Thrombolytic Therapy in Diabetic Patients With Acute Myocardial Infarction

HANS-HENRIK T. HANSEN, MD
SØREN C. KJÆRGAARD, MD
INGE BÜLOW, MD
LARS FOG, MD
PER D. CHRISTENSEN, MD

OBJECTIVE — To compare the frequency of thrombolytic therapy in diabetic and nondiabetic patients with acute myocardial infarction (MI) and to examine why some diabetic patients do not receive thrombolytic therapy.

RESEARCH DESIGN AND METHODS — Retrospective study of all diabetic patients with acute MI admitted to the coronary care unit of Aalborg Hospital within a 3-year period.

RESULTS — Only 35% (43 of 123) of patients with diabetes compared with 47% (404 of 856) of patients without diabetes received thrombolytic therapy ($P < 0.002$). There was no difference in the percentage of patients thrombolyzed among patients admitted to the hospital within 12 h after onset of symptoms. Of diabetic patients who were not thrombolyzed, 60% (48 of 80) arrived at the hospital later than 12 h after onset of symptoms. Among patients who arrived late, 63% (35 of 56) had Q wave infarction and 84% (47 of 56) had symptoms typical of acute MI. Mortality was 29% (16 of 56) in this group. Only one patient did not receive thrombolytic therapy due to diabetic retinopathy.

CONCLUSIONS — Significantly fewer diabetic patients received thrombolytic therapy compared with patients without diabetes. The main reason diabetic patients did not receive thrombolytic therapy was late arrival to the hospital.

Diabetic patients with acute myocardial infarction (MI) receive thrombolytic therapy less often than patients without diabetes (1), although studies have shown that diabetic patients benefit equally well from this treatment as nondiabetic patients (2,3). It is unknown why fewer diabetic patients receive thrombolytic therapy. One reason may be a reluctance to thrombolyze diabetic patients due to the risk of retinal bleeding in patients with retinopathy. Another explanation may be that diabetic patients may have atypical symptoms at the onset of MI (4), which may in turn lead to delayed hospitalization. The purpose of this study was to compare the frequency of thrombolysis in patients with and without diabetes and to study the reasons why diabetic patients did not receive thrombolytic therapy.

RESEARCH DESIGN AND METHODS

— We performed a retrospective study of all patients admitted primarily to Aalborg Hospital with an acute MI in the period from October 1991 to September 1994. Data were assessed from patient records. Patients were defined as having an acute MI if they met at least two of the following criteria: development of Q waves or branch block in electrocardiogram (ECG), chest pain, or a rise in either lactate dehydrogenase >450 U/l (normal range <450 U/l) or creatine kinase B >12 U/l (normal range <6 U/l). The time limit for receiving thrombolytic therapy in our department was 6 h for the first 6 months of the period and 12 h for the latter 30 months. ECG criteria for thrombolytic therapy were: ST-segment elevation of >1 mm in standard leads or 2 mm in precordial leads. Diabetic retinopathy was not an absolute contraindication for giving thrombolytic therapy but depended on the severity. To discriminate between typical and atypical symptoms of acute MI, typical symptoms of acute MI were defined as: chest pain and/or pain in the arms, acute onset of dyspnea, acute pulmonary edema, or syncope with ventricular fibrillation. All other symptoms were regarded as atypical symptoms. The delay was calculated from the onset of symptoms to the arrival at the coronary care unit (CCU). Mortality was calculated as in-hospital mortality. Patients with diabetes were classified as IDDM and NIDDM according to classifications in patient records. Patients, with no prior history of diabetes, who were discharged with antidiabetic therapy were grouped as newly diagnosed diabetic patients. Patients whose blood glucose was >18 mmol/l upon admission who died before a definite diagnosis of diabetes was made, were regarded as unrecognized diabetic patients and grouped as newly diagnosed diabetic patients.

Statistical analysis

The Wilcoxon rank-sum test for unpaired data (Mann-Whitney) was performed when comparing ratio/interval data (age, weight). Other data where variables are binomial were analyzed using the χ^2 test.

RESULTS

— A total of 979 patients with acute MI were hospitalized in the period; 856 patients without diabetes and 123 with diabetes. Twenty patients had IDDM, 96 had NIDDM, and 7 had diabetes diagnosed during hospital stay. Table 1 shows the characteristics of diabetic and nondiabetic patients. Significantly fewer diabetic patients received thrombolytic therapy (35 vs. 47%, $P < 0.002$). The frequency of thrombolysis was similar in patients with and without diabetes admitted to the CCU within 12 h after onset of symptoms. Significantly fewer diabetic patients arrived at the CCU within 12 h after onset of symptoms. In the late presenting group, 8 patients had IDDM

From the Department of Cardiology, Aalborg Hospital, Aalborg, Denmark.
Address correspondence and reprint requests to Hans-Henrik T. Hansen, MD, Department of Cardiology, Aalborg Hospital, Hobrovej 18-22, Box 365, DK-9100 Aalborg, Denmark.
Received for publication 31 October 1995 and accepted in revised form 30 May 1996.
CCU, coronary care unit; ECG, electrocardiogram; MI, myocardial infarction.

