2012 Guidelines of the Taiwan Society of Cardiology (TSOC) for the Management of ST-Segment Elevation Myocardial Infarction

Yi-Heng Li,[1] Hung-I Yeh,[2] Chia-Ti Tsai,[3] Ping-Yen Liu,[1] Tsung-Hsien Lin,[4] Tao-Cheng Wu,[5] Kuo-Chun Hung,[6] Yu-Cheng Hsieh,[7] Guang-Yuan Mar,[8] Chih-Yuan Fang,[9] Kuan-Ming Chiu,[10] Jun-Jack Cheng[11] and Jyh-Hong Chen[1]

ST-segment elevation myocardial infarction (STEMI) is one of the most common cardiovascular diseases in Taiwan. The management strategies for STEMI are to do early diagnosis, minimize delay of medical contact, and administration of reperfusion therapy as rapidly as possible. Initial evaluation in emergency department for STEMI includes concise history taking, physical examination, electrocardiogram and cardiac biomarkers measurement. A 12-lead electrocardiogram should be performed within 10 minutes of emergency department arrival. Oxygen, nitroglycerin, analgesia, dual antiplatelet therapy and anticoagulation drugs should be given immediately. Patients with STEMI should receive reperfusion therapy either by primary percutaneous coronary intervention with door-to-balloon time within 90 minutes or by thrombolytic therapy with door-to-needle time within 30 minutes. The pharmacological treatment after admission includes antiplatelet drugs, anticoagulation drugs, beta blockers, angiotensin converting enzyme inhibitors/angiotensin receptor blockers and statins. STEMI patients should be watched out for hypotension, heart failure or even cardiogenic shock. Mechanical complications, such as acute mitral regurgitation, septum rupture and free wall rupture, cause high mortality after STEMI. Tachy- and bradyarrhythmias are also common in patients with STEMI and should be treated accordingly. Permanent cardiac pacing and implantable cardioverter defibrillator may be necessary after STEMI. Coronary artery bypass grafting surgery may be performed as a definitive or adjunctive revascularization therapy after STEMI. Surgery is also necessary if there are mechanical complications. Before discharge, cardiac rehabilitation should be considered when patients are stabilized. Referral for outpatient rehabilitation should also be encouraged. Antiplatelet drugs, beta blockers, angiotensin converting enzyme inhibitors/angiotensin receptor blockers and statins should be continued after discharge for secondary prevention. Effective hypertension, diabetes and lipid control are important after STEMI.

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[1]Division of Cardiology, Department of Internal Medicine, National Cheng Kung University College of Medicine and Hospital, Tainan; [2]Division of Cardiology, Department of Internal Medicine, Mackay Memorial Hospital and Mackay Medical College; [3]Division of Cardiology, Department of Internal Medicine, National Taiwan University Hospital, Taipei; [4]Division of Cardiology, Department of Internal Medicine, Faculty of Medicine, Kaohsiung Medical University Hospital and Kaohsiung Medical University, Kaohsiung; [5]Division of Cardiology, Department of Internal Medicine, Taipei Veterans General Hospital, Taipei; [6]Second Section of Cardiology, Department of Internal Medicine, Chang Gung Memorial Hospital, Chang Gung University College of Medicine, Taoyuan; [7]Cardiovascular Center, Taichung Veterans General Hospital, Taichung; [8]Division of Cardiology, Department of Internal Medicine, Kaohsiung Veterans General Hospital; [9]Division of Cardiology, Department of Internal Medicine, Chang Gung Memorial Hospital-Kaohsiung Medical Center, Kaohsiung; [10]Department of Cardiovascular Surgery, Far Eastern Memorial Hospital; [11]Division of Cardiology, Department of Internal Medicine, Shin Kong Wu Ho-Su Memorial Hospital, Taipei, Taiwan.

Address correspondence and reprint requests to: Dr. Jyh-Hong Chen, Division of Cardiology, Department of Internal Medicine, National Cheng Kung University College of Medicine and Hospital, No. 138 Sheng Li Road, Tainan 704, Taiwan. Tel: 886-6-235-3535 ext 2389; Fax: 886-6-275-3834; E-mail: jyhhong@mail.ncku.edu.tw

INTRODUCTION

Cardiovascular disease is one of the major leading causes of death in Taiwan and continues to be a public health challenge in the near future. Acute ST-segment elevation myocardial infarction (STEMI) is a common cardiovascular disease and carries a high morbidity and mortality. STEMI is usually caused by acute thrombus formation on a ruptured atherosclerotic plaque in coronary artery. The timely adequate management of patients with STEMI can significantly reduce the mortality.[1] Guidelines for the management of patients with STEMI have been published in North America,[2] Europe[3] and other countries.[4] Adherence to the suggestions from guidelines has been reported to improve the prognosis of patients with STEMI.[5] Although the use of key therapies in patients with STEMI maybe similar, due to the difference in race, geographic location, health care and insurance reimbursement system, there exists variations in the management of STEMI around the world. Considering the situations peculiar to our country, the purpose of the present guideline is to give the health care providers in Taiwan a comprehensive, practical and evidence-based approach that can be applied to the daily clinical practice in the caring of patients with STEMI. Most suggestions in this guideline are based on the international clinical trial results and other major guidelines in the world. In addition to clinical evidences, some of the recommendations for pharmacological and intervention therapies come from the observation studies and expert opinions here in Taiwan. The suggestions in this guideline provide general rules and are not prescriptive. The treatment of STEMI is complex and the clinical situations vary from patient to patient in STEMI. The best treatment for a STEMI patient still depends on the clinical judgment of the in-charged physicians and should be individualized.

PREHOSPITAL CARE

Identification of patients with STEMI

Patients with major cardiovascular risk factors or documented coronary artery disease (CAD) should be educated for the risk of myocardial infarction (MI). It is important to help patients and their family members to understand the risk of MI, recognize its symptoms and avoid any delay for medical contact. Patients should be educated for the classic symptoms of MI which includes sudden onset of chest pain or chest tightness with radiation to arm, lower jaw, upper back or epigastric area. Many patients also experience associated symptoms, such as diaphoresis, shortness of breath, nausea or vomiting. The women, elderly or diabetic patients may experience atypical symptoms, such as shortness of breath, palpitation, and dizziness, as the initial manifestation of MI instead of chest discomfort.

Adequate response to chest pain

Administration of sublingual nitroglycerin (NTG) is important. The patients should sit or lie down and take the sublingual NTG. If chest pain is not improved after 5 minutes, give a second tablet. Call 119 for help immediately if the chest pain has not stopped after another 5 minutes. Family members of patient with multiple cardiovascular risk factors or documented CAD should be advised to receive cardiopulmonary resuscitation (CPR) training. For initial management of the patients with chest pain or sudden collapse, the emergency medical services (EMS) personnel should have advanced cardiac life support (ACLS) training and equipped with a defibrillator. The EMS personnel should also be trained to recognize the symptoms of MI and give the patients initial evaluation and management. These include identification of onset time of chest pain, vital signs evaluation, oxygen administration and basic life support if necessary. Prehospital diagnosis of STEMI is an important method to reduce time to reperfusion therapy. The EMS personnel should be encouraged to perform 12-lead electrocardiogram (ECG) and identify any ST segment elevation. General practitioners also play a major role in the early diagnosis and care of STEMI patients. To obtain 12-lead ECG quickly with precise interpretation is important for diagnosis of STEMI in local clinics. Initial management with chewable aspirin 300 mg, clopidogrel 300 mg, oxygen inhalation, sublingual NTG or intravenous morphine for persistent chest pain in patients with STEMI is suggested if there is no contraindication. The general practitioners should contact percutaneous coronary intervention (PCI)-capable hospitals and transmit 12-lead ECG as soon as possible.

Transportation

Patients with suspected STEMI should be taken to the nearest appropriate hospitals with PCI capability (Figure 1). Until 2010, there are 23 hospitals around Taiwan that have been approved and announced by the Department of Health to perform primary PCI in Taiwan (http://www.doh.gov.tw). During early several hours since chest pain onset, the patient also may be transported to a hospital without PCI facility for thrombolytic therapy if there is no heart failure, shock, or contraindication of thrombolytic therapy. Patient with STEMI who have ongoing chest pain, heart failure, cardiogenic shock, or life threatening arrhythmia should be transferred to PCI-capable hospitals as soon as possible.

EMERGENCY DEPARTMENT ASSESSMENT

Emergency department assessment

Initial evaluation of patients with possible STEMI in emergency department (ED) includes the patient's history, physical examination, ECG and cardiac biomarkers. The optimal strategy for a hospital to rapidly assess and manage STEMI patients in ED should based on a well-established, guideline-oriented, institution-specific written protocol which is developed from the consensus of multidisciplinary teams, including emergency medicine physicians, cardiologists, nurses, laboratory technicians and other appropriate personnel.

Initial evaluation

Early reperfusion therapy is the cornerstone treatment of STEMI and should be always kept in mind when making evaluation of patients in ED. The choice of reperfusion strategy should be made by the emergency medicine physician based on a predetermined, institution-specific, written protocol. For cases in which the initial diagnosis and treatment plan can not be decided by the emergency physician or are not covered directly by an agreed upon protocol, immediate cardiologist consultation is necessary. The time delay from patient arrival at the ED to balloon inflation in the PCI should be less than 90 minutes; alternatively, if thrombolytic therapy is chosen, the door-to-needle time should be less than 30 minutes.

The patient should be placed on a cardiac monitor immediately with resuscitation equipment nearby. A 12-lead ECG should be performed and shown to an emergency medicine physician within 10 minutes of ED arrival. If STEMI is present, the decision to primary PCI or thrombolytic therapy should be made within the next 10 minutes. If the initial ECG is not diagnostic and there is still a highly clinical suspicion for STEMI, serial ECGs at 5- to 10-minute intervals or continuous ST-segment monitoring should be performed. For hospitals without catheterization laboratory, a formal transfer protocol is required so that an expeditious transfer to the nearest intervention facility can be made for the patients who require PCI.

History

The history taking should focus on chest discomfort, associated symptoms, sex and age-related differences in presentation, hypertension, diabetes mellitus, possibility of aortic dissection, risk of bleeding, and history of cerebrovascular disease. The history taken in the ED must be concise and detailed enough but should not delay the reperfusion therapy.

Chest discomfort

The onset time is important. The severity of chest discomfort varies, but is often described as a crushing, vice-like constriction, a feeling equivalent to an "elephant sitting on the chest," or heartburn. The discomfort is substernal but may originate in or radiate to areas such as the neck, jaw, interscapular area, upper extremities, and epigastric area.

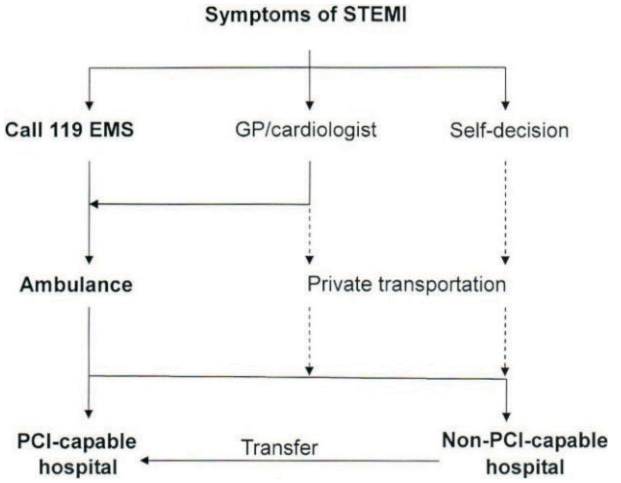

Figure 1. *PCI-capable hospital should provide 24 hours/day, 7 days/week primary PCI service.*

Associated symptoms

The usual associated symptoms include nausea and vomiting. Diaphoresis associated with a pale complexion may also appear, as well as weakness or profound fatigue. Dizziness, lightheadedness, syncope, and paresthesia may occur because of pain and hyperventilation.

Sex- and age-related differences in presentation

Women usually have STEMI at an older age and lag behind men by about 20 years.[6] The most frequent acute symptoms were shortness of breath, weakness, and fatigue. About 43% female MI patients reported no acute chest discomfort/pain.[7] Elderly patients with STEMI are less likely to complain of chest discomfort, but more likely to have shortness of breath, as well as other atypical symptoms such as syncope or unexplained nausea.[8]

Hypertension

Blood pressure should be assessed because severe uncontrolled hypertension is a relative contraindication to thrombolytic therapy.

Diabetes mellitus

Diabetic patients with autonomic neuropathy may have impaired pain recognition. Diabetic patients or physicians may take the symptoms of dyspnea, nausea, vomiting, fatigue, and diaphoresis as the problems of sugar control. Renal dysfunction is also common in diabetics with STEMI.

Possibility of aortic dissection

Severe tearing pain radiating directly to the back should raise the suspicion of aortic dissection, especially in elderly hypertensive patients. It must be kept in mind that the dissection may extend to the proximal aorta and produce aortic regurgitation or cardiac tamponade. If the origin of a coronary artery is involved, it may result in STEMI at the same time.

Risk of bleeding

Patients should be questioned about the bleeding history during previous surgical or dental procedures, peptic ulcer disease, unexplained anemia, or melena. The use of antithrombotic or thrombolytic agents as part of the treatment for STEMI will exacerbate the underlying bleeding problems.

History of cerebrovascular disease

The patient with STEMI frequently has risk factors for stroke. The history and evidence for cerebrovascular disease, including transient ischemic attack, ischemic stroke, intracerebral hemorrhage, or subarachnoid hemorrhage, should be sought. These conditions may influence the choice of reperfusion strategy and use of antithrombotic drugs.

