### **DIAGNOSTIC CRITERIA OF AMI/ACS**

Diagnostic criteria are used to validate clinical diagnoses. Those used in epidemiological studies are here below reported.

# **1. MONICA - Monitoring trends and determinants of CArdiovascular disease** – (1983-84)

Diagnostic Classification

There are the following categories:

(1) definite acute myocardial infarction

(2) possible acute myocardial infarction or coronary death

(3) ischaemic cardiac arrest with successful resuscitation not fulfilling criteria for definite or possible myocardial infarction

(4) no acute myocardial infarction or coronary death

(9) fatal cases with insufficient data, subsequently called "unclassifiable deaths" in collaborative MONICA publications

Allocation of a diagnostic category must follow strictly the definitions provided. The criteria used for the diagnosis of "definite" and "possible" acute myocardial infarction are not necessarily those that would be used by a clinician, but rigid definitions are essential for event analysis.

#### (1) Definite acute myocardial infarction

- a. Definite ECG or
- b. Symptoms typical or atypical or inadequately described, together with probable ECG and abnormal enzymes, or
- c. Symptoms typical and abnormal enzymes with ischaemic or non-codable ECG or ECG not available, or
- d. Fatal cases, whether sudden or not, with naked-eye appearance of fresh myocardial infarction and/or recent coronary occlusion found at necropsy.

(2) Possible acute myocardial infarction or coronary death

- a. Living patients: with typical symptoms whose ECG and enzyme results do not place them in category (1) and in whom there is not good evidence for another diagnosis for the attack, or
- b. Fatal cases whether sudden or not (not in category (1)) where there is no good evidence for another cause of death, clinically or at autopsy.
- i. with symptoms typical or atypical or inadequately described, or
- ii. without typical or atypical or inadequately described symptoms but with evidence of chronic coronary occlusion or stenosis or old myocardial scarring at necropsy; or

iii. with a good history of chronic ischaemic heart disease such as definite or possible myocardial infarction, or coronary insufficiency or angina pectoris in the absence of significant valvular disease or cardiomyopathy.

## (3) Ischaemic cardiac arrest with successful resuscitation not fulfilling criteria for definite or possible myocardial infarction

Spontaneous cardiac arrest not provoked by medical intervention, electrocution, drowning or other gross physical insults, from presumed primary ventricular fibrillation secondary to ischaemic heart disease, in the absence of significant valvular disease or cardiomyopathy.

#### (4) No acute myocardial infarction

- a. Living patients (not in category (1))
  - i. with combinations of symptoms and tests that do not qualify them for the definite category and who do not have typical symptoms that might place them in the possible category, or
  - ii. where illness episode has been explained by another diagnosis
- b. Fatal cases, whether sudden or not, not in category (1) where another diagnosis has been made (clinically or at autopsy)

#### (9) Fatal cases with insufficient data

Cases with no autopsy, no history of typical or atypical or inadequately described symptoms, no previous history of chronic ischaemic heart disease and no other diagnosis. Living patients should not be allocated to this category. It is hoped that most centres will not need this category.

#### A. Electrocardiographic criteria

#### Code 1: Definite ECG

(I) The development in serial records of a diagnostic Q wave

-AND/OR-

(II) The evolution of an injury current which lasts more then one day.

The interpretation of a minimum of two or sometimes three ECG records is therefore necessary for the establishment of these categories.

#### I. Development of Q waves

Progression of Q codes from no Q to a diagnostic Q is sufficient but change from no Q to an equivocal Q or from equivocal to diagnostic Q must be accompanied by deterioration in the ST segment or the T wave. A change in a Q code or in a 4, 5 or 9.2 code must occur within the same lead group but the Q can be in a different lead group to that in which the 4, 5 or 9.2 code is being followed. Note that Minnesota code 1.2.6 is equivalent to No Q code.

