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2020 Focused Update of the 2012 Guidelines of the Taiwan Society of Cardiology for the Management of ST-Segment Elevation Myocardial Infarction

Yi-Heng Li,[1] Cheng-Han Lee,[1,2] Wei-Chun Huang,[3,4,5] Yu-Chen Wang,[6,7,8] Chun-Hung Su,[9,10] Pei-Hsun Sung,[11,12] Shih-Chieh Chien[13] and Juey-Jen Hwang[14]
for The Writing Group of 2020 Focused Update of the 2012 Guidelines of the Taiwan Society of Cardiology for the Management of ST-segment Elevation Myocardial Infarction

One of the major missions of the Taiwan Society of Cardiology is to publish practice guidelines that are suitable for local use in Taiwan. The ultimate purpose is to continuously improve cardiovascular health care from the implementation of the recommendations in the guidelines. Despite recent improvement of medical care, patients with ST-segment elevation myocardial infarction (STEMI) still carry a high morbidity and mortality. There have been many changes in the concepts of STEMI diagnosis and treatment in recent years. The 2020 focused update of the 2012 guidelines of the Taiwan Society of Cardiology for the management of STEMI is an amendment of the 2012 guidelines based on the newest published scientific data. The recommendations in this focused update provide the diagnosis and treatment strategy for STEMI that should be generally implemented in Taiwan. Nevertheless, guidelines never completely replace clinical judgment and medical decision still should be determined individually.

Key Words: Acute myocardial infarction • Guideline • Taiwan

INTRODUCTION

Through early revascularization with primary percutaneous coronary intervention (PCI) and use of guideline-recommended secondary preventive medications, the mortality of ST-segment elevation myocardial infarction (STEMI) continues to decrease in Taiwan.[1] Since the publication of the 2012 Guidelines of the Taiwan Society of Cardiology (TSOC) for the Management of STEMI,[2] some concepts in treating the disease have been modi-

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[1]Division of Cardiology, Department of Internal Medicine, National Cheng Kung University Hospital, College of Medicine, National Cheng Kung University; [2]Institute of Clinical Pharmacy and Pharmaceutical Sciences, College of Medicine, National Cheng Kung University, Tainan; [3]Department of Critical Care Medicine, Kaohsiung Veterans General Hospital, Kaohsiung; [4]School of Medicine, National Yang Ming University, Taipei; [5]Department of Physical Therapy, Fooyin University, Kaohsiung; [6]Division of Cardiology, Department of Internal Medicine, Asia University Hospital; [7]Department of Biotechnology, Asia University; [8]Division of Cardiology, Department of Internal Medicine, China Medical University College of Medicine and Hospital; [9]Division of Cardiology, Department of Internal Medicine, Chung Shan Medical University Hospital; [10]Institute of Medicine, School of Medicine, Chung Shan Medical University, Taichung; [11]Division of Cardiology, Department of Internal Medicine, Kaohsiung Chang Gung Memorial Hospital and Chang Gung University, College of Medicine; [12]Center for Shockwave Medicine and Tissue Engineering, Kaohsiung Chang Gung Memorial Hospital, Kaohsiung; [13]Department of Critical Care Medicine, MacKay Memorial Hospital, Taipei; [14]Division of Cardiology, Department of Internal Medicine, National Taiwan University College of Medicine and Hospital, Taipei, Taiwan.
Corresponding author: Dr. Juey-Jen Hwang, Division of Cardiology, Department of Internal Medicine, National Taiwan University Hospital, No. 7, Chung Shan South Road, Taipei, Taiwan. Tel: 886-2-2312-3456; E-mail: jueyhwang@ntu.edu.tw
All authors contributed equally to this work.
The sequence of authors appeared according to the sequence of chapter they drafted in the guideline.

fied due to emerging new evidences. The purpose of this "focused update" is to revise the 2012 guideline specifically in several areas that the new study results bring in changes of STEMI management. The focused update began with a short review of epidemiology and recent treatment trends of STEMI in Taiwan. STEMI equivalents, defined as patients without typical ST segment elevation on electrocardiography (ECG), but need immediate triage and management as STEMI, were added in the diagnosis section. Revision on the section of prehospital management added new recommendations of early identification of STEMI by emergency medical service (EMS) field triage with prehospital ECG and direct transportation to the nearest PCI-available hospitals. In addition to clopidogrel and ticagrelor, prasugrel was introduced into Taiwan in the end of 2018. There were revised recommendations about the choice of P2Y12 inhibitors for STEMI. There were also revisions to the section on primary PCI, including adequate time intervals from diagnosis to intervention, vascular access and complete revascularization strategy. Cardiogenic shock is still a major cause of mortality in STEMI. Revision on section of cardiogenic shock was added because of recent advances in therapeutic options. For secondary preventive strategies, new pharmacological therapies for diabetes and hypercholesterolemia have been developed and proved to further reduce recurrent cardiovascular (CV) events in high risk patients such as STEMI. The section of long-term pharmacological treatment after discharge was revised and included all these new medical therapies. Finally, a new section of quality care of STEMI was added to indicate the importance of guideline implementation and several quality indicators were proposed.

In 2019, the President and Executive Board of the TSOC decided to revise the 2012 Guidelines of the TSOC for the Management of STEMI and invited several members to form a writing group. The major topics in the guideline were assigned to the members of the writing group and the data from clinical trials as well as other publications in peer-reviewed journals related to the topics were reviewed. New or modified recommendations in this focused update reflect the latest progress in the diagnosis and treatment of STEMI. The readers may refer to the prior guideline about the clinical topics which were not addressed in this focused update.[2] In order to demonstrate the intensities of recommendations, the evidence-based classification system, including class of recommendation (COR) and level of evidence (LOE), was adopted in the guideline. The definitions of COR I to III and LOE A to C were the same as those in the 2018 Guidelines of the TSOC for the management of non ST-segment elevation acute coronary syndrome (ACS).[3]

EPIDEMIOLOGY OF STEMI

Recent epidemiological studies in Taiwan using the Taiwan National Health Insurance Research Database showed that the overall adjusted incidence of acute myocardial infarction (MI) increased progressively from 1999 to 2008.[1,4,5] The age- and sex-adjusted incidence rates (per 100,000 population) of acute MI increased from 30 in 1997 to 49.8 in 2009, which was mainly driven by the increase of non ST-segment elevation myocardial infarction (NSTEMI) and the increasing tendency was noted in both genders.[1,5] However, the adjusted incidence of acute MI remained constant after 2008 and estimated to be 49.8 in 2009 to 50.7 in 2015.[1] The adjusted incidence of STEMI decreased from 16.8 in 2009 to 14.4 in 2015, whereas NSTEMI continuously increased from 32.5 in 2009 to 35.7 in 2015 (Figure 1). The ratio of NSTEMI to STEMI incidence increased from 1.93 in 2009 to 2.47 in 2015.[1] For STEMI, the incidence decreased across all age group except in the young population (< 55 years).[1] There was a 7.7% increase of STEMI from 2009 to 2015 in young men and no sign of decreasing trend in young female.[1] In Taiwan, individuals hospitalized for STEMI were more likely to be younger and were

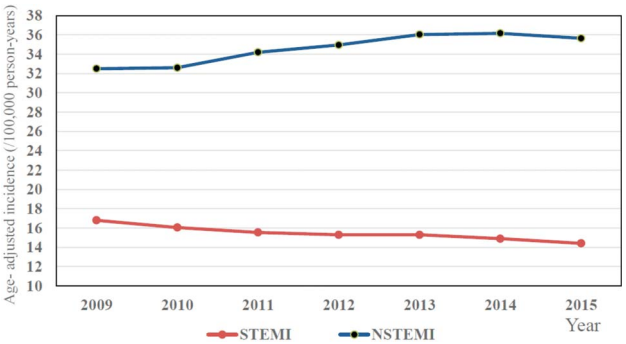

Figure 1. *The recent trends of decreasing incidence of STEMI and increasing incidence of NSTEMI in Taiwan. NSTEMI, non ST-segment elevation myocardial infarction; STEMI, ST-segment elevation myocardial infarction. Adapted from reference 1.*

less likely to have diabetes mellitus and hypertension in comparison with NSTEMI patients.[1] However, the incidence of dyslipidemia was higher in STEMI than NSTEMI patients.[1] For STEMI, the mean age was 1.3 years younger in 2015 compared with that in 2009 and there was a 19.8% increase of dyslipidemia during these years.[1] In Taiwan, most STEMI patients received primary PCI rather than fibrinolytic therapy.[1] Two nationwide ACS registries in Taiwan among different time periods (2008-2010 and 2012-2015) showed that the median door-to-balloon (D2B) time in primary PCI decreased from 96 minutes in the first registry to 71 minutes in the second registry.[6] One retrospective 10-year cohort study in a single medical center in Taiwan also showed that the median D2B time decreased from 142 minutes in 2005 to 69 minutes in 2014.[7] In secondary preventive pharmacological therapies, the in-hospital use of dual antiplatelet therapy (DAPT) (95.1% to 99.6%), angiotensin converting enzyme inhibitor (ACEI)/angiotensin receptor blocker (ARB) (63.8% to 77.5%), beta-blocker (48.8% to 71.4%), and statin (54.4% to 81.2%) all increased significantly between the two ACS registries.[6] The overall crude in-hospital mortality rate of STEMI decreased from 2009 (9.3%) to 2015 (7.6%) in Taiwan.[1] However, the mortality rate was persistently higher in female than male patients and there was no improving trend of mortality in STEMI for female patients.[1] The prescription rate of secondary preventive medications for STEMI in Taiwan was still relatively low compared with the data from Western country.[8]

