

# *ST-Segment Elevation AMI:*

## THE FIRST 12 HOURS

Acute myocardial infarction (AMI) accounts for half of the deaths due to ischemic heart disease and is associated with significant use of resources. Because time from symptom onset is critical, efforts must be made to recognize AMI and prevent complications.

By Michel Le May, MD, FRCPC, FACC



### *Introduction*

Ischemic heart disease remains the greatest cause of mortality in Canada. Acute myocardial infarction (AMI) accounts for half of the deaths due to this disease and is associated with significant use of resources. Guidelines for the treatment of AMI have been provided

by the Canadian Cardiovascular Society<sup>1</sup> and more recently, by the American Heart Association/American College of Cardiology.<sup>2</sup> The purpose of this review is to highlight important features of the early management of ST-segment elevation AMI and to give some insights into new directions for the treatment of this medical emergency.

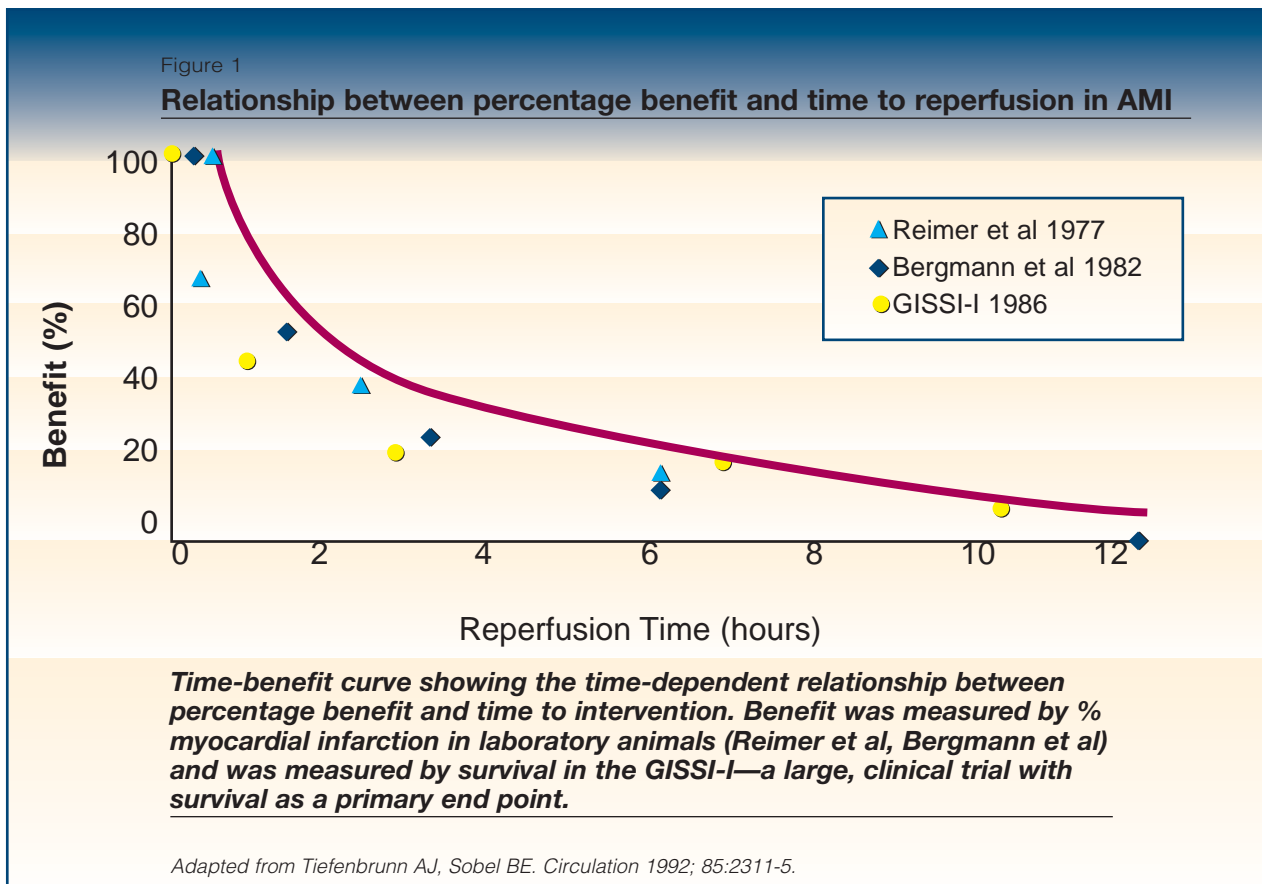
### **About the author...**



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### *Definitions*

Rupture of an atherosclerotic plaque is the primary factor responsible for acute coronary syndromes. Plaque rupture can trigger a cascade of rheologic events involving platelets and coagulation factors leading to occlusive thrombosis of the coronary artery and resulting in downstream myocardial cell death. The presence of ST-segment elevation on the electrocardiogram (ECG) usually indicates trans-