Physical examination

A physical examination should be performed for differential diagnosis of acute chest pain and is also useful for assessing the presence of complications of STEMI (Table 1 and 2). A brief and focused neurological examination to look for evidence of prior stroke should be performed. The physical examination findings are helpful in differential diagnosis. Major pulses may be absent, and a murmur of aortic regurgitation may be present in aortic dissection. A transesophageal echocardiography or computed tomography (CT) scan is useful for diagnosis. Active peptic ulcer disease can be present with chest or epigastric pain, sometimes radiating posteriorly. Free subdiaphragmatic air may be seen on upright chest X-ray in perforations. Pain from pericarditis is usually pleuritic with radiation to shoulder and trapezius ridge and is often relieved by sitting up and leaning forward. A rub is often present. ECG may show PR segment depression with diffuse ST segment elevation but no reciprocal ST segment depression.[9] Pulmonary embolism, with or without infarction, presents with dyspnea and knifelike pleuritic pain, sometimes with hemoptysis. Costochondral pain is described as sharp or sticking, with associated localized tenderness. Pneumothorax may present with acute dyspnea, pleuritic pain, and differential decrease in breath sounds with hyperresonance over lung field. Acute cholecystitis may mimic STEMI, and

Table 1. Basic physical examination in the emergency department

Airway, Breathing, Circulation (ABC)
Vital signs (temperature, blood pressure, heart rate and respiratory rate)
Jugular venous distension
Pulmonary auscultation
Cardiac auscultation
Neurological evaluation of stroke
Systemic hypoperfusion signs

Table 2. Physical findings and possible implications in complicated ST-elevation myocardial infarction patients

Low-grade fever: nonspecific response to myocardial necrosis
Hypertension, tachycardia: high sympathetic tone
Hypotension, bradycardia: high vagal tone
Small volume pulse: low cardiac output
Fast, slow or irregular pulse: atrial or ventricular arrhythmias, heart block
Paradoxical "ectopic" systolic impulse: LV dyskinesis, ventricular aneurysm
Soft S1: Decreased LV contractility, first-degree AV block
Paradoxically split S2: severe LV dysfunction, LBBB
S3 gallop, pulmonary rales, pulsus alternans: LV systolic dysfunction
Hypotension, cool, clammy, cyanotic skin, altered mental status, oligouria: signs of cardiogenic shock
Jugular venous distension with Kussmaul's sign, hypotension, clear lungs: RV infarction
Systolic murmur of mitral regurgitation: papillary muscle rupture
Pericardial friction rub: pericarditis or Dressler's syndrome
Signs of cardiac tamponade: cardiac rupture or aortic dissection
Absent peripheral pulse and murmur of aortic regurgitation: aortic dissection

LV, left ventricular; LBBB, left bundle branch block; CHF, congestive heart failure; RV, right ventricular.

right upper quadrant abdominal tenderness should be sought on physical examination.

Electrocardiogram

A 12-lead ECG should be performed immediately. The 12-lead ECG is at the center of the therapeutic decision pathway[10] and provides prognostic information. Mortality increases with the number of ECG leads showing ST elevation. Left bundle branch block (LBBB) and anterior location of infarction are also important predictors of mortality in the initial 12-lead ECG.[11]

In patients with inferior STEMI, right-sided ECG should be obtained to screen for right ventricular (RV) infarction if there is ST elevation greater than 0.1 mV on V4R. Because the criteria of greater than 0.1 mV in leads V1 through V4 have reduced diagnostic specificity for STEMI in patients with early repolarization, evidences support the use of greater than or equal to 0.2 mV anteroseptal elevation as a preferable threshold for diagnosing STEMI in such patients.[10] When there is marked ST segment depression confined to leads V1 through V4 and accompanied by tall R waves and upright T waves, a posterior wall MI should be suspected. For posterior infarction, confirmatory data from posterior leads (i.e., V7 and V8) as well as 2-dimensional echocardiography may be helpful; the latter tool has a high negative predictive value.[12,13] It is less likely that STEMI is present if the upward-directed ST segment changes are concave rather than convex, except during the earliest stage of STEMI when only hyperacute T waves developed.[14] New or presumably new LBBB are at high risk when presenting with presumed MI, and this ECG presentation is a frequent cause of delay or lack of reperfusion therapy. It is also a situation in which PCI may be preferable to thrombolytic therapy.[15] For LBBB, several ECG criteria can provide independent diagnostic value, including ST elevation greater than or equal to 0.1 mV in leads with a positive QRS, ST depression greater than or equal to 0.1 mV in V1 to V3, and ST elevation greater than or equal to 0.5 mV in leads with a negative QRS.[16,17]

Cardiac biomarkers

Serum cardiac biomarkers [creatine kinase (CK), CK-MB, cardiac-specific troponins, myoglobin] are useful for confirming the diagnosis of MI and also provide valuable prognostic information. However, initiation of reperfusion therapy should not be delayed while awaiting the results of a cardiac biomarker assay. CK-MB rises within 4-8 hours after the onset of STEMI, peaks at an average of 24 hours if no reperfusion and declines to normal in 48 to 72 hours. Troponins rise almost simultaneously with CKMB, usually peak at 24 hours if no reperfusion, but may persist for 7-14 days after MI. Myoglobin is infrequently used in Taiwan. Given the nearly absolute myocardial tissue specificity and high sensitivity for even microscopic myocardial necrosis, cardiac troponins are the preferred biomarkers for diagnosing MI.[18] For patients with ST segment elevation

recognized on the 12-lead ECG, subsequent confirmation of MI should be ascertained by measurement of any of the available cardiac biomarkers. Occasionally, a very small infarct will be missed by CK-MB; therefore, troponin should be measured in patients suspected to have STEMI but have negative serial CK-MBs. CK-MB is the preferred biomarker to diagnose reinfarction and assess reperfusion. In addition to cardiac biomarkers, several routine blood examinations including blood sugar, creatinine, electrolytes, and complete blood cell counts, also have important implications in the management of patients with STEMI. However, reperfusion therapy should not be delayed for laboratory results.

Imaging

Patients with STEMI should have a portable chest X-ray, but this should not delay reperfusion therapy. Echocardiography is helpful to clarify the diagnosis of STEMI if the ECG is confounded by LBBB or pacing or if there is a suspicion of posterior STEMI. Mechanical complications, including acute mitral regurgitation, septal or free wall rupture due to acute infarction, can be detected earlier by echocardiography. Echocardiography can also identify whether there is an intimal flap of aortic dissection extending into aortic root and influence coronary ostium. Transesophageal echocardiography, chest CT scan or magnetic resonance imaging (MRI) scan should be done for differentiating STEMI from aortic dissection in patients for whom this distinction is initially unclear.

EMERGENCY DEPARTMENT MANAGEMENT

Initial management

Oxygen

Pulse oximetry is routinely used to monitor oxygen saturation and detect hypoxemia in the ED. Hypoxemia can worsen myocardial ischemia and oxygen inhalation may reduce myocardial injury.[19] Oxygen 2-4 L/min by nasal prongs or mask is indicated if the oxygen saturation is less than 94% or there is evidence of heart failure. Oxygen can be considered to use in all STEMI patients during the first 6 hours. There is no evidence for continuing routine oxygen use beyond 6 hours in uncomplicated cases.

Nitroglycerin

Nitrate can dilate epicardial coronary arteries to improve coronary flow, reduce preload and afterload, increase collateral supply, and is beneficial for coronary spasm. Because there is no definite effect in cardiovascular risk reduction, it is not necessary to give nitrates routinely.[20] However, patients with ongoing ischemic chest discomfort should receive sublingual NTG (0.4 mg) every 5 minutes for maximal 3 doses if needed and tolerable. Intravenous NTG is indicated for relief of ischemic symptoms, blood pressure control, or management of heart failure. Intravenous NTG is started with 5 mcg/min, and increased every 5 minutes until symptoms relief, a fall in systolic blood pressure (SBP) $\geq$ 30 mmHg of baseline or SBP $<$ 90 mmHg. Nitrate is contraindicated in patients with SBP $<$ 90 mm Hg, right ventricular infarction, or receiving a phosphodiesterase inhibitor for erectile dysfunction within the last 24 hours.[21]

Analgesia

Patients with STEMI usually have severe chest pain associated with higher catecholamine levels which may contribute to coronary contraction, malignant arrhythmia, thrombus formation and anxiety. Control of ischemic chest pain depends on oxygen, opiate analgesics and anti-ischemic agents including beta blockers and nitrate. Nonsteroidal anti-inflammatory drugs (NSAIDs), except aspirin, and cycloxygenase-2 (COX-2) inhibitors, should not be used at the acute stage of STEMI because of the increased risk of prothrombotic effect, death, re-infarction, hypertension, heart failure, and myocardial rupture.[22] The first choice is morphine which could dilate arterial and venous vessels, relieve patients' anxiety, and reduce the respiratory work. Morphine is given 2 to 4 mg intravenously with increments of 2 to 8 mg and repeated at 5- to 15-minute intervals if needed. Intramuscular injection should be avoided. Morphine may cause nausea, vomiting, bradycardia, respiratory depression, or hypotension. If needed, naloxone, 0.1 to 0.2 mg intravenously could be used as the antidote.

Antiplatelet drugs

Both aspirin and clopidogrel should be started in ED for STEMI. Aspirin has been proven to reduce mortality, coronary reocclusion and recurrent ischemic events in patients suffered from acute MI.[23] Aspirin should be

given to STEMI patients not taking aspirin before promptly in ED. The suggested initial loading dose is 300 mg. The chewable form is preferred than the enteric-coated form because it is absorbed more rapidly. The contraindications for aspirin include a known hypersensitivity, active gastrointestinal bleeding, known coagulopathy, or severe hepatic disease. In patients with aspirin intolerance, clopidogrel may be substituted.

Clopidogrel should also be used in STEMI. The COMMIT-CCS-2 study was conducted in Chinese MI patients with 93% ST-segment elevation or bundle branch block and 54% with thrombolysis. It demonstrated clopidogrel on top of aspirin use reduced the composite primary end point of death, re-infarction, or stroke.[24] In the CLARITY-TIMI 28 study, clopidogrel reduced the primary composite efficacy end point of an occluded infarct artery on angiography, death or recurrent MI in STEMI patients receiving thrombolytic therapy.[25] Clopidogrel treatment before and after PCI can significantly reduce the incidence of cardiovascular death or ischemic complications.[26] An initial loading dose of clopidogrel 300 mg in ED is recommended. Loading 600 mg clopidogrel can be considered in patients undergoing PCI to achieve a more rapid onset of effect. Routine glycoprotein (GP) IIb/IIIa inhibitor in ED prior to PCI does not improve cardiovascular outcomes for STEMI patients in Taiwan.[27,28]

Anticoagulation drugs

Intravenous unfractionated heparin (UFH) should be given with an initial bolus 60 U per kg (maximum 4000 U) followed by an intravenous infusion of 12 U per kg per hour (maximum 1000 U per hour). The dose is adjusted to maintain the activated partial thromboplastin time (aPTT) at 1.5 to 2.0 times control (approximately 50 to 70 seconds). For those receiving UFH and planning to receive PCI, UFH should be given in bolus during the PCI procedure to maintain the activated clotting time (ACT) between 250-350 seconds. Heparin-induced thrombocytopenia should be monitored especially in those with prolonged UFH treatment. For patients received thrombolytic therapy, enoxaparin can be considered to replace UFH.

Beta blockers

Clinical trials have shown that beta blocker therapy can reduce the magnitude of infarction, the rate of re-infarction and the frequency of life-threatening ventricular tachyarrhythmias. Oral beta blocker is suggested to start in the first 24 hours for all STEMI patients except those having signs of severe heart failure, active asthma, high-degree atrioventricular block, excessive bradycardia, and hypotension. The relative contraindications to beta blocker therapy includes heart rate less than 60 beats per minute, SBP less than 100 mmHg, signs of peripheral hypoperfusion, PR interval greater than 0.24 second, or reactive airway disease. The suggested medications in ED are listed in the Table 3.

Reperfusion therapy

When STEMI patients enter the ED. the most important point is to consider reperfusion therapy. Rapid restoration of flow in the infarct-related artery can be achieved by primary PCI or thrombolytic therapy. The time from symptom onset, risk of STEMI, time required for transport to PCI-capable hospitals will be considered before the selection of reperfusion therapy and the strategy should be determined as early as possible. The reperfusion therapy should be performed as soon as possible within 12 hours after onset of symptoms.[29]

Primary PCI

Primary PCI is defined as coronary intervention in the infarct-related artery within 12 hours after the symp-

Table 3. Suggested medications in the emergency department

1. Oxygen 2-4 L/min by nasal prongs
2. Sublingual or intravenous NTG for chest pain if no contraindications
3. Intravenous morphine 2 to 4 mg if persistent chest pain
4. Aspirin 300 mg, chewable form preferred
5. Clopidogrel 300 mg
6. Intravenous unfractional heparin with an initial bolus 60 U per kg (maximum 4000 U) followed by an intravenous infusion of 12 U per kg per hour (maximum 1000 U per hour)
7. Beta blocker if no contraindications

tom onset of STEMI without any previous thrombolytic therapy. Randomized controlled trials have suggested that primary PCI is superior to intravenous thrombolysis for the treatment of STEMI. A meta-analysis of 23 randomized trials shows that primary PCI is more effective than thrombolytic therapy in reducing overall mortality, non-fatal re-infarction, stroke, and the combined endpoint of death, non-fatal re-infarction, and stroke.[30] Women and elderly patients get more benefit from primary PCI than thrombolysis.[31,32] In patients presenting with STEMI with multivessel disease, primary PCI should be performed in infarct-related artery only when patients are not hemodynamically compromised.[33,34] The door-to-balloon time for primary PCI should be within 90 minutes and as short as possible.[35]

Thrombolytic therapy

Intravenous thrombolytic therapy is another choice for reperfusion therapy. It could be administered to STEMI patients within 12 hours after symptom onset. The door-to-needle time for thrombolytic therapy should be within 30 minutes and as short as possible. In STEMI patients presenting within 3 hours after symptom onset, thrombolytic therapy is as effective as primary PCI in achieving reperfusion.[29,36,37] Thus STEMI patients are initially sent to a non-PCI capable hospital within 3 hours after symptom onset, immediate thrombolytic therapy could be considered. The patients should be transferred to a PCI-capable hospital for primary PCI if the onset of symptom is more than 3 hours. The commonly used thrombolytic agents in Taiwan include streptokinase (SK), 1.5 million units over 30-60 minutes, and human recombinant tissue plasminogen activator (Alteplase, t-PA), 15 mg intravenous bolus followed by 0.75 mg/kg over 30 minutes then 0.5 mg/kg over 60 minutes intravenous infusion. The total t-PA dose should not exceed 100 mg. Bleeding risk is the most critical consideration of thrombolytic therapy. Intracranial bleeding occurs in an average about 1% of the treated patients. The absolute contraindications for the use of thrombolytic therapy include intracerebral hemorrhage at any time, ischemic stroke within 3 months, central nervous system tumor, major surgery or trauma within 3 weeks, aortic dissection, severe uncontrolled hypertension (SBP > 180 mmHg) and known bleeding disorders.