Recommendation

- More actions should be taken to control the increasing incidence of STEMI in young population in Taiwan. (COR I, LOE C)
- To increase prescription rate of secondary preventive medications for STEMI in Taiwan is necessary. (COR I, LOE C)

DIAGNOSIS OF STEMI

Definition

Diagnosis of acute MI in this guideline is based on definition of the Fourth Universal Definition of MI 2018.[9] It defines acute MI as acute myocardial injury with clinical evidence of acute myocardial ischemia and with detection of a rise and/or fall of cardiac troponin values with at least one value above the 99th percentile upper reference limit with at least one of the following: symptoms of myocardial ischemia; new ischemic ECG changes; development of pathological Q waves; imaging evidence of new loss of viable myocardium or new regional wall motion abnormality in a pattern consistent with an ischemic etiology; identification of a coronary thrombus by angiography or autopsy.[9] Several types of acute MI were defined according to different pathophysiological mechanisms leading to ischemic myocardial injury. The typical STEMI is type 1 MI which is caused by coronary atherosclerosis with atherosclerotic plaque disruption, rupture or erosion and coronary thrombus formation. Most recommendations in this guideline can be applied to this type of MI. Some STEMIs fall into other types of MI which the managements are not included in this guideline.

ECG and biomarker

A 12-lead ECG is the most important diagnostic modality and determines the subsequent management pathways in patients presented with acute chest discomfort. No matter the patients are in an ambulance, local practitioner's clinic, or emergency department, an ECG should be performed immediately if it is available. The ECG should be interpreted as soon as possible to identify any possibility of STEMI or its equivalents by experienced physician, nurse or trained EMS personnel. A rapid transmission of the ECG through smartphone or other ways to emergency physicians or cardiologists not only speeds up the diagnosis of STEMI but also shortens the time for activation of primary PCI team.[10,11] Repeat ECG to follow up the ST-T changes is necessary if the first ECG is normal or equivocal when there are persistent symptoms of myocardial ischemia. Changes of biomarker confirm the presence of myocardial necrosis. Measurement of biomarker should not delay the process for primary PCI. High sensitivity cardiac troponin (hs-cTn) is the recommended biomarker because hs-cTn assays increase diagnostic accuracy for acute MI presenting early after chest pain and allow for a rapid rule-out of acute MI when there are doubts about the diagnosis.[12,13] The detailed recommendations of hs-cTn assays were described previously in the 2018 Guidelines of the TSOC for the management of non ST-segment elevation ACS (Figure 2).[3]

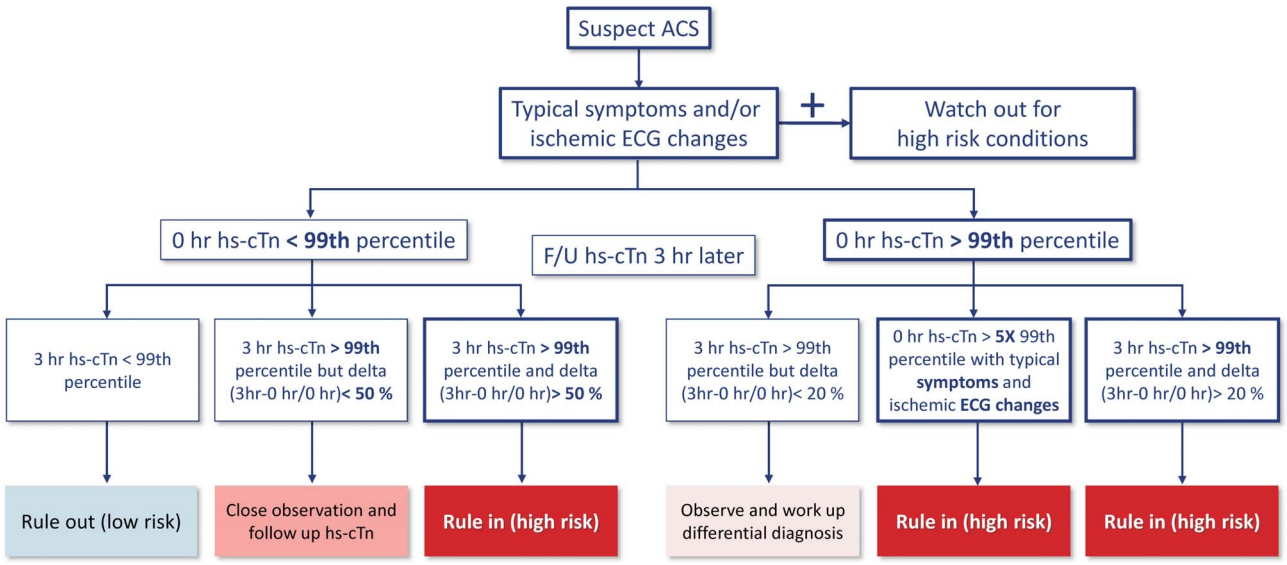

Figure 2. *The detailed recommendations of using high sensitivity cardiac troponin assay to diagnose and rule out acute myocardial infarction. ACS, acute coronary syndrome; ECG, electrocardiography; hs-cTn, high sensitivity cardiac troponin. Adapted from reference 3.*

Recommendation

- A 12-lead ECG should be performed immediately in patients presented with any symptom suggestive of STEMI. (COR I, LOE C)
- Rapid transmission of ECG by smartphone or other ways to emergency physicians or cardiologists for early diagnosis is recommended. (COR I, LOE B)
- Hs-cTn assay is recommended for rapid diagnosis and rule-out of acute MI. (COR I, LOE A)

STEMI equivalents

For rapid triage and primary PCI, this guideline adopts the conventional definition of STEMI as those with symptoms suggestive of myocardial ischemia and ST-segment elevation in at least two contiguous leads on ECG. However, there are several conditions that patients present without typical ST-segment elevation on a standard 12-lead ECG, but should be managed as STEMI equivalents. The first condition is posterior MI. The typical ECG changes of posterior MI include ST segment depression in precordial leads V1-V4 and a R/S ratio greater than 1 in leads V1 or V2.[14] If posterior MI is suspected, posterior leads V7 to V9 of ECG should be done to look for ST segment elevation in these leads.[14,15] Lead V7 is placed at the same level of V6 at the posterior axillary line; lead V8 is on the left side of the back at the tip of the scapula and V9 is placed at left paraspinal region at the same level as V6. The infarct related artery (IRA) in patients with typical ECG abnormalities of posterior MI is left circumflex artery. The second condition is left main MI. The typical ECG changes of left main MI include ST elevation in lead aVR with ST elevation in aVR ≥ V1 and extensive ST depression in leads I, II, and V4-6.[16,17] Patients presented clinical symptoms with these ECG changes require early coronary angiography to define the left main coronary artery anatomy. The third condition is STEMI in preexisting left bundle branch block (LBBB). The ST segment changes in LBBB make it difficult to diagnose STEMI directly. The Sgarbossa ECG criteria, including (1) concordant ST-segment elevation > 1 mm in at least one lead or (2) concordant ST-segment depression > 1 mm in any of the V1 to V3 leads or (3) discordant ST-segment elevation > 5 mm, are used to identify patients with STEMI in patients with preexisting LBBB.[18]

Recommendation

- Even without typical ST segment elevation on standard 12-lead ECG, STEMI equivalents should be managed as STEMI. (COR I, LOE C)

PREHOSPITAL MANAGEMENT

Public awareness of acute MI

STEMI is a time-sensitive disease because prompt treatment after symptoms onset improves patients'

prognosis. Mortality of STEMI could be reduced 1.5% for every 30-minute decrease in reperfusion time.[19] The key to successful treatment is early recognition of symptoms and rapid arrival at a hospital with PCI facility.[20] Patient delay is a critical factor. It commonly due to poor awareness of heart attack symptoms and not calling an ambulance even when acute MI is really occuring.[21] Previous study showed the awareness of acute MI symptoms in citizens ranged from 32.9% (arm or shoulder pain) to 70.2% (difficulty breathing) and 79.1% (chest pain and discomfort).[20] Overall, 67% citizens would call an ambulance if someone had signs of acute MI.[20] Currently, it is roughly estimated that only 10-20% STEMI patients were sent to hospitals by ambulance of EMS in Taiwan. Transportation of suspected STEMI patients by EMS ambulance is much safer because emergency medical technicians (EMT) received cardiopulmonary resuscitation (CPR) training and EMS ambulances are equipped with automated external defibrillator.[22-25] Since 2011, EMS in more than 90% of cities and counties in Taiwan started to set up ECG telemetry system in ambulances which may assist in early diagnosis of STEMI and directly transferring patients to PCI available hospitals. Therefore, ambulance transfer is highly recommended for patients suspected of acute MI with typical chest pain with or without dyspnea, cold sweating or nausea.

