8th Annual Emirates Cardiac Society Conference

ACC Middle East Conference 2017

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Tailoring adjunctive antithrombotic therapy to reperfusion strategy in STEMI

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ACC Middle East Conference 2017

Agenda

- Introduction & different strategies.
- Adjunctive antithrombotics for fibrinolytic therapy.
- Adjunctive antithrombotics for 1ry PCI.
- Algorithm for switching between different P2Y12
- DAPT combined with OAC’s
- Tailoring according to the bleeding and ischemic risk scores.

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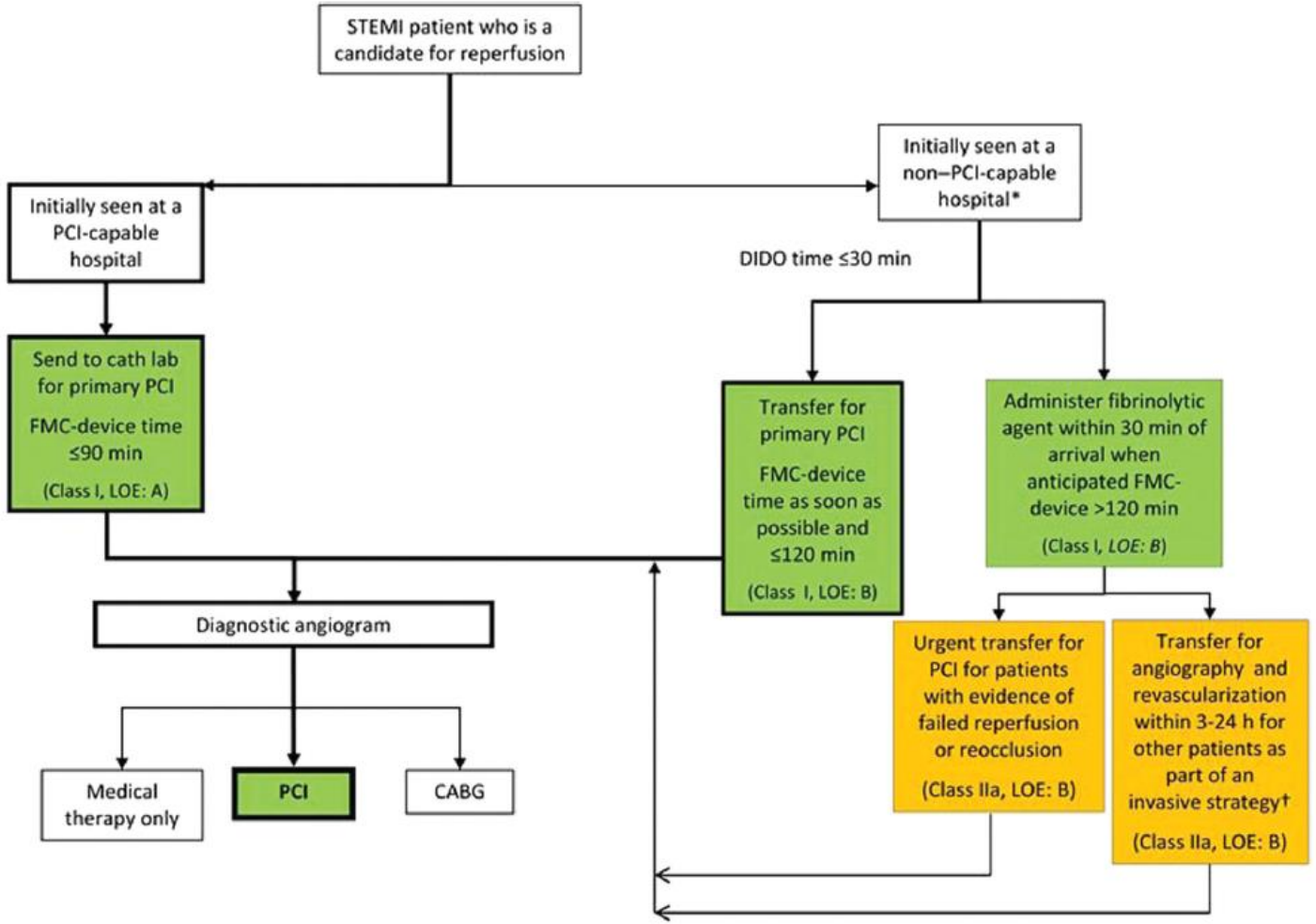
Reperfusion Therapy for Patients with STEMI



