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Acute Myocardial Infarction and Coronary Syndromes: Optimizing Selection of Reperfusion and Revascularization Therapies in the ED

Part I: Fibrinolysis, Procedural Coronary Intervention (PCI), and the Central Role of the Low Molecular Weight Heparin, Enoxaparin, in Fibrinolysis-Mediated Myocardial Reperfusion

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Over the past decade, there have been impressive reductions in mortality, length of hospital stay, and reinfarction reported in large-scale studies of patients with acute myocardial infarction (AMI). Despite these advances, substantial challenges remain in identifying the precise combination and dosing of therapeutic agents—among them fibrinolytics; low molecular weight heparins (LMWHs) such as enoxaparin and unfractionated heparin (UFH); and GP IIb/IIIa inhibitors—that will maximize outcomes while minimizing drug-related adverse events in patients with ST-elevation myocardial infarction (MI).

When one adds the various pharmacological options; possible drug combinations; and myriad procedural, interventional approaches (e.g., angioplasty and stenting) that are available for establishing coronary reperfusion, the decision-making process for cardiologists, emergency physicians, and intensivists becomes even more difficult. Regardless of the modality used to establish reperfusion, there are a number of pathophysiological and clinical issues that must be factored into the efficacy and safety equation when evaluating the optimum medical approaches to AMI management; these include: suboptimal macroperfusion and microperfusion, recurrent ischemia, reinfarction, and intracranial hemorrhage.

What also is clear is that antithrombin agents, especially LMWHs, have continued to play a central—and now an even expanded—role in pharmacological reperfusion therapy for AMI. Until recently, UFH and aspirin, along with a fibrinolytic agent, routinely were administered to most patients with acute coronary ischemia. However,

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two recent landmark trials (Assessment of the Safety of a New Thrombolytic-3 [ASSENT-3] and ENTIRE) support a pivotal role for the LMWH enoxaparin in the setting of fibrinolysis.[1] Unlike UFH, enoxaparin has more predictable kinetics, is less protein-bound, has less potential for platelet activation, and requires no monitoring; this is a combination of benefits that provides a strong rationale for achieving potentially better outcomes when this LMWH is given in combination with fibrinolytic agents.

The track record of enoxaparin's success—and compared to UFH, its superiority—in unstable angina and non-ST elevation MI has been impressive, and therefore, the rapidly evolving story of its outcome-enhancing role in ST-elevation MI should come as no surprise to clinicians who follow reperfusion strategies. Most previous studies comparing enoxaparin to UFH in unstable angina have demonstrated either less reocclusion, enhanced late patency of the infarct-related vessel, or a reduction in reinfarction rate when compared with UFH. The superior outcomes with enoxaparin vs. UFH across the entire spectrum of acute coronary syndromes (ACS), including, most recently, its value in ST-elevation MI as reported in ASSENT-3, have elevated this antithrombin agent to a prominent position among pharmacological modalities used to manage acute coronary ischemia.

As would be expected, glycoprotein GP IIb/IIIa inhibitors also have undergone intensive scrutiny, and in the case of this therapeutic class, the results have been mixed in patients not requiring procedural coronary intervention (PCI), but have been very favorable in patients requiring PCI, especially in the case of coronary stent insertion. Pilot studies with platelet glycoprotein GP IIb/IIIa inhibitors and reduced-dose fibrinolytic agents have shown enhanced patency of the epicardial infarct-related artery, and signs of improved tissue reperfusion. The phase III Global Use of Strategies to Open Occluded Coronary Arteries (GUSTO)-V trial demonstrated a reduction in ischemic complications of AMI with half-dose rPA and abciximab, as compared with full-dose reteplase.[2] The GUSTO-V trial, however, failed to show a significant reduction in 30-day mortality, and there was a significant increase in non-cerebral bleeding complications; this offset potential benefits and dampened enthusiasm for an imminent paradigm shift that routinely would include abciximab as a workhorse drug in fibrinolytic protocols in the absence of PCI.

Although fibrinolysis is widely available and has demonstrated its ability to improve coronary flow, limit infarct size, and improve survival in AMI patients, many individuals with acute infarction are not considered suitable candidates for such treatment. Patients with absolute or relative contraindications to fibrinolytic therapy, cardiogenic shock, non-ST elevation MI (NSTEMI), and/or unstable angina may be ineligible for fibrinolytic therapy. The requirement of administering prompt reperfusion therapy to these patients, as well as the other limitations of fibrinolytic therapy, have led many clinicians to advocate PCI as the primary therapy and treatment of choice for AMI.

PCI, which may include percutaneous transluminal coronary angioplasty (PTCA) or coronary stenting, has many theoretical and practical advantages over fibrinolysis and is becoming the preferred strategy for most patients with AMI. First, there is a larger patient eligibility pool for PCI, a lower risk of intracranial bleeding, and a significantly higher initial reperfusion rate. This strategy always affords earlier definition of coronary artery anatomy and the ability to risk stratify patients, thereby permitting rapid triage to surgical intervention when indicated.

Several trials of various sizes comparing primary PCI with fibrinolysis have been reported in the past 10 years. Interventions in the early trials were performed using PTCA, prior to the current widespread use of coronary stents. Despite a clear and consistent benefit of primary PTCA in restoring patency of the infarct-related artery, differences in mortality in the individual trials have been difficult to evaluate due to small sample sizes and differences in study design, patient selection, and medical therapy. However, recent trials comparing coronary stenting to

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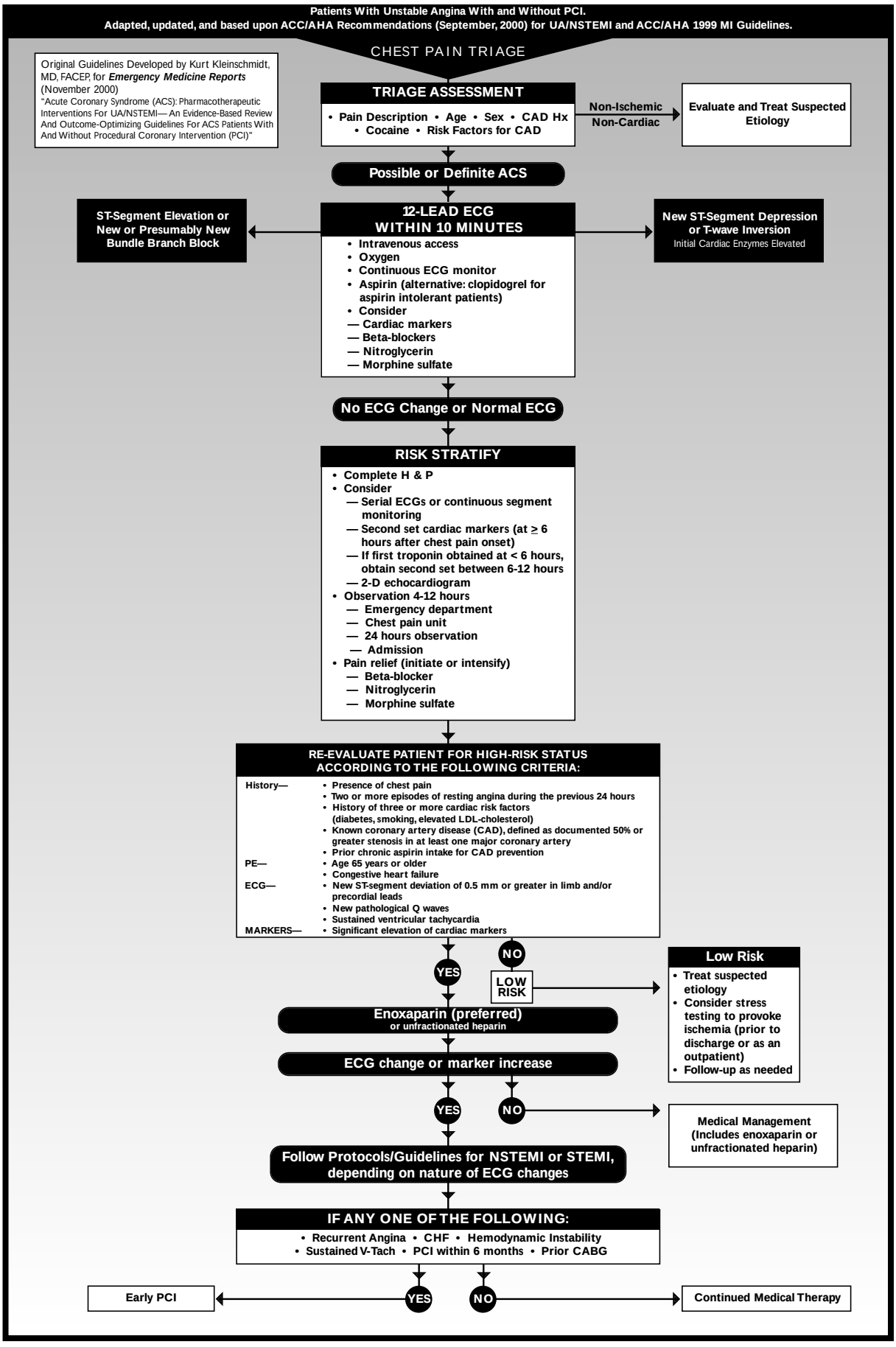
Figure 1. Guidelines for Effective Management of Unstable Angina



fibrinolysis have been more definitive in clarifying the superiority of procedural techniques in the management of appropriately risk-stratified patients with ACS.[3]

With these clinical controversies and treatment options in clear focus, the authors of this landmark review and its accompanying protocols critically evaluate recent clinical trials and outline an evidence-based strategy that employs pharmacological and/or procedural interventions; the indicated interventions are based on risk-group stratification for maximizing outcomes in patients with ST-elevation AMI.

— The Editor

Introduction

A wide range of mechanical and pharmacological options are available for restoring perfusion in coronary arteries that have been occluded by thrombosis in the setting of AMI. These include: 1) PCI (stenting and/or angioplasty); 2) primary fibrinolysis which may include some combination of a fibrinolytic agent, an anticoagulant, and aspirin; or 3) fibrinolysis-facilitated mechanical reperfusion (i.e., pretreatment with a fibrin-specific agent or some combination of a fibrin-specific agent and GP IIb/IIIa platelet antagonist followed by PCI).