PHARMACOLOGICAL TREATMENT AFTER ADMISSION

After initial management and reperfusion therapy, the patients should be sent to coronary care unit (CCU) or intensive care unit (ICU) for monitoring of the vital signs, ECG and pulse oximetry for at least 24 to 48 hours. Routine oxygen can be supplied in the first 6 hours and discontinuation can be considered after reassessment. Antiplatelet drugs, anticoagulation drugs, nitroglycerin, beta blocker, angiotensin-converting enzyme (ACE) inhibitor/angiotensin receptor blocker (ARB), and statins should be considered in STEMI patients.

Antiplatelet drugs

Aspirin

Aspirin should be continued indefinitely with the daily maintenance dose of 100 mg if there is no contraindication. Higher aspirin maintenance dose (> 100 mg) does not gain more benefit. The effects of aspirin daily dose are similar between 75 to 1500 mg and the gastrointestinal side effects increase significantly when daily dose is larger than 325 mg.[38] The clinical benefits become uncertain when the dose is less than 75 mg per day.[38] The observational analysis of the CURE study also showed similar rates of cardiovascular death, MI, or stroke among the patients with acute coronary syndrome (ACS) receiving high (> 200 mg), moderate (101-199 mg) or low (< 100 mg) dose aspirin per day.[39] The rate of major bleeding was increased significantly in those receiving high dose aspirin.

Clopidogrel

Clopidogrel, a thienopyridine, is a prodrug that needs to be metabolized into an active drug to produce platelet P2Y12 inhibitory effect. Aspirin and clopidogrel combination therapy has been shown to have synergistic antiplatelet effect and has become the standard treatment in STEMI regardless of whether patients receive reperfusion with thrombolysis, primary PCI, or not at all.[24-26] Clopidogrel 75 mg per day should be continued for at least 12 months after STEMI. The data from Taiwan Acute Coronary Syndrome Descriptive (T-ACCORD) Registry show that adherence to dual antiplatelet

treatment is associated with a lower total mortality at 1 year.[40] The effect of high dose clopidogrel regimen was tested in the CURRENT-OASIS 7 trial for ACS patients with or without ST segment elevation.[41,42] The clinical outcomes were compared between patients receiving double dose clopidogrel (a 600 mg loading dose on day 1 and 150 mg daily for 6 days, followed by 75 mg daily) or standard dose clopidogrel (a 300 mg loading dose, followed by 75 mg daily). Overall, there were no significant differences in the primary outcome of cardiovascular death, nonfatal MI or nonfatal stroke at 30 days in the two clopidogrel dose regimens.[41] The bleeding risk was lower in standard dose group. However, in the patients who underwent PCI, double-dose clopidogrel regimen significantly reduced the rate of the primary outcome and definite stent thrombosis at 30 days than the standard dose.[42] These data suggest that double dose clopidogrel regimen maybe considered in STEMI patients underwent primary PCI to achieve a more rapid onset and more intensive antiplatelet effect. Ticlopidine is the first generation thienopyridine and is noted for its notorious side effect of neutropenia and thrombocytopenia. Currently, ticlopidine is used only if patients are allergic to clopidogrel.

New antiplatelet drugs

The newer P2Y12 inhibitors, prasugrel and ticagrelor, achieve a greater inhibition of platelet aggregation and have shown a benefit over clopidogrel in the setting of STEMI. The TRITON-TIMI 38 trial compared prasugrel with clopidogrel in 3534 STEMI patients proceed with PCI.[43] Prasugrel significantly reduced the primary endpoint, including cardiovascular death, non-fatal MI, or non-fatal stroke at 30 days. Prasugrel should be avoided in patients with a history of ischemic stroke or transient ischemic attack, patients older than 75 years and those who weigh less than 60 kg because subgroup analysis of the TRITON TIMI-38 trial did not find a net benefit of prasugrel due to higher bleeding risk in these patients. Currently, prasugrel can be used as an alternative to clopidogrel in STEMI patients undergoing primary PCI.

Ticagrelor is an active drug and does not require metabolic transformation. The PLATO trial compared ticagrelor with clopidogrel in 7544 STEMI patients undergoing primary PCI.[44] At 1 year, ticagrelor tended to reduce the primary endpoint of cardiovascular death, MI or stroke [hazard ratio (HR), 0.87; 95% confidence interval, 0.75 to 1.01; p = 0.07]. There was no significant difference in the rates of major bleeding between the two groups.

GP IIb/IIIa inhibitors

The results from recent clinical trials do not support routine use of intravenous GP IIb/IIIa inhibitors in patients with STEMI treated with primary PCI.[45,46] In the current era of dual antiplatelet therapy and routine stenting in patients with STEMI, GP IIb/IIIa inhibitors do not further reduce mortality, recurrent MI or target vessel revascularization at 30 days. There is also no significant benefit to start GP IIb/IIIa inhibitors earlier before primary PCI in prehospital stage or in ED.[27,28,46] Although GP IIb/IIIa inhibitor infusion during primary PCI might improve myocardial perfusion and ST-segment resolution, the drug did not affect the rate of mortality, reinfarction, target lesion revascularization and stroke at 6 months.[47] For various GP IIb/IIIa inhibitors, meta-analysis results demonstrated similar clinical effects in these different agents.[48] Currently, GP IIb/IIIa inhibitors in STEMI should only be used at the time of primary PCI in patients with a large coronary thrombus burden and inadequate loading with a thienopyridine in the ED.[49] In the various clinical trials, the GP IIb/IIIa inhibitors were usually given for 12 to 24 hours after PCI, however, there is no consensus for an optimal duration of GP IIb/IIIa inhibitors therapy.

Anticoagulation drugs

Unfractionated heparin

In STEMI patients undergoing thrombolytic therapy, anticoagulation is usually necessary to improve early coronary patency and reduce reocclusion. In patients treated with fibrin-specific agents (Alteplase, t-PA), intravenous UFH should be continued for 48 hours. However, the role of UFH becomes less important when the less fibrin-specific thrombolytic agents, such as streptokinase, are used. These agents produce a systemic coagulopathy and make these agents themselves strong anticoagulants. In patients treated with primary PCI, additional bolus UFH should be administered as needed during the PCI procedure to keep ACT around 250 to

350 seconds (200-250 seconds if GP IIb/IIIa inhibitors are used). UFH could be continued for 24 to 48 hours after primary PCI or could be considered to stop if coronary flow is restored to TIMI 3 flow and no other high risk features such as large or anterior MI, atrial fibrillation, previous embolism or known LV thrombus.[50] For patients without reperfusion therapy, the optimal duration of UFH is uncertain. It is reasonable to give UFH for 48 hours if there is no contraindication. In these patients, the use of UFH should be individualized and based on patients' clinical conditions.

Enoxaparin

Enoxaparin is a low-molecular-weight heparin that has an excellent bioavailability and preferential anti-Xa activity. In the ExTRACT-TIMI 25 trial, STEMI patients receiving thrombolysis and aspirin were randomized to enoxaparin intravenous 30 mg bolus followed by 1 mg/kg twice daily subcutaneously for up to 8 days, or intravenous bolus of UFH 60 IU/kg followed by infusion of 12 IU/kg/h for 48 hours.[51] Enoxaparin was significantly more effective than UFH in reducing the primary composite endpoint of death or reinfarction at 30 days. Major bleeding rates were more frequent with enoxaparin at 30 days, but the occurrence of intracranial hemorrhage was similar. Therefore, enoxaparin can be considered as an alternative to UFH in STEMI patients who received thrombolytic therapy. In STEMI patients who did not receive any reperfusion therapy, the effect is similar between enoxaparin and UFH. The TETAMI trial compared enoxaparin, 30 mg intravenous bolus, followed by 1 mg/kg subcutaneously twice daily for 2 to 8 days with intravenous UFH in STEMI patients without any reperfusion therapy. There were no significant differences between the enoxaparin and UFH in the combined end point of death, reinfarction, or recurrent angina at 30 days.[52] Due to the similar efficacy profile to UFH, enoxaparin also can be an alternative treatment in non-reperfused STEMI patients. If the patients initially treated with enoxaparin but need PCI later, a dose of 0.3 mg per kg enoxaparin can be given intravenously for PCI if the last subcutaneous dose is 8 to 12 hours earlier. If the last subcutaneous dose was given within the prior 8 hours, no additional enoxaparin is necessary for PCI.[51] The data of comparison enoxaparin and UFH in primary PCI are very limited and large-scale, randomized clinical trials data are lacking.

New anticoagulation drugs

Bivalirudin is a direct thrombin inhibitor with a short biological half-life. In the HORIZONS-AMI trial, bivalirudin was compared with UFH plus GP IIb/IIIa inhibitors in patients with STEMI undergoing primary PCI.[53] Bivalirudin had a lower rate of net adverse clinical events, including major bleeding, death, urgent target vessel revascularization, MI, and stroke at 30 days. The benefit was most significant in reducing major bleeding complications. Therefore, bivalirudin can be used an alternative to UFH in STEMI patients who are invasively managed.

Fondaparinux is a synthetic factor Xa inhibitor which binds to antithrombin III and enhances the AT III-mediated factor Xa inhibition. In the OASIS-6 trial, the effect of fondaparinux was tested in STEMI patients underwent thrombolysis, primary PCI, or no reperfusion therapy and were divided into two groups depending on the need for UFH.[54] Overall, fondaparinux significantly reduced the occurrence of the primary efficacy outcome (death or recurrent MI) at 30 days compared with UFH/placebo. The significant benefits were observed in patients who received thrombolysis or no reperfusion therapy, but not in patients undergoing primary PCI. Accordingly, fondaprinux is recommended as an alternative anticoagulant in STEMI patients treated conservatively, but not in patients undergoing primary PCI.

Nitroglycerin

Sublingual or intravenous nitroglycerin can be given if there are ischemic symptoms in STEMI patients. In addition, intravenous nitroglycerin can be used as a vasodilator for control hypertension, left ventricular dysfunction and heart failure in STEMI patients. Nitroglycerin should not used in patients with hypotension and suspected RV infarction.

Beta blockers

Beta blockers should be initiated after STEMI and continued thereafter if there is no contraindication. Recent studies demonstrated that there is no significant mortality benefit to use intravenous beta blocker therapy immediately (< 24 hours) after the onset of STEMI. In the COMMIT/CCS-2 study, patients received immediate

intravenous metoprolol and followed by oral treatment within 24 hours after MI onset.[55] There was less re-infarction and ventricular fibrillation but more cardiogenic shock in the metoprolol group. Overall, no difference in mortality could be observed. It is reasonable to start early oral beta blocker therapy when the patients' condition is more stable after admission. During the STEMI acute stage, beta blockers should be avoided in patients with evidence of low output state, heart failure, cardiogenic shock, or the presence of any other contraindications to beta blockers.

ACE inhibitors/ARBs

ACE inhibitors should be started within the first 24 hours after STEMI and continued thereafter if there is no contraindication. However, hypotension should be avoided. A number of large randomized clinical trials have demonstrated the benefit of early ACE inhibitors therapy in MI. Meta-analysis of ACE inhibitors trials has consistently demonstrated a significantly favorable effect on survival after MI.[56] The mortality benefit of ACE inhibitors is more prominent in those with left ventricular (LV) dysfunction or heart failure. For patients who can not tolerate ACE inhibitors, ARBs can be considered as alternatives. In VALIANT study, valsartan with a target dose 160 mg twice daily had been shown to be equally effective as captopril 50 mg three times daily in reducing mortality in post-MI patients with heart failure and/or LV dysfunction.[57] In CHARM-alternative study for heart failure, 69.7% of its patients have coronary heart disease as the cause of heart failure. It shows that candesartan to a target dose of 32 mg once daily reduces cardiovascular mortality and morbidity in heart failure patients that are intolerant to ACE inhibitor treatment.[58]

Aldosterone antagonist

In MI patients with heart failure, the suggestion to start aldosterone blocker treatment is completely based on the EPHESUS trial using eplerenone.[59] The early initiation of eplerenone could reduce the mortality rate as early as 30 days post-MI. Although the RALES trial is not a specific MI clinical trial, 55% of its patients have coronary heart disease-related heart failure. RALES study showed aldosterone blocker, spironolactone 25 mg once daily, significantly reduce the mortality in patients with heart failure.[60] Therefore, spironolactone can be considered in STEMI patients with LV dysfunction and heart failure. However, the risk of hyperkalemia should be carefully avoided, especially in the patients with acute or chronic renal failure.

Statins

A lipid profile, including total cholesterol, triglyceride, low-, and high-density lipoprotein cholesterol (LDL-C and HDL-C) should be checked in every STEMI patient within 24 hours of admission. Statin should be given to all STEMI patients and LDL-C should be at least controlled to less than 100 mg/dL. Because the recurrent cardiovascular event is high in post-MI patients, LDL < 70 mg/dL is the optimal target in these patients. Treatment with statins improves both short- and long-term clinical outcomes in STEMI patients. Overall, the suggested pharmacotherapies after admission are listed in the Table 4.

REPERFUSION AND INFARCTION SIZE ASSESSMENT

Determining infarct size is vital in caring for STEMI patients. The extent of infarction is directly related to prognosis, reflects the efficacy of reperfusion therapy and guides future therapeutic decision making. Five major modalities can be applied for sizing an infarction.