1.1 No Q or QS code in the first ECG record followed by a record with a diagnostic Q or QS code (Minn. code 1.1.1 through 1.2.5 plus 1.2.7)

-OR-

1.2 An equivocal Q or QS code (Minn. code 1.2.8 or any 1.3 code) and no major ST segment depression (No Minn. code 4.1 or 4.2) in the first ECG record followed by a record with a diagnostic Q code PLUS a major ST segment depression (Minn. code 4.1 or 4.2)

-OR-

1.3 An equivocal Q finding and no ST segment elevation (No Minn. code 9.2) in the first ECG record followed by a record with a diagnostic Q code PLUS an ST segment elevation (Minn. code 9.2)

-OR-

1.4 An equivocal Q finding and no major T wave inversion (No Minn. code 5.1 or 5.2) in the first ECG record followed by a record with a diagnostic Q code PLUS a major T inversion (Minn. code 5.1 or 5.2)

-OR-

1.5 No Q code and neither 4-1 nor 4-2 in the first ECG followed by a record with an equivocal Q code PLUS a 4.1 or 4.2

-OR-

1.6 No Q code and no 9.2 in the first ECG followed by a record with an equivocal Q code PLUS a 9.2

-OR-

1.7 No Q code and neither 5.1 nor 5.2 in the first ECG followed by a record with an equivocal Q code PLUS a 5.1 or 5.2

-OR-

- II. Evolution of an injury current which lasts more than one day.
- 1.8 An ST segment Elevation (Minn. code 9.2) lasting more than one day (i.e. present on consecutive records of different dates)

#### AND

T wave progression on three or more records from 5.0 to 5.2 or from 5.3 to 5.1, with a more abnormal code present on consecutive records of different dates.

Note: The ST segment elevation does not have to be present in the same lead groups as the T progression, nor does it have to be exactly simultaneous. Q waves will often be present in the same graphs but they are not necessary to the use of this criterion for Definite ECG.

Code 2: Probable ECG

Evolution of repolarisation changes

2.1 No major ST segment depression in one ECG record (no 4.1 or 4.2) and another record with a major ST segment depression (Minn. code 4.1)

- 2.2 No ST segment elevation in one ECG record (no 9.2) and another record with an ST segment elevation (Minn. code 9.2)
- 2.3 No major T wave inversion in one ECG record (no 5.1 or 5.2) and another record with a major T wave inversion (Minn. code 5.1 or 5.2)

Note: Unlike the criteria in the previous classes, the evolution in this class can go in either direction, that is the codes can get better or worse.

Code 3: Ischaemic ECG (in one or more records)

Records not satisfying the above criteria which nonetheless show:

3.1 Minnesota codes 1.1.1 to 1.3.6 excluding 1.2.6 for Q and QS codes.

-AND/OR-

3.2 Minnesota codes 4.1 through 4.3 for ST junction (J) and segment depression.

#### -AND/OR-

3.3 Minnesota codes 5.1 through 5.3 for T wave items.

#### -AND/OR-

3.4 Minnesota code 9.2 for ST segment elevation.

Code 4: Other ECG

All other ECG findings, including normal ECG but note rules for uncodable ECG below.

#### Code 5: Uncodable ECG

The following Minnesota codes lead to suppression of all or most of these items, and a set of ECG records in which such findings are present in all records should be considered uncodable (unless codable Q waves are present, for example in an ECG showing a 7.4)

- 6-1 Third degree A-V block, suppresses all 1,4,5 and 9.2
- 6-4-1 Persistent Wolff-Parkinson White Pattern, suppresses all other codes.
- 6-8 Artificial pacemaker, suppresses all other codes.
- 7-1-1 Complete left bundle branch block, suppresses 1.2.3,1.2.7,1.2.8, 1.3.2, 1.3.6 and all 4, 5 and 9.2 codes but the presence of a codable Q downgrades it to 7.4.
- 7-2-1 Complete right bundle branch block, suppresses 1.2.8, and all 4, 5 and 9.2 codes.
- 7-4 Intraventricular block suppresses all 4, 5, and 9.2 codes.
- 8-2-1 Ventricular fibrillation and asystole, suppress all other codes
- 8-2-2 Idioventricular rhythm, suppresses all other codes.

8-4-1 Supraventricular tachycardia above 140/minute, suppresses all other codes.

#### Code 9: ECG absent

No ECG available or recorded. (Coded as 9, no data).

#### **B.** Symptoms

1 Indicates typical; 2, atypical; 3, other; 4, none; 5, inadequately described; and 9, insufficient data.

Code 1 (typical symptoms) when chest pain is present and characterized by (a) duration of more than 20 minutes and (b) no definite non-cardiac or cardiac non-atherosclerotic cause. If symptom duration is not stated, then code 5 (inadequately described). The duration can be assumed to be 20 minutes if the history implies that the pain lasted while something else was going on, or until something else happened.

