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High Potent Antiplatelet in Pharmacoinvasive Strategy

Lidwina br Tarigan*
Bethesda Hospital-Medicine Faculty UKDW, Yogyakarta, Indonesia

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*Corresponding author
Email:
mercyalidwina@gmail.com

Address:
Jl. Dr. Wahidin Sudirohusodo, Kotabaru, Yogyakarta, Indonesia

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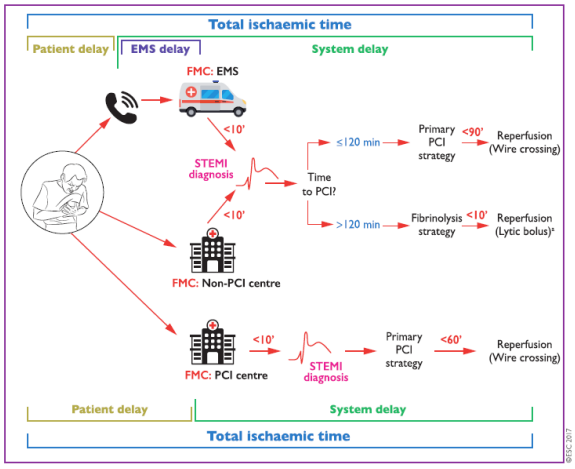
ABSTRACT

ST-segment elevation myocardial infarction (STEMI) accounts for 25–40% of acute coronary syndrome (ACS) cases (1). Several studies and practice guidelines have demonstrated the superiority of primary percutaneous coronary intervention (PCI) over other therapies when performed within 90 minutes of first medical contact FMC) for field transfer and 120 minutes of FMC for patients presenting to non-PCI-capable facility [1-3]. However, some of this superiority is lost when door-to- balloon time exceeds 120 minutes, a situation that can occur when challenging conditions like shortage of skilled manpower, weather, traffic and geography exist. A pharmacoinvasive strategy is recommended for ST-elevation myocardial infarction (STEMI) patients when primary percutaneous coronary intervention (PCI) cannot be achieved in a timely fashion. Pharmacoinvasive strategy was defined as fibrinolysis followed by rescue or urgent PCI or by routine elective PCI (beyond 3 hours of fibrinolytic administration).
Patients treated with a pharmacoinvasive strategy require anticoagulant and antiplatelet therapy before PCI. The prognostic benefit associated with dual antiplatelet therapy (DAPT) following acute coronary syndromes (ACS) has been well established. As such, newer and more potent oral P2Y12 antagonists-prasugrel and ticagrelor-have been preferentially endorsed over clopidogrel in ST elevation myocardial infarction (STEMI) patients following primary percutaneous coronary intervention (PCI). Randomized trials that demonstrated superior efficacy of ticagrelor and prasugrel however excluded STEMI patients treated with a contemporary fibrinolytic pharmacoinvasive strategy. Based on TREAT study patients with STEMI younger than 75 years who initially received clopidogrel can be safely switched to ticagrelor in the first 24 hours after fibrinolysis. Whether this strategy will result in fewer cardiovascular events in the long term remains to be determined.In patients younger than 75 years with STEMI, delayed administration of ticagrelor after fibrinolytic therapy was noninferior to clopidogrel for TIMI major bleeding at 30 days.

Introduction

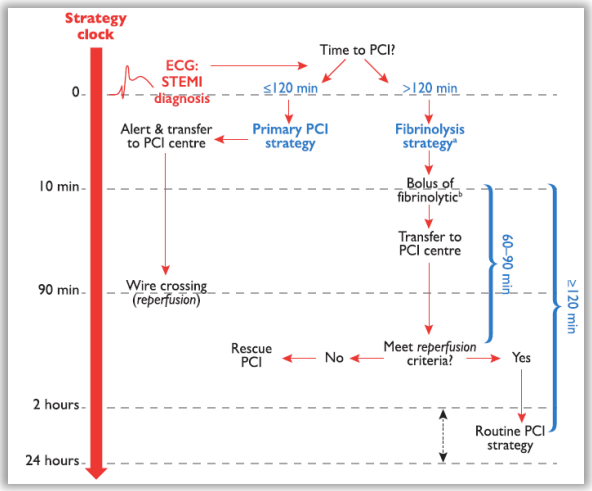
Acute thrombosis induced by a ruptured or eroded atherosclerotic coronary plaque, with or without concomitant vasoconstriction, causing a sudden and critical reduction in blood flow. Atherothrombosis causing total obstruction blood flow named STE-ACS (STEMI) and partial obstruction blood flow named NSTEMI and Unstable Angina (1). There are few electrocardiogram criteria to diagnose STEMI consecutively new ST segment elevation at the J point 2 contiguous lead with ≥ 0.2 mV in men (>40 years old) or ≥ 0.15 mV in women in leads V2-V3 and /or ≥ 0.1 mV in other leads in the absence of LVH and LBBB, new LBBB and symptoms suggestive of ACS and in suspected posterior (circumflex artery related) or right ventricle-related infarction ST elevation in V7, V8 and V9 using a cut off point > 0.05 mV, ST elevation in V3R and



