—**Report on Experiments and Clinical Cases**—

Clinical Course, Timing of Rupture and Relationship with Coronary Recanalization Therapy in 77 Patients with Ventricular Free Wall Rupture Following Acute Myocardial Infarction

Keiji Tanaka[1], Naoki Sato[1], Masahiro Yasutake[1], Shinhiro Takeda[1], Teruo Takano[2] and Shigeo Tanaka[3]

[1]Division of Intensive and Coronary Care Unit, Nippon Medical School Hospital
[2]First Department of Internal Medicine, Nippon Medical School
[3]Department of Cardiovascular Surgery, Nippon Medical School

Abstract

This study aimed to analyze the clinical course, timing of rupture and relationship with percutaneous coronary intervention (PCI) in patients with cardiac free wall rupture (FWR) following acute myocardial infarction (AMI). FWR was observed in 77 (2.3%) of 3,284 patients with AMI in our CCU over 28 years. 47 (61.0%) cases were male and mean of age was 69.8 year old. Rupture occurred on Day 1 of infarction in 46 patients (59.7%). 22 cases (28.6%) had cardiogenic shock before FWR. 10 cases (13.0%) had double rupture preceded by ventricular septal perforation (VSP). 25 cases (32.5%) were treated with thrombolytic agents, and only 10 cases (13.0%) had percutaneous coronary intervention (PCI). Before 1981, when PCI was not indicated, incidence of FWR was 2.7%. After 1988 (the era of PCI), the incidence decreased to 1.1%. FWR and the era showed a significant negative correlation ($r = 0.519$: $P = 0.0056$).

Rupture was abrupt in 51 cases (66.2%: abrupt type) and was gradual in 26 cases (33.8%: oozing type). The percentages of female, patients with cardiogenic shock before rupture, patients treated by thrombolytic agents and survival rate were significantly higher in the slow-onset rupture group than in the abrupt-onset rupture group. The percentage of patients treated by PCI was extremely low (7.8%) in abrupt-onset group.

Of all patients, only 8 (10.4%) survived by emergency operation. One patient with abrupt type survived emergency pericardtomy in the CCU. One patient with abrupt type and 4 patients with oozing type who had emergency operation in operation room survived. 2 patients with oozing type survived by pericardial drainage and strict blood pressure control.

We conclude that early recognition and emergency surgery without thrombolytic therapy may substantially reduce mortality in oozing ruptures. Moreover, immediate and adequate reperfusion by PCI may prevent development of abrupt rupture following acute myocardial infarction. (J Nippon Med Sch 2002; 69: 481–488)

Key words: free wall rupture, acute myocardial infarction, coronary recanalization therapy, oozing type, abrupt type

Correspondence to Keiji Tanaka, MD, Director of Division of Intensive and Coronary Care Unit, Nippon Medical School Hospital, 1–1–5 Sendagi, Bunkyo-ku, Tokyo 113–8603, Japan
E-mail: k-tanaka@nms.ac.jp
Journal Website (http://www.nms.ac.jp/jnms/)

Introduction

It is more than 350 years since the first report of cardiac rupture by William Hearvery in 1649[1]. Though new diagnostic procedures and treatments have been established in coronary care unit (CCU), cardiac free wall rupture (FWR) is still a severe and fatal condition leading to sudden death[2-4]. The common clinical features are known but detailed characteristics concerning the timing of such ruptures is still unknown.

Despite a progressive reduction in acute myocardial infarction mortality over the year, reduction in death related to FWR is controversial. Some investigators have suggested that acute coronary intervention and early recanalization of coronary artery reduces the risk of FWR[5]. However, there are few studies demonstrating a reduction of the risk of FWR achieved by coronary intervention.

The purpose of this study was to analyze the detail clinical characteristics concerning the timing of FWR and to evaluate the effect of thrombolytic therapy and percutaneous coronary intervention (PCI) on the risk of FWR in patients with acute myocardial infarction.

