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Patient Characteristics and Outcomes of Witnessed Out-of-Hospital Cardiac Arrest in Osaka: A 7-Year Emergency Medical Services Perspective in a Large Population

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Abstract:
Objectives: To evaluate the temporal trend of baseline characteristics, resuscitation care characteristics, and outcomes of out-of-hospital cardiac arrests (OHCA) from a large population-based cohort study. ***Methods:*** We enrolled all OHCAs of presumed cardiac etiology in adults (>17 years old) that were witnessed by bystanders and were treated by emergency medical service (EMS) in Osaka Prefecture (population, 8.8 million), Japan from 1999 through 2005. Data were prospectively collected by EMS personnel and physicians in charge using an Utstein-style database. Time course was divided into 7 successive one-year periods. We evaluated changes in demographic and cardiopulmonary resuscitation (CPR)-related factors, and outcomes. Multivariate logistic regression analysis was performed to evaluate the relationship between prognostic factors and outcomes. ***Results:*** Mean age gradually increased over time. The proportion of cases with bystander CPR and with ventricular fibrillation (VF) increased. The time interval from emergency call to the first defibrillation by EMS personnel shortened from 14 to 8 min, while the time to the initiation of CPR by EMS remained 6-7 min. Neurologically favorable outcome 1-month after arrest improved from 1.5% to 4.7% in the entire cohort (Table) and from 5.5% to 16.9% in witnessed VF cases during the observation period. Excluding very-long-duration cardiac arrests (>15 minutes), bystander-initiated cardiac-only resuscitation yielded a higher rate of favorable neurological outcome than no bystander CPR (3.6% versus 2.8%; OR, 1.51; 95% CI, 1.00-2.26), and conventional CPR showed similar effectiveness (3.6%; OR, 1.39; 95% CI, 0.96-2.02).
Conclusion: This study showed the continuous improvement of the chain of survival and outcomes of patients with witnessed OHCA in a large population. Further efforts to increase bystander-initiated cardiac-only resuscitation would improve the outcomes more.

Table: Baseline, Resuscitation Care Characteristics and Outcomes according to time period

		1999 (n=944)	2000 (n=975)	2001 (n=1037)	2002 (n=935)	2003 (n=1005)	2004 (n=967)	2005 (n=1066)
Age, yr, Mean (SD)		68.4 (15.5)	69.4 (15.6)	70.6 (14.8)	70.2 (14.7)	70.4 (15.5)	72.0 (14.7)	71.6 (15.3)
Male, % (n)		63.3 (593)	63.4 (616)	64.8 (669)	62.0 (578)	63.4 (636)	60.5 (585)	63.5 (677)
Presenting rhythm VF, % (n)		17.4 (164)	15.1 (146)	16.6 (170)	19.2 (177)	21.0 (210)	23.0 (221)	22.5 (239)
Bystander CPR, %	Cardiac-only	11.8 (111)	9.7 (94)	12.8 (132)	12.9 (119)	13.3 (133)	15.5 (148)	14.4 (153)

(n)	Conventional CPR	13.3 (125)	15.2 (147)	18.0 (185)	19.5 (180)	19.8 (198)	21.0 (201)	20.8 (222)
Time from call to CPR, min, median (IQR)		7 (6 - 9)	7 (6 - 9)	7 (6 - 9)	7 (6 - 9)	7 (6 - 9)	6 (6 - 9)	7 (6 - 9)
Time from call to defibrillation , min, median (IQR)		14 (12 - 19)	12 (10 - 16)	12 (10 - 16)	11 (9 - 15)	10 (8 - 12)	9 (7 - 12)	8 (7 - 11)
One-month survival, % (n)		4.6 (42)	5.6 (54)	6.6 (68)	7.9 (72)	8.0 (80)	7.8 (74)	9.4 (100)
Neurologically favorable outcome, % (n)		1.5 (14)	2.4 (23)	2.5 (26)	3.0 (28)	3.4 (34)	3.5 (34)	4.7 (50)
SD, standard deviation; IQR, interquartile range								

:

Author Disclosure Block: **T. Iwami**, None; **A. Hiraide**, None; **K. Kajino**, None; **R.A. Berg**, None; **T. Nishiuchi**, None; **Y. Hayashi**, None; **M. Nitta**, None; **T. Hayashi**, None; **H. Ikeuchi**, None; **H. Nonogi**, None; **T. Kawamura**, None.

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Effectiveness Of Cardiac-only CPR Training by Self-learning Video, a 1-hour program, or Both

Author Block: Chika Nishiyama, Taku Iwami, Takashi Kawamura, Masahiko Ando, Kyoto Univ school of public health, Kyoto, Japan; Robert A. Berg, The Univ of Arizona Coll of Med, Arizona, AZ; Naohiro Yonemoto, Kyoto Univ school of public health, Kyoto, Japan; Risa Fukuda, Osaka Univ Graduate school of medicine, Osaka, Japan; Haruyuki Yuasa, Kinki Univ Sch of Med, Osaka, Japan; Akiko Kada, Hiroyuki Yokoyama, Hiroshi Nonogi, J-PULSE Investigators, Natl Cardiovascular Ctr, Osaka, Japan

Abstract:
[Introduction]Despite present efforts to train the general public in CPR, the proportion of bystander CPR is still low. Length of CPR training program and complexity of CPR skills may be barriers to bystander CPR performance. Recently, simple video self-learning has been shown to be an effective CPR training technique.
[Objective]To evaluate the effectiveness of cardiac-only CPR training program by a self-learning video, a 1-hour practical course, or both.
[Method]*Designs:* A randomized controlled trial. ***Participants:*** General public aged 18 years or older. ***Intervention:*** In the video (V) group, participants received the self-learning video before CPR training and then attended a 1-hour cardiac-only CPR training program; in the control (C) group participants attended the training program without a self-learning video. ***Data collection:*** Before and immediately after the training, a 2 minute scenario-based test was conducted and CPR skills were recorded. ***Outcomes:*** The primary outcome measure was the number of correct chest compressions immediately after the training. We also calculated the achievement of correct chest compressions, which meant the proportion of correct chest compressions in relation to the ideal number of chest compressions based on 2005 CPR guideline.
[Result]214 participants were randomly assigned to V (108) and C (106) groups. Before the training, the proportion of attempting chest compression, attempting AED operation, and calling for an AED, and the total number of chest compressions were significantly grater in the V group. After the training, all measured CPR skills of both groups improved substantially compared with pre-training skills, but there were no differences between groups (Table).
[Conclusion]A self-learning video improved CPR skills. However, a 1-hour practical training course was substantially more effective and the addition of a self-learning video did not improve its effectiveness.

Table: CPR Skills of Pre- and Post-training

	Pre-training			Post-training		
	V (n=95)	C (n=87)	p-value	V (n=95)	C (n=87)	p-value
Call for help (119), n (%)	52 (54.7)	22 (25.3)	<0.001	93 (97.7)	85 (97.9)	1.000
Call for an AED, n (%)	40 (42.1)	3 (3.4)	<0.001	90 (94.7)	84 (96.6)	0.720
Attempts of chest compressions, n (%)	88 (92.6)	56 (66.7)	<0.001	95 (100)	87 (100)	1.000

Total number of chest compressions, n	92.8±64.8	49.0±57.3	<0.001	161±31.8	159.0±35.7	0.628
Number of correct chest compressions, n	23.8±39.1	12.9±27.0	0.031	74.7±65.9	88.8±67.0	0.196
Achivement of correct chest compressions, %	13.0±21.4	7.0±14.8	0.031	40.8±36.0	48.5±36.6	0.196
Attemps of AED operation, n (%)	71 (74.7)	25 (28.7)	<0.001	95 (100)	87 (100)	1.000
Correct position of the defibillator pad , n (%)	57 (60.0)	16 (18.4)	<0.001	90 (94.7)	85 (97.7)	0.450
Data are means ± SD unless indicated otherwise , SD: srander deviation						

Author Disclosure Block: **C. Nishiyama**, None; **T. Iwami**, None; **T. Kawamura**, None; **M. Ando**, None; **R.A. Berg**, None; **N. Yonemoto**, None; **R. Fukuda**, None; **H. Yuasa**, None; **A. Kada**, None; **H. Yokoyama**, None; **H. Nonogi**, None; **J. Investigators**, None.