Code 2 (atypical) if symptoms were not typical but there was (a) one or more of atypical pain, acute left ventricular failure, shock, and syncope and (b) the absence of cardiac disease other than ischemic heart disease and (c) no definite non-cardiac or cardiac non-atherosclerotic cause.

Code 3 (other symptoms) when symptoms are well described but do not satisfy the criteria for typical or atypical. Symptoms due to a definite non-cardiac cause or to a definite non-atherosclerotic cardiac cause (eg. pericarditis) should be coded 3.

Code 4 (no symptoms) in nonfatal cases if the patient reported no symptoms in the attack and in fatal cases if the eyewitnesses of the fatal collapse state that the individual was completely normal and uncomplaining before the moment of death.

Code 5 (inadequately described symptoms) for cases otherwise satisfying criteria for typical pain but in which the duration of the pain is not described, so that it is not possible to classify the symptoms as typical.

Code 9 (insufficient data) if information on the presence or character of symptoms is inadequate.

#### C. Serum Enzymes

1 Indicates abnormal; 2, equivocal; 3, nonspecific; 4, normal; 5, incomplete; and 9, insufficient data.

Each MCC should define, with the help of their local hospital laboratories, (a) the cardiac enzyme tests used and (b) the upper limit of normal for each test in each laboratory.

Code 1 (abnormal) if at least one reading is more than twice the upper limit of normal when measured within 72 hours or 3 calendar days of onset of symptoms, admission to hospital, or any recurrence of symptoms.

Code 2 (equivocal) when serum enzyme levels are raised but to less than twice the upper limit of normal.

Code 3 (nonspecific) if serum enzyme levels are raised to more than twice the upper limit of normal but there are explanations other than myocardial infarction, such as liver disease, infections, defibrillation, or surgery.

Code 4 (normal) when the enzyme tests are done in time and are within the limits of normal.

Code 5 (incomplete) where tests are done >72 hours after the onset of acute symptoms or any recurrence.

Code 9 (insufficient data) when serum enzyme tests have not been done or results are unavailable.

#### **D.** Necropsy Findings Summary

1 Indicates definite; 2, equivocal; 4, negative; 8, alive at 28 days or no necropsy performed; and 9, insufficient data.

Code 1 (definite) if there visible to the naked eye was (a) myocardial infarction and/or (b) recent occlusion of a coronary artery (from ante-mortem thrombus or hemorrhage into a plaque or embolism).

Code 2 (equivocal) when the record does not show definite evidence or record any non-cardiac or cardiac, non-atherosclerotic disease causing death but there is (a) old myocardial infarction (scar) and/or (b) occlusion or severe stenosis (>50% reduction of lumen) by atheroma of one or more coronary arteries.

Code 4 (negative) when there is recorded at necropsy (a) no definite evidence as described above and (b) evidence of non-cardiac or cardiac non-atherosclerotic disease causing death.

Code 8 (not relevant) if the patient is alive at 28 days or if necropsy was not done.

Code 9 (insufficient data) when the results of the necropsy were not obtained.

For a more complete overview of MONICA criteria consult the following publication: World Health Organization: WHO Monica Project: MONICA manual. Part IV: Event Registration. http://www.ktl.fi/publications/monica/manual/part4/iv-2.htm#s1-1

#### 2. American Heart Association Criteria (2003)

*Case definitions for Acute Coronary Heart Disease in Epidemiology and Clinical Research Studies.* A statement from AHA Council of Epidemiology and Prevention; AHA Statistics Committee; World Heart Federation Council of Epidemiology and Prevention; European Society of Cardiology Working Group on Epidemiology and Prevention; Centers for Disease Control and Prevention; National Heart, Lung, and Blood Institute.

