

Guidelines for Treating STEMI: Case-Based Questions

As many as 25% of eligible patients presenting with STEMI do not receive any form of reperfusion therapy. The ACC/AHA guidelines highlight steps to improve coronary blood flow and reduce events in patients presenting with STEMI.

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ST-elevation myocardial infarctions (STEMIs) remain a significant health-care burden, with thousands of patients presenting to Canadian emergency departments each year.

The American College of Cardiology (ACC)/American Heart Association (AHA) Guidelines were published last year, reflecting recent advances in the management of STEMI patients. This all-encompassing document highlights discussions in management at the onset of STEMI, including:

- recognition,
- pre-hospital and emergency department (ED) management,
- in-hospital management,
- risk stratification,
- secondary prevention and
- long-term management.

The goals of therapy remain the same—restoration of blood flow in an occluded coronary artery in order to salvage myocardium and improve outcomes (e.g., death, re-infarction and recurrent ischemia). In those for whom successful reperfusion is not achieved, in-hospital mortality is two to three times that of those successfully reperfused.

As Boersma showed, the number of lives saved per thousand is directly related to the time from symptom onset to fibrinolytic therapy (Figure 1). Unfortunately, and of some concern, National Registry of Myocardial Infarction-4 (NRMI-4) data has shown that as many as 25% of eligible patients presenting with STEMI did not receive any form of reperfusion therapy.

Jethro's Case



Jethro is a 66-year-old man with hypertension. He is overweight, sedentary and smokes half-a-pack of cigarettes per day.

His lipids have been borderline in the past and he was recently prescribed

sublingual nitroglycerin for possible atypical angina. After taking three nitroglycerin over a period of half-an-hour, then waiting for another hour and a half, he presents to the emergency department (ED) (with continued retrosternal chest discomfort. (i.e., two hours post chest pain onset).

For more on Jethro, go to page 31.



Are there any new recommendations regarding advice to patients about when to present to an ED?

Previously, it had been commonplace to advise patients to present to the ED if chest discomfort had not resolved after taking two to three nitroglycerin, five minutes apart. The new guidelines suggest that patients call 911 five minutes after taking a *single* sublingual nitroglycerin if the pain does not resolve. Clearly, the intent is to enhance early contact with the medical system so as to optimize the times at which reperfusion therapies can be initiated.

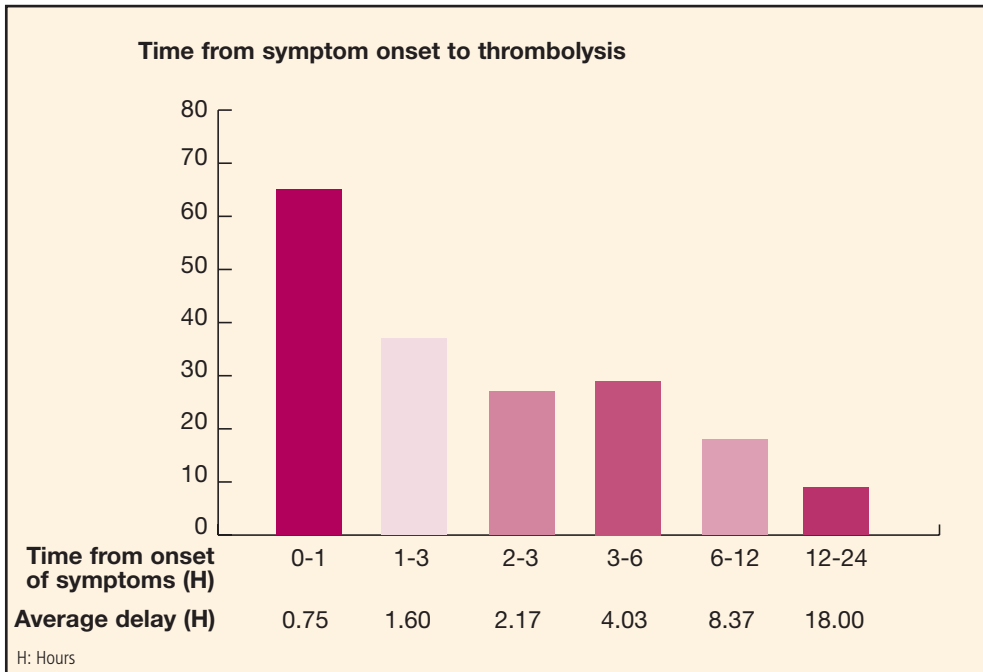


Figure 1. Boersma shows that the number of lives saved per 1,000 patients is directly related to the time from symptom onset to fibrinolytic therapy.



Are there any simple medications that can be given to Jethro to enhance reperfusion in this setting?