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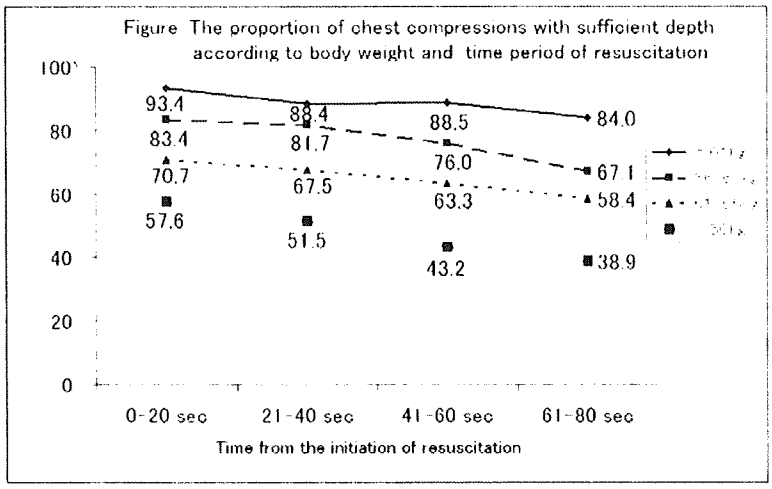
Lay Rescuers' Characteristics Affect Quality of Chest Compressions during cardiac-only resuscitation

Author Block: Chika Nishiyama, Taku Iwami, Takashi Kawamura, Masahiko Ando, Kyoto Univ school of public health, Kyoto, Japan; Robert A. Berg, The Univ of Arizona Coll of Med, Arizona, AZ; Naohiro Yonemoto, Kyoto Univ school of public health, Kyoto, Japan; Risa Fukuda, Osaka Univ Graduate school of medicine, Osaka, Japan; Haruyuki Yuasa, Kinki Univ Sch of Med, Osaka, Japan; Akiko Kada, Hiroyuki Yokoyama, Hiroshi Nonogi, J-PULSE Investigators, Natl Cardiovascular Ctr, Osaka, Japan

Abstract:
[Introduction]Quality of chest compressions has been recognized as a key determinant of successful outcome from cardiac arrest. However, whether the quality of chest compressions varies according to lay rescuers' characteristics including sex, age and body weight are unclear.
[Objective] To evaluate the associations between rescuers' characteristics and the quality of chest compressions.
[Method]*Participants:* General public (18 years or older). ***Data:*** Data were obtained from 182 participates in a 1-hour cardiac-only CPR training program. A 2 minute scenario-based test was conducted and resuscitation skills were recorded automatically. ***Outcomes:*** The primary outcome was the proportion of chest compressions with sufficient depth among the total chest compressions . ***Statistical Analysis:*** Difference in the proportion of sufficient chest compressions according to sex, age (<=50, 51-60, >=61) and body weight (<=50, 51-55, 56-60, >=61Kg) were analyzed using analysis of covariance.
[Result]The proportion of chest compressions with sufficient depth decreased with decreasing of body weight. Female sex and aging were independently associated with poor performance of chest compressions (Table). Time-dependent deterioration of the skills were observed (figure).
[Conclusion]Female sex, higher age, and low body weight of lay rescuers would lower the quality of chest compressions.

Table: Factors associated with insufficient chest compressions

Factors	β	95% CI
Female	-17.4	-33.9 ~ -0.8
Age (years)<=50	reference	
51-60	-10.8	-20.9 ~ -0.4
>=61	-21.4	-33.9 ~ -8.9
Weight (Kg) >=61	reference	
56-60	-3.1	-16.8 ~ 10.6
51-55	-15.4	-30.6 ~ -0.1
<=50	-28.8	-43.0 ~ -14.6
CI: Confidence Interval		



Author Disclosure Block: **C. Nishiyama**, None; **T. Iwami**, None; **T. Kawamura**, None; **M. Ando**, None; **R. Berg**, None; **N. Yonemoto**, None; **R. Fukuda**, None; **H. Yuasa**, None; **A. Kada**, None; **H. Yokoyama**, None; **H. Nonogi**, None; **J. Investigators**, None.

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[3379] Feasibility Of Adrenomedullin Infusion In Patients With Acute Myocardial Infarction -a Possible Cardioprotective Therapy Against Ischemic Injury-

Satoshi Yasuda, Tohoku Univ, Sendai, Japan; Shunichi Miyazaki, Kinki Univ, Sayama, Japan; Noritoshi Nagaya, Yu Kataoka, Teruo Noguchi, Natl Cardiovascular Ctr, Suita, Japan; Isao Morii, Hokusetsu General Hosp, Takatsuki, Japan; Atsushi Kawamura, Kenji Kangawa, Natl Cardiovascular Ctr, Suita, Japan; Kunio Miyatake, Osaka Minami Medical Ctr, Kawachi-Nagano, Japan

Background Adrenomedullin (ADM) is a 52-amino-acid vasodilator peptide that was originally isolated from human pheochromocytoma In the previous experimental study with rat ischemia/reperfusion model, ADM reduced infarct size and inhibited myocyte apoptosis ADM also suppressed the production of oxygen-free-radicals The present study was designed to evaluate the feasibility of intravenous administration of ADM in patients with acute myocardial infarction (AMI)

Methods We studied 10 patients with first AMI (M/F,9/1, mean age,65 years, peak CPK level; 4090 U/L[median]), who were hospitalized within 12 hours of symptom onset. ADM infusion preceded percutaneous coronary intervention (PCI) and was continued at concentration of 0 0125 - 0.025μg/kg/minute for 12 hours. We also studied 10 control AMI patients matched for age, sex and infarct size, who did not receive ADM

Results: During ADM infusion, hemodynamics kept stable except one patient with right ventricular infarction. Urinary levels of 8-iso-prostaglandine F2α, which was measured after the reperfusion therapy with ADM infusion as a marker of oxidative stress, was significantly lower in patients who received ADM than those who did not (76±40 vs 174±21 pmol/mol of creatinine, P<0.01). Infarct area (IA) evaluated by magnetic resonance imaging and brain natriuretic peptide (BNP) levels were also different between the two groups (Table) Conclusions: Intravenous administration of ADM, which possesses a variety of cardiovascular protective actions, is feasible and can be adjunctive to PCI. Suppression of oxidative stress generation may be beneficial for attenuation of left ventricular dysfunction and remodeling following AMI

	IA : 1 month	IA : 3 months	BNP : 1 week	BNP : 1 month	BNP : 3 months
ADM	22±6	16±4	187±121	134±99	103±79
Control	31±15	23±12	214±139	191±132	174±102
P value	0.04	0.06	0.30	0 11	0.02

S. Yasuda, None, S. Miyazaki, None, N. Nagaya, None, Y. Kataoka, None, T. Noguchi, None, I. Morii, None, A. Kawamura, None, K. Kangawa, None, K. Miyatake, None

Session Info: Acute Myocardial Infarction: Improving Ventricular Function and Reducing Infarct Size - Wednesday, November 07, 2007, 02 00 PM-03 15 PM

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Ⅷ. 資料・業績集

Enhanced cardiac production of matrix metalloproteinase-2 and -9 and its attenuation associated with pravastatin treatment in patients with acute myocardial infarction

