Changing Clinical Aspects of Ischemic Heart Disease in Japan

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Abstract: Because of recent advances in medication and revascularization techniques, the clinical prognosis of ischemic heart disease (IHD) patients has markedly improved. The increase in the Japanese population following a Western lifestyle has been associated with an increase in IHD, particularly in the younger population (<50 years). In addition, the number of very old IHD patients who survive other medical illness is also increasing. The increase in IHD the younger population is associated with an increase in the metabolic disorder (obesity, hypertension, hyperlipidemia, and impaired glucose tolerance). Between 1980 and 1990, the mean total cholesterol level of the Japanese general population (≥30 years) increased from 186 to 199 mg/dl in men and from 191 to 207 mg/dl in women. This increase was particularly marked in the younger population of both genders. Diabetes mellitus is also increasing steeply in Japan, and approximately 6,900,000 persons had diabetes in 1998. The prevalence of smoking has decreased, except in younger women, but it is still a problem, with high smoking rates of 55% among men and 13% among women in 1998.

Key words: Ischemic heart disease; Clinical picture; Coronary risk factor

Introduction

The development of new drugs and advances in revascularization techniques have resulted in dramatic improvements in the treatment of ischemic heart disease. However, the incidence of ischemic heart disease in Japan has continued to increase, without showing any tendency to reduce. This can perhaps be explained by the marked changes in the lifestyles and dietary patterns of the Japanese people.

The Incidence and Mortality Rate of Ischemic Heart Disease

Over the past 40 years, the mortality from heart disease in Japan has been broadly flat, or slightly on the decrease. The mortality from ischemic heart disease (IHD), the predominant heart disease encountered in clinical practice, increased until 1970, but thereafter has shown a slow downward trend. This tendency is in sharp contrast to that of cerebrovascular disease, the
mortality from which had decreased to one-third during the same period.

Heart disease is the third leading cause of death in our country. Acute myocardial infarction (MI) accounts for over half of the deaths from heart disease. In 1997, the mortality from MI was estimated to be 46.6 per 100,000 in men, and 42.3 per 100,000 in women. However, advances in diagnostic and therapeutic methods have brought about remarkable improvement in the prognosis of MI in the acute phase.

The incidence of MI or sudden death did not show any significant changes from the 1960’s to the late 1980’s, based on a survey conducted by the epidemiological study group appointed by the Ministry of Health and Labour and Welfare (now reorganized as the Ministry of Health, Labour and Welfare). The age-adjusted prevalence of MI has, however, been on the decline since the 1980’s. Notwithstanding, with the aging of society, the number of patients with MI has actually been increasing.

The average age of patients with MI is 62 to 65 years in men, and 70 to 74 years in women. Thus, the average age at onset of MI is about 10 years higher in women than in men. This statement also holds true for the incidence of MI in the United States and Western Europe.

The incidence of MI has been increasing in both relatively young people and in the elderly. For instance, a study of the age distribution of patients with AMI who were admitted to the Department of Cardiology, Jichi Medical School, showed that the number of inpatients with AMI or unstable angina increased steadily, although not significantly, over the previous three years among subjects under 50 years of age, as well as among those over 80 years of age (Fig. 1).

The increasing incidence of MI and other ischemic heart diseases in the younger generation may be related to rapid progression of coronary arteriosclerosis in this subject population. This assumption is supported by many studies. An epidemiological study demonstrated that the mean serum cholesterol level in the younger population increased by 10 mg from 1980 to 1990. An autopsy study of subjects 1 to 39 years of age revealed that the extent of coronary arteriosclerosis was significantly increased in males in their twenties and thirties between 1991 to 1995 than between 1978 to 1982. Another study reported that the incidence of arteriosclerosis was similar in pediatric subjects 15 years of age in Japan and the United States. In subjects older than 15 years, arteriosclerotic changes were more marked in Japanese than in American subjects.

**Features of Ischemic Heart Disease in the Elderly Population**

Elderly people have been generally defined as those 65 years of age or older in many studies, but a recent survey indicated that there is a common tendency for only people well over 65 years of age to be called elderly. Regardless of the definition considered, which may vary among studies, the features of ischemic heart disease common to the elderly are as follows:

1) Myocardial ischemia is frequently
asymptomatic.

2) A relatively greater proportion of elderly patients with ischemic heart disease have multivascular disease or history of previous MI. Furthermore, in this patient population, heart pump dysfunction or cardiac rupture is more likely to occur as a complication, and the prognosis is often worse.