ECG

All patients diagnosed with STEMI should have follow-up ECGs after reperfusion therapy immediately, at 24 hours upon admission and at hospital discharge to evaluate the success of reperfusion and the extent of in-

Table 4. Suggested pharmacotherpies after admission

1. Aspirin 100 mg and clopidogrel 75 mg per day
2. Intravenous glycoprotein IIbIIIa inhibitor if necessary after PCI
3. Intravenous unfractional heparin to keep aPTT about 2X
4. Sublingual or intravenous NTG for chest pain if no contraindications
5. Beta blocker if no contraindications
6. ACE inhibitors/ARBs if no contraindications
7. Statins
8. Spironolactone for heart failure if no contraindications

farction, as defined partially by the presence or lack of new Q waves. The extent of ST-segment deviation on the baseline ECG provides a semi-quantitative measurement of the amount of jeopardized myocardium and an estimate of the subsequent infarct size. With a QRS scoring system based on the duration and amplitude of individual waveforms within the QRS complex, the infarction size can be estimated from a point score derived and weighted from the 12-lead ECG.[61] However, this method is time consuming and the accuracy is limited in patients with left ventricular hypertrophy or bundle branch block.

Cardiac biomarkers

The conventional means of quantifying infarction use serial CK and CK-MB isoenzyme. The size of MI can be estimated based on the rate of biomarker release, its volume of distribution, and its clearance rate.[62] Satisfactory correlations have been made based on anatomic estimates derived from a postmortem human study.[63] The highly sensitive cardiac troponins (I or T) have a greater myocardial tissue specificity and higher sensitivity than those of other conventional biomarkers. Measuring cardiac troponin T at 72 hours provides an estimate of the infarct size in patients with STEMI who have not received reperfusion therapy.[64] After admission, repeated CK-MB and troponin measurements are required every 6-12 hours until peaking. Cardiac biomarkers should be rechecked if there is any recurrent chest pain during admission.

Radionuclide imaging

The most comprehensive evaluation of STEMI with radionuclide imaging is the technetium sestamibi SPECT method.[65] This method has been validated extensively and provides both early and late imaging to assess the area of ischemic risk as opposed to the ultimate infarct size. Radionuclide angiography with various isotopes can also estimate regional and global LV functions.

Echocardiography

Echocardiography is a useful tool in assessing mechanical complications, global and regional LV functions of STEMI. However, a lag of several days often occurs between successful reperfusion and normalization of wall motion (stunned myocardium), explaining why evaluation is most precise before hospital discharge or at outpatient follow-up. In patients with post-MI chest pain, echocardiography is helpful to distinguish those with recurrent ischemia and new wall motion abnormalities from those with post-infarction pericarditis or noncardiac chest pain.

MRI

Cardiac MRI is a promising method for assessing both the transmural and circumferential extent of infarction.[66] It allows for quantifying the extent of the salvaged area after revascularization as an important parameter for clinical decision-making.[67] This technique may be considered as the new method for infarct location and quantification; however, its development in Taiwan is still at the experimental level. Additional experience and comparison with other methods are warranted.

HEMODYNAMIC DISTURBANCES

Hypotension

In patients with STEMI, hypotension may result from hypovolemia, tachy- or bradyarrhythmias or heart failure. A preshock state of hypoperfusion with normal blood pressure may develop before circulatory collapse, and is manifested by cold extremities, cyanosis, oliguria, or decreased mentation. Initially, rapid intravenous volume loading should be administered and guided by the central venous pressure if there is no clinical evidence of volume overload, such as pulmonary edema. Rhythm and conduction abnormalities should be corrected, such as sinus bradycardia or atrioventricular (AV) conduction block. Inotropic support should be given for hypotension that does not resolve after volume loading. LV function and the presence of a mechanical complication should be assessed by echocardiography. Pulmonary artery catheter monitoring should be performed for patients with progressive hypotension that are not responsive to fluid administration or when fluid administration is contraindicated. Pulmonary artery catheter monitoring is also helpful to differentiate the causes of hypotension, such as hypovolemia, sepsis, or cardiac pumping failure.

Heart failure

In STEMI patients, heart failure may appear during the acute phase and present with dyspnea, orthopnea,

sinus tachycardia, S3 gallop, and pulmonary congestion or edema. Killip classification is used to grade the severity of heart failure and carries prognostic indication (Table 5). Oxygen supplementation should be given to maintain arterial saturation greater than 90%. Morphine sulfate can be used in patients with pulmonary congestion to release anxiety and decrease preload. Beta blockers or calcium channel antagonists should not be administered in patients with low-output state due to heart failure. Low dose short-acting ACE inhibitors, (eg., 6.25 mg captopril) and nitrate can be given to patients unless the systolic blood pressure is less than 100 mmHg or more than 30 mmHg below the baseline. Diuretics with furosemide or bumetanide should be administered to patients with pulmonary congestion but should be cautioned in patients whose systolic blood pressure is less than 100 mmHg or more than 30 mmHg below the baseline.

In severe heart failure, inotropic agents (dobutamine or dopamine) maybe necessary. Intraaortic balloon counterpulsation (IABP) should be performed in patients who do not respond to volume expansion, drug treatment and inotropic agents. When heart failure is complicated by acute renal injury with oligouria and pulmonary edema, forced diuretics should be initiated promptly. If there is no response to diuretics, continuous renal replacement therapy may be beneficial, particularly in the setting of shock or hypotension. IABP is a stabilizing measure for angiography and prompt revascularization. Given the large overall treatment benefit of 13 lives saved per 100 patients treated in the SHOCK trial,[68-70] early revascularization, either PCI or CABG, is recommended for STEMI patients less than 75 years old who develop shock within 36 hours of MI and are suitable for revascularization that can be performed within 18 hours of shock. Echocardiography should be used to evaluate mechanical complications and follow up LV function. Pulmonary artery catheter monitoring is useful to evaluate cardiac performance and LV preload [pulmonary arterial wedge pressure (PAWP)] in STEMI patients with heart failure. Figure 2 summarizes the measures to treat patients with STEMI and concomitant hypotension or shock in the acute stage.

Table 5. Killip classification

Killip 1: No clinical signs of heart failure
Killip 2: Pulmonary rales, an S_3, and elevated jugular venous pressure
Killip 3: Frank pulmonary edema with rales over 50% of the lung fields
Killip 4: Cardiogenic shock

For those who remain in heart failure throughout the hospitalization but can be discharged, low dose beta blockers can be initiated with gradual titration in outpatient clinic. Long-term aldosterone blockade should be prescribed for post-MI patients without significant renal dysfunction (creatinine should be less than or equal to 2.5 mg/dL in men and less than or equal to 2.0 mg/dL in women) or hyperkalemia (potassium should be less than or equal to 5.0 mEq/L) who are already receiving therapeutic doses of an ACE inhibitor, have an LV ejection fraction less than or equal to 0.40, and have either symptomatic heart failure or diabetes.

Cardiogenic shock

Cardiogenic shock is a state of inadequate tissue perfusion due to cardiac dysfunction, which may accompany STEMI as a catastrophic complication with high mortality rate. Inotropic agents and fluid restoration therapy are the initial important management. Emergent PCI for revascularization is beneficial to reduce mortality under adequate mechanical device support. Me-

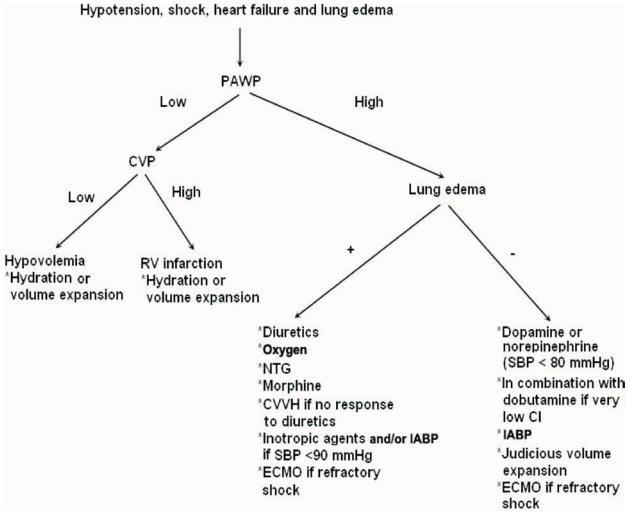

Figure 2. *The management of patients with STEMI and shock is outlined. CI, cardiac index; CVP, central venous pressure; CVVH, continuous venous venous hemofiltration; ECMO, extracorporeal membrane oxygenation; IABP, intraaortic balloon pump; NTG, nitroglycerin; PAWP, pulmonary arterial wedge pressure; RV, right ventricular; SBP, systolic blood pressure.*

chanical devices such as IABP and extracorporeal membrane oxygenator (ECMO) are helpful to stabilize the hemodynamic condition before or during emergent revascularization. IABP improves diastolic coronary blood flow and reduces myocardial work, which made it a useful stabilizing measure for patients in whom cardiac catheterization and revascularization are being considered.[71] ECMO, a cardiopulmonary bypass system placed through either the femoral or intrathoracic vessels, serves to support patients with heart failure and concomitant respiratory failure. Early ECMO-assisted primary PCI improved 30-day outcomes in patients with acute STEMI and profound cardiogenic shock that systolic blood pressure could not be maintained > 75 mmHg after IABP support and intravenous administration of dopamine dose > 60 ug/kg/min.[72] Selected patients with cardiogenic shock that are not candidates for revascularization may be considered for a mechanical support device to serve as a bridge to recovery or subsequent cardiac transplantation. The short-term devices include centrifugal pumps and LV assist devices (LVADs).[73] These systems are limited by their short-term usefulness of less than 1 week and the problems of bleeding and thrombosis. Experience with LVADs implanted in selected patients within 14 days after infarction has shown a survival rate of 67% to cardiac transplantation.[74]

RV infarction

Patients with inferior STEMI and hemodynamic disturbance should be assessed with a right precordial lead V_4R to detect ST-segment elevation and an echocardiogram to screen for RV infarction. RV infarction is characterized by high jugular venous pressure but low PAWP, if no concomitant left ventricular dysfunction is present. Early reperfusion should be achieved if possible. Concomitant sinus arrest or AV block is common. Bradycardia should be corrected either by temporary pacemaker, or permanent pacemaker if no recovery is expected 2 weeks after infarction. RV preload should be optimized, which usually requires large volume challenge in patients with hemodynamic instability. The volume expansion should also be guided by the PAWP to optimize the LV preload. RV afterload should be optimized, which usually requires therapy for concomitant LV dysfunction. Inotropic agents should be used for hemodynamic instability not responsive to volume challenge.

MECHANICAL COMPLICATIONS AND PERICARDITIS

Ischemic mitral regurgitation (IMR)

The presence of pulmonary edema, cardiogenic shock and systolic murmur in STEMI should alert the physicians to the possibility of acute MR and papillary muscle rupture. Severe MR after STEMI, accompanied by cardiogenic shock, carries a poor prognosis. In the SAVE trial, in which patients were treated with an ACE inhibitor after MI, even patients with mild MR have a worse prognosis than those without MR.[75] Post-MI patients with significant severe ischemic MR are usually to be older and more female in Taiwan.[76] PCI for acute STEMI could lower the incidence of ischemic MR.[77] Diagnosis is made by transthoracic or transesophageal echocardiography. In the SHOCK trial, approximately 10% patients with shock presented with severe MR and had an overall hospital mortality of 55%.[78] Mortality with medical treatment only was 71% compared with 40% with surgery.[78] Severe MR, in the absence of papillary muscle rupture, often indicates extensive infarction and severe LV dysfunction. Initial management should include afterload reduction and implantation of IABP. In many cases, the MR will improve over the next several days with aggressive medical management. If surgery is required because of critical coronary anatomy or ongoing ischemia, an intraoperative transesophageal echocardiography should be undertaken to assess the mitral valve. Mitral valve surgery should be undertaken at the same time as coronary artery bypass graft (CABG) surgery for patients with ischemic MR greater than moderate grade.[79]

All patients with papillary muscle rupture should receive urgent surgery. The patient should be stabilized with an IABP, inotropic agents, and afterload reduction to reduce regurgitant volume and alleviate pulmonary congestion. Coronary angiography should be undertaken before surgery. Most patients will require mitral valve replacement, although mitral valve repair has also been used in selected circumstances. Although emergency mitral valve replacement is associated with a relatively high mortality rate, the overall mortality reduction and ventricular function improvement are better compared with medical therapy alone. Delay in operation appears to increase the risk of further myocardial injury, other

organ injury, and subsequent death.[80]

Ventricular septal rupture (VSR)

The frequency of VSR have declined in the reperfusion era, especially after primary PCI and occurs in less than 1% of patients with STEMI in Taiwan.[81] Whereas previous studies indicated the mean time from MI to rupture is 3 to 5 days, data from the GUSTO-I and SHOCK trials indicate that the highest risk for development of a VSR occurs within the first 24 hours after infarction in patients receiving thrombolytic therapy.[82,83] Invasive monitoring is recommended in all patients, together with the judicious use of inotropic agents and a vasodilator to maintain optimal hemodynamics. Insertion of an IABP and prompt surgical repair are recommended for patient with an acute VSR. Although emergency surgery was formerly thought to be necessary only in patients with pulmonary edema or cardiogenic shock, it is now recognized that early surgery is equally important in hemodynamically stable patients.[84,85] Because septal perforations are exposed to shear forces and the rupture site can abruptly expand, resulting in sudden hemodynamic collapse even in patients who appear to be clinically stable. Surgical repair usually involves excision of all necrotic tissue and patch repair of the VSR, together with CABG. Surgical mortality is around 20% to 50% and was reported to be 87% in patients with cardiogenic shock.[83] However, the mortality of surgically treated patients is significantly lower than medically treated patients. In GUSTO-I trial, the mortality rates for surgical or medically treated patients were 47% and 94%, respectively.[82] A limited number of patients with post-infarction VSR can been treated by transcatheter closure with a septal occluding device. At the current time, surgical closure remains the procedure of choice, although percutaneous closure does offer some hope in the future.