Determining which of the aforementioned approaches is appropriate for any given patient can be difficult, and requires a multifactorial assessment. *(See Table 1.)* In this regard, the optimal approach for establishing coronary reperfusion after myocardial infarction depends on a number of clinical factors, among them: patient eligibility for specific interventions (medical vs procedural) based on risk stratification; adherence to risk-stratification protocols; availability of institutional resources for performing interventional techniques; availability of cardiologists with sufficient experience in transcutaneous coronary reperfusion techniques; the ability to provide prompt patient transfer to another hospital for those who may require PCI; and the presence of exclusionary and inclusionary factors that determine patient eligibility for fibrinolysis.

The key point is that selection of a reperfusion strategy is a fluid process that must account for myriad patient, institutional, and risk factors to yield optimal outcomes. See Figures 1-4, in which protocols for managing the spectrum of ACS (unstable angina, non ST-elevation MI, and ST-elevation MI) are presented.

Although the guidelines presented in this comprehensive review prioritize some strategies and agents over others, the dominant approach for a particular patient type identified in the guidelines may not always be the most suitable strategy if institutional, timing, or physician factors are not synchronized with the implementation of a specific intervention. Accordingly, clinical judgment should prevail when applying guidelines articulated in this review.

Fibrinolytic Therapy: The Current Landscape

In appropriately selected patients with AMI, early administration of fibrinolytic agents reduces mortality and is associated with improved short- and long-term clinical outcomes. From a pathophysiological perspective, prompt restoration of patency in the infarct-related artery reduces infarct size and minimizes the extent of myocardial damage, preserves left ventricular function, reduces morbidity, and prolongs survival. Compared to standard therapy, fibrinolysis is associated with a 21% reduction in 30-day mortality.[3] However, these agents also are associated with intracranial hemorrhage in about 0.5-0.9% of patients. In addition, only 30-60% of patients achieve TIMI 3 (normal) flow in the affected epicardial artery within 90 minutes.[3] Because of these drawbacks, safer and more effective fibrinolytic therapies have been developed through bioengineering techniques on the tPA molecule. In addition, the role of combination therapy with adjunctive agents, such as enoxaparin and GP IIb/IIIa inhibitors, is emerging.

Table 1. A Comparison of the Pros and Cons of Thrombolysis and Primary Angioplasty in the Patient with AMI

THROMBOLYTIC	PTCA
• Immediately available	• Few exclusions
• No operator expertise	• Very reasonable outcome
• Proven track record	• Better initial flow
	• Fewer bleeding complications
• *Many exclusions*	• Definition of anatomy
• *More frequent bleeding complications*	• *Not immediately available*
	• *Operator expertise*

Mechanism and Efficacy. From an outcome-effectiveness perspective, it should be stressed that mortality is affected by factors other than epicardial vessel flow. In this regard, reperfusion at the tissue level may be a critical factor in myocardial salvage, and this does not necessarily correlate with epicardial vessel flow. Patients with documented TIMI 3 epicardial flow but poor TIMI myocardial perfusion (TMP) grades (TMP 0 or 1) had a higher mortality rate (5.4%) than those patients with adequate (TMP grade 2 flow) or complete tissue perfusion (TMP grade 3 flow), 2.9% and 0.7%, respectively.[4] Therefore, although survival in studies has been correlated with epicardial vessel flow, there still is still much to be deciphered about perfusion characteristics and predictors of mortality. *(See Figure 5.)*

The ideal fibrinolytic agent provides rapid lysis, enhances tissue-level perfusion, reduces intracranial and systemic hemorrhage, has a long half-life enabling single-bolus administration, has no antigenicity, and has a low reocclusion rate. Enhanced fibrin specificity also is desirable because it permits preferential activation of fibrin-bound plasminogen at the clot surface; this has the potential to increase patency and produce higher initial patency rates, and may be associated with fewer bleeding complications. Greater fibrin specificity also decreases activation of circulating plasminogen and degradation of fibrinogen, resulting in less bleeding and reducing the need for transfusion. Plasminogen activator inhibitor-1 (PAI-1) inhibits fibrinolysis. Greater resistance to the action of PAI-1 would increase the potency of fibrinolytic agents.

Outcome-Optimizing Pharmacological Combinations. Fibrinolytic therapy unequivocally improves survival in patients

presenting with ST-segment elevation AMI. Re-establishing perfusion in the infarct-related coronary artery with the use of fibrinolytic therapy—in essence, reopening the infarct-related artery—increases the opportunity to salvage the ischemic myocardium and, consequently, reduces morbidity and mortality.

Three megatrials comparing tPA to streptokinase have been published. The Gruppo Italiano per lo Studio della Sopravvivenza nell Infarto Miocardico (GISSI)-2 trial[5] and the closely related International Study Group[6] compared a 100 mg infusion of tPA over three hours to streptokinase with or without heparin. The GISSI-2 was the first large-scale mortality trial directly comparing tPA and streptokinase in patients with AMI. The investigators found no difference in mortality between the two treatment groups. More strokes were reported with tPA than with streptokinase (1.3% vs 1%) in the International Study, yet the frequency of confirmed hemorrhagic stroke was similar for both agents. Similar results were found in the Third International Study of Infarct Survival (ISIS-3) trial,[7] the next fibrinolytic megatrial, which compared tPA, streptokinase, and APSAC in approximately 40,000 patients. In marked contrast to current practice, the inclusion criteria allowed entry up to 24 hours after symptom onset yet did not require diagnostic electrocardiographic change. A significant difference in both 35-day mortality and intracerebral hemorrhage was not found.[7]

Vascular Patency and Outcomes. Current fibrinolytic practice was highly affected by the results of the Global Use of Streptokinase and tPA for Occluded Coronary Arteries (GUSTO-I) trial.[8] The purpose of the GUSTO-I trial was to test the hypothesis that early and sustained infarct-vessel patency was associated with better survival rates in patients with AMI.[7] More than 41,000 patients were randomized to four different fibrinolytic strategies: accelerated tPA given over 90 minutes plus IV heparin; a combination of streptokinase plus a reduced dose of tPA along with IV heparin; and two different control groups (streptokinase plus subcutaneous heparin and streptokinase plus IV heparin). Unlike previous trials, tPA was given in a more aggressive, front-loaded 90-minute infusion, which was referred to as the "accelerated" regimen.

In addition to the primary end point of 30-day mortality, the GUSTO investigators explored the relationship between coronary artery patency and degree of normalization of flow in an angiographic substudy; this portion of the larger trial was designed to determine the relationship between early coronary artery patency and outcome. In this trial, accelerated tPA, administered with intravenous heparin, significantly reduced 30-day mortality by 15% as compared to streptokinase with either form of heparin, or the combination of tPA and streptokinase with intravenous heparin. The benefit was highly consistent across virtually all subgroups, including the elderly, location of AMI, and time from symptom onset. These differences remained significant at one-year follow-up.

The angiographic substudy demonstrated a strong relationship between TIMI flow and outcome.[8] Patients with strong forward flow (i.e., TIMI grade 3 flow) at 90 minutes had significantly lower mortality rates compared with patients with little to no flow. The mechanism for this benefit was found to be earlier, more complete infarct-vessel patency with accelerated tPA; this early tPA patency advantage over other agents was lost by 180 minutes after symptom onset. As would be expected, the patients with the higher risk derived the most substantial benefit from accelerated tPA compared to streptokinase in this large study. Patients who received accelerated tPA did suffer more hemorrhagic strokes compared to those who received streptokinase, but the combined end point of death and disabling stroke still favored the accelerated tPA regimen.

Fibrin Specificity. A more recent addition to the fibrinolytic agent literature includes the GUSTO-III investigation.[9] This study compared accelerated tPA to rPA. In this very large trial, rPA was found to be similar to accelerated tPA, with 30-day mortality rates being 7.47% and 7.24%, respectively. The study, however, was designed as a superiority trial, not an equivalence trial and, as such, did not have the power to prove equivalence. However, in patients who present more than four hours after onset of symptoms (a significant number of patients in many institutions) accelerated tPA may be superior to rPA because of its greater fibrin specificity.[9] rPA is a mutant form of tPA that can be administered in a fixed double-bolus dose, with no adjustment required for weight, thus simplifying administration.

The ASSENT-2 trial investigated the use of TNK-tPA, another mutant of wild-type tPA. TNK-tPA has several interesting characteristics and associated potential benefits: 1) its longer half-life allows it to be administered as a single bolus; 2) it is 14 times more fibrin-specific than tPA and even more so than rPA; and 3) it is 80 times more resistant to PAI-1 than tPA. The ASSENT-2 trial randomized approximately 17,000 patients with AMI to single-bolus TNK-tPA (30-50 mg based upon body weight) or accelerated tPA (100 mg total infusion);[10] the primary outcome variable was 30-day all-cause mortality. The investigators found no differences in mortality or intracerebral hemorrhage.[10]

In a subgroup analysis, however, significantly lower 30-day mortality was noted among patients who presented more than four hours after onset of symptoms; furthermore, fewer non-intracranial major bleeding episodes were encountered in the TNK-tPA group. Based on these results, it was concluded that TNK-tPA was equally or minimally more effective, particularly in late presenters. As far as adverse reactions, TNK-tPA also appeared to be modestly safer than accelerated tPA. Finally, due to its single-bolus administration, TNK-tPA is easier to use in the emergency department (ED) as well as in other settings, such as air and ground prehospital environments. Following up on these observations, the ASSENT-3 trial compared TNK-tPA regimens combined with enoxaparin or abciximab vs. a standard TNK-tPA/UFH combination, and demonstrated improved overall efficacy/safety end points using a TNK-tPA/enoxaparin combination (please see below for full discussion).[1]

Candidacy for Fibrinolysis—Patient Screening, Identification, and Stratification

Optimizing outcomes in patients with ACS requires matching patients with strategies that will produce the best results in spe-