Subjects

Of 3,284 patients with acute myocardial infarction admitted to the CCU of our hospital between April, 1973 and December, 2001, 77 patients in whom cardiac rupture was detected were enrolled in this study. Cardiac rupture was confirmed by autopsy in 30 patients; emergency bedside thoracotomy was carried out in 33, operation in 10, and pericardial puncture in 4. Diagnosis of acute myocardial infarction was made according to the New York Heart Association's criteria[6].

The age of the patients ranged from 47 to 87 years, and more than 50% of them were 70 years old or more. The male: female ratio was 1.57: 1. The infarction site was anterior in 13 (16.9%), posterior in 16 (20.8%), anterolateral in 38 (49.4%) and others in 10 (13.5%). All patients had transmural infarction, and only 3 patients had reinfarction. 41 patients (53.2%) had clinical signs of cardiac failure on admission, including 23 patients (29.9%) showing cardiogenic shock. 10 patients (13.0%) had double rupture preceded by ventricular septal perforation (VSP).

Of all patients, only 8 (10.4%) survived by emergency operations. One patient with abrupt type had an emergency thracotomy in the CCU and survived. One patient with abrupt type and 4 patients with oozing type who had emergency operation in operation room survived. 2 patients with oozing type survived after pericardial drainage and strict blood pressure control.

Statistical analysis

A multivariate chi-square test was used to compare categoric variance. Student t test was used for comparison of two mean variables with normal distribution and the Mann-Whitney U test for those with abnormal distribution. A linear regression between year and incidence of FWR was calculated by the least squares methods. Results are expressed as mean ± standard deviation. A level of $p < 0.05$ was accepted as statistically significant

Results

1) Timing of free wall rupture

The time of rupture was defined as the time when sudden cardiac tamponade and shock developed. The interval from onset of infarction to rupture was investigated. As shown in **Fig. 1**, rupture occurred on Day 1 of infarction in 41 patients (53.2%) and on Day 2 or earlier in 50 patients (64.9%). However, prior to blow out, some patients had prodromata (pericardial friction rub, echo free space and/or transient bradycardia-hypotension). In Fig. 1, the patients with these prodromata are indicated by hatched circles. Assuming that the time when these signs appeared was the time of the onset of rupture, the time of rupture was corrected by prodromata. The day of rupture after correction is indicated by dashed lines under the horizontal axis. When the time of rupture was corrected for these signs, 46 patients (59.7%) developed FWR on Day 1, and 60 patients (77.9%) on Day 2 or earlier.