Recommendation

- Increased public awareness of the typical symptoms of acute MI is recommended. (COR I, LOE C)
- Ambulance transfer to PCI available hospitals is recommended for patients with typical symptoms of acute MI. (COR I, LOE C)

Transportation for primary PCI

Compared with fibrinolytic therapy, primary PCI is the preferred reperfusion strategy.[26] In Taiwan, primary PCI is the routine reperfusion therapy for STEMI, whereas fibrinolysis is used only in some special occasions, such as during severe pandemic infectious diseases or in adjacent small islands without PCI available hospitals.[6,27,28] Currently, with a population of 23 million in Taiwan, there are 103 PCI available hospitals. Approved by the national STEMI accreditation system from Taiwan Government, 58 hospitals provide 24-hour service of primary PCI, including 46 hospitals with high grade critical care ability and 12 hospitals with moderate grade critical care ability (Figure 3). Through convenient highway system, ambulances usually could reach a PCI available hospital within 2 hours. However, pre-hospital delay is still a challenging issue in Taiwan due to multifactorial reasons. A well-organized STEMI network among different hospitals and EMS system is critical for optimization of STEMI care.[29-31] A city/county-based STEMI network should have a standard operating procedure to guide EMTs in the ambulance to transport STEMI patients directly to nearby PCI available hospitals and bypass non-PCI hospitals. EMTs could diagnose STEMI by ECG reading themselves or through on-line instruction from hospital staffs by ECG transmission via smartphone or telemetry ECG system in the field.[23-25,32] The network can activate primary PCI team in nearby hospital as soon as possible. EMS ambulance system should be equipped with ECG recorders, automated external defibrillators and auto CPR machines, which could diagnose STEMI in the field and provide critical life-saving treatment.[23,25,32]

STEMI patients can be diagnosed in a hospital without PCI facility or 24-hour PCI capability. Hospitals with 24-hour PCI capability should establish inter-hospital STEMI network with other hospitals in order to transport STEMI patients safely and rapidly. Inter-hospital STEMI network was reported to shorten D2B time, and

Figure 3. *Distribution of hospitals that provide 24-hour primary PCI service in Taiwan. Fibrinolysis is only suggested in special occasions, including special pandemic infection or islands without PCI available hospitals. PCI, percutaneous coronary intervention.*

hospitals with 24-hour PCI capability should take a "no-refusal" principle for all patients transferred for consideration of primary PCI.[33,34] The hospitals with 24-hour PCI capability should have a 24-hour hot line with other non-PCI hospitals. Inter-hospital transmission of ECG and/or laboratory data via smartphone or facsimile in order to early activation of PCI team is necessary. On arrival, the patients should be directly transferred to catheterization laboratory as soon as possible. There should be a feedback system inside the network between non-PCI and PCI hospitals. Figure 4 summarizes the transportation pathways for primary PCI from different places of patient presentation.

Recommendation

- Regional STEMI network should be established to guide direct transportation of STEMI patients to PCI available hospitals. (COR I, LOE B)
- The EMS ambulances should be equipped with ECG recorders, automated external defibrillators and auto CPR machines. (COR I, LOE C)
- The EMTs in ambulance should receive training for ECG recording, interpretation and transmission for early identification of STEMI. (COR I, LOE C)
- Inter-hospital network is recommended to facilitate transfer for primary PCI among non-PCI and PCI available hospitals. (COR I, LOE B)

Pre-hospital medication

Early observational studies showed that upstream clopidogrel treatment before arriving PCI hospitals was associated with a reduction of death or recurrent MI in patients with STEMI treated with primary PCI.[35,36] A later small randomized trial found that clopidogrel 600 mg loading in prehospital phase could not increase the patency rate of IRA before primary PCI, but was associated with a trend toward less adverse clinical event.[37] The ATALANTIC trial randomized STEMI patients to receive ticagrelor either during transfer to a primary PCI hospital or immediately before angiography. The study found

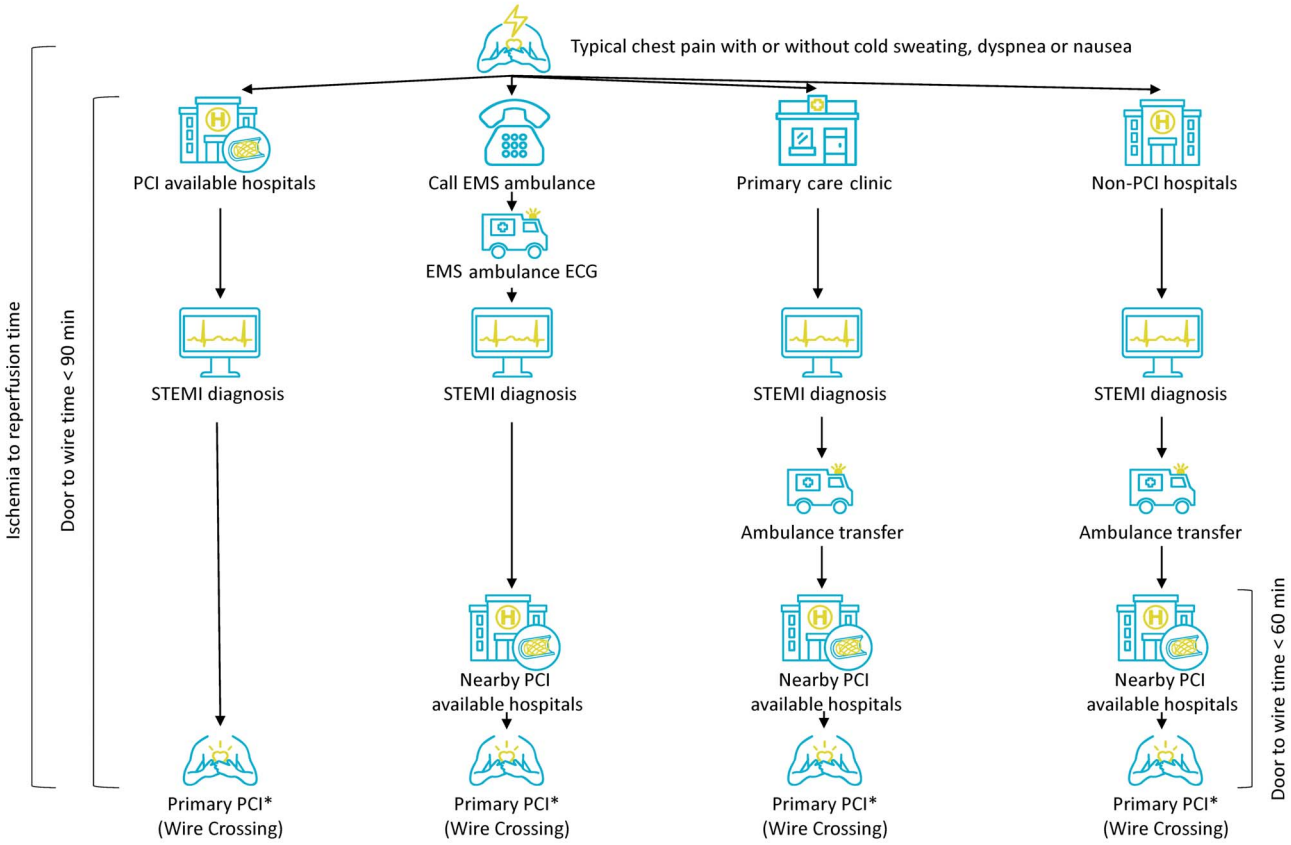

Figure 4. *Recommended transportation pathways and door-to-wire time for primary PCI from different places of patient presentation. PCI, percutaneous coronary intervention; STEMI, ST-segment elevation myocardial infarction. ECG, electrocardiography; EMS, emergency medical service.*

early ticagrelor treatment could not increase ST-segment elevation resolution or Thrombolysis in Myocardial Infarction (TIMI) blood flow in the IRA at initial angiography. But the rates of definite stent thrombosis were lower in 24 hour and 30 days in the prehospital group.[38] Currently, EMTs in 3 cities of Taiwan could administer DAPT in ambulance after on-line instruction by physicians in hospitals after reading ECG from telemetry transmission.

