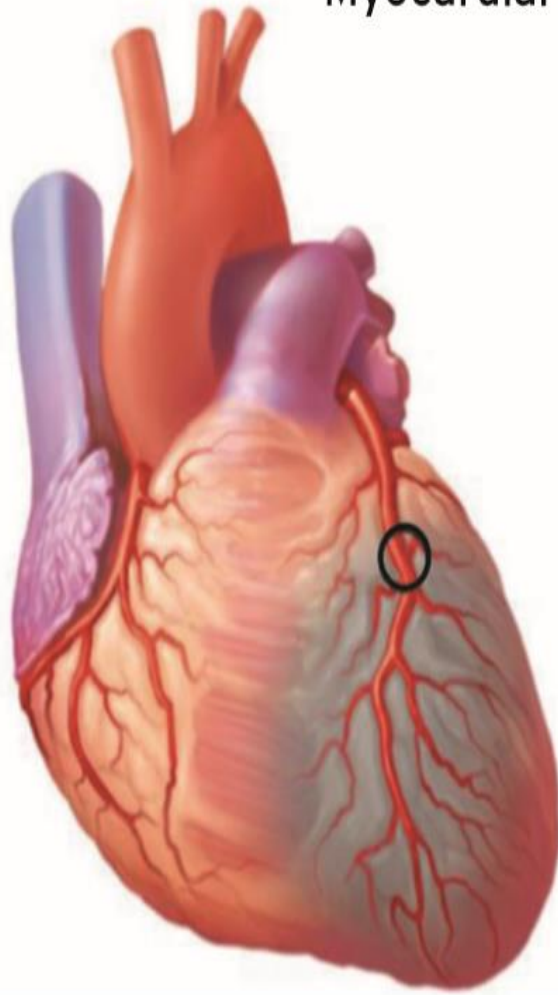


# **KHUYẾN CÁO 2018 VỀ TÁI THÔNG ĐỘNG MẠCH VÀNH: LỰA CHỌN ỨC CHẾ BƠM PROTON PHÙ HỢP**

PGS. TS Phạm Nguyễn Vinh  
Bệnh viện Tim Tâm Đức  
Đại học Y khoa Phạm Ngọc Thạch  
Viện Tim Tp. HCM



