What Could be Changed in the 2012 Taiwan ST-Segment Elevation Myocardial Infarction Guideline?

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The 2012 guidelines of the Taiwan Society of Cardiology for the management of ST-segment elevation myocardial infarction (STEMI) is an important reference commonly used by a variety of medical professionals in Taiwan. However, there are several points that may need to be changed or added to the 2012 edition due to the scientific development. First, timely primary percutaneous coronary intervention (PCI) has become the major reperfusion therapy in Taiwan. Immediate transfer to qualified PCI-capable hospitals by ambulance for all STEMI patients is the preferred strategy. Second, dual antiplatelet therapy with aspirin and P2Y12 inhibitor is important for STEMI patients. The newer P2Y12 inhibitors, ticagrelor or prasugrel, have a more potent platelet inhibitory effect and can be used for STEMI patients prepared for primary PCI if there is no contraindication. Third, aspiration thrombectomy and newer generation drug-eluting stents can be considered during primary PCI. For patients with multivessel disease, typically only an infarct-related artery should be treated at the time of primary PCI. All these evidence-based suggestions together provide an ideal initial treatment strategy for acute STEMI in Taiwan.

Key Words: Guideline ● Myocardial infarction ● Taiwan

INTRODUCTION

The guideline for the Management of ST-segment Elevation Myocardial Infarction (STEMI) of the Taiwan Society of Cardiology was already published in 2012.[1] Due to ethnic-based considerations in the health care system and insurance reimbursement policy in Taiwan

are that different from those in Western countries, the Taiwan Society of Cardiology believes there should be a local "guideline" or "consensus" to guide health care workers in Taiwan in their care of STEMI patients. Most of the recommendations in this guideline come from the international clinical trial results. However, the results of observational studies and expert opinions reached here in Taiwan are also included in the guideline. Recently, new pharmacological therapies and clinical trial results for STEMI management have been released subsequent to the publishing of our current guideline. Based on these new data, there is strong reason to believe that the strategy for optimal care of acute STEMI should be reconfigured in Taiwan. On the other hand, although more than 95% of STEMI patients are treated with primary percutaneous coronary intervention (PCI) in Taiwan,[2] many detailed suggestions for primary PCI were not included in our current guideline. To establish an optimal treatment strategy for STEMI based on the newest evidence, revision of the current guide-

line becomes necessary. The major purpose of this article is to review new evidence in the literature regarding STEMI treatment which has appeared in the most recent several years which are not included in our current guideline. The possibility of applying this recent evidence to our daily clinical practice in Taiwan will be discussed. An ideal initial treatment strategy for acute STEMI in Taiwan is depicted. As we have always emphasized, STEMI is a complex cardiovascular disease with various clinical situations; therefore, despite the progress of therapies for STEMI, the treatment decisions should depend on the in-charge cardiologists' judgment and not on the guideline, and treatment should be individualized from patient to patient.

RAPID TRANSFER FOR PRIMARY PCI

Existing evidence favors the use of rapid primary PCI as the initial reperfusion strategy. One of the merits of our health care system is that Taiwan is a densely populated country with typically easy patient accessibility to PCI-capable hospitals. Since 2009, the Department of Health started to evaluate the ability and quality of primary PCI of hospitals in Taiwan. This has led to the establishment of a well-structured national primary PCI system throughout much of the country. The qualified high-grade primary PCI-capable hospitals in Taiwan are that they can perform primary PCI 24 hours a day and 7 days a week all year around, and to achieve a door-to-balloon (D2B) time < 90 minutes for at least 75% STEMI patients they treat. Up to May 2014, there are 31 qualified high-grade primary PCI-capable hospitals around Taiwan.[3] In addition to these qualified hospitals, there are many other hospitals that can perform primary PCI in daytime. In the western part of Taiwan which has more than 98% population of the country, current transportation system makes it possible to access a PCI-capable hospital within 2 hours which is the critical time for primary PCI transfer.[4] The quality of primary PCI is also improving with a significant decline of D2B time in Taiwan.[5] Therefore, when a possible STEMI patient is encountered, all physicians in Taiwan should consider primary PCI as the first choice of reperfusion strategy when timely transfer is possible. For all suspected STEMI patients who call 119, the emergent medical service

should transport the patients directly to the nearest qualified PCI-capable hospitals as soon as possible. For patients who arrive at a non-PCI-capable hospital, it is strongly recommended that immediate transfer the patients with an ambulance for primary PCI if primary PCI can be performed within 2 hours.[4] General practitioners or emergency physicians in non-PCI-capable hospitals should be aware of the location of the nearest qualified PCI-capable hospitals and help the patients transfer to these hospitals by ambulance (Figure 1). The use of fibrinolytic therapy for STEMI in Taiwan is now only limited to some geographically challenging areas where the estimated transportation time for primary PCI is long. Otherwise, all eligible STEMI patients in Taiwan should receive primary PCI as the initial reperfusion therapy.

