Primary Angioplasty Reduces the Risk of Left Ventricular Free Wall Rupture Compared With Thrombolysis in Patients With Acute Myocardial Infarction

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OBJECTIVES This study aimed to evaluate the effect of primary angioplasty (PA) over the risk of free wall rupture (FWR) in reperfused acute myocardial infarction (AMI).

BACKGROUND It has been suggested that PA reduces the risk of FWR compared with thrombolysis. However, few studies have evaluated this issue, and there are no data demonstrating this hypothesis.

METHODS A total of 1,375 patients with AMI treated with PA (n = 762, 55.4%) or thrombolysis (n = 613, 44.6%) within 12 h after symptoms onset were included. The diagnosis of FWR was made either in the presence of sudden death due to electromechanical dissociation with large pericardial effusion on an echocardiogram or when demonstrated post mortem or at surgery.

RESULTS The overall incidence of FWR was 2.5% (n = 34): 1.8% and 3.3% in patients treated with PA and with thrombolysis, respectively (p = 0.686). The following characteristics were associated with a higher rate of FWR in the univariable analysis: age > 70 (5.2% vs. 1.2%, p < 0.001), female gender (5.1% vs. 1.8%, p = 0.006), anterior location (3.3% vs. 1.4%, p = 0.020) and treatment > 2 h after symptoms onset (3.6% vs. 1.7%, p = 0.043). In the multivariable analysis, age > 70 (odds ratio [OR]: 4.12, 95% confidence interval [CI]: 2.04 to 8.62, p < 0.001) and anterior location (OR: 2.91, 95% CI: 1.36 to 6.63, p = 0.008) were independent risk factors of FWR, whereas treatment with PA was an independent protective factor (OR: 0.46, 95% CI: 0.22 to 0.96, p = 0.0371).

CONCLUSIONS In patients with AMI, PA reduces the risk of FWR in comparison with thrombolysis. (J Am Coll Cardiol 2002;39:598–603) © 2002 by the American College of Cardiology

Primary angioplasty (PA) is the preferred treatment for acute myocardial infarction (AMI) in centers with available infrastructure and well-trained personnel (1). The main advantage of PA over thrombolysis is the achievement of a higher rate of coronary recanalization with a lower risk of intracranial bleeding (2–4).

Left ventricular free wall rupture (FWR) is the second leading cause of in-hospital mortality in patients with AMI (5,6). Some authors have suggested that PA reduces and even avoids the risk of FWR, especially when a successful angiographic result is obtained (7–9). However, few studies have assessed this issue, and there are no data demonstrating a reduction of the risk of FWR achieved by PA. The objective of this study was to evaluate the possible effect of PA in comparison with thrombolysis on the risk of FWR in a consecutive series of patients with AMI reperfused with either PA or with thrombolysis.

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METHODS

Study population and criteria for referring patients to PA or thrombolysis. A total of 1,413 consecutive patients with AMI that were reperfused with either thrombolysis or PA within 12 h after symptoms onset at our institution were retrospectively studied. At our institution, patients that are admitted with the diagnosis of AMI enter a prospective database. The coronary care unit cardiologists are responsible for data entry, quality control, management and analysis. Patients with hypotension (systolic blood pressure <90 mm Hg) of uncertain origin and those having suffered syncope underwent a routine transthoracic echocardiographic study in order to rule out mechanical complications before beginning treatment with thrombolysis or PA. Patients in whom FWR was diagnosed before the reperfusion strategy were not included in the study. Thirty-eight patients underwent rescue angioplasty after failed thrombolysis and were excluded from the study. The remaining 1,375 patients constituted the study population, 613 of whom (44.6%) were treated with thrombolysis, and 762 (55.4%) with PA. The initial 590 patients included in the cohort of patients treated with PA are included in a previous publication (10).