In 2 patients who developed rupture on Day 7 or

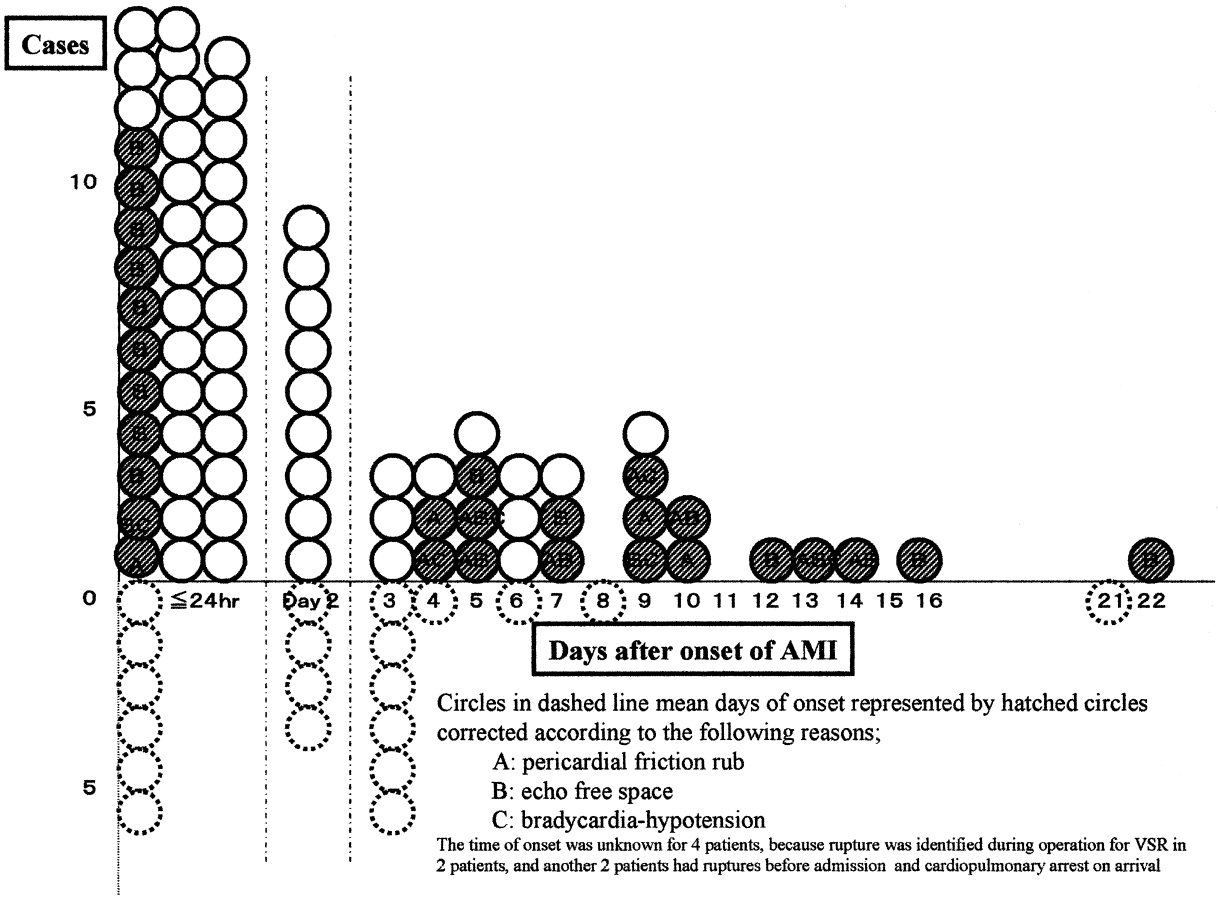


Fig. 1 Day of cardiac rupture

Dashed line circles indicate patients after correction of the day of rupture for the following reasons in patients shown by hatched circles corrected according to following reasons; A : friction rub, B: echo free space, C: bradycardia-hypotension.

The time of rupture was unknown in 4 patients because rupture was detected during operation for ventricular septal perforation in 2 patients, and another 2 patients had ruptures before admission and cardiopulmonary arrest on arrival.

later, chest pain and a re-elevation in the ST segment on ECG appeared a few hours before rupture, suggesting re-infarction. However, since no definite evidence was obtained, the time of rupture was not corrected in these patients. The time of rupture was unknown in 4 patients because ruptures were detected during operation for ventricular septal perforation in 2 patients, and the other patients were admitted for cardio-pulmonary arrest (CPA).

2) Clinical course

Fig. 2 shows the course from the onset of infarction to death after cardiac rupture, expressed in terms of the mean interval between events in all patients excluding survivors. The upper column represents the course in which the time of rupture is defined as the time of blowout. The interval between the onset of infarction and admission in all patients (two patients who had FWR before admission were excluded) was 12.5±49.5 hr. The interval between admission to the CCU and blowout in all patients (four patients who had FWR before admission or VSP were excluded) was 63.8±47.2 hr.

