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Asit R. Gokli
Jay L. Kovar
Terry Kowalenko
Richard M. Nowak

Henry Ford Health System, rnowak1@hfhs.org

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Prehospital Care of Acute Myocardial Infarction: A Review

Asit R. Gokli, MD,* Jay L. Kovar, MD,* Terry Kowalenko, MD,* and Richard M. Nowak, MD*

Each year more than 1 million people in the United States suffer from acute myocardial infarction (MI) with most of the deaths occurring within hours of symptom onset. Over the last 25 years, different prehospital systems have evolved throughout the world which allow early cardiac monitoring and treatment of acute MI patients. Thrombolytic therapy in acute MI has been shown to decrease mortality and preserve left ventricular function when administered early after onset of symptoms. The potential role of Emergency Medical Services or Mobile Coronary Care Units in achieving early thrombolysis is under investigation. Several studies of prehospital interventions to achieve early thrombolysis are reviewed. The use of thrombolytics by prehospital personnel has been found to be feasible, safe, and effective in reducing time delays. However, whether this translates into clinical benefit remains to be seen. (Henry Ford Hosp Med J 1991;39:170-5)

Myocardial infarction (MI) affects more than 1 million people per year in the United States and accounts for over 25% of overall annual deaths (1). Most deaths from acute MI occur shortly after the onset of symptoms and therefore outside of the hospital (2). Recognition of this has led to the development of efficient prehospital care over the last 25 years which has proved to be lifesaving in terms of treating chest pain and serious dysrhythmias with medications and defibrillation.

Over the last decade it has become known that early lysis of an occluding thrombus in the setting of an acute MI results in improved left ventricular (LV) function (3-6), reduction in immediate mortality (7,8), and enhancement of long-term survival (9,10). This has renewed medical interest in the prehospital care of acute MI. Several studies are under way to better define the role of prehospital care of acute MI. The important questions to be answered are: Should thrombolytic therapy be begun in the prehospital setting? Is it feasible, safe, and effective? How can prehospital care of acute MI contribute to early diagnosis and the decision to use thrombolytic therapy?

Developments in Prehospital Care of Acute MI in the United States

The standardization of prehospital emergency medical services (EMS) is a relatively new component of health care. Although the roots of prehospital care date back to military campaigns in the 18th century and hospital transport in the 1860s, prehospital services did little to provide therapeutic interventions and reduce mortality and morbidity until the mid 1960s.

In 1967, in Belfast, Northern Ireland, the first mobile coronary care unit (MCCU) was established. Utilizing cardiac monitoring and defibrillation capabilities, the Belfast group showed positive benefits by prompt and skillful treatment early in the course of acute MI before the patient reached the critical care unit (CCU) in the hospital (11).

Over the years, the administration of antiarrhythmic agents and defibrillation have become well established prehospital interventions. Early defibrillation has been shown to be the single most beneficial prehospital intervention (12). However, the benefits of early prehospital care of acute MI are multifactorial. These include: 1) relief of chest pain; 2) cardiac monitoring for early recognition and prompt treatment of dysrhythmias by pharmacologic agents, defibrillation, and electrical cardiac pacing; and 3) control of blood pressure and heart rate (2). Treatment of autonomic dysfunction (hypotension and bradycardia) associated with acute MI in the prehospital setting has been shown to decrease ultimate mortality and morbidity (13). Besides decreasing mortality, effective, early prehospital care may also prevent extension of MI and the later development of pump failure (2).

Different systems have evolved throughout the world over the last 25 years to treat acute MI during the prehospital phase. In the United States, mobile coronary care has largely been incorporated into the EMS system which is staffed by emergency medical technicians (EMTs) and paramedics (EMTs with specialized training including advanced cardiac life support and an
upgraded level of skills). Timely assessment and therapeutic intervention, not limited to resuscitation, includes treatment of secondary complications of acute MI such as hypotension, hypoxia, bradycardia, pulmonary edema, ventricular fibrillation, and cardiac arrest (14). Thus, in the United States, prehospital care of acute MI is provided by paramedics or EMTs or a combination of both.

