Clinical Characteristics and Prognosis of Patients with Unstable Angina Treated Medically and Surgically

— Results in Patients with ST-segment Elevation and Depression —

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A randomized prospective study was carried out and the therapeutical effects of intensive medical management in the acute stage of unstable angina were compared with those of urgent coronary bypass surgery on patients admitted to Kanazawa Medical University Hospital, who showed an ST elevation or depression during their attacks.

Seventy patients with unstable angina were evaluated clinically, angiographically and hemodynamically: 41 of them had a transient ST elevation (26 treated medically; 15 surgically) and 29 had a transient ST depression (15 treated medically; 14 surgically). The hospital mortality rates were 12.2% for the medical group (3.8% in patients with an ST elevation; 26.7% in an ST depression) and 17.2% for the surgical group (6.7% in an ST elevation; 28.6% in an ST depression). These differences were not significant. The incidence of myocardial infarction among in-patients was 7.3% in the medical group (0% in the patients with an ST elevation; 20% in an ST depression) and 13.8% in the surgical group (13.3% in an ST elevation; 14.3% in an ST depression). These differences were also not significant. On their coronary angiograms, single vessel disease was significantly frequent in unstable angina with an ST elevation and so was triple vessel disease in patients with an ST depression. Left ventricular function was markedly improved in patients with an ST elevation after coronary bypass surgery. However, in unstable angina with an ST depression, there was no amelioration of left ventricular contractility and relaxation.

It is concluded that by medical or surgical treatment, patients with unstable angina showing an ST elevation during their attacks had a fairly better prognosis than those showing an ST depression; the left ventricular function of the ST elevation group was improved considerably after AC bypass surgery, while those of the ST depression group showed no improvement.

Key Words:

Left ventricular contractility
Left ventricular relaxation
Coronary angiogram
Aorto-coronary bypass operation

SINCE the introduction of coronary arterial bypass surgery, a controversy has existed about the management of unstable angina in its acute stage.¹⁻⁶ Are patients with this syndrome managed better by emergency coronary bypass surgery or by intensive medical therapy?⁷⁻¹¹

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TABLE I PATIENTS PROFILE

	No. of patients	Mean age (range) (years)	Surg	Sex		Type of angina		
				male	female	A	B	C
Unstable angina	70	54.4 (25-83)	29	64	6	7 (10.0%)	38 (54.3%)	25 (35.7%)
ST elevation (Group I)	41	54.9 (27-83)	15	37	4	4 (9.8%)	14 (34.1%)	23* (56.1%)
ST depression (Group II)	29	53.4 (25-66)	14	27	2	3 (10.3%)	24* (82.8%)	2 (6.9%)
Stable angina (Group III)	55	54.1 (32-74)	23	46	9			

A = new angina of effort, de novo effort angina; B = changing pattern, worsening effort angina; C = new angina at rest, spontaneous angina (AHA, ISFC/WHO); Surg = number of patients who underwent A-C bypass surgery * = $p < 0.05$

TABLE II PROGNOSIS OF UNSTABLE ANGINA

		Death (%)	AMI (%)	Angina (%)	Poor prognosis (%)
Medical	(n = 41)	5 (12.2)	3 (7.3)	11 (24.4)	19 (46.3)
Group-I (ST ele)	(n = 26)	1 (3.8)	0 (0)	5 (19.2)	6 (23.1)
Group-II (ST dep)	(n = 15)	4 (26.7)	3 (20.0)	6 (40.0)	13 (86.7)
Surgical	(n = 29)	5 (17.2)	4 (13.8)	4 (13.8)	13 (44.8)
Group-I (ST ele)	(n = 15)	1 (6.7)	2 (13.3)	2 (13.3)	5 (33.3)
Group-II (ST dep)	(n = 14)	4 (28.6)	2 (14.3)	2 (14.3)	8 (57.1)

n = number of patients; AMI = number (or %) of patients who developed acute myocardial infarction; Angina = number (or %) of patients who did not become free from anginal attacks during the follow-up period; Poor prognosis = the total number (or %) of patients who died, developed AMI and had continued angina

In addition, are the hemodynamics and the prognosis of unstable angina with an ST segment elevation different from those of patients with an ST depression?¹²⁻¹⁷

To help resolve this issue, we will investigate the left ventricular performance and the angiographic findings of the coronary artery in patients with unstable angina showing an ST segment depression or elevation during their attacks, while comparing the effects of medical and surgical therapies.