The middle column represents the course in which the time of rupture was defined as the time of the appearance of prodromata. The interval between admission to the CCU and cardiac rupture corrected by prodromata was 24.4±47.0 hr. A delay of 39.4 hours was recognized before the blowout from onset of rupture in 22 patients. The interval between rupture and death was 102.7±124.2 hours. This

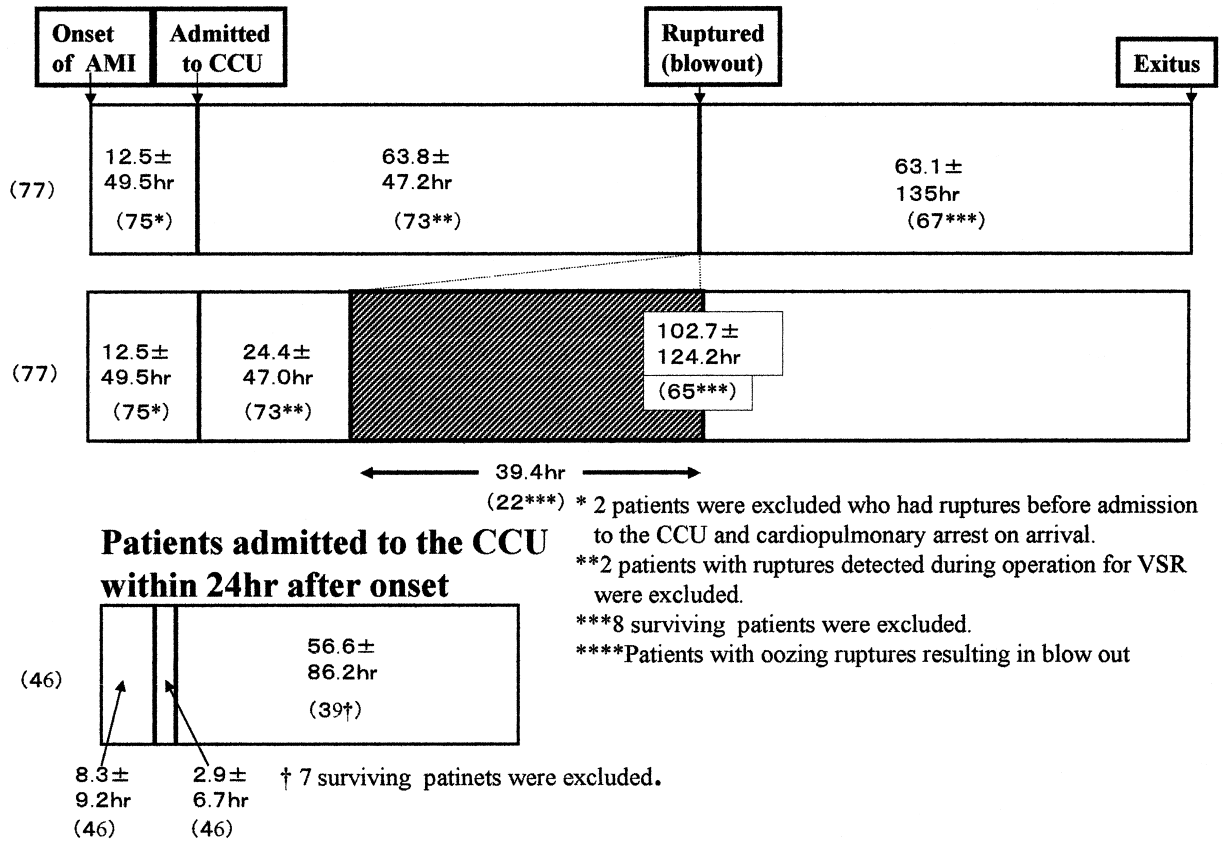


Fig. 2 Mean interval from onset of infarction to death after rupture

* : Two patients who developed ruptures before admission to the CCU and cardiopulmonary arrest on arrival were excluded.

