Acute coronary syndrome

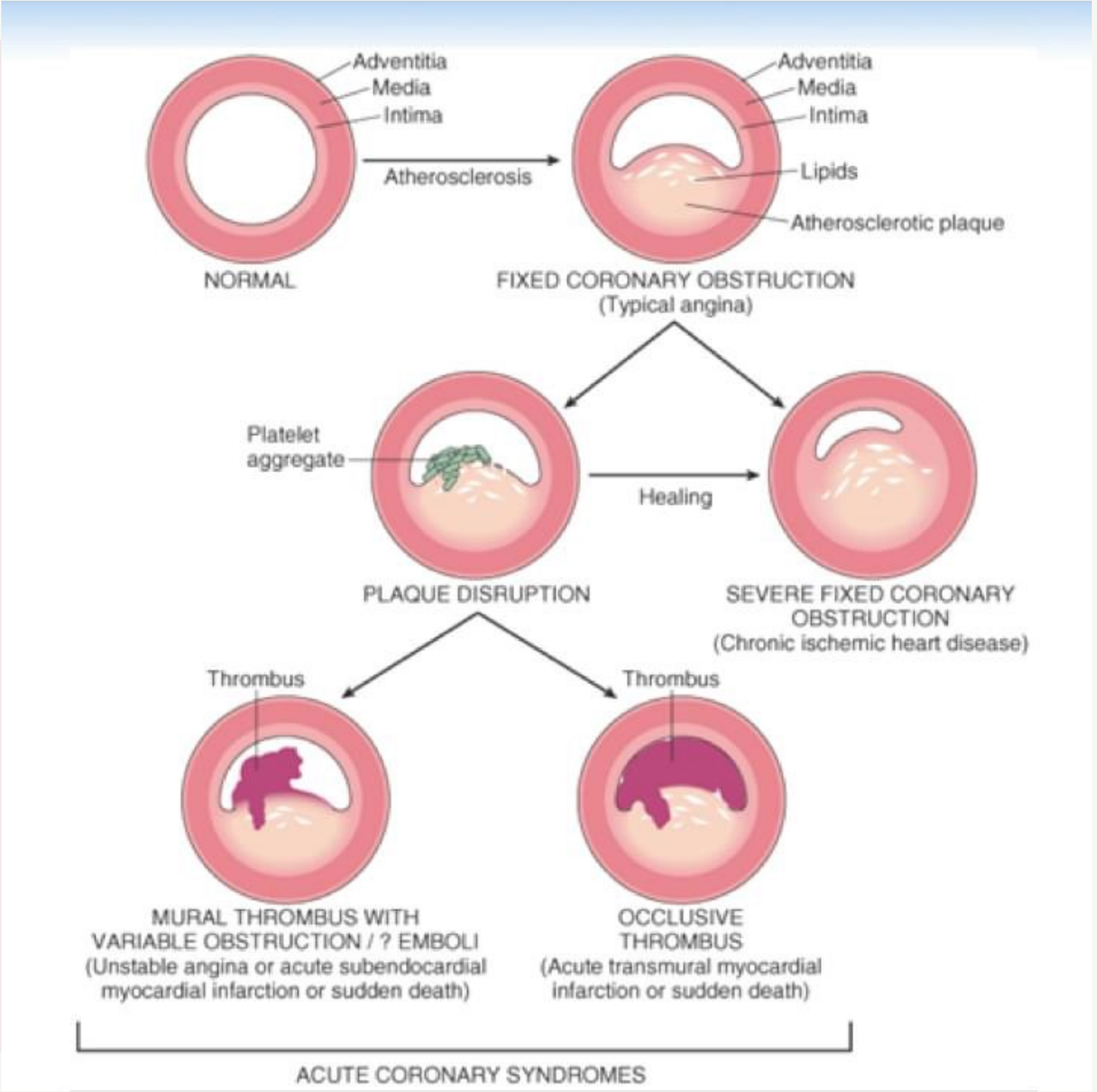
Smart refer

Definition

- Chronic stable angina (CSA) : ขาดแบบเรื้อรัง ค่อยๆ ตีบเป็นเดือน ๆ ปีๆ อาการไม่รุนแรง
- Silent ischemia (SI): ไม่มีเจ็บหน้าอก ตรวจพบโดยบังเอิญ
- Acute coronary syndrome (ACS) : กล้ามเนื้อหัวใจขาดเลือดเฉียบพลัน จากการตีบหรืออุดตันหลอดเลือด แบ่งเป็น 2 รูปแบบใหญ่คือ
    1.ST elevate ACS คือ STEMI
    2.Non-ST elevate ACS ซึ่งแบ่งเป็น Unstable angina (UA) และ NSTEMI

Pathophysiology

- เริ่มจากการสะสมของไขมัน fatty streak -> atherosclerotic plaque
- stable plaque = CSA
- เมื่อไหร่ที่เกิด plaque rupture -> ACS
- partial occlusion -> UA & NSTEMI
- total occlusion -> STEMI



Diagnosis

1.History and Physical examination
- ลักษณะอาการเจ็บแน่นหน้าอก เวลาที่แน่น อาการปวดร้าว
- autonomic symptoms: เหงื่อแตก ใจสั่น
- ประวัติเดิม previous CSA, Old MI
- risk factors: อายุ > 40 ปี HT, DM, DLP, active smoking, family history of CVD