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ABSTRACT

Previous experimental studies have demonstrated that MMPs (matrix metalloproteinases) contribute to LV (left ventricular) remodelling. We hypothesized that cardiac MMPs are activated in patients with AMI (acute myocardial infarction) and, if so, MMP production may be attenuated by statins (3-hydroxy-3-methylglutaryl-CoA reductase inhibitors) through their cardiovascular protective actions. We studied 30 patients, ten control patients with stable angina pectoris and 20 patients with AMI, in whom LV catheterization at the chronic stage was performed 22 ± 12 days (value is mean $\pm$ S.D.) after the onset of AMI. Blood samples were collected from the CS (coronary sinus) and a peripheral artery. In patients with AMI, the levels of MMP-2 and MMP-9 were significantly ($P < 0.05$) higher in the CS than the peripheral artery (MMP-2, 853 ± 199 compared with 716 ± 127 ng/ml; MMP-9, 165 ± 129 compared with 98 ± 82 ng/ml), whereas no significant differences were observed in the patients with angina pectoris. The CS–arterial concentration gradients of MMP-2 and MMP-9 correlated positively with BNP (brain natriuretic peptide) levels (MMP-2, $R = 0.68$, $P < 0.01$; MMP-9, $R = 0.59$, $P < 0.05$) and LV end-diastolic volume index (MMP-2, $R = 0.70$, $P < 0.01$; MMP-9, $R = 0.70$, $P < 0.01$). When patients with AMI treated with 10 mg of pravastatin or without ($n = 10$ in each group) were compared, this statin therapy significantly ($P < 0.05$) decreased the CS–arterial concentration gradients of MMP-2 (69 ± 43 compared with 213 ± 185 ng/ml) and MMP-9 (14 ± 27 compared with 119 ± 84 ng/ml). In conclusion, the enhanced production of cardiac MMP-2 and MMP-9 is associated with LV enlargement and elevated BNP levels in patients with AMI. A pleiotropic effect of statins appears to be associated with the modulation of cardiac MMP activation, which may be potentially beneficial in the attenuation of post-infarction LV remodelling.

Key words: acute myocardial infarction, angina pectoris, brain natriuretic peptide (BNP), metalloproteinase (MMP), remodelling, statin, tissue inhibitor of metalloproteinases (TIMP).

Abbreviations: ACE-I, angiotension-converting enzyme inhibitor; AMI, acute myocardial infarction; Ang II, angiotensin II; AP, angina pectoris; BNP, brain natriuretic peptide; CK, creatine kinase; CRP, C-reactive protein; CS, coronary sinus; LDL, low-density lipoprotein; LV, left ventricular; LVEDVI, LV end-diastolic volume index; LVEF, LV ejection fraction; MMP, matrix metalloproteinase; TGF-β, transforming growth factor-β; TIMP, tissue inhibitor of metalloproteinases; WBC, white blood cell.

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INTRODUCTION

The loss of myocytes as a consequence of AMI (acute myocardial infarction) results in progressive changes in ventricular architecture [1,2]. This process, defined as post-infarction ventricular remodelling, is associated with a higher mortality and a higher incidence of complications, such as the development of heart failure, aneurysm formation and ventricular rupture [3,4]. During the remodelling process, as well as intrinsic changes in cardiac myocytes, it has been recognized that important alterations also occur within the extracellular matrix of the myocardium [5,6].

MMPs (matrix metalloproteinases) belong to a family of zinc-containing endoproteinases responsible for extracellular protein degradation, and are inhibited by specific tissue inhibitors [TIMP (tissue inhibitor of metalloproteinases)] [5,6]. In experimental myocardial infarction, MMPs are up-regulated in myocardial tissues, and are the driving force in extracellular matrix remodelling and infarct expansion [7,8]. Among the MMPs, the importance of MMP-9 during the processes of infarct healing and LV (left ventricular) remodelling has been demonstrated in previous studies using genetically modified mice [9,10]. Infarcted mice with the targeted deletion of MMP-9 had a decreased incidence of early myocardial rupture [9] and progressive LV dilation [10]. However, in the clinical setting, there has been little evidence regarding the production of MMPs in the infarcted human heart.

Statins have various cardiovascular protective actions, including anti-inflammatory and anti-apoptotic actions, independent of their effects on cholesterol levels. A study using a mouse AMI model demonstrated that statin treatment attenuated LV remodelling [11], which was associated with decreased MMP activity [12].

In the present study, we hypothesized that cardiac MMP activation may be associated with the degree of LV enlargement and the level of BNP (brain natriuretic peptide), a biochemical marker of post-infarction remodelling [13,14]. If so, MMP production may be attenuated by statin treatment in patients with AMI.

MATERIALS AND METHODS

Patients

This study included 30 male patients. All of the patients gave their written informed consent prior to participation in the study. The Institutional Ethical Committee on Human Research approved the study protocol. Patients with the following disorders were excluded from the study: prior myocardial infarction, and liver (elevated activities of aminotransferases), kidney (elevated level of creatinine or urea) or lung dysfunction (restrictive or obstructive pattern in spirometry).

The control group consisted of ten patients with stable AP (angina pectoris), who complained of symptoms consistent with Canadian Cardiovascular Society Classification of angina level I, II or III, with evidence of myocardial ischaemia. All of the control patients had no evidence of a previous AMI, and had severe coronary artery stenosis and therefore underwent coronary angioplasty (with adjunctive stenting in five patients). The treated sites were the left anterior descending artery in four patients (40 %), the right or left circumflex artery in four patients (40 %), and both the left anterior descending and right coronary arteries in two patients (20 %).

We also studied 20 patients with AMI who fulfilled the following criteria: typical chest pain >30 min of duration, ST segment elevation > 0.1 mV in two or more ECG leads with the subsequent evolution of a typical infarct pattern, and increased serum CK (creatine kinase) level. A total of 14 patients underwent PTCA (percutaneous transluminal coronary angioplasty) of the infarct-related artery (with adjunctive stenting in nine patients), and the remaining six patients received an intravenous administration of a tissue-type plasminogen activator and/or heparin in the acute phase. In all the patients, coronary angiography immediately after treatment showed a TIMI 3 grade flow in the infarct-related artery. The elapsed time to reperfusion was 4.6 h on average. The infarct sites were in the anterior wall in ten patients (50 %), the inferior wall in seven patients (35 %) and the postero-lateral wall in three patients (15 %). In this study, all of the patients with AMI were treated with the ACE-I (angiotension-converting enzyme inhibitor) enalapril (5 mg) after their hospital admission. Among them, ten patients with hyperlipidaemia (total cholesterol level > 220 mg/dl) were treated with 10 mg of pravastatin; the remaining ten patients did not have hyperlipidaemia and thus did not receive pravastatin. A recent Management of Elevated Cholesterol in the Primary Prevention Group of Adult Japanese (MEGA) trial [14a] has shown a similar decrease in coronary artery disease incidence following treatment with 10–20 mg of pravastatin used in Asia to that observed for 20–40 mg doses used in Europe and the United States.

Cardiac catheterization and analysis of LV function

In patients with AMI, chronic-stage cardiac catheterization was repeated approx. 3–4 weeks after the onset of AMI. A 5 French multipurpose catheter (Cathex) was introduced into the CS (coronary sinus) through the left subclavian vein under fluoroscopic guidance [14]. The position of the catheter tip was confirmed by the injection of contrast medium. Blood samples were collected from the CS before the intravenous administration of heparin. Following the collection of blood samples from the right brachial artery (as peripheral blood samples) through a 6 French sheath, heparin was administered and coronary

angiography and left ventriculography were performed, according to the conventional Judkins' technique. LV pressure was measured using a 2 French high-fidelity micromanometer catheter (Miller Instruments) advanced into the left ventricle via the lumen of a 6 French pig-tail catheter. The restenosis of a treated artery was defined as an arterial narrowing of $>75\%$, as determined by coronary angiography.

LV volume was evaluated angiographically by a cardiologist who was blinded to the results of the biochemical assays. Ventricular silhouettes in a 30° right anterior oblique projection were digitized using an ANCHOR ventriculography analysis system (Siemens-Elema). Using the area-length method, LV end-systolic volume index, LVEDVI (LV end-diastolic volume index) and LVEF (LV ejection fraction) were calculated.

