LUCAS COUNTY

TO: ALL LUCAS COUNTY PARAMEDICS

FROM: Brent Parquette, NREMT-P
Lucas County EMS Continuing Education Program Administrator

DATE: January 22, 2013

SUBJECT: **Continuing Education – February 2013**

In February 2013 we will take a comprehensive look at the 12-Lead ECG in the setting of ACS along with those elusive ACS impostors. Bring your best "interpretive" skills with you to class as we review recent STEMI cases and pertinent ECG data. During class I will also share with you the new ECG criteria for MI and LBBB that have just been released in the **2013 ACCF/AHA Guidelines for the Management of ST-Elevation Myocardial Infarction.**

In an effort to complete the "new" paramedic scope of practice items outlined by the State of Ohio, ***Initiation and Monitoring of Thrombolytic Therapy*** will also be presented at each class during the month. Please take time to read the attached material on thrombolytic therapy to help better prepare you for class.

I look forward to seeing all of you in the coming month of February. If you have any questions or comments please feel free to contact me.

Date	Time	Shift
February 5, 2013 (Tues)	1800 -2200	B
February 6, 2013 (Wed)	1300 – 1700	C
February 7, 2013 (Thurs)	0900 – 1300	A
February 12, 2013 (Tues)	1300 – 1700	C
February 13, 2013 (Wed)	1300 – 1700	A
February 14, 2013 (Thurs)	0900 – 1300	B
February 19, 2013 (Tues)	1800 – 2200	A
February 20, 2013 (Wed)	1300 – 1700	B
February 21, 2013 (Thurs)	0900 – 1300	C
February 26, 2013 (Tues)	0900 – 1300	B

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Thrombolytic Therapy for Acute Myocardial Infarction

Thrombolytic therapy is indicated in patients with evidence of ST-segment elevation MI (STEMI) or presumably new left bundle-branch block (LBBB) presenting within 12 hours of the onset of symptoms if there are no contraindications to fibrinolysis. Patients with STEMI usually have complete occlusion of an epicardial coronary vessel caused by an acute thrombotic obstruction.

Coronary atherosclerosis is a diffuse process characterized by segmental lesions called coronary plaques. The plaque ruptures, exposing the endothelial lining and allowing prothrombotic enzymes and molecular triggers to mix with the blood. Platelets are activated, and the coagulation cascade is amplified resulting in a thrombus that occludes the vessel, preventing the circulation of oxygenated blood. Irreversible ischemia-induced myocardial necrosis may occur within 20-60 minutes of occlusion.

The mainstay of treatment is reperfusion therapy involving either administration of fibrinolytics (pharmacologic reperfusion) or primary percutaneous coronary intervention (PCI) (mechanical reperfusion).

PCI performed within 90 minutes of patient arrival is superior to fibrinolysis with respect to combined endpoints of death, stroke, and reinfarction, but unfortunately, PCI is not widely available at acute care hospitals. Of the nearly 5000 acute care hospitals In the United States, 2200 have catheterization laboratories, and only 1200 of these (< 25%) are capable of performing PCI. Fewer than 10% of patients who are transferred for primary PCI achieve a first door-to-balloon time of less than 90 minutes.

Although primary PCI is the preferred therapy for STEMI, it has severe logistic restraints: treatment is delayed by patient transport, emergency department (ED) delay, and preparation of the catheterization laboratory. Furthermore, a skilled intervention team must be available 24 hours a day. Thrombolysis remains the treatment of choice in STEMI when primary PCI cannot be performed within 90 minutes.

In the 2007 STEMI Focused Update, the writing committee held that at 90 minutes after initiation of fibrinolysis, if there was less than 50% ST-segment resolution in the lead that showed the greatest degree of ST elevation at presentation, fibrinolytic therapy had likely failed to reperfuse the patient. If the judgment was made that fibrinolytic therapy had not resulted in reperfusion, PCI performed at that time was labeled rescue PCI. However, the best subsequent management of patients after fibrinolytic therapy remains unclear.