2.EKG 12-lead
- Significant ST depression (>= 0.1 mV)
- ST elevation with reciprocal changes
- T wave changes

3.Cardiac enzyme

Management in UA/NSTEMI

- Initial

M : Morphine ลดปวด 1-5 mg IV ยกเว้น BP drops

O : Oxygen keep SpO2 > 94% ถ้า SpO2 ดีอยู่แล้วไม่จำเป็นต้องให้

N : Nitrates ถ้าให้ morphine แล้วยังปวดอยู่

A : Anti-platelet

Dual anti-platelet therapy (DAPT)

1. ASA ลด platelet aggregration ลด mortality

Dose: ASA 80-325 mg/day life long C/I bleeding tendency, allergy

2. P2Y12 receptor inhibitor เช่น Clopidogrel, Ticagrelol, Prasugrel เสริมฤทธิ์ยับยั้ง platelet aggregration แต่อาจเพิ่มโอกาสเกิดเลือดออกได้ ควรให้อย่างน้อย 12 เดือน

Dose

- Clopidogrel (PLAVIX)
  If invasive -> load 600 mg then 75 mg OD
  If conservative -> load 300 mg then 75 mg OD (if Age > 75 mg load แค่ 75 mg)
- Prasugrel load 60 mg then 10 mg OD
- Ticagrelor load 180 mg then 90 mg BID

