Effect of Reperfusion Therapy on Cardiac Rupture After Myocardial Infarction in Japanese

Nahoko Ikeda, MD; Takanori Yasu, MD; Norifumi Kubo, MD; Taishi Hirahara, MD;
Yoshitaka Sugawara, MD; Nobuhiko Kobayashi, MD; Shigemasa Hashimoto, MD;
Yoshio Tsuruya, MD; Mikiyoshi Fujii, MD; Muneyasu Saito, MD

Background Cardiac rupture after acute myocardial infarction (AMI) is unpredictable and almost always fatal, so the present study reviewed all the clinical characteristics of patients with cardiac rupture to determine if its occurrence can be predicted.

Methods and Results The clinical characteristics of 1,296 consecutive AMI patients from January 1992 to February 2002 were retrospectively evaluated using multi-logistic analysis. Cardiac rupture occurred in 45 patients (3.5%), comprising left ventricular free wall rupture (n=23), ventricular septal perforation (n=20) and papillary muscle rupture (n=2). Early-phase rupture (within 72 h after AMI onset) was associated with anterior infarction. Of the 45 patients who experienced ruptures, 24 (53.3%) survived to discharge; 21 (46.6%) of the 45 ruptures occurred after admission. Successful reperfusion therapy was performed within 24 h for 840 patients. The incidence of rupture was significantly lower for reperfused patients than for non-reperfused patients (0.6% vs 3.5%, respectively; $p<0.01$). Peak C-reactive protein concentration was a reliable predictor of late-phase rupture ($p=0.01$), but not of early-phase rupture.

Conclusions Reperfusion therapy appears to aid in the prevention of cardiac rupture, especially late-phase rupture. (Circ J 2004; 68: 422–426)

Key Words: Cardiac rupture; Myocardial infarction; Reperfusion

In patients with acute myocardial infarction (AMI), cardiac rupture is the second most common cause of in-hospital death, after pump failure!^{1,2} It is difficult to predict, and almost always fatal. It has been reported that the risk of cardiac rupture is greater for women, hypertensive patients, patients >60 years old sustaining their first infarction^{2,3} and patients with a peak C-reactive protein (CRP) concentration ≥ 20 mg/dl.⁴ However, these associations may change as a result of dramatic improvements in acute phase treatment, including reperfusion therapy by thrombolysis, balloon angioplasty, mechanical circulatory support by intra-aortic balloon pumping (IABP) and percutaneous cardiopulmonary support system (PCPS). Because previous reports have suggested that early- (≤ 72 h after onset of AMI) and late-phase rupture (>72 h after onset of AMI) differ in pathogenesis and mechanisms,^{5,6} in the present study we also divided patients with cardiac rupture into the same 2 groups to determine whether we could predict cardiac rupture following AMI from an analysis of the relationships between clinical background and rupture.

Methods

Patients

Between January 1992 and February 2002, we recruited

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Cardiovascular Division, First Department of Integrated Medicine, Omiya Medical Center, Jichi Medical School, Saitama, Japan
Mailing address: Takanori Yasu, MD, Cardiovascular Division, First Department of Integrated Medicine, Omiya Medical Center, Jichi Medical School, 1-847 Amanuma, Saitama, Saitama 330-8503, Japan. E-mail: tyasu@omiya.jichi.ac.jp

1,296 consecutive AMI patients who had been admitted to the coronary care unit. AMI was diagnosed on the basis of an increase in serum creatine kinase (CK) activity to more than twice the upper limit of normal, accompanied by chest symptoms and electrocardiographic (ECG) changes. Cardiac rupture included free wall rupture (blow-out type, oozing type), ventricular septal perforation (VSP) and

Fig 1. Types of cardiac rupture. (A) Total cardiac ruptures (n=45). (B) Pre hospital ruptures (n=24) occurred before referral from another hospital for surgery. (C) In-hospital ruptures (n=21) occurred after admission to this hospital. PMR, papillary muscle rupture; VSP, ventricular septal perforation.

Fig2. Relationship between time of rupture and site of infarction. Early-phase rupture occurred in 28 patients and was associated with an anterior site. AMI, acute myocardial infarction.

papillary muscle rupture (PMR). Diagnosis of free wall rupture was based on echocardiography followed by pericardiocentesis or surgical or postmortem examination. Blow-out rupture was defined as a free wall rupture with electromechanical dissociation (EMD), and sudden onset of severe hypotension without ECG change, lasting several seconds. Oozing-type free wall rupture required surgical treatment for rapidly increasing pericardial effusion followed by cardiac tamponade. VSP was diagnosed on the basis of abnormal shunt-flow at the interventricular septum on color Doppler echocardiography or a significant increase in oxygen saturation in the right ventricle.