What are Thrombolytics?

Thrombolytics act on plasminogen, converting it into the active enzyme plasmin. Plasmin then “snips up” fibrin in the clot. As the clot breaks apart, blood flow is restored to the myocardium served by the thombosed coronary artery.

Thrombolytics can only effectively “dissolve” an intracoronary thrombus if they are used rapidly after the onset of thrombosis. After a few hours, the clot undergoes a hardening process, which makes it

resistant to breakdown by plasmin. Thus, delays in administering thrombolytics can reduce their effectiveness.

By opening up the thombosed coronary artery, thrombolytics speed healing of the infarcted myocardium. "Borderline" areas of ischemic cardiac tissue may be saved. Long-term cardiac function is improved. Both short-term and long-term risk of death is reduced.

How Do Thrombolytics Differ?

There are five thrombolytics currently used in the U.S. for myocardial infarction: streptokinase (Steptase), alteplase (Activase), anistreplase (Eminase), reteplase (Retavase), and tenecteplase (TNKase). For therapeutic purposes, these products should be regarded as identical in effectiveness, and identical in safety.

All thrombolytics yield the same success rate, with reperfusion of the ischemic myocardium occurring in about 75 percent of patients. The "accelerated" tPA protocol gives earlier reperfusion, but no difference in the final reperfusion rate.

The rate of reocclusion of the (formerly) thrombosed coronary artery is also similar for all thrombolytics, around 20 percent. The rate of reocclusion is reduced by giving aspirin. With tPA, the rate of reocclusion is further decreased with the use of heparin (the data is less clear for streptokinase and anistreplase).

The various thrombolytic agents also yield approximately the same rate, and type, of bleeding complications. About 5 percent of patients will have some problem with bleeding. Just over 1 percent of patients (one out of five who bleed) will have a serious episode of bleeding.

The most feared hemorrhagic complication is intracranial hemorrhage, which occurs with a rate of 0.5 – 1.0 percent. Because of this risk, thrombolytics are contraindicated in patients with history of stroke, brain tumor or AV malformations, or recent CNS surgery. However, some experts feel a history of stroke is only a contraindication if the stroke is recent – within the past two months. The rate of intracranial bleeding is higher with the "accelerated" tPA strategy.

Thrombolytics differ in site action. tPA acts on plasmin only at the site of the clot; streptokinase acts on plasmin systematically; while anistreplase acts on both circulating and clot-bound plasmin. However, this doesn't make any clinical difference, either in success rate or in complication rate. Tenecteplase is more fibrin-specific than tPA and has some resistance to plasminogen inhibitors, but again, this hasn't been shown to affect clinical outcomes.

Thrombolytics differ in serum half-life, but effects at the clot are similar. For example, tPA has a serum half-life of five minutes, but effects at the clot persist for hours. Anistreplase has a serum half-life of around 2 hours, while that of streptokinase is 20 minutes. The half-life of reteplase is 18 minutes; that of tenecteplase, 20 minutes.

The major **CLINICAL** difference between products is possible allergic reactions. Patients allergic to streptokinase may react to streptokinase or anistreplase. About 5 percent of patients given streptokinase will have some sort of allergic reaction. The rate of anaphylaxis is 0.1 percent (one per thousand patients).

The potential for allergy with streptokinase does **NOT** affect overall mortality or morbidity. However, some physicians prefer not to give either streptokinase or anistreplase to patients who have had streptokinase previously, because of the risk of severe allergic reaction.

Which Thrombolytic to Use?

The choice of "best" thrombolytic is a hotly debated question. Each physician must decide: Do I believe the outcomes to be similar enough that I'll go with a cheapstreptokinase? Or do I believe that earlier patency with alteplase or reteplase gives a substantial advantage?

The GUSTO study yielded one unequivocal result: it showed that giving heparin with tPA improves outcome. And like the studies before it, GUSTO showed that tPA has an increased risk of hemorrhagic stroke compared to streptokinase. Unique to the GUSTO study was the finding that tPA is superior for large anterior infarctions when given very early after onset of symptoms.

