Myocardial Infarction Review and Classification

NA-ACCORD Criteria for Events

Each potential MI event is reviewed and classified using standardized criteria.

A reviewer's classification of an event applies only to the specific hospitalization or outpatient situation under review. A reviewer should not be concerned if there is a history of prior incident events identified in the records or in NA-ACCORD reviews. Each event should be judged separately as "Definite," "Probable," or "No/Absent" for a new incident event. Both "Definite" and "Probable" events can be further classified as "Primary" or "Secondary".

Secondary events will be categorized into those that are procedure-related and non-procedure-related. For example, they will include all MIs secondary to hypotension (e.g. sepsis, severe trauma, etc.). When reviewers enter their online review, they will be asked to identify events as Primary or Secondary. If Secondary, they will be further asked to identify type of secondary event using a standardized list of possible causes. All events which occur among patients who have undergone a CABG or PTCA within the prior 48 hours should be classified as a secondary event and based on the appropriate enzyme criteria cut-offs.

1.1 Criteria for Myocardial Infarction

The criteria for MIs include information about chest pain, cardiac enzymes, and ECGs. NA-ACCORD uses state-of-the-art MI adjudication criteria updated from the Universal Definition of Myocardial Infarction and Multiethnic Study of Atherosclerosis (MESA) which developed criteria from the Atherosclerosis Risk in Communities (ARIC) Study ("ARIC Protocol 3, Surveillance Component Procedures, Version 4.0", October 1997) and built on earlier protocols such as the World Health Organization MONICA project developed in the early 1980s. There are differences between the Universal Definition and MESA MI definitions, particularly for cardiac enzyme criteria. In most instances, these differences will result in more patients meeting criteria for MI using the Universal Definition, particularly among patients who have not undergone a procedure. Where differences occur, the more inclusive criteria are used for adjudication. However, to facilitate future cross-study analyses including analyses of HIV-infected vs. HIV-uninfected individuals, differences in criteria are tracked allowing the subset of events that would not be classified as an MI by MESA criteria to be identified and excluded from analyses involving MESA controls.

1.1a Chest pain: Chest pain is defined as an episode of ischemic pain, tightness, pressure, or discomfort in the chest, arm, or jaw. Other atypical pains identified as due to coronary ischemia also qualify. If there is a clear non-cardiac cause, chest pain is considered to be absent. Duration of pain is not considered part of the chest pain criteria.

1.1b Enzyme criteria: Table 1 shows the enzyme criteria. Criteria differ for patients with Coronary Artery Bypass Grafting (CABG) or Percutaneous Transluminal Coronary Angioplasty (PTCA) in the prior 48 hours and for patients in whom (non-CABG or non-PTCA) muscle trauma is present. Total CK or LDH levels alone will not be sufficient to meet cardiac enzyme criteria.

Table 1

NA-ACCORD Algorithm to Classify Cardiac Enzymes as Abnormal, Equivocal or Normal

Enzyme Value	Classification
Troponins:	
Troponins ≤ ULN	Normal
ULN < Troponins	Abnormal
Within 48 hr after PTCA:	
Troponins ≤ ULN	Normal
ULN < Troponins ≤ 3x ULN	Equivocal
3x ULN < Troponins	Abnormal
Within 72 hr after CABG:	
Troponins ≤ ULN	Normal
ULN < Troponins ≤ 5x ULN	Equivocal
5x ULN < Troponins	Abnormal
CK-MB:	
CK-MB ≤ ULN	Normal
ULN < CK-MB	Abnormal
Muscle trauma other than PTCA/CABG:	
CK-MB ≤ ULN	Normal
ULN < CK-MB ≤ 2x ULN	Equivocal
CK-MB > 2x ULN	Abnormal
Within 48 hr after PTCA:	
CK-MB ≤ ULN	Normal
ULN < CK-MB ≤ 3x ULN	Equivocal
3x ULN < CK-MB	Abnormal
Within 72 hr after CABG:	
CK-MB ≤ ULN	Normal
ULN < CK-MG ≤ 5x ULN	Abnormal
5x ULN < CK-MB	
Other enzymes, not preferred:	
CK-MB = "present" where only quantified as "present" or "absent"	Abnormal
CK-MB** ≥ 10% Total CK, if no ULN given	Abnormal
LDH1* : LDH2 > 1	Abnormal
LDH1* ≥ 2x ULN if LDH2 is missing	Abnormal
5% Total CK < CK-MB** < 9% Total CK or CK-MB "weakly present"	Equivocal
ULN < LDH1* < 2x ULN	Equivocal
Data present, but insufficient for above criteria	Incomplete
All other results	Normal