MATERIALS AND METHODS

Criteria for Unstable Angina^{16,18-20}: Three patterns of pain were considered consistent with unstable angina: 1) Chest pain on effort with a recent onset (within 4 weeks) and being progressive in nature, i.e., being provoked by less exertion, becoming more intense and/or persisting longer. 2) Chest pain on effort, being progres-

sive in nature and occurring in patients with chronic stable angina or with previous myocardial infarction. 3) Chest pain at rest, occurring without an obvious provocative factor, lasting longer than 15 min and being intense and recurrent. Acute myocardial infarction was excluded according to the standard criteria.

Patients Profile (Table I): The subjects included 70 patients, ranging in age from 25 to 83, who were hospitalized due to unstable angina and showed transient abnormal ST-T changes during chest pain. These patients were treated medically (41 patients) or surgically (29 patients). Forty-one patients of the 70 had a transient ST segment elevation (Group-I) and 29 a transient ST segment depression (Group-II) during attacks at rest or on effort.

Fifty-five patients with stable angina showing an ST segment depression during attacks were studied as a control group (Group-III). In this group coronary bypass surgery was performed on

23 patients (41.8%). All patients were followed up for at least 3 months after hospitalization, evaluating their clinical course in detail, and the incidence of angina pectoris was followed up for 6 months on the average.

Protocol: All patients admitted to the CCU were treated medically to prevent further myocardial ischemia; medical therapy usually included oral, intravenous or cutaneous administrations of nitrites, Ca^{++} -antagonists and β -blocking agents. During the period when the chest pain was relieved or reduced, a cardiac catheterization study was performed to decide whether or not their coronary arteries and ventricular function permitted surgical treatment. All underwent left heart catheterization and selective coronary angiography using the Judkins technique. Left heart pressure was measured using a micromanometer-tipped catheter. Left ventricular pressure and its first derivative were recorded using a Fukuda MCM-8000 polygraph. From this recording we measured parameters for evaluating left ventricular contractility and relaxation.^{21,22} The left ventricular ejection fraction was calculated from the biplane cine-ventriculograms obtained using an Angiographic Ventricular Dynamics System (Siemens-Elema, AB AVD System).

Significant stenosis of the coronary artery was judged to be present if a 50% or greater segmental reduction in luminal diameter was found in the main left coronary artery or a 70% or greater in the remaining coronary arteries. After catheterization, the above-mentioned medical therapy was resumed in the CCU.

RESULTS

Patients Population and Characteristics

Clinical Features (Table I): The medically treated group and the surgically treated one were similar with respect to age, sex, and a history of smoking, hypertension, hyperlipidemia and other coronary risk factors at the time of entry into the present study. The ST elevation group (Group-I) and the depression group (Group-II) were also similar with respect to above-mentioned factors.

As for the patterns of angina, new angina at rest was observed in 56.1% of Group-I, being significantly higher than those of Group-II ($p < 0.05$). On the other hand, worsening effort angina was significantly more frequent in Group-II than in Group-I ($p < 0.05$).

Follow-up Study (Table II): 1) **Mortality:** During an average follow-up period of 3 months, the mortality rates of the in-patients were 12.2% (5 of 41) in the medical group and 17.2% (5 of 29) in the surgical one, and 4.9% (2 of 41) in Group-I and 27.6% (8 of 29) in Group-II. These differences were statistically not significant, but patients with an ST depression during anginal attack showed a higher mortality rate than patients with an ST elevation, which may be meaningful. 2) **Acute myocardial infarction:** The incidence rate of myocardial infarction during hospitalization was 7.3% (3 of 41) in medically treated patients and 13.8% (4 of 29) in surgically treated ones, including perioperative infarction. Acute myocardial infarction occurred in 4.9% (2 of 41) of Group-I and in 17.2% (5 of 29) of Group-II. These differences were statistically not significant, but there was a higher incidence rate of acute myocardial infarction in patients with surgical therapy or with an ST depression than in those with medical therapy or with an ST elevation, respectively. 3) **Angina pectoris:** In 24.4% (11 of 41) of the medically treated patients and in 13.8% (4 of 29) of the surgically treated ones, angina pectoris was not ameliorated during the 6 months of hospitalization or after discharge. Relief of angina was more common in Group-I than in Group-II during a follow-up period of 6 months, but this difference was not significant. 4) **Summary of the follow-up study:** As mentioned above, there were no significant differences in each item (mortality rate, incidence rate of acute myocardial infarction and freedom from angina) between the medical and surgical therapies. However, the prognosis of unstable angina with reference to a combination of these 3 items was significantly poorer in Group-II than in Group-I.

