What Do Guidelines Say We Should Do in Patients with ST Elevation Myocardial Infarction?

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Abstract
Clinical statements and guidelines dynamically regenerate with rapidly growing new evidence and regulate our daily clinical practice. On the other hand, our obedience on traditional experiences might lead us to manage patients inappropriately. Recently published guidelines on ST elevation myocardial infarction (STEMI) by the European Society of Cardiology (ESC) and American College of Cardiology (ACC) have altered and changed many previously accurate management. The aim of this review is to evaluate the recommendations of the new STEMI guidelines and the inappropriate management practices we perform in our daily practice. (JAEM 2014; 13: 199-203)

Key words: Myocardial infarction, guideline, ST elevation

1. Emergency Management
Recent guidelines recommend assuming acute myocardial infarction (AMI) in any patient who applies to emergency services with the complaints of chest pain. American College of Cardiology (ACC) guidelines recommend obtaining a-12-derivation electrocardiogram (ECG) immediately after the first medical contact (FMC) where European Society of Cardiology (ESC) guidelines recommends not more than in 10 minutes. Furthermore, ESC details the management by utilizing laboratory evaluation and echocardiography but also points out that they should not permit any delay in revascularization therapy. Moreover, ESC also suggests opioid analgesics for chest pain relief and oxygen supplementation in case of dyspnea or hypoxemia (pulse oximetry <95%). Finally, both guidelines recommend primary percutaneous coronary intervention (PCI) as a class I recommendation in all cases if cardiac arrest occurs at FMC (1, 2).

Clinicians should be aware of any ECG abnormality, especially ST-segment elevation AMI and should start therapy without waiting for blood test results. ESC states this as a class I recommendation. Starting long-term high-dose oxygen supplementation in the emergency room or coronary intensive care immediately is not indicated, because it may lead to vasoconstriction. Instead, oxygenation is recommended in patients with oxygen saturation <95%. Additionally, intramuscular injections may lead to hematomas later if patients receive antiaggregant, anticoagulant, or fibrinolytic therapy.

2. Reperfusion Therapy
Reperfusion therapy should be performed in all patients with STEMI if primary PCI (it should absolutely be performed within the first 12 hours of initial symptoms and in 12-24 hours if ischemia insists with obvious clinical and ECG findings) is not capable. Any patients who are candidates for percutaneous intervention should be admitted to a coronary angiography (CAG) laboratory (both ACC and ESC recommend a door-to-needle interval <90 minutes in the FMC) (1, 2).

If the hospital does not contain a CAG laboratory, then the patient should be transferred to another center that is capable of primary intervention in a door-to-balloon interval of less than 120 minutes. In the absence of such a center and if fibrinolytic therapy is available in the first hospital, the patient should receive a fibrinolytic in the first 30 minutes (ESC recommends fibrin-specific agents). Also, the ESC recommends fibrinolytic therapy in any patient who is admitted to the hospital early (<2 hours) with a wide infarction area and low risk of hemorrhage if the FMC-balloon interval is <90 minutes (2).

Both guidelines recommend an immediate transfer in the first 24 hours to a center capable of coronary angiography if 1) reperfusion is unsuccessful after fibrinolysis, 2) the patient experiences re-infarction, heart failure, or cardiogenic shock or 3) symptoms of ischemia do not resolve, and 3 hours within the fibrinolytic therapy if the patient is stable (1, 2).
Diagnosis and transfer of these patients in our country have become extremely rapid after utilization of the Emergency Medical Service (112) of the Turkish Ministry of Health. Centers that are capable of PCI are identified, and such patients are referred to these clinics, especially in megapoles. Despite this, in smaller city hospitals without available CAG laboratories, fibrinolytic therapy is preferred, since there is no nearby center that provides PCI <120 minutes as the FMC-to-balloon interval.

The major mistake in reperfusion therapy is not performing it for patients who are admitted between the 6th and 12th hours of the onset of chest pain. Clinicians still think that reperfusion is indicated in the first 6 hours and manage their patients, as well. Even patients who are admitted later than the 12th hour of initial symptoms are accepted as having subacute myocardial infarction, and despite ECG and clinical findings of ischemia, they do not receive any reperfusion therapy. However, new guidelines are clear in this manner in absolutely starting reperfusion therapy in the first 12 hours and between the 12th and 24th hours depending on ongoing clinical and ECG findings.

