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Pre-hospital factors influencing the time to administration of thrombolytic therapy in acute myocardial infarction in Zagreb region

J. Vincelj, M. Bergovec, I. Sokol, K. Putarek

The present study was conducted to examine the possible relationship between various pre-hospital factors and delays in initiation of thrombolytic therapy (TT) in acute myocardial infarction (AMI). Factors analysed were the time of symptom onset to the time of general practitioner (GP) presentation, time of GP presentation to time of hospital admission, geographic location of patients in the Zagreb region, patient's transportation to the hospital, age and sex of patients.

We studied 184 consecutive patients (123 males and 61 females), mean age 63.3 ± 11.4 years, hospitalized for AMI. TT (intravenous Streptokinase) was administered in 42 (23 %) patients. The mean time from symptom onset to GP presentation was 9.7 ± 14.6 hours in patients who did not receive TT, and 1.3 ± 1.3 hours in patients who received TT ($p < 0.001$). The mean time from GP presentation to hospital admission was 3.2 ± 0.7 hours in patients who did not receive TT and 1.4 ± 0.4 hours in patients who received TT ($p < 0.05$). The mean time from symptom onset to hospital admission was 12.9 ± 15.3 hours in patients who did not receive TT and 2.7 ± 1.6 hours in patients who received TT ($p < 0.001$). The patients who received TT were younger (56 versus 63 years), showed a higher male predominance (83 % versus 67 %), and arrived at the GP and at the hospital sooner than those who did not receive TT.

The results suggested the time elapsed from the onset of symptoms to GP presentation, time from GP presentation to hospital admission, time necessary for transportation to the hospital for a patient from the Dubrava subregion, younger patients and male sex were important factors influencing the time to administration of TT in AMI. *J Clin Bas Cardiol 1998; 1: 30-3.*

Keywords: Thrombolytic therapy, acute myocardial infarction, prehospital factors

Acute myocardial infarction (AMI) is the leading cause of death in the adult population in Croatia. In recent years, stress related war events have contributed towards increased mortality of patients with AMI [1]. The management of AMI has changed radically with the proven efficacy of thrombolysis in reducing mortality and left ventricular damage. Thrombolytic therapy (TT) reduces mortality among patients treated within a few hours of the onset of AMI [2-4]. TT is frequently followed by rapid recanalisation of totally occluded coronary arteries and saves about 30 lives per 1000 patients receiving treatment within 6 h of the onset of symptoms [5]. Time from onset of symptoms of AMI to treatment with TT is a critical determinant in infarct size and mortality [6-9]. For a good outcome, it is necessary for the patient to quickly recognise signs and symptoms of an AMI, for the physician to quickly diagnose the patient with an AMI, and quickly initiate the appropriate treatment, and it is desirable for the physician to identify patients with an AMI presenting with atypical signs and symptoms of this disease process. Minimising the delay between the onset of symptoms and treatment has been found to be most important, as early treatment has been shown to be of greatest benefit [10-12]. Barriers to the delivery of TT within the first hours of symptoms include patient's delay in recognising the symptoms and seeking care, time needed for transportation to the hospital, and in-hospital delay in delivering TT. Several strategies have been implemented to reduce the patient delay by providing information about recognition of chest pain and availability of emergency medical services [13]. After initial reports on the importance of time to treatment in AMI, many hospitals have introduced protocols to reduce the time elapsed from the onset of symptoms to the initiation of TT, termed the call-to-needle time [14, 15]. In this prospective study, pre-hospital factors influencing the time

from onset of symptoms to general practitioner (GP) presentation, time from GP presentation to the initiation of TT, time for transportation to the hospital, age, and sex of patients were evaluated.