The criteria for referring patients for thrombolysis or PA
have varied over the years, depending on the period of time. When participating in Global Use of Strategies to Open Occluded Coronary Arteries (GUSTO) IIb angiographic substudy (11) or in our single-center anterior location AMI study (4), patients were randomly assigned to thrombolysis or PA. When participating in the Primary Angioplasty in Myocardial Infarction (PAMI) II (12), PAMI Stent Pilot study (13), PAMI III (14) and Controlled Abciximab and Device Investigation to Lower Late Angioplasty Complications (CADILLAC) clinical trials, all patients fulfilling inclusion criteria were treated with primary PTCA. When participating in Intravenous nPA for Treatment of Infarcting Myocardium Early (INTIME) I and II studies (15), all patients fulfilling inclusion criteria were treated with thrombolysis. Patients with contraindications for thrombolysis were treated with PA, and those with anterior location or cardiogenic shock were preferably treated with PA during the entire period of study.

**Definitions.** The diagnosis of FWR was made in either of the following situations: 1) sudden death occurred due to electromechanical dissociation associated with large pericardial effusion on an echocardiogram; or 2) FWR was identified post mortem or at surgery (16). Two patients treated with PA and one patient treated with unsuccessful thrombolysis and subsequent rescue angioplasty (excluded from the final study population) suffered coronary perforation during PA and were not considered as having FWR. Free wall rupture was defined as acute when it clinically presented as sudden death due to electromechanical dissociation, whereas it was considered subacute in the remaining cases.

The status on coronary risk factors was coded according to patients’ previously known histories. Patients were considered to have diabetes if they had been previously diagnosed by another physician or if they were being treated with either insulin or oral antidiabetic drugs. Patients were considered to have hypertension if they had been previously diagnosed by another physician or if they were receiving antihypertensive drugs.

**Statistical analysis.** Normally distributed continuous variables are expressed as mean ± SD and compared by the Student t test. Discrete variables are expressed as proportions (percentages) and compared by the chi-square test. A multivariable analysis (step-wise logistic regression) was performed in order to identify independent predictors of FWR in the study population. The multivariable analysis included not only those variables significantly associated with the incidence of FWR in the univariable analysis, but also reperfusion strategy (PA or thrombolysis) and variables that potentially could be related to the risk of FWR, such as treatment with beta-adrenergic blocking agents, hypertension and previous AMI. Associations were considered statistically significant when p < 0.05, although all p < 0.10 are provided.
RESULTS

Baseline characteristics. Baseline characteristics in both groups are shown in Table 1. Patients treated with PA, compared with those treated with thrombolysis, were older and had worse Killip class; longer time from the onset of symptoms; and higher frequency of female gender, hypertension, diabetes and anterior location.

Incidence and predictors of FWR. The incidence of FWR in the whole study population was 2.5% (n = 762) vs. 1.2%, p = 0.001) in patients treated with thrombolysis (n = 1.8% in patients treated with PA (n = 613), p = 0.0053. Hours from symptoms onset (%): 3.3 ± 3.1 vs. 2.9 ± 2.7, p = 0.0279. Hypertension (%): 45.8 vs. 36.4, p = 0.0005. Diabetes mellitus (%): 23.6 vs. 17.7, p = 0.0077. Previous AMI (%): 14.6 vs. 13.3, NS. AMI location (%): Anterior 61.6 vs. 32.1, p < 0.0001; Inferior 32.1 vs. 62.9, p < 0.0001; Lateral 4.6 vs. 2.8, p = 0.0742. Killip class > I (%): 25.6 vs. 14.6, p < 0.0001. Beta-blockers 27.4 vs. 23.7, NS.

AMI = acute myocardial infarction; PA = primary angioplasty.

In the multivariable analysis, two characteristics were independent predictors of FWR: age >70 years (odds ratio [OR]: 4.12; 95% confidence interval [CI]: 2.04 to 8.62; p < 0.001) and anterior location (OR: 2.91; 95% CI: 1.36 to 6.63; p = 0.008). Conversely, treatment with PA was independently associated with a lower incidence of FWR (OR: 0.46; 95% CI: 0.22 to 0.96; p = 0.0371).