*Patients with cardiogenic shock or severe heart failure initially seen at a non–PCI-capable hospital should be transferred for cardiac catheterization and revascularization as soon as possible, irrespective of time delay from MI onset (*Class I, LOE: B*). †Angiography and revascularization should not be performed within the first 2 to 3 hours after administration of fibrinolytic therapy.

So, in dealing with STEMI, we have 2 different clinical scenarios; fibrinolytic therapy or primary PCI

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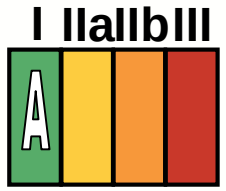
Reperfusion at a Non–PCI-Capable Hospital

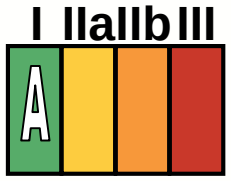
Adjunctive Antithrombotic Therapy With Fibrinolysis

Adjunctive Antiplatelet Therapy With Fibrinolysis



Aspirin (162- to 325-mg loading dose) and clopidogrel (300-mg loading dose for patients ≤75 years of age, 75-mg dose for patients >75 years of age) should be administered to patients with STEMI who receive fibrinolytic therapy.

aspirin should be continued indefinitely and



clopidogrel (75 mg daily) for at least 14 days

and up to 1 year

It is reasonable to use aspirin 81 mg per day in preference to higher maintenance doses after fibrinolytic therapy.

Adjunctive Anticoagulant Therapy With Fibrinolysis

Patients with STEMI undergoing reperfusion with fibrinolytic therapy should receive anticoagulant therapy for a minimum of 48 hours, and preferably for the duration of the index hospitalization, up to 8 days or until revascularization if performed. Recommended regimens include:

a. UFH administered as a weight-adjusted intravenous bolus and infusion to obtain an activated partial thromboplastin time of 1.5 to 2.0 times control, for 48 hours or until revascularization;

b. Enoxaparin administered according to age, weight, and creatinine clearance, given as an intravenous bolus, followed in 15 minutes by subcutaneous injection for the duration of the index hospitalization, up to 8 days or until revascularization; or

c. Fondaparinux administered with initial intravenous dose, followed in 24 hours by daily subcutaneous injections if the estimated creatinine clearance is greater than 30 mL/min, for the duration of the index hospitalization, up to 8 days or until revascularization.

Fibrinolytic therapy

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Recommendations	Class	Level
When fibrinolysis is the reperfusion strategy, it is recommended to initiate this treatment as soon as possible after STEMI diagnosis, preferably in the prehospital setting.	I	A
A fibrin-specific agent (i.e. tenecteplase, alteplase, reteplase) is recommended.	I	B
A half-dose of tenecteplase should be considered in patients ≥75 years of age.	IIa	B
Antiplatelet co-therapy with fibrinolysis		
Oral or i.v. aspirin is indicated.	I	B
Clopidogrel is indicated in addition to aspirin.	I	A
DAPT (in the form of aspirin plus a $P2Y_{12}$ inhibitor) is indicated for up to 1 year in patients undergoing fibrinolysis and subsequent PCI.	I	C

IIa→I

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www.escardio.org/guidelines 2017 ESC Guidelines for the Management of AMI-STEMI (European Heart Journal 2017 - doi:10.1093/eurheartj/ehx095)

Clopidogrel is the P2Y12 inhibitor of choice as co-adjuvant and after fibrinolysis, but **48 h** after fibrinolysis, switch to **prasugrel/ticagrelor** may be considered in patients who underwent PCI.