Methods

The Dubrava University Hospital provides acute care for about 220,000 inhabitants from the east Zagreb area, including Sesvete, Dugo Selo, Vrbovec, and Sv. Ivan Zelina, and to about 17,000 refugees and displaced persons. The study included 184 patients (123 males and 61 females), mean age 63.3 ± 11.4 years, consecutively admitted for AMI to the Intensive Care Unit, Department of Internal Medicine, between October 1995 and July 1996. Definite diagnosis of AMI required two of the following three criteria: typical ischaemic chest pain, new occurrence of abnormal Q waves with evolutionary ST and T wave changes on serial tracings, total serum creatine kinase (CK) two-fold higher than the upper normal limit and CK-MB isoenzyme greater than 10 % of the total CK activity. Criteria for TT included age < 76 years, typical chest pain starting within the previous six h, and ST segment elevation in at least two leads of the electrocardiogram of ≥ 2 mm in V1-V3 or ≥ 1 mm in V4-V6, AVL, II, III, and AVF, and no clear contraindication for TT [16]. Contraindication for TT included history of stroke, gastrointestinal haemorrhage, or ulcer within the previous six months, severe trauma such as major surgery, head injury, or biopsy within the previous two weeks, prolonged cardiac massage in the previous 24 h, persistent severe hypertension, valvulopathy or cardiomyopathy with atrial fibrillation, active pericarditis, known allergy to streptokinase, streptokinase treatment within the previous six months, pregnancy, severe renal or hepatic

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impairment, or some other life-threatening disease [17]. The patients were divided into two groups: 42 (23 %) patients with TT, and 142 (77 %) patients without TT. Forty-two (23 %) patients received 1.5×10^6 units streptokinase infused intravenously over 30–60 minutes. The time of symptom onset, time from symptom onset to GP presentation, time from GP presentation to hospital admission, time from symptom onset to hospital admission, time to initiation of TT, geographic location of the patient's residence in the east Zagreb region, patient's transportation to hospital, age, and sex of patients were analysed. The time of chest pain onset was defined as the time the patient reported that the chest pain had intensified or become prolonged or intolerable, inducing the patient to seek help. The time of GP presentation was defined as the hour and minute of initial presentation to the GP registry. The time of hospital admission was defined as the hour and minute of initial presentation to the hospital registry. Approval of the registry data collection process at the participating hospital may have included human subjects review by institutional review boards.

Statistical Analysis

Data are presented as mean \pm SD. Student's t-test for paired or unpaired data was used where data were normally distributed. Otherwise, Mann-Whitney nonparametric analysis was used. A value of $p < 0.05$ was considered to be the estimate of statistical significance.

Results

Between October 1995 and July 1996, 184 consecutive patients with AMI were included in the study. Among AMI patients, 42 (23 %) patients received TT. The average age of patients with TT was 56.8 ± 8.9 years and 63.3 ± 11.4 years of patients without TT. The clinical characteristics of patients with AMI are described in Table 1. Diabetes mellitus, family history of CAD, and cigarette smokers tended to be more common in patients who received TT than among those who did not receive TT. Hyperlipidaemia and previous MI were similar in both groups. Hypertension is more frequent in patients without TT than with TT. Table 1 also shows the mean time from symptom onset to GP presentation, GP presentation to hospital admission, and symptom onset to hospital admission.

Table 1: Clinical Characteristics of Patients with Acute Myocardial Infarction

| | Thrombolytic therapy | No thrombolytic therapy |
|--|----------------------|-------------------------|
| Number of patients | 42 (23 %) | 142 (77 %) |
| Female/male | 7/35 | 54/88 |
| Mean age (yrs) | 56.8 ± 8.9 | 63.3 ± 11.4 |
| Previous MI | 3 (7 %) | 11 (8 %) |
| Previous stroke | 0 | 9 (6 %) |
| Previous CABG | 0 | 2 (1 %) |
| Diabetes mellitus | 11 (26 %) | 23 (16 %) |
| Hypertension | 21 (50 %) | 82 (58 %) |
| Hyperlipidemia | 8 (19 %) | 26 (18 %) |
| Family history of CAD | 8 (19 %) | 19 (13 %) |
| Cigarette smoker | 24 (57 %) | 45 (32 %) |
| Mean time from symptom onset to GP presentation (hours) | 1.3 ± 1.3 | $9.7 \pm 14.6^*$ |
| Mean time from GP presentation to hospital admission (hours) | 1.4 ± 0.4 | $3.2 \pm 0.7^{**}$ |
| Mean time from symptom onset to hospital admission (hours) | 2.7 ± 1.6 | $12.9 \pm 15.3^*$ |

MI: myocardial infarction, CABG: coronary artery bypass grafting, GP: general practitioner, CAD: coronary artery disease, * $p < 0.001$, ** $p < 0.05$.