mural myocardial ischemia caused by complete occlusion of the coronary artery. If this occlusion is sustained, myocardial necrosis results and Q-waves commonly appear later on the ECG. If the occlusion is incomplete or non-sustained, then flow is interrupted only partly or momentarily, resulting in non-transmural ischemia. The clinical presentation is unstable angina or a non ST-segment elevation AMI, and Q-waves do not usually develop. The correlation between transmural necrosis and the development of Q-waves on the ECG is imperfect. Previously, AMI was classified as transmural or non-transmural. Contemporarily, an ECG classification is preferred. During the first 12 hours of symptom onset, AMI is classified as ST or non-ST-segment elevation. This distinction is important, since current trials indicate that only patients with ST-segment elevation benefit from an immediate reperfusion strategy. After 12

hours of symptom onset, AMI can be further classified as Q or non-Q wave infarction (“transmural” or “non-transmural”).

### *The Most Critical Element: Time*

Delay in treatment decreases the likelihood of survival of patients with AMI. Timely intervention starts with placement of a 911 call, followed by the prompt arrival of trained paramedics, accurate diagnosis in the emergency department and early reperfusion with thrombolysis or percutaneous coronary angioplasty.

Half of the deaths due to AMI occur less than one hour after the onset of symptoms, and the most important contributing mechanism is ventricular fibrillation. The availability of trained paramedics equipped with automated external defibrillators can save lives.

## ST-Segment Elevation AMI

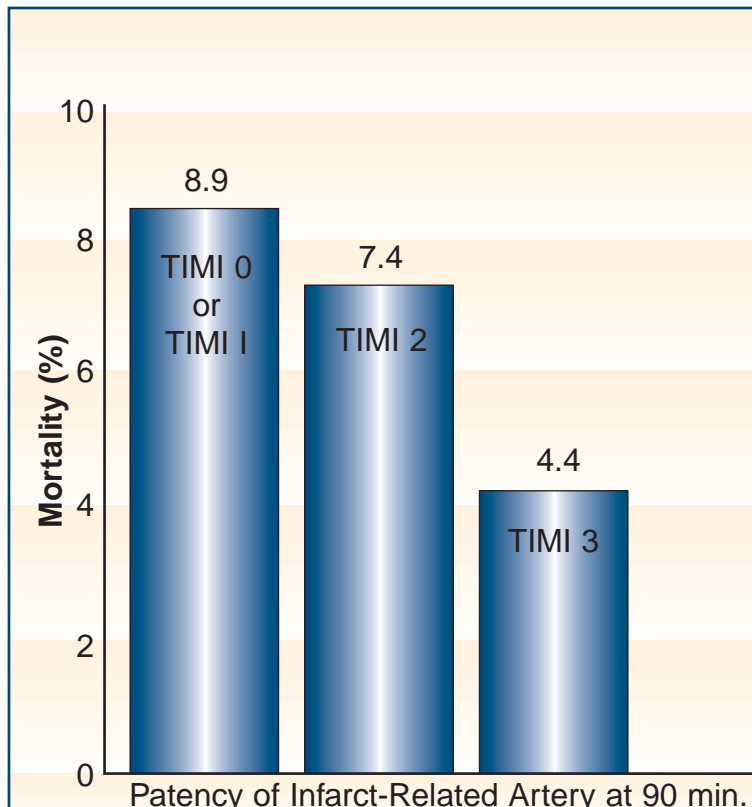


Figure 2

**Thirty day mortality vs. 90-minute TIMI grade flow in GUSTO-1 angiographic substudy (GUSTO, NEJM 1993; 329:1615-22): TIMI grade 0 or 1 vs. TIMI grade 3,  $p+0.0009$ ; TIMI grade 2 vs. TIMI grade 3,  $p+0.08$ .**

Abrupt cessation of coronary flow leads to irreversible injury to myocardial cells. The extent of myocardial necrosis is time dependent, with most of the damage occurring within the first two to four hours. Myocardial salvage can occur if flow is restored promptly.