NEW P2Y12 INHIBITORS

Dual antiplatelet therapy with aspirin and clopidogrel
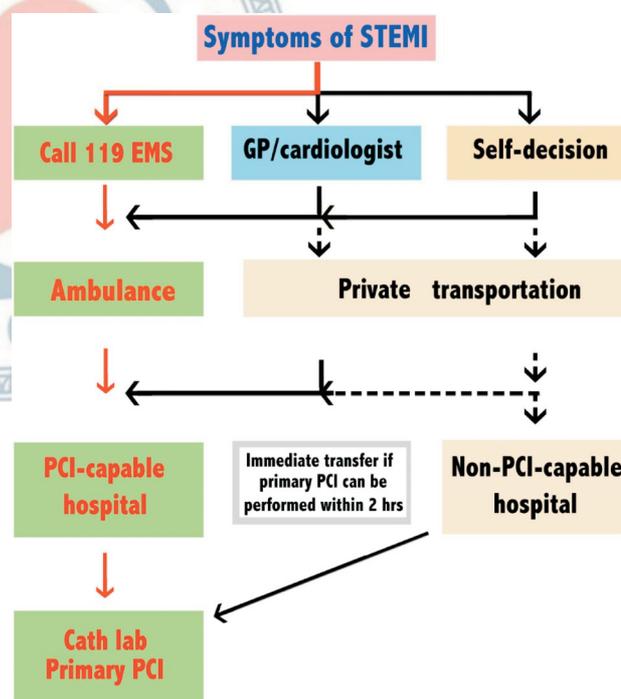
Figure 1. *Rapid primary PCI is the standard reperfusion therapy for patients with acute STEMI in Taiwan. Red continuous line: preferred strategy. Black continuous line: useful strategy. Black dashed line: maybe used but not recommended strategy. EMS, emergent medical service; GP, general practitioner; PCI, percutaneous coronary intervention; STEMI, ST-segment elevation myocardial infarction.*

is the current standard treatment in all STEMI patients, and clopidogrel should be continued at a maintenance dose for at least 1 year if there is no contraindication. However, there is a significant variation of antiplatelet response to clopidogrel among individuals due to different clinical characteristics and genetic polymorphisms that may interfere clopidogrel absorption or metabolism.[6] The newer P2Y12 inhibitors, prasugrel and ticagrelor, have been developed and can achieve a greater inhibition of platelet aggregation. The TRITON-TIMI 38 trial compared prasugrel with clopidogrel in 3534 STEMI patients with PCI.[7] Prasugrel significantly reduced the primary endpoint, including cardiovascular death, non-fatal myocardial infarction (MI), or non-fatal stroke at 30 days. The PLATO trial compared ticagrelor with clopidogrel in 7544 STEMI patients undergoing primary PCI.[8] At 1 year, ticagrelor tended to reduce the primary endpoint of cardiovascular death, MI or stroke (hazard ratio, 0.87, 95% confidence interval, 0.75 to 1.01, p = 0.07). Bleeding is a concern when using prasugrel or ticagrelor. Prasugrel should be avoided in patients with a history of stroke or transient ischemic attack (TIA), older than 75 years and body weight 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. Ticagrelor is also suggested not to be used in patients with a history of intracranial hemorrhage. Because the data are limited, the benefit of ticagrelor in patients with history of ischemic stroke and TIA must be weighed against the risk of bleeding.[9] Currently, ticagrelor is available in Taiwan, but prasugrel is still not accessible. Therefore, for STEMI patients in Taiwan prepared for primary PCI, in addition to aspirin, P2Y12 inhibitors with clopidogrel or ticagrelor should be given as early as possible and continued for at least 1 year if there is no contraindication. For STEMI patients treated medically without intervention, only aspirin and clopidogrel should be administered.

PRIMARY PCI

During the procedure of primary PCI for STEMI, there are several issues that should be taken into consideration. The first is aspiration thrombectomy. Several clinical trials and meta-analysis showed inconsistent results about the benefits from routine manual aspiration thrombectomy with respect to coronary blood flow, ST segment resolution and mortality. A very recent meta-analysis which included 18 clinical trials with 3936 STEMI patients demonstrated that manual catheter aspiration of thrombus is beneficial in reducing adverse cardiovascular events and mortality at 6 to 12 months compared with conventional PCI alone.[10] However, the newest randomized clinical trial, Thrombus Aspiration in ST-Elevation Myocardial Infarction in Scandinavia (TASTE) with a total of 7244 patients with STEMI undergoing primary PCI, could not show any survival benefit of routine aspiration thrombectomy.[11] But aspiration thrombectomy tended to decrease recurrent MI (hazard ratio, 0.61, 95% confidence interval, 0.34 to 1.07, p = 0.09), and stent thrombosis (hazard ratio, 0.47, 95% confidence interval, 0.20 to 1.02, p = 0.06) at 30 days.[11] The other large-scale clinical trial (TOTAL trial, NCT01149044) is still ongoing. At the current stage, it is suggested that manual thrombus aspiration with aspiration catheter can be considered during primary PCI to reduce thrombus burden. However, it is not necessary that the procedure be routinely performed. The second important point is about non-infarct artery PCI at the time of primary PCI. Current international guidelines[12,13] for the management of STEMI do not recommend non-infarct artery PCI in hemodynamically stable patients with multivessel disease at the time of primary PCI. However, a recent randomized clinical trial reevaluated the effect of non-infarct artery PCI in 465 acute STEMI patients with a mean follow-up period of 23 months.[14] The results demonstrated that immediate PCI in non-infarct coronary arteries with major stenosis at the time of primary PCI significantly reduced the risk of adverse cardiovascular events including cardiovascular death or non-fatal MI, as compared to PCI only limited to the infarct artery. An observational study of 1278 STEMI patients in Taiwan found that patients who received delayed staged PCI of non-infarct artery for multivessel disease had better 30-day and 1-year clinical outcomes than those with only infarct-related artery PCI.[15] Up to now, there are no data regarding the comparison between immediate versus delayed (staged) PCI on non-infarct artery in STEMI patients. At the current stage, most guidelines still suggest infarct-related artery PCI only during primary PCI. At the time of primary PCI, non-infarct artery

