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Primary PCI for acute myocardial infarction

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CHAPTER 6

Outcome of Primary Angioplasty for Acute Myocardial Infarction during
Routine Duty Hours versus During Off-Hours.

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On behalf of the Zwolle Myocardial Infarction Study Group

J Am Coll Cardiol, In Press

Abstract

Objectives. We sought to investigate the impact of circadian patterns in the onset of acute myocardial infarction on the practice of primary angioplasty.

Background. A circadian variation in the time of onset of acute myocardial infarction with a peak in the morning hours has been described.

Methods. We studied 1702 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 (08.00-18.00h). There were no differences in baseline clinical characteristics or treatment delays between routine duty hours and off-hours patients. Hospital admission between 08.00 and 18.00 was associated with an angioplasty failure rate of 3.8%, compared to 6.9% between 18.00 and 08.00, $p<0.01$. Thirty day mortality was 1.9% in patients with hospital admission between 08.00 and 18.00, compared to 4.2% in patients with hospital admission between 18.00 and 08.00, $p<0.01$.

Conclusions. Circadian variations may have a profound effect on the practice of primary angioplasty. A majority of patients is treated during routine duty hours. Patients treated during off-hours have a higher incidence of failed angioplasty and consequently a worse clinical outcome, when compared to patients treated during routine duty hours.

Introduction

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

First, is the patient and his disease “acute myocardial infarction” or the presentation of the disease different during these two time periods ? A circadian variation in the time of symptom onset in patients with acute myocardial infarction has been described. In particular, a peak in occurrence in the morning hours is well documented for various cardiovascular events such as acute myocardial infarction, 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 and have confirmed a marked circadian periodicity in the onset of myocardial infarction with a peak incidence between 06.00 and 12.00 hours and a trough at night (1).

Secondly, is care during routine duty hours as good as care during off-hours? The MITRA study group investigated differences in patterns of performance of primary angioplasty between patients presenting during daytime and night-time (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. Both due to the great difference between the number of night-time treated patients in the 8 centres (from 8% to 44%) and the small numbers of patients treated during night-time (23%), selection bias may have played a role in the MITRA analysis. In hospitals, where all patients with acute ST elevation myocardial infarction 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 acute myocardial infarction. Furthermore, we studied the influence of these circadian patterns on clinical outcome in 1702 consecutive patients with acute ST elevation myocardial infarction treated by primary angioplasty during routine duty hours and off-hours.

Methods

Between 1994 and 2000, 1702 consecutive patients with acute ST segment elevation myocardial infarction were treated in our hospital. This cohort has been described before (8). All patients with acute MI 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 PCI center for 11 community hospitals, comprising an area with a maximum distance of 94 km from a referring hospital to our hospital. These patients received aspirin (500 mg iv) and heparin (≥ 5000 IU iv) before transportation to our hospital. In 842 patients the diagnosis of acute MI 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 PCI 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 of all patients. All angiograms were reviewed by two cardiologists, blinded for treatment allocation and clinical data.

Successful angioplasty was defined as: TIMI 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's 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 less than 0.05.

Results

We observed a marked circadian variation in frequency of symptom-onset, hospital admission and first balloon inflation, see Figure 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 08.00 and 18.00 hours. In Table 1 the comparison is shown of the clinical characteristics of patients with symptom-onset between 08.00-18.00 hours and from 18.00-08.00 hours. The comparisons between patients with hospital admission and first balloon inflation between 08.00-18.00 hours and 18.00-08.00 hours 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 3 comparisons there is a significantly higher rate of angioplasty failure from 18.00 to 08.00 hours compared to between 08.00 and 18.00 hours. Thirty day mortality for the 3 comparisons is given in Figure 3, and shows a twofold higher mortality in patients with symptom-onset, hospital admission and first balloon inflation from 18.00-08.00 hours compared to 08.00-18.00 hours. 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 08.00 A.M. and 18.00 P.M. compared to symptom-onset from 18.00 P.M. to 08.00 A.M.

	08.00 – 18.00 N=909	18.00 – 08.00 N=793	P
Age (years±SD)	60.5±11.3	59.7±11.8	>0.1
Male (%)	80.2	79.7	>0.1
Anterior MI (%)	49.3	48.0	>0.1
Previous MI (%)	10.9	12.7	>0.1
MVD (%)	51.7	55.6	>0.1
Diabetes (%)	8.1	8.6	>0.1
Killip class ≥ 2 (%)	11.7	10.6	>0.1
TIMI 2 or 3 * (%)	24.6	29.6	>0.1
Referred patients (%)	21.0	17.5	>0.1
Time delays (min±SD)			
Symptom – Admission	143±80	146±92	>0.1
Admission –1 st balloon	64±29	69±26	>0.1

*before primary angioplasty, MI=myocardial infarction, MVD=multivessel disease, diabetes=history of diabetes before hospital admission, Symptom=symptom-onset, 1st balloon=time of first balloon inflation

Figure 1 Circadian variation in time of symptom onset, hospital admission, first balloon inflation and 30-day Mortality (n=1702)