3) Many elderly patients with ischemic heart disease have concomitant disease, including cerebrovascular disease, restlessness, renal dysfunction, pneumonia, and other organ dysfunctions. In-hospital death among such elderly is also considerably high.

Age is an important risk factor for ischemic heart disease in the elderly. Smoking is thought to be associated with multivascular disease. Comorbidity is frequently observed in elderly patients. The prevalence of hypertension, hyperlipidemia, and diabetes mellitus in this patient population is relatively high. The ratio of females among patients with IHD increases with advancing age of the patients. The prognosis in IHD is significantly dependent on the age of the patient. The more advanced the age, the higher the rate of in-hospital mortality.

According to a research group formed by the Longevity Science Organization, early detection of ischemic heart disease is generally difficult in elderly patients. Their symptoms may be atypical, which may result in missed diagnosis and delayed treatment. Furthermore, the use of catheters during diagnostic procedures frequently causes problems in elderly patients. These factors have contributed to increase in the overall mortality (16.8%) and cardiac death (12.4%), by roughly about 5 times that noted in middle-aged group. One report also pointed out that cardiac death was primarily due to congestive heart failure or heart rupture in the elderly, while in middle-aged patients, cardiogenic shock was the predominant cause of cardiac death.

Changes in Coronary Risk Factors

The incidence of metabolic disorders, such as obesity, hyperlipidemia, and abnormal glucose tolerance has been rapidly increasing in recent years. Preventive measures for these disorders should be instituted in combination with counseling for smoking cessation and blood pressure control. The increased incidence of metabolic diseases has been associated with an increased incidence of ischemic heart disease, especially of MI and severe three-vessel disease. Treatment results and mortality rates in patients with ischemic heart disease have reached levels similar to those in the United States and Western Europe. However, while the incidence of ischemic heart disease has been decreasing in these developed countries as a result of efforts directed at improving lifestyles and advances in therapeutic methods, the incidence curve in Japan remains flat or even increasing.

1. Sex

The incidence of cardiovascular disease is very low in females in their early forties or younger; however, the incidence shows an upward trend in women in their late 40’s and 50’s, i.e., during menopause, and reaches a level similar to that in men in women in their late 60’s. A cohort study on Hisayama-machi residents showed that this tendency has not significantly changed among the three time-periods studied, namely, 1962 to 1970, 1971 to 1979, and 1980 to 1988.

2. Hyperlipidemia

A basic survey of cardiovascular disease by the Ministry of Health and Welfare showed that the serum total cholesterol level (TCL) in males aged 30 years or older increased from 186 to 199 mg/dl during the 10 years from 1980 to 1990, while in females aged 30 years or older, during the same period, the level changed from 191 to 207 mg/dl. The proportion of subjects with serum TCL equal to 220 mg/dl or over
was the largest in subjects in their forties (31.1%) among males and in subjects in their sixties (52.6%) among females. The proportion of people with the specified TCL or over has continued to increase gradually. The average serum TCL has also increased after 1990, especially in younger people.

Elevated TCL is associated with a higher incidence of ischemic heart disease. The risk in males with a serum TCL of 200 is 1.7 to 2.0, relative to those whose TCL is 160 to 170. When the TCL level increases to 220 or over, the risk ratio jumps to 2 to 5 relative to those with a TCL of 160 to 170. The risk ratios are similar for females. HMG-CoA reductase inhibitors, which were introduced into clinical practice as anti-hyperlipidemic agents in the 1990’s, have been confirmed to effect a decrease in the incidence and mortality rate of MI.

3. Hypertension

The average blood pressure is known to be correlated with the incidence of coronary artery disease. The Hisayama-machi cohort study showed that the systolic blood pressure level was related to the incidence of coronary arteriosclerosis, but the incidence of coronary artery disease had not changed over time.

The prevalence of severe hypertension has decreased, while the number of patients with mild diastolic hypertension or borderline hypertension has been on the increase. The average systolic blood pressure has shown a continued tendency to decrease in both males and females since 1961.

4. Diabetes mellitus

The prevalence of diabetes mellitus has been increasing year by year. According to the 1998 epidemiological survey, the number of diabetic patients was estimated to be approximately 6.9 million. This may be attributable to genetic disposition and changes in lifestyles. Excessive fat intake due to adoption of westernized diet patterns and physical inactivity have led to an increased incidence of obesity.

The incidence of the first episode of ischemic heart disease in diabetic patients is as high as the recurrence rate in non-diabetic patients with previous MI. The relative risk of MI is greater than 2.0 in diabetic patients in Japan.