Figure 2. Guidelines for Effective Management of Non ST-Elevation MI

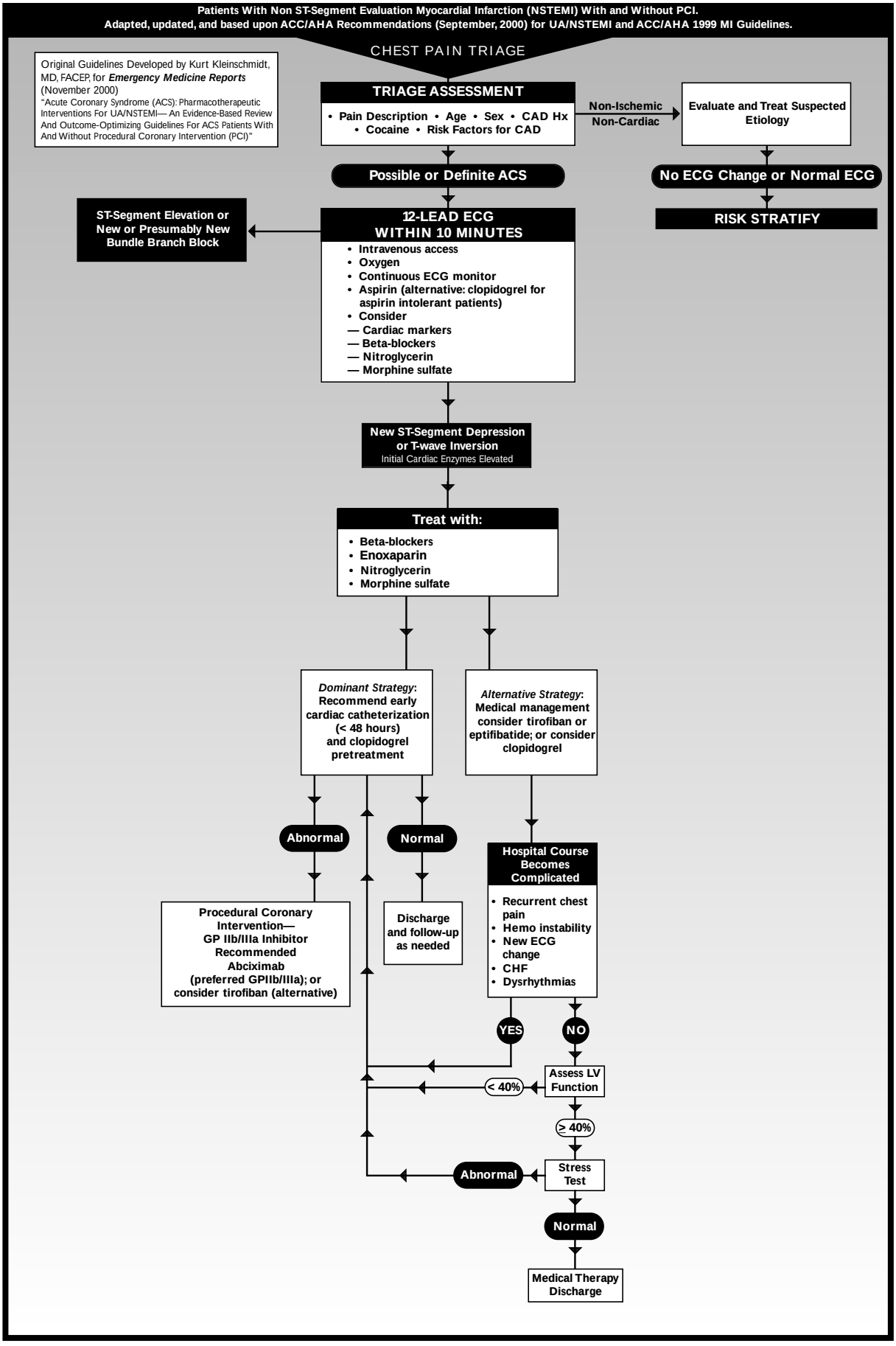
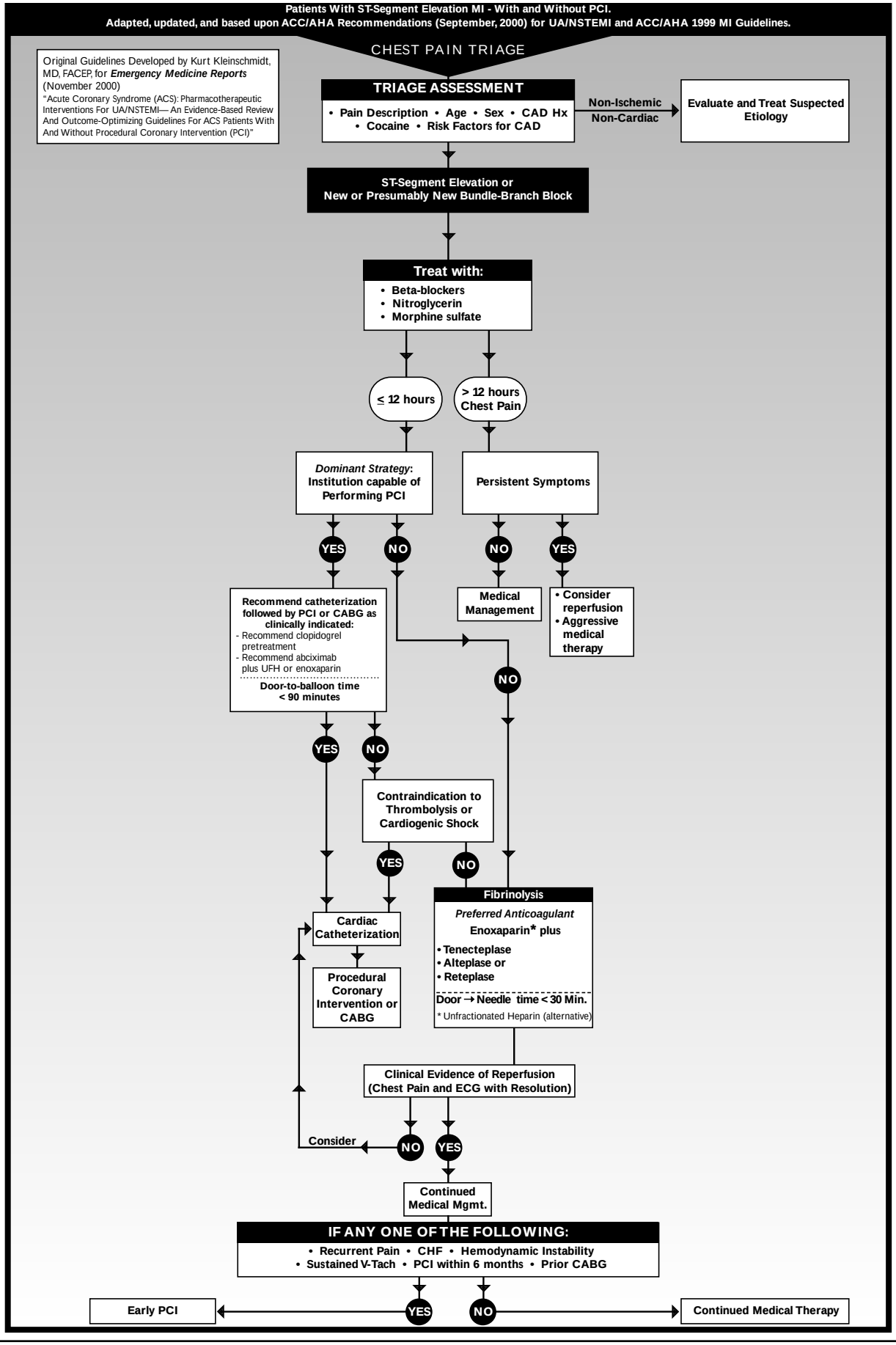


Figure 3. Guidelines for Effective Management of ST-Elevation MI



cific clinical subgroups. Identifying those patients who represent ideal candidates for fibrinolysis, and who are likely to have outcomes at least as favorable as they would with procedural interventions, has become an area of intense focus among cardiologists and emergency physicians. A number of factors that should be considered when assessing patients with AMI for either procedural or fibrinolytic therapy are discussed in the following sections. *(See Figure 6.)*

Perhaps one of the most important aspects of managing patients with acute coronary ischemic syndromes is the ability to risk-stratify patients according to whom will benefit most from either pharmacology or procedure-mediated reperfusion. It has been difficult to generate a deterministic patient selection process that will guarantee an optimal outcome for each individual case. Although a number of risk-stratification tools have been suggested by clinical experts and associations, the TIMI risk factor analysis has emerged as one of the most widely accepted approaches for identifying patients who will likely benefit from specific strategies.

Among the factors included in the TIMI risk-stratification scheme are the following: 1) presence of chest pain; 2) significant elevation of cardiac markers; 3) history of three or more cardiac risk factors (i.e., diabetes, smoking, elevated LDL-cholesterol, etc.); 4) age 65 or older; 5) known coronary artery disease (CAD), defined as documented 50% or greater stenosis in at least one major coronary artery; 6) prior chronic aspirin intake for CAD prevention; 7) two or more episodes of resting angina during the 24 hours prior to presentation; and 8) new ST-segment deviation of 0.5 mm or greater in limb and/or precordial leads.

Patient Age. In general, published trials do not provide evidence to support withholding fibrinolytic therapy on the basis of a patient's age alone. In fact, the Fibrinolytic Therapy Trialist's (FTT) Collaborative Group concluded that "clearly, age alone should no longer be considered a contraindication to fibrinolytic therapy."[11] At the same time, it must be recognized that patients older than age 75 have a higher incidence of hemorrhagic stroke than younger patients. Moreover, the recent GUSTO-V trial suggested inferior outcomes when abciximab was combined with UFH and TNK-tPA in patients older than age 75.[2]

Time from Chest Pain Onset, Therapeutic Window. The generally accepted therapeutic window for administration of a fibrinolytic agent after the onset of ST-segment elevation AMI is 12 hours. Considerable data support this time period.[5-13] Without question, the earlier the treatment is initiated, the greater the likelihood that the patient will experience a good outcome. This is the case in patients within the first six hours of AMI. Delayed administration (i.e., those occurring between six and 12 hours after AMI onset) also confers benefit, although of a lesser magnitude.[14]

The Late Assessment of Fibrinolytic Efficiency (LATE) trial, which compared fibrinolytic therapy with placebo, found a significant 26% decrease in 35-day mortality in patients treated with tPA, heparin, and aspirin 6-12 hours after the onset of symptoms.[15] There is no significant decrease in mortality among patients treated 12-24 hours after symptom onset. These studies, then, clearly establish benefit from 0 to 12 hours in patients who otherwise are appropriate candidates for fibrinolytic therapy. Treatment beyond that time is not supported by results of currently available trials. The single exception may be a patient with a "stuttering" pattern of chest pain between 12 and 24 hours after symptom onset. This emphasized the importance of an adequate history. If there is evidence of marked ST-segment elevation on a 12-lead ECG, the patient should be considered a potential fibrinolytic candidate.