#### **Classification of AMI**

	Biomarker Findings								
	Cardiac Symptoms or Signs Present				Cardiac Symptoms or Signs Absent				
ECG Findings	Diagnostic	Equivocal	Missing	Normal	Diagnostic	Equivocal	Missing	Normal	
Evolvine diagnostic	Definite	Definite	Definite	Definite	Definite	Definite	Definite	Definite	
Positive	Definite	Probable	Probable	No	Definite	Probable	Possible	No	
Non specific	Definite	Possible	No	No	Definite*	Possible	No	No	
Normal or other ECG findings	Definite	Possible	No	No	Definite*	No	No	No	

Classification of case is at highest level allowed by combinations of 3 characteristics (cardiac signs and symptoms, ECG findings, biomarkers).

\*In absence of diagnostic troponin, downgrade to possible.

#### **Definitions of IHD**

The definition of a IHD case depends on symptoms, signs, biomarkers, and ECG and/or autopsy findings. These data may vary in quantity, quality, and timing. On the basis of the extent and diagnostic quality of data, definite, probable, and possible cases of fatal and nonfatal AMI, procedure-related events, and angina pectoris are defined. The recommendations emphasize biomarkers in a setting in which signs, symptoms, and/or ECG findings suggest acute ischemia.

## Definition of Terms

Cardiac Biomarkers

Cardiac biomarkers are blood measures of myocardial necrosis, specifically CK, CK-MB, CK-MBm, or troponin (cTn). The order of diagnostic value is cTn\_CK-MBm\_CK-MB\_CK.

A. *Adequate set of biomarkers*: At least 2 measurements of the same marker taken at least 6 hours apart B. *Diagnostic biomarkers*: At least 1 positive biomarker in an adequate set (see A above) of biomarkers showing a rising or falling pattern in the setting of clinical cardiac ischemia and the absence of noncardiac causes of biomarker elevation

C. *Equivocal biomarkers*: Only 1 available measurement that is positive, or a rising or falling pattern not in the setting of clinical cardiac ischemia or in the presence of nonischemic causes of biomarker elevation

D. Missing biomarkers: Biomarkers not measured

E. *Normal biomarkers*: Measured biomarkers do not meet the criteria for a positive biomarker (see F below)

F. *Positive biomarkers*: At least 1 value exceeding the 99<sup>th</sup> percentile of the distribution in healthy populations or the lowest level at which a 10% coefficient of variation can be demonstrated for that laboratory

#### Cardiac Symptoms and Signs

Cardiac symptoms and signs are findings from patient interview and examination.

A. *Cardiac symptoms*: Presence of acute chest, epigastric, neck, jaw, or arm pain or discomfort or pressure without apparent noncardiac source. More general, atypical symptoms, such as fatigue, nausea, vomiting, diaphoresis, faintness, and back pain, should not be used as a diagnostic criterion, although they are clinically useful in arriving at the correct diagnosis.

B. *Cardiac signs*: Acute congestive heart failure or cardiogenic shock in the absence of non-IHD causes.

#### **ECG** Findings

One or more ECG(s) may be collected in a possible cardiac event. These should be adjudicated or classified when possible.

The evolution of ECG findings may be demonstrated between the ECG(s) associated with the event or between a previously recorded ECG and the event ECG(s). In cases in which only a single event ECG is available, an evolving diagnostic ECG pattern can be recorded only if a previous study ECG is available (eg, if there is no previous study ECG and only 1 event-related ECG, there can be no classification of "evolving diagnostic" ECG).

Precise measurement guidelines for measurement of wave onset and offset to determine wave duration and voltage must be followed. Most events likely to be AMI occur in settings not controlled by epidemiology researchers, so that most ECG(s) will be hard copy, with varying levels of quality. The most extensively used measurement system for visual ECG findings is the Minnesota Code. These measurement guidelines should be coupled with validated biologically acceptable degrees of change in ECG wave forms to code an evolution of change. Another coding system that standardizes the measurement of ECG wave patterns is the Novacode (an extension of the Minnesota Code), which was designed for clinical trial ascertainment of AMI. More details on ECG coding are available on the Minnesota ECG Coding Center web site (www.epi.umn.edu/ecg).

The categories are as follows:

- A. Evolving diagnostic ECG
- B. Positive ECG
- C. Nonspecific ECG
- D. ECG negative for ischemia

#### Postmortem Consistent With AMI

Postmortem findings consistent with AMI are a cardiac pathology consistent with recent coronary occlusion or AMI  $\leq$  28 days old.