Thrombolysis improves survival when given within 12 hours of the onset of symptoms. Figure 1 depicts the relationship between benefit and time, from symptom onset to reperfusion. The magnitude of benefit is greatest when reperfusion is established early. The reduction in mortality may be as high as 30% to 50% for patients receiving thrombolysis within six hours of the onset of chest pain,

compared to only 7.5% for patients treated between 6 to 12 hours of the onset of symptoms.

Furthermore, to improve left ventricular (LV) function and survival, coronary flow must be restored not only early, but also to a completely normal level. The Thrombolysis In Myocardial Infarction (TIMI) investigators developed an angiographic score to grade coronary flow in patients with AMI. TIMI grade 0-1 flow represents, essentially, no flow in a completely occluded infarct-related artery. TIMI-2 flow means flow is present but sluggish; and TIMI-3 means flow is normal. The Global Utilization of Streptokinase and t-PA for Occluded coronary arteries (GUSTO-1) trial<sup>3</sup> clearly demonstrated the important relationship between survival and the early restoration of TIMI grade 3 flow. (Figure 2)

### *Recognition and Diagnosis of AMI*

Because time from symptom onset is critical for survival, efforts must be made to recognize the problem early to prevent complications. The general public must become aware of the symptoms or signs that may suggest AMI. Then a 911 emergency call may be initiated without delay to ensure rapid arrival of trained paramedics and rapid transport to the nearest hospital. In the emergency room, vital signs, a 12-lead ECG, and a targeted history should be obtained immediately. The pain of AMI is usually severe and may be associated with dyspnea or nausea. Elderly patients may present with dyspnea alone, without ischemic chest discomfort. A fourth heart sound is common, reflecting LV stiffness. The presence of a third heart sound is worrisome as it indicates significant LV dysfunction and is associated with a worse outcome. Crackles in the lung fields

Table 1

**Killip classification of patients with acute myocardial infarction**

<b>Class</b>	<b>Clinical Findings</b>	<b>% of patients</b>	<b>Hospital mortality rate, %*</b>
I	No rales; no S-3	30 to 40	2 to 4
IIa	Rales <50% of lungs; no S-3	20 to 30	3 to 5
IIb	Rales <50% of lungs; S-3 present	10 to 20	10 to 15
III	Rales >50% of lungs; Pulmonary edema	5 to 10	45
IV	Shock	10	80 to 100

\* mortality reported in the pre-thrombolytic era

may also be due to heart failure. The Killip classification is a useful bedside method to assess prognosis. The data provided in Table 1 was collected in the pre-thrombolysis era. However, as demonstrated in the GUSTO-1 study, the relationship between higher Killip class and mortality persists in the thrombolytic era. The jugular venous pressure may be elevated in patients presenting with inferior wall AMI associated with right ventricular (RV) infarction, and with inspiration, the jugular venous pressure may be seen to increase paradoxically (Kussmaul's sign). If primary angioplasty is a consideration, arterial access will be needed, and documentation of adequate peripheral pulses, therefore, is important.



Pericarditis and aortic dissection may present with chest pain and are contraindications to thrombolysis. The pain of pericarditis is typically pleuritic; while pericarditis complicates AMI in 5 to 10% of patients, its presentation is usually absent in the first 12 hours. The presence of a pericardial rub or the characteristic diffuse ST-segment elevation on a 12-lead ECG confirms the diagnosis of pericarditis. The pain of aortic dissection may migrate from the anterior chest to the back and is usually worse at inception. On occasion, the aortic tear can extend into a coronary artery, obstruct flow and cause AMI. The chest x-ray may show a widened mediastinum and the diagnosis is confirmed by



### High-risk patients can be quickly identified by risk stratification.

trans-esophageal echocardiography or by computerized tomography.

The paramedics providing expeditious recognition of AMI may have obtained the 12 lead ECG in the field. If not available upon arrival to the emergency department, the ECG should be obtained within 5 to 10 minutes and promptly reviewed by the staff physician. ST-segment elevation AMI is defined as ST-segment elevation of  $>1$  mm (0.1 mV) in two or more contiguous electrocardiographic leads. The presence of a presumably new left bundle-branch-block in a patient with symptoms compatible with ischemia, constitutes evidence of AMI. ST-segment elevation in the right precordial leads (V3R, V4R) helps to confirm RV infarction.