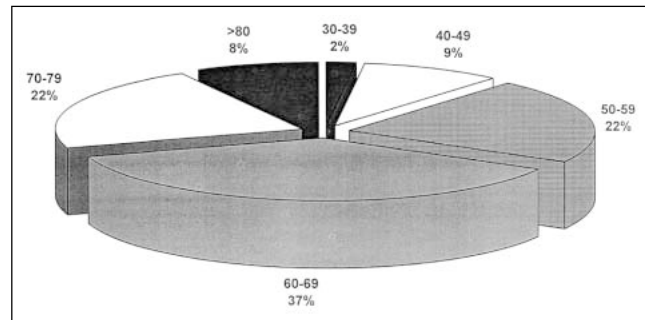


Figure 1: Distribution of patients with AMI according to age

tal admission, and symptom onset to hospital admission. The mean time from symptom onset to GP presentation was longer for patients who did not receive TT (9.7 ± 14.6 hours) than for patients who received TT (1.3 ± 1.3 hours) ($p < 0.001$). The mean time from GP presentation to hospital admission was longer for patients who did not receive TT (3.2 ± 0.7 hours) than for patients who received TT (1.4 ± 0.4 hours) ($p < 0.05$). The mean time from symptom onset to hospital admission was longer for patients who did not receive TT (12.9 ± 15.3 hours) than for patients who received TT (2.7 ± 1.6 hours) ($p < 0.001$). Among AMI patients, only 84 (46 %) patients arrived at the hospital within six hours from the onset of symptoms, and 42 (50 %) patients of those from Dubrava subregion. However, 50 % of AMI patients did not call 94 (Emergency Medical Aid), but went directly to the hospital emergency unit, having been transported to the hospital by family members or friends. Figure 1 shows the distribution of patients with AMI according to age. Approximately 60 % of the AMI patients are between 50 and 69 years. The number of patients aged over 75 years was 24 (13 %), and 9 (4 %) of those admitted to the hospital within 6 h from symptom onset. The number of patients with newly developed LBBB was 4 (2 %), and all patients admitted to the hospital 8 hours after onset of symptoms. Mean time from hospital admission to initiation of TT was 41.6 ± 24 minutes. The time from symptom onset to time of starting TT (call-to-needle time) is shown in Figure 2. In the group of 42 patients who received TT, it was initiated within two hours from the onset of symptoms in 17 %, within 2–4 hours in 57 %, and within 4–6 hours in 26 % of patients. The time from hospital admission to initiation of TT (door-to-needle time) is shown in Table 2. Of the 42 patients who received TT, 26 % received treatment < 30 minutes after hospital admission, 55 % within 30–60 minutes, and 19 % > 60 minutes after admission.

Discussion

Thrombolytic therapy for AMI was used in 23 % of the patients, which is less than the rate of 35 % in the USA [18, 19]. Thus, the use of thrombolytic therapy has increased steadily from 1995 through to 1997 in Croatia. Delay from symptom onset to arrival at the hospital was a major determinant for the initiation of thrombolytic therapy. This study revealed that the time elapsed from symptom onset to the hospital admission, from symptom onset to GP presentation, and from GP presentation to hospital admission was very long in AMI patients. Pre-hospital delay, however, is still longer than the current optimal recommendation [18]. These results have been shown by a large number of AMI patients who do not recognise AMI symptoms, and did not call 94 Emergency Medical Aid. The results suggested that a great proportion (77 %) of AMI patients waited for a very long time (9.7 hours) before seeking medical help because they failed to