Most patients are advised to ingest 160 mg to 325 mg of chewable acetylsalicylic acid (ASA) as soon as possible after calling 911, or immediately upon arrival in the ED. Current ACC/AHA guidelines suggest clopidogrel for patients receiving thrombolytic therapy who are unable to take ASA because of hypersensitivity or major gastrointestinal intolerance. Now, many physicians feel that clopidogrel should be given in addition to ASA and continued for eight to 16 days after presentation, based on the overall relative and absolute risk reduction demonstrated in the CLopidogrel as an Adjunctive Reperfusion and TherapY (CLARITY) trial and CIOpidogrel and Metoprolol Myocardial Infarction Trial (COMMIT).



Should one type of heparin be used over another? If Jethro were 76 years old instead of 66, would it affect the decision?

The Guidelines don't advise one heparin over another. However, low molecular weight heparin may be used as an alternative to unfractionated heparin in the management of many conditions, including post-thrombolytic therapy in patients with STEMI. The utilization of low-molecular heparin has been adopted by some centres, but others express concern over evidence from the Assessment of the Safety and Efficacy of a New Thrombolytic regimen-3 (ASSENT-3) study that shows patients over age 75 who receive thrombolytic therapy and enoxaparin have an increased risk for bleeding. Three trials showed enhanced

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perfusion and less occlusion using low-molecular weight heparin. Our own current practice is to use enoxaparin in patients younger than age 75 and to use unfractionated heparin in those older than age 75.

? In light of data suggesting that primary coronary intervention (PCI) has advantages over thrombolytic therapy, should the treating physician withhold thrombolytics and transfer Jethro to the nearest centre?

Table 1 shows situations where one form of reperfusion therapy is favoured over the other. The Keely metanalysis (Figure 2) would suggest a definite benefit of PCI over thrombolysis in reduction of death, MI, stroke or all combined. However, the first problem with this metanalysis is that it includes several trials where the thrombolytic of choice was streptokinase. Once these trials are excluded, the differences are less apparent.

More on Jethro

Jethro has now been in the ED for approximately 20 minutes. A decision has been made, after giving him acetylsalicylic acid (ASA) and clopidogrel, to initiate more definite reperfusion therapy. His current location is a centre without cardiac catheterization lab facilities, but it is a short ambulance drive to a centre with the facilities.

If Jethro were to be transferred, there must not be a delay of greater than one hour. Nallamouthu demonstrated a decrease in the mortality advantage of PCI when PCI is delayed 60 minutes, compared to when a patient could have received a thrombolytic. A similar metanalysis to Keely's (Figure 3) demonstrated that, early after the onset of symptoms, there is no particular advantage of either form of reperfusion therapy, whereas later, PCI has an advantage.

As a result of these metanalyses and a multitude of studies, current ACC/AHA guidelines suggest that patients who present within three hours can be treated equally effectively with PCI and thrombolysis and those who present after three hours have an advantage with PCI. Jethro has arrived at the ED within the three-hour window and, therefore, can be given thrombolytic therapy with equal benefit as a patient who presented at a centre with PCI facilities.

Table 1 Preferred reperfusion therapies	
Fibrinolysis <i>Preferred when:</i>	Invasive strategy <i>Preferred when:</i>
<ul style="list-style-type: none"> • Patient presents early (three hours or less from symptom onset) • Delay to invasive strategy/ prolonged transfer: Door-to-balloon—door-to-needle time > one hour • No access to a skilled catheterization laboratory (invasive strategy not an option) 	<ul style="list-style-type: none"> • Patient presents late (three hours or greater from symptom onset) • Door-to-balloon—door-to-needle time < one hour • High-risk STEMI: Cardiogenic shock or Killip \geq three • Contraindications to fibrinolysis
STEMI: ST-elevation myocardial infarction	

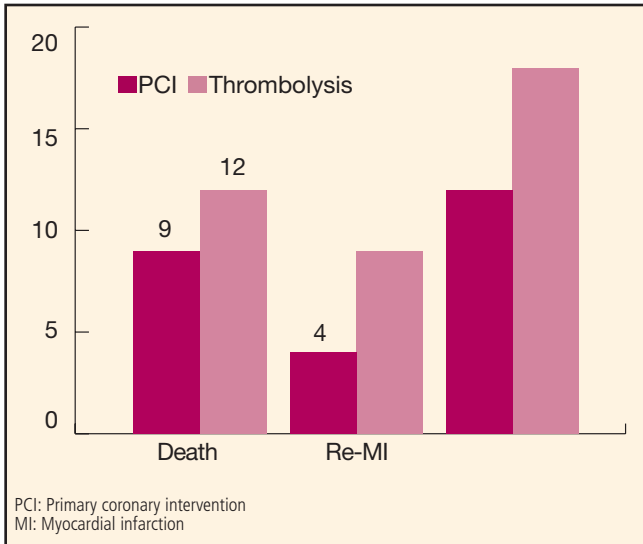


Figure 2. Keely meta-analysis: PCI vs. thrombolysis (23 trials).