Recent advances in thrombolytic therapy in acute MI and its time-dependent character have led to a new emphasis on the prehospital care of acute MI.

**Historical Review of Thrombolytics in Acute MI**

Acute transmural MI is a thrombotic process (15). Coronary artery thrombus causing total occlusion of the infarct-related vessel is present in 80% to 90% of patients with acute MI. In about 15% to 20% of patients, an intraluminal thrombus is present which causes subtotal occlusion of the infarct-related vessel.

DeWood et al (16), performing cardiac catheterization and coronary angiography in 210 MI patients within 6 hours of the onset of symptoms, found that 87% of patients had total occlusion of the infarct-related vessel.

Working with animal models, Reimer and Jennings et al (17, 18) studied the time course of myocardial necrosis after coronary occlusion. They demonstrated that coronary artery occlusion followed by variable lengths of ischemia and then by reperfusion resulted in predictable degrees of myocardial necrosis. This myocardial necrosis proceeds from the subendocardial to the subepicardial layers of the myocardium in a wavefront of necrosis in a time-dependent manner. Early reperfusion occurring within minutes of occlusion of the vessel resulted in minimal to no myocardial necrosis, whereas reperfusion occurring later in the time course resulted in a variable amount of subendocardial necrosis.

Initial human studies with thrombolytic agents utilized intracoronary administration of streptokinase (SK). In 1979, Feit and Rentrop (19) demonstrated reestablishment of distal blood flow after administration of SK directly into the coronary thrombus. Anderson et al (20) studied 50 patients and demonstrated that intracoronary SK administered at 2.7 hours after the onset of symptoms resulted in a seven-point difference in ejection fraction (EF) and thus significant myocardial salvage compared to patients with acute MI who received routine CCU care. Khaja et al (21) studied 40 patients who received intracoronary SK at an average of 4.8 hours after the onset of symptoms of acute MI. No improvement was seen in EF compared to the control group. The difference in improvement in EF in the Anderson (20) and Khaja (21) studies was mainly due to a significant difference in time to treatment (2.7 versus 4.8 hours). The Western Washington randomized trial demonstrated that intracoronary SK administered within the first 6 hours of the onset of symptoms reduced 30-day mortality rates. This benefit persisted at one-year postinfarction when intracoronary SK had resulted in total coronary reperfusion (8,22).

Emergency cardiac catheterization and coronary angiograms involve significant time delay, usually about 90 to 180 minutes. Many hospitals are not equipped for cardiac catheterization and so this mode of therapy is available to few patients with acute MI. Thus, medical research has focused on the intravenous (IV) administration of thrombolytics.

The Intravenous Streptokinase in Acute Myocardial Infarction study found that patients treated within 1.5 hours of the onset of symptoms had significantly shorter time to peak creatine kinase (CK) interval, smaller area under CK-MB curve, and higher global or infarct-related regional EFs compared to patients treated within 1.5 to 4 hours after acute MI (23).

Fine et al (24) found that IV thrombolytic therapy administered within 2 hours of symptoms in patients with acute anterior wall MI resulted in smaller infarct size compared to patients treated within 2 to 4 hours from time of symptoms.

Gruppo Italiano per lo Studio della Streptochinasi nell’ Infarto Miocardico (GISSI), a multicenter, placebo-controlled, randomized trial, also utilized IV SK (25). This study conclusively showed a reduction in overall mortality of 18% in patients treated with IV SK compared to patients who received routine CCU care. Patients treated within 3 hours of the onset of symptoms had a 23% reduction in in-hospital mortality. In patients who received IV SK within 1 hour of the onset of symptoms, the in-hospital mortality was reduced by 47% compared to the control group. This survival advantage persisted at one-year follow-up.