Study Protocol

The present study design was a retrospective single-center case-control study. We reviewed the clinical characteristics of all the patients: age, gender, previous history of myocardial infarction, ST segment elevation on ECG, wall motion abnormalities and pericardial effusion on echocardiography, sites of coronary arterial lesions, grade of collateral flow, peak plasma concentrations of CK and CRP,

Fig3. Early- and late-phase rupture. PMR, papillary muscle rupture; VSP, ventricular septal perforation.

Fig4. Mortality of patients with cardiac rupture: 24 (53.3%) of 45 with cardiac rupture survived to the end of the study period. Percutaneous cardiopulmonary support system (PCPS) was used in 14 patients, 6 of whom survived. PMR, papillary muscle rupture; VSP, ventricular septal perforation.

and reperfusion therapy including direct percutaneous transluminal coronary angioplasty (PTCA) and thrombolysis. Reperfusion therapy consisted of administration of thrombolytic agents (urokinase or tissue plasminogen activator (t-PA)) intravenously or into the infarct-related coro-

Table 1 Relationships Between Clinical Factors and Total In-Hospital Cardiac Ruptures

	Total in-hospital rupture (n=21)	Non-rupture (n=1,251)	p (vs non-rupture)
Acute reperfusion	5 (19%)	838 (67%)	<0.001
Pericardial effusion	4 (19%)	37 (3%)	0.052
M:F	14:7	950:301	0.067
Anterior MI	16 (76%)	600 (48%)	0.097
Dyskinesia	11 (52%)	250 (20%)	0.124
ST elevation (mm)	11.0±8.2	8.2±8.9	0.140
Age (years)	68±10	62±11	0.191
Thrombolytic therapy	5 (24%)	212 (17%)	0.218
Max CRP (mg/dl)	11.9±8.6	8.1±5.3	0.101
CRBBB	3 (14%)	75 (6%)	0.433
Max CK (mg/dl)	3,314±2,770	2,660±2,283	0.542
History of MI	3 (14%)	250 (20%)	0.802
Collateral vessel	1 (5%)	225 (18%)	0.999

CK, creatine kinase; CRBBB, complete right bundle branch block; CRP, C-reactive protein; MI, myocardial infarction.

Table 2 Relationships Between Clinical Factors and the 2 Phases of Cardiac Rupture, and Comparison of Each Phase

	Early rupture (n=10)	Late rupture (n=11)	Non-rupture (n=1,251)
Acute reperfusion	4 (40%)*	1 (9%)*	838 (67%)
Pericardial effusion	2 (20%)	2 (18%)	37 (3%)
M:F	7:3	7:4*	950:301
Anterior MI	9 (90%)*	7 (64%)	600 (48%)
Dyskinesia	3 (30%)#	8 (73%)	250 (20%)
ST elevation (mm)	11.0±9.6	11.4±7.2	8.2±8.9
Age (years)	67±10*	70±11	62±11
Thrombolytic therapy	2 (20%)	3 (27%)	212 (17%)
CRP (mg/dl)	8.3±8.9	15.2±7.1*	8.2±5.3
CRBBB	3 (30%)#	0 (0%)	75 (6%)
Max CK (mg/dl)	4,391±3,451	2,112±1,403	2,660±2,283
History of MI	1 (10%)	2 (18%)	250 (20%)
Collateral vessels	0 (0%)	1 (9%)	225 (18%)

CK, creatine kinase; CRBBB, complete right bundle branch block; CRP, C-reactive protein; MI, myocardial infarction.

* $p < 0.05$ vs non-rupture group; # $p < 0.05$ vs late rupture.

nary artery, PTCA, or a combination of PTCA and thrombolytic therapy. Successful recanalization was defined as thrombolysis in myocardial infarction (TIMI) with grade 2 flow or greater. Patients who had cardiac rupture were divided into 2 groups on the basis of time of rupture: early phase (≤ 72 h of AMI onset) and late phase (> 72 h after onset).

Statistics

Data are expressed as mean $\pm$ SD. Multiple logistic regression analysis was used to assess the effects of various factors on cardiac rupture in hospital. Chi-square analysis was used to assess differences among categorical variables. A p -value less than 0.05 was considered to indicate statistical significance.

Results

Details of Cardiac Ruptures

Left ventricular free wall rupture (including blow-out

type (n=12) and oozing type (n=11)), VSP (n=20) or PMR (n=2) occurred in 45 (3.5%) of the 1,296 patients (Fig 1A). Early-phase rupture occurred in 28 of the 45 patients and was associated with an anterior site of infarction ($p=0.022$). Late-phase rupture occurred in 12 patients, and was not associated with any specific infarction site (Fig 2). In 24 patients, rupture occurred before referral to this hospital for surgery; most of these patients had VSP (n=17) (Fig 1B). Approximately half (n=10) of the in-hospital ruptures were the blow-out type (Fig 1C), which occurred more often in the early phase (Fig 3).