Biochemical assessment

Blood samples were centrifuged and serum was stored at -80 °C until assay. A sandwich enzyme immunoassay was performed to determine MMP-2 level (Fuji Chemical Industries) [15]. In addition, the level of MMP-9, another gelatinase-like MMP-2, and that of MMP-13, an interstitial collagenase, were analysed using MMP Biotrak enzyme-linked immunoadsorbent assay kits (Amersham Biosciences). The levels were back-calculated from the standard curve determined with the enzyme-linked immunoadsorbent assay kits using a 96-well microplate reader (Emax; Molecular Devices). These kits detect the pro-enzyme and the pro-enzyme complexed with TIMP. The detection limits were 0.5 ng/ml for MMP-2, 0.6 ng/ml for MMP-9 and 0.03 ng/ml for MMP-13.

We also measured levels of TIMP-1 (Fuji Chemical Industries) and TIMP-2 (Amersham Biosciences) using sandwich enzyme immunoassays [15]. The detection limits for TIMP-1 and TIMP-2 were 1.2 and 8.0 ng/ml respectively.

BNP was measured using specific immunoradiometric assay kits (Shionogi). The sensitivity of these kits was 2 pg/ml. Ang II (angiotensin II) and TGF-β (transforming growth factor-β) levels were also measured, as reported previously [16].

The serum CRP (C-reactive protein) level was measured by N Latex CRP II monoassay using a nephelometric analyser (BN II; Dade Behring). The lower detection limit of this test was 0.06 mg/dl. Total cholesterol, triacylglycerol (triglyceride) and HDL (high-density lipoprotein) cholesterol concentrations were determined by enzymatic methods using a Toshiba TBA 80M analyser. LDL (low-density lipoprotein) was calculated using Fredewald's formula. We also measured WBC (white blood cell) number.

Statistical analysis

The two groups were compared by Student's t test. Measurements from the CS and the peripheral artery were compared within a group by ANOVA. When a significant difference among groups was indicated by the initial analysis, individual paired comparisons were determined using the Student–Newman–Keuls method. A linear regression line was calculated by the least-square method to assess the correlation between two parameters. To investigate independent predictors, we used multivariate logistic regression analysis. In all cases, differences were considered significant at $P < 0.05$. Results are presented as means $\pm$ S.D., or medians.

Table 1 Clinical characteristics

*$P = 0.05$ and **$P < 0.01$ compared with control (patients with stable AP).

Characteristic	Patients with AMI ($n = 20$)	Patients with stable AP ($n = 10$)
Age (years)	66 ± 9	67 ± 6
Peak CK (units/l)	1986 (801–8574)	–
Cardiac function		
LVEF (%)	48 ± 7**	58 ± 7
LVEDVI (ml/m^2)	95 ± 18**	55 ± 21
Vessels $>75\%$ stenosed (n)	1.5 ± 0.7	1.6 ± 0.7
Risk factors (n)		
Hypertension	11 (55%)	7 (70%)
Diabetes mellitus	15 (75%)	6 (60%)
Hyperlipidaemia	10 (50%)	6 (60%)
Smoking	12 (60%)	6 (60%)
Biochemical parameters†		
Total cholesterol (mg/dl)	193 ± 27	198 ± 20
LDL (mg/dl)	120 ± 30	122 ± 31
WBC count (cells/μl)	6615 ± 1571	5600 ± 1063
CRP (mg/dl)	0.34 ± 0.33*	0.13 ± 0.06
Medication used (n)		
ACE-I	20 (100%)	4 (40%)
β-Blockers	11 (55%)	6 (60%)
Statins	10 (50%)	6 (60%)
Calcium antagonists	7 (35%)	5 (50%)
Nitrates	4 (20%)	2 (20%)
Aspirin	20 (100%)	10 (100%)

† Data obtained on the day when cardiac catheterization was performed.

RESULTS

The baseline clinical characteristics of the patients with AMI and the control patients with AP (without evidence of AMI) are summarized in Table 1. In the patients with AMI, cardiac function data were obtained at chronic-stage cardiac catheterization performed 22 ± 12 days after the onset of AMI. Coronary angiography revealed 90% stenosis of the infarct-related artery in two patients and 100% stenosis in three patients. These five patients with restenosis had received intravenous thrombolysis alone in the acute stage. In the remaining 15 patients, the treated

Table 2 Comparisons of BNP, MMP and TIMP levels in the CS and peripheral artery

*$P < 0.05$ compared with levels in artery; †$P < 0.05$ compared with control (patients with stable AP).

	Patients with AMI ($n = 20$)		Patients with stable AP ($n = 10$)	
Peptide	CS	Artery	CS	Artery
BNP (pg/ml)	400 ± 376*†	126 ± 176	54 ± 25	52 ± 25
MMP-2 (ng/ml)	853 ± 199*†	716 ± 127	631 ± 44	630 ± 46
MMP-9 (ng/ml)	165 ± 129*†	98 ± 82	68 ± 25	71 ± 24
MMP-13 (ng/ml)	0.05 ± 0.04	0.05 ± 0.02	0.04 ± 0.02	0.04 ± 0.02
TIMP-1 (ng/ml)	155 ± 59	150 ± 53	130 ± 33	134 ± 32
TIMP-2 (ng/ml)	112 ± 18	108 ± 14	94 ± 11	97 ± 16

sites remained patent. With the exception of cardiac function (LVEF and LVEDVI) and the prevalence of ACE-I use, clinical characteristics were similar between patients with AMI and AP.

Enhancement of cardiac MMP production in patients with AMI

Table 2 shows the comparison of BNP, MMP and TIMP levels between blood samples from the CS and peripheral artery. In patients with AMI, levels of BNP, MMP-2 and MMP-9 were significantly ($P < 0.05$) higher in the CS than in the peripheral artery, whereas the levels of MMP-13, TIMP-1 and TIMP-2 were similar. In control patients with AP, no significant differences in the levels of BNP, MMPs and TIMPs were observed between the CS and peripheral artery. These findings indicate that the production of MMP-2 and MMP-9, as well as that of BNP, is enhanced in an infarcted heart.

Correlation of cardiac MMP production with post-infarction LV remodelling

In patients with AMI, the CS–arterial concentration gradients of MMP-2 and MMP-9 correlated positively with those of BNP and LVEDVI respectively (Figure 1), but not with LVEF, peak CK level and circulating WBC counts. These myocardial gradients were not different between patients with and without progression to restenosis (MMP-2, 87 ± 32 compared with 152 ± 173 ng/ml; MMP-9, 83 ± 86 compared with 61 ± 82 ng/ml).

Comparisons between pravastatin-treated patients with AMI and non-pravastatin-treated patients with AMI

We then compared levels of MMPs between ten patients treated with 10 mg of pravastatin and ten patients not treated with pravastatin (Table 3). Although the total cholesterol level before treatment was higher ($P < 0.05$) in the pravastatin-treated patients with AMI (223 ± 7 mg/dl in treated patients compared with 195 ± 17 mg/dl in