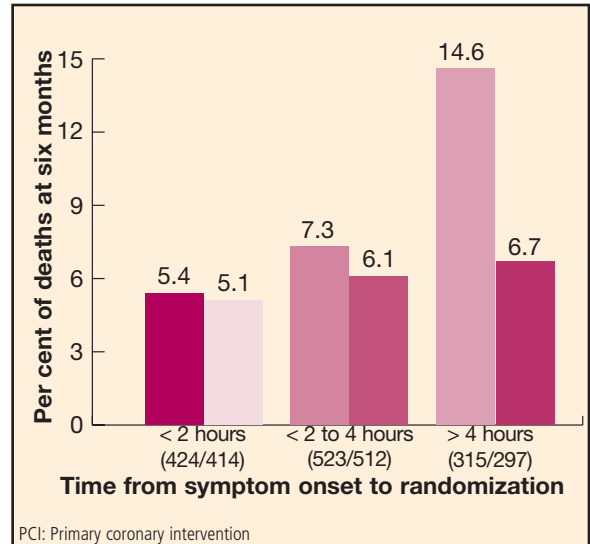


Figure 3. Time to treatment: PCI vs. thrombolysis (10 trials).

? **The DANAMI trial suggests that even transfer improves outcomes with PCI. Do you agree?**

The DANish trial in Acute Myocardial Infarction (DANAMI) found no difference in outcomes in patients who presented to non-PCI referral hospitals and were transferred to a PCI centre as compared to those who initially presented to PCI centres. Both PCI groups appeared to do better than the thrombolysis group.

However, there was a non-statistical difference in death

between both PCI groups and the thrombolysis group. Most of the benefit achieved was based on recurrent MI.

Biases of the study include a very low rate of rescue angioplasty in the patients treated with thrombolytic therapy and patients who failed to show evidence of reperfusion were given repeat thrombolytic therapy, known to increase the risk of bleeding and cerebrovascular accidents.

Also, the average transport time in the DANAMI trial was 30 minutes over an average distance of 50 kilometres—a total transport time of just over 90 minutes. Data from the NRMI-4 suggests that, in the US, only 5% of patients achieve a door-to-balloon time of less than 90 minutes; similar data is available in Canada.

The Guidelines suggest that hospitals should establish multi-disciplinary teams to develop guideline-based, institution-specific written protocols for triaging and managing patients who are seen in the pre-hospital setting or who present to the ED with symptoms suggestive of STEMI. It is felt that it is not possible to choose a superior reperfusion approach for all patients and all clinical settings at all times of the day.

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What is clear is that timely reperfusion remains critical and mortality and subsequent events are related to the early achievement of patency. Some simple measures to achieve early patency include:

- attempts at shortening the time between the patient's onset of chest pain and contact with the medical system,
- using chewable ASA,
- early clopidogrel loading and
- possibly considering enoxaparin.

The choice of reperfusion therapy will vary at different sites and in different cities. Recent and ongoing studies are examining the benefits of a facilitated approach—thrombolytic therapy followed by angioplasty—and the results appear promising.




Should Jethro be started on other therapies?

An oral beta-blocker should be administered as early as possible, unless otherwise contraindicated. An intravenous (IV) beta-blocker could be used if Jethro has hypertension or tachycardia in the absence of significant congestive heart failure.

IV nitroglycerin is indicated for the relief of ongoing chest discomfort, control of hypertension and/or management of congestive heart failure. Caution should be exercised in using nitrates when systolic blood pressure is less than 90 mmHg or when one suspects a right ventricular infarction. It should not be administered to patients who have received therapy for erectile dysfunction in the last 24 hours. Some studies have shown survival benefit when nitrates are prescribed for patients with anterior wall MIs. It is not necessary to continue nitrates beyond 48 hours and there is no evidence to support their long-term use in the absence of ongoing chest discomfort.

Risk stratification is now being performed earlier and subsequent therapies need not be initiated in the first 24 hours. It is important

that patients be continued on ASA indefinitely, clopidogrel for a period of one to two weeks and clearly longer if they undergo coronary intervention. All patients with acute MIs should be discharged on an angiotensin-converting enzyme (ACE) inhibitor unless intolerant. Patients who have clinical or radiologic evidence of congestive heart failure or who have an ejection fraction of less than 40% and are intolerant of an ACE inhibitor should be prescribed an angiotensin II receptor blocker (ARB).

More data would be required to prescribe an ARB in ACE inhibitor-intolerant patients who do not have decreased ventricular function or heart failure. Patients should be continued on oral beta-blockers and will need aggressive management of lipids to achieve low-density lipoprotein targets of at least 2.5 mmol/L. 

Resources

1. Heart and Stroke Foundation of Canada: The Changing Face of Heart Disease and Stroke in Canada. Ottawa, Canada; 1999.
2. Dahlöf B, Devereux RB, Kjeldsen SE, et al: Cardiovascular morbidity and mortality in the Losartan Intervention for end point reduction in hypertension study (LIFE): A randomized trial against atenolol. *Lancet* 2002; 359(9311):995-1003.