PCI is limited to those cases with multiple lesions and hemodynamic instability or those with multiple lesions where the definite infarct location is ambiguous. The non-infarct artery PCI can be performed electively later. Third, stent implantation is now performed almost routinely during primary PCI. Bare-metal stents (BMS) decrease the risk of restenosis compared with balloon angioplasty only, and drug-eluting stents (DES) further reduce restenosis rate compared with BMS. However, in a highly thrombogenic milieu of coronary lesions in STEMI, the risk of stent thrombosis of DES becomes a safety concern during primary PCI. Findings from recent meta-analyses have shown that newer generation DESs, other than first generation sirolimus and paclitaxel-eluting stent, have less stent thrombosis and target vessel revascularization compared to BMS.[16-18] The data suggest that newer generation DES can be used safely in STEMI patients treated with primary PCI. One-year dual antiplatelet therapy is important in patients who received DES. If patients have an increased risk of bleeding, need subsequent surgical procedures or have indication for long-term anticoagulation, BMS should be considered in these patients during primary PCI.

CONCLUSIONS

In Taiwan, primary PCI becomes the first line reperfusion therapy for STEMI and almost all STEMI patients received primary PCI. The major effort now should be focused on decreasing the treatment delay by rapid transfer of STEMI patients with ambulance to PCI-capable hospitals. Any delay in the health care system should be reduced as much as possible after the first medical contact of the STEMI patients. A performance monitoring system should be established in all PCI-capable hospitals to improve the quality of care. Rapid platelet inhibition with aspirin and P2Y12 inhibitor is an essential treatment in STEMI. In addition to clopidogrel, there are new P2Y12 inhibitors (prasugrel and ticagrelor) with more potent antiplatelet effects that can be used in STEMI patients prepared for primary PCI. For STEMI patients who received medical treatment without PCI, aspirin and clopidogrel is still the standard therapy. The procedural aspects of primary PCI are also important. Clinical trials have shown conflicting results about rou-
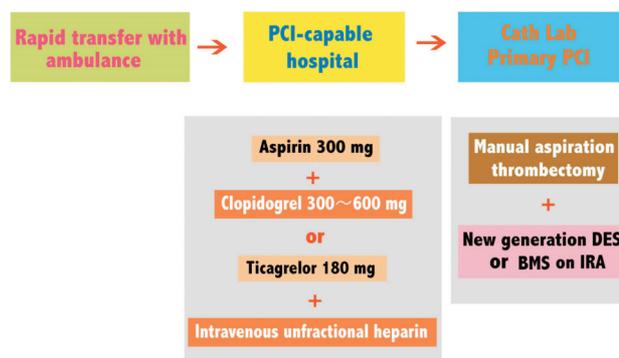
Figure 2. *The ideal initial treatment for acute STEMI in Taiwan. BMS, bare-metal stent; DES, drug-eluting stent; IRA, infarct-related artery; PCI, percutaneous coronary intervention.*

tine manual aspiration thrombectomy before stenting. Currently, manual catheter aspiration of thrombus is not a routine procedure but can be performed to reduce thrombus burden during primary PCI. For STEMI patients with multivessel disease, only infarct-related artery PCI should be undertaken during primary PCI. The non-infarct artery PCI could be performed in a later stage but not at the time of primary PCI except there are other considerations. Compared to the first generation DES, the newer generation DES has thinner struts and reduced polymer thickness, and has been shown to have less stent thrombosis and restenosis than BMS. But if the patients' bleeding risk is high or cannot tolerate 12-month dual antiplatelet therapy, BMS should be used. An ideal initial treatment for acute STEMI in Taiwan is depicted in Figure 2. As we have always emphasized, due to the varieties of patient situations, the optimal therapy for each patient still depends on the cardiologist's clinical judgment and preference.

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