Fibrinolytic therapy *(continued)*

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Recommendations	Class	Level
Anticoagulation co-therapy with fibrinolysis		
Anticoagulation is recommended in patients treated with lytics until revascularization (if performed) or for the duration of hospital stay up to 8 days. The anticoagulant can be:	I	A
• Enoxaparin i.v. followed by s.c. (preferred over UFH).	I	A
• UFH given as a weight-adjusted i.v. bolus followed by infusion.	I	B
• In patients treated with streptokinase: fondaparinux i.v. bolus followed by an s.c. dose 24 hours later.	IIa	B
Transfer after fibrinolysis		
Transfer to a PCI-capable centre following fibrinolysis is indicated in all patients immediately after fibrinolysis.	I	A

Doses of fibrinolytic agents and antithrombotic co-therapies *(continued)*

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Drug	Initial treatment	Specific contra-indications
Doses of antiplatelet co-therapies		
Aspirin	Starting dose of 150–300 mg orally (or 75–250 mg intravenously if oral ingestion is not possible), followed by a maintenance dose of 75–100 mg/day	
Clopidogrel	Loading dose of 300 mg orally, followed by a maintenance dose of 75 mg/day. In patients ≥75 years of age: loading dose of 75 mg, followed by a maintenance dose of 75 mg/day.	

Weight-adjusted i.v. tenecteplase, aspirin, and clopidogrel given orally, and enoxaparin i.v. followed by s.c. administration until the time of PCI (revascularisation), comprise the antithrombotic cocktail most extensively studied as part of a pharmacoinvasive strategy

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Reperfusion at a PCI-Capable Hospital

Antithrombotic Therapy to Support Primary PCI for STEMI

Antiplatelet Therapy to Support Primary PCI for STEMI

Aspirin 162 to 325 mg should be given before primary PCI.

After PCI, aspirin should be continued indefinitely.

A loading dose of a $P2Y_{12}$ receptor inhibitor should be given as early as possible or at time of primary PCI to patients with STEMI. Options include:

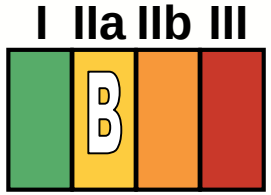
- Clopidogrel 600 mg; or
- Prasugrel 60 mg; or
- Ticagrelor 180 mg

Antiplatelet Therapy to Support Primary PCI for STEMI

$P2Y_{12}$ inhibitor therapy should be given for 1 year to patients with STEMI who receive a stent (BMS or DES) during primary PCI using the following maintenance doses:

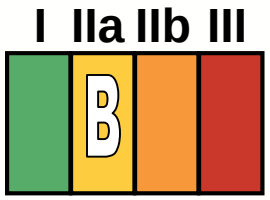
- Clopidogrel 75 mg daily; or
- Prasugrel 10 mg daily; or
- Ticagrelor 90 mg twice a day*

*The recommended maintenance dose of aspirin to be used with ticagrelor is 81 mg daily.



It is reasonable to use 81 mg of aspirin per day in preference to higher maintenance doses after primary PCI.

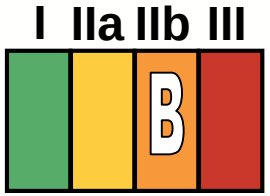
Antiplatelet Therapy to Support Primary PCI for STEMI



It is reasonable to start treatment with an intravenous GP IIb/IIIa receptor antagonist at the time of primary PCI (with or without stenting or clopidogrel pretreatment) in selected patients with STEMI who are receiving UFH.

- Abciximab: 0.25 mg/kg IV bolus, then 0.125 mcg/kg/min (maximum 10 mcg/min); or
- High-bolus-dose tirofiban: 25 mcg/kg IV bolus, then 0.15 mcg/kg/min; or
- Double-bolus eptifibatide: 180 mcg/kg IV bolus, then 2 mcg/kg/min; a 2nd 180-mcg/kg bolus is administered 10 min after the 1st bolus.

