women in 2007, accounting for 10.0%, 9.8% and 9.8% of all deaths, respectively [3]. Although women have a greater life expectancy than men, the prevalence of coronary artery disease is high in women [4]. Care of menopausal women is thus an important issue for health care institutions in Taiwan.

Metabolic Syndrome

Metabolic syndrome (MetS) represents a cluster of risk factors for CVD, including atherogenic dyslipidemia, elevated blood pressure, elevated glucose, a prothrombotic state, and a proinflammatory state [5]. People with MetS are at high risk of diabetes and CHD and suffer increased mortality from CVD [6,7]. MetS was first defined in the Third Report of the National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) [5]. Subsequent studies have revealed ethnic difference in the development of intra-abdominal fat accumulation and in the risk of CVD. Asian races are more susceptible to intra-abdominal fat accumulation and more susceptible to CVD than Caucasians, even at a lower body mass index [8,9]. The diagnostic cutoffs for MetS in the Adult

Table. Diagnostic criteria for metabolic syndrome in Taiwanese adults in 2006

Measures	Cut-off points
Increased waist circumference (central obesity)	≥ 90 cm in men, ≥ 80 cm in women
Elevated BP	Systolic BP ≥ 130 mmHg or diastolic BP ≥ 85 mmHg, or drug treatment for hypertension
Reduced high-density lipoprotein-cholesterol	Men: ≤ 40 mg/dL; women: ≤ 50 mg/dL
Elevated fasting glucose	≥ 90 mg/dL or drug treatment for elevated glucose
Elevated triglycerides	≥ 150 mg/dL

BP = blood pressure.

Treatment Panel III criteria were, therefore, modified to account for these ethnic differences [8]. The definition of MetS used in Taiwan is in accordance with the MetS criteria for Taiwanese from the Bureau of Health Promotion in Taiwan. The Table summarizes the diagnostic criteria for MetS in Taiwanese patients [10].

The prevalence of MetS varies according to the diagnostic criteria, population, age, sex, and area. The prevalence of MetS among Taiwanese adults was 19.5% in men and 13.8% in women in 2005, according to the MetS criteria for Taiwanese [11]. However, there was a surge in the incidence of MetS in perimenopausal and postmenopausal Taiwanese women, from 24.2% in Taiwan metropolitan women aged 40–64 years, to 51.8% in women ≥ 65 years [12]. Methods for the treatment and prevention of MetS in perimenopausal and postmenopausal women are, therefore, urgently required.

In addition to CVD, MetS is also highly associated with non-alcoholic fatty liver disorders [13]. Non-alcoholic fatty liver disorders, rather than hepatitis B, are now the leading cause of abnormal liver function in Taiwan [14].

Menopause and Components of MetS

Body composition

Two patterns of body fat distribution have been observed; android or apple-shaped body composition (central obesity) represents intra-abdominal fat accumulation, while gynoid or pear-shaped composition represents fat accumulation in the gluteofemoral region. Central obesity with intra-abdominal fat deposition is associated with a higher risk of diabetes, hypertension and CVD [15]. For a 1-cm increase in abdominal circumference, the relative risk of a CVD event is increased by 2% [16].

The menopausal transition accelerates intra-abdominal fat accumulation, with a decrease in lean body mass. These changes in body composition may be attributed to the aging process, hormonal changes, or changes in physical activity [16]. A study by Gambacciani et al [17] revealed that menopausal transition, rather than the aging process, contributed to intra-abdominal fat accumulation in perimenopausal and postmenopausal women. On the other hand, a study by Kanaley et al [18] showed that the level of physical activity, but not menopausal state or age, accounted for intra-abdominal fat accumulation in menopausal women. Chang et al [19] reported that age, menopause and central obesity were all independent and significant risk factors for CVD in Chinese women.