Free wall rupture

Cardiac rupture occurs in 1% to 6% of all patients admitted with STEMI.[86-88] Cardiac rupture is observed most frequently in patients with their first MI, those with anterior infarction, the elderly, and women. Other risk factors include hypertension during the acute phase of STEMI, lack of previous angina and MI, lack of collateral blood flow, Q waves on the ECG, and use of corticosteroids or non-steroid analgesics. The frequency of cardiac rupture has two peaks: an early peak within 24 hours and a late one from 3 to 5 days after STEMI. Early rupture is related to the initial evolution of infarction before significant collagen deposition, and late rupture is related to expansion of the infarct-related ventricular wall. The most important determinants in preventing rupture are successful early reperfusion and the presence of collateral circulation.[86,87] Echocardiography is mandatory in the diagnosis of free wall rupture and pseudoaneurysm. Pericardiocentesis for relief of tamponade and emergency surgical repair may be lifesaving. The patient should be sent to operating room as soon as possible. Most series of patients reaching the operating room for management of this complication are small, with the surgical mortality rate in these patients being up to 60%.[89,90]

Ventricular aneurysm

Ventricular aneurysm after STEMI usually occurs on the anterior aspect of the LV in association with left anterior descending artery total occlusion and a large area of infarction. Clinical consequences include heart failure, thromboembolism, and ventricular arrhythmias. In patients who receive PCI and exhibit patent infarct-related artery have a significantly reduced incidence of LV aneurysm formation.[91] The need for surgery of ventricular aneurysm early after STEMI is rare, but it may be necessary for control of heart failure or intractable ventricular arrhythmias unresponsive to conventional therapy. Patients with severe LV dysfunction have an increased surgical mortality that has been reported to be as high as 19% for an LV ejection fraction less than 0.20.[92] Operation survivors can have functional improvement and a 60% 5-year survival rate.[93]

Pericarditis

Pericarditis in STEMI usually occurs in patients with extensive necrosis across the full thickness of the myocardial wall. Therefore, patients with pericarditis are prone to have larger infarcts, a lower ejection fraction, and a higher incidence of heart failure. Pericarditis appears up to several weeks after STEMI. Pericardial effusion can be evident on echocardiography but is rarely of hemodynamic importance. A small effusion is not diagnostic of pericarditis because it can be demonstrated in the majority of patients with STEMI.[94] Aspirin is the

treatment of choice, but higher doses (650 mg every 4 to 6 hours) may be required. Several small studies showed that colchicine could successfully treat or prevent the recurrence of acute pericarditis after the conventional therapy failed. Colchicine may be administered at 0.6 mg every 12 hours, with or without a loading dose.[95] NSAIDs may be considered for pain relief; however, they should not be used for extended periods. Corticosteroids are associated with scar thinning in the infarct zone and myocardial rupture, thus, should not be used except as a last resort. Antithrombotic therapy can be continued safely but requires vigilance for increasing pericardial effusion or signs of cardiac tamponade. Impending cardiac tamponade is an indication for prompt termination of antithrombotic therapy.

ARRHYTHMIAS IN STEMI

Cardiac arrhythmias are common in patients with STEMI and occur most frequently early after development of symptoms. The mechanisms for ventricular tachyarrhythmias include loss of transmembrane resting potential, reentrant mechanisms due to dispersion of refractoriness in the border zones between infarcted and nonischemic tissues,[96] and the development of foci of enhanced automaticity. Reperfusion arrhythmias appear to involve washout of toxic metabolites and of various ions such as lactate and potassium.[97] Atrial arrhythmias have additional causes, such as excessive sympathetic stimulation, increased atrial stretch due to heart failure or AV valvular insufficiency, proarrhythmic effects of pericarditis, and atrial infarction. Bradyarrhythmias may be due to overstimulation of vagal afferent receptors and resulting cholinergic stimulation, as well as ischemic injury of conducting tissues.

Ventricular arrhythmias

Ventricular fibrillation or pulseless ventricular tachycardia

Ventricular fibrillation (VF) or pulseless ventricular tachycardia (VT) should be treated with an unsynchronized electric shock with an initial monophasic shock energy of 360 J; if unsuccessful, a second and subsequent shocks of 360 J should be given. For biphasic defibrillators, providers should use the manufacturer's recommended energy dose (eg., initial dose of 120 to 200 J).[98] The maximal dose should be used if the effective dose range is not known. VF or pulseless VT that is refractory to electric shock should be treated with epinephrine (1 mg every 3-5 minutes) and amiodarone (300 mg or 5 mg/kg, IV bolus) followed by a repeat unsynchronized electric shock. Further management of VF or pulseless VT should be performed according to ACLS guideline.[99] Prophylactic administration of antiarrhythmic therapy in STEMI is not recommended. Routine use of prophylactic antiarrhythmic drugs (ie, lidocaine) is not indicated for suppression of isolated ventricular premature beats, couplets, runs of accelerated idioventricular rhythm, or nonsustained VT.

Ventricular tachycardia

Sustained (more than 30 seconds or causing hemodynamic collapse) polymorphic VT should be treated as VF as described previously. It is necessary to manage refractory polymorphic VT by aggressive attempts to reduce myocardial ischemia and adrenergic stimulation, including therapies such as beta blockade, IABP use, and consideration of emergency PCI/CABG. It is also necessary to aggressively normalize serum potassium to greater than 4.0 mEq/L and magnesium to greater than 2.0 mg/dL. If the patient has bradycardia to a rate less than 60 beats per minute or long QTc, temporary pacing at a higher rate may be instituted.

Sustained monomorphic VT associated with angina, pulmonary edema, or hypotension (SBP less than 90 mmHg) should be treated with a synchronized 100 J monophasic or biphasic electric shock. Increasing energies may be used if not initially successful. Brief sedation is desirable if hemodynamically tolerable. Sustained monomorphic VT not associated with angina, pulmonary edema, or hypotension could be initially treated with intravenous amiodarone: 150 mg infused over 10 minutes; repeat 150 mg every 10 to 15 minutes as needed and follow by maintenance infusion of 1 mg/min over 6 hours; then 0.5 mg/min over the next 18 hours. The total cumulative dose, including additional doses given during cardiac arrest, must not exceed 2.2 g over 24 hours. Procainamide and sotalol can also be considered.[97] Synchronized electrical cardioversion starting at monophasic or biphasic energies of 100 J with brief sedation can be

used if drug therapies fail.

Ventricular premature beats

Treatment of isolated ventricular premature beats, couplets, and nonsustained VT is not recommended unless they lead to hemodynamic compromise. Before the present era of care of the STEMI patient with antiplatelet therapy, beta-blockade, ACE inhibitors and reperfusion therapy, it was thought that ventricular warning arrhythmias preceded VF. Careful monitoring has refuted this concept, and treatment of these rhythm disturbances is not recommended unless they lead to hemodynamic compromise.

Accelerated idioventricular rhythms and accelerated junctional rhythms

Antiarrhythmic therapy is not indicated for accelerated idioventricular rhythm and accelerated junctional rhythm.

Implantable cardioverter defibrillator implantation

Generally speaking, an implantable cardioverter-defibrillator (ICD) can be considered for patients with VF or hemodynamically significant sustained VT with LV systolic dysfunction after STEMI if the arrhythmia is not due to ischemia, reinfarction or any other reversible causes. In the 2008 revised ACC/AHA guideline,[100] ICD is indicated in the following 3 groups of patients after MI: (1) patients with LV ejection fraction less than or equal to 35% due to prior MI who are at least 40 days post-MI and are in NYHA functional Class II or III, (2) patients with LV dysfunction due to prior MI who are at least 40 days post-MI, have an LV ejection fraction less than or equal to 30%, and are in NYHA functional Class I, and (3) patients with nonsustained VT due to prior MI, LV ejection fraction less than or equal to 40%, and inducible VF or sustained VT at electrophysiological study.

Atrial fibrillation/atrial flutter and supraventricular arrhythmias

Sustained atrial fibrillation/atrial flutter

Sustained atrial fibrillation/atrial flutter with hemodynamic compromise or ongoing ischemia should be treated with synchronized cardioversion with an initial monophasic shock of 200 J for atrial fibrillation and 50-100 J for flutter, preceded by brief sedation whenever possible. The shock dose should be increased gradually if the initial shock fails. The recommended initial biphasic energy dose for cardioversion of atrial fibrillation is 120 to 200 J.[99] For episodes of atrial fibrillation that do not respond to electrical cardioversion or recur after a brief period of sinus rhythm, antiarrhythmic therapy is indicated to slow down the ventricular rate. These pharmacological agents include intravenous amiodarone and intravenous digoxin, especially in patients with LV dysfunction and heart failure. In patients with sustained atrial fibrillation/atrial flutter with ongoing ischemia but without hemodynamic compromise, intravenous beta blockers, diltiazem or verapamil can be considered before electric cardioversion. In patients with sustained atrial fibrillation/atrial flutter but without hemodynamic compromise or ischemia, rate control is usually indicated. In addition, patients with sustained atrial fibrillation or flutter should be given anticoagulant therapy.

Reentrant paroxysmal supraventricular tachycardia

Reentrant paroxysmal supraventricular tachycardia can be treated with the following measures: (1) vagal maneuvers, including Valsalva maneuver or carotid sinus massage (2) intravenous adenosine (3) intravenous beta blockers with metoprolol, esmolol or atenolol and (4) intravenous verapamil or diltiazem. Beta blockers, verapamil, and diltiazem should not be used in patients with LV dysfunction and heart failure. Digoxin, amiodarone or cardioversion can be considered in these patients. Cardioversion of reentrant SVT generally requires less energy with an initial energy of 50-100 J is often sufficient.

Atrial premature beats

Treatment of atrial premature beats is not indicated.

Bradycardia

Symptomatic sinus bradycardia, sinus pauses greater than 3 seconds, or sinus bradycardia with a heart rate less than 40 beats/minute and associated hypotension or signs of hemodynamic compromise should be treated with intravenous bolus of atropine 0.5 mg every 3 to 5 minutes (maximal 3 mg). Dopamine intravenous infusion (2-10 mcg/kg/min) also can be used. If bradycardia is persistent, transcutaneous or transvenous temporary

pacing should be instituted. Atropine is usually ineffective in type II second degree or third degree AV block. Temporary pacing is necessary.

Permanent pacing in STEMI

Permanent cardiac pacing should be considered for persistent conduction disturbances (≥ 14 days) due to STEMI. Permanent ventricular pacing is indicated for persistent second degree AV block in the His-Purkinje system with alternating bundle branch block or third-degree AV block within or below the His-Purkinje system after STEMI. Permanent ventricular pacing is also indicated for transient advanced second- or third-degree infranodal AV block and associated bundle branch block. If the site of block is uncertain, an electrophysiological study may be necessary. For persistent and symptomatic second- or third-degree AV block, permanent ventricular pacing is also indicated. Permanent ventricular pacing may be considered for persistent second or third degree AV block at the AV node level, even there is no symptom. Overall, the criteria for patients with STEMI and AV block do not necessarily depend on the presence of symptoms. Furthermore, the requirement for temporary pacing in STEMI does not by itself constitute an indication for permanent pacing.

Permanent ventricular pacing is not recommended for: (1) transient AV block in the absence of intraventricular conduction defects, (2) transient AV block in the presence of isolated left anterior fascicular block, (3) new bundle branch block or fascicular block in the absence of AV block, (4) persistent asymptomatic first-degree AV block in the presence of bundle branch or fascicular block. Indications for permanent pacing after STEMI in patients experiencing AV block are related in large measure to the presence of intraventricular conduction defects.

Pacing mode selection in STEMI patients

All patients who have an indication for permanent pacing after STEMI should be evaluated for ICD or biventricular pacing (cardiac resynchronization therapy) indications. It is reasonable to implant a permanent dual-chamber pacing system in STEMI patients who need permanent pacing and are in sinus rhythm. It is reasonable that patients in permanent atrial fibrillation or flutter receive a single-chamber ventricular device.

CABG SURGERY IN STEMI

To optimize the treatment of STEMI, timely reperfusion of the occluded coronary artery is critical. PCI has improved short- and long-term outcome in patients with STEMI and is now the preferred treatment strategy. However, coronary angiography also identifies patients suitable for CABG during the acute and subacute phase of STEMI. In patients with a coronary anatomy not eligible for PCI, CABG is also served as the primary reperfusion modality either in the acute phase or after stabilization. Most of time, CABG is performed after PCI as a definitive or adjunctive revascularization therapy after STEMI.[101] CABG after STEMI is indicated for both ischemic and anatomical reasons if one of the following criteria is met: (1) persistent or recurrent ischemia refractory to medical therapy, (2) cardiogenic shock, (3) a concomitant procedure for postinfarction VSR or MR, or (4) primary reperfusion therapy within 24 hours if the coronary anatomy is unsuitable for PCI.[101] Meanwhile, CABG is also considered as a treatment option in the absence of ongoing ischemia when an anatomical indication is present. Such lesions include significant left main disease, three-vessel disease and two-vessel disease with significant involvement of the proximal left anterior descending coronary artery and either depressed left ventricular function or noninvasive evidence of ischemia.

Timing of surgery

The mainstay for the treatment of STEMI is early revascularization with either thrombolytic therapy or PCI. CABG plays a role in different clinical scenarios. It could be elective after MI recovery, urgent or emergent. Emergency or urgent CABG in patients with STEMI should be undertaken in the following circumstances: (1) failed PCI with persistent chest pain or hemodynamic instability in patients with coronary anatomy suitable for surgery, (2) persistent or recurrent ischemia refractory to medical therapy in patients who have coronary anatomy suitable for surgery, who have a significant area of myocardium at risk, and who are not candidates for PCI, (3) at the time of surgical repair of postinfarction VSR or MR, (4) cardiogenic shock in patients less than 75 years old with ST-segment elevation or left bundle-branch block or posterior MI who develop shock within

36 hours of MI and are suitable for revascularization that can be performed within 18 hours of shock, unless further support is futile because of the patient' s wishes or contraindications/unsuitability for further invasive care, (5) life-threatening ventricular arrhythmias in the presence of greater than or equal to 50% left main stenosis and/or triple-vessel disease.

