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Progression of Coronary Artery Disease

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Abstract The coronary artery disease is progressive, which implies two processes ; one time-dependent and anothetr time-independent. Nonocclusive progression occurs in relation to time, while progression to occlusion does not depend directly on time. The chronic nonocclusive progression has a pattern of stepwise course mixed with slow progression phase and rapid progression phase. The acute occlusive progression occurs unexpectedly at any stage of nonocclusive progression. Thus, the coronary artery disease is not supposed to progress linearly and may have a chaotic course.

Key words : Angina pectoris, Acute myocardial infarction, Coronary artery disease

The natural history of coronary artery disease has not been the primary topic of many of the published papers, and the information that can be gleaned from them, particularly with respect to the time factor, is often incomplete. Serial angiographic studies may help us to understand the development of coronary artery disease, and there is a wealth of such data on file. Previous studies[1-14] have included in their definition of progression of coronary artery disease the whole spectrum of lumen reduction, including coronary artery occlusion. However, whereas coronary artery occlusion is considered as an acute process, coronary atherosclerosis considered as a chronic process. This report is a review of the evidence relating to the two processes of coronary artery progression ; chronic progression and acute progression.

Chronic Nonocclusive Progression

Coronary atherosclerosis is a degenerative arterial disease which in time can progress and produce vessel stenosis, with reduced myocardial blood flow in the later phase of the disease. Autopsy studies from the Korean and Vietnam wars have demonstrated that atherosclerotic lesions in the coronary and systemic circulations may be present in the third decade of life[15,16]. However, most of the affected persons will not become symptomatic or have any signs of coronary artery disease detectable by available diagnostic tests for many years (subclinical stage, Fig. 1). At some time after initiation of the coronary lesions, the patient may develop manifestations of coronary artery disease (clinical stage, Figure 1). It has been generally documented that a stenosis of 75 percent lumen diameter reduction will sufficiently impede augmented blood flow as to cause myocardial ischemia under conditions of imposed stress[17].

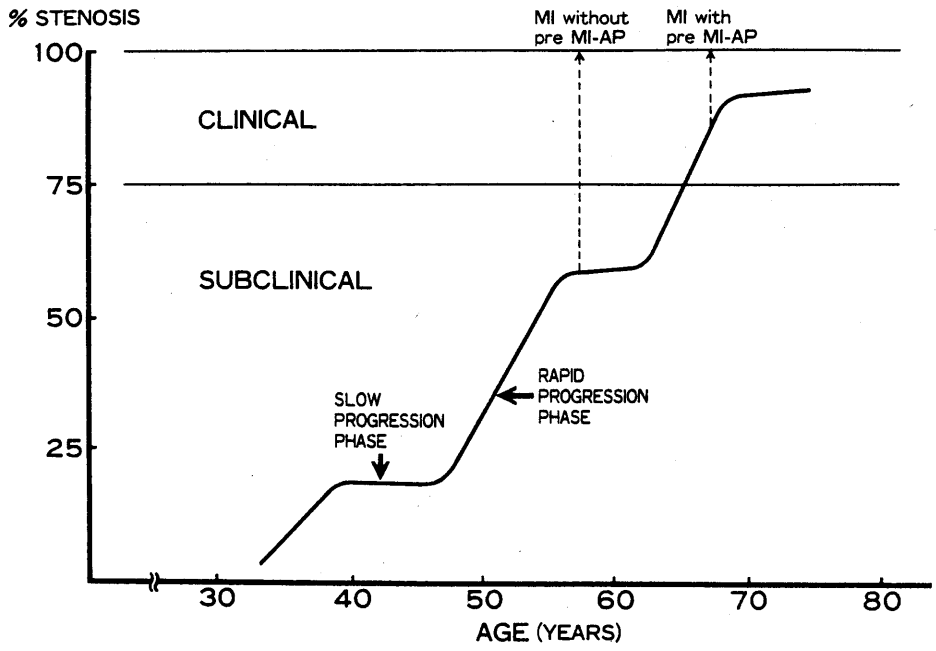

Fig. 1 Progression of coronary artery disease. Coronary artery disease begins in the middle age, initially has an asymptomatic process and then a symptomatic period. Nonocclusive progression of coronary artery disease (solid line) is constituted of rapid progression phase and slow progression phase. Occlusive progression of coronary artery disease (dotted line) can occur at any time in the course of coronary artery disease. Some patients have myocardial infarction (MI) with angina (AP) before infarction and some have myocardial infarction without angina before infarction.