#### *Risk Stratification*

In the GUSTO-1 study, multi-variable analysis identified age as the most significant factor influencing 30-day mortality, with rates of 1.1% in patients  $<45$  years and 20.5% in patients  $>75$  years. Other factors most signifi-

cantly associated with increased mortality were systolic blood pressure ( $<100$  mm Hg), higher Killip class, heart rate  $>100$  bpm, and anterior AMI. The mortality for anterior AMI was 9.9% versus 5.0% for inferior AMI. Further analysis in patients with inferior AMI revealed the magnitude of precordial ST-segment depression (sum of leads V1 to V6) adds significant independent prognostic information. The risk of 30-day mortality increases by 36% for every 0.5 mV of precordial ST-segment depression. A detailed analysis from the Gruppo Italiano per lo Studio della Streptochinasi nell'Infarto miocardico (GISSI-I) trial<sup>4</sup> shows the number of leads with ST-segment elevation is more important than infarction location. Mortality ranged from 6.4% for patients with ischemic changes in two or three leads, up to 21.7% for patients with changes in eight to nine leads.

The height of the ST-segment elevation has been correlated with both large infarction and poor survival. Patients with high ST-segment elevation on admission (*e.g.* the sum of ST-segment elevation  $>20$  mm) have a mortality of 10% within 30 days of presentation, compared

Table 2

**Contraindications to Thrombolysis in AMI****Absolute**

- Aortic dissection
- Acute pericarditis
- Active bleeding (does not include menses)
- Previous hemorrhagic stroke at any time; recent non-hemorrhagic stroke

**Relative**

- Non-hemorrhagic stroke >1 year
- Known intracerebral disease (AV malformation, malignancy)
- Severe uncontrolled hypertension (systolic BP>200 mm Hg) and/or diastolic BP>120)
- Major trauma <2 weeks
- Prolonged (>10 min) CPR
- Major surgery < 3 weeks
- Pregnancy
- Current use of anticoagulants
- Bleeding diathesis
- Gastrointestinal hemorrhage <6 mos.
- Allergy to streptokinase
- Non-compressible vascular puncture

to 2.3% in patients with low ST- segment elevation, sums of 12 mm or less.

The presence of cardiogenic shock defined as sustained hypotension (systolic blood pressure <90 mm Hg) or the need for intravenous inotropes and/or intra-aortic balloon counterpulsation to support the blood pressure, is associated with very poor survival. These patients are best managed by prompt referral to tertiary centres equipped with a catheterization facility, such that revascularization can be done by either percutaneous transluminal coronary angioplasty or surgery. Thrombolysis for cardiogenic shock is generally much less effective, but should be considered when significant transportation delays (greater than one hour) are anticipated.

### *Treatment and Management*

#### **Acetylsalicylic acid (ASA)**

Once the diagnosis of AMI is suspected, all patients should receive 160 to 325 mg chewable ASA. The Second International Study of Infarct Survival (ISIS-2)<sup>5</sup> demonstrated a 23% reduction in mortality at the 35-day follow-up. ASA can be given by the paramedics or immediately upon arrival to the emergency department.

#### **Thrombolytic therapy**

Reperfusion of the obstructed coronary artery achieved with thrombolysis leads to improved survival. Criteria for thrombolysis are:

- 1) Ischemic chest discomfort >20 minutes

- duration with onset <12 hours, **and**;
- 2) ST-segment elevation >0.1mV (1 mm) in two or more contiguous leads, **or**;
  - 3) New or presumably new left bundle-branch-block.

Patients presenting with ST-segment depression generally do not benefit from thrombolysis. Contraindications to thrombolysis are listed in Table 2.

Thrombolysis is available in any community hospital and the current goal is to achieve a door-to-needle time of less than 30 minutes. The mortality from AMI in patients >75 years old is much higher. The relative survival benefit of thrombolysis in the elderly is present, albeit smaller. Advanced age, hypertension, and low body weight (<60 kg) augment the risk of intracranial hemorrhage. Nonetheless, except for very small AMI, thrombolysis should not be withheld unless a contraindication is present.