Antiplatelet Therapy to Support Primary PCI for STEMI



It may be reasonable to administer intravenous GP IIb/IIIa receptor antagonist in the precatheterization laboratory setting (e.g., ambulance, ED) to patients with STEMI for whom primary PCI is intended.

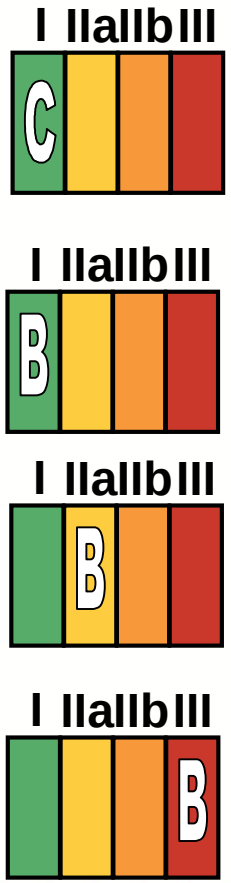
It may be reasonable to administer intracoronary abciximab to patients with STEMI undergoing primary PCI.

Continuation of a $P2Y_{12}$ inhibitor beyond 1 year may be considered in patients undergoing DES placement.

Prasugrel should not be administered to patients with a history of prior stroke or transient ischemic attack.

Harm

Anticoagulant Therapy to Support Primary PCI



For patients with STEMI undergoing primary PCI, the following supportive anticoagulant regimens are recommended:

- UFH, with additional boluses administered as needed to maintain therapeutic activated clotting time levels, taking into account whether a GP IIb/IIIa receptor antagonist has been administered; or
- Bivalirudin with or without prior treatment with UFH.

In patients with STEMI undergoing PCI who are at high risk of bleeding, it is reasonable to use bivalirudin monotherapy in preference to the combination of UFH and a GP IIb/IIIa receptor antagonist.

Fondaparinux should not be used as the sole anticoagulant to support primary PCI because of the risk of catheter thrombosis.

Periprocedural and postprocedural antithrombotic therapyc in patients undergoing primary percutaneous coronary intervention

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Recommendations	Class	Level
Antiplatelet therapy		
A potent $P2Y_{12}$ inhibitor (prasugrel or ticagrelor), or clopidogrel if these are not available or are contra-indicated, is recommended before (or at latest at the time of) PCI and maintained over 12 months unless there are contra-indications such as excessive risk of bleeding.	I	A
Aspirin (oral or i.v, if unable to swallow) is recommended as soon as possible for all patients without contra-indications.	I	B
GP IIb/IIIa inhibitors should be considered for bailout if there is evidence of no-reflow or a thrombotic complication.	IIa	C
Cangrelor may be considered in patients who have not received $P2Y_{12}$ receptor inhibitors.	IIb	A

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www.escardio.org/guidelines 2017 ESC Guidelines for the Management of AMI-STEMI (European Heart Journal 2017 - doi:10.1093/eurheartj/ehx095)

Periprocedural and postprocedural antithrombotic therapy in patients undergoing primary percutaneous coronary intervention

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Recommendations	Class	Level	
Anticoagulant therapy			
Anticoagulation is recommended for all patients in addition to antiplatelet therapy during primary PCI.	I	C	
Routine use of UFH is recommended.	I	C	
In patients with heparin-induced thrombocytopenia, bivalirudin is recommended as the anticoagulant agent during primary PCI.	I	C	
Routine use of enoxaparin i.v. should be considered.	IIa	A	IIb→IIa
Routine use of bivalirudin should be considered.	IIa	A	I→IIa
Fondaparinux is not recommended for primary PCI.	III	B	

Routine post-procedural anticoagulant therapy is not indicated after primary PCI, except when there is a separate indication for either full-dose anticoagulation [due, for instance, to atrial fibrillation (AF), mechanical valves, or LV thrombus) or prophylactic doses for the prevention of venous thromboembolism in patients requiring prolonged bed rest.