Thus, IV thrombolytic therapy given to patients with acute MI appears to lyse the occluding thrombus, reestablish perfusion to the ischemic myocardium, and prevent or limit myocardial necrosis in a time-dependent manner. The “golden period” appears to be the first 2 to 4 hours after the onset of symptoms, during which maximum benefit could be achieved from thrombolytic therapy as indicated by reduction in mortality and preservation of residual LV function.

**Interventional Delays in Thrombolytic Therapy**

The optimal goal of thrombolytic therapy in acute MI is to administer the thrombolytic agent at the earliest time, within minutes if possible, and most certainly within the first 2 to 4 hours of the onset of symptoms. Unfortunately, only a small proportion of patients receive thrombolytic therapy within this time frame (27-29).

The causes of delay in initiating thrombolytic therapy are multifactorial and include: 1) patient delay in recognizing acute MI symptoms and seeking medical help; 2) EMS delays in response time, on-scene time, and transport time; and 3) delays in the Emergency Department (ED).

**Patient delay**

Investigations in patient recognition and response times have revealed that up to 44% of acute MI patients do not seek medical assistance until more than 4 hours after the onset of symptoms (30). Older patients and those from lower socioeconomic groups wait longer prior to seeking medical help (31). Only 30% to 50% of patients with acute MI activate EMS; the remainder use other means of transport and walk in to the ED (32). The most common reason for delay in seeking medical care is patient denial. Other reasons include mistaking symptoms of acute MI for...
more benign medical conditions, being alone at home at time of symptom onset and thus being unable to activate EMS, and attempting to contact personal physician first (33). Limited public awareness campaigns conducted in Sweden (34) and America (35) have failed to produce significant increases in the number of MI patients who present early for medical treatment. To be effective, public awareness programs need to be of longer duration and repeated frequently.

EMS delay

The EMS "response time," or time from system activation to EMS arrival at the patient’s side, averaged about 8 minutes in one multicenter study (36). Difficult access to the patient due to physical barriers at the scene can contribute to long response times (37). Also, there are limitations due to weather and traffic conditions.

The "on-scene time" is the time from EMS arrival at the patient’s side until transport is initiated. This time involves evaluation of patient by history and physical examination, electrocardiographic data acquisition, insertion of IV lines, base station contact with a controlling physician, and initial in-field therapies. In a review of eight major prehospital study groups, Kereiakes et al (36) demonstrated an average on-scene time of 26 minutes for patients with chest pain.

The EMS "transport time," time from initiation of patient transport to arrival in the ED, averaged 13 minutes in a multicenter urban study. In rural areas transport times can be much longer especially if aeromedical transport is not available.

Emergency Department delay

Once the patient suffering from an acute MI arrives in the ED, whether conveyed by EMS or private transport, rapid diagnosis and administration is fraught with delays. Factors contributing to the delay include registration and collection of demographic data, triage by a nurse and initial physician evaluation, IV access, collection of blood, ECG and a chest x-ray, consultation with the patient’s private physician or cardiologist, and acquisition of the thrombolytic agent from the pharmacy. Sharkey et al (38) reported an average 20-minute wait after arrival in the ED before the initial ECG was obtained, and an additional 70 ± 40 minutes before thrombolytics were administered.

Prehospital Thrombolytics

Thrombolytic therapy in the setting of an acute MI can reduce mortality and morbidity, but its effectiveness is inversely related to time (10,25). Maximum benefit of thrombolytic therapy is achieved when it is administered within 2 to 4 hours of the onset of symptoms (10,25). Significant time delay to treatment could be prevented if thrombolytic therapy could be initiated by the first trained medical team to come in contact with the patient. In the prehospital setting, this would be either paramedic-staffed EMS or physician-staffed MCCU. Several studies have focused on the feasibility, safety, and effectiveness of prehospital administration of thrombolytics in acute MI.

Koren et al (39) studied the use of IV SK in the prehospital setting. The MCCU physician was able to obtain and interpret an initial ECG in the field and begin thrombolytic treatment with IV SK. The average time from onset of symptoms to treatment was 1.7 ± 0.8 hours. Patients who received treatment in the first 1.5 hours of symptom onset, versus those who received treatment between 1.5 and 4 hours of symptom onset, had a significantly higher global LVEF (56% ± 15% versus 47% ± 14%) and infarct-related regional EF (51% ± 19% versus 34% ± 20%).