Table 1—*Patient characteristics*

	Nondiabetic patients	Diabetic patients	*P* value
n	856	123	
Age (years)*	65.5 ± 11.3	68.6 ± 13.2	0.005
Typical symptoms	724 (85)	107 (87)	NS
Q wave infarctions (%)	582 (68)	78 (63)	NS
Thrombolytic therapy (%)	404 (47)	43 (35)	0.002
Thrombolytic therapy in patients admitted within 12 h†	332 (57)	35 (49)	NS
Delay <12 h (%)	582 (68)	67 (58)	0.003
Complications in thrombolytic therapy‡	18 (4)	2 (5)	NS
Length of hospital stay (days)*	7.4 ± 4.8	7.3 ± 6.0	NS
Mortality (%)	110 (13)	34 (28)	0.00002
Reasons for not giving thrombolytic therapy§			
Delay >12 h (%)	202 (45)	48 (60)	
Delay <12 h without ECG criteria for thrombolysis (%)	150 (33)	24 (30)	
Other contraindications (%)	100 (22)	8 (10)‖	

*Figures are mean values ± SD. †Percentages are given for patients admitted to CCU within 12 h of symptoms. ‡Percentages are given for patients thrombolyzed. §Percentages given in parentheses are of nonthrombolyzed patients. ‖Only one patient with diabetic retinopathy. NS, nonsignificant.

(14%), 16 patients (29%) were treated with insulin, and 24 patients (43%) had had diabetes for >10 years. In the early presenting group, comparable figures were 12 (18%), 19 (28%), and 26 (39%). There were no significant differences between these figures. Of 43 thrombolyzed diabetic patients, 8 died (19%), compared with 26 of 80 nonthrombolyzed diabetic patients (33%). This difference did not reach statistical significance.

The main reason diabetic patients were not thrombolyzed was late arrival to the CCU. Fifty-six patients arrived later than 12 h after onset of symptoms. Eight of these patients were thrombolyzed due to signs of ongoing ischemia. In the late presenting group, 35 patients (63%) had Q wave infarction. In the late presenting group, 16 patients (29%) died in the hospital, which was not different from the mortality in the early presenting group (18 of 67 patients; 27%). Forty-seven of the patients with late arrival (84%) experienced typical symptoms of MI. In patients who arrived within 12 h, 60 patients (90%) had symptoms typical of MI (not significant). The remaining patients presented with symptoms such as vomiting, dizziness, and malregulated diabetes. In our material, only one patient did not receive thrombolytic therapy due to diabetic complications. This patient had severe diabetic retinopathy. This patient had an anterior Q wave infarction and died in the hospital.

CONCLUSIONS — The benefits of thrombolyzing diabetic patients with acute MI are well documented (2,3). There has been a reduction in in-hospital mortality from 30 to 14% (3) since the introduction of thrombolytic therapy in the treatment of acute MI. The thrombolytic therapy is safe in diabetic patients (2). In our study, we saw no episodes of cerebral hemorrhages and only two bleeding episodes requiring transfusion. We saw no cases of retinal bleeding in diabetic patients in our study, which is in accordance with the fact that, to our knowledge, only one case of retinal bleeding in a patient with diabetes has been reported (5).

Thus, there is no reason why diabetic patients should not be given thrombolytic therapy as often as nondiabetic patients. Our study, however, indicates that diabetic patients receive thrombolytic therapy significantly less often than nondiabetic patients. This finding is in accordance with other reports (1,6); however, these reports did not specify reasons why diabetic patients were not thrombolyzed.

In our study, we found that arrival at the CCU later than 12 h after onset of symptoms was the main reason why diabetic patients were not thrombolyzed. The reason for late arrival in our study is unknown. In the late presenting group, only 16% had symptoms atypical of acute MI, such as dizziness, vomiting, and malregulated diabetes. This percentage did not differ from that seen in diabetic patients with early arrival. Patients with autonomic neuropathy have a higher frequency of silent ischemia (7), thus it is possible that diabetic patients with autonomic neuropathy experience less pain in the course of MI. Our study, however, could not address whether there was a higher occurrence of autonomic neuropathy among patients in the late presenting group. We found no difference in the percentage of patients with IDDM, insulin treatment, and long duration of diabetes between the early and late presenting group; however, this could be due to the small number of patients in each group. Another explanation for the late arrival may be that diabetic patients exhibit a high degree of self-care and thus have a higher threshold for seeking medical care.

It has recently been recommended that thrombolytic therapy should not be withheld from diabetic patients (8). Our study shows that in our hospital in a 3-year period thrombolytic therapy was withheld from only one patient due to diabetic complications. The majority of diabetic patients were not thrombolyzed due to late arrival at the CCU. This leads to the recommendation that diabetologists and general practitioners should inform their diabetic patients of the necessity to seek medical care without delay at the onset of chest pain, acute dyspnea, or chest discomfort.

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