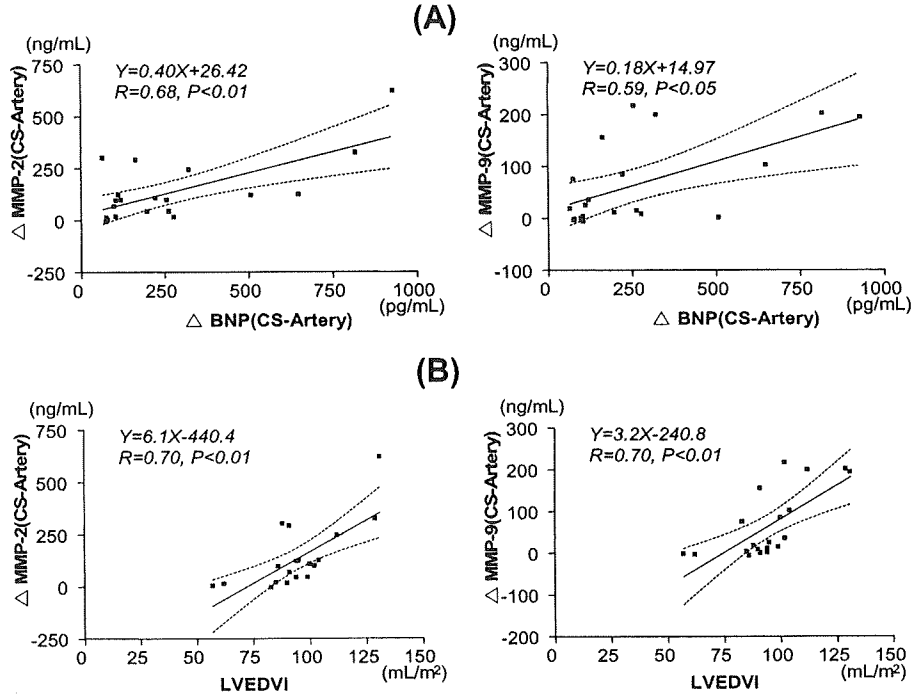

Figure 1 Correlations between CS–arterial concentration gradients of MMP-2 and -9 and BNP (A) and LVEDVI (B) in 20 patients with AMI

Table 3 Comparisons of MMPs between pravastatin-treated and non-pravastatin-treated patients

*$P < 0.05$ compared with levels in artery; †$P < 0.05$ compared with levels in non-pravastatin-treated patients. CS–artery, CS–arterial concentration gradient.

	Patients with AMI						Patients with stable AP					
	Pravastatin-treated ($n = 10$)			Non-pravastatin-treated ($n = 10$)			Pravastatin-treated ($n = 6$)			Non-pravastatin-treated ($n = 4$)		
MMP (ng/ml)	CS	Artery	CS–artery	CS	Artery	CS–artery	CS	Artery	CS–artery	CS	Artery	CS–artery
MMP-2	808 ± 182	739 ± 158	69 ± 43†	897 ± 216*	684 ± 84	213 ± 185	631 ± 53	624 ± 51	7 ± 23	629 ± 32	639 ± 43	−9 ± 53
MMP-9	94 ± 61†	80 ± 59	14 ± 27†	236 ± 142*	117 ± 100	119 ± 84	68 ± 20	72 ± 16	−4 ± 4	68 ± 20	69 ± 29	0 ± 5
MMP-13	0.06 ± 0.06	0.03 ± 0.03	0.03 ± 0.06	0.03 ± 0.02	0.05 ± 0.03	−0.01 ± 0.03	0.03 ± 0.04	0.04 ± 0.02	−0.01 ± 0.01	0.04 ± 0.02	0.03 ± 0.02	0.01 ± 0.03

non-treated patients), no significant differences were observed after treatment between the two groups (183 ± 31 mg/dl in treated patients compared with 201 ± 20 mg/dl in non-treated patients). Levels of CRP (0.18 ± 0.13 mg/dl in treated patients compared with 0.50 ± 0.40 mg/dl in non-treated patients; $P = 0.03$) and the CS–arterial concentration gradients of MMP-2 and MMP-9 (Table 3) were significantly different between the two groups. However, the concentration gradients of TGF-β and Ang-II were similar between patients treated with pravastatin and those not treated (Ang-II, 19.5 ± 20.2 compared with 36.9 ± 32.4 pg/ml respectively; TGF-β, 1.2 ± 3.3 compared with 2.1 ± 4.7 pg/ml respectively).

We then performed multivariate analysis for the predictors of CS–arterial concentration gradients of MMP levels, including age, sex, coronary risk factors, peak CK, infarct site (anterior wall), CRP, TIMP, pravastatin treatment, LVEF and LVEDVI. The association between pravastatin treatment and cardiac MMP-2 production was modest, with an odds ratio of 0.074 (95 % confidence interval, 0.005–1.109; $P = 0.06$), and did not reach statistical significance.

DISCUSSION

The major findings of the present clinical study are that after AMI, the cardiac production of MMP-2 and MMP-9 is enhanced and associated with LV enlargement and BNP secretion, and that the pleiotropic effect of statins appears to be associated with the modulation of cardiac MMP activation.

Among the MMP species, MMP-2 and MMP-9 play an important role in LV remodelling, as these MMPs are activated in the myocardium and it has been reported that the targeted deletion of these MMPs prevents post-infarction cardiac dysfunction and rupture [9,10]. In the clinical setting, circulating MMP-2 and MMP-9 levels have been measured in previous studies of patients with AMI [17–19]; however, these results were conflicting. Squire et al. [17] reported that circulating MMP levels were inversely correlated with LV dilatation, whereas Matsunage et al. [18] and Nakaya et al. [19] found that serum MMP levels and activity were positively correlated with LV dilatation. In addition, circulating MMP levels could be affected at the acute stage following reperfusion therapy and by the clinically vulnerable state [20–23]. In the present study, we focused on cardiac production of MMP [14], and the measurement was performed at the clinically stable stage following AMI. As shown in Table 2, despite similar levels of TIMPs, significant differences in levels of BNP, MMP-2 and MMP-9 were observed between the CS and the peripheral artery in patients with AMI. To our knowledge, this is the first study demonstrating the enhanced production of MMP-2 and MMP-9 in a human infarcted heart. Moreover, as shown

in Figure 1, the CS–arterial concentration gradients of MMP-2 and MMP-9 correlated positively with those of BNP and LVEDVI. Taking into account the delicate balance between MMPs and TIMPs in tissue remodelling, the present findings indicate that excessive cardiac production of MMPs may play an important pathological role in the progression of post-infarction LV dysfunction.

A previous experimental study of an AMI model using BNP-transgenic mice demonstrated a potential interaction of BNP with inflammation [24]. The overexpression of BNP leads to neutrophil infiltration and MMP-9 expression in the infarct region and increases the incidence of cardiac rupture. These findings suggest the significance of inflammatory reaction in the heart accompanied by changes in LV function. 3-Hydroxy-3-methylglutaryl-CoA reductase inhibitors, such as statins, exert various cardiovascular protective effects beyond their lipid-level lowering actions [12,25]. These pleiotropic effects include the inhibition of inflammatory responses. In the present study, we have shown that the CS–arterial concentration gradients of MMP-2 and MMP-9 were smaller in the pravastatin-treated group than in the non-pravastatin-treated group, which was accompanied by a decrease in CRP level. These findings indicate that pravastatin may modulate cardiac MMP production in patients with AMI, probably via its anti-inflammatory effects. Similar observations of decreased circulating MMP-2 levels in patients with AMI treated with 10 mg of paravastain have been reported previously [19].

There are several potential limitations of the present study. First, this study was not randomized. Pravastatin was administered to a small number of patients with AMI with hyperlipidaemia. In such a pro-inflammatory state, tissue MMPs might have been activated before treatment [26], which could affect the results. Therefore prospective studies will be required to determine if pravastatin has a causal role in reducing cardiac MMP production in patients with AMI. Secondly, the present study was carried out over the short term, whereas ventricular remodelling is known to progress over months or years. Thirdly, previous studies have shown that the renin–angiotensin system is also involved in the induction of post-infarction ventricular remodelling [27] and can be inhibited by statins [28,29]. However, we have shown that the CS–arterial concentration gradients of Ang II were similar between pravastatin-treated patients and non-pravastatin-treated patients. This may be related, in part, to the fact that all our patients with AMI had been treated with 5 mg of enalapril.

In conclusion, the present study demonstrates the enhancement of MMP production in an infarcted heart. Pleiotropic effects of statins may be associated with the modulation of cardiac MMP activation, which is potentially beneficial in the attenuation of post-infarction LV remodelling.

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Unstable Angina and Non-ST Elevation Acute Coronary Syndrome

— Epidemiology and Current Management in Japan (Japan Multicenter Investigation for Cardiovascular Disease-D (JMIC-D) Committee) —

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Background A multicenter study was conducted to assess the current medical management of unstable angina (UA) and non-ST-elevation acute coronary syndrome in Japan.