V4R, using a cutoff point > 0.05 mV and > 0.1 mV in men < 30 year (2). ESC STEMI 2017 Flowchart for STEMI Reperfusion Strategy (1)

Discussion

Timing and logistical factors influence choice of reperfusion strategy. Time to reperfusion according to patient ability to recognize symptom, mode of transportation to the hospital, inter hospital transfer challenges (distance, traffic patterns, climatic conditions and etc). Health care resource also influence reperfusion strategy such as PCI vs non-PCI capable hospital, dependence of operator expertise/volume, availability of a 24/7 service and availability of pre hospital system for diagnosis and treatment (3, 4,5). A primary PCI strategy is recommended over fibrinolysis within indicated time frames (1). What if primary PCI cannot be performed timely after STEMI diagnosis? ESC STEMI 2017 recommended fibrinolytic therapy is recommended within 12 hours of symptom onset in patient without contraindication.



Pharmacoinvasive strategy was defined as fibrinolysis followed by rescue or urgent PCI or by routine elective PCI (beyond 3 hours of fibrinolytic administration). There is a prospective country registry about Efficacy and Safety of Pharmacoinvasive Strategy Compared to Primary Percutaneous Coronary Intervention in the Management of ST-Segment Elevation and coming a conclusion pharmacoinvasive strategy have comparable outcomes to those treated with primary PCI with no increased risk of major bleeding (6).

Patients treated with a pharmacoinvasive strategy require a potent antiplatelet therapy before fibrinolytic, before PCI and after PCI. Results from the ISIS-2 trial comparing aspirin and streptokinase alone and in combination in patients with AMI. Aspirin was effective in reducing mortality alone and was additive when given with streptokinase. From ISIS-2 Collaborative Group (7). Clarity TIMI 28 Study design Double-blind, randomized, placebo-controlled trial in 3491 patients, age 18-75 years with STEMI < 12 hours giving aspirin, fibrinolytic and heparin randomize patients with clopidogrel 300 mg Loading dose, 75 mg maintenance with placebo. All patients performed Coro angiography in 2-8 days and follow up clinical result for 30 days. Result from this trial is 36 % in the odds of an occluded infarct-related artery or death/MI by angiography (NNT 16), 20 % reduction in CV death, MI, or recurrent ischemia leading to urgent revascularization through 30 days (NNT=36) and no excess in TIMI major or minor bleeding (including in those undergoing CABG) or ICH. According to STEMI guidelines 2017 DAPT in the form of ASA + P2Y12 inhibitor in indicated for up to 1 year in patients undergoing fibrinolytic and subsequent PCI. Clopidogrel is the P2Y12 inhibitor of choice as co adjuvant and after fibrinolytic, but 48 hours after fibrinolytic, switch to ticagrelor or prasugrel may be considered in patients who underwent PCI (3).

The long-term pharmacodynamic effects of Ticagrelor versus Clopidogrel in patients undergoing early percutaneous coronary intervention (PCI) after fibrinolytic therapy is unknown.

SET FAST study design 212 patients undergoing PCI within 24 h of Tenecteplase (TNK), Aspirin, and Clopidogrel for ST-elevated myocardial infarction (STEMI) were randomized at four Canadian sites to receive additional Clopidogrel or Ticagrelor initiated prior to PCI. The platelet reactivity units (PRU) were measured with the Verify Now Assay before study drug administration (baseline), at 4 and 24 h post PCI, and follow-up appointment. Ticagrelor achieved superior platelet Inhibition vs Clopidogrel in Fibrinolytic-treated STEMI patients (8). The bleeding safety of ticagrelor in patients with ST-elevation myocardial infarction treated with fibrinolytic therapy remains uncertain. TREAT study evaluate the short-term safety of ticagrelor when compared with clopidogrel in patients with ST-elevation myocardial infarction treated with fibrinolytic therapy. A multinational, open label, randomized, phae III trial to asses safety and efficacy of ticagrelor vs clopidogrel in patients age 18-75 yesrd, diagnosed with STEMI < 24 hours prior to randomization, with documented cardiac ischaemic symptoms due to atherosclerosis treated with pharmacological thrombolysis and the result is ticagrelor did not increase TIMI major bleeding at 30 days compared with clopidogrel in STEMI patients treated with fibrinolytic (9)

Conclusion

Primary PCI is preferred option for reperfusion strategy in STEMI patients, if Primary PCI cannot be offered in timely manner, pharmacoinvasive strategy is an option and has a comparable outcome to primary PCI. TREAT provides additional safety data, supporting the use of high potent antiplatelet: ticagrelor + aspirin in STEMI including patient with fibrinolytic. In patients younger than 75 years with STEMI, delayed administration of ticagrelor after fibrinolytic was non inferior to clopidogrel for TIMI major bleeding at 30 days.

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