#### **Case Classifications for IHD**

#### I. Nonfatal events

A. Definite AMI

- 1. Evolving diagnostic ECG, or
- 2. Diagnostic biomarkers
- B. Probable AMI

1. Positive ECG findings plus cardiac symptoms or

signs plus missing biomarkers, or

2. Positive ECG findings plus equivocal biomarkers

#### C. Possible AMI

1. Equivocal biomarkers plus nonspecific ECG findings,

or

2. Equivocal biomarkers plus cardiac symptoms or

signs, or

3. Missing biomarkers plus positive ECG

D. Unrecognized AMI

1. Appearance, in a nonacute setting, of a new diagnostic Q wave with or without ST-T– wave depression, or ST elevation

E. Medical procedure-related event

1. Cardiac events after (up to 28 days) a medical procedure (eg, general surgery) with criteria for definite, probable, and possible AMI identical to those described above (I.A–C)

2. May be reported separately as procedure-related cardiac events or combined with overall event rates

3. If the medical procedure was performed for the treatment of acute ischemia (eg, angioplasty, coronary bypass surgery), an event should be classified as described above (I.A–C) and not considered procedure-related

F. Unstable angina pectoris

1. New cardiac symptoms and positive ECG findings with normal biomarkers

- 2. Changing symptom pattern and positive ECG findings with normal biomarkers
- G. Stable angina pectoris

1. Cardiac symptoms in a pattern that remains constant in presentation, frequency, character, and

duration over time

#### II. Fatal events (hospitalised patients)

- A. Definite fatal AMI
  - 1. Death within 28 days of hospital admission in AMI cases defined in I.A
  - 2. Postmortem findings consistent with AMI within 28 days
- B. Probable fatal MI

1. Death within 28 days of hospital admission in cases defined in I.B

2. Death within 6 hours of hospital admission with cardiac symptoms and/or signs. Other confirmatory data (biomarkers, ECG) are absent or not diagnostic.

#### C. Possible fatal coronary event

1. Death within 28 days of hospital admission in cases defined in I.C, I.F, and I.G

2. Post-mortem findings show old infarct and/or  $\geq$  50% atherosclerotic narrowing of coronary arteries

For a more complete overview of AHA criteria consult the following publication: *Luepker VR*, *Apple FS*, *Chistenson RH*, *Crow RS*, *Fortmann SP*, *Goff D*, *Goldberg RJ*, *Hand MM*, *Jaffe AS*, *Julian DG*, *Levy D*, *Manolio T*, *Mendis S*, *Mensah G*, *Paj k A*, *Prineas R*, *Reddy S*, *Roger V*, *Rosamond WO*, *Shahar E*, *Sharrett R*, *Sorlie P*, *Tunsall-Pedoe H*. *Case definitions for acute coronary heart disease in epidemiology and clinical research studies*. *Circulation 2003; 108: 2543-2549*.

#### 3. Nomenclature for AMI/ACS proposed by British Cardiac Society (2004)

The clinical and cardiac marker manifestations are determined by the volume of myocardium affected and the severity of ischaemia. Despite the similarities in disease mechanism the time course and severity of cardiac complications vary substantially across the spectrum of ACS. Similarly, treatment patterns differ.

BCS proposes that the spectrum of ACS should be subdivided as follows:

- ACS with unstable angina
- ACS with myocyte necrosis
- ACS with clinical Acute Myocardial Infarction (AMI).

	Markers	ECG	Pathology
ACS with unstable angina	Troponin (TnT) and creatine-kinase (CK- MB) undetectable	ST or T non- elevation or transient ST elevation or normal	Partial coronary occlusion (plaque disruption, intra- coronary thrombus, micro- emboli)
ACS with myocite necrosis	TnT elevation, < 1.0 ng/ml	ST o T elevation or transient ST elevation or normal	Partial coronary occlusion (plaque disruption, intra- coronary thrombus, micro- emboli), more extended than that provoked by angina
ACS with clinical myocardial infarctionTnT elevation, > 1.0 ng/ml +/- CK-MB elevation		ST elevation or ST non- elevation or T inversion: may evolve Q waves	Complete coronary occlusion (plaque disruption, intra- coronary thrombus, micro- emboli)

#### SPECTRUM OF ACUTE CORONARY SYNDROME (ACS)

BCS recommends that the term "unstable angina" should be reserved for patients with a clinical syndrome, but with undetectable troponin or CK-MB markers.