## Myocardial Infarction Type 1

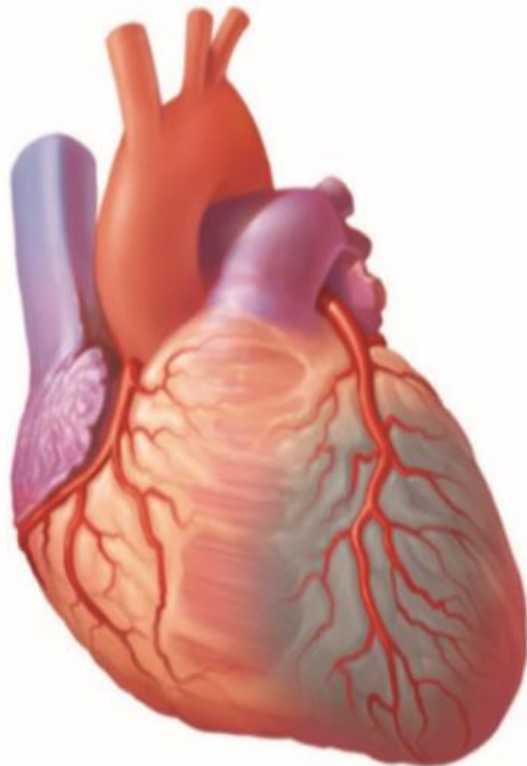


Plaque rupture/erosion with occlusive thrombus



Plaque rupture/erosion with non-occlusive thrombus

## Myocardial Infarction Type 2



Atherosclerosis and oxygen supply/demand imbalance



Vasospasm or coronary microvascular dysfunction

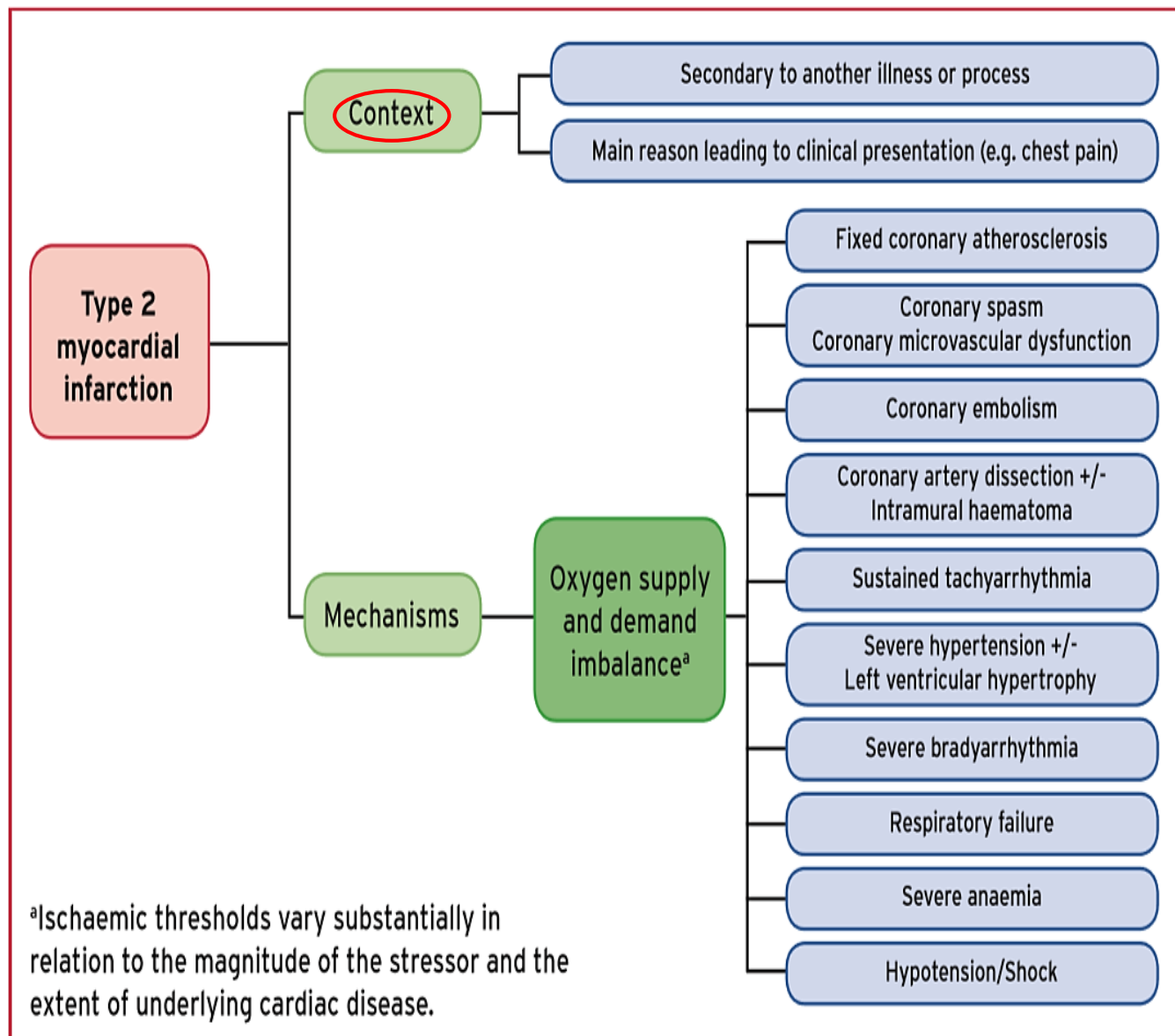


Non-atherosclerotic coronary dissection



Oxygen supply/demand imbalance alone

# Type 2 MI: Clinical context and pathophysiological mechanisms



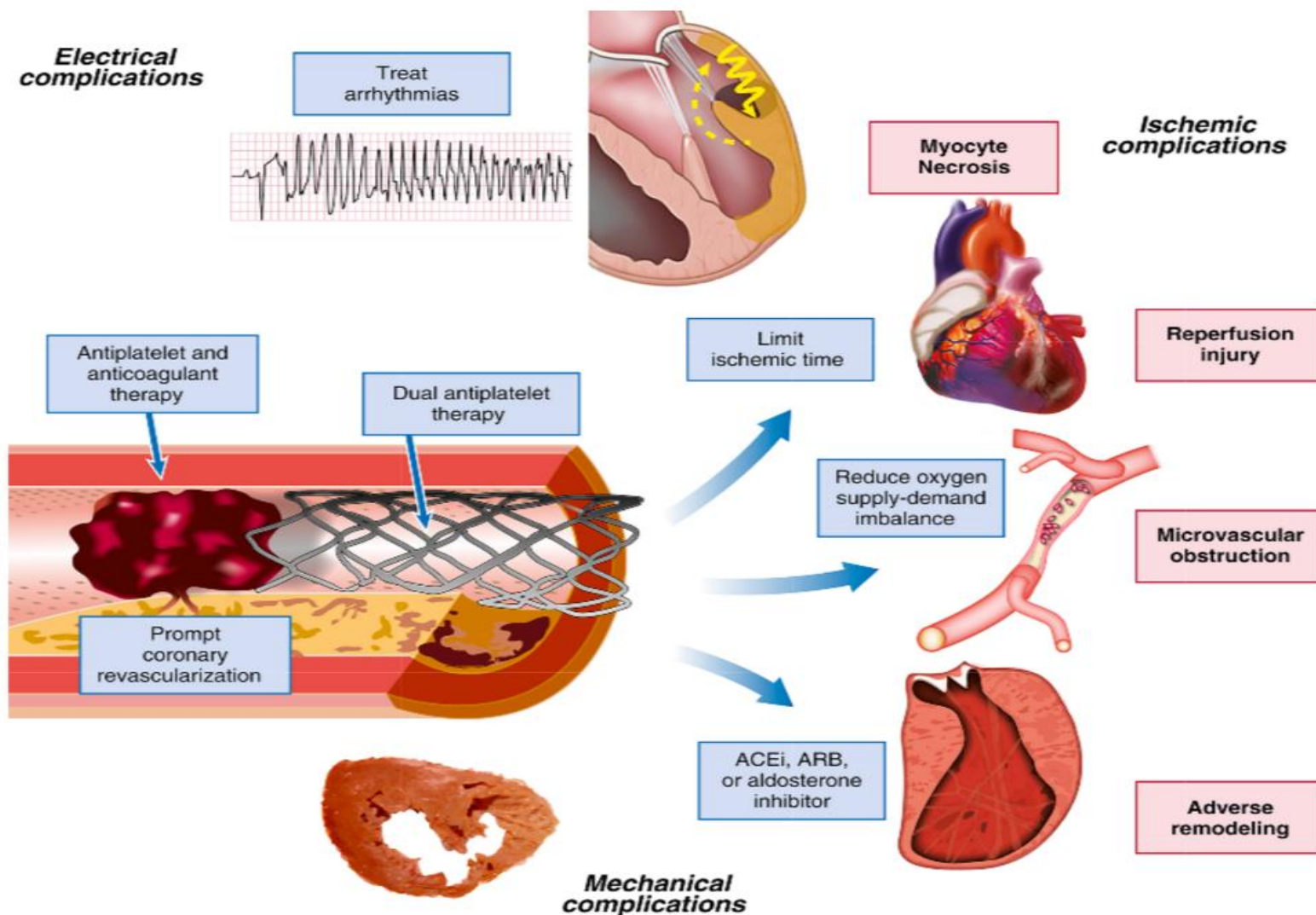
TL: Thygesen K et al. Fourth universal definition of myocardial infarction 2018. European Heart Journal (2018) 00, 1–33. doi:10.1093/eurheartj/ehy462



Pham  
Nguyen  
Vinh

<sup>a</sup>Ischaemic thresholds vary substantially in relation to the magnitude of the stressor and the extent of underlying cardiac disease.

# Các biến chứng của NMCT và mục tiêu điều trị





**ESC**

European Society  
of Cardiology

European Heart Journal (2018) **00**, 1–96

doi:10.1093/eurheartj/ehy394

**ESC/EACTS GUIDELINES**

---

# **2018 ESC/EACTS Guidelines on myocardial revascularization**

**The Task Force on myocardial revascularization of the European Society of Cardiology (ESC) and European Association for Cardio-Thoracic Surgery (EACTS)**

**Developed with the special contribution of the European Association for Percutaneous Cardiovascular Interventions (EAPCI)**

# Indications for revascularization in patients with stable angina or silent ischaemia

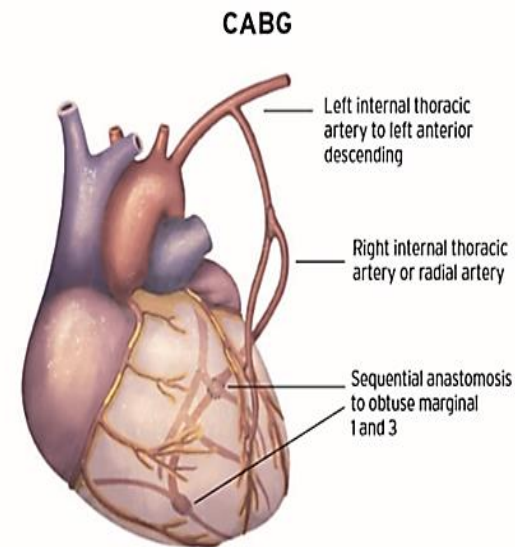
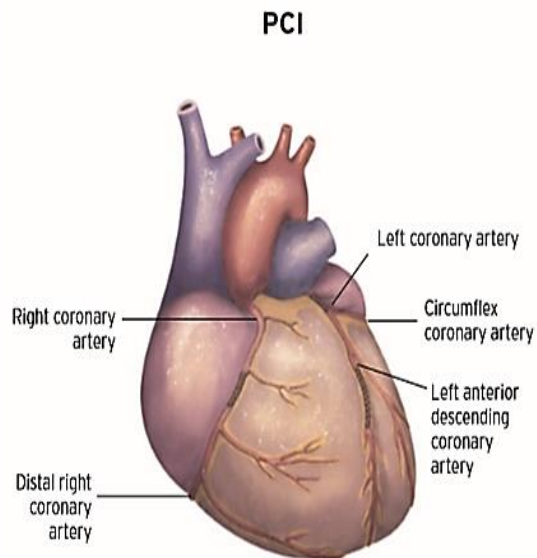
Extent of CAD (anatomical and/or functional)		Class <sup>a</sup>	Level <sup>b</sup>
<b>For prognosis</b>	Left main disease with stenosis >50%. <sup>c 68–71</sup>	I	A
	Proximal LAD stenosis >50%. <sup>c 62,68,70,72</sup>	I	A
	Two- or three-vessel disease with stenosis >50% with impaired LV function (LVEF ≤35%). <sup>c 61,62,68,70,73–83</sup>	I	A
	Large area of ischaemia detected by functional testing (>10% LV) or abnormal invasive FFR. <sup>d 24,59,84–90</sup>	I	B
	Single remaining patent coronary artery with stenosis >50%. <sup>c</sup>	I	C
<b>For symptoms</b>	Haemodynamically significant coronary stenosis <sup>c</sup> in the presence of limiting angina or angina equivalent, with insufficient response to optimized medical therapy. <sup>e 24,63,91–97</sup>	I	A

FFR = fractional flow reserve; iwFR = instantaneous wave-free ratio. (a) Class of recommendation; (b) Level of evidence; (c) With documented ischaemia or a haemodynamically relevant lesion defined by FFR < 0.80 or iwFR < 0.89 (see section 3.2.1.1), or >90% stenosis in a major coronary vessel; (d) Based on FFR < 0.75 indicating a prognostically relevant lesion (see section 3.2.1.1); (e) In consideration of patient compliance and wishes in relation to the intensity of anti-anginal therapy

# Decision-making between PCI and CABG among patients with stable multivessel and/or left main CAD

DAPT = dual antiplatelet therapy; LIMA = left internal mammary artery; RIMA = right internal mammary artery; MVD = multivessel coronary artery disease; RA = radial artery; SYNTAX = Synergy between Percutaneous Coronary Intervention with TAXUS and Cardiac Surgery; (a) Consider no-touch off-pump CABG in case of porcelain aorta.

TL: Neumann FJ et al. 2018 ESC/EACTS Guidelines on myocardial revascularization. European Heart Journal (2018) 00, 1–96. doi:10.1093/eurheartj/ehy394



## FAVOURS PCI

### Clinical characteristics

- Presence of severe co-morbidity (not adequately reflected by scores)
- Advanced age/frailty/reduced life expectancy
- Restricted mobility and conditions that affect the rehabilitation process

### Anatomical and technical aspects

- MVD **SYNTAX score 0-22**
- Anatomy likely resulting in incomplete revascularization with CABG due to poor quality or missing conduits
- Severe chest deformation or scoliosis
- Sequelae of chest radiation
- Porcelain aorta

## FAVOURS CABG

### Clinical characteristics

- Diabetes
- Reduced LV function (EF  $\leq 35\%$ )
- Contraindication to DAPT
- Recurrent diffuse in-stent restenosis

### Anatomical and technical aspects

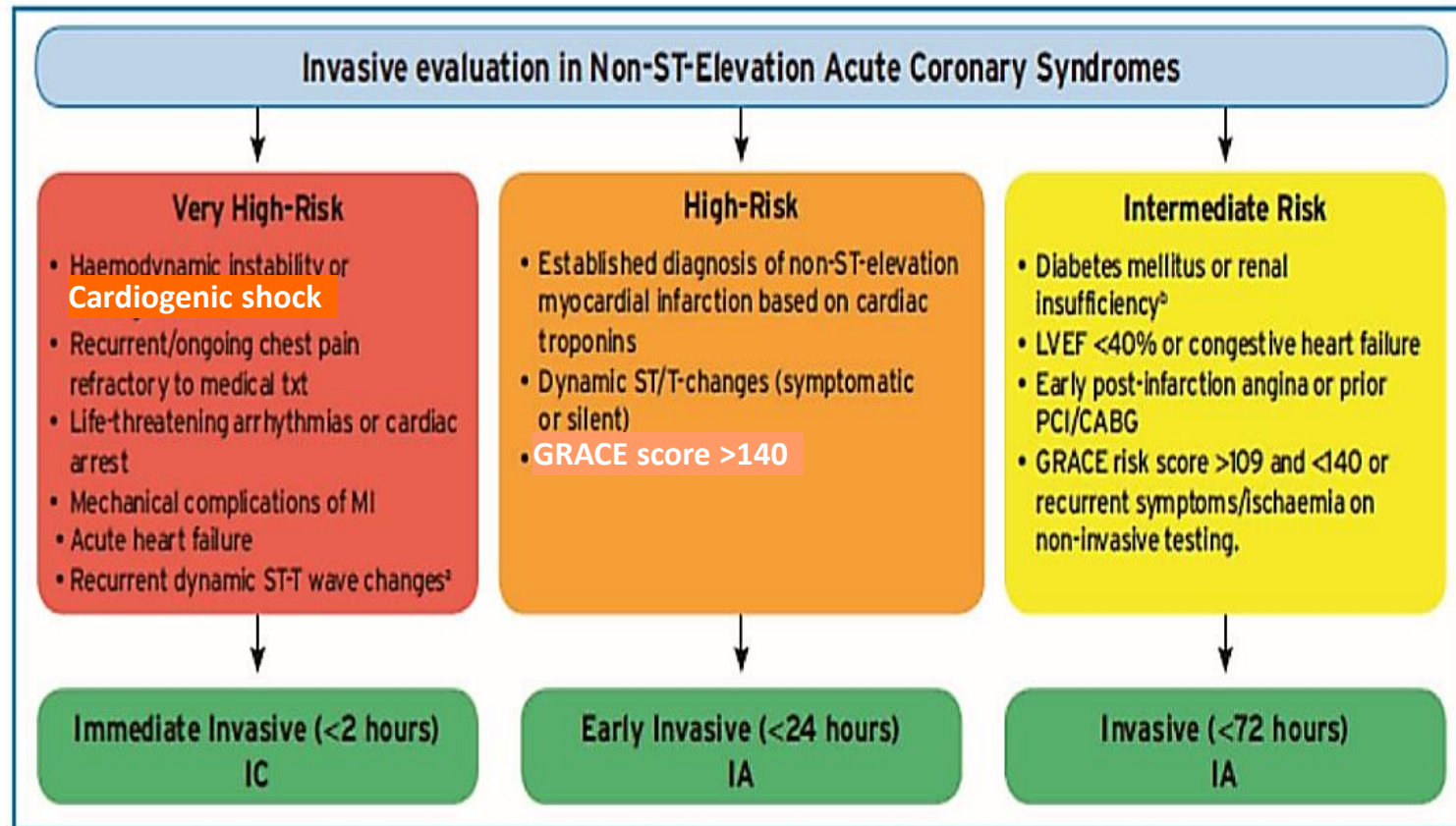
- MVD **SYNTAX score  $\geq 23$**
- Anatomy likely resulting in incomplete revascularization with PCI
- Severely calcified coronary artery lesions limiting lesion expansion