Recommendation

- Early use of DAPT (aspirin and P2Y12 inhibitor) in ambulance may be considered after on-line instruction by physicians in hospitals if no contraindication. (COR IIb, LOE C)

Out-of-hospital cardiac arrest

STEMI can be presented with out-of-hospital cardiac arrest (OHCA). After CPR and return of spontaneous circulation, emergency coronary angiography and PCI should be performed in awake or comatose patients with OHCA with suspected STEMI. Therapeutic hypothermia with targeted temperature management (TTM) should be considered because TTM after return of spontaneous circulation in cardiac arrest patients leads to improvements in mortality and neurological outcomes.[39,40] Previous study showed, after cardiac catheterization and TTM, there was a survival rate of 56% of the OHCA patients and most of the survivors had good neurological outcome.[41] However, previous studies using prehospital cold intravenous fluid resulted in worse outcomes including decreased rate of return of spontaneous circulation, increased chance of pulmonary edema, and increased incidence of diuretic use.[42,43]

Recommendation

- Primary PCI is recommended in STEMI patients with cardiac arrest post return of spontaneous circulation. (COR I, LOE B)
- TTM is recommended in comatose STEMI patients with cardiac arrest after return of spontaneous circulation. (COR I, LOE B)
- Prehospital cooling in ambulance with rapid infusion with cold saline is not recommended in STEMI patients with cardiac arrest post return of spontaneous circulation. (COR III, LOE B)

ANTIPLATELET THERAPY

DAPT with aspirin and P2Y12 inhibitor is the cornerstone therapy for STEMI. Clopidogrel was used in STEMI patients for many years and was the only P2Y12 inhibitor recommended in the 2012 Taiwan STEMI Guidelines.[2] New generation P2Y12 inhibitors, prasugrel and ticagrelor, showed superior efficacy compared with clopidogrel in improving clinical outcomes but at the expense of bleeding. Choosing either clopidogrel or potent P2Y12 inhibitors needs more consideration of the balance between clinical benefit and bleeding risk.

Clopidogrel

In large randomized studies, combination of clopidogrel with aspirin was associated with reduced ischemic event and mortality rate for STEMI, regardless of reperfusion strategies.[44,45] Four observational studies in Taiwan showed DAPT with aspirin and clopidogrel for more than 9 to 12 months significantly reduced ischemic risk and mortality rate in patients with ACS with or without PCI.[46-49] In patients receiving elective PCI, clopidogrel 600 mg loading dose was associated with more rapid and higher platelet inhibition than 300 mg dose.[50,51] But in the CURRENT–OASIS 7 trial, clopidogrel 600 mg loading dose did not reduce ischemic events but lead to higher major bleeding risk comparing with 300 mg loading dose in patients with ACS. However, in the subgroup analysis for patients receiving PCI, higher clopidogrel loading dose significantly reduced the rates of 30 days primary outcomes and stent thrombosis.[52] A meta-analysis demonstrated that higher clopidogrel loading dose with 600 mg was associated with reduced ischemic events and similar bleeding risk comparing with standard clopidogrel 300 mg loading dose in patients undergoing PCI.[53] In Taiwan, a loading dose of 300 mg to 600 mg clopidogrel is recommended for STEMI depending on patients' clinical conditions. There are some drawbacks of clopidogrel including slower onset time and drug response variability. Clopidogrel is an inactive prodrug and requires a 2-step metabolism to become an active metabolite,[54] which may be responsible to its slower drug onset and may lead to increased ischemic events in ACS patients with coronary thrombus formation. Furthermore, the prevalence of cytochrome P450 2C19 polymorphism with clopidogrel resistance is not uncom-

mon and may increase CV risk in ACS patients.[55,56] The percentage of CYP2C19 reduced function alleles carrier in Asian population is much higher than that in Caucasian population.[57,58] Therefore, newer P2Y12 inhibitors such as prasugrel or ticagrelor have been developed to overcome these unmet clinical needs of clopidogrel.

Prasugrel

Comparing with clopidogrel, prasugrel (60 mg loading and 10 mg daily dose) provides faster and greater platelet inhibitory effects in patients undergoing PCI.[59] The TRITON–TIMI 38 trial randomized 13608 ACS patients to receive either prasugrel or clopidogrel. The study found prasugrel reduced more ischemic events compared with clopidogrel [hazard ratio (HR) 0.82, 95% confidence interval (CI) 0.73-0.93], but also increased the risk of major bleeding (HR 1.40, 95% CI 1.05-1.88).[60] In the subgroup analysis for STEMI patients, the efficacy of prasugrel was consistent (HR 0.79, 95% CI 0.65-0.97) irrespective of the PCI timing.[61] It is worth of noticing that the post-hoc analysis of the TRITON-TIMI 38 study demonstrated that prasugrel was associated with net clinical harm due to a trend toward more major bleeding (p = 0.06) in patients with a history of ischemic stroke or transient ischemic attack (TIA). Patients aged 75 years or older and who were weighing less than 60 kg also had no clinical benefit from prasugrel.[60] Therefore, prasugrel is contraindicated in patients with prior history of stroke/TIA and should be used cautiously in patients with old age or low body weight.

In Taiwan and Japan, reduced-dose prasugrel (20 mg loading and 3.75 mg daily dose) is available due to the concern of bleeding risk in Asians. The reduced-dose regimen was studied in the PRASFIT-ACS trial which was conducted in Japan with the similar study design as the TRITON-TIMI 38 study. In the PRASFIT-ACS trial, about 50% of the study population was STEMI and those with prior ischemic stroke/TIA were excluded. After randomizing 1363 ACS patients undergoing PCI, the reduced-dose prasugrel was associated with a trend of 23% risk reduction (HR 0.77, 95% CI 0.56-1.07) of adverse CV events and similar risk of non-coronary artery bypass graft (CABG) major bleeding compared with clopidogrel.[62] A post-marketing observational study (PRASFIT--Practice I) enrolled 732 Japanese ACS patients receiving both PCI and reduced-dose prasugrel from 2014 to 2015 and 60% of the patients were STEMI. The rates of TIMI major bleeding and major adverse CV events were 1.6% and 3.1%, respectively during the observational period indicating the safety and efficacy of this regimen.[63] There was another larger nationwide registry study in Japan including 62737 ACS patients undergoing PCI in 2016. After propensity score matching, there were 12016 patients in the clopidogrel or prasugrel group, respectively. STEMI patients accounted for 30.7% in clopidogrel and 32.6% in prasugrel group. Compared with clopidogrel, reduced-dose prasugrel was associated with higher bleeding risk [odds ratio (OR) 1.65, 95% CI 1.10-2.51], similar rates of mortality (OR 1.11, 95% CI 0.89-1.38), and similar risk of stent thrombosis (OR 1.29, 95% CI 0.73-2.30). In subgroup analysis for STEMI patients, reduced-dose prasugrel was associated with numerically higher rate of bleeding than clopidogrel (0.67% vs. 0.47%; OR 1.44, 95% CI 0.76-2.78).[64] Therefore, larger randomized controlled trials are needed in the future to confirm the efficacy and safety of reduced-dose prasugrel in ACS or STEMI patients.

Ticagrelor

Another newer P2Y12 inhibitor, ticagrelor (180 mg loading and 90 mg twice daily dose), is an active drug that does not require hepatic metabolism for activation. The platelet inhibitory ability of ticagrelor is greater and faster than clopidogrel. In addition, ticagrelor binds to P2Y12 inhibitors reversibly, which lead to faster onset after platelet binding and offset after discontinuing the drug.[65] In the PLATO study, ticagrelor was associated with reduced combined risk of CV death, MI, or stroke compared with clopidogrel (HR 0.84, 95% CI 0.77-0.92) in 18,624 ACS patients. However, ticagrelor also increased the rate of non-CABG major bleeding (4.5% vs. 3.8%, p = 0.03).[66] The benefits of ticagrelor over clopidogrel in STEMI subgroup were consistent with those from the overall PLATO results. In STEMI patients receiving primary PCI, ticagrelor also reduced risks of MI, total mortality and definite stent thrombosis without increasing major bleeding risk.[67] In the TREAT study, STEMI patients receiving fibrinolysis were randomized to ticagrelor or clopidogrel with a median of 11.4 hours after fibrinolytic therapy. Ticagrelor was non-inferior to clopidogrel for TIMI major bleeding at 30 days in this study.[68] After 12 months follow-up, ticagrelor was associated with similar ischemic and bleeding events compared with

clopidogrel.[69] The largest real world data comes from SWEDEHEART registry which included 45073 ACS patients in Sweden from 2010 to 2013. In this study, ticagrelor versus clopidogrel was associated with a lower composite ischemic risk (HR 0.85, 95% CI 0.78-0.93) and a higher risk for re-admission with bleeding (HR 1.20, 95% CI 1.04-1.40) which was similar to the results in the PLATO study.[70] However, in Asia, data from small randomized control trials and observational studies comparing ticagrelor with clopidogrel in STEMI or ACS patients demonstrated conflicting results.[71-76] In Taiwan, three observational studies comparing ticagrelor with clopidogrel in ACS patients showed reduced ischemic risk without increasing major bleeding risk in patients receiving ticagrelor.[77-79]