Reteplase offers "convenience in dosing" when compared to alteplase. Early data indicate that it may give earlier arterial patency than either tPA or streptokinase, but it has not been compared directly to alteplase for overall mortality and incidence of stroke.

Indications and Administration

First, the drug must be reconstituted. Tenecteplase and reteplase are ready in about one minute. For streptokinase or tPA, the typical time form physician order to administration is 12 to 15 minutes. In some hospitals, the delay can be 45 to 60 minutes for pharmacy preparation.

Complexity of administration differs. Tenecteplase is given as a 5-second IV bolus. Anistreplase can be given as a single IV push over two minutes. Reteplase is given as two bolus injections 30 minutes apart. Streptokinase and tPA must be given by infusion pump, requiring additional setup time. Streptokinase is given as a single infusion over 60 minutes. Under the accelerated 90 minute protocol, tPA is given as a small initial bolus, then at varying rates over 90 minutes.

Thrombolytics may be used for other situations, such as clotted dialysis fistula, pulmonary embolism, or DVT when appropriate. To order thrombolytics for myocardial infarction, you need only satisfy four conditions: (1) typical chest pain, (2) typical ST segment changes, (3) absence of contraindications, and (4) expected benefits are greater than the risk.

Criteria for Thrombolytic Therapy

A. Typical Chest pain
- Over 15 minutes
- Less than 6 hours
- Not responsive to nitroglycerin

B. Typical ECG Changes
- ST segment elevation in two or more contiguous leads of over 1mm in limb leads or 2mm in chest leads

C. Absence of major contraindications

D. Expected benefit greater than risk if "relative" contraindications are present

Thrombolytics can be started in the emergency room, in the field by paramedics, or even in the doctor's office. To wait for CCU admission or cardiology consultation decreases myocardial salvage.

Monitoring the Thrombolytic Patient

Take frequent vital signs and monitor with ECG all patients to whom you give thrombolytics. The patient should be admitted to a monitored hospital bed, with oxygen and IV. Reperfusion often occurs about one hour after thrombolytics are started. The patient should be monitored for signs of reperfusion. Serial CPK's and serial ECG's should be obtained. Factors that may indicate reperfusion are:

- **ü** Resolution of the chest pain is 80 percent accurate
- **ü** Resolution of ST segment elevation is 75 percent accurate
- **ü** Early "premature" peaking of CK is 50 percent accurate
- **ü** Arrhythmia (PVC's or brief V-Tach) often occurs as blood reaches ischemic myocardium

Pain relief and ST segment normalization together are highly accurate at predicting reperfusion. PVC's and runs of V-Tach often occur as the ischemic myocardium is reperfused, and (while not "evidence" that reperfusion has occurred) may serve as a marker of the time of reperfusion.
As blood reaches ischemic tissue, CK is washed out, causing dramatic peaking of CK earlier than would be expected. CK normally elevates four to six hours following infarction, with a peak at 24 hours. When reperfusion occurs, however, CK elevates in minutes, and peaks within a few hours. Some centers will draw CK levels every 15 minutes to monitor for evidence of reperfusion, but most will simply follow clinical status and serial ECG's. Even in patients with no signs of reperfusion, nearly 50 percent will have cleared the thrombus.

Other Factors in Therapy

Beta blockers are often given to decrease myocardial oxygen consumption, and to reduce the incidence and severity of reperfusion arrhythmia. Beta blockers reduce arrhythmias, although they haven't been clearly shown to improve acute-phase mortality. Beta blockade is part of most thrombolytic treatment protocols.