** : Two patients with ruptures confirmed during operation for ventricular septal perforation were also excluded.

*** : Eight surviving patients were excluded.

**** : Patients with oozing ruptures resulting in blowout.

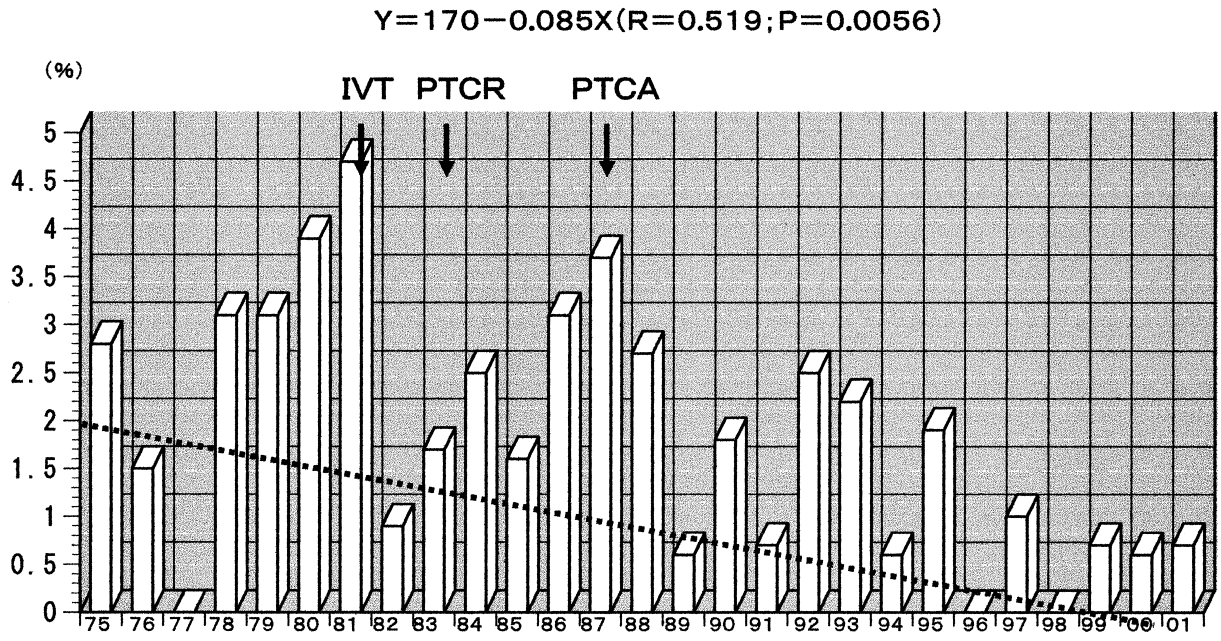
interval was relatively long because the subjects included patients with successful repair of the rupture site in emergenct bedside operations. The longest interval was 129 days in all patients excluding survivors.

The lower column shows the course in 46 patients who developed rupture within 24 hours after the onset of infarction. The interval between the onset of infarction and admission was 8.3±9.2 hr and the interval between admission to the CCU and blowout was 2.9±6.7 hr. One patient developed rupture 2 hours after chest pain, which was the shortest interval. Another patient was brought to hospital in a state of CPA 4 hours after onset of infarction, and rupture was confirmed by autopsy. In all patients, rupture occurred 6～12 hours after onset of infarction. The interval between rupture and death was 56.6±86.2 hours in this group.

3) Influence of reperfusion therapy and annual change in the incidence of FWR

Acute coronary recanalization therapy was performed on 31 patients (40.3%) before VFR. Among the 31 patients, 25 cases (32.5%) were treated with intravenous thrombolytic agents (urokinase in 20 and tissue plasminogen activator in 5). Only 4 cases (5.2%) underwent direct percutaneous transluminal coronary angioplasty (PTCA), and only 6 cases (7.8%) had both intravenous thrombolysis and PTCA.