Methods and Results This study presents the results of a nationwide questionnaire survey of 770 sites and a case report investigation performed at 20 sites. The questionnaire survey revealed that the number of acute myocardial infarction (AMI) patients treated annually was 1.56-fold greater than the number of UA patients. Non-ST-elevation AMI accounted for 17% of all patients with AMI. Analysis of case reports for 885 UA patients showed extensive use of invasive treatment. In the UA patients, the cumulative incidence of a composite endpoint (all-cause mortality, AMI, and urgent coronary revascularization) was 2% at 1 month and 9% at 6 months. Stratified analysis with respect to the composite endpoint through 6 months showed a significantly lower incidence in patients treated with a calcium-channel blocker than in patients not treated with a calcium-channel blocker.

Conclusions In Japan, fewer patients are hospitalized annually for treatment of UA than for AMI. The largest percentage of UA patients had Braunwald class III disease. Non-ST-elevation AMI is managed in Japan according to the principle of early invasive treatment, resembling the treatment for ST-elevation AMI. The outcome of treatment is better for Japanese UA patients than for Japanese AMI patients. (*Circ J* 2007; **71**: 1335–1347)

Key Words: Acute coronary syndromes; Epidemiology; Non-ST elevation; Unstable angina

According to the Population and Vital Statistics of Japan for 2003, heart disease is the second leading cause of death, and ischemic heart disease, including acute myocardial infarction (AMI), is the most frequent cause of cardiac death[1] If the aging of society continues, mortality from ischemic heart disease will increase further, so more effort should be made to improve treatment.

In 2002, the Japanese Circulation Society established guidelines for the diagnosis and treatment of acute coronary syndrome (ACS), but most of the clinical data used as the basis for the guidelines was gathered overseas[2] Because of differences in the pathophysiology of ACS between Japanese and Caucasians[3] the Japanese ACS guideline should be based on data obtained from Japanese patients.

Several multicenter studies on the treatment of AMI have already been conducted in Japan[4] but there have been few studies of unstable angina (UA). According to recent recommendations for treatment of ACS made by the Japanese Circulation Society, as well as the relevant American and European societies, the treatment of individual patients should not be based on diagnoses such as AMI or UA, but on whether ST changes are found on admission[2,5] In Japan, none of the multicenter studies has compared baseline characteristics, treatment, and outcomes in patients with ST-elevation and non-ST-elevation ACS, except for a few single-center studies[6,7]

Accordingly, we launched the Japan Multicenter Investigation for Cardiovascular Disease-D (JMIC-D) to investigate the number of patients with UA and non-ST-elevation ACS and the current management practices for both disease manifestations in Japan, with the aim of using the results to optimize specific therapeutic recommendations.

Methods

This study comprised a questionnaire survey (study 1) and a case report investigation (study 2). The questionnaire survey was designed to investigate the number of hospitalized patients with UA or AMI, and the treatment policies for these conditions at the participating sites. The case report investigation was designed to obtain detailed treatment and outcome data for individual patients. All statistical tests were 2-sided with an α=0.05 significance level. Between-group comparisons were tested using chi-square tests or Fisher's exact test where appropriate. In this study,

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3. Jichi Medical School Omiya Medical Center	*Muneyasu Saito (Changes to Saitama kinen Hosipital)*
4. Sekishinkai Sayama Hospital	*Masami Sakurada (Moved to Tokorozawa Heart Clinic)*
5. Nippon Medical School Hospital	*Teruo Takano, Keiji Tanaka*
6. Nippon Medical School Chiba Hokusoh Hospital	*Kyouichi Mizuno*
7. Yokohama Rosai Hospital	*Kenichi Katoh*
8. Yokohama City University Medical Center	*Kazuo Kimura*
9. Toyohashi Heart Center	*Shigenori Ito (Moved to Moriyama Municipal Hospital, City of Nagoya)*
10. Nagoya Daini Red Cross Hospital	*Haruo Hirayama*
11. National Cardiovascular Center	*Hiroshi Nonogi*
12. Kansai Rosai Hospital	*Shinsuke Nanto*
13. Osaka Police Hospital	*Kazuhisa Kodama, Atsushi Hirayama*
14. Osaka City Central Hospital	*Kazuo Haze*
15. Sakurabashi Watanabe Hospital	*Kenshi Fujii*
16. Osaka Koseinenkin Hospital	*Tatsuya Sasaki*
17. Matsushita Memorial Hospital	*Hiroki Sugihara*
18. Wakayama Medical University	*Yoshiaki Tomobuchi*
19. Kobe City General Hospital	*Shigefumi Morioka*
20. Kumamoto Chuo Hospital	*Shuichi Oshima*

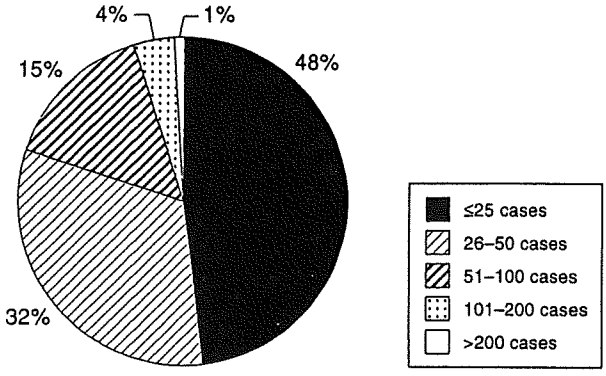

Fig 1. Approximate number of unstable angina (UA) patients hospitalized in 2000 at 582 cardiovascular care sites.

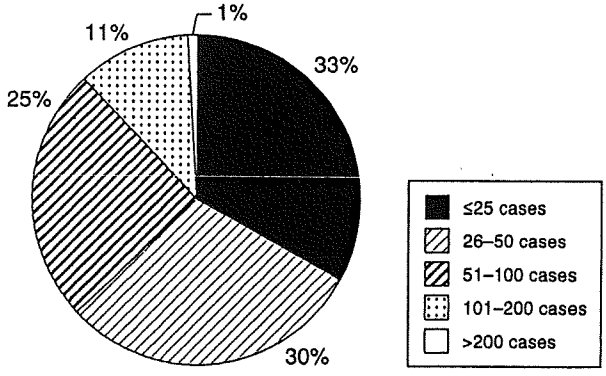

Fig 2. Approximate number of acute myocardial infarction (AMI) patients treated in 2000 at 580 cardiovascular care sites.

UA was defined according to the Braunwald Classification with creatine kinase (CK) and CK-MB isozyme values not greater than twice the respective upper limits of normal; a diagnosis of AMI was made if the CK and CK-MB values exceeded twice the upper limits of normal and the time from onset to admission was within 24 h.

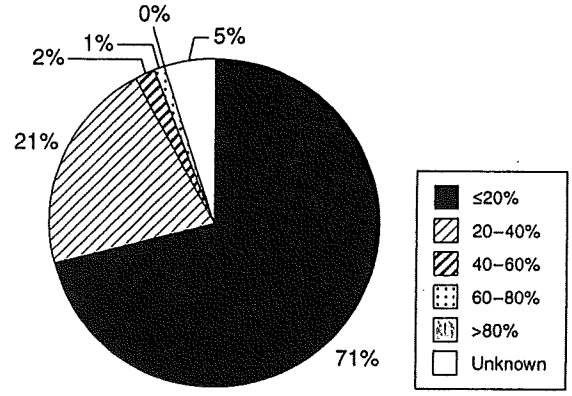

Fig 3. Approximate percentage of patients with non-ST elevation acute myocardial infarction (AMI) among all AMI patients at 574 responding sites.

Study 1: Questionnaire Survey

A questionnaire composed of the 8 questions listed below was sent to the 770 sites certified for cardiovascular care by the Japanese Circulation Society. To increase the response rate and to avoid null answers, multiple choice responses to the questions were set, as shown in parentheses below.

UA (1) Approximate number of hospitalized UA patients during the year from January to December 2000 (≤25; 26–50; 51–100; 101–200; >200).