### Need for concomitant interventions

- Ascending aortic pathology with indication for surgery
- Concomitant cardiac surgery



# Selection of non-ST-elevation acute coronary syndrome treatment strategy and timing according to initial risks stratification



© ESC 2018

CABG = coronary artery bypass grafting; GRACE = Global Registry of Acute Coronary Events; LVEF = left ventricular ejection fraction; MI = myocardial infarction; PCI = percutaneous coronary intervention.

<sup>†</sup>Particularly intermittent ST-elevation; <sup>‡</sup>Estimated glomerular filtration rate <60mL/min/1.73m<sup>2</sup>

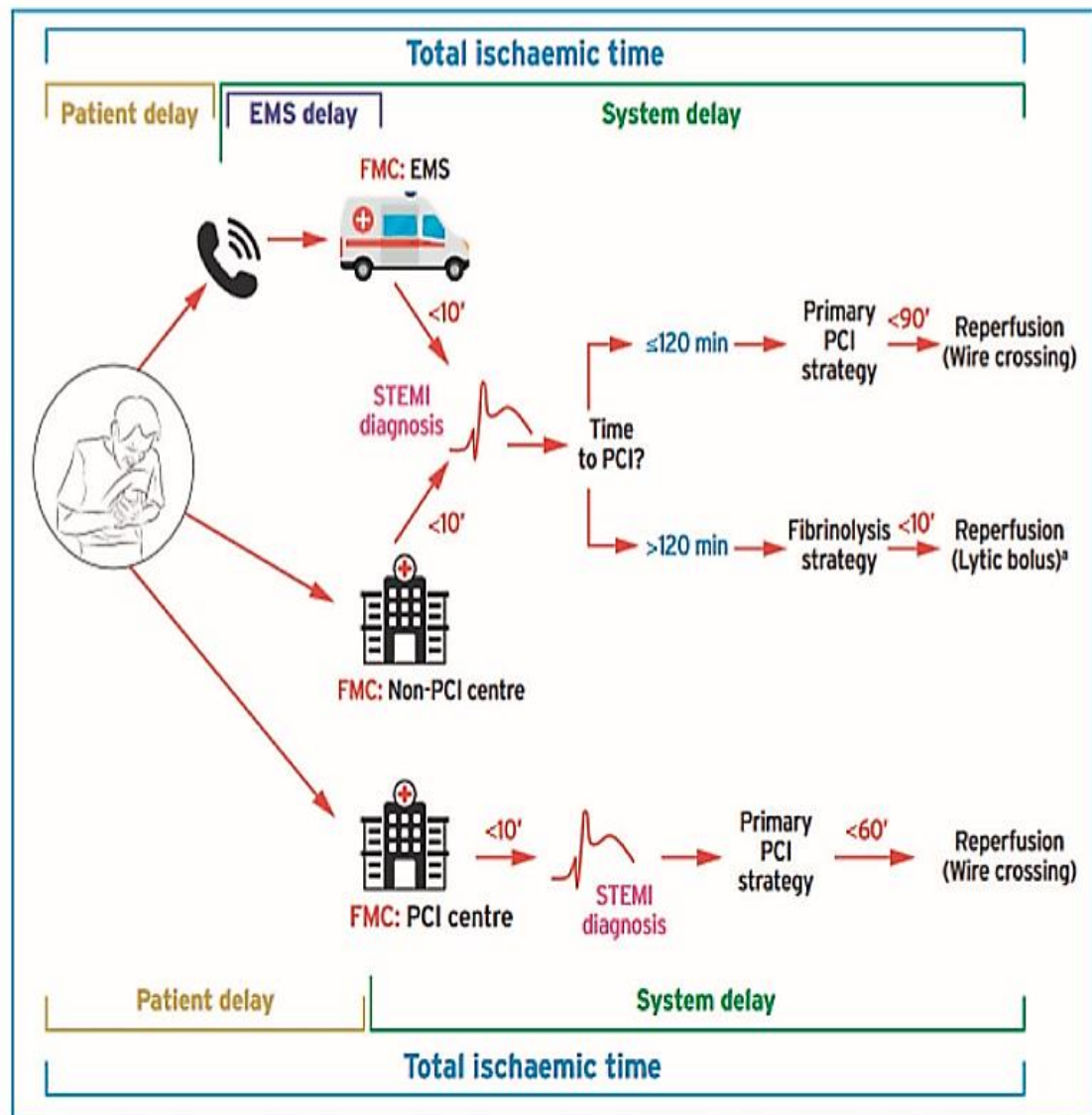
According to ESC NSTEMI-ACS 2015 Guidelines

# Modes of patient's medical contact, components of ischaemia time, and flow chart for reperfusion strategy selection.

TL: Neumann FJ et al. 2018 ESC/EACTS Guidelines on myocardial revascularization. European Heart Journal (2018) 00, 1–96.  
doi:10.1093/eurheartj/ehy394



Pham  
Nguyen  
Vinh



The recommended mode of patient presentation is by alerting the EMS (call national emergency number: 112 or similar number according to region). When STEMI diagnosis is made in the out-of-hospital setting (via EMS) or in a non-PCI centre, the choice of reperfusion strategy is based on the estimated time from STEMI diagnosis to PCI-mediated reperfusion (wire crossing). System delay for patients alerting the EMS starts at the time of phone alert, although FMC occurs when the EMS arrives at the scene. EMS = emergency medical service.

FMC = first medical contact; PCI = percutaneous coronary intervention; STEMI = ST-segment elevation myocardial infarction. \*denotes minutes.

\*Patients receiving fibrinolysis should be transferred to a PCI centre immediately after administration of the lytic bolus.

# Primary PCI for myocardial reperfusion in STEMI: procedural aspects (strategy and technique)

Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
<b>Strategy</b>		
Routine revascularization of <u>non-IRA lesions</u> should be considered in patients with multivessel disease <u>before hospital discharge</u> . <sup>211–214</sup>	IIa	A
CABG should be considered in patients with ongoing ischaemia and large areas of jeopardized myocardium if PCI of the IRA cannot be performed.	IIa	C
In <u>cardiogenic shock</u> , routine revascularization of non-IRA lesions is <u>not recommended</u> during primary PCI. <sup>190</sup>	III	B
<b>Technique</b>		
Routine use of thrombus aspiration is not recommended. <sup>223–226,228</sup>	III	A