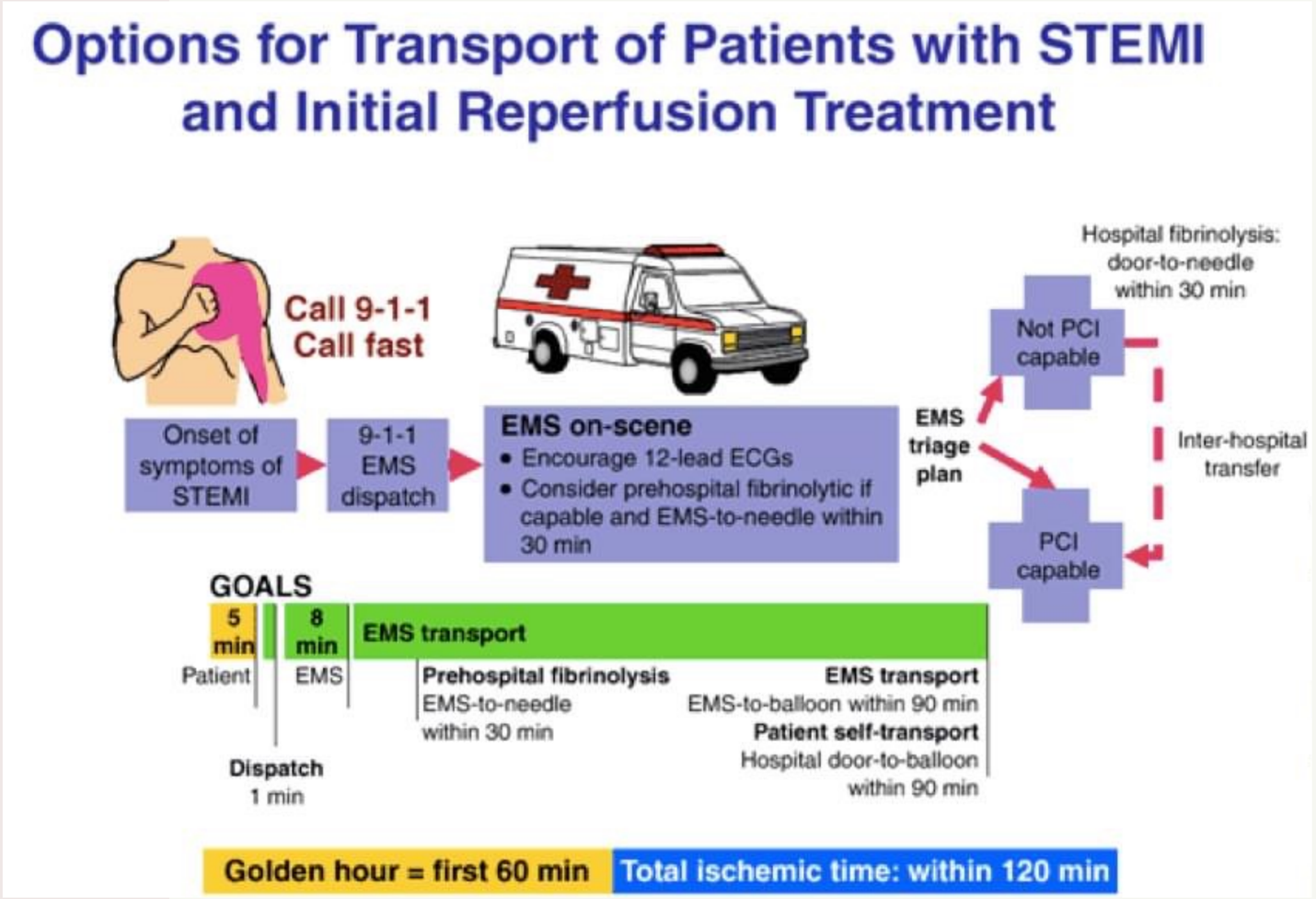
Management in STEMI

- Initial: same UA/NSTEMI
- Reperfusion:
  - PCI
  - Fibrinolytic

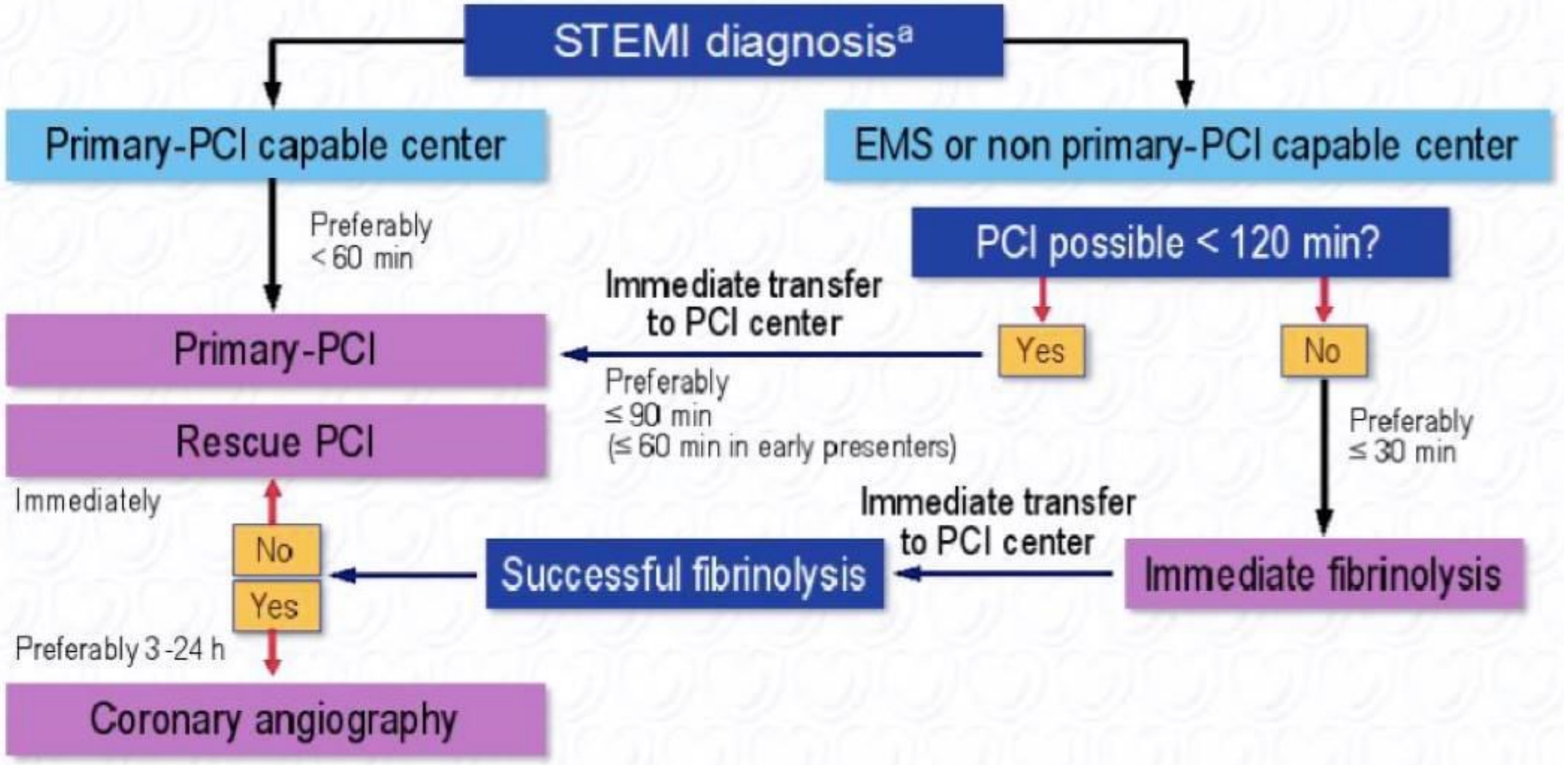
Management in STEMI

- 1st contact to PCI < 120 min
- Door to PCI < 90 min
- Door to needle < 30 min

Contraindication ต่อ Fibrionolytic ที่ควรรู้คือ
Intracranial hemorrhage, hemorrhagic stroke at anytime, AVM, mass or tumor in brain, coagulopathy, recent stroke, MI



Prehospital and in-hospital management, and reperfusion strategies within 24 h of FMC



[a] The time point the diagnosis is confirmed with patient history and ECG ideally within 10 min from the first medical contact (FMC). All delays are related to FMC (first medical contact).

Cath = catheterization laboratory; EMS = emergency medical system; FMC = first medical contact; PCI = percutaneous coronary intervention; STEMI = ST-segment elevation myocardial infarction.