Percutaneous Cardiopulmonary Support and Survival

Twenty-four (53.3%) of the 45 patients survived. PCPS was used to rescue 14 patients from a state of shock (VSP (n=3), free wall oozing rupture (n=1), blow out type (n=9), PMR (n=1)), 6 of whom survived (VSP (n=2), free wall oozing rupture (n=1), blow out type (n=2), PMR (n=1)) (Fig 4).

Table 4 Clinical Background of the Patients With In-Hospital Ruptures

Age	Gender	Rupture type	Rupture time	MI site	BP (mmHg)	Killip	RT	CRP	CK
52	M	Blow out	7 h	Anterior	95/60	4	—	0.2	2,842
71	M	Blow out	7 h	Anterior	105/55	2	+	0.2	2,265
55	F	Blow out	9 h	Anterior	125/85	2	—	0.1	1,420
69	M	Blow out	10 h	Anterior	100/60	2	—	19.3	7,609
66	M	Blow out	12 h	Non anterior	160/90	1	—	0.5	3,095
76	F	Oozing	17 h	Anterior	130/65	1	+	2.4	2,815
78	M	Oozing	36 h	Anterior	100/60	1	—	17.1	5,573
76	F	Blow out	36 h	Anterior	110/75	2	—	21.6	614
67	M	Oozing	37 h	Anterior	100/60	2	+	14.2	5,550
55	M	Blow out	40 h	Anterior	150/100	2	+	7.3	12,130
81	M	PM rupture	3 d	Non anterior	55/40	4	—	17.4	760
73	F	VSP	3.5 d	Anterior	110/60	3	—	18.8	992
85	M	Blow out	4 d	Non anterior	100/70	1	—	0.8	1,807
70	F	Oozing	4 d	Anterior	100/60	1	—	15	3,195
51	M	Oozing	4 d	Anterior	100/60	2	+	15.2	4,893
65	M	VSP	4 d	Anterior	140/80	1	—	15.4	2,810
52	M	Oozing	5 d	Anterior	110/60	2	—	6.1	1,234
68	F	Oozing	7 d	Non anterior	105/60	1	—	19.7	1,962
77	M	Blow out	7 d	Non anterior	130/80	2	—	28.5	307
78	M	Blow out	8 d	Anterior	100/60	4	—	13.1	
65	F	VSP	16 d	Anterior	110/55	1	—	17.3	3,160

BP, blood pressure (mmHg); CK, creatine kinase (mg/dl); CPR, cardiopulmonary resuscitation; CRP, C-reactive protein (mg/dl); IABP, intraaortic balloon pumping; MI, myocardial infarction; OMI, old myocardial infarction (—: not exist, +: exist); PCPS, percutaneous cardiopulmonary support; RT, reperfusion therapy (—: not performed or failed reperfusion, +: successful reperfusion therapy); t-PA, tissue plasminogen activator (—: not used, +: used).

Table 3 Management of Cardiac Rupture After Acute Myocardial Infarction

Blow-out rupture	(Pericardiocentesis) PCPS, surgical repair
Oozing rupture	(Pericardiocentesis) Oxygenation, colloid infusion, dobutamine; surgical repair
Papillary muscle rupture	IABP (PCPS), surgical repair
Ventricular septal perforation	
Qp/Qs≤2	If hemodynamic state permits, wait for 2 weeks from onset of AMI; surgical repair
Qp/Qs≥2	IABP (PCPS), surgical repair

IABP, intra-aortic balloon pumping; PCPS, percutaneous cardiopulmonary support.

Analysis of Clinical Factors

We analyzed the clinical factors of patients with in-hospital cardiac rupture (n=21; Tables 1,2) and found that on multiple logistic regression analysis recanalization of the infarction-related artery most strongly reduced the risk of rupture (especially in the late phase). Occurrence of in-hospital rupture was lower in reperfused patients (n=5, 0.6%) than in non-reperfused patients (n=16, 3.5%, $p<0.01$) (Fig 5). The clinical factor that was secondarily associated with early-phase rupture was anterior myocardial infarction (MI) ($p=0.044$). Peak CRP concentrations were significantly higher in patients with late-phase rupture than in those without rupture ($p=0.011$), but there was no significant difference between patients with early-phase rupture and those without rupture (Table 2).

