

## **S2 Appendix. Definitions of cardiovascular events.**

### **1. Myocardial Infarction**

Non-fatal myocardial infarction was defined as experiencing at least one of the following conditions:

- (1) Electrocardiographic (ECG) abnormality fulfilling the definitive diagnostic criteria at the time of event
- (2) Ischemic chest pain and elevated cardiac enzyme levels fulfilling the diagnostic criteria at the time of event
- (3) Ischemic chest pain, elevated cardiac enzyme levels, and ECG abnormality fulfilling the suspected criteria at the time of event
- (4) New ECG abnormality fulfilling the definitive diagnostic criteria at the time of event; however, it should not have fulfilled the definitive diagnostic criteria at the previous test
- (5) Elevated cardiac enzyme

### **2. Angina Pectoris**

- (1) A case fulfilling all of the following symptoms (chest pain and chest discomfort):
  - Pain, discomfort, or strangulation including any part of the sternum
  - Symptoms appear at the time of exertion or stress, usually lasting over 30 seconds (the degree of exertion or stress does not matter)
  - Mostly, symptoms appear within 10 minutes after relieving rest or exertion
  - Symptoms usually improve within 2 to 5 minutes after nitroglycerin administration. However, this condition isn't applicable when nitroglycerin has never been administered
- (2) A case without any symptoms
  - Hospitalization for the diagnosis and treatment of angina pectoris within the observation period and diagnosed as angina pectoris

### **3. Asymptomatic Myocardial Ischemia Including Painless Myocardial Infarction**

- (1) New ECG abnormality suggesting myocardial ischemia
- (2) A case fulfilling at least one of the following conditions:
  - Myocardial ischemia has been confirmed by radioisotope examination
  - Significant stenosis or occlusion of the coronary artery has been confirmed by coronary angiogram or multislice computed tomography

### **4. Congestive heart failure**

A case fulfilling at least one of the following conditions, and clinically diagnosed as congestive heart failure:

- (1) Non-acute heart failure
- (2) Accompanied with marked respiratory distress
- (3) Marked pulmonary edema in the chest X-ray front view
- (4) Markedly high levels of brain natriuretic peptide (when measuring)
- (5) Need for strict fluid balance control

## **5. Arrhythmia**

A case with at least one of the following conditions:

- (1) Ventricular fibrillation
- (2) Sustained ventricular tachycardia
- (3) Torsades de pointes
- (4) High-grade atrioventricular block (complete atrioventricular block)
- (5) Sick sinus syndrome
- (6) Atrial fibrillation
- (7) Atrial flutter

## **6. Cerebrovascular Disease**

The following three types of events are targeted for diagnosing cerebrovascular disease:

- (1) Cerebral infarction
- (2) Cerebral hemorrhage
- (3) Subarachnoid hemorrhage

For diagnosis, all of the following conditions should be fulfilled:

- Cerebral infarction, cerebral hemorrhage, or subarachnoid hemorrhage appeared recently and clear and objective focal neurological deficit observations were confirmed
- Observations lasted more than 24 hours
- Neurological observations were not due to extracranial disorders
- Cerebrovascular disease could be classified as cerebral hemorrhage, cerebral infarction, or subarachnoid hemorrhage with computed tomography or magnetic resonance imaging or autopsy records within 3 weeks of onset

## **7. Peripheral Artery Disease**

A case fulfilling at least one of the following conditions:

- (1) Vascular intermittent claudication
- (2) Unilateral disappearance or weakness of the femoral artery pulse
- (3) Unilateral disappearance or weakness of the dorsalis artery and posterior tibial artery pulse
- (4) Disappearance or weakness the dorsalis artery and/or posterior tibial artery pulse
- (5) Ankle brachial index  $< 0.8$
- (6) Angiography confirmed stenosis (more than 75% stenosis or collateral circulation)
- (7) Lower leg gangrene or ulcer