Thrombolytic use in the region around Amarillo, Texas, in patients with ST elevation myocardial infarction

Kelly S. McMaster, MBA^a, Totini Chatterjee, BS^a, Drew McBrayer, BA^a, and David Brabham, DO^b

^aDepartment of Internal Medicine, Texas Tech University Health Sciences Center School of Medicine–Amarillo, Amarillo, Texas; ^bDepartment of Internal Medicine, Cardiology Center of Amarillo and Texas Tech University Health Sciences Center School of Medicine–Amarillo, Amarillo, Texas

ABSTRACT

Appropriate administration of thrombolytic therapy is particularly important for ST elevation myocardial infarction (STEMI) patients who are unable to access primary percutaneous coronary intervention (PCI) in a timely manner. We evaluated the current state of thrombolytic therapy in the Panhandle region of West Texas where access to primary PCI is poor. The medical records of 79 patients transferred from 20 outlying facilities to the two hospitals in Amarillo, Texas, for STEMI in 2016 were retrospectively evaluated for time of onset of chest pain, initial electrocardiogram findings, medication reconciliation, and any contraindications to thrombolytic therapy. Medical record review allowed the patients to be sorted into one of five predefined categories based on our findings. The most common error discovered was failure to deliver the appropriate accompanying medications with thrombolytic therapy, noted in 43% of patients. Other errors included failure to deliver thrombolytic therapy in patients who met no clear contraindications to thrombolytic therapy (21%) and administering thrombolytic therapy to patients who had not suffered STEMI (4%). Thirteen percent of patients were appropriately treated with thrombolytic therapy and 19% of patients met a contraindication to thrombolytic therapy and were not treated with thrombolytic therapy, as was appropriate.

KEYWORDS Acute coronary syndrome; dual antiplatelet therapy; ST-elevation myocardial infarction; thrombolytic therapy

Acute coronary syndrome (ACS) is a common condition affecting millions of people worldwide. The guidelines for treating ACS are clear in their recommendations that patients with ST segment elevation myocardial infarction (STEMI) should be urgently reperfused, preferably with primary percutaneous coronary intervention (PCI). Though primary PCI is the gold standard, patients presenting with STEMI to rural facilities are unlikely to undergo primary PCI in a timely manner. Therefore, thrombolytic therapy is particularly useful in these settings. Amarillo, Texas, serves the population of the Panhandle region of West Texas, and primary PCI is readily available within city limits. However, the 20 rural facilities that treat patients with ACS outside of Amarillo, Texas, are not equipped with primary PCI capabilities and therefore should regularly be treating STEMI patients with thrombolytic therapy prior to transferring these patients to Amarillo for higher-level care. Due to our interest in the current state of thrombolytic therapy in the Panhandle region of West Texas, we systematically reviewed the appropriateness of delivery of thrombolytic therapy in the facilities surrounding Amarillo, Texas, for the year 2016.

METHODS

The medical records of all patients with STEMI in 2016 who were transferred from the 20 outlying facilities to the two hospitals in Amarillo, Texas, were evaluated retrospectively. Records were evaluated for time of onset of chest pain, initial electrocardiogram findings, medication reconciliation, and any contraindications to thrombolytic therapy. An onset of chest pain within 12 hours was considered to be within the target window for delivery of thrombolytic therapy. Initial electrocardiograms were evaluated by a board-certified interventional cardiologist to determine whether the patient had in fact suffered a STEMI. STEMI was defined as (1) new ST elevation at the J point in at least two contiguous leads of ≥ 2 mm (0.2 mV) in men or ≥ 1.5 mm (0.15 mV) in women in leads V2–V3 and/or of ≥ 1 mm (0.1 mV) in other contiguous chest leads or the limb leads; (2) new or presumed new left bundle branch block; or (3) isolated posterior myocardial infarction.¹

It was then determined whether the patient had been given thrombolytic therapy at the outside facility and whether the appropriate accompanying medications were given along with the thrombolytic therapy. Each patient treated with thrombolytic therapy should have received both of the following medications: (1) dual antiplatelet therapy (DAPT), 162–325 mg aspirin with 300 mg of

Corresponding author: Kelly S. McMaster, MBA, Department of Internal Medicine, Texas Tech University Health Sciences Center School of Medicine–Amarillo, 1400 S. Coulter Street, Amarillo, TX 79106 (e-mail: kelly.mcmaster@ttuhsc.edu)

clopidogrel (75 mg is sufficient in patients >75 years) and (2) anticoagulation, either a 60 U/kg bolus of unfractionated heparin or a 30 mg intravenous bolus followed by 1 mg/kg subcutaneous low-molecular-weight heparin (the bolus may be eliminated in patients >75 years). The contraindications to thrombolytic therapy are defined by the ACLS Fibrinolytic Checklist for STEMI (Table 1).