European Heart Journal (2012) 33, 2569–2619
doi:10.1093/eurheartj/ehs215

www.escardio.org/guidelines

EUROPEAN SOCIETY OF CARDIOLOGY®

Management of Cardiovascular Conditions (1)

Hypertension

- Target BP : < 140/90 mmHg
- Medication of choice : ACEI/ARB (preferred if albuminuria), dihydropyridine CCB, thiazide-like diuretics, β-blocker (if previous MI or HF)
- *More intensive target < 130/80 mmHg may be considered in high-risk patients with 10-year ASCVD risk ≥ 15% and at low risk for hypotension and/or adverse drug effects.*

- Recommendation in-line with ACC/AHA 2017 Hypertension Guideline and assumes the universal benefit derived from lower BP on CV outcomes based on **SPRINT trial** (N = 9,361 non-diabetic patients; intensive BP control (SBP < 120 mmHg) ↓ primary CV outcomes (5-point MACEs) by 25%).
- In contrast, **ACCORD BP trial** (which directly studied in 4,733 diabetic patients with ASCVD or multiple CV risk factors) failed to show a reduction in CV outcomes (3-point MACEs) in the intensive arm (SBP < 120 mmHg).
- Such apparently divergent results could be due to differences in the study designs, chance, and/or different mechanisms underlying cardiovascular comorbidities among DM and non-DM patients.

Hyperlipidemia

- Recommendation based on AHA/ACC 2018 Blood Cholesterol Guideline
- ASCVD risk factors : e.g. HT, DM, smoking, family Hx of premature CVD, CKD, albuminuria

(1) Statin

Primary Prevention

- Age 40-75 yrs regardless of ASCVD risk → moderate-intensity statin (class I)
- Age 40-75 yrs + multiple ASCVD risk factors → high-intensity statin with target ↓ LDL ≥ 50% (class IIa)

Secondary Prevention

- Age ≤ 75 yrs + prior ASCVD → high-intensity statin with target ↓ LDL ≥ 50% (class I)
- Age > 75 yrs + prior ASCVD → high or moderate-intensity statin as tolerable with target ↓ LDL ≥ 30% (class IIa); discuss risk and benefit before initiating statin in this group of patients.

Very high-risk* : Multiple major ASCVD events OR 1 major ASCVD event + multiple high-risk conditions

Major ASCVD events :

- Recent ACS < 12 months
- Hx of MI (other than recent ACS)
- Hx of ischemic stroke
- Symptomatic PAD (Hx of claudication with ABI < 0.85, or previous revascularization or amputation)

High-risk conditions :

- Age ≥ 65 yrs
- Heterozygous familial hypercholesterolemia
- Hx of prior CABG or PCI outside of major ASCVD events
- ***DM***
- HT
- CKD (eGFR 15-59 ml/min)
- Current smoking

High-intensity statins

- Atorvastatin 40-80 mg/day
- Rosuvastatin 20-40 mg/day
  (max. in Asians = 20 mg/day)

Moderate-intensity statins

- Atorvastatin 10 mg/day
- Rosuvastatin 10 mg/day
- Simvastatin 20-40 mg/day
- Pravastatin 40 mg/day
- Lovastatin 40 mg/day
- Fluvastatin 40 mg BID

(2) Combination Therapy

IMPROVE-IT trial : ezetimibe (10 mg) + simvastatin (40 mg) combination (avg LDL 54 mg/dl) ↓ 5-point MACEs by 6.4% and ↓ CV death by 10% compared to simvastatin alone (avg LDL 70 mg/dl) in post-ACS patients at avg. 6 yrs; subgroup analysis showed enhanced benefit of this combination in DM (↓ RR of 3-point MACEs by 15%) and in non-DM with high TIMI risk score (↓ RR of composite 3-point MACEs by 18%).

■ ***Drugs with proven CV benefit***

- If LDL still ≥ 70 mg/dl despite on maximally tolerated statin → add ezetimibe (class IIa)
- If LDL still ≥ 70 mg/dl despite on maximally tolerated statin + ezetimibe → add PCSK9i after discussing net benefit, safety, and cost.

ODYSSEY LONG TERM trial : adding alirocumab 150 mg SC q 2 wks in patients with high CV risk and LDL ≥ 70 mg/dl despite receiving max. tolerated statin ↓ LDL 62% from baseline at 24 weeks, and ↓ 4-point MACEs at 78 wks by 48% in post hoc analysis.