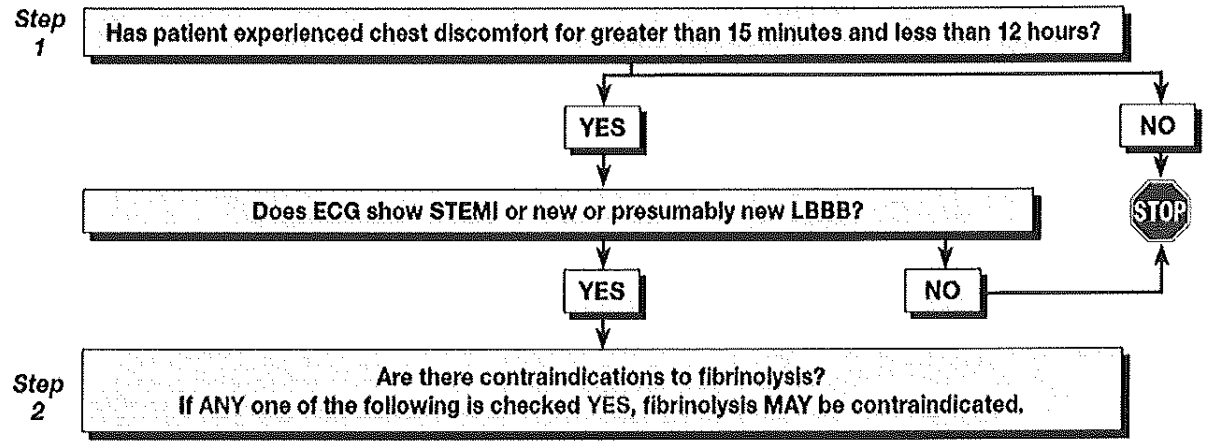
Low dose aspirin has been shown to decrease risk of rethrombosis. Give every MI patient chewable aspirin immediately, unless contraindicated.

Heparin may be given to prevent reformation of the thrombosis. Heparin is clearly helpful with tPA. The role and proper dosage of heparin have not been clearly established for streptokinase and anistreplase.

"Acute phase" cardiac catheterization is controversial. The MI patient can certainly be given thrombolytics in the small hospital with no "cath lab." Immediate coronary angioplasty should be considered for patients with large infarctions who fail to reperfuse. Angioplasty is also indicated for patients with contraindications to thrombolytics or those with cardiogenic shock.

Sample: Fibrinolytic (Thrombolytic) Checklist

***Note:** This checklist is intended only as a tool for the pre-hospital identification of patients with significant contraindication(s) to the administration of fibrinolytics in the acute ST elevation M.I. (STEMI) setting. It is not intended to be a comprehensive list of all factors to be considered prior to administration of these agents. Significant contraindications may warrant the triage of these patients to facilities capable of percutaneous intervention (PCI). This list can also be used to determine if a possible ischemic stoke victim, is a candidate for ischemic stroke reperfusion.



Systolic BP >180 to 200 mm Hg or diastolic BP >100 to 110 mm Hg	○ **YES**	○ NO
Right vs left arm systolic BP difference >15 mm Hg	○ **YES**	○ NO
History of structural central nervous system disease	○ **YES**	○ NO
Significant closed head/facial trauma within the previous 3 weeks	○ **YES**	○ NO
Stroke >3 hours or <3 months	○ **YES**	○ NO
Recent (within 2-4 weeks) major trauma, surgery (including laser eye surgery), GI/GU bleed	○ **YES**	○ NO
Any history of intracranial hemorrhage	○ **YES**	○ NO
Bleeding, clotting problem, or blood thinners	○ **YES**	○ NO
Pregnant female	○ **YES**	○ NO
Serious systemic disease (eg, advanced cancer, severe liver or kidney disease)	○ **YES**	○ NO

Step 3 — **Is patient at high risk?**
If ANY one of the following is checked YES, consider transfer to PCI facility.

Heart rate ≥100/min AND systolic BP <100 mm Hg	○ **YES**	○ NO
Pulmonary edema (rales)	○ **YES**	○ NO
Signs of shock (cool, clammy)	○ **YES**	○ NO
Contraindications to fibrinolytic therapy	○ **YES†**	○ NO
Required CPR	○ **YES**	○ NO

†Consider transport to primary PCI facility as destination hospital.

Receiving Physician/Hospital: _____ Time: _____
Paramedic No. _____ Signature: _____