Discussion

Acute Reperfusion and Cardiac Rupture

Successful reperfusion of the ischemic myocardium was the factor most strongly associated with prevention of cardiac rupture in both the early and late phases, which is consistent with the findings of previous reports.⁷⁻⁹ Successful

Peak time	OMI	t-PA	Management	Result
104h	—	—	PCPS + Ope	Alive
15h	—	—	PCPS + Ope	Alive
6h	—	+	PCPS	Dead
10h	—	—	PCPS	Dead
11h	—	+	Conventional CPR	Dead
17h	—	—	Ope	Alive
13h	+	—	IABP + Ope	Dead
—	—	—	PCPS + Ope	Dead
28h	—	—	PCPS + Ope	Alive
4h	—	—	Conventional CPR	Dead
—	—	+	IABP + Ope	Dead
36h	—	—	IABP + Ope	Dead
—	+	—	Conventional CPR	Dead
16.5h	—	—	Ope	Alive
17h	—	+	IABP + Ope	Alive
19h	—	—	IABP + Ope	Dead
24h	+	+	Ope	Alive
24h	—	—	Ope	Alive
72h	—	—	PCPS + Ope	Dead
—	—	—	PCPS	Dead
24h	—	—	Ope	Alive

Fig 5. Reperfusion therapy and cardiac rupture. Rupture occurred significantly less in reperfused patients (0.6%) than in non-reperfused patients (3.5%, $p<0.001$).

early reperfusion of the infarct-related coronary artery while maintaining integrity of the downstream microvasculature limits ongoing necrosis, salvages the myocardium, and may prevent the development of shock in many vulnerable patients. Most of the present patients with cardiac rupture who received reperfusion therapy had an early-phase rupture, which occurred more frequently at an anterior site of infarction, and most (70%) were the blow-out type. In anterior MI, loss of contraction at the apex may result in a further decrease in apical wall thickness in systole, thus increasing tensile stress per unit cross-sectional area of the apical wall. That suggests an important role for mechanical factors in the development of early-phase rupture. In pathological studies, Becker and van Mantgem have classified cases of cardiac rupture into 3 types:⁵ type I rupture is characterized as an abrupt, slit-like myocardial tear correlating clinically with a recent infarction (<24h); type II rupture has an area of myocardial erosion, indicative of a slowly progressive tear; and type III rupture correlates with older infarctions, and the fatal tear typically occurs where an aneurysm has formed. The blow out rupture is thought to be a type I rupture.

We performed direct PTCA in 93% of reperfused patients, and thrombolysis was performed in 6.4%. In this small number, thrombolytic therapy had no statistical effect on the incidence of cardiac rupture, although many reports indicate that thrombolytic therapy accelerates myocardial rupture. Primary angioplasty restores coronary patency more frequently than thrombolysis.^{10,11} Intramyocardial hemorrhage following reperfusion injury may lead to myocardial tears, especially in patients who receive thrombolytic therapy.¹²⁻¹⁶

CRP Concentration and Cardiac Rupture

It has been reported that the peak CRP concentration in plasma is an important predictor of cardiac rupture and left

ventricular remodelling^{4,17,18} Intramyocardial hemorrhage and pericarditis, resulting from slow leakage of blood into the pericardial space early after MI, can participate in local cardiac inflammation, causing marked and persistent elevation of serum CRP. However, in the present study, CRP was only a useful predictor of late-phase rupture, not of early-phase rupture. In the early-phase rupture group, rupture may have occurred before the CRP concentration peaked.

Management of Cardiac Rupture

Contemporary methods for management of cardiac rupture after AMI are summarized in Table 3.^{6,19,20} In Japan, mechanical support by PCPS in cardiogenic shock was introduced in the 1990s^{21,22} and since then, the survival rate of cardiac rupture has risen.^{23,24} The clinical backgrounds of the present patients with in-hospital rupture are shown in Table 4. Two cases of blow-out free wall rupture were salvaged using PCPS followed by surgery. Their coronary arteries were obstructed at the proximal site of the left anterior descending artery. One of these 2 patients has returned to work, but the other suffered hypoxic brain damage. The time from rupture to start of PCPS is the key to protecting the brain. Conservative strategies that may be used successfully in selected subgroups of patients have been suggested by other researchers.^{6,25,26}

Study Limitations

This was a retrospective single-center study, and the number of patients with cardiac rupture was small. Therefore, the present results should be viewed as preliminary, requiring confirmation by larger clinical trials.

Conclusions

Reperfusion therapy appears to aid in the prevention of cardiac rupture, especially late-phase rupture. Serum peak CRP concentration is an independent predictor of late-phase cardiac rupture. However, reperfusion therapy does not adequately prevent ruptures in patients with anterior MI, in whom ruptures are more likely to occur in the early phase. Further research is needed in the areas of pharmacological and mechanical hemodynamic support, refinement of revascularization strategies, and outcome modeling.

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