* In the presence of liver disease or hemolytic disease, troponins or CK-MB are required for diagnosis of myocardial infarction; LDH levels should not be used.

** CK and CK-MB must be in same units for this criterion.

1.1c ECG criteria:

The following ECG tracings are identified by the sites and included in the review packet:

a. The first two ECGs after admission;
b. The last ECG recorded before discharge; and
c. The last ECG recorded on day 3 (or the first ECG thereafter) following admission or an in-hospital event.

The above ECG's will be provided to the Events Review Committee members who will review the ECG's and classify them into the categories listed below using clinical criteria.

1.2 MI Criteria: Table 2 shows the diagnostic categories of MI according to the ECG criteria, enzyme categories, and chest-pain history.

Table 2
NA-ACCORD Diagnostic Criteria for MI

Cardiac Pain Present **Cardiac Enzymes**

ECG Pattern *	Abnormal	Equivocal*	Incomplete	Normal
Evolution of Major Q-Wave	Definite MI	Definite MI	Definite MI	Definite MI
Evolution of ST Elevation with or without Q-wave Or New LBBB	Definite MI	Probable MI	Probable MI	No MI
Evolution of ST-T Depression/inversion alone Or Evolution of Minor Q-waves alone	Definite MI	Probable MI	No MI	No MI
Single ECG with Major Q-Wave Or Single ECG with LBBB, described as new	Definite MI	Probable MI	No MI	No MI
Normal, Absent, Uncodable, other	Definite MI	No MI	No MI	No MI

Cardiac Pain Absent **Cardiac Enzymes**

ECG Pattern *	Abnormal	Equivocal*	Incomplete or Missing	Normal
Evolution of Major Q-Wave	Definite MI	Definite MI	Definite MI	Definite MI
Evolution of ST Elevation with or without Q-wave Or New LBBB	Definite MI	Probable MI	No MI	No MI
Evolution of ST-T Depression/inversion alone Or Evolution of Minor Q-Wave alone	Definite MI	No MI	No MI	No MI
Single ECG with Major Q-Wave Or Single ECG with LBBB, described as new	Definite MI	No MI	No MI	No MI
Normal, Absent, Uncodable, other	Probable MI	No MI	No MI	No MI

*Note that some of the Definite MIs listed in the Abnormal enzyme column, would be downgraded to Probable MI in the MESA criteria due to different definitions of Abnormal. This will be done in the analysis as needed depending on whether MESA or Universal criteria are being used.

Although frequently not available, among patients with abnormal cardiac enzymes, the presence by imaging of a new loss of viable myocardium or a new regional wall motion abnormality will also meet criteria for a Definite MI. Imaging techniques can include echocardiography, radionuclide ventriculography, myocardial perfusion scintigraphy, magnetic resonance imaging (MRI), positron emission tomography (PET), and computed tomography (CT).

Note that if a patient is determined to have an MI, reviewers will then be asked if an MI is thought to be primary or secondary. A secondary MI occurs when a patient has an MI in the setting of another major event that likely contributed significantly to the MI. For example, a patient having an MI in the setting of bacteremia and severe sepsis would be classified as having had an MI, secondary, due to sepsis. All MIs within 48 hours after PTCA or CABG should be classified as secondary to these procedures.

In addition, reviewers will also be asked to mark all criteria that indicated an MI:

- Abnormal cardiac enzymes

  Enzyme criteria used:

  - Standard
  - PTCA
  - CABG
  - Muscle trauma exists (for CK-MB)
- Chest pain
- ECG changes
- Loss of viable myocardium or regional wall abnormality by imaging

A subset of patients may not have had an MI but still have confirmed coronary artery disease of a severity that requires an intervention. Therefore, for patients who are found not to have an MI, reviewers will also be asked if the patient underwent a cardiac intervention such as CABG or PTCA.