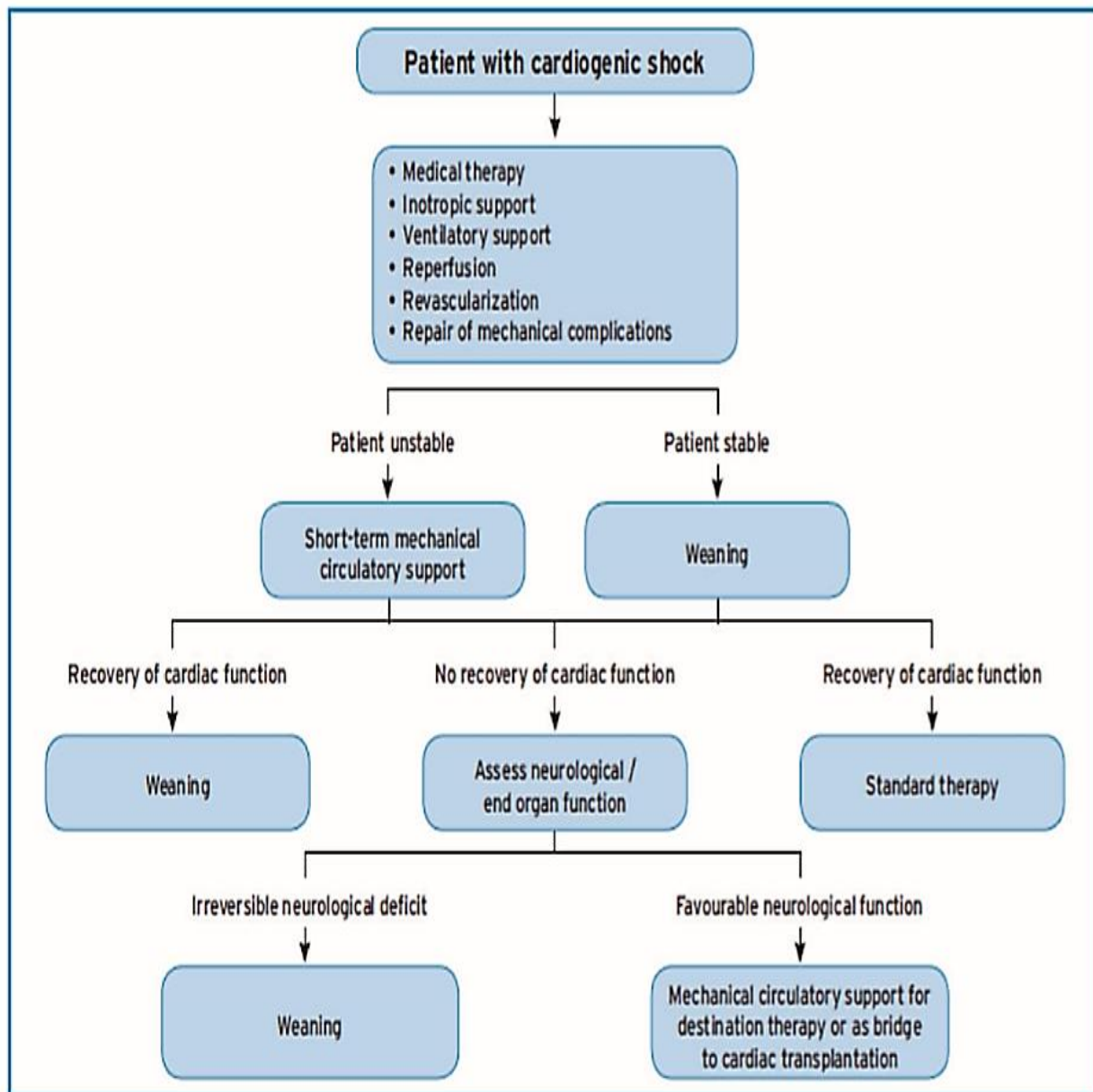


# Algorithm for the management of patients with cardiogenic shock

TL: Neumann FJ et al. 2018 ESC/EACTS Guidelines on myocardial revascularization. European Heart Journal (2018) 00, 1–96. doi:10.1093/eurheartj/ehy394



Pham  
Nguyen  
Vinh

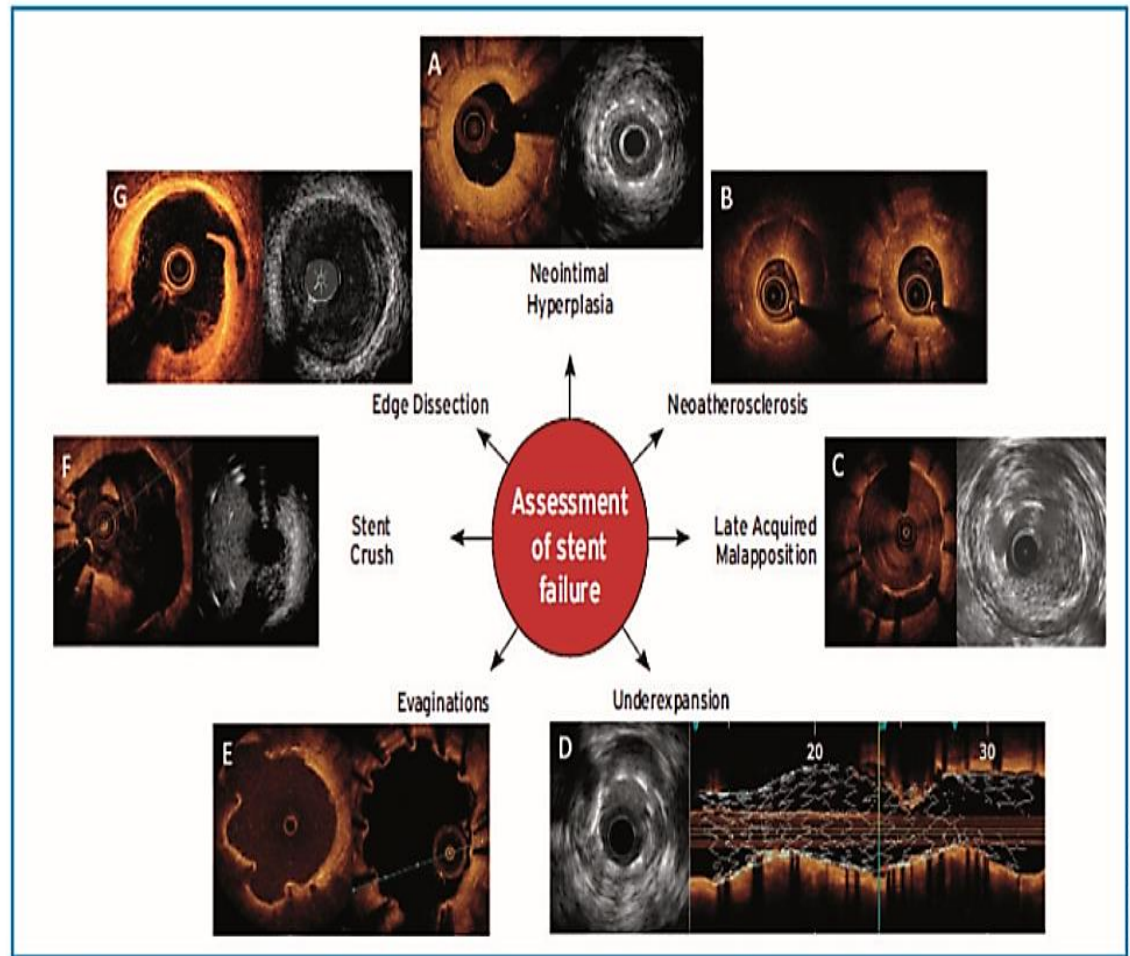


# Intracoronary imaging for the assessment of stent failure

TL: Neumann FJ et al. 2018 ESC/EACTS Guidelines on myocardial revascularization. European Heart Journal (2018) 00, 1–96.  
doi:10.1093/eurheartj/ehy394



Pham  
Nguyen  
Vinh



Examples of intravascular imaging findings (IVUS or OCT) in patients with stent failure. Panel A displays OCT (left) and IVUS (right) examples of in-stent restenosis due to excessive neointimal hyperplasia. Panel B displays two OCT examples of in-stent restenosis due to neoatherosclerosis. Panel C displays OCT (left) and IVUS (right) examples of late acquired malapposition. Panel D displays IVUS (left) and longitudinal OCT reconstruction (right) images of stent underexpansion. Panel E displays two OCT examples of in-stent evaginations, a typical finding of delayed arterial healing. Panel F displays OCT (left) and IVUS (right) examples of stent crush. Panel G displays an OCT (left) and IVUS (right) case of coronary dissection at the stent edge.

IVUS = intravascular ultrasound; OCT = optical coherence tomography.

Intracoronary images for this figure were kindly provided by Drs Nicolas Amabile, Fernando Alfonso, and Gennaro Sardella.

## Recommendations for the prevention of ventricular arrhythmias by revascularization

Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
A <u>primary PCI strategy</u> is recommended in patients with <u>resuscitated cardiac arrest</u> and an ECG consistent with <u>STEMI</u> . <sup>395,397,436,437</sup>	I	B
Urgent angiography (and PCI if indicated) should be considered in patients with <u>resuscitated cardiac arrest without diagnostic ST-segment elevation</u> but with a high suspicion of ongoing myocardial ischaemia.	IIa	C
In patients with electrical storm, urgent coronary angiography and revascularization (as required) should be considered.	IIa	C



## Recommendations for the prevention and treatment of AF in the setting of myocardial revascularization

Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
Perioperative oral beta-blocker therapy is recommended for the prevention of post-operative AF after CABG surgery. <sup>412,438</sup>	I	B
Restoration of sinus rhythm by electrical cardioversion or antiarrhythmic drugs is recommended in post-operative AF with haemodynamic instability.	I	C
Perioperative amiodarone should be considered as prophylactic therapy to prevent AF after CABG surgery. <sup>412,439</sup>	IIa	A
Long-term anticoagulation should be considered in patients with AF after CABG or PCI who are at risk of stroke, considering the individual stroke and bleeding risk. <sup>440,441</sup>	IIa	B
Rate control and anticoagulation should be considered as the initial management of asymptomatic post-operative AF. <sup>442</sup>	IIa	B
Antiarrhythmic drugs should be considered for symptomatic post-operative AF after CABG or PCI in an attempt to restore sinus rhythm.	IIa	C
Surgical occlusion or exclusion of the LAA may be considered for stroke prevention in patients with AF undergoing CABG surgery. <sup>432–434</sup>	IIb	B

