Outcome of Primary Angioplasty for Acute Myocardial Infarction During Routine Duty Hours Versus During Off-Hours

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OBJECTIVES
We sought to investigate the impact of circadian patterns in the onset of acute myocardial infarction (AMI) on the practice of primary angioplasty.

BACKGROUND
A circadian variation in the time of onset of AMI with a peak in the morning hours has been described.

METHODS
We studied 1,702 consecutive patients with acute ST-segment elevation myocardial infarction treated with primary angioplasty. We observed circadian variation in frequency of symptom onset, hospital admission, and first balloon inflation. Circadian patterns of symptom onset, hospital admission, and balloon inflation are similar.

RESULTS
A majority of patients have symptom onset (53%), hospital admission (53%), and first balloon inflation (52%) during routine duty hours (0800 to 1800 h). There were no differences in baseline clinical characteristics or treatment delays between routine duty hours and off-hours patients. Hospital admission between 0800 and 1800 was associated with an angioplasty failure rate of 3.8%, compared with 6.9% between 1800 and 0800, p < 0.01. Thirty-day mortality was 1.9% in patients with hospital admission between 0800 and 1800, compared with 4.2% in patients with hospital admission between 1800 and 0800, p < 0.01.

CONCLUSIONS
Circadian variations may have a profound effect on the practice of primary angioplasty. A majority of patients are treated during routine duty hours. Patients treated during off-hours have a higher incidence of failed angioplasty and consequently a worse clinical outcome than patients treated during routine duty hours. (J Am Coll Cardiol 2003;41:2138–42) © 2003 by the American College of Cardiology Foundation

Primary angioplasty is gradually becoming accepted as the treatment of choice for acute myocardial infarction (AMI). However, this means that this type of care has to be available 24 h a day. It would be of interest to study whether this treatment modality and its outcome are as good during off-hours as during normal working hours. To analyze this issue, we must take in account two important and independent variables.

First, are patients and their disease “AMI” or is the presentation of the disease different during these two time periods? A circadian variation in the time of symptom onset in patients with AMI has been described. In particular, a peak in occurrence in the morning hours is well documented for various cardiovascular events such as AMI, unstable angina, sudden cardiac death, transient myocardial ischemia, and ischemic stroke (1–6). Determinations of plasma creatine kinase activity have permitted objective assessment of the time of onset of myocardial infarction (MI) and have confirmed a marked circadian periodicity in the onset of MI, with a peak incidence between 0600 and 1200 hours and a trough at night (1).

Second, is care during routine duty hours as good as care during off-hours? The Maximal Individual Therapy in Acute Myocardial Infarction (MITRA) study group investigated differences in patterns of performance of primary angioplasty between patients presenting during daytime and nighttime (7). From a total of 491 patients, 77% came during the day and only 23% during the night. Patients in the night group had a shorter time to presentation. There was no significant difference between the two groups in clinical outcome. Because of the great difference between the number of nighttime-treated patients in the eight centers (from 8% to 44%) and the small number of patients treated during nighttime (23%), selection bias may have played a role in the MITRA analysis. In hospitals, where all patients with acute ST-elevation MI are treated by primary angioplasty, it has not been studied whether circadian variations in time of either symptom onset or treatment have an effect on clinical outcome.

Therefore, we sought to investigate the influence of circadian variation on symptom onset, hospital admission, and first balloon inflation in patients presenting with AMI. Furthermore, we studied the influence of these circadian
patterns on clinical outcome in 1,702 consecutive patients with acute ST-elevation MI treated by primary angioplasty during routine duty hours and off-hours.

**METHODS**

Between 1994 and 2000, 1,702 consecutive patients with acute ST-segment elevation MI were treated in our hospital. This cohort has been described before (8). All patients with AMI presenting within 6 h after symptom onset were included. The protocol was approved by our institutional review board. Electrocardiographic criteria were ST-segment elevation of ≥1 mm in two or more contiguous leads. Acute myocardial infarction was diagnosed in 860 patients by the ambulance crew or at one of our 11 referring hospitals. We are the only referral percutaneous coronary intervention center for 11 community hospitals, in an area with a maximum distance of 94 km from a referring hospital to our hospital. These patients received aspirin (500 mg intravenous) and heparin (≥5,000 IU intravenous) before transportation to our hospital. In 842 patients the diagnosis of AMI was established in our hospital. These patients received aspirin and heparin intravenously before immediate transportation to the catheterization laboratory. None of the patients received fibrinolytic therapy or glycoprotein IIb/IIIa blockers before angiography. All primary percutaneous coronary intervention procedures, both during routine duty hours and off-hours, were performed by the senior staff.