Doses of antiplatelet and anticoagulant co-therapies in primary PCI

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Doses of antiplatelet and parenteral anticoagulant co-therapies in primary PCI	
Antiplatelet therapies	
Aspirin	Loading dose of 150-300 mg orally or of 75-250 mg i.v. if oral ingestion is not possible, followed by a maintenance dose of 75-100 mg/day.
Clopidogrel	Loading dose of 600 mg orally, followed by a maintenance dose of75 mg/day.
Prasugrel	Loading dose of 60 mg orally, followed by a maintenance dose of 10 mg/day. In patients with body weight ≤60 kg, a maintenance dose of 5 mg/day is recommended. Prasugrel is contra-indicated in patients with previous stroke. In patients ≥75 years, prasugrel is generally not recommended, but a dose of 5 mg/day should be used if treatment is deemed necessary.

www.escardio.org/guidelines 2017 ESC Guidelines for the Management of AMI-STEMI (European Heart Journal 2017 - doi:10.1093/eurheartj/ehx095)

Doses of antiplatelet and anticoagulant co-therapies in primary PCI *(continued)*

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Doses of antiplatelet and parenteral anticoagulant co-therapies in primary PCI	
Antiplatelet therapies *(continued)*	
Ticagrelor	Loading dose of 180 mg orally, followed by a maintenance dose of 90 mg b.i.d.
Abciximab	Bolus of 0.25 mg/kg i.v. and 0.125 µg/kg/min infusion (maximum 10 µg/min) for 12 hours.
Eptifibatide	Double bolus of 180 µg/kg i.v. (given at a 10-min interval) followed by an infusion of 2.0 µg/kg/min for up to 18 hours.
Tirofiban	25 µg/kg over 3 min i.v., followed by a maintenance infusion of 0.15 µg/kg/min for up to 18 hours.

Doses of antiplatelet and anticoagulant co-therapies in primary PCI*(continued)*

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Doses of antiplatelet and parenteral anticoagulant co-therapies in primary PCI	
Parenteral anticoagulant therapies	
UFH	70-100 IU/kg i.v. bolus when no GP IIb/IIIa inhibitor is planned 50-70 IU/kg i.v. bolus with GP IIb/IIIa inhibitors.
Enoxaparin	0.5 mg/kg i.v. bolus.
Bivalirudin	0.75 mg/kg i.v. bolus followed by i.v. infusion of 1.75 mg/kg/hour for up to 4 hours after the procedure.

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Algorithm for switching between oral $P2Y_{12}$ inhibitors in the acute setting

