Natural History and Prognosis of Ischemic Heart Disease

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1) Forty-four cases with myocardial rupture (33 with free wall rupture, 9 with interventricular septal perforation and 2 with papillary muscle rupture), all of which were ascertained by autopsy and/or at surgery, were analyzed. When the following 7 risk factors were actively managed in the acute stage of myocardial infarction, the incidence of myocardial rupture was significantly reduced: a) high blood pressure on admission, b) physical and emotional instability, c) recurrent chest pain, d) aged females, e) no history of angina or myocardial infarction, f) large myocardial infarction on ECG and g) the first 10 days after the attack of myocardial infarction. If cardiogenic shock occurs, surgery should be performed as soon as possible; if not, it should be delayed 3 weeks.

2) The natural history of ischemic heart disease was analyzed in 400 medically-treated patients with significant coronary artery disease. They had been followed up continuously and periodically for more than one year. The prognosis of the patients with 3-vessel disease or left main trunk disease, those with poor left ventricular function ($EF < 30\%$) and of old age (≥ 60) and those who had a history of ischemic heart disease was poor.

3) Follow-up study was done in 30 patients with variant angina. They often had life-threatening arrhythmias during attacks (8 ventricular tachycardia or ventricular fibrillation, 8 serious bradyarrhythmia). All patients with variant angina should be treated medically at first, and only patients with organic coronary artery disease and chest pain on effort in spite of the medical treatment should be considered as candidates for AC bypass surgery.

SURGICAL treatment of ischemic heart disease is very popular in Western countries, and recently it has been increased also in Japan.¹ However, there are many problems remaining in the medical and surgical management for severe cases. In order to clarify these problems, the following studies were conducted from the medical view point.

Myocardial Rupture in Acute Stage of Myocardial Infarction

Out of a total of 4,750 consecutive autopsies

Key Words:

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Free wall rupture
Papillary muscle rupture
IVS perforation

there were 234 cases with acute myocardial infarction (MI), including 40 cases complicated by myocardial rupture. Forty-four cases having this complication (40 autopsy cases and 4 surgical cases) were analyzed: 33 with free wall rupture, 9 with interventricular septal (IVS) perforation and 2 with papillary muscle rupture. The site of MI in the 33 with free wall rupture was anterior in 23 and infero-posterior in 10. All of the 9 cases with IVS perforation were anterior MI and 2 with papillary muscle rupture were infero-posterior. The age of the patients ranged from 54 to 92 (mean, 71.2), consisting of 21 males and 23 females.

Annual incidence of myocardial rupture in autopsy cases is shown in Fig. 1. The total myocardial ruptures in the past 9 years were 40

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Fig.1. Annual incidence of myocardial rupture in autopsy cases with myocardial infarction.

Black arrow: The date of the 42nd Annual Meeting of Japanese Circulation Society, when we began to make every effort to avoid risk factors.

TABLE I OUTCOME OF MYOCARDIAL RUPTURE

Free wall rupture	33 cases		sudden death
IVS perforation	9 cases	Shock (—) 5 cases	surgery 4 cases
		Shock (+) 4 cases	death within 3 days
PM rupture	2 cases	Shock (+) 2 cases	death within 1 day

IVS = interventricular septum; PM = papillary muscle

out of 234 MI (17.1%). On the 42nd annual meeting of Japanese Circulation Society² and on the 7th Asian-Pacific Congress of Cardiology³, we presented the following risk factors for myocardial rupture: 1) high blood pressure on admission, 2) physical and emotional instability, 3) recurrent chest pain, 4) aged female, 5) no history of angina or MI, 6) large MI on ECG and 7) within the first 10 days.

Since then, we have made every effort to eliminate these risk factors in the acute stage of MI. As a result, the incidence of myocardial rupture has been dramatically reduced since 1978. In 1981, only 2 cases of myocardial rupture were found among 45 autopsy cases with MI (4.4%).

Case 1: A 69-year-old male developed pansystolic murmur with thrill several hours after the onset of anterior MI. Perforation of the IVS was diagnosed by bed-side catheterization with oximetry. Because of no significant hemodynamic deterioration, he had been treated

medically with close observation for the next 3 weeks. A left ventriculogram confirmed perforation of the IVS in the apex. On selective coronary angiogram, the right coronary artery was branched off from the left anterior descending artery, indicating the presence of a single coronary artery, and a 75% stenosis of the left anterior descending artery was observed just before the branching off of the right coronary artery (white arrow in Fig. 2). Hemodynamic deterioration occurred following angiography and the patient underwent surgery.