Thrombolytic therapy does not always achieve complete reperfusion of the infarct-related artery. In the GUSTO-1 study<sup>3</sup>, TIMI grade 3 flow was achieved in 54% of patients with accelerated t-PA, compared to only 33% with streptokinase. Reteplase (r-PA) achieves survival benefits comparable to t-PA<sup>6</sup>, and is currently available as a double bolus intravenous treatment. Tenecteplase (TNK) gives equivalent survival benefits to alteplase (t-PA)<sup>7</sup>, and is given as a single weight adjusted bolus. This agent is currently available in the United States and is in the approval process for use in Canada. Intravenous heparin must be used for at least 48 hours after administration of plasminogen activators to prevent early reocclusion.

Regardless of the specific thrombolytic agent considered, it is always better to give any thrombolytic agent early than to give the best thrombolytic agent late. Unfortunately, thrombolysis is used in only 50% of eligible patients. Strategies to improve diagnosis, reduce “door-to-needle” time, and increase the availability of thrombolysis, are needed.

### *Primary Angioplasty*

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Percutaneous transluminal coronary angioplasty in the setting of AMI (primary angioplasty) provides equivalent, if not superior, clinical benefits, compared to thrombolysis. It should be considered as an alternative when patients have important contraindications to thrombolysis (e.g. recent stroke, recent surgery, active bleeding problem). Also, in patients presenting with cardiogenic shock, thrombolysis has not been associated with significant clinical benefit, and primary angioplasty is often the preferred option. Primary bypass surgery is occasionally another option in the context of severe left main disease, or failed angioplasty. As for thrombolysis, time to reperfusion with primary angioplasty is critical. A short symptom onset to balloon inflation time is associated with a more favorable prognosis. Ideally, the door to first balloon inflation time should be under 90 minutes.

Rescue angioplasty should be considered in those patients in which evidence suggests failure of thrombolysis. For example:

- 1) Unabated chest pain associated with persistent ST-segment elevation two hours after initiation of thrombolysis.
- 2) Deteriorating hemodynamic status.
- 3) Reinfarction.

Recently, we have demonstrated superior clinical benefits of stent implantation in the infarct-related artery (primary stenting) over thrombolysis with accelerated t-PA.<sup>8</sup> In centers where facilities and experienced interventionists are available, primary stenting offers an attractive alternative to thrombolysis.

### *Beta-adrenergic Blockers*

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Intravenous beta-adrenergic blockers also improve survival in AMI. Contraindications to beta-adrenergic blockers include:

- Bradycardia;

- Heart block;
- Moderate to severe heart failure;
- Asthma, and;
- Severe chronic obstructive pulmonary disease.

Metoprolol can be given as 5 mg IV every five minutes, to a maximum of 15 mg, followed by oral therapy (50 to 100 mg BID).

### *Other concomitant therapy*


Nitroglycerin given sublingually by the paramedics or in the emergency department helps reduce ischemic chest pain by vasodilatation of the coronary arteries and the venous capacitance (preload). Following its administration, complete resolution of pain and of ST-elevation suggests a diagnosis of coronary spasm. When RV infarction is present, nitroglycerin should be avoided, or used with caution, as the RV cardiac output is very preload-dependent. Angiotensin-converting enzyme inhibitors given orally within 24 hours of AMI provide an additional small survival benefit. To avoid confounding variables associated with hypotension, the author usually starts ACE-inhibitors after 12 hours, unless hypertension is present.

### *Future Directions*

Several trials are currently under way to determine if combination treatment will improve angiographic or clinical outcomes of AMI. The GUSTO IV ST-elevation AMI trial is a large phase-3 randomized study designed to compare survival in patients treated with thrombolysis alone (reteplase) *versus* half-dose reteplase plus abciximab, a platelet glycoprotein receptor antagonist. Recruitment is complete, and results will be available in the next few months.

The CAPITAL AMI study, a local multi-centre study to be conducted in Ottawa,

Ontario, starting in June 2001, will compare Combined Angioplasty and Pharmacological Intervention *versus* Thrombolysis Alone in acute myocardial infarction. Patients with extensive AMI will be randomized in local hospitals and will receive TNK as a single intravenous bolus. Once the TNK bolus is given, patients randomized to the combined arm will be transported immediately to the catheterization facility at the Ottawa Heart Institute for angioplasty. Clinical outcomes and cost-effectiveness will be assessed.

Future directions in the management of AMI may include routine acquisition of the ECG by trained paramedics with improved computer ECG interpretations. With appropriate guidelines/algorithms to screen patients appropriately, bolus thrombolytic therapy may be given in the field, achieving ultra-short symptom-to-needle times and, hopefully, improved survival. 

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