FOURIER trial : adding evolocumab 140 mg SC q 2 wks or 420 mg SC monthly on top of background statin Rx in patients with established ASCVD and LDL ≥ 70 mg/dl ↓ 59% mean LDL compared to placebo at 48 wks and ↓ primary 5-point MACEs by 15% and ↓ 20% key secondary 3-point MACEs at 26 mo; median LDL in intervention gp. = 30 mg/dl.

■ ***Drugs with no proven CV benefit but may be considered under specific circumstances***

- Fibrate
- Niacin
- Laropiprant
  (PGD2 receptor inhibitor)

→ Thai guideline recommends fibrate or niacin in patients with TG ≥ 500 mg/dl to prevent pancreatitis.

ACCORD study : statin + fibrate combination provided no additional CV benefit compared to statin alone except in men with TG ≤ 204 mg/dl and HDL ≤ 34 mg/dl.
AIM-HIGH study : statin + niacin combination provided no additional CV benefit and may ↑ risk of ischemic stroke by 39%.
HPS2-THRIVE study : statin + laropiprant combination provided no additional CV benefit and ↑ risk of new-onset DM by 32% and up to 55% of patients with preexisting DM faced ↑ disturbance in diabetic control.

References :

Management of Cardiovascular Conditions (2)

Antiplatelets

- Primary prevention : must weigh risk & benefit carefully before initiating antiplatelet agents.
  - ► Low dose ASA (75-162 mg/day) may be considered in DM patients aged 40-70 yrs who are at high risk for ASCVD but not high risk for bleeding.
  - ► ASA is potentially harmful in patients aged > 70 yrs due to ↑ risk of bleeding.
  - ► Benefit of ASA is controversial in DM patients aged < 40 yrs with no other major ASCVD risk factors.
- Secondary prevention :
  - ► Low dose ASA (75-162 mg/day)
- Clopidogrel 75 mg/day is an alternative if ASA-allergic.

Cardiovascular Outcomes

All SGLT-2 inhibitors and some GLP-1 RAs have evidence of added cardiovascular benefit beyond improved glycemic control in DM patients at high CV risk or with established ASCVD.

Benefit on ASCVD Reduction

SGLT-2 inhibitors : ***EMPAGLIFLOZIN, CANAGLIFLOZIN, DAPAGLIFLOZIN***

- ► **EMPA-REG OUTCOME study** : adding empagliflozin in DM with established CVD ↓ primary CV events (3-point MACEs) by 14% at 3 yrs.
- ► **CANVAS study** : adding canagliflozin in DM with high CV risk or established CVD ↓ primary CV events (3-point MACEs) by 14% at 5.7 yrs. but was associated with ↑ risk of lower extremity amputation.
- ► **DECLARE-TIMI 58 study** : adding dapagliflozin in DM with established ASCVD or at high risk for ASCVD ↓ primary CV endpoints (3-point MACEs) by 7% at 4.2 yrs.

GLP-1 RAs : ***LIRAGLUTIDE, SEMAGLUTIDE, ALBIGLUTIDE, DULAGLUTIDE***

- ► **LEADER study** : adding liraglutide in DM with ASCVD or high CV risks ↓ primary CV outcomes (3-point MACEs) by 13% at 3.8 yrs.
- ► **SUSTAIN-6 study** : adding semaglutide in DM with ASCVD or high CV risks ↓ primary CV events (3-point MACEs) by 26% at 2.1 yrs.
- ► **HARMONY OUTCOMES study** : adding albiglutide in DM with ASCVD ↓ primary CV endpoints (3-point MACEs) by 22% at 1.6 yrs.
- ► **REWIND study** : adding dulaglutide in DM with ASCVD or CV risk factors ↓ primary CV outcomes (3-point MACEs) by 12% at 5.4 yrs.