Case 2: A 59-year-old male suddenly developed cardiogenic shock with pulmonary edema on the 9th day of acute inferior MI. Four hours later, he died in spite of intensive medical treatment. The post-mortem examination revealed acute inferior MI with posterior papillary muscle rupture (Fig. 3).

The outcome of the myocardial rupture is shown in Table I. All of the 33 cases with free wall rupture resulted in immediate death. The

Fig.2. A 69-year-old male developed pansystolic murmur with thrill several hours after the onset of acute anterior myocardial infarction. His left ventriculogram revealed a perforation of the interventricular septum in the apex (black arrow). On selective coronary angiogram, the right coronary artery branched off from the left anterior descending artery (single coronary artery) and a 75% stenosis of the left anterior descending artery was present just before the branching off of the right coronary artery (white arrow).
Abbreviations: ICS = intercostal space; PSM = pansystolic murmur; CAP = carotid artery pulse

patients with IVS perforation (9 cases) and papillary muscle rupture (2 cases) could be divided into 2 groups: with shock (6 cases) and without shock (5 cases) following the occurrence of the rupture. Patients with shock died within 3 days in spite of intensive medical treatment, and in 4 out of the 5 patients without shock, surgery was delayed more than 3 weeks when the tissue could be repaired. Two of the 4 operated cases were survived and the remaining one without surgery was died of renal failure 4 weeks after the rupture.

We could reduce the incidence of myocardial rupture by taking the above-mentioned risk factors into consideration. As far as we know, no previous literature exists concerning the successful prevention of myocardial rupture. Bates et al⁴ have listed 5 factors which indicate an increased risk of rupture: 1) recurrent chest pain, 2) sustained hypertension, 3) first MI, 4) less than 5 days since MI and 5) 80 years and

older; whereas we presented 7 risk factors as stated above^{2,3}. Among these risk factors, physical and emotional instability and recurrent chest pain were able to be corrected, and sustained hypertension, which is also one of the most important risk factors, was treated with sublingual nifedipine or nitroprusside infusion.

The diagnosis of myocardial rupture is relatively easy. Most patients with free wall rupture result in sudden death and an electro-mechanical dissociation is observed. When a new heart murmur occurs following acute MI, IVS perforation or papillary muscle rupture is suggested. Perforation of the IVS is relatively easily differentiated from papillary muscle rupture by bedside right heart catheterization with sequential oximetry and 2-D echocardiography.

Patients with myocardial rupture should be treated surgically, but most of the free wall ruptures have no chance for surgical treatment

Fig. 3. A 59-year-old male suddenly developed cardiogenic shock with pulmonary edema on the 9th day after acute inferior myocardial infarction. Rupture of the posterior papillary muscle (white arrow) was found at autopsy.

Fig. 4. The cumulative survival curves according to the number of diseased coronary arteries. Abbreviations: VD = vessel disease; LMT = left main trunk

Fig. 5. Cumulative survival curves according to left ventricular function. EF = ejection fraction

because of sudden death. Giuliani et al⁵ have recommended that surgery for IVS perforation should be delayed as long as possible, ideally 3 to 6 weeks. In the present study, 4 cases out of

the 9 IVS perforation and both cases with papillary muscle rupture developed cardiogenic shock soon after rupture, and died within 3 days without surgery. Several authors have also

Fig. 6. The cumulative survival curves according to age.

Fig. 7. The cumulative survival curves in angina and infarction.

reported that IVS perforation and papillary muscle rupture can be repaired successfully even in the early post-infarction stage.⁶⁻⁹ In our treatment of patients with IVS perforation, as recommended by Radford,⁹ intra-aortic balloon pumping must be instituted promptly when cardiogenic shock is present; invasive studies are performed within 6 hours thereafter. Surgical repair is carried out within the next 12 hours. If cardiogenic shock is not present, surgery should be delayed 3 weeks.