Emergent CABG after failed thrombolytic therapy or PCI

Emergent CABG after failed thrombolytic therapy or PCI should be undertaken in patients with persistent chest pain or hemodynamic instability and suitable coronary anatomy. CABG may be performed as primary reperfusion in patients who have suitable anatomy and who are not candidates for or who have had failed fibrinolysis/ PCI and who are in the early hours (6 to 12 hours) of evolving STEMI.

Elective CABG after STEMI

The indications of elective CABG after STEMI depend on patients' conditions, coronary anatomy, extent of myocardial ischemia and time eclipse after STEMI.

Elective CABG is recommended for patients after STEMI who have significant left main coronary artery stenosis. Elective CABG is recommended for patients after STEMI who have left main equivalent including significant (greater than or equal to 70%) stenosis of the proximal left anterior descending and proximal left circumflex artery. Elective CABG is also recommended for patients after STEMI who have 3-vessel disease and the survival benefit is greater when LV ejection fraction is less than 0.50. Elective CABG is recommended in patients after STEMI who have 2-vessel disease with significant proximal left anterior descending artery stenosis and either LV ejection fraction less than 0.50 or demonstrable ischemia on noninvasive testing. Elective CABG is recommended in patients in whom revascularization is not optimal or possible and who have ongoing ischemia not responsive to maximal nonsurgical therapy. Elective CABG is beneficial for patients after STEMI who have 1- or 2-vessel CAD without significant proximal left anterior descending artery stenosis but with a large area of viable myocardium and high-risk criteria on noninvasive testing. Elective CABG is beneficial for patients after STEMI who have developed post-MI angina despite maximal noninvasive therapy, when surgery can be performed with acceptable risk.

In patients who have had an STEMI, CABG mortality is elevated for the first 3 to 7 days after infarction, and the benefit of revascularization must be balanced against this increased risk. Beyond 7 days after infarction, the criteria for revascularization described in following sections are applicable. Elective CABG is reasonable in patients after STEMI who have proximal left anterior descending artery stenosis with 1-vessel disease. This recommendation becomes strong if extensive ischemia is documented by noninvasive study and/or LV ejection fraction is less than 0.50. Elective CABG may be useful for patients after STEMI who have 1- or 2-vessel CAD without significant proximal left anterior descending artery stenosis but who have a moderate area of viable myocardium and demonstrable ischemia on noninvasive testing. Elective CABG is reasonable in bypassable 1- or 2-vessel disease causing life-threatening ventricular arrhythmias after STEMI. This recommendation becomes strong if the arrhythmia is resuscitated sudden cardiac death or sustained ventricular tachycardia.

CABG after STEMI and antiplatelet drugs

Antiplatelet and anticoagulant therapies are administered to all patients with STEMI. Therefore, more bleeding, transfusion and reopen for hemostasis after CABG are expected in this stage. Consistently, the use of these antiplatelet and anticoagulant medications prior to CABG has been associated with increased bleeding complications but not with in-hospital or 30-day mortality in patients undergoing CABG. In patients requiring CABG, clopidogrel should be withheld for 5 to 7 days before CABG. However, this recommendation cannot be followed in most patients presenting with STEMI who require urgent CABG.

For patients with STEMI and cardiogenic shock referred for emergent CABG, blood component therapy will be the only treatment to control bleeding. Platelet transfusion is the cure for antiplatelet therapy. Care should be given to balance the hemostasis with potential graft occlusion. For lacking of antidote, low-molecule-weight heparin is not a preferred choice in patients with STEMI expected to have an emergent operation. Similarly, GP IIb/IIIa inhibitors with longer half-life are not

recommended in this clinical scenario. If CABG is performed as definitive or adjunctive revascularization after STEMI, tailored adjustment of antiplatelet or anticoagulant therapy should be considered. In addition to aspirin, parenteral heparin could be given for patients with remaining ischemic symptoms. Platelet count should be monitored when CABG is expected. If clinical circumstances permit, clopidogrel should be withheld for 5 days before the performance of elective CABG surgery.

IMMEDIATE BEFORE AND AFTER DISCHARGE

Patient education and cardiac rehabilitation

Stable patients that considered to be discharged after STEMI should be followed by appropriate management. The key components of management in this stage include education, assessment, drug therapy, lifestyle modification, and cardiac rehabilitation.

Before discharge, all STEMI patients should be educated about and actively involved in planning for adherence to the lifestyle changes and drug therapies that are proved effective for secondary prevention of CAD. Recommendations regarding healthy diet, smoking cessation, achievement of ideal body weight, diabetes control, blood pressure control (less than 130/80 mmHg) and encouragement of a minimum of 30 to 60 minutes of activity (preferably daily, or at least 3 times weekly) should be an integral part of patient education. Beta blockers, aspirin and statins should be used for all patients following STEMI. ACE inhibitors or ARBs are indicated for patients with heart failure and/or reduced LV ejection fraction and are likely protective in most patients. Patients and their family members should receive discharge instructions about recognizing acute cardiac symptoms and appropriate actions to take in response (ie, call 119 if symptoms are unimproved or worsening 5 minutes after onset or post 1 sublingual nitroglycerin) if symptoms recur. Family members of STEMI patients should be advised to learn CPR.

Referral for outpatient rehabilitation should also be strongly encouraged. The concept of cardiac rehabilitation following MI is not new but is gaining acceptance as an essential part of the service to these patients recently. Cardiac rehabilitation and secondary prevention programs, when available, are recommended for patients with STEMI, particularly those with multiple modifiable risk factors and/or those moderate- to high-risk patients in whom supervised exercise training is warranted.[102,103] Adherence to these goals in patients with STEMI will lead to better long-term outcomes and reduction in cardiac death, recurrent MI, stroke, and need for coronary revascularization.

Long-term pharmacological treatment after discharge

Antiplatelet drugs

Antiplatelet drugs should be prescribed after discharge. Aspirin is recommended with a daily dose 100 mg if there is no contraindication. Clopidogrel 75 mg per day should be routinely added for 12 months to all STEMI patients regardless of whether they receive thrombolytic therapy, primary PCI or do not receive any reperfusion therapy. If patients are scheduled for surgery, clopidogrel is recommended to be discontinued 5 days before. For aspirin, in general the benefit of continuous use outweighs the risk of bleeding. Maintenance of aspirin before surgery has been shown to prevent vascular events during and after surgery. However, given that the risk and benefit of aspirin varied case by case, the cardiologist should be consulted regarding the use or stop of aspirin before surgery.

Inhibition of renin-angiotensin-aldosterone-system

ACE inhibitors should be given to patients with anterior infarction, pulmonary congestion, or LV ejection fraction less than 0.40, in the absence of hypotension (SBP less than 100 mmHg or less than 30 mmHg below baseline) or known contraindications to that class of medications.[56,104] ACE inhibitors after STEMI should be started with low dose and increase steadily to achieve a full dose within 24 to 48 hours if possible.[105,106] For those STEMI patients intolerant to ACE inhibitors and who have either clinical or radiological signs of heart failure or LV ejection fraction less than 0.40, ARBs should be administered. Valsartan[57] and candesartan[58] have established efficacy for this recommendation.

Long-term aldosterone blockade is another means of inhibiting the renin-angiotensin-aldosterone system. In the post-STEMI setting, it should be considered for

long-term usage in patients without significant renal dysfunction (estimated creatinine clearance should be greater than 30 mL per minute) or hyperkalemia (potassium should be less than or equal to 5.0 mEq/L) who are already receiving therapeutic doses of an ACE inhibitor or ARB, have a LV ejection fraction of less than or equal to 0.40 or symptomatic heart failure. Given the fact that the risk of hyperkalemia is greatest in patients with creatinine clearance estimated to be less than 50 mL/minute, close monitoring of potassium levels is indicated for those patients. The risk-to-benefit ratio should be carefully weighed in such patients.

Beta blockers

Oral beta blocker therapy should be initiated in the first 24 hours for patients who do not have any of the following: (1) signs of heart failure, (2) evidence of a low output state, (3) increased risk for cardiogenic shock, such as in patients with age greater than 70 years, SBP less than 120 mmHg, sinus tachycardia greater than 110 bpm or heart rate less than 60 bpm, (4) other relative contraindications to beta blockade, such as PR interval greater than 0.24 seconds, second- or third-degree heart block, active asthma, or reactive airway disease. It is reasonable to administer an IV beta blocker to patients who are hypertensive. Patients with early contraindications within the first 24 hours of STEMI should be reevaluated for candidacy for beta blocker therapy as secondary prevention. Patients with moderate or severe LV failure should receive beta blocker therapy as secondary prevention with a gradual titration scheme. Beta-blockade should be initiated before discharge for secondary prevention. For those who remain in heart failure throughout the hospitalization, low doses should be initiated, with gradual titration on an outpatient basis.

Blood pressure control

The patients with STEMI should be informed of their blood pressure and the treatment goal if hypertension exists during hospitalization. After discharge, it is recommended the blood pressure goal is < 130/80 mmHg for secondary prevention.[107] Besides, initiation of lifestyle modification along with weight control, increased physical activity, moderate alcohol consumption, decreased sodium usage and increased consumption of fresh fruits, vegetables, and low-fat dairy products is important for hypertension control.[107] The blood pressure should be treated initially with beta-blockers and/or ACE inhibitors, with the addition of other drugs such as thiazides as needed to achieve the blood pressure goal. ARBs are alternative choices if patients are intolerant to ACE inhibitors. Overall, the details of hypertension control can be found in the 2010 Guidelines of the Taiwan Society of Cardiology for management of hypertension.[107]

Diabetes management

Glucose metabolic disturbances are common in patients with STEMI and impaired glucose tolerance is a significant risk factor for future cardiovascular events after MI.[108] Therefore, oral glucose tolerance test can be performed before or shortly after discharge.[109] In patients with established diabetes, the effort should be made to keep $HbA_1C \leq 7.0\%$. Intensive life modification, such as diet control, regular exercise, and weight reduction, usually together with pharmacotherapy is highly recommended to achieve the goal. Thiazolidinediones should not be used in those who have New York Heart Association class III or IV heart failure.[110,111] In addition, rosiglitazone is not recommended after MI. In patients with impaired fasting glucose or impaired glucose tolerance, only lifestyle modification is recommended.

Lipid management

Many studies have demonstrated the benefits of lipid-lowering agents in patients after ACS for prevention of recurrent ischemic events and mortality. In addition to drug therapy, it is important to encourage patients to start dietary therapy. In patients with acute STEMI within 24 hours of hospitalization, fasting lipid profile should be assessed. Adequate lipid-lowering agents should be administered before discharge and statin is the drug of choice. At least, the LDL-C goal should be less than 100 mg/dL. It is reasonable to lower LDL-C to less than 70 mg/dL in STEMI patients.[112] High dose statin has been proved to be more effective to reach the treatment goal in ACS clinical trials. If patients can not tolerate statins or have contraindications, other lipid-lowering agents may be considered. However, the clinical trial evidence of these agents in ACS is lacking. If triglycerides are 200 to 499 mg/dL, non-HDL-C should be less than 130 mg/dL. Fibrate or

niacin is indicated before LDL-lowering therapy for the patients with triglyceride more than 500 mg/dL to prevent pancreatitis.

Hormone therapy

The incidence of cardiovascular diseases increases after menopause and postmenopausal women have a significantly higher incidence of cardiovascular diseases compared to premenopausal women at any age. Epidemiological findings suggest the causative role of ovarian hormone deficiency in the development of cardiovascular diseases in women.[113] In early postmenopausal women, ovarian hormone replacement therapy (HRT) may be cardioprotective because of the responsiveness of the endothelium to estrogens that also buffer the detrimental effects on coagulation of HRT. But in late postmenopausal women, HRT has either a worthless effect or even a detrimental effect because of the predominance of the procoagulant or plaque-destabilizing effects over the vasoprotective effects.[114] Therefore, HRT has beneficial cardiovascular effects in younger women while it may have detrimental effect on coagulative balance and vascular inflammation and has little effect on cardiovascular functions in older women. Postmenopausal women should not receive combination estrogen and progestin therapy for primary or secondary prevention of CAD. Concordantly, HRT with estrogen plus progestin should not be given to postmenopausal women after STEMI for secondary prevention.[115-117] Postmenopausal women who are already taking estrogen plus progestin at the time of STEMI should not continue hormone therapy. In summary, the previous advice that HRT is beneficial in postmenopausal women to prevent and treat CAD is no longer valid. It is recommended that the use of HRT be discontinued in women who have STEMI.

CONCLUSION

The successful treatment of STEMI depends on rapid reperfusion therapy and adherence to the guideline suggested pharmacological management in hospital and at discharge. According to the results from Taiwan ACS full spectrum registry,[118] reperfusion therapy was carried out in 82.2% of 1703 STEMI patients at the time of admission in Taiwan. Primary PCI was performed over 95% of the patients and thrombolytic therapy was administered in only about 3%. The median door-to-balloon time was 96 minutes. The door-to-balloon time was within 60 minutes in about 50% of these patients. In patients received thrombolytic therapy, the median door-to-needle time of 65 minutes and only 12.8% of these patients were within 30 minutes. In Taiwan, dual antiplatelet therapy with aspirin and clopidogrel was used in 82% of the STEMI patients at discharge. Beta blocker was used in 57%, ACE inhibitor was used in 53% and statin was used in 65% of these patients at discharge. Overall, there is a gap between the real world practice in Taiwan and guideline recommendations. Therefore, the Taiwan Society of Cardiology decided to establish the local ACS guideline to close the gap and improve the quality of STEMI care. The first meeting for the Taiwan ACS guideline was held in Taipei on January 9, 2011 by the Taiwan Society of Cardiology and determined to publish STEMI guideline first in Taiwan. The writing group of the guideline for the STEMI was created by the Taiwan Society of Cardiology in March 2011. Individual members from different hospitals in their area of expertise were invited to contribute to the different sections of the guideline. There were discussions at meetings for the writing members and opinion leaders in Kaohsiung on April 23, 2011 and in Taipei on April 24, 2011. The preliminary draft of the guideline was presented at the Annual Scientific Session of the Taiwan Society of Cardiology in Taipei on May 14, 2011. After several revisions, the manuscript was sent to the executives, controllers and committee leaders of the Taiwan Society of Cardiology in July 2011 for final approval. The suggestions and recommendations in the guideline need to be implemented in our daily clinical practice. The Taiwan Society of Cardiology will keep playing an active role in promoting the implementation of the guideline in Taiwan through frequent continuing medical education. The ultimate goal is to significantly decrease the morbidity and mortality of STEMI in Taiwan.