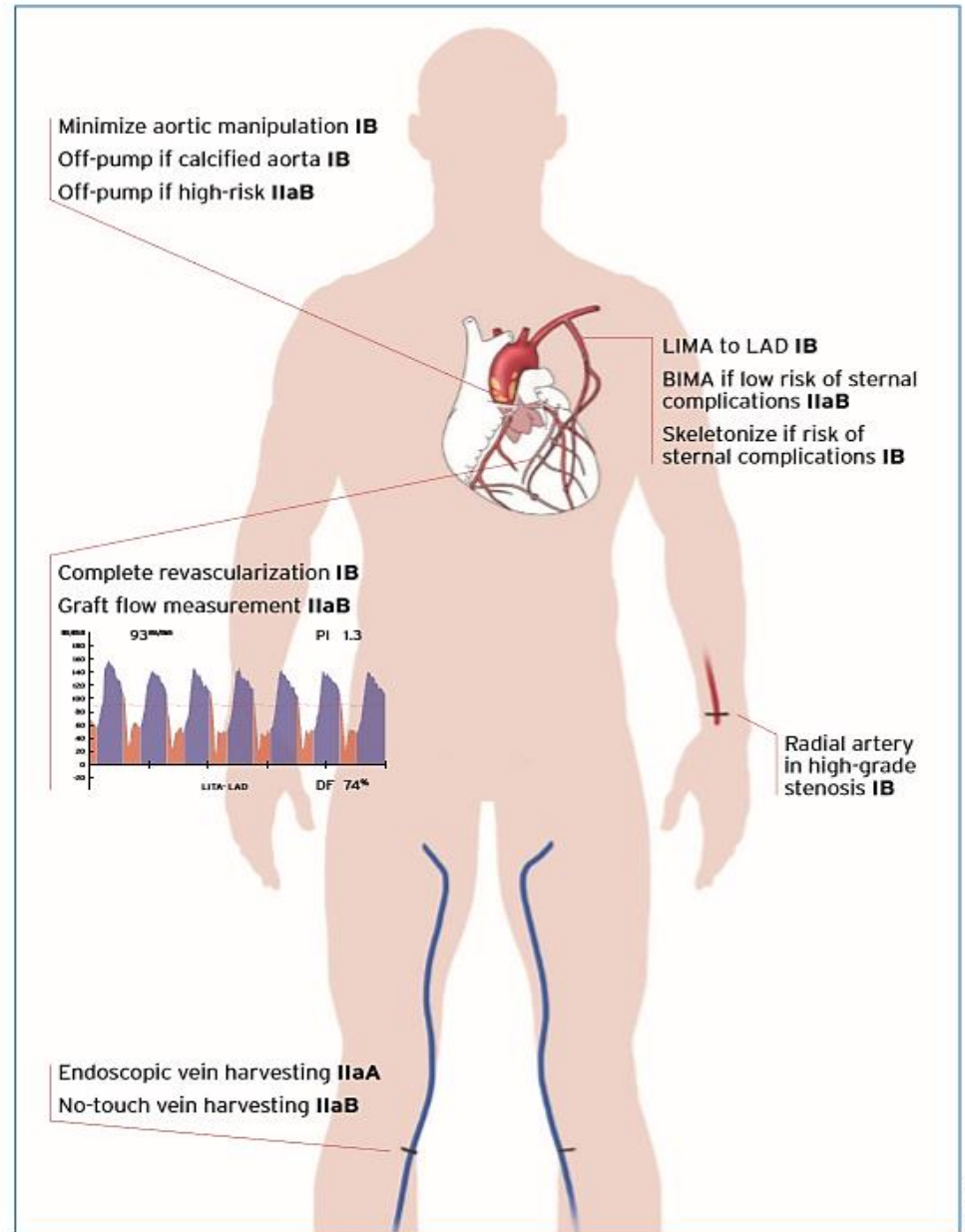
TL: Neumann FJ et al. 2018 ESC/EACTS Guidelines on myocardial revascularization. European

Heart Journal (2018) 00, 1–96. doi:10.1093/eurheartj/ehy394

# Technical aspects of CABG

BIMA = bilateral internal mammary artery; CABG = coronary artery bypass grafting; IMA = internal mammary artery; LAD= left anterior descending coronary artery

TL: Neumann FJ et al. 2018 ESC/EACTS Guidelines on myocardial revascularization. European Heart Journal (2018) 00, 1–96.  
doi:10.1093/eurheartj/ehy394



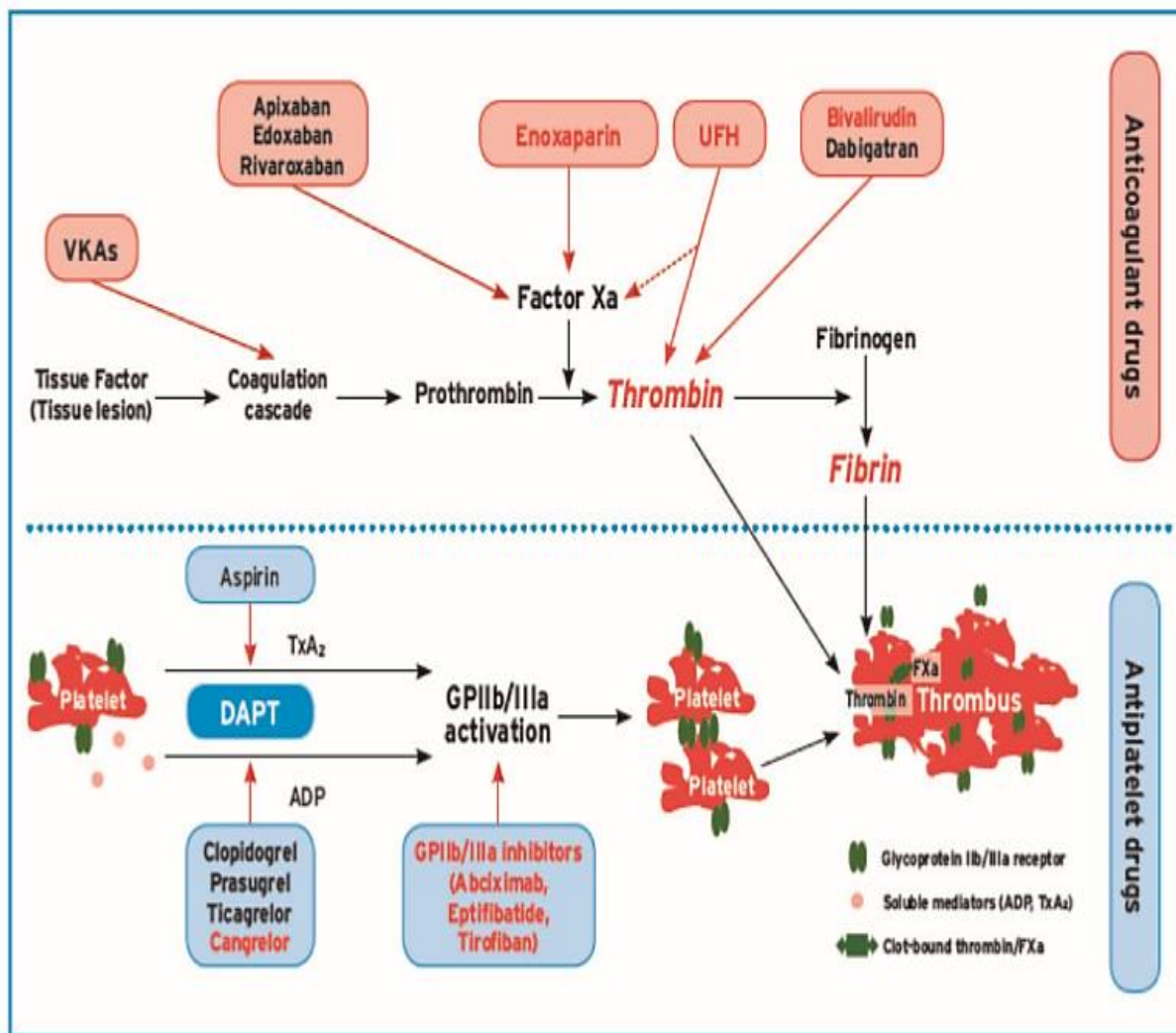


## Antithrombotic treatment for myocardial revascularization and its pharmacological targets.

TL: Neumann FJ et al. 2018  
 ESC/EACTS Guidelines on myocardial revascularization. European Heart Journal (2018) 00, 1–96.  
 doi:10.1093/eurheartj/ehy394



Pham  
 Nguyen  
 Vinh



The figure illustrates anticoagulant and antiplatelet drugs being used during and after myocardial revascularization (percutaneous coronary intervention or coronary artery bypass grafting). Drugs with oral administration are shown in black letters and drugs with preferred parenteral administration in red. ADP = adenosine diphosphate; DAPT = dual antiplatelet therapy; FXa = factor Xa; GP = glycoprotein; TxA<sub>2</sub> = thromboxane A<sub>2</sub>; UFH = unfractionated heparin; VKAs = vitamin K antagonists.

## Doses of antiplatelet and anticoagulant drugs used during and after myocardial revascularization (1)

Antiplatelet drugs	
Aspirin	Loading dose of 150–300 mg orally or 75–150 mg i.v. if oral ingestion is not possible, followed by a maintenance dose of 75–100 mg/day.
Clpidogrel	Loading dose of 600 mg orally, followed by a maintenance dose of 75 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 is recommended. In patients aged >75 years, prasugrel is generally not recommended, but a dose of 5 mg should be used if treatment is deemed necessary.
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 h.
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 h.
Tirofiban	Bolus of 25 µg/kg over 3 min i.v., followed by an infusion of 0.15 µg/kg/min for up to 18 h.
Cangrelor	Bolus of 30 µg/kg i.v. followed by 4 µg/kg/min infusion for at least 2 h or duration of procedure, whichever is longer.