Although the timing is the most important fact in reperfusion treatment, because of challenges, such as insufficient knowledge of ECG and experience of the first clinician who takes care of the patient, waiting for serum marker results, delays in the cardiology consultation, ambulance arrival or CAG stuff to come together, fibrinolysis initiation (which should be <30 minutes) and FMC-balloon interval (which should be <30 minutes) are also delayed, unfortunately.

1.1 Primary Percutaneous Intervention Therapy

Both guidelines recommend performing primary PCI in STEMI patients applying in the first 12 hours and at any time for patients having concomitant cardiogenic shock or heart failure (HF) as a class I recommendation. ESC guidelines recommend primary PCI as a class I recommendation in patients with obvious clinical and ECG findings of ischemia who apply between the 12th and 24th hours, where ACC determines the same intervention in the same patient population as a class Ila recommendation. Both of the guidelines recommend primary PCI as a class IIb recommendation in asymptomatic patients applying in the same time interval (1, 2). ACC does not recommend intervention for uninvolved arteries in ischemia (class III), whereas ESC does not recommend intervention to totally occluded artery in stable patients without any ischemic symptoms within the first 24 hours of symptom onset (class III) (1).

Additionally, both guidelines recommend stenting instead of a balloon. ACC recommends bare-metal stents (BMS) as a class I recommendation for patients who have a high risk for bleeding and are inappropriate for dual antiplatelet therapy (DAPT) for 2 years, whereas ESC recommends drug-eluting stents (DES) in patients who are not contra-indicated to receive DAPT as a class Ilb recommendation. Again, both guidelines recommend usage of thrombectomy catheters as a class Ila recommendation. Finally, ESC recommends radial artery intervention for experienced clinicians as a class Ila recommendation (1, 2).

Besides, ACC recommends emergency coronary artery by-pass graft surgery (CABG) for STEMI patients. Patients having ischemia, cardiogenic shock, severe HF, and mechanical defects who have coronary anatomy that is amenable to PCI are candidates for CABG as a class I recommendation. But, for patients without cardiogenic shock, this indication in the first 6 hours is a class IIb recommendation (1).

Experienced clinics are known to perform successful interventions in STEMI patients. Despite this, guidelines are not followed especially strictly in daily practice. Stable patients applying later than 24 hours with totally occluded arteries without any obvious symptoms of ischemia undergo inaccurate interventions. Additionally, besides infarction-related arteries, it is a common fault to perform interventions in other arteries unrelated to infarction.

Another mistake is to forward the patient to urgent surgery instead of performing reperfusion intervention for the culprit vessel if the patient has 3-vessel disease in CAG performed during STEMI.

We are familiar with extremely expensive thrombectomy catheters that our social security system does not cover, which means that additional bills are paid by the patient. Thus, only limited numbers of clinics buy and use such devices, as well as DES, since it is unethical to ask any patients or accompanying relatives if more expensive but effective stents can be used or not, although ESC recommends them.

2.1.1 Antiplatelet therapy in centers performing primary PCI

Aspirin should be given orally or intravenously in a loading and maintenance dose if the patient is unable to swallow before intervention in patients with STEMI (class I). Again, both guidelines recommend loading and maintenance doses of one of the ADP receptor blockers (clopidogrel, prasugrel, or ticagrelor) (class I). At this point, ESC points out that clopidogrel should only be used when ticagrelor or prasugrel is unavailable or contra-indicated, whereas prasugrel should be used in patients under 75 years old who did not receive clopidogrel previously and have no transient ischemic attack (TIA) or stroke history. There are no limitations for ticagrelor in ESC guidelines (2).

None of the guidelines recommends glycoprotein IIb/IIIa receptor blockers (GP2b/3a RB) as a class I recommendation. ACC recommends glycoprotein IIb/IIIa inhibitors as a class Ila recommendation in selected patients who receive unfractionated heparin (UFH), whereas ESC defines these patients in detail as having thrombus, diagnosed thrombotic complications, slow flow, or no reflow. Use double boluses of eptifibatide and a high-dose bolus of tirofiban should not be forgotten. Finally administration of these drugs during transfer and administration to all patients are class IIb recommendations (1, 2).

Intravenous (IV) aspirin is available in only a few centers and thus can not always be applied to patients who can not swallow aspirin tablets. For this reason, unfortunately, the right management is impossible in such centers.