5. Overweight

The Framingham Study has reported that obesity was a risk factor for ischemic heart disease, independent of smoking, serum total cholesterol level, systolic blood pressure, impaired glucose tolerance, and hypercardia. A tendency towards increase in the number of obese subjects has been observed in our country. Impaired glucose tolerance, hyperlipidemia, and hypertension are strongly related to obesity, especially to abdominal fat obesity.

6. Cigarette smoking

Cigarette smoking has been confirmed to be associated with both increased morbidity rate and mortality rate from ischemic heart disease. The number of pack years of cigarette smoking is strongly correlated with the risk of coronary artery disease. The relative risk of smokers to non-smokers is 1.73 for males and 1.90 for females. Although the number of smokers has been gradually decreasing, the percentage of smokers is still remarkably high in Japan as compared to that in the United States and Western Europe. The smoking rates among Japanese males reached its peak (83.7%) in 1966, and subsequently showed a downward trend, decreasing to 55.2% in 1998. The smoking rate among females has, however, remained unchanged (13.3%) during the same period. The absence of reduction in the smoking rate in young female smokers in their twenties and thirties is a matter of particular concern, since this would be expected to result in a higher incidence of ischemic heart disease in the future.
Advances in the Treatment of Ischemic Heart Disease

Advances in the treatment and diagnostic methods of ischemic heart disease have brought about marked improvement in the prognosis of MI in the acute phase. Such advances include the establishment of coronary care units (CCUs) in many medical institutions throughout the country, earlier reperfusion therapy, strategic drug therapy using β-blockers, angiotensin-converting enzyme (ACE) inhibitors, and angiotensin II receptor blockers (ARB). In particular, earlier revascularization has greatly contributed to reduction in the incidence of cardiac rupture and inhibition of prolonged myocardial remodeling, which has resulted in much improved prognosis in a large number of patients with ischemic heart disease.

Mechanical assist devices, such as intraaortic balloon pumping (IABP) and percutaneous cardiopulmonary support (PCPS) have also been confirmed to be effective in improving the survival rate in cases of acute MI. In addition, risk factor monitoring and secondary prevention by medication (using statins, ARB, ACE inhibitors, and antithrombotic agents) have also played a role in improving the prognosis of MI.

MI is often accompanied by heart failure (15 to 27%), cardiogenic shock (15 to 18%), and cardiac rupture (4 to 5%). The mortality rate among MI patients with these complications is high both in Japan and in Western countries.

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In-hospital mortality from AMI was estimated to be 29% in the 1960’s, 21% in the 1970’s, 16% in the 1980’s, and 10% in the 1990’s in the United States and Western Europe. In Japan, the mortality was calculated to be 30.5% from 1982 to 1985, when CCUs were scarcely established in medical institutions, but decreased to 9.4% after CCUs became a commonplace. Percutaneous transluminal coronary angioplasty (PTCA) and percutaneous transluminal coronary recanalization (PTCR) have been shown to reduce the incidence of formation of ventricular aneurysm. In-hospital mortality from AMI at the Department of Cardiology, Jichi Medical School Hospital was 4.7% in 2001, and the mortality even among patients with acute MI classified as Killip class IV decreased to the 40% range.

Despite advances in the methods of treatment of ischemic heart disease, the short-term prognostic factors nonetheless remain old age, female sex, previous history of hypertension, diabetes mellitus, or MI, Killip class III or more advanced, and no reperfusion therapy.
risk factors still significantly increase the mortality rate (See Fig. 2. Mortality rate by Killip classification stage).

Concerning the long-term prognosis, death rates after one year, three years, and five years after an episode of MI were 6.2%, 7.6 to 12%, and 18 to 19.1%, respectively in Japan. In Western countries, the corresponding rates were 8 to 14.1%, 14 to 33%, and 19 to 39%, respectively, which indicate that the prognosis is better in Japan than in Western countries. This difference is probably attributable to the preference for low fat diet and low rates of previous multivessel disease or MI among Japanese subjects. Improvements in survival rates after MI have, however, produced an increase in the number of patients at higher risk who are older, have more severe multivessel disease and more severe cardiac dysfunction. This may complicate the clinical picture of ischemic heart disease further in the future.

Conclusion

Change in the lifestyles of Japanese people has resulted in an increased incidence of ischemic heart disease in both the younger generation and in the elderly. The ever-increasing number of ischemic heart disease patients among relatively younger people highlights the importance of management of patients at higher risk of coronary artery disease and primary preventive measures. Furthermore, the increase in the incidence of ischemic heart disease in the high-risk elderly population also points to the importance of effective treatment and management of these patients so as to maintain the quality of life and avoid a bedridden life in these patients.

REFERENCES