Weiss et al (26) showed similar results with prehospital thrombolytics using IV SK. The time from onset of symptoms to administration of IV SK averaged 63 ± 19 minutes in the field compared to 114 ± 54 minutes for a similar group of acute MI patients who received IV thrombolytics in-hospital. This study also showed smaller infarct size and better residual EF in the prehospital SK group compared to the in-hospital SK group.

Roth et al (40) studied recombinant tissue-type plasminogen activator (rt-PA) use in acute MI in the prehospital MCCU (n = 74) and in-hospital (n = 44) setting and found prehospital use of rt-PA safe and feasible. However, this study failed to show significant clinical advantage of prehospital administration of rt-PA over in-hospital rt-PA administration (time to treatment = 94 ± 36 minutes versus 137 ± 15 minutes).

Applebaum et al (41) used IV SK in 13 patients suffering from acute MI in the prehospital setting using a MCCU. In this study, patients waited 33 ± 17 minutes after onset of acute MI symptoms to call the ambulance. Ambulance arrival time was 5 ± 3 minutes. An additional 32 minutes were required before IV SK therapy was initiated. Thus, time from onset of acute MI symptoms to initiation of thrombolytic therapy averaged 66.7 minutes. No major complications were noted. A reduction in time delay of 30 to 60 minutes was achieved by prehospital use of thrombolytics. These investigators concluded that prehospital thrombolytic therapy is safe and reduces time delay to treatment.

Castaigne et al (42,43) conducted a two-part study to determine the feasibility and safety of prehospital thrombolytics and whether prehospital thrombolytics caused delay in the patient’s arrival to the hospital. Phase I of the study evaluated the diagnostic accuracy of MCCU physicians. Of the 294 patients evaluated and judged as having unstable angina or acute MI in the field, 282 were confirmed as candidates for thrombolysis by the in-hospital team. Phase II of this study was a randomized, placebo-controlled trial. Patients who were diagnosed in the field as having acute MI (n = 100) received either anisoylated plasminogen streptokinase activator complex (APSAC) (n = 57) or placebo (n = 43). Patients who received placebo in the field received APSAC upon arrival in the hospital if indicated. APSAC was given in the field with a median time delay of 131 minutes after the onset of acute MI symptoms whereas the median time delay to in-hospital administration of APSAC was 180 minutes. Thus, there was an average savings of 50 minutes in the prehospital group. No difference was observed in the complication rate in each treatment group regarding arrhythmias, hypotension, hemorrhage, or death. In-field administration of APSAC did not delay patient arrival to the hospital.

However, this study failed to show any difference in the early post APSAC EF in the two groups. This study demonstrates that prehospital thrombolytic use is feasible and safe and significantly reduces time delay to treatment.

In the above studies, all ambulances/MCCUs were staffed by physicians. Physicians evaluated the patients on the scene, obtained and interpreted ECGs, initiated thrombolytic therapy, and managed complications. In the United States, prehospital care is rendered by highly trained paramedics. The question then arises as to whether specially trained paramedics working in collaboration with physicians can safely initiate thrombolytic therapy in the field.

With the ability of transmitting 12-lead ECGs from the field to a base hospital where a physician can interpret the ECG and make decisions regarding in-field thrombolysis, prehospital thrombolytic therapy has become a real possibility.

