10.   Definition of cardiovascular diseases

10.1   *Nosologic definitions*

Acute myocardial infarction: myocardial cell death due to prolonged ischaemia[63] .

Acute coronary syndrome: it is a big category which includes myocardial infarction, both Q-wave and non-Q-wave, and unstable angina. Unstable angina is an acute ischaemia without myocardial necrosis.

Angina pectoris: a pain in the chest and/or adjacent area associated with myocardial ischaemia but without myocardial necrosis[63]. It is an old term used to describe myocardial ischemia without necrosis. It is generally divided into unstable, which is part of acute coronary syndrome, and stable angina.

Ischaemic heart diseases and coronary heart diseases: are commonly due to the obstruction of coronary arteries by atheromatous plaques. These include acute myocardial infarction, other symptomatic and asymptomatic (silent) myocardial ischaemia, old myocardial infarction, angina pectoris, and other forms of chronic ischaemic heart disease. Generally speaking, congestive heart failure, cardiac arrhythmias and sudden death recognise the same etiology. There are also non-atherosclerotic causes of obstructive coronary artery diseases (CAD). Myocardial ischaemia may also occur in the absence of obstructive CAD, as in the case of aortic valve disease, hypertrophic cardiomiopathy, idiopathic dilated cardiomiopathy, and luetic aortitis [64]; they are rare.

Heart failure: it is a pathophysiological state in which an abnormality in cardiac function is responsible for the failure of the heart to pump blood at a rate commensurate with the requirements of metabolising tissues[63]. Hypertension, myocardial infarct, and coronary heart disease are the major causes of heart failure.

*Cerebrovascular accidents: s*troke is characterised by rapidly developing clinical symptoms and signs of focal, at times global, loss of cerebral function lasting more than 24 hours or leading to death, with no apparent cause other than that of vascular origin [63].

There are four main types of stroke: two caused by blood clots or other particles and two by haemorrhage. Ischaemic stroke (thrombosis and embolism) is the most common, accounting for about 70-80% of all strokes [63].

Cerebral thrombosis: it occurs when a blood clot (thrombus) forms and blocks blood flowing in an artery that supplies blood to part of the brain. Blood clots usually form in arteries damaged by atherosclerosis [63].

Cerebral embolism: it occurs when a clot (an embolus) or some other particle formed in a blood vessel, usually in the heart, is carried in an artery leading to or in the brain, blocking the flow of blood. The most common cause of embolism is atrial fibrillation[64].

Subarachnoid haemorrhage: it occurs when a blood vessel on the surface of the brain ruptures and bleeds into the space between the brain and the skull [64].

Intracerebral haemorrhage: it occurs when a defective artery in the brain bursts, flooding the surrounding tissue with blood [64].

Other cardiovascular diseases: include rheumatic heart disease, hypertensive heart diseases, other forms of heart diseases, atherosclerosis, aortic aneurysm, acute cor pulmonale, dysrhythmias, acute pulmonary oedema and venous thromboembolic diseases.

10.2   *Nosographic definitions*

Table 12 shows the diseases and their codes following the ICD, 8th, 9th, and 10th Revisions. Most countries have adopted ICD-10 Revision, however ICD-9 is still used by almost all countries for coding HDRs, because of the classification of procedures (ICD9-CM)[65-67]. In 1996 the Nordic Medico-Statistical Committee (NOMESCO) published the Classification of Surgical Procedures adopted in the five Nordic Countries (Denmark, Sweden, Finland, Norway, and Iceland)[68].

10.3   *Standardised diagnostic criteria*

Diagnostic criteria are used to validate clinical diagnoses. Those used in standardised studies are here reported in detail.

10.3.a MYOCARDIAL INFARCTION

WHO criteria [46]

Myocardial infarction is defined as definite on the basis of history, ECG, enzyme and necropsy, as follows:

1) ECG with unequivocal serial changes, or 2) typical history or atypical history together with equivocal ECG and elevated enzymes, or 3) typical history and elevated enzymes with negative or non available ECG, or 4) fatal cases whether sudden or not, with naked-eye appearance of fresh myocardial infarction and/or recent coronary occlusion at necropsy (ante-mortem thrombus, haemorrhage into an atheromatous plaque or embolism).

MONICA criteria [24]

Non-fatal coronary events are classified as *definite* and *possible*. The major difference with the WHO criteria is the use of the Minnesota code, a quantitative system for coding ECGs [69,70].

A *definite non-fatal event* is defined as:

(1) Progression of Minnesota codes on serial ECGs;

- Progression from no Q-wave to a definite Q-wave; or

- A lesser Q-wave progression combined with progressive ST-segment depression, developing ST-segment elevation, or progressive T-wave inversion; or
- Persistent ST-segment elevation with progressive T-wave inversion in sequential daily ECGs; or

(2) Cardiac enzyme levels two times the normal cut-off point, either with typical symptoms and an abnormal ECG, or with lesser symptoms and an ECG progression labelled *probable*.