At necropsy, the aorta of most middle aged subjects has lesions of several different types and stages within a single segment, ranging from small, focal proliferations of smooth-muscle cells to large white fibrous plaques and from fatty spots to large fibro-fatty lesions[18]. In a large series of repeated angiograms of the aorta and its major branches, DeBakey[19] recognized three groups—(1) patients, mainly relatively young, having individual lesions that appear and rapidly progress in the course of one to three years, (2) patients with gradual progression, and (3) patients in whom the disease seems to be static over many years. He suggested that atherosclerosis is not necessarily a continuously progressing disease and may even be self-limited. Previous reports indicated that the frequency of progressive arterial changes increased as the interval between the two angiographic studies increased[2,10–12]. In the series of 262 patients with obstructive coronary artery disease, Kramer et al[10]. reported that 128 patients had progressive changes and the remainder did not. In patients with nonprogressive changes between the two angiographic studies, the coronary artery disease had progressed to the degree recognized at first angiographic study. Nonprogression of coronary artery disease means no change of stenosis occurred in the interval between the two angiographic studies. However, these nonprogressive patients have progressed previously and may progress in some time in future. Therefore, progression of coronary artery disease most likely does not occur linearly, and may have a pattern of stepwise course mixed with slow progression phase and rapid progression phase (Fig. 1). When the interval between the two angiographic

studies is long, the interval more frequently includes the rapid progression phase. When the interval between the two angiographic studies is short, some intervals will include a rapid progression phase and others will have only a slow progression phase. Therefore, the progression of coronary artery disease appears to be related to time. The interval of rapid and slow progression phase, and rapidity (progression/time) may be different from one patient to another. In one patient, the course of coronary artery progression may be variable. It is still unknown which factors are related to rapid or slow progression in different patients and to different stages in the same patient. Kramer et al[20]. observed the relation of risk factors to the progression of coronary artery disease. No significant difference could be found between the progressive and nonprogressive groups in relation to family history, blood pressure, diabetes, smoking habits, weight, cholesterol level, triglyceride level, initial ECG and initial catheterization findings. The results showed progression was more frequent in patients younger than 50 years than it was in patients 50 years and older and as the severity of the lesion increases, which was consistent with other studies[1,2,5,14]. There have been conflicting results in the relation of risk factors such as smoking status, hypertension, diabetes, and cholesterol level to the progression of coronary artery disease[2-4,6,7,14,20]. The rapid progression could have a different mechanism from the slow progression. The risk factor may be related to the certain stage of progression process, either rapid progression or slow progression. Coronary artery disease is not static, but rather, is an actively progression process. The progression appears to be a multistage process. A multistage process of coronary artery disease and the relation of risk factor to rapid or slow progression might be observed in more than three sequential angiographic studies.

Acute Occlusive Progression

Some patients have angina pectoris before acute myocardial infarction, and others do not[21-23]. Matsuda et al[21]. observed the relation between types of angina before myocardial infarction and the level of physical activity at the onset of myocardial infarction. In patients with chronic stable angina before myocardial infarction, most of the anginal attacks were precipitated by effort, however, the subsequent myocardial infarction occurred during varying degrees of physical activity. The degree of physical activity that precipitated angina before myocardial infarction was different from that at the onset of myocardial infarction. In patients without angina before myocardial infarction, myocardial infarction occurred during varying degrees of physical activity. Patients with either no angina or chronic stable angina before myocardial infarction had myocardial infarction without any warning compared to those with unstable angina.

In angiographic observation after myocardial infarction, most of the patients had significant stenosis in the artery reponsible for myocardial infarcton[21,24]. In necropsy cases of fatal myocardial infarction, most of the patients had old atherosclerotic plaque[25]. These date suggest that the significant fixed underlying stenosis exist in the artery responsible for myocardial infarction prior to infarction. When patients were divided according to the presence or absence of angina before myocardial infarction, patients without angina before infarction more frequently had lesions of less than 50 per cent than patients with angina before infarction[21]. It is tempting to speculate that some patients without angina before infarction do not have significant severe fixed underlying stenoses before myocardial infarction. On the other hand, most of patients with angina before infarction had lesions of more than 50 per cent in the artery responsible for myocardial infarction. Patients with exertional angina before infarction apparently have significant fixed underlying stenosis before infarction. Exercise is the most common anginal precipitating factor in patients with angina before infarction and angina during exercise is believed to be related to inability of a fixed coronary reserve to meet the increased myocardial oxygen demands[26]. Although the symptom of angina may not always be related to the pathoanatomy of the coronary artery, the presence or absence of angina may reflect to the presence or absence of fixed severe coronary narrowing before myocardial infarction. If exertional angina is related to significant coronary stenosis and the worsening of angina is related to the progression of stenosis, the unpredictable myocardial infarction could be caused by a different mechanism from chronic nonoc-