Primary angioplasty was associated with a lower rate of FWR, irrespective of AMI location (risk ratio [RR]: 0.64 [95% CI: 0.27 to 1.54] in anterior AMI; RR: 0.21 [95% CI: 0.03 to 1.73] in inferior AMI) and gender (RR: 0.60 [95% CI: 0.24 to 1.48] in men; RR: 0.66 [95% CI: 0.33 to 1.30] in women). Primary angioplasty reduced the risk of FWR, especially in elderly patients but not in those 70 years old or younger (RR: 0.47 [95% CI: 0.19 to 1.17] in patients >70 years old; RR: 1.03 [95% CI: 0.32 to 3.34] in patients ≤70 years) (Fig. 1).

DISCUSSION

The incidence of FWR in the present series was 2.5%, which does not differ from that of previous studies in patients with AMI treated conservatively or with thrombolysis (5,6,19). There was no statistical difference in this incidence between patients treated with PA (1.8%) and those treated with thrombolysis (3.3%). In the multivariate analysis, however, PA was independently associated with lower incidence of FWR. Therefore, the major finding of the present study is that PA was independently associated with a lower incidence of FWR.

Effect of successful coronary recanalization over the risk of FWR. The reduction in the rate of FWR achieved by PA probably resulted from the earlier and more effective coronary recanalization. Although little is known about the pathophysiology of FWR, there are some data suggesting that a sustained and complete coronary occlusion might be a necessary condition. Cheriex et al. (20) demonstrated that

Table 2. Characteristics Associated With the Risk of FWR in the Univariable Analysis

<table>
<thead>
<tr>
<th>Incidence of FWR</th>
<th>p Value</th>
<th>Incidence of FWR</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt;70 yrs</td>
<td>&lt;0.001</td>
<td>Diabetes</td>
<td>NS</td>
</tr>
<tr>
<td>Age ≤70 yrs</td>
<td>1.2%</td>
<td>Yes</td>
<td>1.4%</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td>No</td>
<td>2.4%</td>
</tr>
<tr>
<td>Male</td>
<td>1.8%</td>
<td>Previous AMI</td>
<td>NS</td>
</tr>
<tr>
<td>Female</td>
<td>5.1%</td>
<td>Yes</td>
<td>1.6%</td>
</tr>
<tr>
<td>Time from onset</td>
<td></td>
<td>No</td>
<td>2.2%</td>
</tr>
<tr>
<td>&gt;2 h</td>
<td>3.6%</td>
<td>Anterior location</td>
<td>0.020</td>
</tr>
<tr>
<td>&lt;2 h</td>
<td>1.7%</td>
<td>Yes</td>
<td>3.3%</td>
</tr>
<tr>
<td>Hypertension</td>
<td></td>
<td>No</td>
<td>1.4%</td>
</tr>
<tr>
<td>Yes</td>
<td>2.5%</td>
<td>Thrombolysis</td>
<td>NS</td>
</tr>
<tr>
<td>No</td>
<td>1.9%</td>
<td>PA</td>
<td>1.8%</td>
</tr>
</tbody>
</table>

AMI = acute myocardial infarction; FWR = free wall rupture; PA = primary angioplasty.
most patients with FWR identified by autopsy have complete occlusion or incomplete reperfusion of the infarct-related artery. In the study by Morishima et al. (21), patients with severe no-reflow after PA had larger infarctions and a higher risk of FWR. Finally, in a recent study (10), we observed that in patients with AMI referred to PA, the presence of a TIMI flow grade 0 at the initial angiogram is statistically associated with higher risk of FWR.

Taking into consideration these data, an early restoration of coronary patency should theoretically reduce the frequency of FWR. In the study of Nakamura et al. (22), patients with AMI that were reperfused had a lower incidence of FWR compared with patients not reperfused, especially when a successful coronary reperfusion is obtained. Although contradictory data exist, thrombolytic therapy seems not to increase the risk of FWR (23,24).