Before 1981 when PCI was not indicated in our CCU, the incidence of FWR was 2.7%. After 1988 (the era of PCI: above 80% of AMI patients are treated with PCI now), the incidence decreased to 1.1%. 55 patients (71.4%) with FWR were admitted to our CCU before 1988. The linear regression



IVT; Intravenous Thrombolysis
PTCR; Percutaneous Transluminal Coronary Recanalization PTCA; Percutaneous Transluminal Coronary Angioplasty

Fig. 3 A linear regression between year and incidence of FWR was calculated by the least squares methods. FWR and the era showed a significant negative correlation (y = 170 − 0.085x: r = 0.519: P = 0.0056). IV; Intravenous Thrombolysis PTCR; Percutaneous Transluminal Coronary Recanalization

between year and incidence of FWR was calculated by the least squares methods. FWR and the era showed a significant negative correlation (y = 170−0.085x: r = 0.519: P = 0.0056).

4) Rapid- and slow-onset rupture groups

Patients with prodromata of rupture were classified as the slow-onset rupture group, and those without prodromata as the rapid-onset rupture group. The clinical characteristics of the two groups are compared in **Table 1**. The age of the patients, site of infarction and incidence of arrhythmias or VSP were similar between the two groups. The percentage of females was higher in the oozing group than in the abrupt group (P = 0.034). The incidence of cardiac failure (Killip II or III) was relatively high in the oozing group (P = 0.163) and that of cardiogenic shock (Killip IV) before blowout was significantly higher in the oozing group than in the abrupt group (P = 0.003). The CTR (cardiothoracic ratio) was also higher in the oozing rupture group (60.6 ± 6.6 vs 54.8 ± 5.6. P = 0.0014).

Concerning treatment, the percentages of patients treated with thrombolytic agents and IABP (intra-aortic balloon pumping) were higher in the oozing rupture group (P = 0.035, 0.001, respectively). 13 patients (59.1%) out of 22 with oozing rupture resulting in blowout had intravenous thrombolytic agents. The percentage of patients treated with thrombolytic agents did not differ from those of patients without FWR before 1988 but decreased to about 20% after 1988. Only 10 patients in both groups (7.8% in the abrupt group and 23.1% in the oozing group) were treated by PTCA (percutaneous transluminal coronary angioplasty). This percentage was extremely low compared with patients without cardiac rupture. The survival rate of abrupt type was 3.9% and that of oozing type was 23.1%.

Discussion

The incidence of cardiac rupture following acute myocardial infarction has been reported to be 2～24%[7]. This differences reported may be because the diagnosis of this condition is mainly based on autopsy findings, and the incidence is affected by the autopsy rate.

Table 1 Difference between clinical characteristics of abrupt type and oozing type

		Abrupt type (51) †	Oozing type (26) ††
Age		69.1 ± 7.5	70.2 ± 9.4
Sex		Male 36, Female 15	Male 11, Female 15*
Infarction site	anterior	10 (19.6%)	4 (15.4%)
	posterior	10 (19.6%)	7 (26.9%)
	anterolateral	24 (47.1%)	13 (50.0%)
	others	7 (13.7%)	2 (7.7%)
Complication	heart failure	9 (17.6%)	8 (30.8%)
	cardiogenic shock	8 (15.7%)	14 (53.8%) *
	arrhythmia	33 (64.7%)	18 (69.2%)
	VSR	6 (11.8%)	4 (15.4%)
Treatment	thrombolytic agent	12 (23.6%)	13 (50.0%) *
	PTCA	4 (7.8%)	6 (23.1%)
	digitalis	4 (7.8%)	4 (15.4%)
	catecholamine	17 (33.3%)	15 (57.7%)
	IABP	4 (7.8%)	12 (46.2%) *
	others	31 (60.8%)	16 (61.5%)
CTR		54.8 ± 5.6%	60.6 ± 6.6%*
Survival		2 (3.9%)	6 (23.1%) *

† 2 patients with CPA on arrival were included *< 0.05

†† 2 patients with ruptures detected during operation of VSP were included.

The incidence we investigated by methods such as emergency bedside thoracotomy, pericardocentesis or autopsy was 2.3%.