Previous Myocardial Infarction or Coronary Artery Bypass Grafting. In the setting of AMI, a previous MI should not preclude consideration for treatment with fibrinolytic agents, although there is evidence that procedural intervention may be preferable.[11] Without treatment, there is a potential for greater loss of function in the newly infarcting region of the myocardium. Although the GISSI-1 trial shows no treatment benefits with fibrinolytic therapy in patients with previous MI,[16] the ISIS-2 trial demonstrates a 26% relative mortality rate reduction in patients with previous MIs who were treated with fibrinolytic therapy.[12] The FTT Collaborative Group meta-analysis further demonstrates that patients with a history of a past MI who receive fibrinolytic therapy for recurrent acute infarction have a mortality rate of 12.5%, compared with 14.1% among control patients.[11]

Many studies have reported successful fibrinolysis in AMI patients with prior coronary artery bypass graft (CABG). Complete thrombotic occlusion of the bypass graft is the cause of AMI in approximately 75% of cases, as opposed to native vessel occlusion. It has been suggested that because of the large mass of thrombus and absent flow in the graft, conventional fibrinolytic therapy may be inadequate to restore flow. Because patients who have undergone CABG may be relatively resistant to fibrinolytic therapy, they should be considered for direct angioplasty or combined fibrinolysis and rescue angioplasty.[17]

Stroke. A history of previous stroke or transient ischemic attack (TIA) is a major risk factor for hemorrhagic stroke after treatment with fibrinolytic therapy. A history of previous ischemic stroke should remain a strong relative contraindication to fibrinolytic therapy. A history of previous hemorrhagic stroke should remain an absolute contraindication.

Recent Surgery and Trauma. Recent surgery or trauma is considered a relative contraindication to fibrinolytic therapy. However, the term recent has been variably interpreted in fibrinolytic therapy trials. In the GISSI-1 trial, patients were excluded if they had surgery or trauma within the previous 10 days.[16] In the Anglo-Scandinavian Study of Early Thrombolysis (ASSET) trial, patients were excluded for surgery or trauma within the previous six weeks.[18] Other fibrinolytic therapy trials have not defined "recent surgery or trauma." It is prudent to consider alternative interventions such as angioplasty—if available—in patients who have had an AMI within 10 days of surgery or significant trauma.

Elevated Blood Pressure. Current evidence indicates that patients with a history of chronic hypertension should not be excluded from fibrinolytic therapy if their blood pressure is under control at the time of presentation or if it can be predictably lowered to acceptable levels using standard therapy for ischemic chest pain. In this regard, the admission blood pressure

Figure 4. Acute Coronary Syndrome Management

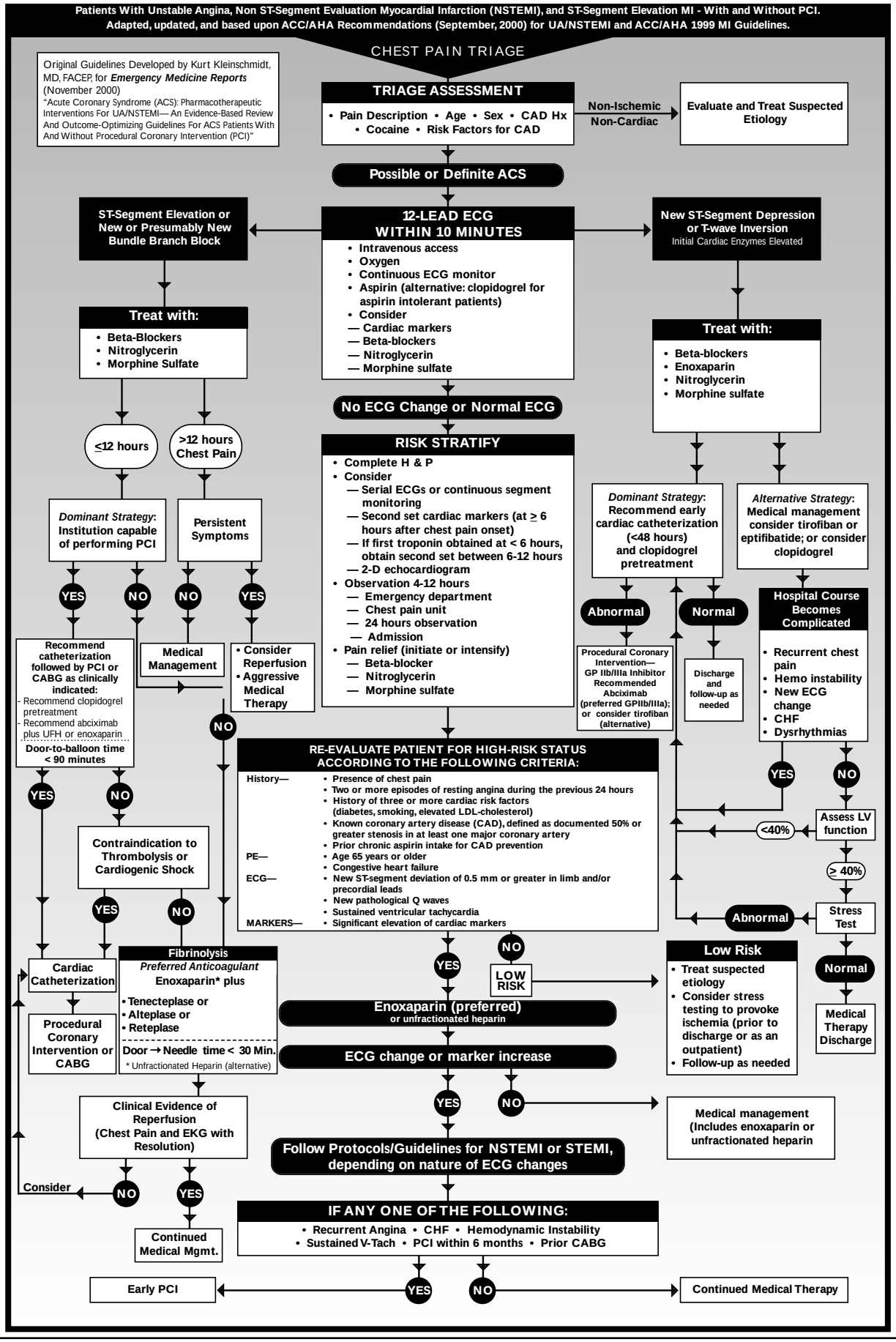
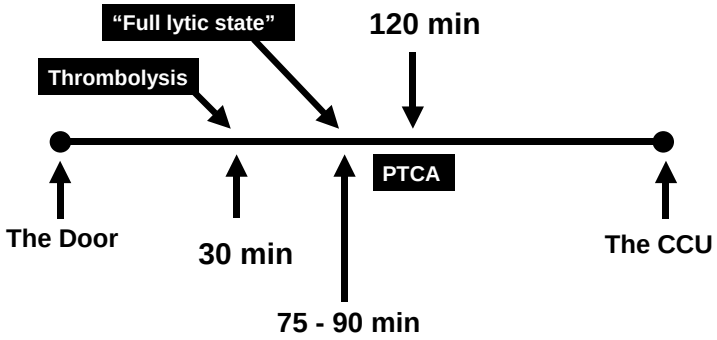


Figure 5. Time Line Comparing Thrombolysis vs. Primary Angioplasty in the AMI Patient



A "full thrombolytic state" is not reached for at least 45-60 minutes after administration of the thrombolytic agent. Therefore, if a time-line is considered regarding various treatment options and the time to expected full benefit, actual reperfusion may not occur for at least 75-90 minutes in the thrombolytic-managed patient, assuming a 30-minute door-to-drug interval. This time to benefit period is not dissimilar from the patient undergoing primary PTCA with the catheter balloon across the lesion at 120 minutes after ED arrival.

also is an important indicator of intracerebral hemorrhage risk.

The FTT Collaborative Group meta-analysis demonstrates that the risk of cerebral hemorrhage increases when patients have a systolic blood pressure greater than 150 mmHg on admission, and that it further increases when systolic blood pressure is 175 mmHg or greater.[11] Despite an increased mortality rate during days 0 and 1, the FTT Collaborative Group meta-analysis demonstrates an overall long-term benefit of 15 lives saved per 1000 in patients with systolic blood pressures greater than 150 mmHg and 11 lives saved per 100 for patients with systolic blood pressures of 175 mmHg or greater.[11] Although the FTT Collaborative Group meta-analysis appears to indicate an acceptable risk-benefit ratio for patients with substantially increased systolic blood pressure, a persistent blood pressure greater than 200/120 mmHg generally is considered an absolute contraindication to fibrinolytic therapy.

The benefit of fibrinolytic therapy in patients with hypotension remains controversial. The GISSI-1 and GISSI-2 trials show no apparent reduction of mortality rate with fibrinolytic therapy among patients classified in either Killip class III or IV.[5,16] These findings have led to the previous claim that primary angioplasty, not fibrinolytic therapy, should be used in patients with cardiogenic shock. The FTT Collaborative Group meta-analysis, however, does not support this hypothesis.[11] In its meta-analysis, patients with an initial systolic blood pressure of less than 100 mmHg who were not treated with fibrinolytic therapy had a very high risk of death (35.1%), and those who were treated with fibrinolytic therapy had the largest absolute benefit (60 lives saved per 1000 patients).[11] Based on this evidence, the FTT Collaborative Group suggests that hypotension, heart failure, and perhaps even shock should not be contraindications to fibrinolytic therapy.[11] The value of PCI in these patients also has been established. Overall, the data support immediate treatment directed to myocardial reperfusion, regardless of the method (PCI or fibrinolysis) as indicated by clinical judgment.

Menstrual Bleeding. Previously, there has been concern regarding whether menstruating women with AMI should be considered candidates for fibrinolytic therapy. Because natural estrogen is cardioprotective, there has been little experience with fibrinolysis among premenopausal women. Significant adverse effects, however, have not been reported by clinicians who administer fibrinolytic therapy to such patients. Gynecologists indicate that any excessive vaginal bleeding that may occur after receiving fibrinolytic therapy should be readily controllable by vaginal packing and, therefore, can be considered a compressible site of bleeding.