Coronary Angiographic Findings

Frequency and severity of coronary occlusive disease assessed by arteriography is summarized in Fig. 1. Single vessel disease was present in 22 patients (53.7%) of Group-I, 3 (10.3%) of Group-II and 16 (38.1%) of Group-III. There was a significant difference between Group-I and Group-II ($p < 0.05$), and between Group-II and Group-III ($p < 0.05$). Double vessel disease was present in 11 patients (26.8%) of Group-I, 3 (10.3%) of Group-II and 10 (23.8%) of Group-III. These differences were not statistically significant. Triple vessel disease was present in one patient (2.4%) of Group-I, 20 (69.0%) of Group-

Fig.1. Frequency and severity of coronary occlusive disease assessed by arteriography in 3 groups.

Single = single vessel disease; Double = double vessel disease; Triple = triple vessel disease; LMT = left main trunk; G-I = Group-I (ST elevation); G-II = Group-II (ST depression); G-III = Group-III (stable angina). ** $p < 0.005$, * $p < 0.05$

II and 16 (38.1%) of Group-III. There was a significant difference between Group-I and Group-II ($p < 0.05$), and between Group-I and Group-III ($p < 0.0005$). Normal coronary angiogram was present in 7 patients (17.1%) of Group-I and one (3.4%) of Group-II. Significant stenosis of the left main coronary artery was visualized only in 2 patients (6.9%) of Group-II and not in any other group. In short, we found that single vessel disease was significantly frequent in patients with an ST elevation and that triple vessel disease was significantly frequent in patients with an ST depression.

Left Ventricular Hemodynamics

Left Ventricular Hemodynamics in Unstable and Stable Angina (Tables III and IV): Twenty-seven patients of Group-I, 21 of Group-II and 39 of Group-III were evaluated. LV max dp/dt/IIT (IIT: integrated isometric tension), Vpm (peak measured velocity), Vmax (maximum velocity of shortening) and $K (= 1/T)$ (T: time constant of the LV pressure fall during the isometric relaxation period) were smaller in unstable angina with an ST elevation or depression than in stable angina with an ST depression. As shown in Table

IV, 15 medical and 12 surgical patients of Group-I and 9 medical and 12 surgical patients of Group-II were evaluated at resting state. There was a significant difference in the ejection fraction, Vmax, LV negative dp/dt and K between the medical group and the surgical one both with an ST elevation. There was no difference in aortic pressure, end-diastolic pressure and LV max dp/dt/IIT between the 2 groups. On the other hand, in Group-II left ventricular function was not so disturbed in the surgical group, as in the medical one. From these data, we found that the patients with the more disturbed left ventricular function in Group-I, therefore, may be advised to undergo bypass surgery, and that Group-II patients with a similar malfunction received medical treatment.

Changes of Left Ventricular Hemodynamics before and after A-C Bypass Surgery in Unstable and Stable Angina (Table V): Twelve patients of Group-I, 7 of Group-II and 22 of Group-III were investigated before and after surgery. In Group-I, there was a significant difference in the ejection fraction, LVEDP and K between their values before and after surgery. Namely, the ejection fraction increased from 53.6 ± 13.1 to

TABLE III LEFT VENTRICULAR PERFORMANCE IN UNSTABLE AND STABLE ANGINA

	AoSP/AoDP (mmHg)	HR (beats/min)	LVEDP (mmHg)	LVmax dp/dt (mmHg/sec)	LVmax dp/dt / IIT	Vpm (ml/sec)	Vmax (ml/sec)	LVneg dp/dt (mmHg/sec)	K (sec ⁻¹)	EF (%)
Group-I (n = 27)	141.8 / ±23.6 / ±12.3	74.5 ±10.4	16.7 ±7.1	1512.7 ±204.9	458.3 ±121.1	1.07 ±0.23	1.42 ±0.23	1747.0 ±329.2	21.2 ±4.9	60.6 ±12.5
Group-II (n = 21)	143.3 / ±23.4 / ±21.5	76.4 ±14.7	15.3 ±5.5	1646.2 ±355.7	453.0 ±126.3	1.07 ±0.27	1.44 ±0.45	1731.2 ±270.7	20.7 ±2.9	58.0 ±12.9
Group-III (n = 39)	136.9 / ±29.5 / ±15.7	76.2 ±13.8	15.5 ±6.2	1557.7 ±304.0	497.6 ±142.8	1.19 ±0.31	1.51 ±0.29	1640.4 ±419.1	22.7 ±5.1	58.6 ±11.9