Cellular ECG equipment can provide hard copies of the 12-lead ECGs to the paramedic as well as to the physician at the base hospital. At the same time, the paramedic can relay pertinent patient medical history and other information to the physician. Based on all of the previous data, the base physician then decides whether thrombolytic therapy should be begun in the field. Grim et al (44,45) demonstrated the feasibility and accuracy of cellular telephone transmission of a 12-lead ECG from the transporting ambulance to the hospital. Aufderheide et al (46) demonstrated that paramedics were able to obtain prehospital ECGs 94.6% of the time (157 of 166 eligible patients). The paramedic-performed ECGs required one-third the time of that needed to perform ECGs in the ED (8.4 ± 5.1 minutes versus 24.2 ± 21.6 minutes). The prehospital ECGs increased on-scene time by an average of 5.2 minutes compared to a retrospectively evaluated group of paramedic-transported patients (26.8 ± 7.8 minutes versus 21.6 ± 7.6 minutes). There was a high concordance between prehospital and ED 12-lead ECG diagnosis (99.3% for acute MI and 92.8% for angina). This study also demonstrated that prehospital 12-lead ECGs were diagnostic in 54.2% of all acute MI patients with a specificity of 99.2% and positive predictive value of 92.8%. These values far exceed those achieved by paramedics using single-lead telemetry (positive predictive value 32.7%).

Grim et al (47) demonstrated that emergency physicians can accurately make the decision to administer thrombolytic therapy in the field based on the 12-lead ECG and historical information provided by the paramedics. However, only 4.2% of patients evaluated for chest pain (2 of 48) were actually candidates for in-field thrombolysis.

Several studies have shown that the acquisition of the prehospital ECGs and their transmission to base hospital and protocol-driven assessment of history, physical examination, and risk factors for administration of thrombolytic therapy do not increase either on-scene or transport time (14,48). Grim et al (47) reported an average time from arrival at the scene to arrival at the hospital of 28 ± 6 minutes in the prehospital ECG group compared to 27 ± 6 minutes in the control group without prehospital ECG. The Field Ambulance Study of Thrombolysis in Myocardial Infarction demonstrated a significant decrease in the average time delay to initiation of thrombolytic therapy in the hospital by prehospital ECGs (48 ± 12 minutes with prehospital ECG compared to 68 ± 29 minutes for patients without prehospital ECGs) (48). Thus, prehospital acquisition of ECG with either its transmission to the base hospital or by presenting the 12-lead ECG upon the patient’s arrival to the ED can significantly reduce ED time delay to thrombolytic therapy without increasing EMS on-scene or transport time.

Using strict criteria for the diagnosis of acute MI of 1) 1 mm ST elevation in contiguous ECG leads, 2) "reciprocal" ST depression of at least 0.5 mm in at least one ECG lead, and 3) an interpretive comment suggesting "injury" or "infarction," O'Rourke et al (49) demonstrated that paramedic diagnosis of acute MI was feasible and accurate without telemetry, provided that patients with prior Q wave infarctions were excluded.

The actual administration of thrombolytic therapy in the prehospital setting, either on-scene or during transport, has reduced average time delay to treatment by 30 to 86 minutes (31,40,48). SK, rt-PA, and APSAC all have been studied in the prehospital setting and show no reduction in safety or efficacy (32). Initial studies were conducted using continuous IV infusion of SK. Castaigne et al (42) have suggested APSAC for use in the prehospital setting since the single IV bolus dose obviates the need of continuous infusion. Purvis et al (50) and McKendall et al (51) have demonstrated high (exceeding 90%) infarct artery patency rate on coronary angiograms performed 90 minutes after an initial bolus of rt-PA. The more common complications of hypotension and reperfusion arrhythmias are usually self-limited and easily treated in the field by the paramedics (52).

Of the 2,472 patients prospectively evaluated for chest pain during phase I of the Myocardial Infarction Triage and Intervention (MITI) trial, 677 (27%) had clinical findings suggestive of acute MI (53). Of the 522 patients in whom in-field ECGs were obtained, 107 were eligible for prehospital thrombolytic therapy based on diagnostic changes of acute MI on ECG. Thus only 107 (4.2%) of the 2,472 chest pain patients evaluated were potential candidates for prehospital thrombolytics. The Cincinnati Heart Project also showed a low accrual rate of acute MI patients with only 20 (4.2%) acute MIs identified out of 477 patients evaluated for chest pain (54). In the Nashville prehospital rt-PA trial, only three (3.5%) of the 85 patients were found to be actual candidates for rt-PA in the field over a six-month period (54).