The Electrocardiogram. Combined with the patient's history and physical examination, the 12-lead ECG is the key determinant of eligibility for fibrinolysis. The electrocardiographic findings include two basic issues: 1) ST-segment elevation of 1 mm or more in two or more anatomically contiguous standard limb leads and 2 mm or more elevation in two or more contiguous precordial leads; or 2) new or presumed new left bundle-branch block (LBBB). No evidence of benefit from fibrinolytic therapy is found in patients with ischemic chest pain who lack either appropriate ST-segment elevation or the new development of LBBB.

Patients with LBBB and AMI are at an increased risk of experiencing a poor outcome; accordingly, these patients should be rapidly and aggressively managed in the ED with appropriate reperfusion therapies.[11,19] This observation was noted prior to the introduction of fibrinolytic agents and continues to be true today. In patients with AMI, new-onset LBBB is a clinical marker for a significantly worse prognosis in terms of higher mortality, lower left ventricular ejection fraction, and increased incidence of cardiovascular complications.[11,19] The development of new LBBB in the setting of AMI suggests proximal occlusion of the left anterior descending artery; such an obstruction places a significant portion of the left ventricle in ischemic jeopardy. Despite this increased risk of a poor outcome, patients with LBBB are less likely to receive fibrinolytic agents than are patients with ST elevation without LBBB. It should be stressed that patients with new-onset LBBB show significant benefit when treated with fibrinolytic therapy.[11]

Patients with AMI in the anterior, inferior, or lateral anatomic locations benefit from administration of fibrinolytic therapy. The relatively favorable prognosis associated with inferior infarction without fibrinolytic therapy requires larger sample sizes to detect a significant survival benefit. The large ISIS-2 trial demonstrated a statistically significant mortality benefit from fibrinolytic therapy in patients with inferior AMI: The mortality at five weeks is 6.5% for streptokinase plus aspirin vs. 10.2% for placebo.[12] Patients with inferior AMI who have coexisting right ventricular infarctions as detected by additional-lead ECGs are likely to benefit because a significant portion of the myocardium is involved. Acute, isolated posterior wall myocardial infarction, diagnosed by posterior leads, may represent yet another electrocardiograph-

Figure 6. Drug Dosing Guidelines for ACS

Aspirin	Initial 162.5-325 mg (non-enteric coated) po followed by 81-325 mg po per day
IV nitroglycerin:	Initial dose 5 mg/min IV; increase dose by 5-10 mg/min until relief of ischemic chest pain, or mean arterial pressure decreased by 30% if hypertensive (but never a systolic blood pressure < 90 mm Hg; utilize for approximately 24 hrs
Metoprolol (Lopressor):	5 mg IV q 5 min x 3 followed in 15 min by 25-50 mg po q6 hr x 24 hrs, titrate dose to HR/BP; switch to twice daily or qd (extended-release formulation) regimen prior to hospital discharge
Unfractionated heparin:	60 U/kg IV bolus (maximum 4000 U) followed by 12 U/kg/hr (maximum 1000 U/hr); measure aPTT at 4-6 hrs and titrate dose to aPTT of 50-70 sec (or titration specific range) using a weight-based dosing nomogram.
Enoxaparin (Lovenox):	**Dose for NSTE/ACS:** 1 mg/kg sc q12 hr **Dose for STE/ACS:** 30 mg IV bolus followed immediately by 1 mg/kg sc q12 hr **Dose for PCI in patients with NSTE/ACS:** If last dose administered < 8 hrs, no supplemental enoxaparin (or unfractionated heparin) dose needed; if last dose administered more than 8 hours (and less than 12 hrs), administer 0.3 mg/kg IV bolus Avoid in patients with CrCL < 30 mL/min
Morphine sulfate:	2-4 mg IV bolus; repeat and titrate if necessary for complete pain relief
Alteplase (tPA)*:	15 mg bolus followed by 0.75 mg/kg IV over 30 min (max 50 mg) followed by 0.5 mg/kg (max 35 mg) over 60 min (Max dose = 100 mg)
Reteplase (rPA, Retavase)*:	10 U IV bolus x 2, 30 min apart
Tenecteplase (TNKase)*:	< 60 kg = 30 mg IV bolus 60-69.9 kg = 35 mg IV bolus 70-79.9 kg = 40 mg IV bolus 80-89.9 kg = 45 mg IV bolus ≥ 90 kg = 50 mg IV bolus
Clopidogrel (Plavix):	Initial dose—300 mg (4, 75 mg tablets) po then 75 mg po qd beginning Day 2; For NSTE/ACS in aspirin intolerant patients, administer 75 or 300 mg as initial dose followed by 75 mg po qd.
Abciximab (ReoPro):	**Dose for PCI and STE/ACS:** 0.25 mg/kg IV bolus followed by 0.125 mg/kg/min, max 10 mg/min x 12 hrs; no dosage adjustment in renal insufficiency; not recommended for medical management of NSTE/ACS
Tirofiban (Aggrastat):	**Dose for PCI:** 10 mg/kg IV bolus over 3 min followed by 0.15 mg/kg/min x 18-24 hrs **Dose for NSTE/ACS:** 0.4mg/kg IV bolus over 30 min followed by 0.1 mg/kg/min x 48-72 hrs Not recommended for STE/ACS; for patients with CrCL < 50 mL/min, decrease maintenance and infusion rates by 50%
Eptifibatide (Integrilin):	**Dose for PCI and NSTE/ACS:** 180 mg/kg IV bolus, followed by an infusion of 2 mg/kg/min with a second 180 mg/kg IV bolus administered 10 min after the first bolus; continued infusion for x 18-48 hrs; Limited data suggests reducing the maintenance infusion to 1 mg/kg/min for patients with SCr 2.0-4.0 mg/dL; Avoid in patients with SCr > 4.0 mg/dL.

ic indication for fibrinolysis. Although improved outcomes are unproven in large fibrinolytic trials, patients with isolated posterior AMI may be considered possible candidates for reperfusion therapy.

In general, the larger the size of the myocardial infarct, the greater the mortality reduction with fibrinolytic therapy. The size of an AMI, and therefore the associated risk of cardiovascular complications and death, are reflected either by the absolute number of leads showing ST-segment elevation on the ECG or a summation of the total ST-segment deviation from the baseline (i.e., both ST-segment depressions and elevations).

The current evidence strongly indicates that fibrinolytic therapy should not be used routinely in patients with ST-segment depression only on the 12-lead ECG. The mortality rate actually may be increased by administration of fibrinolytics in this patient subgroup. The Thrombolysis in Myocardial Infarction (TIMI)-3 trial demonstrated a significant difference in outcome in fibrinolytic-treated patients with only ST-segment depression: 7.4% incidence of death compared with 4.9% in the placebo group.[20] These findings also are supported in the FTT Collaborative Group meta-analysis, which demonstrated that the mortality rate among patients with ST-segment depression who received fibrinolytic therapy is 15.2%, compared with 13.8% among controls.[19]

Recent Cardiopulmonary Resuscitation (CPR). CPR is not a contraindication to fibrinolytic therapy unless CPR has been prolonged (> 10 minutes) or extensive chest trauma from manual compression is evident.[21] Although the in-hospital mortality rate is higher in AMI patients who experience cardiac arrest and then receive ED-based fibrinolytic agents, no difference is found in the rates of bleeding complications. No hemothorax or cardiac tamponade occurred in those cardiac arrest patients receiving fibrinolytics.[21]

Low Molecular Weight Heparin (Enoxaparin)—A Central Role in Fibrinolytic Regimens

The most important advance in fibrinolysis-mediated management of AMI is the emerging, evidence-based support defining a pivotal role for enoxaparin as part of a TNK-tPA based, fibrinolytic regimen. In this regard, the recently published ASSENT-3 trial was designed to compare the effectiveness and safety of enoxaparin vs. UFH as part of a full-dose TNK-tPA regimen.[1] This landmark trial enrolled 6095 patients with AMI of fewer than six hours duration, and randomly assigned patients to one of three regimens: 1) full-dose TNK-tPA plus enoxaparin for a maximum of seven days (enoxaparin group; n = 2040); 2) half-dose TNK-tPA with weight-adjusted, low-dose UFH and a 12-hour infusion of abciximab (abciximab group; n = 2017); and 3) full-dose TNK-tPA with weight-adjusted, UFH for 48 hours (UFH group; n = 2038). The primary end points were the composites of 30-day mortality, in-hospital reinfarction, or in-hospital refractory ischemia (efficacy end point); and the above end point plus in-hospital intracranial hemorrhage or in-hospital major bleeding complications (efficacy plus safety end point).

Of special importance is the finding that the combination of full-dose TNK-tPA plus enoxaparin produced the lowest 30-day mortality rates (5.2%) in patients with AMI reported in similar, large, clinical trials evaluating fibrinolytic strategies in similar patient populations. Consistent with this finding is that there were significantly fewer efficacy end points in the enoxaparin and abciximab groups than in the UFH group: 233 of 2037 (11.4%) vs. 315 of 2038 (15.4%; relative risk [RR] 0.74 95% [confidence interval (CI) 0.63-0.87], P = 0.0002) for enoxaparin, and 223 of 2017 (11.1%) vs. 315 of 2038 (15.4%; RR 0.72 [CI 0.61-0.84], P < 0.0001) for abciximab. The same was true for the efficacy plus safety end point: 280 of 2037 (13.7%) vs. 347 of 2036 (17.0%; RR 0.81 [CI 0.70-0.93], P = 0.0037) for enoxaparin, and 287 of 2016 (14.2%) vs. 347 of 2036 (17.0%; RR 0.84 [CI 0.72-0.96], P = 0.01416) for abciximab.

The investigators concluded that the TNK-tPA plus enoxaparin or abciximab regimens reduced the frequency of ischemic complications in AMI, producing an overall relative reduction in primary adverse end points of about 26% in the enoxaparin-TNK-tPA and abciximab groups as compared to the UFH group. However, in light of its ease of administration, better safety profile, and lower cost as compared to the abciximab-UFH-TNK-tPA combination, the enoxaparin-TNK-tPA arm emerged as the most attractive reperfusion regimen.