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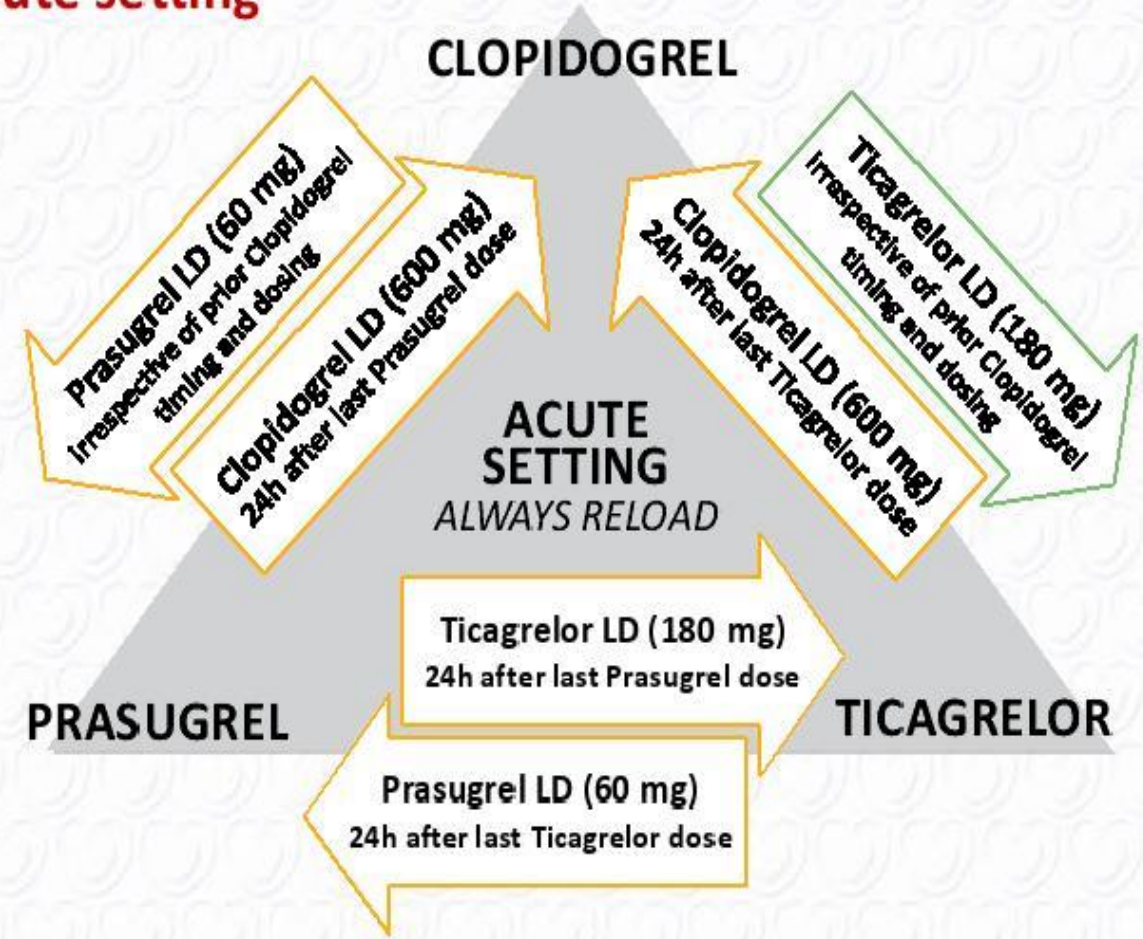

2017 ESC Focused Update on DAPT in Coronary Artery Disease, developed in collaboration with EACTS
(European Heart Journal 2017 - doi:10.1093/eurheartj/ehx419)

Switching between oral $P2Y_{12}$ inhibitors

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Recommendations	Class	Level
In patients with ACS who were previously exposed to clopidogrel, switching from clopidogrel to ticagrelor is recommended early after hospital admission at a loading dose of 180 mg irrespective of timing and loading dose of clopidogrel, unless contra-indications to ticagrelor exist.	I	B
Additional switching between oral $P2Y_{12}$ inhibitors may be considered in cases of side effects/drug intolerance according to the proposed algorithms.	IIb	C

Maintenance antithrombotic strategy after ST-elevation myocardial infarction

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Recommendations	Class	Level
Antiplatelet therapy with low-dose aspirin (75–100 mg) is indicated.	I	A
DAPT in the form of aspirin plus ticagrelor or prasugrel (or clopidogrel if ticagrelor or prasugrel is not available or is contra-indicated) is recommended for 12 months after PCI unless there are contra-indications such as excessive risk of bleeding.	I	A
A PPI in combination with DAPT is recommended in patients at high risk of gastrointestinal bleeding.	I	B
In patients with an indication for oral anticoagulation, oral anti-coagulants are indicated in addition to antiplatelet therapy.	I	C

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Take Home Message

- Antithrombotic management of STEMI should be tailored according to the treatment strategy as well as drug availability.
- Both duration and choice of DAPT depends on bleeding as well as ischemic risk and the need for OAC's.

Thank you