A subset of patients will meet review criteria for an MI however clinically they may not have had an actual event. Typically these are patients who meet criteria for an MI due to an elevated troponin and have no other evidence suggestive of an MI (no major ECG changes, nl CK-MBs, etc.) and who have a reason for a potential false positive troponin value such as renal failure. These patients should be reviewed according to standard review criteria (and therefore classified as having a definite or probably MI). However, after completing the review, if clinically, the patient is likely to not have had an MI, and there is no other evidence suggestive of an MI besides the elevated troponin, then please check the box indicating that the patient has a credible reason for a potential false positive value. These reasons could include renal failure (particularly with troponin T), severe sepsis, myocarditis (particularly with troponin I), severe or acute heart failure, massive pulmonary embolism, or acute pericarditis.

Finally, for all probable or definite events, reviewers will be asked about any mention of tobacco use (current or past), cocaine or crack use, and a family history of MI. Although ideally this question is referring to a family history of premature CAD, most chart documentation is not thorough enough to include ages of relatives and so any family history of CAD will be acceptable.

1.3 Criteria for Resuscitated Cardiac Arrest

A category of resuscitated cardiac arrest is an additional non-fatal outcome. This diagnosis is reserved for patients who were in full arrest (asystole or ventricular fibrillation and pulseless) and who underwent cardio-pulmonary resuscitation (including cardioversion) successfully. Cardiac arrest secondary to non-cardiac conditions, such as respiratory arrest, should not be classified as resuscitated cardiac arrest. Because post-arrest enzymes are difficult to interpret, in general, attempts to classify MI will not be made in patients with resuscitated cardiac arrest. To classify an event as a Resuscitated Cardiac Arrest, all of the criteria below must be met:

a. The absence of a clear-cut non-cardiac cause. Presence of cardiac symptoms (e.g., chest pain) is confirmatory but not necessary.
b. The person must have lived at least 24 hours after resuscitation.

2 Review Process

Reviewers will have three weeks (from when they receive the packet) to review all potential events. All potential events will be reviewed by 2 Physician Reviewers (not from the NA-ACCORD site where the event originated). Reviewers will complete online review forms. The results between reviewers will be compared by the Coordinating Center and any disagreement resolved as stated below.

2.1 Committee Review

Occasionally investigations will be reviewed by the entire Cardiac subgroup. This is done to ensure quality control. A selection of 10 to 20 training cases will be assembled for new reviewers for training and consistence purposes. In addition, a selected number of additional cases will reviewed by the entire committee each subsequent year for quality control purposes. Key teaching points from these selected cases will then be reviewed with all reviewers via conference call to minimize potential drift in methods of adjudication.

2.2 Disagreement Resolution

All conflicting diagnoses will be resolved by a "Third Reviewer".

The third reviewer diagnosis will be considered final. If the two reviewers do not agree, another reviewer will be assigned to act as the final reviewer and will complete a review. This independent Adjudication reviewer will discuss the case with the first two reviewers. The Adjudication reviewer will enter his/her decision online, and this will be considered the final diagnosis for that endpoint.

2.3 Reviewer Responsibilities

Reviewers are responsible for doing several things:

- Review investigations and have the results entered online within three weeks of receipt of the investigation review packet.
- Communicate with other Reviewers (when necessary) to resolve disagreements and submit results within three weeks of notification of disagreement.
- Act as a tie-breaker when two other Reviewers can not agree.

All questions or concerns with the process should be relayed directly to the NA-ACCORD Data Core. Chart reviewers at each site will also have no direct involvement in the Review Process (unless they are also a Physician Reviewer).

Appendix A. Important Definitions

Procedure-related events: The NA-ACCORD Review Committee classifies events as procedure-related or not. This classification requires clinical judgment and will be determined at Review.

Aborted MI: Because most people who receive thrombolytic therapy have elevations of enzymes and ECG changes, NA-ACCORD does not include a separate category for aborted MI.