From a practical, time-to-treat myocardial salvage perspective, the convenience factor of the enoxaparin regimen should not be under-emphasized. The abciximab arm required initiation of two infusions (abciximab plus UFH) and administration of three IV boluses (TNK-tPA, abciximab, and heparin). In contrast, the enoxaparin arm was appropriately convenient, requiring two simple bolus infusions, one of TNK-tPA and one of enoxaparin.

These practical advantages, combined with a lower bleeding rate and maintenance of overall effectiveness in terms of safety and efficacy across the full-spectrum of high-risk patient subgroups with AMI (i.e., including the elderly and diabetic subsets), supports a paradigm shift to enoxaparin-TNK-tPA or enoxaparin in combination with other fibrin-specific thrombolytics, as the preferred pharmacotherapeutic approach to fibrinolysis-mediated therapy of AMI. Although the ASSENT-3 trial evaluated a fibrinolytic regimen consisting of TNK-tPA, it is reasonable to suggest that enoxaparin also should be the preferred anticoagulant agent, over UFH, when used in combination with other fibrinolytic agents such as tPA and rPA.

There are several findings that support the "workhorse" role of enoxaparin in combination with TNK-tPA and other fibrinolytics as the optimal regimen for appropriately selected patients with AMI. First, the results obtained in ASSENT-3 with half-dose TNK-tPA plus abciximab are very similar to those with half-dose reteplase and abciximab seen in GUSTO-V, and support the hypothesis that a more potent antiplatelet agent increases flow in the infarct-related coronary artery.[2] However, in both trials, the benefits of abciximab in a fibrinolytic regimen were obtained at the cost of a higher rate of thrombocytopenia, major bleeding complications, and blood transfusions, thereby mitigating its attractiveness. Moreover, as is the case in GUSTO-V, no benefit, and perhaps even harm, was observed in ASSENT-3 patients treated with the abciximab/half-dose fibrinolytic regimen who were older than age 75, which reinforces the need for

caution regarding the use of this combination in elderly patients. In contrast to GUSTO-V, ASSENT-3 also suggested an inferior result, compared to heparin, for the abciximab regimen in diabetic patients, a finding that should prompt additional investigation.

Further support for enoxaparin's safety and efficacy in AMI has been forthcoming from the second trial of Heparin and Aspirin Reperfusion Therapy (HART II) in 400 patients with AMI that compared enoxaparin (30 mg intravenous bolus then 1 mg/kg subcutaneously every 12 hours) with UFH intravenous infusion as adjunct to a 90-minute regimen with a maximum of 100 mg human recombinant tPA and aspirin. Enoxaparin was found to be at least as effective as UFH for achieving TIMI grades 3 and 2 flow, and for preventing reocclusion, without increasing the risk of major bleeding. This study showed that enoxaparin was effective and safe in patients with AMI and that it may be a convenient substitute for UFH in conjunction with fibrinolytics in this indication.[22]

Pharmacoeconomic Implications. A number of studies support the observation that enoxaparin reduces the incidence of adverse cardiovascular end points, including recurrent myocardial infarction and need for revascularization, without increasing major bleeding in patients with ACS, including unstable angina and acute ST-elevation myocardial infarction.[1,23-25] These clinical benefits are associated with economic benefits in terms of reduced expenditure on revascularization procedures, the requirement for additional drug therapies and drug administration. Accordingly, several pharmacoeconomic analyses have been conducted on the use of enoxaparin in ACS.[26-29]

Enoxaparin has been shown to be associated with a cost savings compared with UFH in the management of unstable angina and non-ST-segment elevation myocardial infarction in health economic studies from Canada, the United States, the United Kingdom, South America, and France.[26-29] These cost savings accrue from reductions in administration costs (primarily associated with the ease of administration of subcutaneous enoxaparin compared with intravenous UFH); the amount of nursing time required (which also increases the availability of nurses); the need for revascularization procedures (and any complications arising from these procedures); and the duration of hospitalization.[28]

Percutaneous, Procedural Coronary Intervention (PCI)

Although fibrinolysis is widely available and has been documented to improve coronary flow, limit infarct size, and improve survival in AMI patients, many individuals with acute infarction simply are not considered suitable candidates for such treatment. In this regard, patients with absolute contraindications to fibrinolytic therapy, certain relative contraindications, cardiogenic shock, and/or unstable angina may be ineligible to receive fibrinolytic therapy.

The mandate to implement prompt reperfusion therapy in these patients, as well as the other limitations of fibrinolytic therapy, have encouraged many clinicians to advocate PTCA, and more recently, another PCI (stenting), as the primary treatment modalities for the majority of patients with AMI. Indeed, PCI has many theoretical advantages over fibrinolysis, including a greater pool of potentially eligible patients, a lower risk of intracranial bleeding, a significantly higher initial reperfusion rate, earlier delineation of coronary artery architecture with rapid triage to surgical intervention, and more precise risk stratification, which may facilitate safe and earlier hospital discharge.

Several trials of varying sizes comparing primary PTCA with fibrinolysis have been reported in the past 10 years. Interventions in the early trials were performed using PTCA prior to the current widespread use of coronary stents, the current PCI of choice. Despite a clear and consistent benefit of primary PTCA in restoring patency of the infarct-related artery, differences in mortality in the individual trials were difficult to evaluate due to the smaller sample sizes in the studies.

The Primary Angioplasty in Myocardial Infarction (PAMI) trial enrolled 395 patients who were randomly assigned to undergo primary PTCA or to receive tPA.[17] Compared with standard-dose tPA, primary PTCA reduced the combined occurrence of nonfatal reinfarction or death, was associated with a lower rate of intracranial hemorrhage, and resulted in a similar left ventricular function. The results of the Netherlands trial indicate that primary angioplasty was associated with a higher rate of patency of the infarct-related artery, a less severe residual stenotic lesion, better left ventricular function, and less recurrent myocardial ischemia and infarction than patients receiving streptokinase.[30]

In a substudy of the GUSTO-IIb trial,[31] the authors randomly assigned 1138 patients with AMI to either primary PTCA or accelerated tPA. The composite end point of the study included death, nonfatal reinfarction, and nonfatal disabling stroke, all occurring within 30 days of the AMI. Of those patients assigned to primary PTCA therapy, 83% were candidates for such treatment and underwent angioplasty 1.9 hours after ED arrival for a total elapsed time from chest pain onset to therapy of 3.8 hours. Ninety-eight percent of the patients assigned to fibrinolytic therapy received tPA 1.2 hours after hospital arrival. The occurrence of the composite end point was encountered significantly less often in the PTCA group (9.6%) compared to the tPA group (13.7%) at 30 days.

When the individual components of the 30-day composite end point were considered separately, the incidence of death (5.7% vs 7%), infarction (4.5% vs 6.5%), and stroke (0.2% vs 0.9%) occurred at statistically similar rates for both treatment groups (PTCA and tPA), respectively. Additional evaluation in the form of a meta-analysis by Weaver and colleagues reviewed 10 major studies comparing fibrinolysis vs. primary PTCA in more than 2600 patients.[32] The 30-day mortality was found to be significantly lower in the PTCA group (4.4%) vs. the patients treated with fibrinolytics (6.5%). Primary PTCA also was associated with a significant reduction in total stroke and hemorrhagic strokes.

The longer-term results of primary PTCA, however, are less clear. The GUSTO-IIb study showed no overall mortality advantage of primary PTCA at six months;[31] conversely, two-year follow-up from the PAMI trial found a significant reduction in hospital readmission, recurrent ischemia, target vessel revascularization, and reinfarction, with a trend toward a reduction in mortality in the PTCA group, compared to treatment with fibrinolysis.[17]

Much of the previous literature comparing the acute reperfusion therapies in the AMI patient does not include or evaluate the use of coronary stenting as the PCI of choice. However, more recent studies suggest the introduction of intracoronary stenting likely will favorably alter the outcomes of AMI patients, making stent placement a superior method of management for appropriately selected patients at institutions where physicians are experienced with this procedure.

Coronary Stenting. Support for the primary—and based on recent data, superior—role of coronary stenting in patients with ST-elevation MI comes from investigators involved in the Stent versus Thrombolysis for Occluded Coronary Arteries in Patients with Acute Myocardial Infarction Study (STOPAMI).[33] The purpose of this study was to assess whether coronary stenting combined with blockade of platelet glycoproteins GP IIb/IIIa produces a greater degree of myocardial salvage than fibrinolysis with an accelerated infusion of tPA.

In this study, a total of 140 patients with ST-elevation MI were enrolled in a randomized trial, with 71 assigned to receive a stent plus abciximab, and 69 to receive intravenous tPA. The primary end point was the degree of myocardial salvage, determined by means of serial scintigraphic studies, and the secondary end point was a composite of death, reinfarction, and stroke within six months after randomization. In the group that received a stent plus abciximab, the median size of the final infarct was 14.3% of the left ventricle, as compared with a median of 19.4% in the tPA group. The cumulative incidence of death, reinfarction, or stroke at six months was lower in the stent group than in the tPA group (8.5 vs 23.2%, P = 0.02, relative risk, 0.34; 95% confidence interval, 0.13-0.88).[33] The investigators concluded that in patients with AMI, coronary stenting plus abciximab produces a greater degree of myocardial salvage and a better clinical outcome than does fibrinolysis with a tissue plasminogen activator.

Primary Angioplasty in Patients with Failed Fibrinolysis and Cardiogenic Shock. Current trial data suggest that rescue angioplasty may be advantageous in patients whose infarct-related arteries fail to reperfuse after fibrinolytic therapy.[34] Some centers routinely catheterize patients after fibrinolytic therapy to determine whether successful reperfusion has occurred and to perform angioplasty if necessary and anatomically feasible. Other centers catheterize patients after fibrinolytic therapy only if there is clinical evidence that the infarct-related artery has failed to open, such as continued chest pain or persistent ST-segment elevation.