The most frequent mistake committed in our country is not giving a loading dose of ADP receptor blockers in the pre-intervention period. Loading doses of these drugs are not being applied in many clinics because of the possibility of referral of these patients to urgent surgery after CAG and the resistance of cardiovascular surgeons in operating these patients who receive such medications. As a general practice, loading doses are given after primary intervention in many clinics.

Because of problems in payment by the social security system of our country, the experience with ADP receptor blockers other than clopidogrel is extremely low. Thus, misuse of these drugs are also little. But, it should not be forgotten that ESC guidelines recommend other antiaggregants instead of clopidogrel.

Finally, although GP2b/3a RBs are recommended for selected patients, they are never used in some clinics, even is indicated, because of high costs.
2.1.2 Anticoagulant Therapy in Primary PCI Centers
Both guidelines recommend anticoagulant therapy with UFH (using activated clotting time=ACT level for follow-up) or bivalirudin and discourage fondaparinux in patients in whom primary intervention was performed. Moreover, ACC does not mention any enoxaparin usage, while ESC recommends enoxaparin instead of UFH (class IIb) (1, 2).

Since bivalirudin is not available in our country and there is not too much experience with fondaparinux in cardiology clinics, we do not notice any misuse. But, a common error is not to regulate dosages of UFH according to ACT and to start enoxaparin instead of UFH, since it is easier to administer.

2.2 Fibrinolytic Therapy
Fibrinolytic therapy is a class I recommendation within the first 12 hours of chest pain if the clinic has no CAG laboratory, FMC-balloon interval is >120 minutes, and there is no contra-indication of fibrinolysis. If the patient is admitted in the first 12-24 hours of pain with obvious clinical ischemia and ongoing ECG abnormality, fibrinolysis is recommended as a class IIb recommendation. ESC also recommends fibrinolytic therapy for patients who are admitted within the first 2 hours of chest pain with wide infarction, low bleeding possibility, and FMC-balloon interval >90 minutes (class IIa).

Pre-hospital administration of fibrinolytic (class IIa), especially with fibrin-specific agents (class I), is encouraged by ESC. Fibrinolysis is discouraged in patients with ST depression, except those with true posterior MI and ST elevation in aVR.

Finally, immediate transfer to a CAG unit is recommended in cases of unsuccessful reperfusion with fibrinolysis, reinfarction, HF, cardiogenic shock, and ongoing symptoms of ischemia. If the patient is stable and fibrinolysis is successful, transfer is recommended in 3-24 hours.

Fibrinolytic therapy is frequently administered because of former experiences and difficulties in reaching centers capable of CAG, although primary interventions are performed frequently. Absolute and relative contraindications of fibrinolytics should be realized very well. An accompanying clinician should be ready to follow up and treat any complication that will occur during fibrinolysis, like hypotension, hypertension, and arrhythmia. Another error in the management of these patients is to transfer patients to clinics capable of CAG too late, 3-4 days after fibrinolytic therapy.

2.2.1 Antiplatelet Therapy in Clinics Administering Fibrinolysis
These patients have to receive aspirin and clopidogrel. According to ACC, aspirin should be given continuously at a dose of 162-325 mg, whereas clopidogrel should be given at least 14 days but for 1 year preferably at a dose of 300 mg to patients <75 years old and at 75 mg for those >75 years old (1). None of the guidelines recommends GP2b/3a RBs to patients who receive fibrinolics (1, 2).

Although clopidogrel should be given, as well as aspirin, directly to any patient with STEMI, either lack of knowledge or former habits cause low dose or any treatment with clopidogrel.

2.2.2 Anticoagulant Therapy in Clinics Administering Fibrinolysis
Again, both guidelines recommend anticoagulation, and UFH infusion has to be monitored with aPTT (targeting 1.5-2 times normal value) follow-ups. If enoxaparin is preferred, then the dosage should be adjusted according to patient age at loading boluses and maintenance doses. Similarly, fondaparinux is also convenient in patients who receive fibrinolitics (1, 2).

The most frequent mistake in daily practice is to administer IV heparin at a constant dose of 1000 U/hour instead of adjusting a given dose according to aPTT monitoring. Administration of clinically effective anticoagulants (enoxaparin and fondaparinux) in such patients may help to minimize this mistake. Additionally, another fact not to miss is to adjust the dose of enoxaparin in patients >75 years old.