Medical record review allowed the patients to be sorted into one of five predefined groups: (1) Appropriate thrombolytic therapy delivered to the appropriate STEMI patient, (2) failure to deliver thrombolytic therapy to the appropriate STEMI patient, (3) delivery of thrombolytic therapy to a patient who did not have STEMI, (4) delivery of thrombolytic therapy to the appropriate STEMI patient without appropriate accompanying medications, and (5) appropriate failure to deliver thrombolytic therapy in a patient with STEMI who met absolute or relative contraindications to thrombolytic therapy.

RESULTS

A total of 79 patients were transferred from 20 outlying facilities to the two hospitals in Amarillo, Texas, for STEMI in 2016. Of those 79 patients, 10 patients (13%) with STEMI were appropriately given thrombolytic therapy along with the appropriate accompanying medications; 17 patients (21%) with STEMI were not given thrombolytic therapy when they

Table 1. Contraindications to thrombolytic therapy

Type	Contraindication
Absolute	<ul style="list-style-type: none"> Any prior intracranial hemorrhage Known structural cerebral vascular lesion (e.g., arteriovenous malformation) Known malignant intracranial neoplasm (primary or metastatic) Ischemic stroke within 3 months EXCEPT acute ischemic stroke within 3 hours Suspected aortic dissection Active bleeding or bleeding diathesis (excluding menses) Significant closed-head trauma or facial trauma within 3 months
Relative	<ul style="list-style-type: none"> History of chronic, severe, poorly controlled hypertension Severe uncontrolled hypertension on presentation (SBP > 180 mm Hg or DPB > 110 mm Hg) History of prior ischemic stroke >3 months, dementia, or known intracranial pathology not covered in contraindications Traumatic or prolonged (> 10 minutes) cardiopulmonary resuscitation or major surgery (<3 weeks) Noncompressible vascular punctures For streptokinase/anistreplase: prior exposure (>5 days ago) or prior allergic reaction to these agents Pregnancy Active peptic ulcer Current use of anticoagulants: the higher the international normalized ratio, the higher the risk of bleeding

SBP indicates systolic blood pressure; DBP, diastolic blood pressure.

Figure 1. Appropriateness of delivery of thrombolytic therapy.

met no clear contraindications; 3 patients (4%) without STEMI were given thrombolytic therapy; 34 patients (43%) with STEMI were appropriately given thrombolytic therapy but failed to receive the appropriate accompanying medications; and 15 patients (19%) with STEMI met either absolute or relative contraindications to thrombolytic therapy and were therefore not given thrombolytic therapy (Figure 1).

By far the most common mistake made by the outlying facilities in the management of STEMI patients with thrombolytic therapy was failure to use the correct accompanying medications (Figure 1). Of the 34 patients with STEMI who received thrombolytic therapy without the appropriate accompanying medications, 12 patients (35%) did not receive DAPT, 10 patients (30%) did not receive any anticoagulation or the correct dosage of anticoagulation, and 12 patients (35%) received neither DAPT, anticoagulation, or correct dosage of anticoagulation (Figure 2).

Seventeen patients met either an absolute or relative contraindication and were not given thrombolytic therapy: 1 patient was transferred to Amarillo and was treated with primary PCI within 120 minutes, as per guidelines; 2 patients were not given thrombolytic therapy due to delayed presentation following onset of chest pain; 5 patients were incorrectly diagnosed with STEMI but were not given thrombolytic therapy for unknown reasons; 1 patient had recently undergone placement of a ventriculoperitoneal shunt; 1 patient suffered closed-head trauma shortly before arriving at the facility for chest pain; 3 patients were chronically anticoagulated; 1 patient had uncontrolled blood pressure and presented with systolic blood pressure >180; and 1 patient was not given thrombolytic therapy due to his age >85 years and concern for dementia.

DISCUSSION

In the United States, an ACS incident occurs every 25 seconds. Every minute, an ACS-related death occurs.² An increasing number of centers are utilizing checklists to assess patients with suspected ACS. However, to date, no standardized method has been established for the delivery of thrombolytics.

Figure 2. Types of errors in accompanying medications. DAPT indicates dual antiplatelet therapy.

Thrombolytic therapy has been used for more than 40 years to treat ACS. It primarily works by dissolving large clots in blood vessels, restoring blood flow and thereby halting ischemic damage to organs and tissues.³ With this therapy it is possible to return blood flow to nearly 75% of patients if the therapy is administered within the 2-hour window of symptom onset to thrombolytic delivery. Because better outcomes are associated with quicker delivery of thrombolytic therapy, the time between arrival to the treatment facility and thrombolytic administration should be less than 30 minutes. The benefit is greatest when the medication is administered within the first 4 hours after the onset of symptoms and particularly within the first 70 minutes.⁴ Therefore, it is not necessary to wait for the results of cardiac biomarkers such as creatine kinase-MB and troponin I.