Patients with AMI who present with cardiogenic shock, which occurs in up to 10% of cases, demand special attention because this population has a mortality rate of almost 80%.[22] Fibrinolysis is not effective in this subgroup of AMI patients, most likely due to a significantly lower coronary perfusion pressure; in the shock state, it is felt that the occlusive thrombus is not adequately exposed to the fibrinolytic agent, which may account for the clinical failure of the drug. In reviewing large fibrinolytic trials such as GISSI-1[11] and ISIS-2,[12] AMI patients presenting in cardiogenic shock did not benefit from fibrinolysis. Conversely, primary PCI has been investigated in more than 600 patients in several small studies; a cumulative analysis of this data revealed a significantly lower mortality rate (45%) compared to placebo and/or historical controls.[35]

The Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock (SHOCK) trial compared the outcomes of AMI patients presenting in cardiogenic shock;[36] patients were randomly assigned to emergency revascularization (primary PTCA without stenting or emergent CABG) or initial medical stabilization including fibrinolysis. The primary end point was mortality from all causes at 30 days; six-month survival was the secondary end point. Overall mortality at 30 days did not differ significantly between the revascularization and medical therapy groups (46.7% vs 56%, respectively). Six-month mortality was lower in the revascularization group than in the medical therapy group. The authors concluded that in AMI patients with cardiogenic shock, emergency revascularization did not significantly reduce overall mortality at 30 days. After six months, however, there was a significant survival benefit. The prespecified subgroup analysis of patients younger than age 75 showed an absolute reduction of 15.4% in 30-day mortality and 21.4% in six-month mortality in the revascularization group. Therefore, when catheterization facilities are not available in patients with cardiogenic shock, fibrinolytic therapy should be given to eligible patients, and urgent transfer to a facility with interventional capabilities should be strongly considered.[36] *(For more information on acute coronary syndromes, please see* Emergency Medicine Reports *Nov. 6 and 20, and Dec. 4, 2000, issues (2000;21:257-272, 273-284, 285-296.)*

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Physician CME Questions

57. The theoretical and practical advantages of PCI over primary fibrinolysis include:
    A. larger patient eligibility pool.
    B. lower risk of intracranial bleeding.
    C. significantly higher initial reperfusion rate.
    D. All of the above

58. The GUSTO-III trial revealed that, because of its greater fibrin specificity, accelerated tPA may be superior to rPA in what group of patients?
    A. Those who present more than four hours after onset of symptoms
    B. Those who present within one hour of symptom onset
    C. Those who present within 30 minutes of symptom onset
    D. Those who present within two hours of symptom onset

59. Which of the following factors is included in the TIMI risk-stratification scheme?
    A. Age 65 or older
    B. Known coronary artery disease (CAD)
    C. Two or more episodes of resting angina during the 24 hours prior to presentation
    D. Prior chronic aspirin intake for CAD prevention
    E. All of the above

60. The generally accepted therapeutic window for administration of a fibrinolytic agent after the onset of ST-segment elevation AMI is:
    A. 2 hours.
    B. 4 hours.
    C. 18 hours.
    D. 12 hours.
    E. 24 hours.

61. No evidence of benefit from fibrinolytic therapy is found in patients who:
    A. have ST-elevation.
    B. have ST-elevation and present fewer than four hours after chest pain onset.
    C. lack either appropriate ST-segment elevation or the development of a new LBBB.
    D. None of the above

62. In the ASSENT-3 trial, the combination of full-dose TNK-tPA plus enoxaparin produced 30-day mortality rates of about:
    A. 1.2%.
    B. 5.2%.
    C. 10%.
    D. 22.2%.
    E. None of the above

63. In the STOPAMI Trial, comparing coronary stenting plus abciximab vs. primary fibrinolysis with tPA, the investigators concluded that a greater degree of myocardial salvage was seen in:
    A. the coronary stenting group.
    B. the tPA group.

64. Fibrinolysis is not effective in patients with AMI who present with cardiogenic shock. This is most likely due to:
    A. a significantly lower coronary perfusion pressure.
    B. a significantly higher coronary perfusion pressure.
    C. the occlusive thrombus being overexposed to the fibrinolytic agent.
    D. None of the above

Emergency Medicine Reports CME Objectives

To help physicians:

- quickly recognize or increase index of suspicion for specific conditions;
- understand the epidemiology, etiology, pathophysiology, and clinical features of the entity discussed;
- be educated about how to correctly perform necessary diagnostic tests;
- take a meaningful patient history that will reveal the most important details about the particular medical problem discussed;
- apply state-of-the-art therapeutic techniques (including the implications of pharmaceutical therapy discussed) to patients with the particular medical problems discussed;
- understand the differential diagnosis of the entity discussed; understand both likely and rare complications that may occur;
- and provide patients with any necessary discharge instructions.

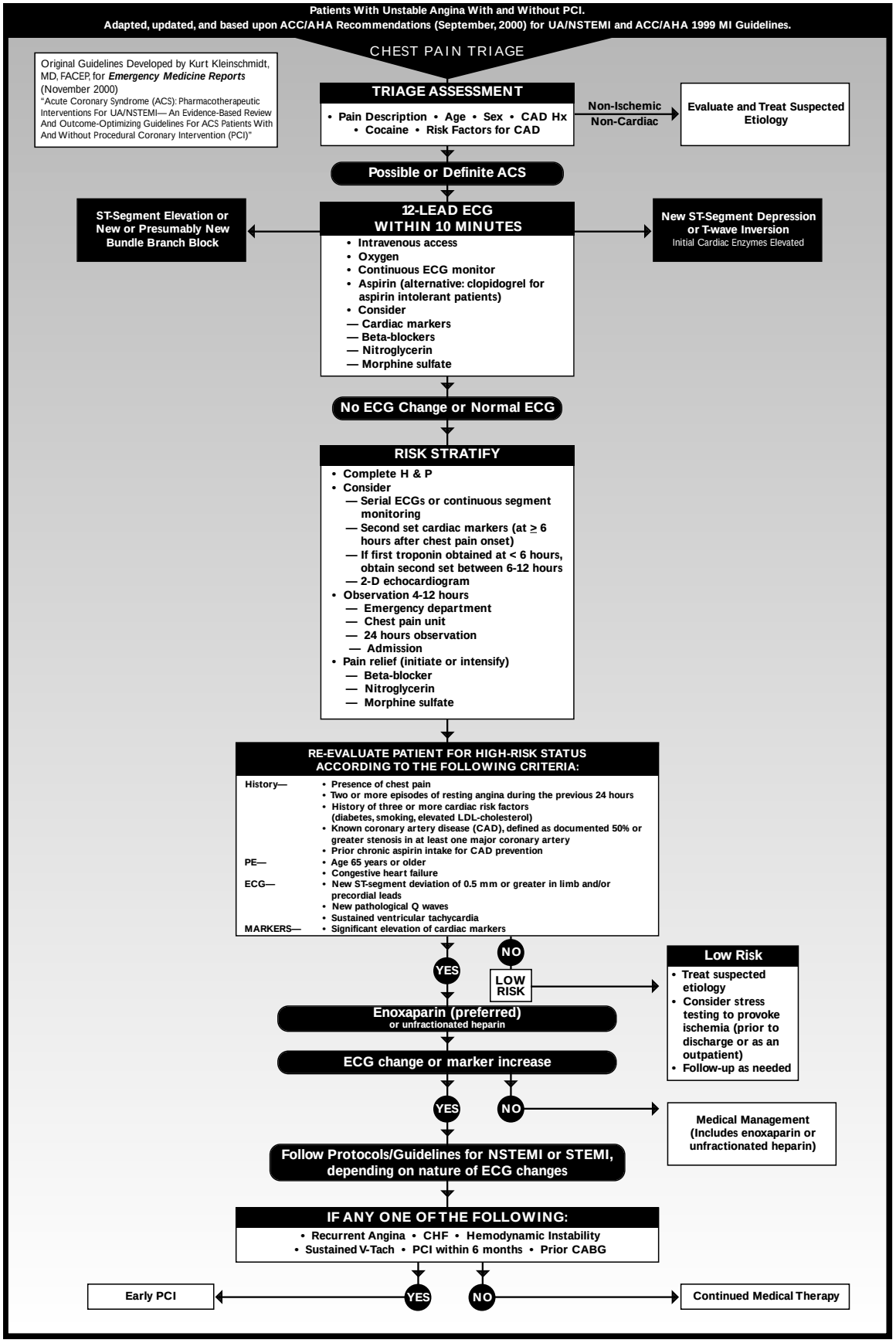
In Future Issues:

AMI and Coronary Syndromes: Part II

Emergency Medicine Reports
The Practical Journal for Emergency Physicians

AMI and Coronary Syndromes: Part I

Guidelines for Effective Management of Unstable Angina



Guidelines for Effective Management of Non ST-Elevation MI

Patients With Non ST-Segment Evaluation Myocardial Infarction (NSTEMI) With and Without PCI.
Adapted, updated, and based upon ACC/AHA Recommendations (September, 2000) for UA/NSTEMI and ACC/AHA 1999 MI Guidelines.

Original Guidelines Developed by Kurt Kleinschmidt, MD, FACEP, for ***Emergency Medicine Reports*** (November 2000)
"Acute Coronary Syndrome (ACS): Pharmacotherapeutic Interventions For UA/NSTEMI— An Evidence-Based Review And Outcome-Optimizing Guidelines For ACS Patients With And Without Procedural Coronary Intervention (PCI)"

CHEST PAIN TRIAGE

TRIAGE ASSESSMENT
- Pain Description • Age • Sex • CAD Hx
- Cocaine • Risk Factors for CAD

Non-Ischemic / Non-Cardiac → **Evaluate and Treat Suspected Etiology**

Possible or Definite ACS

No ECG Change or Normal ECG → **RISK STRATIFY**

12-LEAD ECG WITHIN 10 MINUTES

ST-Segment Elevation or New or Presumably New Bundle Branch Block

- Intravenous access
- Oxygen
- Continuous ECG monitor
- Aspirin (alternative: clopidogrel for aspirin intolerant patients)
- Consider
  - — Cardiac markers
  - — Beta-blockers
  - — Nitroglycerin
  - — Morphine sulfate

New ST-Segment Depression or T-wave Inversion
Initial Cardiac Enzymes Elevated

Treat with:
- Beta-blockers
- Enoxaparin
- Nitroglycerin
- Morphine sulfate

Dominant Strategy: Recommend early cardiac catheterization (< 48 hours) and clopidogrel pretreatment

Alternative Strategy: Medical management consider tirofiban or eptifibatide; or consider clopidogrel