## Doses of antiplatelet and anticoagulant drugs used during and after myocardial revascularization (2)

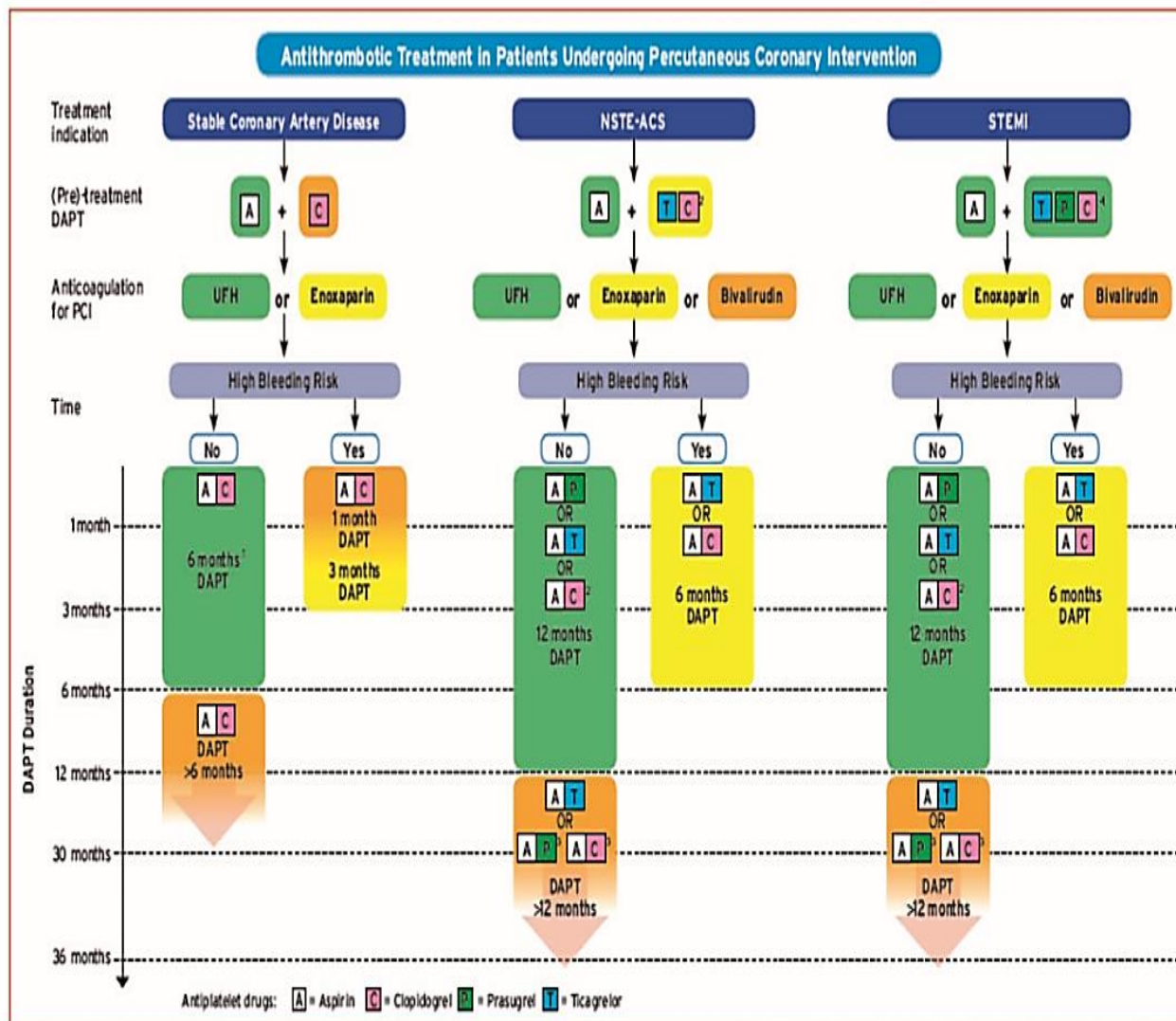
Anticoagulant drugs for PCI	
Unfractionated heparin	<ul style="list-style-type: none"> <li>• 70–100 U/kg i.v. bolus when no GP IIb/IIIa inhibitor is planned.</li> <li>• 50–70 U/kg i.v. bolus with GP IIb/IIIa inhibitors.</li> </ul>
Enoxaparin	0.5 mg/kg i.v. bolus.
Bivalirudin	0.75 mg/kg i.v. bolus followed by i.v. infusion of 1.75 mg/kg/h for up to 4 h after the procedure as clinically warranted.
Oral anticoagulant drugs (concomitant treatment after PCI)	
Vitamin K antagonists (e.g. warfarin, phenprocoumon)	Dosing is based on INR value and the respective clinical indication.
Apixaban	Maintenance doses of 5 and 2.5 <sup>a</sup> mg b.i.d.
Dabigatran	Maintenance doses of 150 and 110 mg b.i.d.
Edoxaban	Maintenance doses of 60 and 30 <sup>a</sup> mg/day
Rivaroxaban	Maintenance doses of 20 and 15 <sup>a</sup> mg/day, and 2.5 mg b.i.d. (vascular dose).

TL: Neumann FJ et al. 2018 ESC/EACTS Guidelines on myocardial revascularization. European Heart Journal (2018) 00, 1–96. doi:10.1093/eurheartj/ehy394

# Algorithm for the use of antithrombotic drugs in patients undergoing PCI

High bleeding risk is considered as an increased risk of spontaneous bleeding during DAPT (e.g. PRECISE-DAPT score > 25). Colour-coding refers to the ESC classes of recommendations (green= class I; yellow= class IIa; and orange = class IIb).

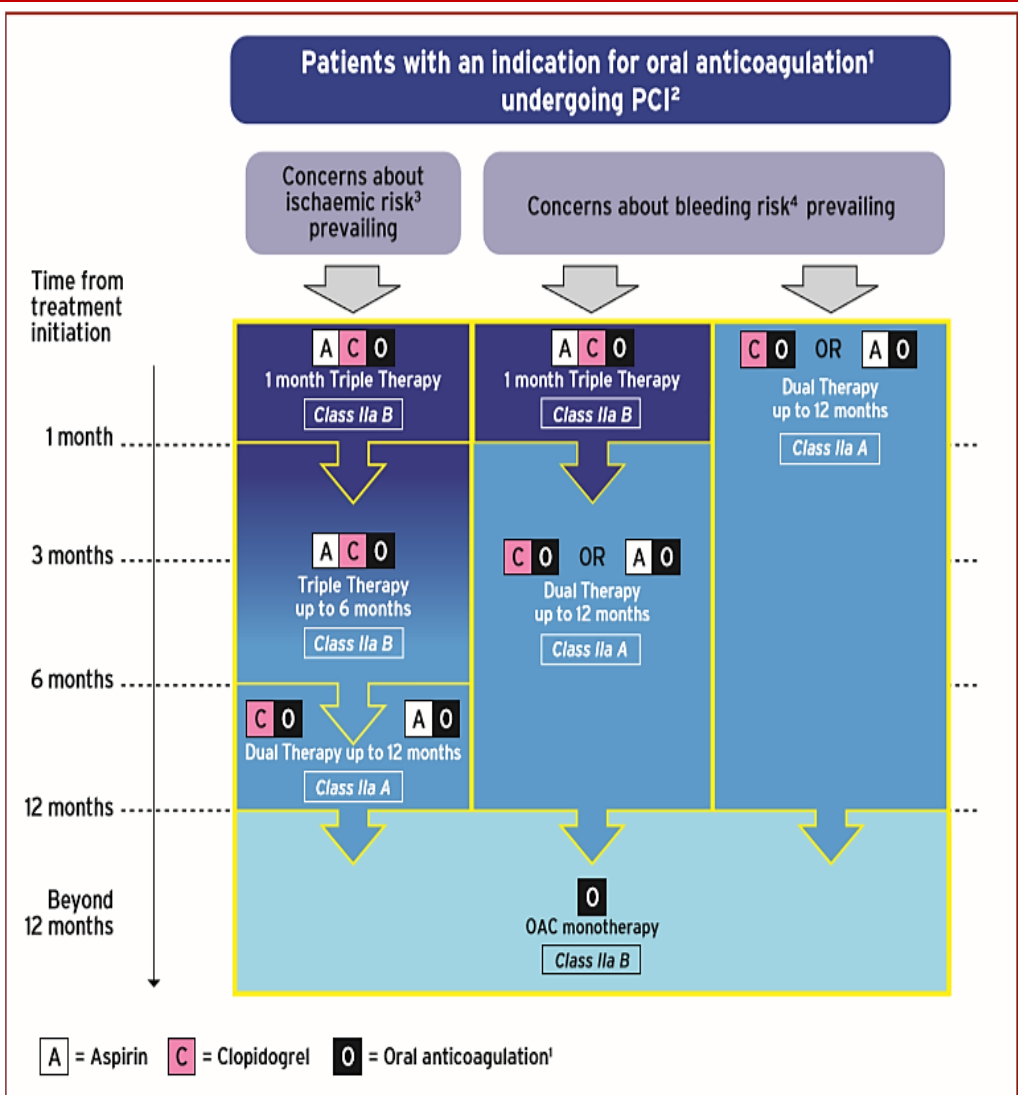
\* Ticagrelor > Clopidogrel



DAPT = dual antiplatelet therapy; DCB = drug-coated balloon; NSTEMI-ACS = non-ST-elevation acute coronary syndrome; PCI = percutaneous coronary intervention; PRECISE-DAPT = Predicting bleeding Complications in patients undergoing Stent implantation and subsequent Dual Antiplatelet Therapy; STEMI = ST-elevation myocardial infarction; UFH = unfractionated heparin.  
 Colour-coding refers to the ESC classes of recommendations (green = Class I; yellow = Class IIa; orange = Class IIb).  
 \*After PCI with DCB 6 months DAPT should be considered (class IIa) - \*Clopidogrel if patient is not eligible for a treatment with prasugrel or ticagrelor; or in a setting of DAPT de-escalation (Class IIb).  
 †Clopidogrel or prasugrel if patient is not eligible for a treatment with ticagrelor - \*Pretreatment before PCI (or at the latest at the time of PCI) clopidogrel if potent P2Y12 inhibitors are contraindicated or not available. (For scores see Supplementary Table 4).  
 High bleeding risk is considered as an increased risk of spontaneous bleeding during DAPT (e.g. PRECISE-DAPT score > 25)

# Algorithm for dual antiplatelet therapy in patients with an indication for OAC undergoing PCI

\* A + Clopidogrel



TL: Neumann FJ at al. 2018 ESC/EACTS Guidelines on myocardial revascularization. European Heart Journal (2018) 00, 1–96. doi:10.1093/eurheartj/ehy394



Colour-coding refers to the number of concomitant antithrombotic medication(s). Triple therapy denotes treatment with DAPT plus oral anticoagulant (OAC). Dual therapy denotes treatment with a single antiplatelet agent (aspirin or clopidogrel) plus OAC.  
 ABC = Age, Biomarkers, Clinical history; AF = atrial fibrillation; HAS-BLED = Hypertension, Abnormal renal/liver function, Stroke, Bleeding history or predisposition, Labile INR, Elderly, Drugs/alcohol concomitantly; VKA = vitamin K antagonist.  
<sup>1</sup>Non-vitamin K antagonist oral anticoagulant (NOAC) preferred over VKA in patients with non-valvular AF. (Class IIaA).  
<sup>2</sup>Periprocedural administration of aspirin and clopidogrel during PCI is recommended irrespective of the treatment strategy.  
<sup>3</sup>High ischaemic risk is considered as an acute clinical presentation or anatomical/procedural features which might increase the risk for myocardial infarction.  
<sup>4</sup>Bleeding risk can be estimated by HAS-BLED or ABC score.