clusive progression of coronary artery disease. The acute occlusive event of myocardial infarction could occur at any stage of nonocclusive progression of coronary artery disease (Fig. 1). Some patients have myocardial infarction in mild stenosis of coronary artery disease and some have myocardial infarction in severe stenosis of coronary artery disease. The coronary artery occlusion of myocardial infarction is not a termination of chronic nonocclusive progression of coronary artery disease.

The atheromatous lesion per se is generally not responsible for totally occluding the vessel. Coronary thrombi are usually superimposed on or adjacent to atherosclerotic plaques ; the mechanism by which thrombosis occurs in these stenotic areas remains controversial. Thus, the acute clinical event of myocardial infarction does not appear to be related to the progression of the basic atheroma to total obstruction.

The report of Kramer et al[13]. is in support of this conclusion, in which they analyzed the results of 62 patients who had myocardial infarction in the interval between the two angiographic studies. Thirty-five per cent of the patients did not have disease progression. Bruschke et al[2]. reported similar findings in their series of 256 parients with follow-up coronary angiograms. Eight of their 30 patients who had repeat catheterizations with interim myocardial infarctions had no significant disease progresson. Pichard et al[27]. observed the angiographic appearance of the infarct-related artery in 130 patients with a history of acute myocardial infarction. The slow spontaneous lysis of the thrombus may be completed in several months in less than half of the patients and may never reach completion in a significant number of patients. A similar repair or lytic process does not seem to occur in the atherosclerotic plaque, since most patients without total obstruction remain with severe narrowing in the infarct-related artery. Recent studies in which coronary arteriography was performed on patients within the first few hours after the onset of acute myocardial infarction have demonstrated that coronary artery supplying the area of evolving infarction is totally occluded in the majority of these individuals[28,29]. If fibrinolytic agents are infused into the coronary artery, patency is achieved in a high percentage of cases. Angiography performed after fibrinolytic therapy usually demonstrates either residual high-grade stenotic lesion or mildly or moderately narrowed lesion at the site where coronary artery occlusion had existed. Fresh thrombi have been recovered from the majority of patients with acute myocardial infarction undergoing emergency coronary bypass surgery[29]. Hence, acute myocardial infarction may occur without evidence of progression of the basic atherosclerotic lesions.

Postmortem studies also reveal a duality of the progressive pathologic process leading to fatal acute myocardial infarction[30-32]. Atherosclerosis develops in a time-dependent manner. It develops in a chronic fashion until vessel occlusion occurs with atheromatous material or thrombus in an acute, time-independent manner. From the sequential angio-graphic observation, Kramer et al[13]. suggested that two processes, one time-dependent and another time-independent, determine the rate of progression in coronary artery disease. Nonocclusive progression occurred in relation to time, while progression to occlusion did not depend directly on time. Furthermore, the likelihood of the acute occlusive event occurring is directly related to the severity of lumen diameter reduction. Patients with more severe stenosis have more frequency of occurrence of acute myocardial infarction.

The progression of coronary artery disease does not occur linearly. The nonocclusive progression of coronary artery disease has multistage and is time-dependent ; while the occlusive progression is time-independent. The occlusive progression of coronary artery disease could be caused by a different mechanism from the nonocclusive progression. Some risk factors may be more related to the occlusive progression. Other risk factors may be more related to the nonocclusive progression. It has been reported that smoking status, while strongly predictive of myocardial infarction, is only weakly related to angina pectoris[33]. Therapeutic consideration should be paid to the understanding of the pattern of this progression of the coronary artery disease. In the course of nonocclusive progression, the control of factors related to progression might be a primary management. In the occlusive progression, the mean of prevention of acute occlusion and the restoration of coronary artery blood flow immediately after occlusion should be considered.

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