Non-fatal events are placed in the category *possible* if a typical prolonged chest pain (20 minutes) occurs together with lesser or no ECG and enzyme findings.

Fatal coronary events are classified as *definite*, *possible*, and *unclassifiable*.

Events are *definite* if they satisfy the following criteria:

- definite criteria reported for non-fatal events; or
- when autopsy shows recent myocardial infarction or coronary thrombosis.

Possible coronary death involves suggestive terminal symptoms, or a CHD history in the absence of chronic occlusive CHD, or old myocardial infarction without pathological findings suggestive of a fatal disease.

Limitations of the coronary MONICA criteria [45]

The MONICA Project provides thorough information on mortality and morbidity, diagnostic criteria, standardisation, validation, quality control and data comparability for the years 1985-1994. Consistent methodology and diagnostic criteria were used to identify coronary events over time. The methodology was expensive, however. Available indicators were attack rate and fatality rate. There are some aspects that limit the study's generalisability:

- the age group under surveillance was limited to 35-64 year old individuals;
- areas selected for the study were those registering 100 to 300 coronary deaths in men below age 65 years;
- the selected areas were not necessarily representative of the whole country;
- it could not identify silent forms of myocardial infarction and misdiagnosed events.

New Criteria of the Joint ESC/ACC Committee for the Redefinition of Myocardial Infarction [71]

Recently, sensitive and specific serologic biomarkers have become available for the identification of very small myocardial infarctions that would not have been detected earlier. The biomarker of myocardial damage is cardiac troponine, which has nearly absolute myocardial tissue specificity, as well as a high sensitivity.

The application of these new, more sensitive criteria for MI will potentially cause the rise of MI incidence and the fall of case fatality rate. Thus, the new definition of MI may confuse efforts to

follow trends of disease rates in populations. Continued tracking of these trends will require methods for adjusting to the new criteria.

Criteria for acute, evolving or recent AMI

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

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

    (a) Ischaemic symptoms;

    (b) Development of pathologic Q-waves on the ECG;

    (c) ECG changes indicative of ischaemia (ST-segment elevation or depression); or

    (d) Coronary artery intervention (e.g., coronary angioplasty).

(2) Pathologic findings of an acute MI.

Criteria for established MI (past)

Anyone of the following criteria satisfies the diagnosis for established MI:

(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 normalised, depending on the time elapsed since the infarct developed.

(2) Pathologic findings of a healed or healing MI.

Limitations of the Joint ESC/ACC criteria[72]

These new criteria, based on the rise and fall of the cardiac troponine marker, can be observed if myocardial infarction comes under care immediately after the onset of symptoms and the patient survives for several days, in order to guarantee the fall of the biochemical marker. Therefore the definition is not comprehensive of fatal cases.

10.3.b UNSTABLE ANGINA

According to the New Criteria of the Joint ESC/ACC Committee unstable angina is defined as an ACS with no ST-segment elevation at the ECG and no elevation of biochemical markers such as troponine or CK-MB measured by mass assay [71].

10.3.c ISCHAEMIC HEART DISEASE

The LSHTM questionnaires for angina pectoris on effort and myocardial infarction identify the characteristics of ischaemic pain - i.e., occurrence usually on walking, in certain chest site, usually causing the individual to slow his pace or stop, and promptly relieved by rest. ECG Minnesota Code provides a framework for uniform reporting in reasonably homogeneous, precisely defined classes, and includes instructions to reduce coding variability. Definition of the Minnesota ECG Codes are

given in the Publication of Rose and Blackburn[34,35]; diagnostic criteria for IHD are reported in the publication of Keys [36]:

- major Q-waves corresponding to Minnesota Codes 1.1
- lesser Q-waves plus major T-wave findings, corresponding to Minnesoda Codes 1.2 plus 5.1 or 1.2 plus 5.2
- major specific resting ECG abnormalities corresponding to one of the following Minnesota Codes: 1.2, 1.3; 5.1, 5.2; 6.1, 6.2; 7.1, 7.2, 7.4 or 8.3.

10.3.d HEART FAILURE

Framingham Criteria [23]

Criteria for HF as specified in the Framingham Study may be distinguished into major and minor criteria.

Major criteria include:

- paroxysmal nocturnal dyspnoea
- neck vein distension
- rales
- radiographic cardiomegaly (increasing heart size on chest X-ray film)
- acute pulmonary oedema
- third sound gallop
- increased central venous pressure (>16 cm H_2O in the right atrium)
- circulation time $\geq$25 seconds
- hepatojugular reflux
- pulmonary oedema, visceral congestion or cardiomegaly at autopsy
- weight loss $\geq$4.5 kg in 5 days in response to treatment of HF.