Comparisons between P2Y12 inhibitors

When comparing the efficacy and safety between newer P2Y12 inhibitors (prasugrel/ticagrelor) and clopidogrel in STEMI patients undergoing PCI, a meta-analysis demonstrated that newer P2Y12 inhibitors versus clopidogrel significantly reduced all-cause death, major adverse CV events and stent thrombosis with similar risk in bleeding.[80] Another meta-analysis showed that both prasugrel and ticagrelor were associated with better clinical outcomes than clopidogrel, and prasugrel was even superior to ticagrelor in STEMI patients undergoing primary PCI.[81] In addition, there was a retrospective analysis from Korea using claim data from the Health Insurance Review and Assessment Service with 40706 acute MI patients undergoing PCI between 2010 to 2015 and 35% of the study population were STEMI. In this study, newer P2Y12 inhibitors including prasugrel and ticagrelor both had favorable effect on reducing 30-day mortality.[82] Furthermore, according to the data from KAMIR-NIH registry, treatment with both prasugrel and ticagrelor in ACS patients were shown to improve major adverse CV events-free survival rate compared to clopidogrel. The difference of major adverse CV events rate between prasugrel and ticagrelor in overall population and STEMI subgroups were not significant.[83] For head to head comparison of the efficacy and safety between the two newer P2Y12 inhibitors in ACS patients, a retrospective cohort analysis from claims database showed that patients received ticagrelor had both reduced ischemic and bleeding events compared with patients treated with prasugrel.[84] However, in a large randomized control trial, the ISAR-REACT 5 study, which recruited 4018 ACS subjects and 41% of whom were STEMI patients, prasugrel was associated with significantly reduced ischemic composite risks including death, MI, or stroke than ticagrelor, and the incidence of bleeding was statistically insignificant between the two groups.[85]

Based on current available evidences, standard-dose ticagrelor and prasugrel should be the preferred P2Y12 inhibitor in STEMI patients. However, if concerns about bleeding prevail over ischemia, it is reasonable to choose clopidogrel rather than newer P2Y12 inhibitors. High bleeding risk features include old age, chronic kidney disease, anemia, low body weight, combination therapy with oral anticoagulant, prior intracranial hemorrhage, or history of previous major bleeding. Furthermore, based on Asians' data, reduced-dose prasugrel (20 mg loading and 3.75 mg daily maintenance dose) may also be considered in STEMI patients undergoing primary PCI in Taiwan. The selection of different P2Y12 inhibitors, different dose regimens, and the trade-off between ischemic and bleeding risk should be individualized to acquire the maximal net clinical benefit for STEMI patients.

Recommendation

- Ticagrelor (180 mg loading dose, 90 mg twice daily), prasugrel (60 mg loading dose, 10 mg daily dose), or clopidogrel (300-600 mg loading dose, 75 mg daily dose) is recommended in STEMI patients undergoing primary PCI unless contraindicated and ticagrelor or prasugrel is preferred to clopidogrel. (COR I, LOE B)
- Clopidogrel rather than ticagrelor or prasugrel may be considered in patients with increased bleeding risk features. (COR IIa, LOE C)
- Reduced dose of prasugrel (20 mg loading dose, 3.75 mg daily dose) may be considered in STEMI patients undergoing PCI based on Asian data. (COR IIa, LOE B)

PCI STRATEGY

Door-to-wire time

D2B time of primary PCI has been regarded as an important metric for STEMI patients because it could influence the clinical outcomes of the patients.[86-88] Previous international guidelines as well as 2012 Taiwan

STEMI guidelines have focused on the importance of D2B time.[2] However, later studies found that the total ischemia time, including the time from symptom onset to STEMI diagnosis and the time from STEMI diagnosis to primary PCI, is a more important determinant of clinical outcomes.[89-91] That is why much more effort now is devoted to shorten the total ischemia time by pre-hospital diagnosis of STEMI and early activation of PCI team. Due to the progress of PCI technique, balloon dilation is not always the first intervention step performed during primary PCI, therefore, the term has further evolved to medical contact-to-device time. Wire crossing the lesion in IRA is always necessary before any intracoronary procedure, therefore, the wire time instead of device time is preferred in our guideline. In Taiwan, if STEMI has already been diagnosed in primary care clinic, non-PCI hospital or in ambulance and transferred for primary PCI, a door-to-wire time ≤ 60 minutes is suggested in the transferred PCI available hospitals. In fresh cases that need time to diagnose STEMI, a door-to-wire time ≤ 90 minutes is suggested in PCI available hospitals.

Recommendation

- For patients with already diagnosed STEMI that are transferred for primary PCI, a door-to-wire time ≤ 60 minutes in PCI available hospitals is recommended. (COR I, LOE C)
- In fresh cases that need time to diagnose STEMI, a door-to-wire time ≤ 90 minutes in PCI available hospitals is recommended. (COR I, LOE B)

PCI procedures

The RIVAL trial was a large scale clinical trial that randomly allocated 7021 ACS patients including 1958 STEMI patients to radial or femoral artery access during PCI. The composite primary outcome of death, MI, stroke or non-CABG major bleeding at 30 days occurred significantly fewer in the radial group compared with the femoral group in patients with STEMI (HR 0.60, 95% CI 0.38-0.94) and in high volume radial centers (HR 0.49, 95% CI 0.28-0.87).[92] The radial procedural volume was important and independently associated with the primary outcome.[93] The MATRIX trial included a total of 8404 ACS patients (4008 STEMI) undergoing PCI and randomized to radial or femoral access. The 30-day co-primary outcomes were major adverse CV events (MACE), defined as all-cause mortality, MI and stroke. The net adverse clinical events were defined as MACE or non-CABG major bleeding. The radial access group was associated with reduced MACE [risk ratio (RR) 0.85, 95% CI 0.74-0.99] and net adverse clinical events (RR 0.83, 95% CI 0.73-0.96). The difference was mainly driven by fewer non-CABG major bleeding and reduction of all-cause death.[94] Therefore, the radial access has become the favorable choice during primary PCI and is especially recommended to be performed by an experienced operator at high volume center.

The EXAMINATION study randomly assigned 1504 patients with STEMI to receive everolimus-eluting stent (EES) or bare-metal stent (BMS). The results showed both rates of target lesion revascularization and stent thrombosis were reduced in recipients of EES at 1 year.[95] Similarly, the COMFORTABLE AMI trial randomly assigned 1161 STEMI patients to receive biolimus-eluting stents or BMS in primary PCI. The group of biolimus-eluting stents with a biodegradable polymer was associated with reduced composite of cardiac death, target vessel-related reinfarction, and ischemia-driven target-lesion revascularization in STEMI patients at 1 year.[96] Based on these evidences, new generation drug-eluting stent (DES) is recommended during primary PCI for STEMI. The TASTE trial randomly assigned 7244 STEMI patients undergoing PCI to manual thrombus aspiration followed by PCI or to PCI only. The results revealed routine thrombus aspiration before PCI as compared with PCI alone did not reduce 30-day and 1-year mortality. In addition, this strategy did not reduce total mortality or the composite of death from any cause, rehospitalization for MI, or stent thrombosis up to 1 year.[97,98] A later and larger scale TOTAL study with 10732 STEMI patients also reported routine manual thrombectomy did not reduce the risk of CV death, recurrent MI, cardiogenic shock, or class IV heart failure within 180 days. In addition, this strategy in TOTAL trial was associated with an increased rate of stroke within 30 days, which was not observed in TASTE trial.[99-101] In summary, with compared to PCI alone, recent clinical trials have not shown any clinical benefit with routine thrombectomy during primary PCI.