Natural History of Ischemic Heart Disease

Aorto-coronary (AC) bypass surgery has recently increased in our country, but still not so many as in Western countries. While it relieves symptoms in most cases, the effect of the surgery on survival is still controversial. The

Fig. 8. Incidence of serious accidents during the follow-up period from one to 7 years. VT = ventricular tachycardia; VF = ventricular fibrillation; AMI = acute myocardial infarction; CVA = cerebro-vascular accident

TABLE II ELECTROCARDIOGRAPHIC FINDINGS IN VARIANT ANGINA

Site of ST elevation	Serious arrhythmia	
	VT or VF	Bradyarrhythmia
Anterior	16	5
Inferior	10	1
Anterior + Inferior	4	2
Total	30	8

survival rate was analyzed in medically-treated patients according to the number of stenotic vessels, left ventricular function, age and history of MI.

During the 7-year period from 1975 to 1981, more than 1000 patients underwent selective cine-coronary angiography using the Sones or the Judkins technique in Mie University hospital. Of these, 400 consecutive patients, who had significant coronary artery disease and could be followed continuously and periodically for more than one year in our hospital, were analyzed. Significant coronary artery disease was defined as that having a 75% or greater occlusion of at least one major coronary artery according to AHA classification.¹⁰ The patients were divided into 3 groups according to the ejection fraction (EF): $EF > 50\%$, $50 \geq EF \geq 30\%$ and $EF < 30\%$. They were also divided into 4 age groups: ≤ 39 , 40-49, 50-59 and ≥ 60 .

The cumulative survival curves related to the number of diseased coronary arteries are shown in Fig. 4. Prognosis is especially poor in left main trunk disease and 3-vessel disease. The 3-year survival rates in 1-, 2- and 3-vessel disease

Fig.9. A 28-year-old male, who suffered from a small anterior infarction about one year ago, developed "variant type angina". His ECG at rest showed the presence of the old anterior infarction, and small apical defect (black arrow) was shown on ^{201}Tl myocardial imaging. During methacholin-provoked anginal attack, marked ST elevation was observed on ECG (I, aVL and V_2-V_6) and ^{201}Tl myocardial imaging demonstrated an extensive perfusion defect except for the lateral wall.

and left main trunk disease were 97.8, 94.1, 64.7 and 44.4%, respectively.

The cumulative survival curves related to left ventricular function are shown in Fig. 5, which indicated significantly poor prognosis in patients with the EF of less than 30%.

The cumulative survival curves related to age are shown in Fig. 6. Prognosis is poor in patients

above 60 years of age.

When MI group was compared with the angina group in the medically-treated patients, prognosis is significantly better in the latter (Fig. 7), in which only 2 sudden deaths occurred during the follow-up period (Fig. 8).

As in other reports,¹¹⁻¹⁴ the prognosis of the medically-treated patients with 3-vessel disease

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Fig.10. A 60-year-old male with WPW syndrome was diagnosed as variant angina clinically and angiographically. He suffered from a severe anginal attack and soon died from arrhythmia. Initially ST elevation was observed on the anterior leads, which was followed by the same finding on the inferior leads. Then, he developed bradycardia and died from ventricular tachycardia.

or left main trunk disease was quite poor in our study, and surgical treatment must be considered according to age, left ventricular function and graftability of the coronary artery in each patient. In aged patients (≥ 60) with poor left ventricular function ($EF < 30\%$) prognosis with medical treatment is poor, but these patients often have a high risk for surgery, too. The

indication and timing for surgery should be carefully decided by cardiologists and surgeons in co-operation.

AC bypass surgery for ischemic heart disease is done in anticipation of 1) symptomatic relief, 2) improvement of exercise tolerance, 3) prevention of MI or arrhythmia and 4) prolongation of life expectancy. In this study, prognosis of

TABLE III TREATMENT OF VARIANT ANGINA

Organic CAD (+) 13	AC Bypass	4	Perioperative MI (Death 1)	2
	Medical treatment	9	Angina at rest	0
Organic CAD (-) 17	Medical treatment	17	Angina on effort (Death 1)	2
			Angina at rest	0
			Angina on effort	0

CAD = coronary artery disease; AC = aorto-coronary; MI = myocardial infarction

anginal patients was excellent with medical treatment as compared with MI patients. Therefore, we would like to re-emphasize the importance of medical treatment, which includes the removal of coronary risk factors.

