CHAPTER 7

PATIENT ELIGIBILITY

7.1 INTRODUCTION

All patients, admitted to the Emergency Room (ER), Coronary Care Unit (CCU), or other specialized units of the hospital, or affiliated hospitals, and who have the diagnosis of unstable angina or suspected myocardial infarction (MI), should be considered for study eligibility. Patients should be evaluated for eligibility for T3 as soon as possible. In order to screen and enroll patients within 24 hours of an ischemic episode it will be necessary to have an efficient notification system in operation within each participating hospital.

7.2 NOTIFICATION SYSTEM

The staff in the Emergency Room (ER), Coronary Care Unit (CCU), or intermediate care ward are responsible for initial notification of the T3 staff. The staff of these departments should be well informed of the general objective of the T3 Study and the type of patients who will be suitable for the study. They should immediately notify T3 staff of potentially eligible T3 patients. By reviewing a log of all patients admitted to the ER/CCU with a diagnosis of unstable angina or suspected myocardial infarction, the Principal Investigator at each Clinical Center will verify that the T3 staff was notified of all such admissions. The T3 staff (primarily the Research Coordinator) will fill out a Screening Log Sheet verifying time of admission to ER/CCU, and noting inclusion and exclusion criteria for each patient. If the patient seems eligible for the study, the T3 fellow will immediately review the patient's record and contact the Cardiology Attending, who is on call for T3, to discuss the patient's eligibility. T3 staff, with the participation of the Cardiology Attending, will inform the patient about the study purpose and ask for informed consent.

In previous studies notification of the Triage staff by ER/CCU/intermediate care ward personnel of a potential patient has been found to be difficult and frequently delayed. Posting of signs and regular personal communication by the investigators with the hospital staff are necessary to maintain a high level of awareness of the T3 Study. The Research Coordinator on call should be available at all times in the hospital. If he/she is unable to respond immediately to the call, the Research Coordinator should initiate notification of the T3 staff member or fellow on back up call and the Cardiology Attending on call.

7.3 ELIGIBILITY CRITERIA: T3A

Since prospective classification of patients with non-Q-wave MI as distinct from those with unstable angina is often impossible, the eligibility criteria (inclusion criteria plus exclusion criteria) are the same for the two conditions.

7.3.1 Inclusion Criteria - T3A

All patients who have experienced an episode of rest pain, presumed to be ischemic in origin and lasting five or more minutes (but no longer than six hours) which was present within the 12 hours prior to the time of enrollment, will be evaluated for enrollment in the study. Patients may be eligible if pain is present within the 12 hours prior to enrollment. Pain need not start within the 12-hour period.

In addition, the patient must have evidence of coronary artery disease. Such evidence may consist of either of the following:

1. New or presumably new ECG evidence of myocardial ischemia in a standard 12-lead ECG obtained during any attack of pain within the 12 hours before enrollement. This may consist of transient or persistent ST-segment depression of at least 0.10 mV (0.80 seconds after the J-point) in two or more contiguous leads, OR transient or persistent T-wave inversion in two or more contiguous leads, OR transient (< 30 minutes in duration) ST-segment elevation of at least 0.10 mV in two or more con-

tiguous leads. "New" ST-segment or T-wave changes are defined as those not present on an ECG recorded during the year prior to the qualifying episode of pain. (If a previous ECG is not available, ST-segment or T-wave changes noted on recordings obtained prior to randomization that can be ascribed to no other cause [e.g., digitalis, electrolyte disturbance] will be considered "presumably new.") ECG changes persisting after the termination of ischemic pain may be used as "new" changes.

2. Documented coronary artery disease manifest as either a documented prior myocardial infarction or at least 70% luminal diameter narrowing of a major coronary artery on a prior coronary angiogram. This angiogram may be a previous angiogram or an angiogram obtained during or shortly following the qualifying episode of rest pain.

7.3.2 Exclusion Criteria - T3A

Patients who fulfill the above inclusion criteria but who manifest any of the following exclusion criteria at the time of randomization will not be eligible for the study.

1. Pain radiating to the back or having other characteristics suggestive of aortic dissection.
2. Constant ischemic pain of more than six hours duration.
3. Age $\geq$ 76 years or < 21 years.
4. Left bundle branch block.
5. New or presumably new ST-segment elevation of at least 0.10 mV in two or more contiguous leads not reverting to < 0.10 mV within 30 minutes of administration of therapy (e.g. nitroglycerin).
6. A treatable cause for angina pectoris--e.g., arrhythmia, severe anemia, hypotension, or hyperthyroidism.
7. Acute pulmonary edema (rales heard over more than two-thirds of the lung fields that do not clear with cough).