Recommendation

- Radial access is recommended over femoral access in

experienced operators and high volume centers for primary PCI. (COR I, LOE A)
- New generation DESs are recommended for primary PCI. (COR I, LOE A)
- Thrombus aspiration during primary PCI is an optional but not a routine procedure during primary PCI. (COR I, LOE A)

Complete revascularization

About 40% of patients with acute MI carried multiple complex coronary lesions in multiple coronary arteries on angiography and these patients had poorer left ventricular function and increased risk for recurrent ischemia.[102] Whether to completely revascularize these non-culprit lesions or only treat culprit lesion during the index procedure of primary PCI is a common dilemma.[103,104] In addition, the optimal timing of complete revascularization also remains uncertain. Previous randomized trials have compared routine non-culprit lesion PCI with optimal medical therapy alone in patients with multivessel disease (MVD) who underwent primary PCI for STEMI, regardless of whether revascularization was performed during index or staged procedure. Although the results almost consistently revealed significant reduction in repeat revascularizations in the group of complete revascularization, none of which were powered for the hard end points of death or MI.[105-109] In a meta-analysis, compared to culprit lesion-only PCI, complete revascularization significantly reduced the combined end points of death or MI (OR 0.71, 95% CI 0.52-0.96). In addition, the benefit of routine non-culprit lesion PCI was only observed among patients who performed during the index primary PCI but not staged procedure.[110] Recently, the COMPLETE trial randomized 4041 STEMI patients with MVD but without cardiogenic shock who had undergone successful culprit-lesion primary PCI to a strategy of either complete revascularization with PCI of angiographically significant non-culprit lesions or no further revascularization. At a median follow-up of 3 years, the first co-primary outcome of CV death or MI was significantly lower in the complete-revascularization group than culprit-lesion-only PCI group (HR 0.74, 95% CI 0.60-0.91). In this study, all non-culprit lesion PCIs were staged procedures either during the index hospitalization or within 45 days after discharge. This study was statistically powered to concluded that routine staged complete revascularization was superior to culprit lesion only PCI in reducing the risk of CV death, new MI, or ischemia driven revascularization in STEMI patients with MVD and without cardiogenic shock.[111]

In STEMI patients with MVD and cardiogenic shock (CS), the CULPRIT-SHOCK trial randomized 706 patients to either PCI of the culprit lesion only or multivessel PCI. At 30 days, the end points of death or renal replacement therapy were significantly lower in the culprit lesion only group and these benefits were maintained at 1 year.[112,113] In addition, a large-scale observational study also showed that culprit lesion only PCI in STEMI patients with CS had lower mortality rate than multivessel PCI at 30 days and at 1 year.[114] Figure 5 summarizes the current recommendations for PCI strategy for STEMI in Taiwan.

Recommendation
- In hemodynamically stable STEMI patients with MVD, immediate or staged PCI (< 45 days) for complete revascularization is recommended. (COR I, LOE A)
- In STEMI patients with CS and MVD, routine non-culprit lesion revascularization during primary PCI is not recommended. (COR III, LOE B)

CARDIOGENIC SHOCK

Definition and classification

Although there were some variations of the definition, CS complicating acute MI is generally defined as systolic blood pressure (BP) < 90 mmHg for ≥ 30 minutes with end-organ hypoperfusion ± hemodynamic criteria (cardiac index ≤ 2.2 L/min/m^2 and wedge pressure ≥ 15 mmHg) based on largest randomized controlled trials.[112,115,116] Recently, the Society of Cardiovascular Angiography and Interventions unified CS definition and recommended a classification system with 5 stages: A: at risk for CS development (e.g., anterior wall MI), B: beginning or pre-shock (clinical evidence of relative hypotension or tachycardia without hypoperfusion), C: classical CS (hypoperfusion requiring pharmacological or mechanical intervention), D: doom (worse with failing to respond to initial interventions), and E: extremis [cardiac arrest with ongoing CPR and/or extracorporeal membrane oxygenation (ECMO)].[117] The classification system not only

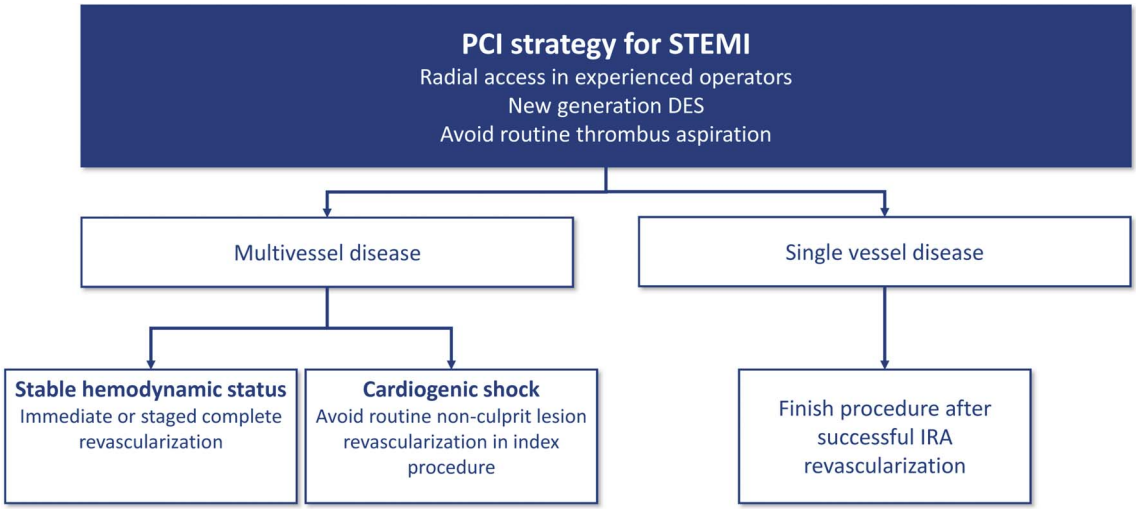

Figure 5. *Recommended PCI strategy for STEMI in Taiwan. DES, drug-eluting stent; IRA, infarct-related artery; PCI, percutaneous coronary intervention; STEMI, ST-segment elevation myocardial infarction.*

makes different CS trials more comparable but also emphasizes the effectiveness of early intervention on the phase of pre-shock or early shock.[118,119]

Pathophysiology

The incidence of CS with acute MI ranges from 3% to 13%.[120,121] Ventricular myocardial dysfunction following acute MI accounts for the majority of CS, comprising around 80% and 7% for left and right ventricular failure, respectively. The remaining 13% of CS victims result from mechanical complications, including acute mitral regurgitation (~7%), ventricular septal defect (~4%) and free wall rupture (~2%).[122] Impaired myocardial systolic and diastolic function subsequent to acute MI induce hypoperfusion and lung congestion leading to tissue ischemia and hypoxia.[123] It also chemically or biologically elicits a serial release of inflammatory cytokines or inducible nitric oxide synthase resulting in vasodilation which further decreases systemic and coronary perfusions and aggravates pre-existing pumping impairment.[124] The catastrophic vicious cycle results in 40-50% mortality rate of CS even in the era of early revascularization and mechanical circulatory support (MCS).[124,125]

Management

Management should be initiated at pre-shock phase when hypotension appears as the first sign of CS. Echocardiography should be performed immediately to exclude mechanical complications of acute MI as the potential causes of CS. Intra-aortic balloon pumping (IABP) can be considered as a strategy to unload left ventricle and increase coronary perfusion if there is unstable hemodynamics due to mechanical complications. However, IABP should not be performed routinely in patients with CS complicating acute MI.[116] Emergent coronary angiography is strongly recommended and revascularization strategy should be determined after heart team evaluation. PCI to open the occluded culprit vessel can be performed but routine non-culprit lesions revascularization during the initial PCI is not recommended.[112,113] In patients with CS after initial treatment, complete revascularization during the index hospitalization maybe beneficial.[126]

Patients with CS should be treated with fluids, vasopressors, and inotropes to prevent or rescue multiple organ dysfunction syndrome (MODS).[127] If hemodynamic instability remains after fluid resuscitation with saline or Ringer's lactate > 200 mL in 15-30 minutes, pharmacological circulatory support with vasopressor (e.g., norepinephrine) and/or ventricular support with inodilator (e.g., dobutamine or levosimendan) should be considered.[128] The patients are closely monitored in intensive care units. Pulmonary artery catheter for diagnostic evaluation and therapeutic guidance may be considered if necessary.[129] Ultrafiltration may be considered for organ decongestion in acute cardiorenal syndrome with fluid overload and poor response to forceful diuretic therapy.[130] Although those resuscitated from cardiac ar-

rest or lethal arrhythmia are generally treated with hypothermia for neuroprotection, the effects of therapeutic hypothermia on hemodynamic or clinical outcomes in CS are still controversial.[131,132] For those with refractory shock or deteriorating organ dysfunctions, growing evidences have shown appropriate use of MCS could reduce catecholamine dosage, improve hemodynamics, and serve as bridge to recovery, destination, transplantation, or family's decision.[133-135] Nevertheless, there are still limited data from randomized clinical trials on when and how to use MCS devices properly in CS during acute MI. The survival outcome of CS with acute MI might be affected by different study designs, indications, and limitations of the MSC devices.[136]

Several reviews have concluded that a successful management of CS with acute MI depends on the following important components including early reperfusion therapy, early hemodynamic support, adequate left ventricular unload, and good quality of post-MI care.[137-139] A meta-analysis of 1,866 CS patients supported with ECMO has shown the MCS-associated complication rates were up to 50%, 40%, 30% and 15% for acute kidney injury, major bleeding, infection, and limb ischemia/neurologic deficit, respectively, implicating ECMO can result in survival to discharge but may be associated with considerable morbidity.[140] Prevention or prompt management of MCS-associated complications probably increases the chance of survival of CS. Although recent systematic review and meta-analysis have found MODS following CS could be prevented by short-term MCS if it is used at optimal timing at stages B or C of CS, with sufficient blood flow support with 2-7 L/min and without MCS-related complications, the overall survival rate was similar compared with control group.[137,141] Therefore, routine use of MCS in unselected patients with CS complicating acute MI is still not suggested. The MCS should be applied after heart team evaluation and according to operator's experience and patient's conditions. Figure 6 summarizes the recommendations of evaluation and management of CS complicating acute MI.