Values are given as mean ± SD. n = number of patients; Group-I = unstable angina (ST elevation); Group-II = unstable angina (ST depression); Group-III = stable angina; AoSP = aortic systolic pressure; AoDP = aortic diastolic pressure; HR = heart rate; LVEDP = left ventricular end-diastolic pressure; LVmax dp/dt = maximum dp/dt of the left ventricle; IIT = integrated isometric tension; Vpm = peak measured velocity; Vmax = maximum velocity of shortening; neg = negative; K = P(t) poe-Kt; EF = ejection fraction

TABLE IV LEFT VENTRICULAR PERFORMANCE IN UNSTABLE ANGINA IN MEDICAL AND SURGICAL CASES

	AoSP/AoDP (mmHg)	HR (beats/min)	LVSP (mmHg)	LVEDP (mmHg)	LV _{max} dp/dt (mmHg/sec)	LV _{max} dp/dt / IIT	V _{pm} (ml/sec)	V _{max} (ml/sec)	LV _{neg} dp/dt (mmHg/sec)	K (sec ⁻¹)	EF (%)	
Group-I	M (n = 15)	143.9 / 80.4 ±24.6 ±11.4	75.1 ±10.9	144.9 ±22.6	14.8 ±7.1	1575.9 ±200.7	466.3 ±78.2	1.13 ±0.20	1.50 ±0.17	1848.9 ±318.1	23.1 ±4.5	64.9 ±11.2
	S (n = 12)	139.1 / 82.6 ±23.1 ±13.7	73.7 ±10.1	142.3 ±23.2	19.1 ±6.5	1433.7 ±189.0	448.3 ±163.4	0.998 ±0.25	1.33 ±0.27	1619.6 ±309.2	18.9 ±4.4	55.9 ±12.5
Group-II	M (n = 9)	138.3 / 76.3 ±21.8 ±17.4	74.6 ±14.4	141.6 ±20.7	16.3 ±4.9	1616.3 ±239.5	444.3 ±107.4	1.02 ±0.25	1.34 ±0.31	1800.3 ±194.5	20.2 ±2.6	54.9 ±13.3
	S (n = 12)	147.1 / 79.7 ±24.7 ±24.8	77.7 ±15.3	147.6 ±30.1	14.5 ±5.96	1668.6 ±432.5	459.6 ±143.3	1.10 ±0.29	1.53 ±0.53	1679.4 ±314.4	21.2 ±3.2	62.3 ±11.5

Values are given as mean ± SD. M = patients treated medically; S = patients treated surgically. Other abbreviations are the same as in Table III.

TABLE V CHANGES OF LEFT VENTRICULAR PERFORMANCE BEFORE AND AFTER A-C BYPASS SURGERY IN UNSTABLE AND STABLE ANGINA

	AoSP/AoDP (mmHg)		LVEDP (mmHg)		LV ^{max} dp/dt (mmHg/sec)		LV ^{max} dp/dt / IIT		V _{pm} (ml/sec)		V _{max} (ml/sec)		LV ^{neg} dp/dt (mmHg/sec)		K (sec ⁻¹)		EF (%)			
	b	a	b	a	b	a	b	a	b	a	b	a	b	a	b	a	b			
Group-I (n = 12)	139.1 ±	82.6 ±	126.2 ±	77.6 ±	19.1 ±	13.3 ±	1433.7 ±	1645.7 ±	448.3 ±	508.2 ±	0.99 ±	1.25 ±	1.33 ±	1.55 ±	1619.6 ±	1750.6 ±	18.9 ±	24.4 ±	53.6 ±	72.8 ±
	23.1	13.7	17.8	11.1	6.5	3.6	189.0	438.3	163.4	193.9	0.25	0.33	0.27	0.41	309.2	340.0	4.4	4.8	13.1	9.2
Group-II (n = 7)	152.4 ±	84.7 ±	128.3 ±	74.7 ±	14.1 ±	16.6 ±	1525.9 ±	1689.5 ±	437.8 ±	549.0 ±	1.15 ±	1.20 ±	1.46 ±	1.55 ±	1581.2 ±	1646.8 ±	21.8 ±	26.1 ±	52.9 ±	52.4 ±
	28.5	15.0	18.6	11.9	5.8	7.8	249.5	482.6	132.7	152.8	0.32	0.43	0.35	0.32	330.4	360.5	2.7	6.3	14.5	11.2
Group-III (n = 22)	135.6 ±	79.5 ±	131.6 ±	76.2 ±	14.9 ±	15.9 ±	1534.9 ±	1595.3 ±	496.2 ±	494.4 ±	1.19 ±	1.12 ±	1.53 ±	1.50 ±	1620.7 ±	1631.6 ±	21.9 ±	23.3 ±	58.1 ±	62.7 ±
	29.5	13.3	22.5	17.8	4.5	5.0	216.4	307.1	145.8	161.3	0.31	0.26	0.26	0.28	425.5	305.2	4.5	5.7	13.1	13.1