# Medical therapy, secondary prevention, and strategies for follow-up (1)

TL: Neumann FJ et al. 2018 ESC/EACTS Guidelines on myocardial revascularization. European Heart Journal (2018) 00, 1–96.  
doi:10.1093/eurheartj/ehy394



Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
After CABG or PCI for AMI, participation in a cardiac rehabilitation programme is recommended to improve patient outcomes. <sup>777</sup>	I	A
It is recommended that <u>secondary prevention measures</u> , including medical therapy and <u>lifestyle changes</u> , are started and reinforced after myocardial revascularization. <sup>683,778–785</sup>	I	A
It is recommended that patients are <u>re-evaluated</u> after myocardial revascularization (e.g. at <u>3 months and thereafter</u> , at least on an annual basis) in order to reassess symptoms and adherence to secondary prevention measures, and reinforce medical therapy and lifestyle changes when appropriate.	I	C

## Medical therapy, secondary prevention, and strategies for follow-up (2)

TL: Neumann FJ et al. 2018 ESC/EACTS Guidelines on myocardial revascularization. European Heart Journal (2018) 00, 1–96.  
doi:10.1093/eurheartj/ehy394



Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
<b>Symptomatic patients</b>		
Coronary angiography is recommended in patients with intermediate- to high-risk findings <sup>c</sup> at stress testing.	<b>I</b>	<b>C</b>
An imaging stress test should be considered in patients with prior revascularization over stress ECG. <sup>786</sup>	<b>IIa</b>	<b>B</b>
<b>Asymptomatic patients</b>		
Surveillance by non-invasive imaging-based stress testing may be considered in high-risk patient subsets 6 months after revascularization.	<b>IIb</b>	<b>C</b>
After high-risk PCI (e.g. unprotected LM stenosis), late (3–12 months) surveillance angiography may be considered, irrespective of symptoms.	<b>IIb</b>	<b>C</b>
Routine non-invasive imaging-based stress testing may be considered 1 year after PCI and >5 years after CABG.	<b>IIb</b>	<b>C</b>

# Chiến lược giảm chảy máu liên quan đến can thiệp ĐMV

- Anticoagulant doses adjusted to bodyweight and renal function, especially in women and elderly patients.
- **Radia** approach preferred.
- **Proton pump inhibitors in patients on DAPT** at higher than average risk of gastrointestinal bleeds (i.e. history of gastrointestinal ulcer/haemorrhage, anticoagulant therapy, chronic NSAIDs/corticosteroid use, or two or more among age  $\geq 65$  years, dyspepsia, gastrooesophageal reflux disease, *Helicobacter pylori* infection, and chronic alcohol use).
- In patients on **OAC**
  - PCI performed without interruption of VKAs or NOACs.
  - In patients on VKAs, do not administer UFH if INR value  $>2.5$ .
  - In patients on NOACs, regardless of the timing of the last administration of NOACs, add additional low-dose parenteral anticoagulation (e.g. enoxaparin 0.5 mg/kg i.v. or UFH 60 IU/kg).
  - Aspirin indicated but avoid pretreatment with P2Y<sub>12</sub> inhibitors.
  - GPIIb/IIIa inhibitors only for bailout of periprocedural complications.

DAPT = dual (oral) antiplatelet therapy; GPIIb/IIIa = glycoprotein IIb/IIIa; INR = international normalised ratio; NOACs = non-vitamin K antagonist oral anticoagulants; NSAIDs = non-steroidal anti-inflammatory drugs; OACs = oral anticoagulants; PCI = percutaneous coronary intervention; UFH = unfractionated heparin; VKAs = vitamin K antagonists.





# Điều trị lâu dài sau can thiệp ĐMV

- Các thuốc giúp kéo dài đời sống
- Thay đổi lối sống:
  - Ăn chay (Vegans)?
  - Ăn kiểu paleo?
  - Ăn chế độ trung dung?
  - Tập thể dục
- Vấn đề kháng kết tập tiểu cầu kép

# Điều trị lâu dài sau tái lưu thông ĐMV

- Siêu âm tim trước và sau tái thông ĐMV
- Giảm cân
- Thể dục: 30-60 phút/ngày
- Ổn định đường huyết, huyết áp, lipid máu
- LDL-C < 70 mg% hoặc < 50 mg%
- Chế độ ăn: vegans (nguyên TT Mỹ B.Clinton); paleo food; rau củ quả, tinh bột kèm cá
- Chống trầm cảm<sup>+++</sup>
- Chủng ngừa cúm mỗi năm
- Các thuốc kéo dài đời sống: UCMC, chẹn beta, statins, chống kết tập tiểu cầu

# Các bệnh nhân đặc biệt cần khảo sát TNGS bằng hình ảnh sớm

- Tất cả b/n ST chênh sau can thiệp hoặc BCĐMV tối khẩn cần khảo sát trước ra viện hoặc rất sớm sau ra viện
- Bệnh nhân có nghề nghiệp cần an toàn cao (TD: phi công, tài xế...) hoặc vận động viên
- Sử dụng thuốc ức chế 5 –phosphodiesterase (sildenafil, tadalafil...)
- Bệnh nhân đột tử được cứu sống
- Bệnh nhân tái lưu thông ĐMV không hoàn toàn
- Bệnh nhân có biến chứng khi can thiệp (bóc tách, NMCT chu phẫu, gỡ bỏ nội mạc khi BCĐMV...)
- Bệnh nhân ĐTĐ
- Bệnh nhiều nhánh ĐMV kèm tổn thương còn sót lại hoặc TMCT yên lặng

# Cytochrome P450 và các thuốc ức chế bơm proton

# Cytochrome P450

- Một nhóm enzymes nằm trong heme, ở vị trí màng của endoplasmic reticulum
- Hai nhiệm vụ sinh học:
  - Chuyển hóa các chất nội sinh
  - Lọc các chất ngoại sinh

# Cytochrome P450 Families

Family	Subfamily	Subtype
<b>CYP1</b>	<b>A</b>	<b>1A1, 1A2</b>
<b>CYP2</b>	<b>A</b>	<b>2A6</b>
	<b>B</b>	<b>2B6</b>
	<b>C</b>	<b>2C8, 2C9, 2C10, 2C18, 2C19</b>
	<b>D</b>	<b>2D6</b>
	<b>E</b>	<b>2E1</b>
<b>CYP3</b>	<b>A</b>	<b>3A3, 3A4, 3A5, 3A7</b>

# Tính đa dạng di truyền

Một vài enzymes CYP P450 có đa kiểu hình di truyền, chia ra các nhóm:

- Chất chuyển hóa rộng rãi (Extensive Metabolisers, EM)
- Chất chuyển hóa trung gian (Intermediate Metabolisers, IM)
- Chất chuyển hóa kém (Poor Metabolisers, PM)