These discrepancies in the results among different studies probably reflect the complexity of the relationship between menopausal status and body fat. Inconsistent conclusions may be due to ethnic bias or different methodologies. Irrespective of the etiology of intra-abdominal fat accumulation, the incidence an abnormal waist circumference was shown to increase dramatically in perimenopausal and postmenopausal women in Taiwan; the incidence increased from 10.7% in women aged 40–49 years to 22.8% in women aged 50–59 years, and to about 40% in women ≥ 65 years.

Insulin resistance

Insulin resistance is one of the most important pathophysiologic components of MetS. However, the effect of menopausal transition on insulin resistance remains to be determined. Some studies revealed a decrease in insulin sensitivity in postmenopausal women compared with premenopausal women [20–22], but others failed to find such a relationship [23,24]. Furthermore, the aging process and changes in body fat distribution may also contribute to a decrease in insulin sensitivity in postmenopausal women.

DeNino et al [20] found a reduction in insulin sensitivity only in older women > 60 years of age. Age-related differences in visceral fat accumulation could explain only a modest part of the decline in insulin sensitivity in nonobese women. Otsuki et al [22] demonstrated that menopausal state was associated with elevated fasting plasma glucose. However, most previous studies were based on indirect measurements of insulin sensitivity.

A recent study by Toth et al [24], using direct measurement of insulin sensitivity (hyperinsulinemic–euglycemic clamp technique), revealed that menopausal status did not affect insulin sensitivity. Further studies are needed to determine the relationship between menopausal transition and insulin sensitivity.

An epidemiologic study by Lin et al [12] demonstrated that the prevalence of high glucose levels was 11.6% and 34.1% in Taiwanese metropolitan women aged 40–64 and ≥ 65 years, respectively. The study by Chang et al [19] demonstrated that menopausal status was an independent risk factor for glycosylated hemoglobin A_{1c} in Taiwanese women; menopausal women had higher levels than premenopausal women.

Blood pressure

Premenopausal women usually have lower blood pressure than age-matched men. The rise in systolic blood pressure in postmenopausal women is steeper when compared with that in men [25], which results in marked increase in the prevalence of hypertension in postmenopausal women. The mechanisms responsible for rapid increases in blood pressure in postmenopausal women may be related to hormone changes during menopausal status and to other complex factors, including a change in the estrogen to androgen ratios, activation of the rennin–angiotensin system, increased endothelin levels, obesity, increased oxidative stress, and a higher sympathetic activity [26]. However, the relationship between menopause and hypertension remains controversial. Several studies revealed no relationship between menopause and hypertension [27]. The rise in systolic blood pressure does not occur during the menopausal transition or immediately after menopause, but rather develops over a number of years after menopause [28]. These inconsistent results indicate the complexity in the pathophysiology responsible for the increases in systolic blood pressure in postmenopausal women.

Although the systolic blood pressure increases with advancing age, the mean diastolic blood pressure decreases gradually from the sixth decade on [28]. Chow et al [1] found that postmenopausal women in Taiwan had a higher systolic blood pressure and diastolic blood pressure than age-matched men. However, Torng et al [29] revealed that the increases in blood pressure in postmenopausal women in Chin-Shan area were not significant after being adjusted for age and body mass index. The prevalence of abnormal blood pressure (systolic pressure ≥ 130 mmHg or diastolic pressure ≥ 85 mmHg) in Taiwanese metropolitan women aged 40–65 years and > 65 years was 44.2% and 84.1%, respectively [12].

High-density lipoprotein cholesterol (HDL-C) and triglycerides

HDL-C has a protective effect on the cardiovascular system. Previous studies have demonstrated an inverse relationship between blood levels of HDL-C and the incidence of CHD. Low blood levels of HDL-C are associated with an increased risk of coronary artery disease. The relative risk of coronary artery disease in women with HDL-C < 40 mg/dL was comparable with the relative risk of low-density lipoprotein cholesterol (LDL-C) > 160 mg/dL. HDL-C is, therefore, a better predictor of CHD than LDL-C [30].