It has been thought that a delay in CCU admission was an important factor in FWR. However, some investigators have questioned such a relation. In this study, the interval between the onset of infarction and admission to the CCU did not differ from patients without FWR and ruptures occurred 6～12 hours after onset of infarction in 46 patients. One patient developed a rupture 2 hours after chest pain. Another patient was brought to hospital in a state of CPA 4 hours after onset of infarction. These observations show that a delay is not a major factor. The speed with which myocardial necrosis developes, the size of myocardial necrosis and early reperfusion of the culprit coronary artery are important factors. Cheriex EC et al[8] demonstrated that myocardial rupture typically occurs in an infarcted area without reperfusion by means of coronary angiograpy.

Timing of rupture

Rupture occurred within 1 week (peak myocardial softening period) in most patients, and rarely after 1 week or more[9]. Figueras et al found that 55% of patients ruptured within 2 days and 87% within 6 days[10]. In this study, the interval between the onset of infarction and cardiac rupture was most frequently within 24 hours; 59.7% of patients developed rupture during this period. The reason why the time that onset of rupture is earlier than in other articles is that the time was fixed by prodromata.

Several studies reported that cardiac rupture had an acute, subacute or slow course[11～13]. We classified cardiac ruptures into abrupt type and oozing type. The patients with prodromata of rupture were classified as oozing type and those without the signs as abrupt type. Abrupt rupture was similar to acute rupture, and oozing rupture was thought to be about the same as subacute rupture. The percentage of females was larger in the oozing group and the incidence of preexisting cardigenic shock was significantly higher in the oozing group than in the abrupt group. The frequency of patients treated with thrombolytic agents or IABP was also higher in the oozing rupture group.

Relationship of reperfusion therapy

Reperfusion therapy is one of the most effective treatments for acute myocardial infarction, but the effect on left ventricular free wall rupture remains to be determined.

In the cases who developed rupture within 24 hours, the mean interval between the onset of infarction and rupture was 8.3 hours. This 8 hours after the onset of infarction corresponds to the time soon after completion of coronary thrombolytic therapy. This may be one of the reasons that the relationship between thrombolytic therapy and cardiac rupture has been discussed.

Controversy remains about the actual relationship between the use of thrombolytic agents and frequency of rupture[14~16]. Early thrombolytic therapy may reduce the incidence of cardiac rupture[14,15], but on the other hand the late use of thrombolytic agents appears to increase the incidence of rupture[15,16]. In this study, thrombolytic agents such as urokinase were administered only to 25 patients (33.8%), which suggests no close association between thrombolytic therapy and cardiac rupture. However, it should be noted that thrombolytic agents were more frequently used in the oozing rupture group (50.0%) than in the abrupt rupture group (23.6%). When thrombolytic agents are used without recognition of the above mentioned signs of rupture in the oozing rupture group, blowout may develop.

Only 10 patients (13.0%) in both groups were treated by PTCA. A successful reperfusion by early PTCA and stenting may have prevented the development of both types of cardiac rupture[17,18]. Brodie et al[18] reviewed the timing and mechanism of death in 1,184 consecutive patients with AMI treated with primary angioplasty from 1984 to 1995. Of 98 deaths, 48 (49%) occurred early on day 0 or 1. The incidence of death from left ventricular rupture was 0.4%. In contrast to thrombolytic therapy, the incidence of death from myocardial rupture and bleeding complications is low. Accordingly, it is expected that the incidence of cardiac rupture can be reduced if PTCA is performed earlier. But on the other hand, the increase in the number of cases with coronary arterial rupture caused by PTCA should be paid attention to[19].

Conclusion

We concluded that early recognition[20] and emergency surgery without thrombolytic therapy may substantially reduce mortality in oozing rupture. Moreover, immediate and adequate reperfusion by PTCA may prevent development of cardiac rupture following acute myocardial infarction.

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