REFERENCES

1. Lambert L, Brown K, Segal E, et al. Association between timeliness of reperfusion therapy and clinical outcomes in ST-eleva-

tion myocardial infarction. *JAMA* 2010;303:2148-55.
2. Antman EM, Anbe DT, Armstrong PW, et al. ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction -- executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 1999 Guidelines for the Management of Patients with Acute Myocardial Infarction). *J Am Coll Cardiol* 2004;44:671-719.
3. The task force on the management of ST-segment elevation acute myocardial infarction of the European Society of Cardiology. Management of acute myocardial infarction in patients presenting with persistent ST-segment elevation. *Eur Heart J* 2008;29: 2909-45.
4. China Society of Cardiology of Chinese Medical Association; Editorial Board of Chinese Journal of Cardiology. Guideline for diagnosis and treatment of patients with ST-elevation myocardial infarction. *Zhonghua Xin Xue Guan Bing Za Zhi* 2010; 38:675-90.
5. Eagle KA, Montoye CK, Riba AL, et al. Guideline-based standardized care is associated with substantially lower mortality in Medicare patients with acute myocardial infarction. *J Am Coll Cardiol* 2005;46:1242-8.
6. Wenger NK. You've come a long way, baby: cardiovascular health and disease in women: problems and prospects. *Circulation* 2004;109:558-60.
7. McSweeney JC, Cody M, O'Sullivan P, et al. Women's early warning symptoms of acute myocardial infarction. *Circulation* 2003;108:2619-23.
8. Weaver WD, Litwin PE, Martin JS, et al. for the MITI Project Group. Effect of age on use of thrombolytic therapy and mortality in acute myocardial infarction. *J Am Coll Cardiol* 1991;18: 657-62.
9. Spodick DH. Diagnostic electrocardiographic sequences in acute pericarditis: significance of PR segment and PR vector changes. *Circulation* 1973;48:575-80.
10. Menown IB, Mackenzie G, Adgey AA. Optimizing the initial 12-lead electrocardiographic diagnosis of acute myocardial infarction. *Eur Heart J* 2000;21:275-83.
11. Mauri F, Gasparini M, Barbonaglia L, et al. Prognostic significance of the extent of myocardial injury in acute myocardial infarction treated by streptokinase (the GISSI trial). *Am J Cardiol* 1989;63:1291-5.
12. Matetzky S, Freimark D, Chouraqui P, et al. Significance of ST segment elevations in posterior chest leads (V7 to V9) in patients with acute inferior myocardial infarction: application for thrombolytic therapy. *J Am Coll Cardiol* 1998;31:506-11.
13. Cheitlin MD, Armstrong WF, Aurigemma GP, et al. ACC/AHA/ASE 2003 guideline update for the clinical application of echocardiography: summary article: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (ACC/AHA/ASE Committee to Update the 1997 Guidelines for the Clinical Application of Echocardiography). *Circulation* 2003;108:1146-62.
14. Wang K, Asinger RW, Marriott HJ. ST-segment elevation in conditions other than acute myocardial infarction. *N Engl J Med* 2003;349:2128-35.
15. Fibrinolytic Therapy Trialists' (FTT) Collaborative Group. Indications for fibrinolytic therapy in suspected acute myocardial infarction: collaborative overview of early mortality and major morbidity results from all randomised trials of more than 1000 patients. *Lancet* 1994;343:311-22.
16. Sgarbossa EB, Pinski SL, Barbagelata A, et al. for the GUSTO-1 (Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries) Investigators. Electrocardiographic diagnosis of evolving acute myocardial infarction in the presence of left bundle-branch block. *N Engl J Med* 1996;334:481-7.
17. Sgarbossa EB. Value of the ECG in suspected acute myocardial infarction with left bundle-branch block. *J Electrocardiol* 2000; 33:87-92.
18. Alpert JS, Thygesen K, Antman E, Bassand JP. Myocardial infarction redefined: a consensus document of the Joint European Society of Cardiology/American College of Cardiology Committee for the redefinition of myocardial infarction. *J Am Coll Cardiol* 2000;36:959-69.
19. Maroko PR, Radvany P, Braunwald E, Hale SL. Reduction of infarct size by oxygen inhalation following acute coronary occlusion. *Circulation* 1975;52:360-8.
20. ISIS-4 (Fourth International Study of Infarct Survival) Collaborative Group. ISIS-4: a randomised factorial trial assessing early oral captopril, oral mononitrate, and intravenous magnesium sulphate in 58,050 patients with suspected acute myocardial infarction. *Lancet* 1995;345:669-85.
21. Come PC, Pitt B. Nitroglycerin-induced severe hypotension and bradycardia in patients with acute myocardial infarction. *Circulation* 1976;54:624-8.
22. Gislason GH, Jacobsen S, Rasmussen JN, et al. Risk of death or reinfarction associated with the use of selective cyclooxygenase-2 inhibitors and nonselective nonsteroidal antiinflammatory drugs after acute myocardial infarction. *Circulation* 2006;113: 2906-13.
23. ISIS-2 (Second International Study of Infarct Survival) Collaborative Group. Randomised trial of intravenous streptokinase, oral aspirin, both, or neither among 17,187 cases of suspected acute myocardial infarction: ISIS-2. *Lancet* 1988;2:349-60.
24. Chen ZM, Jiang LX, Chen YP, et al. Addition of clopidogrel to aspirin in 45,852 patients with acute myocardial infarction: randomised placebo controlled trial. *Lancet* 2005;366:1607-21.
25. Sabatine MS, Cannon CP, Gibson CM, et al. Addition of clopidogrel to aspirin and fibrinolytic therapy for myocardial infarction with ST-segment elevation. *N Engl J Med* 2005;352: 1179-89.
26. Sabatine MS, Cannon CP, Gibson CM, et al. Effect of clopidogrel pretreatment before percutaneous coronary intervention in patients with ST-elevation myocardial infarction treated with fibrinolytics: the PCI-CLARITY study. *JAMA*

2005;294:1224-32.
27. Fang CC, Jao YT, Chen Y, et al. Glycoprotein IIb/IIIa inhibitor (tirofiban) in acute ST-segment elevation myocardial infarction. *Angiology* 2009;60:192-200.
28. Yip HK, Wu CJ, Chang HW, et al. Impact of tirofiban on angiographic morphologic features of high-burden thrombus formation during direct percutaneous coronary intervention and short-term outcomes. *Chest* 2003;124:962-8.
29. Bassand J, Danchin N, Filippatos G, et al. Implementation of reperfusion therapy in acute myocardial infarction. A policy statement from the European Society of Cardiology. *Eur Heart J* 2005;26:2733-41.
30. Keeley EC, Boura JA, Grines CL. Primary angioplasty versus intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review of 23 randomised trials. *Lancet* 2003; 361:13-20.
31. Tamis-Holland JE, Palazzo A, Stebbins AL, et al. Benefits of direct angioplasty for women and men with acute myocardial infarction: results of the Global Use of Strategies to Open Occluded Arteries in Acute Coronary Syndromes Angioplasty (GUSTO II-B) Angioplasty Substudy. *Am Heart J* 2004;147: 133-9.
32. Goldenberg I, Matetzky S, Halkin A, et al. Primary angioplasty with routine stenting compared with thrombolytic therapy in elderly patients with acute myocardial infarction. *Am Heart J* 2003;145:862-7.
33. Kornowski R, Mehran R, Dangas G, et al. Prognostic impact of staged versus "one-time" multivessel percutaneous intervention in acute myocardial infarction: analysis from the HORIZONS-AMI (harmonizing outcomes with revascularization and stents in acute myocardial infarction) trial. *J Am Coll Cardiol* 2011;58: 704-11.
34. Vlaar PJ, Mahmoud KD, Holmes DR Jr, et al. Culprit vessel only versus multivessel and staged percutaneous coronary intervention for multivessel disease in patients presenting with ST-segment elevation myocardial infarction: a pairwise and network meta-analysis. *J Am Coll Cardiol* 2011;58:692-703.
35. Rathore SS, Curtis JP, Chen J, et al. Association of door-to-balloon time and mortality in patients admitted to hospital with ST elevation myocardial infarction: national cohort study. *BMJ* 2009;338:b1807.
36. Boersma E, Maas AC, Deckers JW, Simoons ML. Early thrombolytic treatment in acute myocardial infarction: reappraisal of the golden hour. *Lancet* 1996;348:771-5.
37. Steg PG, Bonnefoy E, Chabaud S, et al. Impact of time to treatment on mortality after prehospital fibrinolysis or primary angioplasty: data from the CAPTIM randomized clinical trial. *Circulation* 2003;108:2851-6.
38. Antithrombotic Trialists' Collaboration. Collaborative meta-analysis of randomised trials of antiplatelet therapy for prevention of death, myocardial infarction, and stroke in high-risk patients. *BMJ* 2002;324:71-86.
39. Peters RG, Mehta SR, Fox KA, et al. Effects of aspirin dose when used alone or in combination with clopidogrel in patients with acute coronary syndromes: observations from the Clopidogrel in Unstable angina to prevent Recurrent Events (CURE) Study. *Circulation* 2003;108:1682-7.
40. Cheng CI, Chen CP, Kuan PL, et al. The causes and outcomes of inadequate implementation of existing guidelines for antiplatelet treatment in patients with acute coronary syndrome: the experience from Taiwan Acute Coronary Syndrome Descriptive Registry (T-ACCORD Registry). *Clin Cardiol* 2010;33:E40-8.
41. Mehta SR, Bassand JP, Chrolavicius S, et al. Dose comparisons of clopidogrel and aspirin in acute coronary syndromes. *N Engl J Med* 2010;363:930-42.
42. Mehta SR, Tanguay JF, Eikelboom JW, et al. Double dose versus standard-dose clopidogrel and high dose versus low-dose aspirin in individuals undergoing percutaneous coronary intervention for acute coronary syndromes (CURRENT-OASIS 7): a randomised factorial trial. *Lancet* 2010;376:1233-43.
43. Montalescot G, Wiviott SD, Braunwald E, et al. Prasugrel compared with clopidogrel in patients undergoing percutaneous coronary intervention for ST-elevation myocardial infarction (TRITON-TIMI 38): double-blind, randomised controlled trial. *Lancet* 2009;373:723-31.
44. Steg PG, James S, Harrington RA, et al. Ticagrelor versus clopidogrel in patients with ST-elevation acute coronary syndromes intended for reperfusion with primary percutaneous coronary intervention: A Platelet Inhibition and Patient Outcomes (PLATO) trial subgroup analysis. *Circulation* 2010;122:2131-41.
45. Mehilli J, Kastrati A, Schulz S, et al. Abciximab in patients with acute ST-segment-elevation myocardial infarction undergoing primary percutaneous coronary intervention after clopidogrel loading: a randomized double-blind trial *Circulation* 2009;119: 1933-40.
46. Van't Hof AW, Ten Berg J, Heestermans T, et al. Prehospital initiation of tirofiban in patients with ST-elevation myocardial infarction undergoing primary angioplasty (On-TIME 2): a multicentre, double-blind, randomised controlled trial *Lancet* 2008; 372:537-46.
47. Liu CP, Lin MS, Chiu YW, et al. Additive benefit of glycoprotein IIb/IIIa inhibition and adjunctive thrombus aspiration during primary coronary intervention: results of the Initial Thrombosuction and Tirofiban Infusion (ITTI) trial. *Int J Cardiol* 2012;156:174-9.
48. De Luca G, Ucci G, Cassetti E, et al. Benefits from small molecule administration as compared with abciximab among patients with ST-segment elevation myocardial infarction treated with primary angioplasty: a meta-analysis *J Am Coll Cardiol* 2009; 53:1668-73.
49. Kushner FG, Hand M, Smith Jr SC, et al. 2009 focused updates: ACC/AHA guidelines for the management of patients with ST-elevation myocardial infarction (updating the 2004 guideline and 2007 focused update) and ACC/AHA/SCAI guidelines on percutaneous coronary intervention (updating the 2005 guideline and 2007 focused update): a report of the American College