Comparison between PA and thrombolysis. Primary angioplasty achieves the restoration of coronary patency more frequently than thrombolysis (2–4). The effect of PA on the risk of FWR, however, has not been evaluated in detail. In most series of patients with AMI treated with PA, this incidence is very low (0% to 0.8%), especially when a successful angiographic result is obtained (7–9). However, in most randomized studies comparing PA with thrombolysis, the incidence of FWR has not been well studied. In the studies by Zijlstra et al. (3), Grines et al. (2) and an angiographic substudy of GUSTO IIb (11), the incidence of FWR is not reported.

In our institution, there is a great awareness of the early diagnosis and management of FWR, and every patient with AMI and hypotension undergoes an immediate transthoracic echocardiogram in order to rule out FWR (10,16). In our anterior location AMI randomized study, the incidence of FWR was higher in patients treated with thrombolysis than in those treated with primary percutaneous transluminal coronary angioplasty (8.1% vs. 3.7%) (4). Although these differences did not reach statistical significance, this reduction in the risk of FWR could be important in accounting for the lowering of mortality obtained by PA compared with thrombolysis. We have recently reported a frequency of FWR of 2.2% in 590 patients treated with PA, a frequency not different from that of a series of patients treated conservatively or with thrombolysis (10). However, elderly patients and those with anterior location are preferably referred to PA, both factors being associated with a higher incidence of FWR (10,25,26). To overcome this possible selection bias, we performed a multivariable analysis that included patients with AMI treated with either PA or thrombolysis during the same period of time. For the first time, we have demonstrated that PA is a protective factor for FWR compared with thrombolysis. Other factors related to the risk of FWR (advanced age, anterior location and female gender) were similar to that of previous studies (10,25,26).

In this study, the incidence of FWR in patients treated with PA was slightly lower (1.8%) than that previously reported (2.2%) (10). This could be related to a progressively less restrictive criteria for referring patients to PA (especially more patients with non-anterior location AMI), although the influence of an improvement on the results of PA cannot be excluded (18).
According to our results, the benefit given by PA seems to be independent of AMI location and gender. Nevertheless, PA may be especially beneficial for patients over 70, the risk of FWR being similar irrespective of the reperfusion strategy applied in younger patients.

**Conclusions and practical implications.** In patients with AMI that are treated with reperfusion strategies, PA independently reduces the risk of FWR in comparison with thrombolysis. Therefore, apart from reducing the rate of recurrent ischemia and intracranial bleeding, there could be another reason for preferring PA as a reperfusion strategy for AMI.

**Study limitations.** This study has some limitations. First, it is a retrospective study, and theoretically, FWR could be present in some patients before thrombolysis or PA. The biggest challenge of this study was to identify all cases of FWR. However, at our institution, every patient with AMI suffering hypotension, syncope or other hemodynamic instability undergoes an immediate transthoracic echocardiographic study, and the possibility that FWR was present before PA or thrombolysis is very low. The criteria we used to define FWR have been previously validated and demonstrated a very high diagnostic accuracy (16). Secondly, although the study population was large, it could be considered relatively small, taking into consideration the relatively low incidence of FWR. However, the study population was large enough to obtain a statistically significantly lower incidence of FWR in patients treated with PA in the multivariable analysis. Moreover, this is a non-randomized study. However, there are not very likely to be new randomized studies on PA versus thrombolysis in patients with AMI, and available studies provide very few data about this FWR. Finally, some authors have suggested that thrombolysis could increase the risk of FWR by means of producing more intramyocardial hemorrhage (27). So, it could be argued that the lower incidence of FWR in patients treated with PA compared with thrombolysis in our study could be due partly to an increased risk in the group of patients treated with thrombolysis. However, an increased risk of FWR in patients treated with thrombolysis compared with placebo has not been demonstrated (23,24).

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