Minor criteria include:

- bilateral ankle oedema
- nocturnal cough
- dyspnoea on ordinary exertion
- hepatomegaly
- pleural effusion
- decrease in vital capacity by 33% from maximal value recorded
- tachycardia (rate $\geq$120 beats/min)

Diagnosis of HF is given for two major or one major and two minor criteria [23].

Boston Criteria [73]

Criterion	Point value [*]	
Category I: history		
Rest dyspnoea	4	
Orthopnea	4	
Paroxysmal nocturnal dyspnoea	3	
Dyspnoea while walking on level area	2	
Dyspnoea while climbing	1	
Category II: physical examination		
Heart rate abnormality	1	*if 91 to 110 beats per minute*
	2	*if more than 110 beats per minute*
Jugular venous elevation	2	*if greater than 6 cm* H_2O
	3	*if greater than 6 cm* H_2O *plus hepatomegaly or oedema*
Lung crackles	1	*if basilar*
	2	*if more than basilar*
Wheezing	3	
Third heart sound	3	
Category III: chest radiography		
Alveolar pulmonary oedema	4	
Interstitial pulmonary oedema	3	
Bilateral pleural effusion	3	
Cardio thoracic ratio greater than 0.50	3	
Upper zone flow redistribution	2	

[*] The composite score (the sum of the subtotal from each category) has a possible maximum of 12 points. The diagnosis of heart failure is classified as *definite* at a score of 8 to 12 points, *possible* at a score of 5 to 7 points, and *unlikely* at a score of 4 points or less.

ESC definition of HEART FAILURE[74]

1. Symptoms of heart failure (at rest and during exercise)

<p align="center">and</p>

2. Objective evidence of cardiac dysfunction (at rest)

<p align="center">and</p>

3. Response to treatment directed towards heart failure (in cases where the diagnosis is in doubt)

Criteria 1 and 2 should be fulfilled in all cases.

Limitations of HF case finding

To obtain an exhaustive picture regarding HF, which does not necessarily require routine hospitalisation, review of GP records or ad hoc surveys are necessary.

In HDRs, HF can be found under different diagnoses. Therefore if validation studies on HF are carried out these codes should be taken into account [75]:

- heart failure: ICD-9 428, ICD-10 I50

- hypertensive heart disease: ICD-9 402, ICD-10 I11

- other primary cardiomyopathies: ICD-9 425.4, ICD-10 I42.5, I42.8

- alcoholic cardiomyopathy: ICD-9 425.5, ICD-10 I42.6

- secondary cardiomyopathy, unspecified: ICD-9 425.9, ICD-10 I42.9

- chronic cor pulmonale: ICD-9 416.9, ICD-10 27.9

10.3.e STROKE

WHO criteria [76]

The recommended WHO stroke definition is *a focal (or at times global) disturbance of cerebral function lasting more than 24 hours (or leading to death) with no apparent cause other than that of vascular origin. Transient episodes of cerebral ischaemia were excluded by definition.* Cerebrovascular lesions discovered at autopsy without having shown clinical manifestations in life were not registered as stroke. A careful review of the patient's history is required to differentiate a previous stroke from previous TIA, as the two episodes may be misclassified.

This definition is normally used in longitudinal studies [77]. When possible, incidence studies should register TIA because mild strokes are often misdiagnosed as TIA [78].

MONICA criteria[79]

Definite stroke is a *rapid development of focal signs (or global) or disturbance of cerebrovascular function lasting more than 24 hours (unless interrupted by surgery or death), with no apparent cause other than that of vascular origin; this category includes patients presenting clinical signs and symptoms suggestive of subarachnoid haemorrhage, intracerebral haemorrhage, or cerebral ischaemic infarct. The term "global" refers to patients with subarachnoid haemorrhage or deep coma but it excludes coma of systemic vascular origin such as shock, Stokes-Adams syndrome or hypertensive encephalopathy.*

This definition of stroke includes reference to a focal or global disturbance of the cerebral function. One or more of the following definite focal signs must be present to make a diagnosis of stroke: unilateral or bilateral motor impairment (including un-coordination), unilateral or bilateral sensory

impairment, aphasia/dysphasia (non-fluent speech), hemianopia (half-sided impairment of visual fields), diplopia, forced gaze (conjugate deviation), apraxia of acute onset, ataxia of acute onset (muscular un-coordination), perception deficit of acute onset.

Time dimension has to be met and the signs should have developed from a presumed vascular origin.

Limitations of stroke case finding

The above criteria were developed to allow comparisons of stroke rates in communities with different availability of diagnostic image technologies (CT and MRI) necessary for stroke type definition (ischaemic and hemorrhagic).