The 2013 American College of Cardiology Foundation/American Heart Association guideline for management of STEMI recommends use of thrombolytic therapy in patients with symptom onset within 12 hours who cannot receive primary PCI within 120 minutes of first medical contact.⁵ Most of the patients residing within the Panhandle region of West Texas are served by outlying community hospitals and will not be able to reach a cardiac catheterization lab within 120 minutes. Therefore, it is imperative that thrombolytic therapy is properly managed in these settings and that an emphasis is placed on when to deliver thrombolytic therapy, when to abstain, and which medications need to be delivered in conjunction. The most common error we found was that of appropriate delivery of thrombolytics but lack of accompanying medications, which includes both anticoagulation and DAPT.

Numerous trials have demonstrated the positive outcomes in STEMI patients treated concurrently with thrombolytic therapy and DAPT. In the COMMIT/CCS-2 trial, 45,852 patients with suspected STEMI were randomly assigned to receive clopidogrel or placebo, with half of the patients receiving

thrombolytic therapy. This study found much better outcomes for the group treated with clopidogrel, including fewer deaths, repeat myocardial infarctions (MIs), and strokes.⁶ A statistical difference was also found in terms of reinfarction, stroke, and death in the hospital between the clopidogrel group and the placebo group ($P = 0.002$).⁶

In the CLARITY-TIMI 28 trial, 3491 patients with STEMI age 75 years or younger received thrombolytic therapy, anticoagulation, and aspirin. They were subsequently randomized to take either clopidogrel or placebo. The clopidogrel group had fewer reocclusions and recurrent MIs than the placebo group. They also had better results in terms of cardiovascular death, MI, and recurrent ischemia leading to urgent revascularization.⁷ A 36% reduction was seen in the odds of an occluded infarct-related artery, death, or recurrent MI by the time of angiography when patients were treated with a loading dose of 300 mg of clopidogrel and a daily dose of 75 mg thereafter.⁷ Furthermore, a 20% reduction was found at the 30-day endpoint in total deaths from cardiovascular causes, recurrent MI, and recurrent ischemia leading to the need for urgent revascularization.

The use of anticoagulation with thrombolytic therapy has also proven to be beneficial. A 1996 meta-analysis of over 60,000 patients treated with thrombolytic therapy discovered a reduction in the short-term risk of death with the addition of intravenous or high-dose subcutaneous heparin.⁸ Although the efficacy of anticoagulant therapy in this setting has been proven, there is controversy as to whether any agent is superior to another. All of these agents have benefits and risks that would make them more suitable in particular patient groups.

1. Sabatine MS, Cannon CP, Gibson M, et al; CLARITY-TIMI 28 Investigators. Addition of clopidogrel to aspirin and fibrinolytic therapy for myocardial infarction with ST-segment elevation. *N Engl J Med*. 2005;352(12):1179–1189.
2. Sabatine MS, McCabe CH, Gibson M, Cannon CP. Design and rationale of clopidogrel as adjunctive reperfusion therapy—thrombolysis in myocardial infarction (CLARITY-TIMI) 28 Trial. *Am Heart J*. 2005;149(2):227–233.
3. Collins R, MacMahon S, Flather M, et al. Clinical effects of anticoagulant therapy in suspected acute myocardial infarction: systematic overview of randomised trials. *BMJ*. 1996;313(7058):652–659.
4. Thygesen K, Alpert JS, Jaffe AS, Simoons ML, Chaitman BR, White HD. Third universal definition of myocardial infarction. *Circulation*. 2012;126:2020–2035.
5. Wachira JK, Stys TP. Cardiovascular disease and bridging the diagnostic gap. *S D J Med*. 2013;66(9):366–369.
6. Sherry S. The origin of thrombolytic therapy. *J Am Coll Cardiol*. 1989;14(4):1085–1092. doi:10.1016/0735-1097(89)90493-2.
7. Fibrinolytic Therapy Trialists' Collaborative Group. Indications for fibrinolytic therapy in suspected acute myocardial infarction: collaborative overview of early mortality and major morbidity results from all randomised trials of more than 1000 patients. *Lancet*. 1994;343(8893):311–322.
8. O'Gara PT, Kushner FG, Ascheim DD, et al; American College of Emergency Physicians, Society for Cardiovascular Angiography and Interventions. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction. *J Am Coll Cardiol*. 2013;61(4):e78–e140.