Studies to date have conclusively shown reduction in time delay to treatment of 30 to 70 minutes with prehospital thrombolysis. However, data on clinical benefit from this time saving is not clear. Randomized trials of prehospital thrombolysis have shown improved survival without improved residual LV function (55), improved LV function with no difference in survival (43), and no difference in survival or LV function (56). Data from the MITI and European Myocardial Infarction Project (EMIP) trials which are currently in progress will hopefully yield a more definitive answer regarding whether reduction in time delay to treatment of 30 to 70 minutes by prehospital thrombolytic therapy translates into improved survival and improved residual LV function. Phase II of the MITI trial, which began in October 1988, is a prospective evaluation of the benefit of paramedic administration of rt-PA (53). A total of 800 patients will be randomized to receive rt-PA in the field or in the
hospital after prehospital diagnosis of acute MI by 12-lead ECGs. LVEFs will be measured to judge the benefit of prehospital versus in-hospital thrombolytic therapy. The main goal of EMIP, a prospective, double-blind, randomized, multicenter international study, is to evaluate the benefit/risk ratio of prehospital thrombolytic therapy compared with in-hospital thrombolysis, with total mortality as the major endpoint. Patients suspected of having acute MI receive APSAC in the field or in the hospital. The goal is to include 10,000 patients in this study.

**Barriers to Prehospital Thrombolysis**

About half of all patients suffering from acute MI activate EMS while the others arrive in the ED by other means of transport (42% in Seattle, 44% in Minneapolis, and 57% in Goteborg) (38,32,35). Thus prehospital administration of thrombolytic therapy would reach only half of all patients with acute MI. Due to adherence to strict inclusion and exclusion criteria for prehospital thrombolysis, only about 4% of patients evaluated for chest pain would be candidates for prehospital thrombolysis (53). This would translate into few prehospital thrombolytic treatments given. Gibler et al (54) noted a decline in paramedic skill because of infrequent use of thrombolytic therapy. Thus it would be necessary to train paramedics to give thrombolytics in the field and then periodically retrain them to prevent decline in their skills. The cost of equipping the ambulance with electrocardiographic and communication equipment may be prohibitive. The costs of stocking the thrombolytic agents in the field and wastage of these agents due to expiration or breakage may also be excessive. There could be additional medicolegal risk for the ED physicians as well as the paramedics due to faulty diagnosis from inaccurate history and increased complications. Interference with cellular telephone transmission could delay prehospital thrombolysis.

**Conclusion**

The time-dependent efficacy of thrombolytic therapy in acute MI has revitalized interest in the prehospital care of acute MI. Thrombolytic therapy within 2 to 4 hours of symptom onset is desirable. Patient delay in seeking medical attention and low usage of the EMS system is a major component in delay to thrombolytic treatment, with as many as one-half of patients waiting 4 or more hours before seeking medical attention. In-hospital time delay to thrombolytic treatment of 60 minutes is common despite enhanced general awareness, transfer of responsibility for initiating thrombolysis to the emergency physicians, and stocking of thrombolytic agents in the ED. The acquisition of prehospital 12-lead ECG has been shown to reduce hospital time delay to thrombolytic therapy in acute MI patients. Potential time savings of 30 to 60 minutes have been observed with this strategy. Prehospital diagnosis of acute MI using 12-lead ECG has been found to be feasible and accurate. The use of all three current forms of thrombolytic agents (SK, rt-PA, and APSAC) in the prehospital setting is feasible and safe and reduces time delay to treatment. However, clinical benefit from this reduction in time delay has not been conclusively shown. Low public use of EMS, few patients meeting criteria for in-field thrombolysis, the high cost of equipping the ambulance and training paramedics, along with increased medicolegal risks may make prehospital administration of thrombolysis impractical at the present time. We await the results from ongoing studies of large numbers of patients to help answer this question.

**References**