**Data collection and analysis.** Demographic data and clinical data were recorded at baseline, and follow-up until 30 days was completed on all patients. All angiograms were reviewed by two cardiologists, blind to treatment allocation and clinical data.

Successful angioplasty was defined as Thrombolysis in Myocardial Infarction 3 flow and a residual lumen diameter ≥50%. Statistical analysis was performed using SPSS 10.0. Differences between group means were tested by two-tailed Student t test. A chi-square statistic was calculated to test differences between proportions. The Fisher exact test was used when the expected value of cells was smaller than 5. Statistical significance was defined as a p value of <0.05.

**Abbreviations and Acronyms**

AMI = acute myocardial infarction
MI = myocardial infarction
MITRA = Maximal Individual Therapy in Acute Myocardial Infarction

![Figure 1](image-url). Circadian variation in time of symptom onset, hospital admission, first balloon inflation, and 30-day mortality (n = 1,702). The bars designate the number of patients of the variables: Symptom Onset, Hospital Admission, and 1st Balloon Inflation. The lines demonstrate more clearly the variation during the day with respect to Symptom Onset, Hospital Admission, 1st Balloon Inflation, and 30-Day Mortality. *30-day mortality.
RESULTS

We observed a marked circadian variation in frequency of symptom-onset, hospital admission, and first balloon inflation (Fig. 1). Figure 1 also reveals a circadian variation in 30-day mortality. The patterns of frequency of symptom onset, hospital admission, and first balloon inflation are similar, with some shift in time. As a consequence, a majority of patients have symptom onset (53%), hospital admission (53%), and first balloon inflation (52%) during routine duty hours of our hospital, between 0800 and 1800 h. Table 1 shows a comparison of the clinical characteristics of patients with symptom onset between 0800 and 1800 h and from 1800 to 0800 h. The comparisons between patients with hospital admission and first balloon inflation between 0800 and 1800 h and 1800 to 0800 h showed a similar pattern (data not shown). With respect to age, gender, infarct location, previous infarctions, presence of multivessel disease, diabetes, Killip class, and antegrade flow in the infarct-related artery, there is no difference between the groups irrespective of categorization based on symptom onset, hospital admission, or first balloon inflation, and there are no differences between the groups with regard to any of these baseline clinical characteristics.

The difference in failed angioplasty procedures between patients treated within routine duty hours and patients treated during off-hours is shown in Figure 2. For all three comparisons there is a significantly higher rate of angioplasty failure from 1800 to 0800 h compared with between 0800 and 1800 h. Thirty-day mortality for the three comparisons is given in Figure 3 and shows a twofold higher mortality in patients with symptom onset, hospital admission, and first balloon inflation from 1800 to 0800 h compared with 0800 to 1800 h. Mortality and angioplasty failure are strongly related; 30-day mortality after successful angioplasty was 2.2%, versus 17% after failed angioplasty.

Table 1. Clinical Characteristics of Patients With Symptom Onset Between 0800 and 1800 Compared With Symptom Onset From 1800 to 0800

<table>
<thead>
<tr>
<th></th>
<th>0800–1800 (n = 909)</th>
<th>1800–0800 (n = 793)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs ± SD)</td>
<td>60.5 ± 11.3</td>
<td>59.7 ± 11.8</td>
<td>&gt;0.1</td>
</tr>
<tr>
<td>Male (%)</td>
<td>80.2</td>
<td>79.7</td>
<td>&gt;0.1</td>
</tr>
<tr>
<td>Anterior MI (%)</td>
<td>49.3</td>
<td>48.0</td>
<td>&gt;0.1</td>
</tr>
<tr>
<td>Previous MI (%)</td>
<td>10.9</td>
<td>12.7</td>
<td>&gt;0.1</td>
</tr>
<tr>
<td>MVD (%)</td>
<td>51.7</td>
<td>55.6</td>
<td>&gt;0.1</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>8.1</td>
<td>8.6</td>
<td>&gt;0.1</td>
</tr>
<tr>
<td>Killip class ≥ 2 (%)</td>
<td>11.7</td>
<td>10.6</td>
<td>&gt;0.1</td>
</tr>
<tr>
<td>TIMI 2 or 3* (%)</td>
<td>24.6</td>
<td>29.6</td>
<td>&gt;0.1</td>
</tr>
<tr>
<td>Referred patients (%)</td>
<td>21.0</td>
<td>17.5</td>
<td>&gt;0.1</td>
</tr>
<tr>
<td>Time delays (min ± SD)</td>
<td>143 ± 80</td>
<td>146 ± 92</td>
<td>&gt;0.1</td>
</tr>
<tr>
<td>Symptom—admission</td>
<td>64 ± 29</td>
<td>69 ± 26</td>
<td>&gt;0.1</td>
</tr>
<tr>
<td>Admission—1st balloon</td>
<td></td>
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*Before primary angioplasty

Diabetes = history of diabetes before hospital admission; MI = myocardial infarction; MVD = multivessel disease; Symptom = symptom-onset; 1st balloon = time of first balloon inflation; TIMI = Thrombolysis In Myocardial Infarction.