Recommendation

- Early heart team approach is recommended for treatment of mechanical complications as well as revascularization strategy in acute MI with CS. (COR I, LOE C)
- Emergency coronary angiography is recommended for acute MI patients with CS, followed by PCI of culprit vessel if coronary lesion is suitable, otherwise, emergency CABG is an alternative. (COR I, LOE B)

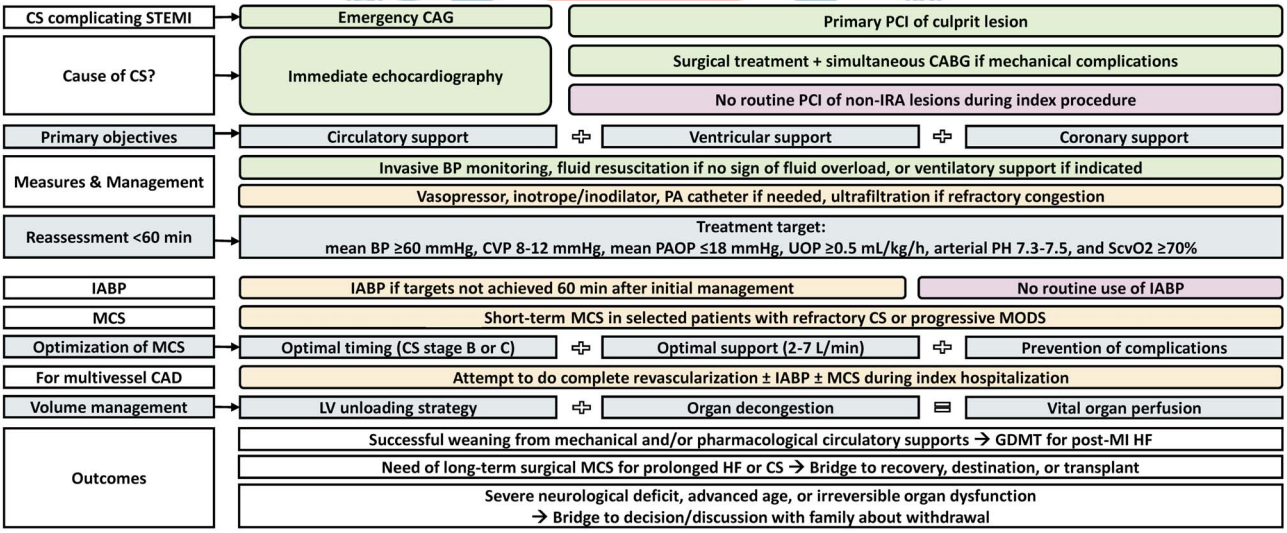

Figure 6. *Evidence-based algorithm for evaluation and management of cardiogenic shock complicating AMI. The recommendations were mainly based on the latest reviews and international guidelines. Class I, II, III recommendations were depicted with light green, light yellow, and pink colors, respectively. AMI, acute myocardial infarction; BP, blood pressure; CABG, coronary artery bypass grafting surgery; CAD, coronary artery disease; CAG, coronary angiography; CS, cardiogenic shock; CVP, central venous pressure; GDMT, guideline-directed medical therapy; HF, heart failure; IABP, intra-aortic balloon pumping; IRA, infarct-related artery; LV, left ventricular; MCS, mechanical circulatory support; MODS, multiple organ dysfunction syndrome; PAOP, pulmonary artery obstructive pressure; PCI, percutaneous coronary intervention; ScvO2, central venous oxygen saturation; STEMI, ST-segment elevation myocardial infarction; UOP, urine output.*

- For MI patients with CS and MVD, attempt of complete revascularization during index hospitalization is reasonable. (COR IIa, LOE B)
- Short-term mechanical support device (e.g., percutaneous cardiopulmonary support, ECMO, or ventricular assist device) with/without IABP may be considered as a rescue therapy in patients with refractory CS. (COR IIb, LOE C)

POST-MI MEDICAL THERAPIES

Aggressive control of risk factors with evidence-based medical therapies substantially improved prognosis of STEMI. Recent report from the TSOC ACS-Diabetes Mellitus Registry revealed a higher adherence rate of guideline-directed medical therapies could reduce about 40% CV events.[142] Repetitive and careful assessment of treatment goal achievement and medical adherence is crucial from acute to chronic stage of MI.[143] Additional efforts to enhance patients' drug adherence, such as using single-pill combination or participation of educational programs, are necessary.[144,145]

Hypertension

The Taiwan STEMI and hypertension guidelines both recommend a BP goal < 130/80 mmHg in STEMI patients.[2,146] Although more intensive treatment with systolic BP < 120 mmHg appeared to benefit high-risk individuals in the SPRINT study,[147] implementing this result to all STEMI patients in Taiwan might not be practical because of the method of BP measurement used in the SPRINT study and the concern of J-curve phenomenon of BP.[147-149] Effective medical regimens, including long-acting beta-blocker, ACEI/ARB and calcium channel blocker (CCB) are recommended to optimize BP control.[146] Beta-blocker, ACEI/ARB and/or mineralocorticoid receptor antagonist (MRA) are especially beneficial in STEMI patients with heart failure or depressed left ventricular ejection fraction.[146] MRA should not be used in those with creatinine clearance < 30 mL/min/1.73 m^2 or potassium level > 5 mEq/L. Routine administration of beta-blocker, ACEI or ARB in all STEMI patients was supported by international guidelines.[150,151] But baseline heart rate, comorbidity and beta receptor selectivity are likely to influence the efficacy of beta-blocker.[152-155]

Recommendation

- It is recommended to control BP < 130/80 mmHg in STEMI patients by long-acting beta-blocker, ACEI/ARB and/or CCB. (COR I, LOE B)
- Beta-blocker, ACEI/ARB and/or mineralocorticoid receptor antagonist are recommended for STEMI patients with heart failure and reduced ejection fraction if there is no contraindication. (COR I, LOE B)
- Routine use of ACEI/ARB for all STEMI patients is reasonable if no contraindication. (COR IIa, LOE A)
- Routine use of beta-blocker for all STEMI patients may be beneficial if no contraindication. (COR IIa, LOE B)

Diabetes

A treatment goal of HbA1c < 7% is recommended in patients with STEMI. However, clinicians can modify the HbA1c target based on patient's general condition and risk of hypoglycemia. A less stringent HbA1c target < 8% is reasonable if patients had hypoglycemic history, limited life expectancy, advanced micro- or macrovascular complications and extensive comorbid conditions. In contrast, individuals with least hypoglycemic risk are also eligible to have more stringent target of < 6.5%.[156] Metformin remains the usual first-line anti-diabetic agent.[157] Thiazolidinedione (TZD), sodium/glucose co-transporter 2 inhibitor (SGLT-2i) or glucagon-like peptide-1 receptor agonist (GLP-1 RA) are recommended as second-line therapies in coronary artery disease since favorable CV outcomes had been observed in relevant clinical studies.[157] Concerning the increased risk of development of post-MI heart failure, TZD is not generally recommended to all STEMI patients as a second-line agent and should be administered with caution. In patients with STEMI and heart failure, SGLT-2i can be considered as the first line therapy because the drug has been proved to improve the prognosis of heart failure with reduced ejection fraction in recent clinical trial.[158]

Recommendation

- It is recommended to control HbA1c < 7% in STEMI patients. The target of HbA1c could be individualized according to patient's condition (< 6.5% to < 8%). (COR I, LOE B)
- Metformin is recommended as the first-line therapy. (COR I, LOE B)
- The priority for add-on therapy includes SGLT-2i and

GLP-1 RA. (COR IIa, LOE A)
- SGLT-2i is recommended for STEMI patients with heart failure and reduced ejection fraction. (COR I, LOE B)