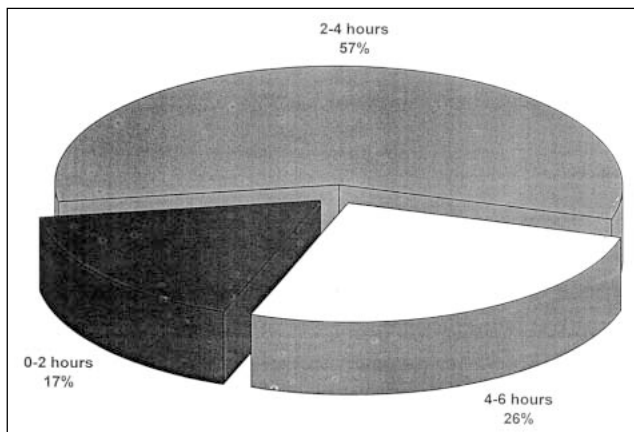


Figure 2: Time elapsed from symptom onset to initiation of TT in patient with AMI (call-to-needle time)

recognise the AMI symptoms. Previous investigations found shorter times from symptom onset to GP presentation, and from symptom onset to hospital admission in patients who recognised their AMI symptoms, believed that the symptoms represented an actual AMI, and perceived the symptoms to be serious [20–25]. This prospective study suggested a prolonged time elapsed from symptom onset to GP presentation, from GP presentation to hospital admission, time for transportation to the hospital, younger patients and male sex to be important prehospital factors influencing the time to administration of TT in AMI. In this evaluation of patient delay, older patients, female sex, and residence outside the Dubrava subregion were each related to a longer delay. It is possible, however, that unmeasured factors (eg, patient's response to symptoms of AMI, education about AMI symptoms, severity of illness) could explain the disparity in unusually prolonged time from symptoms onset to GP presentation. Despite considerable medical education about the benefit of early treatment with TT the findings from this study demonstrated that only 26 % of patients received TT within 30 minutes of hospital admission, and 55 % of patients within 60 minutes of arrival.

Reduction of the patient decision time, transportation time, and time from symptom onset to hospital admission appears to be the basis for future approaches in the management of AMI. The GP should attend the patient from call for help to the administration of TT (call-to-needle time). The time elapsed until care is provided should not exceed 90 minutes (fast track) [18]. Shortening the time from the onset of symptoms to the initiation of TT represents an alternative strategy for improving clinical outcome in AMI. A GISSI study found that the interval between the onset of symptoms and the decision to seek help was primarily responsible for the delay in the initiation of TT [26]. Educational programs informing the public of the symptoms of AMI and the importance of early intervention may help in reducing this delay. Improvements in the speed and efficiency of emergency care procedures might also be expected to expedite delivery of TT.

Table 2: Time elapsed from hospital admission to the initiation TT (door-to-needle time)

| Time (minutes) | Number of patients |
|----------------|--------------------|
| < 30 | 11 (26 %) |
| 30–60 | 23 (55 %) |
| > 60 | 8 (19 %) |

TT: thrombolytic therapy

We suggest that the present situation should be improved by proper public education to seek medical help as soon as symptoms begin that could represent AMI, including chest pain, chest discomfort, syncope, and faintness, and earliest possible transfer to the hospital. In summary, in this evaluation of call-to-needle time, older patients, female sex, unrecognised AMI symptoms, and the duration of transfer to the hospital were each related to longer delay time.

Conclusions

Thrombolytic therapy for AMI was used in 23 % of patients. The results suggested that the time elapsed from onset of symptoms to GP presentation, time from GP presentation to hospital admission, time for transportation to the hospital, a patient from the Dubrava subregion, younger patients and male sex are important factors influencing the time to administration of TT in AMI. We are inclined to believe that educating patients to recognise AMI symptoms, and fast transfer to the hospital would greatly improve the present, quite unfavourable situation.

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