Figure 2. Failed primary angioplasty in patients treated within normal duty hours and off-hours.
DISCUSSION

The first principal finding of our study is that there is a circadian variation in the time of symptom onset, hospital admission, and treatment of AMI. As a consequence of the distribution in time of onset of MI, a majority of primary angioplasty procedures are performed in only 10 of the 24 h of the day, during regular routine duty hours between 0800 and 1800 h. The second and more important finding is the observation that patients treated during off-hours have worse outcome. Patients with symptom onset, hospital admission, and first balloon inflation during these off-hours have a higher rate of angioplasty failure and, consequently, a higher 30-day mortality.

From a theoretical perspective three mechanisms may be involved in this phenomenon. First, patients presenting during the day may have different baseline clinical characteristics associated with improved procedural and clinical outcome. For instance, an increased risk of congestive heart failure has been reported among infarctions with nighttime onset (9). In our study we looked at the baseline clinical characteristics including Killip class, and could find no differences between daytime and nighttime infarctions. It seems therefore unlikely that this mechanism has played a major role in our study. A potential confounder may be the reported onset of symptoms and therefore the ischemic time in nighttime patients. In (awake) patients during the day, the onset of symptoms is almost the time of occlusion of the epicardial vessel. Hence, the reported onset of symptoms and ischemic time is fairly reliable. However, it is conceivable that nighttime (normally sleeping) patients have an occlusion of an epicardial vessel and only experience the chest discomfort in a later phase of the AMI. Thus, although the reported ischemic time is equal in both groups, patients with AMI during the night may have had a longer ischemic time.

Second, the efficacy of reperfusion therapy may, in part, be dependent on the time of day. Circadian variations have been documented for platelet aggregation (10,11), coronary flow (12), viscosity (13), cortisol levels (14), epinephrine levels (15), and activated partial thromboplastin time and thrombin time (10,16). Levels of tissue-type plasminogen activator and other factors related to natural fibrinolytic activity suggest potential for enhanced fibrinolysis in the evening hours (17–20). Finally, a circadian pattern has been described in the efficacy of streptokinase and tissue-type plasminogen activator to reestablish flow in coronary arteries with acute thrombotic occlusion (21–23). Therefore, the efficacy of reperfusion, as has been documented for several thrombolytic agents (21–23), may be related to the circadian variation in the balance between prothrombotic mechanisms and the natural fibrinolytic system (10–20). This balance may certainly influence the ability to obtain brisk antegrade flow in the infarct-related artery, and therefore this mechanism may, in part, be involved in procedural success or failure of primary angioplasty.

Third, the quality of care may be dependent on the time of day. Outcome after primary angioplasty has been reported to be related to the time delay from hospital admission to first balloon inflation (24) and to hospital and physician volume (25–27), and therefore it is conceivable
that the quality of care delivered during day or night may differ through variations in performance of physicians, catheterization laboratory, and coronary care staff. Furthermore, even in high-volume centers there may be marked intercenter variability in outcome for patients treated with primary angioplasty (28). Quality of care is difficult to measure, and whether this mechanism is involved in our study cannot be ascertained. Time from hospital admission to first balloon inflation has an impact on clinical outcome, probably as a surrogate for quality of care. However, in our study, there was no circadian variation in hospital admission to first balloon time. This suggests a similar quality of care, in particular as our hospital has been dedicated to an optimal quality of care for large numbers of patients with AMI, every hour a day, seven days a week, for many years. Nevertheless, this mechanism seems likely to explain, at least in part, our findings.

The relative importance of the second and third potential mechanisms (is it the patient or is it quality of care?) that may explain our findings cannot be analyzed in our data. Methods to assess quality of care should be developed that are applicable in patients treated with percutaneous interventional procedures for acute ST-segment elevation MI. If the circadian variation in the balance between natural prothrombotic and fibrinolytic factors plays an important role as an underlying factor that may explain our findings, adjunctive pharmacotherapies that have a positive influence on this balance should be developed.

Conclusions. Circadian variations have a profound effect on the practice of primary angioplasty. A majority of patients are treated during routine duty hours, and these patients have a higher procedural success rate and a better clinical outcome compared with the patients treated during off-hours.

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REFERENCES


APPENDIX