# CYP2C Subfamily

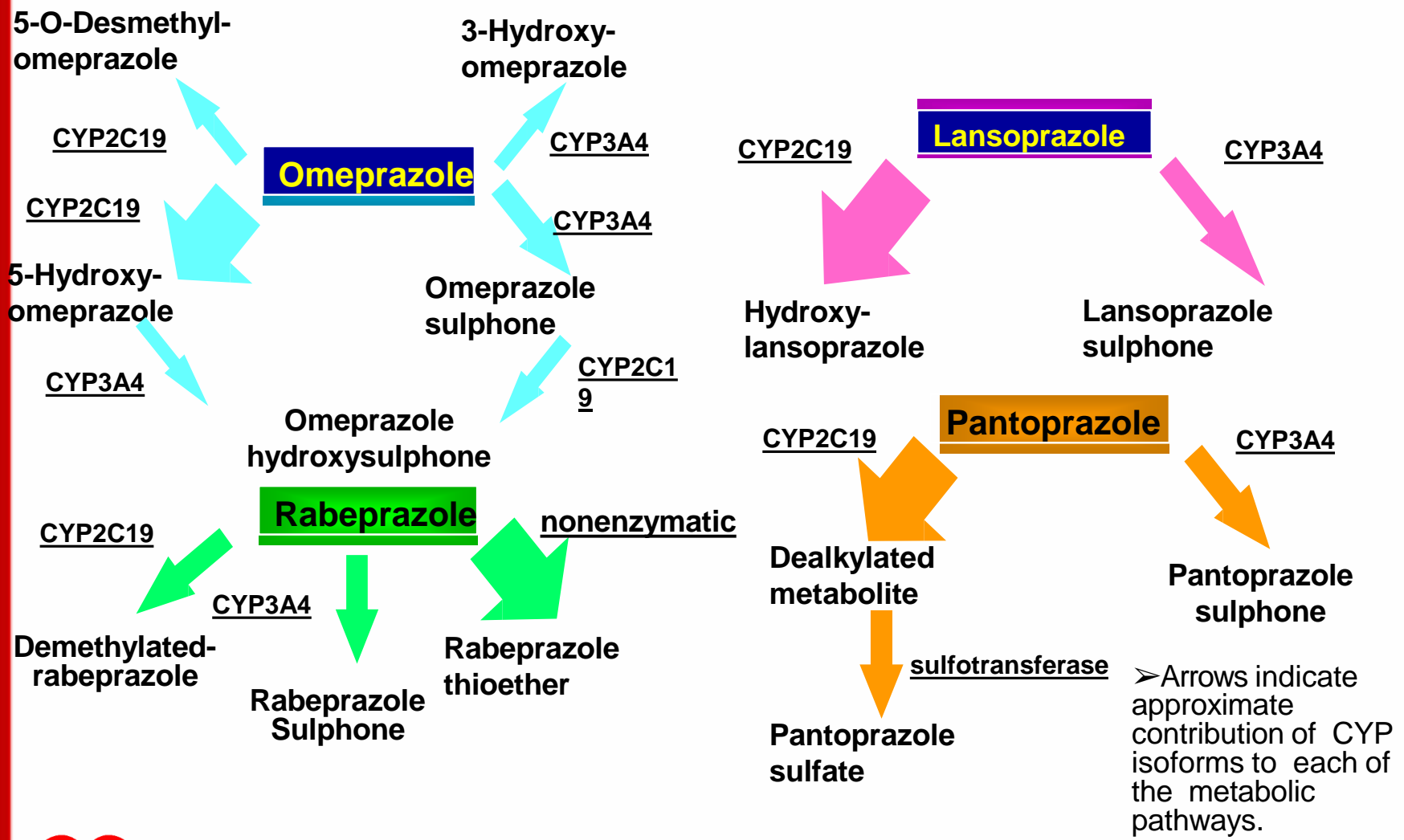
- Enzyme chính là 2C19
- Hoạt tính có 2 kiểu
- Tần suất PMs:
  - 2-6% ở người Caucasians
  - Tới 22% ở người châu Á
- Khiếm khuyết chính là đột biến CYP2C19m1
- Khiếm khuyết phụ là CYP2C19m2 (chỉ có ở người châu Á)



# Phân bố kiểu hình CYP2C19 theo chủng tộc khác nhau

	<b>N</b>	<b>EM</b>	<b>IM</b>	<b>PM</b>
<b>Chinese</b>	<b>121</b>	<b>26.4%</b>	<b>49.6%</b>	<b>24.0%</b>
<b>Japanese</b>	<b>96</b>	<b>36.5%</b>	<b>45.8%</b>	<b>17.7%</b>
<b>Thai</b>	<b>121</b>	<b>37.2%</b>	<b>47.1%</b>	<b>15.7%</b>
<b>Vietnamese</b>	<b>90</b>	<b>40.0%</b>	<b>40.0%</b>	<b>20.0%</b>
<b>Caucasians</b>	<b>1,356*</b>	<b>72.6%</b>	<b>25.3%</b>	<b>2.1%</b>

# Các đường chuyển hóa của PPIs và các đồng dạng Cyt P450



Pham  
Nguyen  
Vinh

Ishizaki, T. and Horai, Y. : Aliment. Pharmacol Ther. 1999: 13 (Suppl.3); 27-36

# Hoạt tính dược học của Rabeprazole và chất chuyển hóa

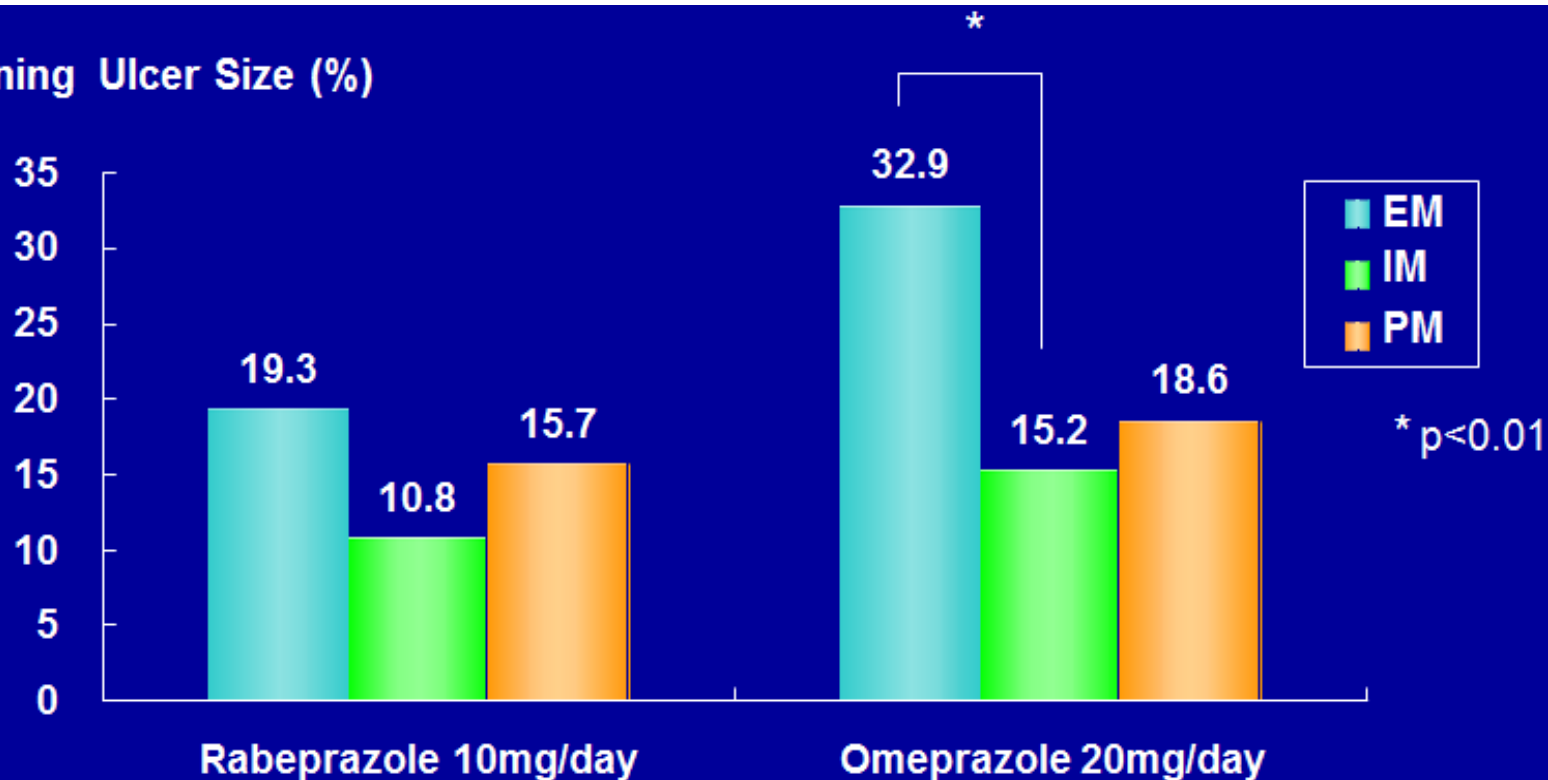
Compound	Pharmacologically Active or Inactive
Rabeprazole sodium	Active (IC <sub>50</sub> : 0.20μM)
Thioether	Inactive (IC <sub>50</sub> : ≥100μM)
Sulfone	Inactive (IC <sub>50</sub> : >100μM)
Desmethyl ( <i>metabolites by CYP2C19</i> )	Active (IC <sub>50</sub> : 0.29μM)
Desmethyl Thioether	Inactive (IC <sub>50</sub> : >100μM)
Mercapturic Acid	Inactive (IC <sub>50</sub> : >100μM)
Thioether Carboxylic Acid	Inactive (IC <sub>50</sub> : >100μM)

- IC<sub>50</sub> for H, K, - ATPase Inhibition

# Hiệu quả lành sẹo sớm loét tiêu hóa

Remaining Ulcer Lesion by Phenotype (%) after 2-week therapy of rabeprazole or omeprazole

Remaining Ulcer Size (%)



Number of patients:

Rabeprazole group: 12 for EM, 18 for IM, 6 for PM

Omeprazole group: 15 for EM, 17 for IM, 5 for PM

Ando et. al. DDW 2002, San Francisco

# Tóm tắt: ảnh hưởng của di truyền đa dạng CYP2C19 trên ức chế bơm protons

- Ethnic differences
- Pharmacokinetics
- Onset and potency of acid inhibitory effect
- Clinical outcomes

# Rabeprazole

- Ít phụ thuộc CYP2C19 trong chuyển hóa
- Rất ít ảnh hưởng của CYP2C19
- Hiệu quả hằng định trên tất cả các chất chuyển hóa, do đó:
  - Không cần quan tâm đến trạng thái chuyển hóa
  - Không tốn chi phí khảo sát tình trạng bệnh (Td: trắc nghiệm di truyền)

# Kết luận

- Điều trị bệnh ĐMV:
  - Thuốc giảm TMCB
  - Thuốc kéo dài đời sống
  - Thời điểm tái lưu thông ĐMV: phù hợp
- Điều trị kháng kết tập tiểu cầu kép: KC 2018 → có thể trên 1 năm
- Lựa chọn đúng ức chế bơm proton khi sử dụng clopidogrel kèm aspirin: rabeprazole hoặc pantoprazole