3. Other Treatment Strategies

3.1 Glycose
ESC recommends regulating blood glycose level between 90-200 mg/dL as a class IIa recommendation in hyperglycemic patients with diabetes but discourages using glucose-potassium-insulin infusion routinely (class III) (2).

Serum glycose levels increase in AMI due to stress. Closely monitoring serum glycose levels and regulating glycosia strictly may cause hypoglycemia episodes. Hypoglycemia may lead to clinical deterioration by a sympathomimetic stimulus. Moreover, some clinics still use glucose-potassium-insulin infusion routinely.

3.2 Beta-blockers and Verapamil
Oral beta-blockers should be initiated in the first 24 hours of STEMI unless contraindicated and should be continued during hospitalization and after discharge. Intravenous beta-blocker is a class IIa recommendation for patients whose hypertension and tachycardia are not secondary to HF (1, 2). Beta-blockers are contraindicated in cases of hypotension or HF.

ESC recommends verapamil (class IIb) for patients without HF but absolute contraindications for beta-blockers (2).

Habits on administering IV beta-blockers routinely to any patient with STEMI give rise to an increase in mortality in patients with HF. Despite this, uncontrolled use of IV beta-blockers is ongoing. Furthermore, it is a common mistake to start IV beta-blockers despite contraindications due to lack of a detailed physical examination and ECG evaluation.

Diltiazem is another drug frequently used in our country to replace when beta-blockers are contraindicated, even if it does not take part in any of the guidelines. Such drugs are absolutely contraindicated in patients with HF.

3.3 Renin-angiotensin-aldosterone System Inhibitors
Angiotensin-converting enzyme inhibitors (ACEIs) should be initiated in the first 24 hours in patients with HF, left ventricular dysfunction, diabetes, or anterior wall infarction who do not have any contraindications (class I). It is a class IIa recommendation to initiate routine ACEI in all patients (1). Angiotensin receptor blockers (ARBs) may replace ACEIs in patients who can not tolerate.

Aldosterone antagonists that are not contraindicated should be initiated simultaneously with ACEIs or beta-blockers in patients with HF, left ventricular ejection fraction <40%, or diabetes, along with close monitoring for renal failure and hyperpotassemia as a class I recommendation (1).

Patients with ventricular systolic dysfunction and anterior wall ischemia are usually normotensive. But, these patients are those who have a class I recommendation for ACEI initiation. Avoiding starting
ACEIs in these normotensive STEMI patients is a frequent mistake because of the fear of consequent hypotension as a complication. Besides, ARB is the first choice in some clinics instead of ACEI for the same reasons.

Although it is a class I recommendation, aldosterone antagonists are also rarely initiated in STEMI patients.

### 3.4 Lipid Therapy

Both guidelines recommend obtaining a fasting lipid profile as soon as possible. Irrespective of initial cholesterol levels, according to both guidelines, it is a class I recommendation to initiate and continue high-dose statin in STEMI patients if there are no contraindications (1, 2). Besides, ESC recommends re-obtaining LDL levels 4-6 weeks after STEMI and adjusting the therapy, targeting and LDL level <70 mg/dL as a class IIa recommendation (2).

Despite these, lipid therapy is still managed according to ATP III guidelines, and usually, lipid-lowering therapy is never initiated if LDL level is <130 mg/dL. Because of social security payment rules in our country, we cannot initiate high-dose statin without obtaining a lipid profile. Furthermore, the targeted LDL level according to guidelines (<70 mg/dL) is lower than our security system accepts (lipid-lowering therapy can only be accepted if serum LDL is >130 mg/dL).

### 3.5 Anticoagulant Therapy

Anticoagulation with vitamin K antagonists is obligatory for obviously indicated patients [CHADS2 ≥ 2 atrial fibrillation (AF), mechanical heart valve, venous thromboembolism, hypercoagulability]. If the patient has mural thrombi, continuing anticoagulation for a minimum of 3 months is recommended (class IIa) (1). Additionally, ACC recommends achieving an INR of 2.0–2.5 in patients under DAPT and adding anticoagulation if anterior apical wall dyskinesia or aki-nesia exists (1).

Some clinicians hesitate adding anticoagulants to DAPT, especially to patients who live in rural areas that are far away from hospitals. For this reason, anticoagulation is not initiated, despite being indicated, especially in patients with AF.