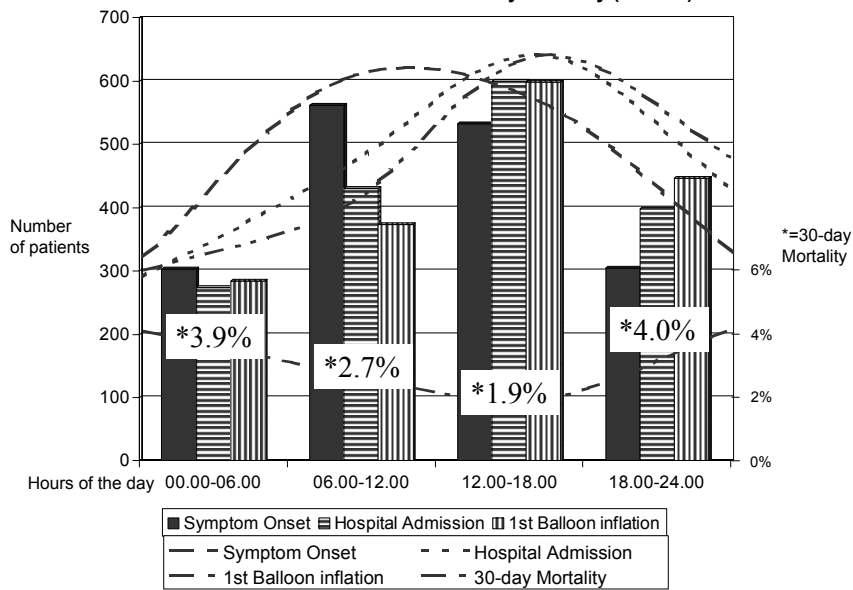


Figure 2

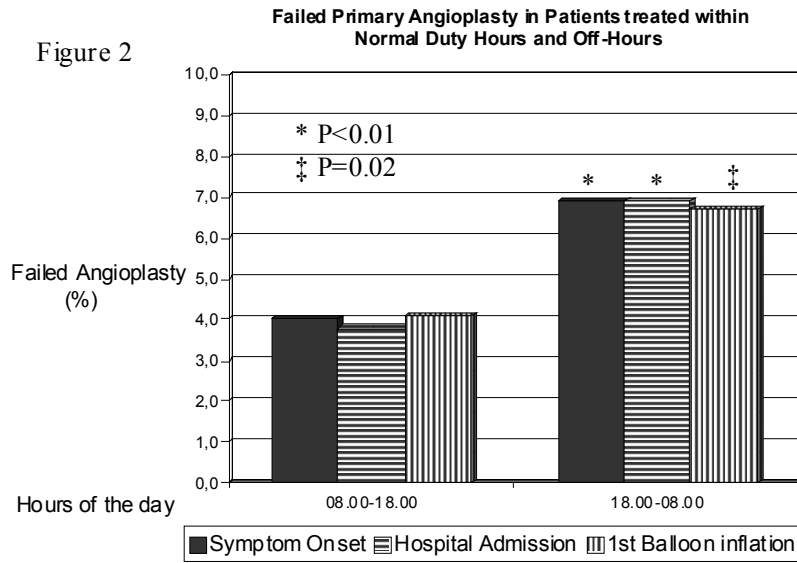
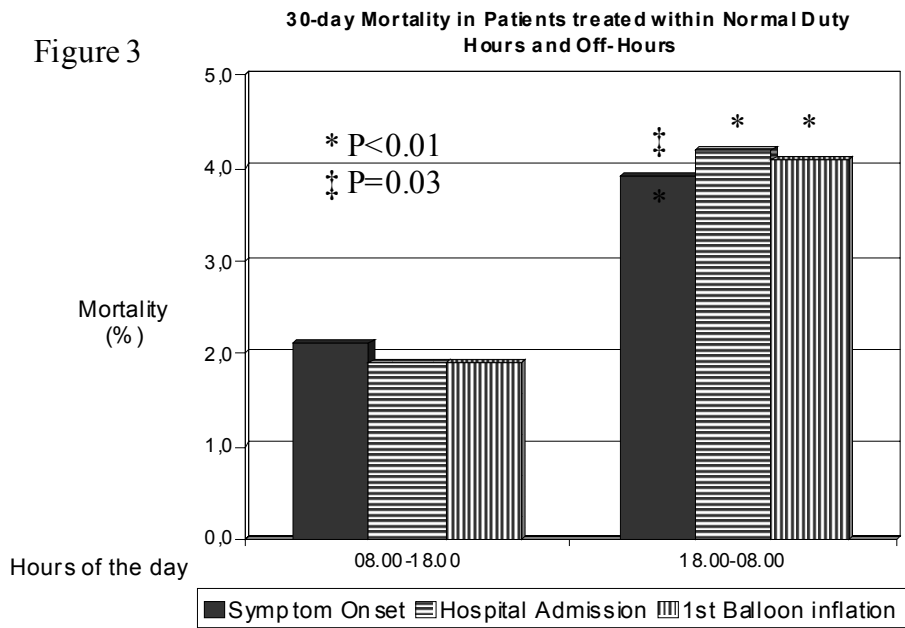


Figure 3



Discussion

The first principle finding of our study is that there is a circadian variation in the time of symptom-onset, hospital admission and treatment of acute myocardial infarction. As a consequence of the distribution in time of onset of myocardial infarction, a majority of primary angioplasty procedures is performed in only 10 of the 24 hours of the day, during regular routine duty hours between 08.00 and 18.00 hours. 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. Firstly, 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 acute myocardial infarction. Thus, although the reported ischemic time is equal in both groups, patients with acute myocardial infarction during the night may have had a longer ischemic time.

Secondly, 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

issue-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 re-establish 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.

Thirdly, the quality of care may be dependent on the time of the 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 due to 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 it serves 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 acute myocardial infarction, every hour a day, 7 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 myocardial infarction. 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 is treated during the routine duty hours and these patients have a higher procedural success rate and a better clinical outcome when compared to the patients treated during off-hours.

Appendix:

Zwolle Myocardial Infarction Study Group : MJ de Boer, JHE Dambrink, ATM Gosselink, AWJ van 't Hof, JCA Hoorntje, JP Ottervanger, H Suryapranata, F Zijlstra

Secretarial Assistance: VRC Derks.

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