Values are given as mean ± SD. b = before surgery; a = after surgery. Other abbreviations are the same as in Table III.

72.8 ± 9.2%, LVEDP decreased from 19.1 ± 6.5 to 13.3 ± 3.6 mmHg and K increased from 18.9 ± 4.4 to 24.4 ± 4.8 sec⁻¹. On the other hand, there was no significant amelioration of left ventricular contractility and relaxation in Group-II after surgery.

DISCUSSION

Clinical Characteristics of Patients with Unstable Angina

In a subtype of angina, "new angina at rest or spontaneous angina", there was a significantly larger number of patients with an ST elevation during pain attacks than those with an ST depression. On the other hand, in another subtype of angina, "changing pattern or worsening effort angina", there was a significantly larger number of patients with an ST depression than those with an ST elevation. Angiographic studies of the coronary artery showed a characteristic distribution of each vessel disease between the patients with an ST elevation and those with an ST depression. Namely, in single vessel disease there was a significantly larger number of patients with an ST elevation than those with an ST depression, and in triple vessel disease a significantly larger number of patients with an ST depression than those with an ST elevation. A normal coronary artery was noted in 7 patients with an ST elevation and only in one with an ST depression. Disease of the left main coronary artery was found only in 2 patients with an ST depression during attacks. Recent studies^{14,23,24} suggest that an involvement of the left main coronary artery in unstable angina may be more prevalent than previously thought. In our study, however, only about 7% of unstable angina with an ST depression had a significant stenosis of the left main coronary artery.

Results of Medical versus Surgical Treatment of Unstable Angina with an ST Elevation or an ST Depression

During the follow-up period, there were no significant differences between medically and surgically treated patients in mortality rate, incidence rate of acute myocardial infarction and persistence of angina pectoris. However, as shown in Table II under the item of "poor prognosis", medically treated patients with an ST depression had a significantly poorer clinical course than those with an ST elevation.

Hemodynamics in Unstable Angina with an ST Elevation or Depression Treated Medically or Surgically

Several studies of the hemodynamic changes occurring in patients with unstable angina have been reported in the literature. Cannon and his associates¹⁵ have noticed 3 groups of patients based on the particular hemodynamic changes which preceded or were associated with the attacks of pain. These changes were an increase in heart rate, an increase in both heart rate and brachial artery pressure, or an increase of brachial artery and pulmonary artery pressures without an increase in heart rate. They suggested that there may be various pathogenic mechanisms for the occurrence of "spontaneous" or resting angina in patients with occlusive coronary artery disease but that the mechanism and associated hemodynamic changes may be specific in individual patients. Maseri²⁵ has observed in unstable angina with an ST segment elevation that the initial event was an increase in a negative dp/dt of the left ventricle, then a decrease in a positive dp/dt , and finally an increase in left ventricular end-diastolic pressure, all reflecting an acute deterioration of the left ventricular function. In our laboratory, we observed that the LV max dp/dt , V_{pm} , V_{max} and $K (= 1/T)$ were smaller in unstable angina than in chronic stable angina. These results may suggest that in patients with unstable angina both contractility and relaxation of the left ventricle have a tendency to deteriorate.

Although an extensive literature has recently appeared concerning the indications and results of aorto-coronary bypass surgery using a saphenous vein for patients with unstable angina^{2,7,8,9} few studies have described their hemodynamic status, comparing it before and after surgery. An important method for evaluating whether this surgical procedure has succeeded or not is a postoperative hemodynamic analysis in these patients. Our data supports that the patients with an ST elevation during angina attacks considerably improved in their left ventricular function after A-C bypass surgery, whereas the patients with an ST depression had no significant amelioration of the left ventricular function after surgery. Thus, it is suggested that the patients with unstable angina of an ST elevation type, whose coronary angiogram frequently reveals single vessel disease, show a good response to both medical and surgical managements.

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