Hypercholesterolemia

Low-density lipoprotein cholesterol (LDL-C) remains the primary target for screening, diagnosis and management of dyslipidemia.[159,160] Current Taiwan lipid guidelines for high risk patients recommend a LDL-C goal < 70 mg/dl for patients with acute MI and < 55 mg/dl for acute MI in diabetic patients.[160] The major evidence-based lipid-lowering medications for ACS were limited to statin and ezetimibe in the past. Previous meta-analysis demonstrated that reduction of LDL-C with statin or nonstatin therapy was associated with similar risk reduction of major vascular events.[161] Due to its potency and scientific evidences, statin is the first-line therapy. In Taiwan, titration to high intensity statin (atorvastatin 40 mg/day or rosuvastatin 20 mg/day) or use statin plus ezetimibe combination therapy is suggested to treat to LDL-C goal in patients with acute MI.[160] A number of patients may develop adverse effects after taking high or any dose of statins.[162] This population has suboptimal LDL-C control and increased risk of CV events.[163] Recently published randomized controlled trials, FOURIER and ODYSSEY OUTCOMES studies, showed that add-on proprotein convertase subtilisin/kexin type 9 inhibitors (PCSK9i) to statin therapy could further reduce 50-60% of LDL-C and obtain a 15% relative risk reduction of CV events in patients with stable ASCVD and recent ACS.[164,165] In the ODYSSEY OUTCOMES trial with recent ACS, the preset LDL-C target of PCSK9i group was 25 to 50 mg/dL and the mean achieved LDL-C level at 48-month follow-up was 53 mg/dL.[165] Intensification of LDL-C control by these potent agents could help STEMI patients to attain the current treatment LDL-C goal much more easier. However, due to the drugs are still very expensive, PCSK9i is usually suggested as the last resort after using maximally tolerated statin and ezetimibe.[166,167] Figure 7 summarizes the recommendations of the treatment target and drug of choice for long term post-MI medical therapies.

Recommendation
- It is recommended to control LDL-C < 70 mg/dL in STEMI patients. (COR I, LOE A)
- A lower target of LDL-C < 55 mg/dL can be considered in STEMI patients. (COR IIa, LOE B)
- LDL-C control should be intensified by statin plus nonstatin therapies, including ezetimibe and/or PCSK9i with full consideration of clinical efficacy, patient's preference as well as cost-effectiveness. (COR I, LOE A)

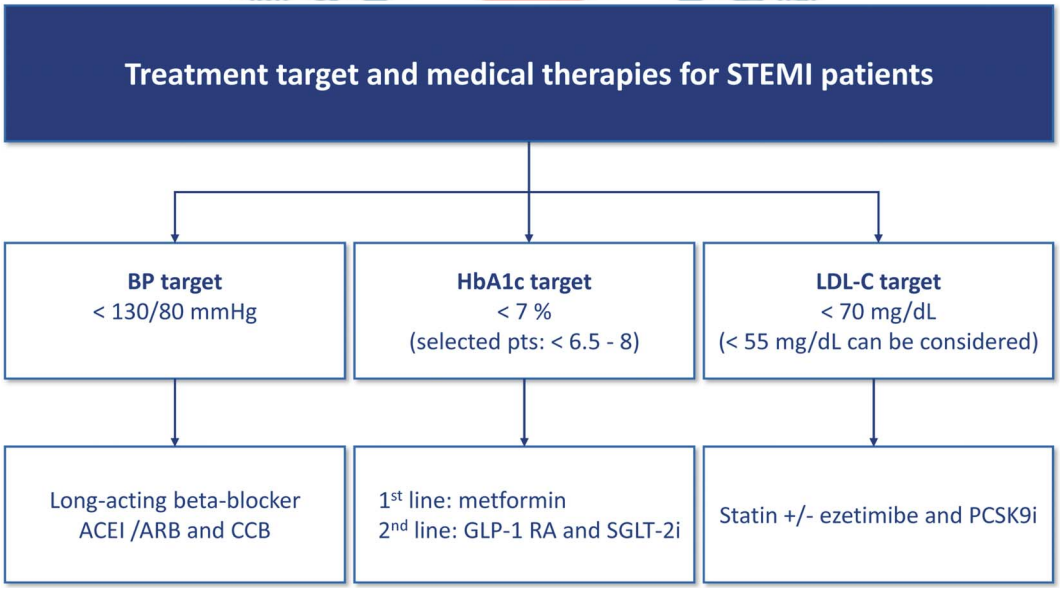

Figure 7. *Recommended treatment targets and medical therapies for STEMI patients. ACEI, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; BP, blood pressure; CCB, calcium channel blocker; GLP-1 RA, glucagon-like peptide-1 receptor agonist; LDL-C, low-density lipoprotein cholesterol; PCSK9i, proprotein convertase subtilisin/kexin type 9 inhibitor; SGLT-2i, sodium/glucose co-transporter 2 inhibitor.*

QUALITY CARE OF STEMI

To reduce the gap between clinical practice and guideline recommendations in STEMI care, a quality evaluation system should be established.[168,169] The quality care of STEMI depends on regularly tracking time intervals of reperfusion therapy, monitoring measurable quality indicators and timely feedback to network stakeholders. The major purpose is for continuous quality improvement of STEMI. The quality indicators, which can measure and compare the quality of health service provider, are divided into three dimensions, including structure, process and outcome indicators (Table 1).[170,171] The pre-hospital and hospital-based treatment delays or in-hospital medications can be monitored by routine audit meeting and updated STEMI management protocols. If the

Table 1. STEMI quality indicators

Dimension	Process	Setting	Indicators
Structure indicator	Diagnosis	Pre-hospital	• Ambulance equipped with telemetry pre-hospital ECG recorders • Ambulance equipped with automated external defibrillators • Ambulance equipped with auto CPR machines • City-based network system to record key factors and time to reperfusion
	Treatment	Hospital	• Single call to activate STEMI team • 24-hour service of catheterization laboratory
Process indicator	Diagnosis	Pre-hospital	• EMTs perform telemetry pre-hospital ECG for patients with typical symptoms of acute MI
	Diagnosis	Hospital	• Door to ECG time • Evaluation of LVEF before discharge
	Treatment	Emergent department	• Aspirin at arrival • P2Y12 receptor inhibitor at arrival
	Treatment	Catheterization laboratory	• Symptom onset to door time • Door to wire time
	Treatment	In-hospital	• Aspirin prescribed at discharge • P2Y12 receptor inhibitor prescribed at discharge • Beta blocker prescribed at discharge • Statin prescribed at discharge • ACEI or ARB or ARNI prescribed at discharge for LV systolic dysfunction (EF ≤ 40%) • Aldosterone antagonist prescribed at discharge for LV systolic dysfunction (EF ≤ 40%) • Cardiac rehabilitation referral from an inpatient setting • Immediate angiography for resuscitated OHCA in STEMI patients • Therapeutic hypothermia for comatose STEMI patients with OHCA • Smoking cessation advice or counseling before discharge
	Quality	Follow up	• Participation in ≥ 1 national STEMI accreditation system and/or other STEMI certification system
Outcome indicator	Quality	In-hospital	• In-hospital mortality
	Quality	Follow up	• 30-day mortality • 30-day readmission rate • 30-day re-infarction rate • 1-year mortality • 1-year readmission rate • 1-year re-infarction rate

ACEI, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; ARNI, angiotensin receptor-neprilysin inhibitor; CPR, cardiopulmonary resuscitation; ECG, electrocardiography; EF, ejection fraction; EMT, emergency medical technicians; LV, left ventricle; MI, myocardial infarction; OHCA, out-of-hospital cardiac arrest; PCI, percutaneous coronary intervention; STEMI, ST-segment elevation myocardial infarction.

targets of quality indicators are not met, quality improvement program should be initiated to improve performance of the system and further maintain quality targets.

In Taiwan, a national STEMI accreditation system was developed by government to monitor the care quality of STEMI in hospitals that performs primary PCI every 3 years. The monitored items include door to ECG time, DAPT use, door to wire time in primary PCI, and other standard operation procedures of STEMI care. The hospitals with 24-hour PCI capability have to reach the following targets: (1) more than 80% of STEMI patients have door to ECG time < 10 minutes, (2) more than 80% of STEMI patients received DAPT, (3) more than 75% of STEMI patients have door to wire time in primary PCI < 90 minutes for those initially presented with ischemic symptoms and more than 70% of STEMI patients have door to wire time in primary PCI < 60 minutes for those diagnosed STEMI referred for primary PCI. The national STEMI accreditation system established the basic requirements for STEMI quality care in Taiwan.[27] The Joint Commission of Taiwan is a non-government organization with the missions of hospital accreditation, certification and healthcare quality inspection. The Joint Commission of Taiwan built up a Taiwan AMI Certification Hospitals system to help the hospitals to pursue a better quality of care for AMI. Taiwan AMI Certification Hospitals system has 3 categories and 27 detailed items. The three categories include STEMI teamwork and management, STEMI patients and family care and STEMI quality improvement. The ultimate purpose is to further improve the comprehensive care of AMI.

Recommendation

- Participation of national STEMI accreditation system and other certification system are recommended to audit the time delay and critical quality targets achievement for STEMI. (COR I, LOE C)
- STEMI quality control system, including monitoring quality indicators and regular quality care meetings, should be established in hospitals. (COR I, LOE C)

CONFLICTS OF INTEREST

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