episodes, 33% had accompanying symptom, while 67% were asymptomatic. 2) The exercise testing performed in the morning induced an ischemic attack in 58 (60%) of 96 patients. Of the 58 attacks, 46 were associated with ST segment elevation on the ECG. The exercise test performed in the afternoon induced ischemic attack in 30 (33%) of 90 patients and the inducibility was significantly lower than that in the morning (p < 0.01). 3) Hyperventilation test induced an ischemic attack in 68 (69%) of 99 patients. 4) The inducibility of ischemic attack with exercise test and hyperventilation test was significantly correlated with the activity of the disease (both p < 0.01). 5) Propranolol did not suppress the exercise-induced attack in any of the 34 patients in whom ischemic attack was induced with exercise testing after placebo. In contrast, both diltiazem and nifedipine significantly suppressed the exercise-induced attack (the inducibility after these drugs was 15% and 16%, respectively). 6) Of the 106 study patients, 29 (27%) were considered to have spasm in the left coronary artery, 33 (31%) in the right coronary artery and 44 (42%) in both the left and right coronary arteries (i.e., multivessel coronary spasm). Most of patients (82%) with multivessel spasm did not show significant organic stenosis in the arteriogram. 7) Of 104 patients with intracoronary injection of acetylcholine, coronary spasm was induced in 95 patients (91%).

In conclusion, the clinical aspects described above characterize coronary spasm as a pathogenesis of angina pectoris. In the consideration of the therapeutic strategy, it is important to base the diagnosis of coronary spastic angina on these clinical characteristics. This is especially true in patients with angina and without significant coronary artery disease in whom the provocative procedure for coronary spasm failed or in those in whom coronary arteriography is not performed. Calcium antagonists are extremely effective in preventing ischemic attack due to coronary spasm, whereas beta-blockade may be harmful. Finally, multivessel coronary spasm is not a rare phenomenon; it occurs in relatively many patients with variant angina, especially in those without significant coronary artery disease.

3. Pathophysiological Findings, Treatment and Prognosis of Angina Pectoris

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Subjects and Methods

Long-term prognosis of patients with angina pectoris

The long-term prognosis of 1883 (98.2%) of 1918 patients with angina pectoris who underwent routine coronary angiography (CAG) was studied. The percentage of patients with significantly (more than 70%) obstructed vessels in single vessel disease (SVD) was 29.0%, double (DVD), 25.0%, triple (TVD), 20.5% and left main trunk (LMT), 5.4%. There were 20.1% of the patients with no fixed stenosis and 24.7% with coronary artery spasm.

The 1308 patients who did not undergo coronary artery bypass surgery (CABS) or coronary angioplasty (PTCA) within 90 days after CAG were defined as medically treated patients.

The another 883 patients who underwent CABS at this hospital were defined as surgically treated patients.

Long-term prognosis of patients with silent myocardial ischemia (SMI) following acute myocardial infarction (MI)

Subjects was a total of 525 survivors from acute MI. Episodes of SMI were diagnosed from 12 lead EKG during rehabilitation practice, treadmill test and/or thallium exercise scintigraphy during a hospitalization period of about 4 weeks. The subjects were classified into the following three groups: a control group of patients without angina nor SMI
(309 cases, 58.9%), SMI group of patients with SMI and without angina (59 cases, 11.2%), and AP group of patients with angina pectoris (157 cases, 29.9%). Follow-up rate was 99%.

Mechanisms and treatment of impending MI

Impending MI was defined in this study according to the following criteria: 1) new onset, recurrent or worsening angina, 2) more than two episodes of chest pain at rest with ischemic ST-T changes in spite of extensive medical treatment, and 3) at least one anginal attack prolonged for more than 15 min after intravenous nitroglycerin. The 62 impending MI patients were divided into the following two groups according to the ST segment displacement during the chest pain attacks: with at least one episode of ST segment elevation with chest pain, group E (35 patients), and with ST segment depression, group D (27 patients).

Results

Figure 1a) shows the cumulative survival curves. It is unequivocal that the prognoses were affected by the numbers of diseased vessels. There were no significant prognostic differences between the medical and surgical patients. However, as shown in Fig. 1b), the difference was significant in the patients with TVD or LMT.

Regarding the baseline characteristics, previous MI, non-Q wave MI and multivessel coronary artery disease were significantly more frequent in the SMI group and AP group than in the control group. Angina prior to MI was more frequent in the AP group than in the other groups.

As shown in Fig. 2, the total and cardiac mortality rate and incidence of recurrent MI were higher in the SMI group and likewise in the AP group than in the control group.

There was no significant difference in the baseline characteristics between the two groups, except for a significantly higher proportion of new onset or recurrent angina in group E and worsening angina in group D. As indicated in Fig. 3, group E had a significantly higher incidence of SVD (54%), and group D a higher incidence of TVD or LMT (82%). Intracoronary thrombus in the ischemia

![Cumulative survival curves after coronary angiography (CAG) in patients with angina pectoris. FS, fixed stenosis; SVD, single vessel disease; DVD, double vessel disease; TVD, triple vessel disease; LMT, left main trunk lesion.](image)

![Cumulative survival curves in medical (---) and surgical (-----) patients with TVD or LMT.](image)

![Comparison of cumulative survival, cardiac mortality and MI recurrence curves in the following three groups: SMI group (-----), AP group (------) and control group (-----) (*, p <0.05).](image)
related vessel was present in 34 patients of group E, while in only 6 of group D. In contrast, complex coronary lesions such as eccentric narrowing with irregular borders, ulceration or dissection were documented with higher incidence in group D (Fig. 3).

Regarding the results of treatment, thrombolysis with intracoronary urokinase was assessed to be effective in 15 patients of group E, but in only one of group D. As a final effective therapeutic procedure, PTCA was predominantly chosen for group E (22 patients), and CABS for group D (20 patients).

Discussion

In the last 20 years, the prognosis of angina pectoris has been markedly improved. However, the prognosis complies with development of MI. As seen in the present results, if it would be possible to diagnose expeditiously and examine in detail impending MI, worsening or new onset angina, SMI and multivessel coronary artery disease, infallibly effective treatment regimens are possible based on a understanding of the pathophysiology.

It is true that not a small number of patients with angina pectoris have acute MI due to a delay of hospitalization. Furthermore, a sudden MI onset from stable angina or from a seemingly healthy state are not infrequent. In the majority of cases of angina pectoris, the morbid state changes with time, then susceptibility to acute MI sets in. Moreover, the pathogenic mechanisms of angina pectoris and MI are not necessarily the same. These factors prohibit the means to find a reliable method to prevent MI onset.

The optimal treatment based on a full-scale classification of angina pectoris will be possible after the elucidation of the mechanisms of the changing status of angina and sudden MI onset.