Unstable angina requires supporting evidence of coronary disease (abnormal ECG or prior documented coronary disease).

The term "ACS with myocyte necrosis" should be reserved for patients with a typical clinical syndrome plus an increased troponin concentration below the diagnostic threshold (that is, troponin T < 1.0 ng/ml or AccuTnI < 0.5 ng/ml)

The term "clinical myocardial infarction" should be reserved for patients in the context of a typical clinical syndrome and a marker increase above the diagnostic threshold.

BCS proposes that the threshold for defining clinical AMI be set at 1.0 ng/ml for troponin T or 0.5 ng/ml for AccuTnI (or equivalent threshold with other troponin I methods)

Therefore, BCS recommends that in the context of a typical ACS clinical myocardial infarction should be diagnosed when the maximum troponin T increase is > 1.0 ng/ml or AccuTnI > 0.5 ng/ml (and/or new Q waves develop on the ECG).

Individual laboratories that use other troponin I assays will need to estimate an equivalent troponin I concentration.

It is well recognised that the myocardium can be damaged after percutaneous coronary intervention (PCI) and cardiac markers may increase in up to a third of patients. It is important to bear in mind, just as with spontaneous MI, that cardiac enzyme release after PCI should be integrated with clinical, angiographic, and ECG data to assess prognosis properly. Troponin concentrations should not be considered in isolation. BSC recommends systematic measurement of troponins after PCI (> 6 hours) as part of quality control standards.

The figure reported below describes the spectrum of acute coronary syndrome.

ACS with unstable angina	ACS with myocyte necrosis	ACS with clinical myocardial infarction
Marker: Tn (Troponin) and CK- MB (creatine kinase) undetectable	Marker: Troponon elevated TnT < 1.0 ng/ml	Marker: Tn (Troponin) and CK- MB (creatine kinase) undetectable
ECG: ST↓or T↓or transient ST↑ or normal		ECG: ST♠or ST↓ or T inversion: may evolve Q waves
Risk of death (from hospitalisation to 6 months): 5-8%	Risk of death (from hospitalisation to 6 months): 8-12%	Risk of death (from hospitalisation to 6 months): 12-15%
Pathology (plaque disruption, intra- coronary thrombus, micro-emboli): partial coronary occlusion		Pathology (plaque disruption, intra- coronary thrombus, micro-emboli): complete coronary occlusion
Left Ventricular function: no measurable dysfunction		Left Ventricular function: systolic dysfunction, LV dilatation

For a more complete overview of BCS criteria consult the following publication: Fox KAA, Birkhead J, Wilcox R, Knight C, Barth J. British Cardiac Society Working Group on the definition of myocardial infarction. Heart 2004; 90: 603-609.

#### 4. European Society of Cardiology/American College of Cardiology Criteria (2000)

#### Criteria for definition of acute, evolving or recent myocardial infarction

Either one of the following criteria satisfies the diagnosis for an acute, evolving or recent myocardial infarction:

(1) Typical rise and gradual fall (troponin) or more rapid rise and fall (CK-MB) of biochemical markers of myocardial necrosis with at least one of the following:

- (a) ischemic symptoms;
- (b) development of pathologic Q waves on the ECG;
- (c) ECG changes indicative of ischemia (ST segment elevation or depression); or
- (d) coronary artery intervention (e.g., coronary angioplasty).

(2) Pathologic findings of an acute MI.

#### Criteria for established myocardial infarction

Any one of the following criteria satisfies the diagnosis for established myocardial infarction:

(1) Development of new pathologic Q waves on serial ECGs. The patient may or may not remember previous symptoms. Biochemical markers of myocardial necrosis may have normalized, depending on the length of time that has passed since the infarct developed.

(2) Pathologic findings of a healed or healing myocardial infarction.

For a more complete overview of ESC/ACC criteria consult the following publication: The Joint European Society of Cardiology/American College of Cardiology Committee. Myocardial infarction redefined. A consensus document of The Joint European Society of Cardiology/American College of Cardiology Committee for the Redefinition of Myocardial Infarction. Eur Heart J 2000; 21: 1502-1513.