(2) Treatment with heparin immediately after hospital arrival, excluding bolus administration for coronary angiography and/or revascularization (for all patients apart from those with contraindications; only for refractory patients not responding to appropriate antianginal treatment or for severe cases; not used in principle).

(3) Timing of coronary angiography (immediately after arrival at hospital; after stabilization by drug treatment; not performed if stabilized by drug treatment; no definite policy).

(4) Use of heparin after percutaneous coronary intervention (PCI) (not used in principle; for some patients; for all patients in principle).

AMI (1) Approximate number of hospitalized AMI patients during the year from January to December 2000

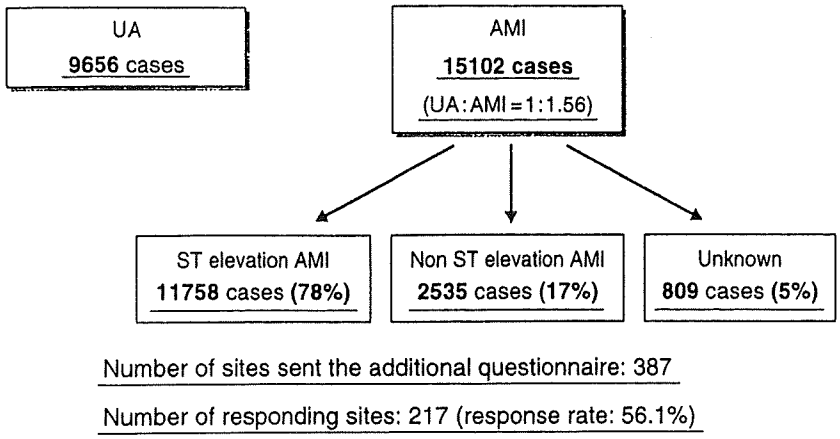

Fig 4. Number and ratio of unstable angina (UA) and acute myocardial infarction (AMI) patients: results from the additional questionnaires.

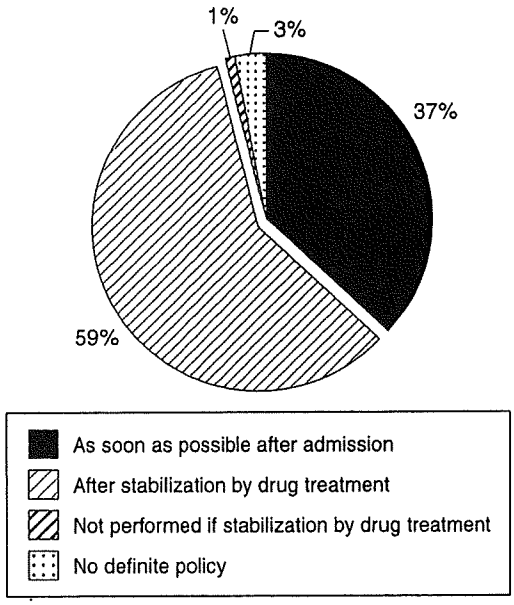

Fig 5. Timing of coronary angiography for unstable angina (UA) patients. Number of responding sites: 574.

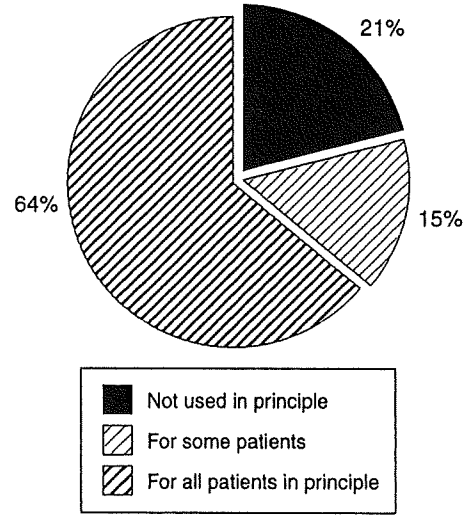

Fig 7. Use of Heparin after percutaneous coronary intervention (PCI). Number of responding sites: 521.

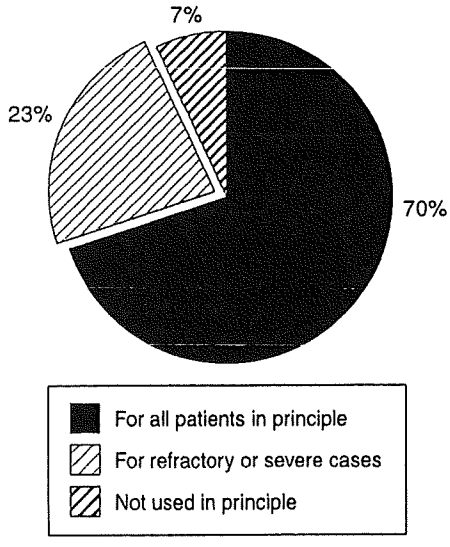

Fig 6. Treatment with heparin immediately after admission. Number of responding sites: 582.

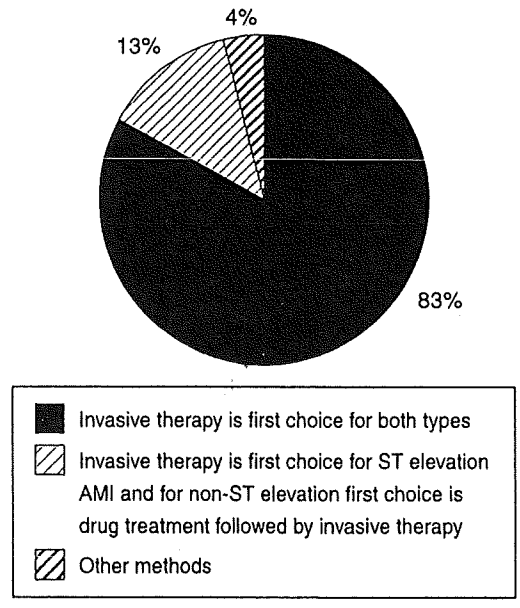

Fig 8. Treatment principles for ST elevation and non-ST elevation acute myocardial infarction (AMI) at 576 responding sites.

Table 2 Baseline Characteristics of Patients With UA

Sex	
M	652 (74%)
F	233 (26%)
Age (years)	
Median	67 (Max: 93 Min: 27)
Mean±SD	66.2±10.8
Concomitant disease	
Hypertension	
Yes	514 (58%)
No	371 (42%)
Diabetes	
Yes	328 (37%)
No	557 (63%)
Hyperlipidemia	
Yes	373 (42%)
No	512 (58%)
Cerebrovascular disease	
Yes	75 (8%)
No	810 (92%)
Renal disease	
Yes	81 (9%)
No	804 (91%)
Liver disease	
Yes	24 (3%)
No	861 (97%)
Previous disease	
MI	
Yes	221 (25%)
No	664 (75%)
History of PTCA, stent	
Yes	198 (22%)
No	684 (77%)
Unknown	3 (0.3%)
History of CABG	
Yes	39 (4%)
No	845 (95%)
Unknown	1 (0.1%)
Time from onset to admission (h)	
Median	15.75 (Max: 1,258 Min: 0)
Mean±SD	70.11±140.8
Duration of hospitalization (days)	
Median	12 (Max: 259 Min: 0)
Mean±SD	18.35±22.10
Braunwald class	
I	225 (25%)
II	112 (13%)
III	548 (62%)
A	87 (10%)
B	775 (88%)
C	23 (3%)
ECG abnormality on admission	
ST deviation	
No change	376 (42%)
Elevation	130 (15%)
Depression	364 (41%)
Elevation + Depression	4 (0.5%)
Unknown	11 (1%)

UA, unstable angina; MI, myocardial infarction; PTCA, percutaneous transluminal coronary angioplasty; CABG, coronary artery bypass graft.