of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, *J Am Coll Cardiol* 2009;54: 2205-41.
50. Yip HK, Chang HW, Wu CJ, et al. A safe and effective regimen without heparin therapy after successful primary coronary stenting in patients with acute myocardial infarction. *Jpn Heart J* 2000;41:697-711.
51. Antman EM, Morrow DA, McCabe CH, et al. Enoxaparin versus unfractionated heparin with fibrinolysis for ST-elevation myocardial infarction, *N Engl J Med* 2006;354:1477-88.
52. Cohen M, Gensini GF, Maritz F, et al. The safety and efficacy of subcutaneous enoxaparin versus intravenous unfractionated heparin and tirofiban versus placebo in the treatment of acute ST-segment elevation myocardial infarction patients ineligible for reperfusion (TETAMI): a randomized trial. *J Am Coll Cardiol* 2003;42:1348-56.
53. Stone GW, Witzenbichler B, Guagliumi G, et al. Bivalirudin during primary PCI in acute myocardial infarction. *N Engl J Med* 2008;358:2218-30.
54. Yusuf S, Mehta SR, Chrolavicius S, et al. Effects of fondaparinux on mortality and reinfarction in patients with acute ST-segment elevation myocardial infarction: the OASIS-6 randomized trial. *JAMA* 2006;295:1519-30.
55. Chen ZM, Pan HC, Chen YP, et al. Early intravenous then oral metoprolol in 45,852 patients with acute myocardial infarction: randomised placebo-controlled trial. *Lancet* 2005;366:1622-32.
56. ACE-Inhibitor Myocardial Infarction Collaborative Group. Indications for ACE inhibitors in the early treatment of acute myocardial infarction: systematic overview of individual data from 100,000 patients in randomised trials. *Circulation* 1998;97: 2202-12.
57. Pfeffer MA, McMurray JJ, Velazquez EJ, et al. Valsartan, captopril, or both in myocardial infarction complicated by heart failure, left ventricular dysfunction, or both. *N Engl J Med* 2003; 349:1893-906.
58. Granger CB, McMurray JJ, Yusuf S, et al. Effects of candesartan in patients with chronic heart failure and reduced left-ventricular systolic function intolerant to angiotensin-converting-enzyme inhibitors: the CHARM-alternative trial. *Lancet* 2003;362:772-6.
59. Pitt B, Remme W, Zannad F, et al. Eplerenone, a selective aldosterone blocker, in patients with left ventricular dysfunction after myocardial infarction. *N Engl J Med* 2003;348:1309-21.
60. Pitt B, Zannad F, Remme W, et al. The effect of spironolactone on morbidity and mortality in patients with severe heart failure. *N Engl J Med* 1999;341:709-17.
61. Sevilla DC, Wagner NB, Anderson WD, et al. Sensitivity of a set of myocardial infarction screening criteria in patients with anatomically documented single and multiple infarcts. *Am J Cardiol* 1990;66:792-5.
62. Buja LM, Willerson JT. Infarct size: can it be measured or modified in humans? *Prog Cardiovasc Dis* 1987;29:271-89.
63. Hackel DB, Reimer KA, Ideker RE, et al. Comparison of enzymatic and anatomic estimates of myocardial infarction size in man. *Circulation* 1984;70:824-35.
64. Licka M, Zimmermann R, Zehelein J, et al. Troponin T concentrations 72 hours after myocardial infarction as a serological estimate of infarct size. *Heart* 2002;87:520-4.
65. Gibbons RJ, Miller TD, Christian TF. Infarct size measured by single photon emission computed tomographic imaging with (99m) Tc-sestamibi: a measure of the efficacy of therapy in acute myocardial infarction. *Circulation* 2000;101:101-8.
66. Ibrahim T, Nekolla SG, Hornke M, et al. Quantitative measurement of infarct size by contrast-enhanced magnetic resonance imaging early after acute myocardial infarction: Comparison with single-photon emission tomography using Tc99m-sestamibi. *J Am Coll Cardiol* 2005;45:544-52.
67. Friedrich MG, Abdel-Aty H, Taylor A, et al. The salvaged area at risk in reperfused acute myocardial infarction as visualized by cardiovascular magnetic resonance. *J Am Coll Cardiol* 2008; 51:1581-7.
68. Hochman JS, Sleeper LA, Webb JG, et al. for the Should We Emergently Revascularize Occluded Coronaries for Cardiogenic Shock (SHOCK) Investigators. Early revascularization in acute myocardial infarction complicated by cardiogenic shock. *N Engl J Med* 1999;341:625-34.
69. Hochman JS, Sleeper LA, White HD, et al. for the SHOCK Investigators: one-year survival following early revascularization for cardiogenic shock. *JAMA* 2001;285:190-2.
70. Menon V, Slater JN, White HD, et al. Acute myocardial infarction complicated by systemic hypoperfusion without hypotension: report of the SHOCK trial registry. *Am J Med* 2000; 108:374-80.
71. Chang SN, Hwang JJ, Chen YS, et al. Clinical experience with intra-aortic balloon counterpulsation over 10 years: a retrospective cohort study of 459 patients. *Resuscitation* 2008;77:316-24.
72. Sheu JJ, Tsai TH, Lee FY, et al. Early extracorporeal membrane oxygenator-assisted primary percutaneous coronary intervention improved 30-day clinical outcomes in patients with ST-segment elevation myocardial infarction complicated with profound cardiogenic shock. *Crit Care Med* 2010;38:1810-7.
73. Pennington DG, Smedira NG, Samuels LE, et al. Mechanical circulatory support for acute heart failure. *Ann Thorac Surg* 2001; 71:S56-9.
74. Chen JM, DeRose JJ, Slater JP, et al. Improved survival rates support left ventricular assist device implantation early after myocardial infarction. *J Am Coll Cardiol* 1999;33:1903-8.
75. Lamas GA, Mitchell GF, Flaker GC, et al for the Survival and Ventricular Enlargement Investigators. Clinical significance of mitral regurgitation after acute myocardial infarction. *Circulation* 1997;96:827-33.
76. Chung SY, Lin FC, Chua S, et al. Clinical profile and outcome of first acute myocardial infarction with ischemic mitral regurgitation. *Chang Gung Med J* 2008;31:268-75.
77. Chua S, Hung J, Chung SY, et al. Primary percutaneous coronary intervention lowers the incidence of ischemic mitral regurgitation in patients with acute ST-elevated myocardial infarc-

tion. *Circ J* 2010;74:2386-92.
78. Thompson CR, Buller CE, Sleeper LA, et al. Cardiogenic shock due to acute severe mitral regurgitation complicating acute myocardial infarction: a report from the SHOCK Trial Registry. Should we use emergently revascularize occluded coronaries in cardiogenic shock? *J Am Coll Cardiol* 2000;36:1104-9.
79. Byrne JG, Aranki SF, Cohn LH. Repair versus replacement of mitral valve for treating severe ischemic mitral regurgitation. *Coron Artery Dis* 2000;11:31-3.
80. Tepe NA, Edmunds LH. Operation for acute postinfarction mitral insufficiency and cardiogenic shock. *J Thorac Cardiovasc Surg* 1985;89:525-30.
81. Yip HK, Fang CY, Tsai KT, et al. The potential impact of primary percutaneous coronary intervention on ventricular septal rupture complicating acute myocardial infarction. *Chest* 2004;125:1622-8.
82. Crenshaw BS, Granger CB, Birnbaum Y, et al. for the GUSTO-I (Global Utilization of Streptokinase and TPA for Occluded Coronary Arteries) Trial Investigators. Risk factors, angiographic patterns, and outcomes in patients with ventricular septal defect complicating acute myocardial infarction. *Circulation* 2000; 101:27-32.
83. Menon V, Webb JG, Hillis LD, et al. Outcome and profile of ventricular septal rupture with cardiogenic shock after myocardial infarction: a report from the SHOCK Trial Registry. Should we emergently revascularize Occluded Coronaries in cardiogenic shock? *J Am Coll Cardiol* 2000;36:1110-6.
84. Lemery R, Smith HC, Giuliani ER, Gersh BJ. Prognosis in rupture of the ventricular septum after acute myocardial infarction and role of early surgical intervention. *Am J Cardiol* 1992;70: 147-51.
85. Skillington PD, Davies RH, Luff AJ, et al. Surgical treatment for infarct-related ventricular septal defects: improved early results combined with analysis of late functional status. *J Thorac Cardiovasc Surg* 1990;99:798-808.
86. Nakamura F, Minamino T, Higashino Y, et al. Cardiac free wall rupture in acute myocardial infarction: ameliorative effect of coronary reperfusion. *Clin Cardiol* 1992;15:244-50.
87. Pollak H, Nobis H, Mlczoch J. Frequency of left ventricular free wall rupture complicating acute myocardial infarction since the advent of thrombolysis. *Am J Cardiol* 1994;74:184-6.
88. Becker RC, Gore JM, Lambrew C, et al. A composite view of cardiac rupture in the United States National Registry of Myocardial Infarction. *J Am Coll Cardiol* 1996;27:1321-6.
89. McMullan MH, Maples MD, Kilgore TL, Hindman SH. Surgical experience with left ventricular free wall rupture. *Ann Thorac Surg* 2001;71:1894-8.
90. Slater J, Brown RJ, Antonelli TA, et al. Cardiogenic shock due to cardiac free-wall rupture or tamponade after acute myocardial infarction: a report from the SHOCK Trial Registry. Should we emergently revascularize occluded coronaries for cardiogenic shock? *J Am Coll Cardiol* 2000;36:1117-22.
91. Chen JS, Hwang CL, Lee DY, Chen YT. Regression of left ventricular aneurysm after delayed percutaneous transluminal coronary angioplasty (PTCA) in patients with acute myocardial infarction. *Int J Cardiol* 1995;48:39-47.
92. Di Donato M, Sabatier M, Montiglio F, et al. Outcome of left ventricular aneurysmectomy with patch repair in patients with severely depressed pump function. *Am J Cardiol* 1995;76: 557-61.
93. Di Donato M, Toso A, Maioli M, et al. for the RESTORE Group. Intermediate survival and predictors of death after surgical ventricular restoration. *Semin Thorac Cardiovasc Surg* 2001;13: 468-75.
94. Cheitlin MD, Alpert JS, Armstrong WF, et al. ACC/AHA guidelines for the clinical application of echocardiography: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Clinical Application of Echocardiography). *J Am Coll Cardiol* 1997;29:862-79.
95. Adler Y, Finkelstein Y, Guindo J, et al. Colchicine treatment for recurrent pericarditis: a decade of experience. *Circulation* 1998; 97:2183-5.
96. Karagueuzian HS, Mandel WJ. Electrophysiologic mechanisms of ischemic ventricular arrhythmias: experimental and clinical correlations. *Cardiac arrhythmias: their mechanisms, diagnosis, and management*. 3rd ed. Philadelphia: J. B. Lippincott; 1995, p. 563-603.
97. Carmeliet E. Cardiac ionic currents and acute ischemia: from channels to arrhythmias. *Physiol Rev* 1999;79:917-1017.
98. Field JM, Hazinski MF, Sayre MR et al. Part 1: executive summary: 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. *Circulation* 2010;122:S640-56.
99. Neumar RW, Otto CW, Link MS, et al. Part 8: Adult Advanced Cardiovascular Life Support: 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. *Circulation* 2010;122:S729-67.
100. ACC/AHA/HRS 2008 Guidelines for Device-Based Therapy of Cardiac Rhythm Abnormalities: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the ACC/AHA/NASPE 2002 Guideline Update for Implantation of Cardiac Pacemakers and Antiarrhythmia Devices). *J Am Coll Cardiol* 2008;51:e1-62.
101. Eagle KA, Guyton RA, Davidoff R, et al. ACC/AHA 2004 Guideline Update for Coronary Artery Bypass Graft Surgery: Summary Article: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Update the 1999 Guidelines for Coronary Artery Bypass Graft Surgery). *Circulation* 2004;110; 1168-76.
102. Dalal HM, Zawada A, Jolly K, et al. Home based versus centre based cardiac rehabilitation: cochrane systematic review and meta-analysis. *BMJ* 2010;340:b5631.
103. Marchionni N, Fattirolli F, Fumagalli S, et al. Improved exercise

tolerance and quality of life with cardiac rehabilitation of older patients after myocardial infarction: results of a randomized, controlled trial. *Circulation* 2003;107:2201-6.
104. Latini R, Maggioni AP, Flather M, et al. ACE inhibitor use in patients with myocardial infarction. Summary of evidence from clinical trials. *Circulation* 1995;92:3132-7.
105. GISSI-3: effects of lisinopril and transdermal glyceryl trinitrate singly and together on 6-week mortality and ventricular function after acute myocardial infarction. Gruppo Italiano per lo Studio della Sopravvivenza nell'infarto Miocardico. *Lancet* 1994;343: 1115-22.
106. ISIS-4: a randomised factorial trial assessing early oral captopril, oral mononitrate, and intravenous magnesium sulphate in 58,050 patients with suspected acute myocardial infarction. ISIS-4 (Fourth International Study of Infarct Survival) Collaborative Group. *Lancet* 1995;345:669-85.
107. Chiang CE, Wang TD, Li YH, et al. 2010 Guidelines of the Taiwan Society of Cardiology for management of hypertension. *J Formos Med Assoc* 2010;109:740-73.
108. Bartnik M, Malmberg K, Norhammar A, et al. Newly detected abnormal glucose tolerance: an important predictor of long-term outcome after myocardial infarction. *Eur Heart J* 2004;25: 1990-7.
109. Ryden L, Standl E, Bartnik M, et al. Guidelines on diabetes, pre-diabetes, and cardiovascular diseases: executive summary. The Task Force on Diabetes and Cardiovascular Diseases of the European Society of Cardiology (ESC) and of the European Association for the Study of Diabetes (EASD). *Eur Heart J* 2007;28:88-136.
110. Wang CH, Weisel RD, Liu PP, et al. Glitazones and heart failure: critical appraisal for the clinician. *Circulation* 2003;107:1350-4.
111. Nesto RW, Bell D, Bonow RO, et al. Thiazolidinedione use, fluid retention, and congestive heart failure: a consensus statement from the American Heart Association and American Diabetes Association. *Circulation* 2003;108:2941-8.
112. Grundy SM, Cleeman JI, Merz CN, et al. Implications of recent clinical trials for the National Cholesterol Education Program Adult Treatment Panel III guidelines. *Circulation* 2004;110: 227-39.
113. Colditz GA, Willett WC, Stampfer MJ, et al. Menopause and the risk of coronary heart disease in women. *N Engl J Med* 1987;316:1105-10.
114. Prentice RL, Langer R, Stefanick ML, et al. Combined postmenopausal hormone therapy and cardiovascular disease: toward resolving the discrepancy between observational studies and the Women's Health Initiative clinical trial. *Am J Epidemiol* 2005;162:404-14.
115. Grady D, Herrington D, Bittner V, et al. Cardiovascular disease outcomes during 6.8 years of hormone therapy: Heart and Estrogen/progestin Replacement Study follow-up (HERS II). *JAMA* 2002;288:49-57.
116. Hulley S, Grady D, Bush T, et al. Randomized trial of estrogen plus progestin for secondary prevention of coronary heart disease in postmenopausal women. Heart and Estrogen/progestin Replacement Study (HERS) Research Group. *JAMA* 1998;280: 605-13.
117. Rossouw JE, Anderson GL, Prentice RL, et al. Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results from the Women's Health Initiative randomized controlled trial. *JAMA* 2002;288:321-33.
118. Shyu KG, Wu CJ, Mar GY, et al. Clinical characteristics, management and in-hospital outcomes of patients with acute coronary syndrome – observations from the Taiwan ACS Full Spectrum Registry. *Acta Cardiol Sin* 2011;27:135-44.