8. Other major illness--e.g., a major infection; active cancer within the past five years; active severe hepatic disease; hemodynamically significant valvular, myocardial, or congenital heart disease; or renal failure with serum creatinine > 3 mg/ml.
9. A documented MI (CK-MB greater than normal, if available, or total CK greater than two times the upper limit of normal; MB takes precedence over total CK) within the past 21 days (excluding suspected infarction within 12 hours of enrollment).
10. Systolic arterial blood pressure less than 90 mm Hg on at least two recordings obtained 15 minutes apart.
11. Inability to cooperate with the protocol.
12. A female of childbearing potential.
13. PTCA within the previous six months.
14. Prior coronary artery bypass surgery.
15. Oral anticoagulation therapy at the time of initial enrollment.
16. Heparin allergy or known intolerance.
17. Thrombolytic therapy within prior 72 hours.
18. Contraindications to thrombolytic therapy:
    a. Past or present bleeding disorder or active bleeding.
    b. Any confirmed recording of systolic pressure exceeding 180 mm Hg, diastolic pressure exceeding 110 mm Hg on two measurements during the presenting illness prior to randomization and prior to the administration of a blood pressure lowering drug (e.g., nitroglycerin, calcium antagonist, or vasodilator), or uncontrolled hypertension at any time prior to entry (diastolic blood pressure > 110 mm Hg on several measurements).
    c. Any history of cerebrovascular disease, including any form of stroke and/or transient ischemic attack.

d. Prolonged cardiopulmonary resuscitation with one minute or more of external cardiac massage within the last two weeks.

e. Severe trauma within the prior six months.

f. History of parenteral or other drug abuse.

g. Significant surgical procedure within the last two months.

h. Active peptic ulcer disease within the past six months.

i. Invasive procedure (or lithotripsy) within the preceding 14 days that would significantly increase the risk of hemorrhage, such as biopsy, cardiac catheterization, or unsuccessful central venous puncture.

j. Probable pericarditis.

7.3.2.1 T3A Angiographic Exclusion Criteria

Patients should be excluded from T3A if any one of the following angiographic exclusion criteria apply:

1. < 60% stenosis in a major coronary segment.
2. ≥ 50% stenosis of LMCA.
3. Presence of extensive coronary diseae such that emergency coronary artery bypass grafting of the culprit vessel(s) is necessary to prevent hemodynamic collapse.

   This criterion will allow those patients with active ischemia and critical obstructions supplying viable myocardium considered to be vital to prevent hemodynamic collapse, to receive emergent (within 24 hours) coronary bypass surgery.
4. Patients should be excluded from T3A, who are found to have only a single old total occlusion supplying non-viable myocardium. An "old total occlusion" is defined as a total occlusion that is presumed to have occurred at a time remote from the qualifying episode, such as a prior MI > 3 weeks prior to enrollment, or a total occlusion viewed angiographic-

ally to have characteristics consistent with an old age, such as vasa vasorum, bridging collaterals and absence of a stump beyond proximal side branches (Stone et al, JACC 1990).

5. Presence of a true posterior MI documented at angiography with the following: (1) a "new" or "presumably new" total occlusion in the artery supplying the posterior wall of the heart, (2) no collateral blood flow to the posterior wall of the heart, and (3) a qualifying episode of ischemic pain occurring within six hours of angiography. (A time frame of six hours has been added to this exclusion criterion to define that group of patients in whom open label thrombolytic therapy is medically indicated.)

7.4 ELIGIBILITY CRITERIA: T3B

Since prospective classification of patients with non-Q-wave MI as distinct from those with unstable angina is often impossible, the eligibility criteria (inclusion criteria plus exclusion criteria) will be the same for the two conditions.

7.4.1 Inclusion Criteria - T3B

All patients who have experienced an episode of rest pain, presumed to be ischemic in origin and lasting five or more minutes (but no longer than six hours) which was present within the 24* hours prior to the time of enrollment, will be evaluated for enrollment in the study. Patient may be eligible if pain is present within the 24 hours prior to enrollment. Pain need not start within the 24-hour period.

In addition, the patient must have evidence of coronary artery disease. Such evidence may consist of one of the following:

1. New or presumably new ECG evidence of myocardial ischemia in a standard 12-lead ECG obtained during any attack of pain within the 24 hours before enrollment. This may consist of transient or persistent ST-segment depression of at least 0.10 mV (0.80 seconds after the J-point) in two or more contiguous

leads, OR transient or persistent T-wave inversion in two or more contiguous leads, OR transient (< 30 minutes in duration) ST-segment elevation of at least 0.10 mV in two or more contiguous leads. "New" ST-segment or T-wave changes are defined as those not present on an ECG recorded during the year prior to the qualifying episode of pain. (If a previous

*Prior to the November 11, 1990 protocol modification, the qualifying epidose of pain had to be present within the 12 hours prior to enroll ment. Qualifying ECGs also had to be from this same 12-hour period.