### 4. Suggestions for Post-STEMI Complications

#### 4.1 Cardiogenic Shock

Primary PCI is indicated in STEMI patients with cardiogenic shock, if incapable, fibrinolysis should be performed regardless of admission time (class I). An intra-aortic balloon pump should be inserted if possible (class IIa) (2). ESC recommends the use of dopamine, dobutamine (class IIa), levosimendan (class IIb), and ultrafiltration (class IIa) in patients with HF Killip III. Epinephrine use in patients with HF Killip IV is a class IIb recommendation (2).

Owing to the high mortality of these patients, many unexperienced clinicians avoid performing intervention and prefer medical therapy. Although it is a class I recommendation, fibrinolytic therapy is avoided or delayed in patients do not receive intervention as a common mistake.

#### 4.2 Arrhythmias

Beta-blockers or non-dihydropyridine calcium channel blockers (verapamil, diltiazem) may be initiated in patients with AF who do not have HF. But, if hypotension and HF occur due to rapid ventricular response, digitalis or amiodarone is the drug of choice. If medical therapy is not effective and can not heal the HF, ischemia, or hemo-dynamics of the patient, then cardioversion is indicated. Besides, medical cardioversion with amiodarone can be performed in stable patients with new onset of AF. Digoxin, verapamil, sotalol, metoprolo-l, and others are discouraged for use for medical cardioversion of AF, as well as rhythm control.

ESC recommends cardioversion in sustained ventricular tachycardia (VT) or ventricular fibrillation (VF). If sustained monomorphic VT episodes repeat, then amiodarone (class IIa) and lidocaine or so-talol (class IIb), added to cardioversion, is recommended. Furthermore, it is a class IIa recommendation to terminate VT by transcath-eter pacing in these patients. Finally, IV beta-blockers in addition to other therapies are a class Ila recommendation in patients with non-sustained VT episodes (2).

If the patient has polymorphic VT, IV beta-blocker or amiodar-one (by paying attention to QT interval), correcting electrolyte im-balances, magnesium supplementation, and performing CAG to exclude ischemia are class I recommendations. Whereas transvenous pacing and isoproterenol therapy are class Ila recommendations, li-docaine is a class IIb recommendation (1, 2).

In clinical practice, patients having newly onset AF during STEMI receive amiodarone. However, digoxin, verapamil, sotalol, and meto-prolol are preferred as antiarrhythmic, and hypotension and HF are ignored and cardioversion is delayed.

Although lidocaine is a class IIb recommendation in these patients, it is frequently used due to habits. Besides, terminating VT by transcatheter pacing or beta-blocker therapy is rarely admin-istered.

#### 4.3 ICD Implantation

An ICD is recommended in patients experiencing ventricular tachycardia or fibrillation within the first 48 hours of STEMI that is unrelated to ischemia, re-infarction, or metabolic causes (class I) (1, 2). Social security regulations and old-fashioned knowledge on the subject cause rare ICD implantation in our country.

#### 1.4 Pericarditis

In the case of pericarditis, the pain responds to high-dose aspirin (class I), and if needed, acetaminophen, colchicine, and opioid analgesics as additives (class IIa) are recommended. Glucocorticoids and non-steroidal anti-inflammatory drugs (NSAIDs) should be avoided (class III) (1, 2).

STEMI patients are misdiagnosed as re-infarction after elevation of ST segments in ECG due to pericarditis. Common errors in these patients are performing recurrent CAG although not indicated, mis-diagnosing pericarditis as myalgia, and starting NSAIDs.

#### 5. Discharging

ESC recommends 24-hour observation at least in coronary intensive care units as a class 1 recommendation; selected cases with low risk may be hospitalized in earlier (nearly, 72 hours later) patients (class IIb) (2).

Sometimes, patients with STEMI are discharged the next day after CAG, as in elective patients in whom percutaneous intervention is performed. Nevertheless, it does not mean myocardial healing when arterial lesions are opened up. Despite this, some clinicians quickly discharge their patients after stenting as if he/she is healed. This is also the result of social security payments that equalize STEMI pa-tients with elective CAG-indicated ones.
**Peer-review:** Externally peer-reviewed.


**Conflict of Interest:** The authors declared no conflict of interest.

**Financial Disclosure:** The authors declared that this study has received no financial support.

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