Although some studies found that menopausal women had significantly lower levels of HDL-C [31,32], others showed an increase [31] or no change [22] in HDL-C levels. Taiwanese women had significantly lower LDL-C and higher HDL-C levels than Framingham women [29,33,34]. The more favorable lipoprotein profiles in Taiwanese women may be attributed to lower dietary total fat, saturated fatty acids and cholesterol, and more dietary polyunsaturated fatty acids [35]. Thus, the association between menopausal status and HDL-C levels still remained to be determined. Several studies have focused on the relationship between menopausal status and HDL-C concentrations in Taiwanese women, but the results have been inconsistent. A cohort study in the Chin-Shan community, a rural area in North Taiwan, failed to demonstrate any reduction in serum HDL-C levels after menopause [29]. The study by Chang et al [19] revealed that menopausal status was not an independent risk factor for HDL-C levels in Taiwanese women [19], while other reports have shown that postmenopausal women in Taiwan had significantly higher HDL-C levels than premenopausal women [29,33,34]. However, the risk of low HDL-C levels in metropolitan Taiwanese women increased with age, with a prevalence of 56.4% in women aged 40–65 and 62.7% in those aged > 65 years [12]. These inconsistent results may reflect differences in lifestyles between different areas, as metropolitan women tend to have a relatively sedentary lifestyle.

Previous studies in Taiwan demonstrated that menopausal transition was associated with an increased triglycerides level [19,29,33,34]. These results were consistent with studies in other ethnic populations [32,34]. The prevalences of high triglycerides levels were 19.3% and 33.2% in metropolitan Taiwanese women aged 40–65 and ≥ 65 years, retrospectively [12].

Lifestyle and MetS

Obesity and sedentary lifestyle are the most important factors contributing to the development of MetS.

Lifestyle intervention is, hence, the first and most important strategy for its treatment. However, there have been surprisingly few studies focusing on the effects of lifestyle intervention on MetS, especially in menopausal women. Previous studies have revealed that lifestyle interventions with changes in diet and regular aerobic exercise over periods of >6 months could effectively improve most components of MetS [36–38]. However, these interventions had no significant effect on HDL-C concentrations [36–38].

Regular aerobic exercise for >6 months without dietary intervention could significantly increase HDL-C concentrations [39]. It is possible that the apparently limited effect of lifestyle intervention on HDL-C may be because dietary changes cause a decrease in HDL-C, which cancels out the favorable effects of exercise.

A previous study in Taiwanese women revealed that an 8-week lifestyle intervention program could significantly improve four of the five components of MetS, but that the HDL-C concentration was markedly reduced [40]. These results indicated that short-term exercise programs could not improve HDL-C levels enough to compensate for the detrimental effects of dietary control. Lifestyle interventions for longer than 8 weeks are needed to clarify this relationship.

In addition to their effects on the components of MetS, lifestyle interventions can also improve physical fitness, insulin sensitivity, liver function, and quality of life [40,41]. Adequate and regular aerobic exercise is especially important for menopausal women. Rapid loss of lean body mass, as well as rapid bone loss, occurs during the perimenopausal period. Regular aerobic exercise may effectively prevent and treat MetS. In addition, regular exercise may help to maintain lean body mass in perimenopausal and postmenopausal women, and prevent disability due to muscle wasting in older women.

Conclusion

The prevalence of MetS has increased markedly in Taiwanese menopausal women in recent years, especially in metropolitan areas. The development of strategies for preventing and treating MetS, together with the management of menopausal symptoms, osteoporosis and cancer screening women, is becoming one of the most important issues in the health care of menopausal. An inappropriate lifestyle, including a lack of physical activity and excessive caloric intake, is the major contributor to MetS. Lifestyle interventions, therefore, provide the key first step in the prevention and management of MetS. Gynecologists in Taiwan play a major role in the health care of menopausal women and, therefore, need to increase their efforts to effectively manage MetS.

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