ECG is not available, ST-segment or T-wave changes noted on recordings obtained prior to randomization that can be ascribed to no other cause [e.g., digitalis, electrolyte disturbance] will be considered "presumably new.") ECG changes persisting after the termination of ischemic pain may be used as "new" changes.

2. New or presumably new ECG evidence of myocardial ischemia obtained during the presenting illness, but more than 24 hours before enrollment in T3. The ECG evidence should be obtained no more than seven days prior to enrollment. ECGs obtained during an episode of pain associated with ST-T-wave deviation (as described above), occurring at a referring hospital or physician's office within the seven days prior to enrollment may be used as evidence of coronary artery disease provided a legible copy of the ECG is available.
3. Coronary artery disease confirmed by a documented prior myocardial infarction, or at least 70% luminal diameter narrowing of a major coronary artery on a prior coronary angiogram, or a positive exercise thallium test, defined as the presence of both of the following criteria:
    1) $\geq$ 1 mm ST segment depression during exercise or recovery compared to baseline, and
    2) the presence of at least one definite reversible thallium or Sesta-MIBI perfusion defect.

7.4.2 Exclusion Criteria - T3B

Patients who fulfill the above inclusion criteria but who manifest any of the following exclusion criteria at the time of randomization will not be eligible for the study.

1. Pain radiating to the back or having other characteristics suggestive of aortic dissection.
2. Constant ischemic pain of more than six hours duration.

3. Age $\geq$ 76* years or < 21 years.
4. Left bundle branch block.
5. New or presumably new ST-segment elevation of at least 0.10 mV in two or more contiguous leads not reverting to < 0.10 mV within 30 minutes of administration of therapy (e.g. nitroglycerin).
6. A treatable cause for angina pectoris--e.g., arrhythmia, severe anemia, hypotension, or hyperthyroidism.
7. Acute pulmonary edema (rales heard over more than two-thirds of the lung fields that do not clear with cough).
8. Other major illness--e.g., a major infection; active cancer within the past five years; active severe hepatic disease; hemodynamically significant valvular, myocardial, or congenital heart disease; or renal failure with serum creatinine > 3 mg/ml.
9. A documented MI (CK-MB greater than normal, if available, or total CK greater than two times the upper limit of normal; MB takes precedence over total CK) within the past 21 days (excluding suspected infarction within 24 hours of enrollment).
10. Systolic arterial blood pressure less than 90 mm Hg on at least two recordings obtained 15 minutes apart.

*Prior to the November 11, 1990 protocol modification, the upper limit of the exclusion criteria for age was $\geq$ 76 years. On November 11, 1990 the upper limit of the exclusion criteria was changed to $\geq$ 80 years. On November 11, 1991 the upper limit was changed back to $\geq$ 76 years.

11. Inability to cooperate with the protocol.

12. A female of childbearing potential.

13. PTCA within the previous six months.

14. Prior coronary artery bypass surgery.

15. Oral anticoagulation therapy at the time of initial enrollment.

16. Coronary arteriography within the prior 30 days.

17. Heparin allergy or intolerance.

18. Thrombolytic therapy within prior 72 hours.

19. Contraindications to thrombolytic therapy:

    a. Past or present bleeding disorder or active bleeding.

    b. Any confirmed recording of systolic pressure exceeding 180 mm Hg, diastolic pressure exceeding 110 mm Hg on two measurements during the presenting illness prior to randomization and prior to the administration of a blood pressure lowering drug (e.g., nitroglycerin, calcium antagonist, or vasodilator), or uncontrolled hypertension at any time prior to entry (diastolic blood pressure > 110 mm Hg on several measurements).

    c. Any history of cerebrovascular disease, including any form of stroke and/or transient ischemic attack.

    d. Prolonged cardiopulmonary resuscitation with one minute or more of external cardiac massage within the last two weeks.

    e. Severe trauma within the last six months.

    f. History of parenteral or other drug abuse.

    g. Significant surgical procedure within the last two months.

h. Active peptic ulcer disease within the past six months.

i. Invasive procedure (or lithotripsy) within the preceding 14 days that would significantly increase the risk of hemorrhage, such as biopsy, cardiac catheterization, or unsuccessful central venous puncture.

(j) Probable pericarditis.

7.5 CONSENT

Prior to enrollment, informed consent should be sought from the patient and the attending physician. A model consent form is included in Chapter 8, and has been provided to all centers. This form, or a modification based on the local Institutional Review Board recommendations, should be completed for all enrolled patients.

T3 MANUAL OF OPERATIONS

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