Table 3 Baseline Characteristics of Patients With AMI

Sex	
M	727 (78%)
F	210 (22%)
Age (years)	
Median	66 (Max: 96 Min: 28)
Mean±SD	65.2±12.2
Concomitant disease	
Hypertension	
Yes	512 (55%)
No	425 (45%)
Diabetes	
Yes	312 (33%)
No	625 (67%)
Hyperlimidemia	
Yes	349 (37%)
No	588 (63%)
Cerebrovasculer disease	
Yes	68 (7%)
No	869 (93%)
Renal disease	
Yes	63 (7%)
No	874 (93%)
Liver disease	
Yes	16 (2%)
No	921 (98%)
Previous disease	
MI	
Yes	149 (16%)
No	785 (84%)
Unknown	3 (0.3%)
History of PTCA, stent	
Yes	97 (10%)
No	838 (89%)
Unknown	2 (0.2%)
History of CABG	
Yes	25 (3%)
No	911 (97%)
Unknown	1 (0.1%)
Time from onset to admission (h)	
Median	3.0 (Max: 29 Min: 0)
Mean±SD	5.35±5.75
Duration of hospitalization (days)	
Median	21 (Max: 257 Min: 0)
Mean±SD	25.53±22.24
ECG abnormality on admission	
Elevation	782 (83%)
ST deviation	
Non elevation	133 (14%)
No change	34
Depression	99
Elevation + Depression	15 (2%)
Unknown	7 (1%)

AMI, acute MI. Other abbreviations as in Table 2.

(≤25; 26–50; 51–100; 101–200; >200).

(2) Approximate percentage of patients with ST-elevation AMI among all AMI patients (≥80%; 60–80%; 40–60%; 20–40%; ≤20%; unknown).

(3) Treatment principles (first-line treatment) for ST-elevation and non-ST-elevation AMI (invasive therapy is first choice for both types; invasive therapy is first choice for ST-elevation and for non-ST-elevation first choice is drug treatment followed by invasive therapy; other methods).

Study 2: Case Report Investigation

Twenty sites (Table 1) were randomly selected from among those participating in the questionnaire survey (study 1) and were requested to submit case reports for 50 consecutive patients treated for UA and 50 treated for AMI after January 2000. A case report was to include the following information.

Demographic Data and Clinical Profile Sex, age, concomitant disease, previous disease, time from onset to admission, Braunwald classification (only for UA patients), and ECG findings. Hypertension, hyperlipidemia, diabetic, kidney disease, and liver disease that were concomitant diseases were diagnosed by individual investigator based on the diagnostic standard of each site.

Treatment Findings of coronary angiography, details

Table 4 Details of Treatment of Patients With UA

Coronary Angiography	
Yes	*810 (92%)*
No	*75 (8%)*
Time from admission to angiography (h)	
Median	*28.4 (Max: 333 Min: 0)*
Mean±SD	*58.02±68.44*
Coronary vessel with significant stenosis before intervention	
0 vessel	*78*
1 vessel	*360*
2 vessels	*217*
3 vessels	*170*
LMT	*59*
Unknown	*4*
Culprit vessel	
LMT	*43*
LAD	*424*
LCX	*178*
RCA	*229*
Graft or other	*13*
Stenosis of culprit vessel before intervention	
100%	*85*
99%	*229*
90%	*339*
75%	*73*
50%	*6*
25%	*5*
0%	*59*
Unknown	*14*
TIMI flow past the culprit lesion before intervention	
0	*73*
1	*39*
2	*142*
3	*505*
Unknown	*56*
Revascularization	
Yes	*647 (73%)*
No	*238 (27%)*
Interventional procedure	
PTCA	*519 (80%)*
Stent	*406 (63%)*
ICT	*13 (2%)*
IVCT	*5 (1%)*
CABG	*101 (16%)*
Other	*31 (5%)*
Time from admission to revascularization (h)	
Median	*57 (Max: 5,857.25 Min: 0)*
Mean±SD	*144.97±296.28*
Stenosis after intervention	
100%	*5*
99%	*2*
90%	*4*
75%	*1*
50%	*30*
25%	*214*
0%	*280*
Unknown	*111*
TIMI Flow after intervention	
0	*11*
1	*1*
2	*3*
3	*508*
Unknown	*124*
Treatment with continuous heparin infusion	
Yes	*606 (68%)*
No	*279 (32%)*
Max daily dosage (units)	
Median	*12,000 (Max: 38,400 Min: 480)*
Mean±SD	*12,692±4,236*
Duration (days)	
Median	*3 (Max: 43 Min: 1)*
Mean±SD	*4.31±3.51*
Treatment with antiplatelet medication after admission	
Yes	*842 (95%)*
No	*43 (5%)*
ASA alone	*286*
Ticlopidine alone	*14*
ASA + Ticlopidine	*349*
ASA + Other	*61*
Ticlopidine + Other	*3*
Other alone	*16*
ASA + Ticlopidine + Other	*99*
Unknown	*14*

LMT, left main trunk; LAD, left anterior descending coronary artery; LCX, left circumflex coronary artery; RCA, right coronary artery; TIMI, Thrombolysis In Myocardial Infarction; ICT, intracoronary thrombolysis; IVCT, intravenous thrombolysis; ASA, acetylsalicylic acid. Other abbreviations as in Table 2.

Table 5 Details of Treatment of Patients With AMI

Coronary angiography	
Yes	*917 (98%)*
No	*20 (2%)*
Time from admission to reperfusion therapy (h)	
Median	*1.0 (Max: 1,426.5 Min: 0)*
Mean±SD	*15.6±81.1*
Coronary vessel with significant stenosis before reperfusion	
0 vessel	*10 (1%)*
1 vessel	*481 (52%)*
2 vessels	*253 (28%)*
3 vessels	*161 (18%)*
LMT	*33 (4%)*
Unknown	*1 (0.1%)*
Culprit vessel	
LMT	*22 (3%)*
LAD	*436 (51%)*
LCX	*163 (19%)*
RCA	*321 (38%)*
Graft or other	*9 (1%)*
Unknown	*70 (7%)*
Stenosis of culprit vessel before reperfusion	
100%	*496*
99%	*229*
90%	*107*
75%	*13*
50%	*3*
25%	*5*
0%	*0*
Unknown	*64*
TIMI flow past the culprit lesion before reperfusion	
0	*479*
1	*89*
2	*140*
3	*136*
Unknown	*73*
Reperfusion therapy	
Yes	*855 (91%)*
No	*82 (9%)*
Reperfusion therapy modality	
PTCA	*765 (89%)*
Stent	*558 (65%)*
ICT	*72 (8%)*
IVCT	*62 (7%)*
CABG	*36 (4%)*
Other	*59 (7%)*
Time from admission to reperfusion (h)	
Median	*1.5 (Max: 2,798.75 Min: −22.5)*
Mean±SD	*27.76±163.44*
Stenosis after reperfusion therapy	
100%	*15 (1.8%)*
99%	*11 (1.3%)*
90%	*5 (0.6%)*
75%	*15 (1.8%)*
50%	*81 (9.5%)*
25%	*317 (37.1%)*
0%	*362 (42.3%)*
Unknown	*49 (5.7%)*
TIMI flow after reperfusion therapy	
0	*20 (2%)*
1	*13 (2%)*
2	*45 (5%)*
3	*703 (82%)*
Unknown	*74 (8%)*
Treatment with continuous heparin infusion	
Yes	*766 (82%)*
No	*170 (18%)*
Unknown	*1 (0.1%)*
Max daily dosage (units)	
Median	*14,400 (Max: 80,000 Min: 480)*
Mean±SD	*14,051±5,304*
Duration (days)	
Median	*4 (Max: 212 Min: 1)*
Mean±SD	*5.09±8.71*
Treatment with antiplatelet medication after admission	
Yes	*905 (97%)*
No	*32 (3%)*
ASA alone	*218*
Ticlopidine alone	*11*
ASA + Ticlopidine	*394*
ASA + Other	*71*
Ticlopidine + Other	*2*
Other alone	*2*
ASA + Ticlopidine + Other	*190*
Unknown	*17*

Abbreviations as in Tables 2–4.