Variant Angina

Variant angina was described by Prinzmetal et al.¹⁵ more than 20 years ago, and recently coronary spasm has been considered to be its mechanism.^{16,17} Natural history of variant angina has not been established as yet. The purpose of this study is to evaluate the long-term natural history and the indication and timing for AC bypass surgery in variant angina associated with significant organic coronary artery disease.

From 1975 to 1981, 30 patients were clinically diagnosed as having variant angina (angina at rest with transient, reversible ST-segment elevation). Thirteen of these had significant organic coronary artery disease angiographically, i.e., a 75% or greater occlusion of at least one major coronary artery after a sublingual administration of isosorbide dinitrate. Seventeen has no significant coronary artery disease. Their ECG findings during the attacks and the effects of treatment (medical and surgical) were evaluated.

Out of the 30 patients, ST elevation was observed during attacks on the anterior leads of the ECG in 16, on the inferior leads in 10 and on both the anterior and the inferior leads in 4 (Table II). Life threatening arrhythmia during spontaneous and/or provoked attacks were ventricular tachycardia or ventricular fibrillation in 8 cases and serious bradyarrhythmia, such as complete AV block or sinus arrest, in 8. Ventricular tachycardia or ventricular fibrillation tends to occur in patients with ST elevation on the anterior leads of the ECG and bradyarrhythmia in patients with ST elevation on the inferior leads. There was no relation between

these arrhythmia and the presence of organic coronary artery disease.

Case 3: A 28-year-old male, who suffered from small anterior MI about one year ago, recently has developed "variant type angina". His ECG at rest showed old anterior MI and ²⁰¹Tl myocardial imaging demonstrated a small defect at the apex. During the attack, which was provoked by methacholine administration, marked ST elevation was observed on leads I, aVL and V₂-V₆, and ²⁰¹Tl myocardial imaging demonstrated an extensive perfusion defect except for the lateral wall (Fig. 9). If this kind of attack continues for more than 5 min., the patient will develop serious hemodynamic deterioration, which may cause sudden death.

Case 4: A 60-year-old male with WPW syndrome was diagnosed as having variant angina clinically and angiographically. In spite of nifedipine administration (10 mg TID), he suddenly developed anginal attack at 7:55 in the morning. On ECG, ST elevation was observed on the anterior leads (V₁-V₆) at first, which was followed by the same finding on the inferior leads (II, III and aV_F). Then, he developed extreme bradycardia and died from ventricular tachycardia (Fig. 10).

In these 2 cases, the attacks of variant angina themselves were very serious from the hemodynamic and electrocardiographic points of view, and intensive medical follow-up must be necessary to control these attacks.

Results of treatments for variant angina are shown in Table III. AC bypass surgery was performed on 4 out of 13 cases with organic coronary artery disease. Two of them developed MI due to perioperative coronary spasm and one of them died. In the medically-treated cases with organic coronary artery disease, chest pain completely disappeared with medical treatment at rest, but chest pain on effort still remained in

2 cases. Only these 2 cases should have been treated surgically. In 17 cases with no organic coronary artery disease, medical treatment is sufficient to control anginal attack.

Patients with variant angina often suffer from life-threatening arrhythmias during attack and occasionally die suddenly as in Case 4. In variant angina, a functional factor (coronary vasospasm) and an organic factor (coronary sclerosis) are considered to co-exist in most cases. Coronary vasospasm seems to be well controlled by appropriate medical treatment such as nitrate and Ca^{++} -antagonist.

Surgical treatment for patients with organic coronary artery disease is still controversial because myocardial infarction is apt to occur due to perioperative coronary vasospasm.¹⁸ Shubrooks et al.¹⁹ have stated that most patients with significant organic coronary artery disease become well after AC bypass surgery. On the other hand, Severi et al.²⁰ concluded that the prognosis of patients with variant angina receiving appropriate medical therapy is reasonably good after the acute phase, even in the presence of severe organic coronary artery disease.

In conclusion, all patients with variant angina should be treated medically at first, and only patients with organic coronary artery disease and chest pain on effort even with maximal medical treatment, should be considered as candidates for AC bypass surgery.

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