Abnormal → Procedural Coronary Intervention— GP IIb/IIIa Inhibitor Recommended Abciximab (preferred GPIIb/IIIa); or consider tirofiban (alternative)

Normal → Discharge and follow-up as needed

Hospital Course Becomes Complicated
- Recurrent chest pain
- Hemo instability
- New ECG change
- CHF
- Dysrhythmias

YES / **NO**

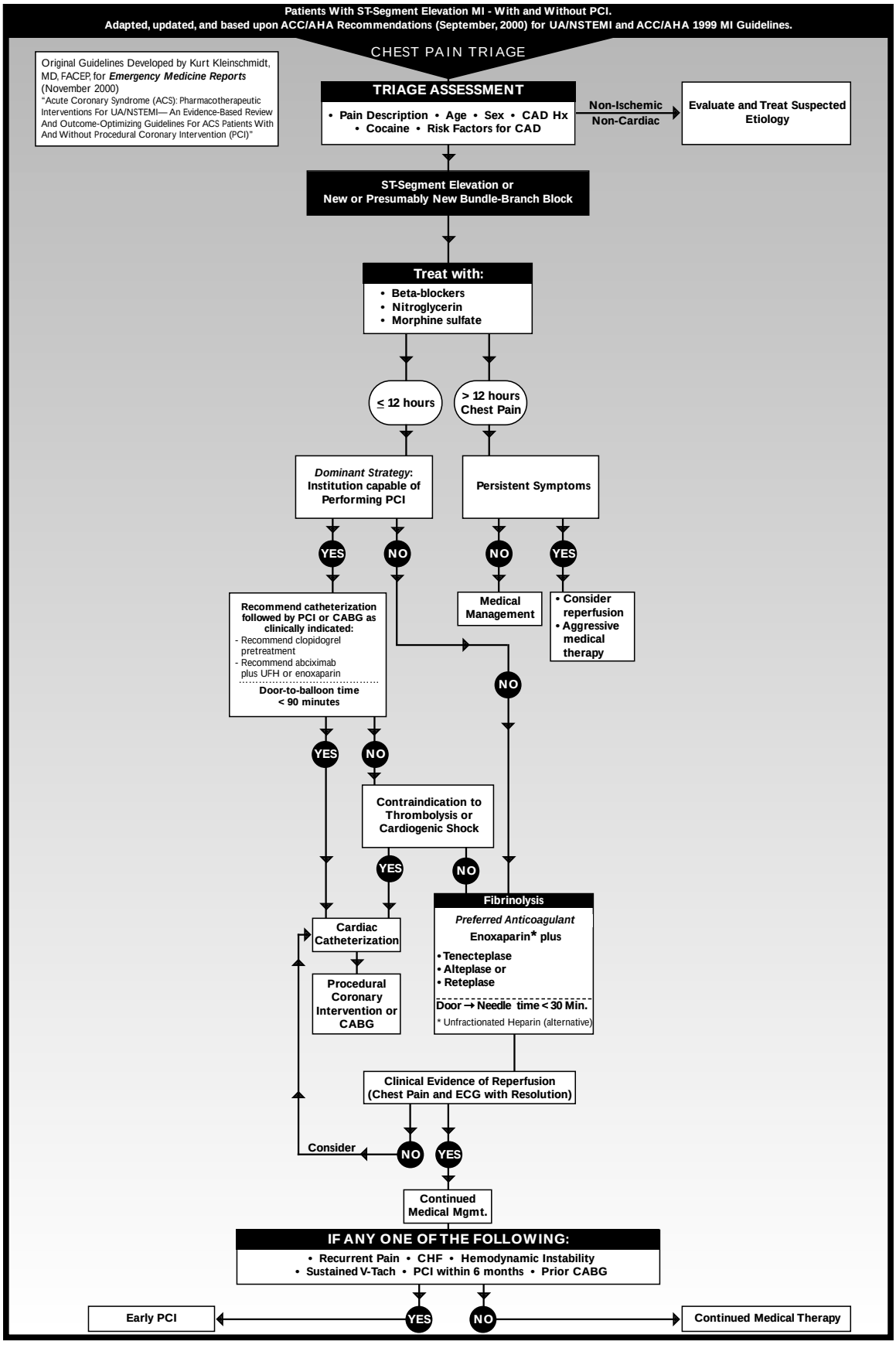
< 40% ← **Assess LV Function**

≥ 40% → **Stress Test**

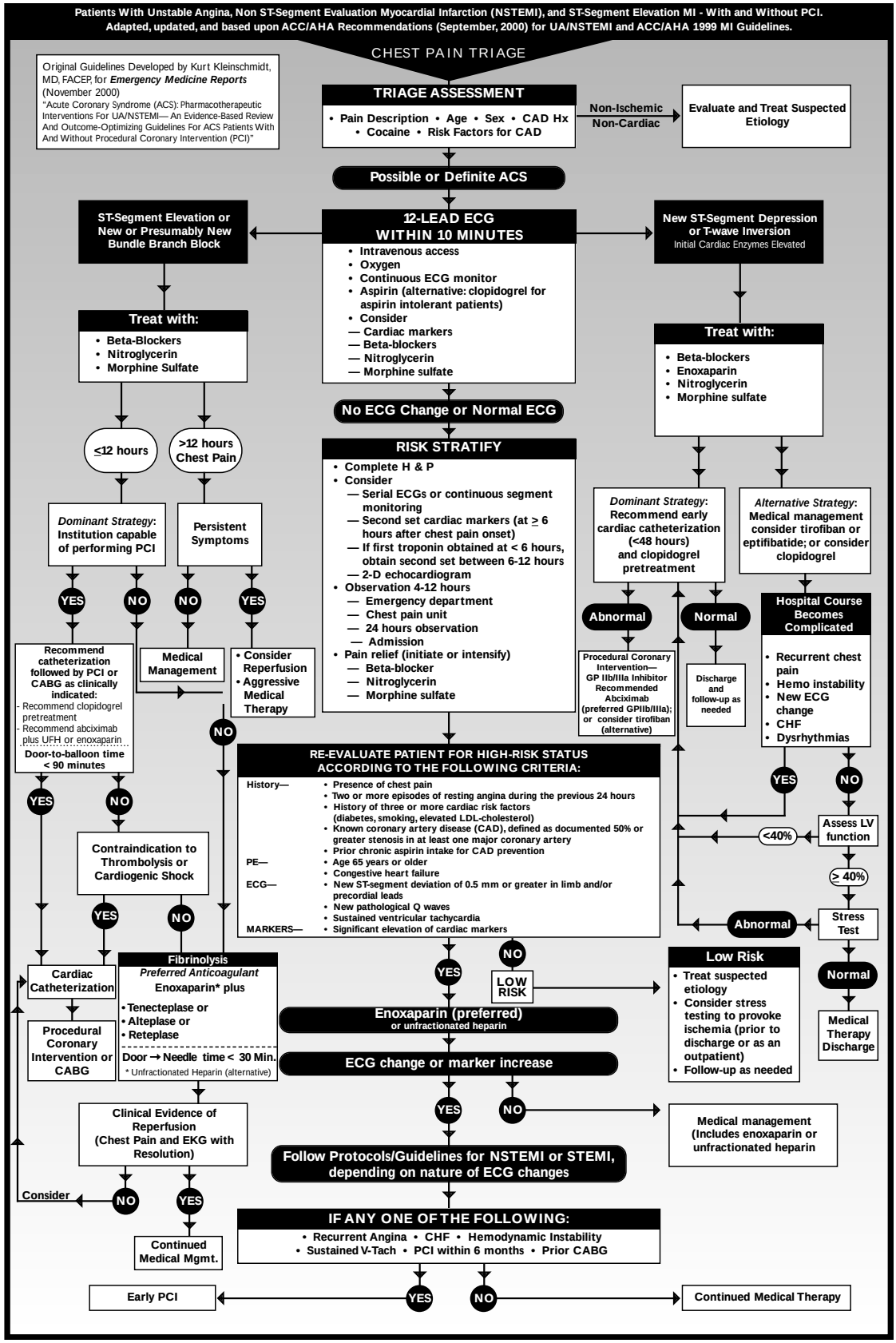
Abnormal → (to Procedural Coronary Intervention)

Normal → **Medical Therapy Discharge**

Guidelines for Effective Management of ST-Elevation MI



Acute Coronary Syndrome Management



Supplement to *Emergency Medicine Reports*, October 8, 2001: "Acute Myocardial Infarction and Coronary Syndromes: Optimizing Selection of Reperfusion and Revascularization Therapies in the ED. Part I: Fibrinolysis, Procedural Coronary Intervention (PCI), and the Central Role of the Low Molecular Weight Heparin, Enoxaparin, in Fibrinolysis-Mediated Myocardial Reperfusion." *Authors:* **William R. Brady, MD, FACEP, FAAEM,** Associate Professor, Residency Program Director, and Vice Chairman, Department of Emergency Medicine, University of Virginia School of Medicine, Charlottesville, VA; **Gideon Bosker, MD, FACEP,** Assistant Clinical Professor, Yale University School of Medicine, New Haven, CT; Associate Clinical Professor, Oregon Health Sciences University, Portland, OR; **Kurt Kleinschmidt, MD, FACEP,** Associate Professor, Department of Emergency Medicine, University of Texas Southwestern Medical School, Dallas, TX.

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Wednesday, November 14, 2001 2:00 to 3:40 p.m. EST

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Saint Vincents Hospital Speakers:

Toni G. Cesta, PhD, RN, FAAN, Director of Case Management
Eileen Hanley, RN, MBA, Manager, the Supportive Care Program
Suzanne Pugh, RN, Nurse Manager, Emergency Department
Richard Westfal, MD, Medical Director, Emergency Department

On the morning of September 11, 2001, a Code Three was called at Saint Vincents Hospital in Manhattan, and staff mobilized for what many thought was a routine disaster drill. It wasn't. Two hijacked airliners had slammed into the twin towers of the World Trade Center, ultimately destroying both buildings. In the confusing hours that followed, the number of dead and injured was unknown, and area hospitals braced for the worst.

At Saint Vincents Hospital, a Level 1 Trauma Center two miles from the World Trade Center Complex, dedicated professionals rose to the unique challenge of responding to the attack:

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- offering comfort, counsel, and vital information to family members of the victims; and
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Over for details on CE and CME

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