Benefit on Heart Failure Reduction

SGLT-2 inhibitors : ***EMPAGLIFLOZIN, CANAGLIFLOZIN, DAPAGLIFLOZIN***

- ► **EMPA-REG OUTCOME study** : adding empagliflozin in DM with established CVD ↓ HF hospitalization by 35% at 3 yrs.
- ► **CANVAS study** : adding canagliflozin in DM with high CV risk or established CVD ↓ HF hospitalization by 23% at 5.7 yrs.
- ► **DECLARE-TIMI 58 study** : adding dapagliflozin in DM with ASCVD or at high risk for ASCVD ↓ HF hospitalization by 27% at 4.2 yrs.
- ► **DAPA-HF study** : adding dapagliflozin in HFrEF patients ↓ composite outcomes (CV death, HF hosp, worsening HF) by 26% at 18 months.

DPP-4 inhibitors

- ► No added CV benefit on ASCVD or HF proven for any DPP-4 inhibitors (from **EXAMINE, TECOS, CARMELINA studies**).
- ► **SAVOR-TIMI 53 study** : saxagliptin was associated with ↑ rate of HF hospitalization by 27%.

Septic shock

Smart refer

Definition

- Infection : การติดเชื้อ (microbial invasion)
- Septicemia : การติดเชื้อในกระแสเลือด บางครั้งอาจเขียนเป็น ’Bacteremia’, ‘viremia’, ‘fungemia’ กรณีรู้เชื้อ
- Sepsis : การติดเชื้อที่มีผลให้เกิดการตอบสนอง/การอักเสบทั่วร่างกาย (SIRS : Systemic inflammatory response syndrome)
- Severe Sepsis : SIRS + > 2 organ dysfunctions
- Sepsis-induced hypotension : Sepsis + Hypotension; fluid responsive
- Septic Shock : Sepsis + Hypotension despite adequate volume resuscitation or been given vasopressor

Sepsis

ในอดีตเราจะจำมาเสมอว่า Sepsis = SIRS + infection
และจำมาตลอดเช่นกันว่า SIRS มีแค่ 4 ข้อเอา 2/4
1.BT > 38.3 or BT < 36
2.RR>20/min or PaCO2 < 32 mmHg
3.PR > 90/min
4.WBC > 12,000 or < 4,000 or Band > 10%

แต่ใน Surviving sepsis ตัวใหม่จะแบ่งการวินิจฉัย sepsis ให้ละเอียดมากขึ้นโดยแบ่งเกณฑ์เป็น 5 ข้อใหญ่
1.General Variables e.g. BT>38.3 or < 36, PR>90, RR>20, Alteration of consciousness, hyperglycemia (>120 mg/dl, no DM)
2.Inflammatory variables e.g. WBC>12,000, <4,000, band>10%, CRP, or procalcitonin > 2SD
3.Hemodynamic variables e.g. Hypotension, MAP < 70 mmHg, ScVO2 < 70%
4.Organ dysfunction e.g. hypoxemia (P/F ratio < 300), Oliguria, abnormal coagulogram
5.Tissue perfusion variables e.g. serum lactate > 2 mmol/L. delayed cap refill time

Early goal direct therapy

Goal ที่ต้องทำให้ถึงภายใน 6 ชั่วโมง (6-hours bundle) มีดังต่อไปนี้ ตามลำดับ

1.CVP goal แยกเป็นใส่ท่อหรือไม่ใส่ท่อช่วยหายใจแล้วต่อ mechanical ventilation เนื่องจากเวลาใส่ท่อช่วยหายใจจะทำให้ venous return เข้าสู่หัวใจลดลง เลือด pool อยู่ใน large vein มากขึ้น RA pressure จะมากขึ้นกว่าปกติ จึงต้องใช้ goal ที่สูงกว่าเดิม ตรงนี้ต้องระวังเวลาจำเพราะมีหน่วย cmH2O และ mmHg CVP 8–12 mmHg (12-15 mmHg ถ้า on positive pressure ventilation) แต่ถ้าเป็นหน่วย cmH2O จะเป็น 12-15 cmH2O และ 15-20 cmH2O ตามลำดับ ถ้าระดับ CVP ยังไม่ถึง goal ให้ทำ fluid challenge test

2.MAP > 65 mmHg หลังจากที่ได้ CVP ถึง goal แล้วเราต้องทำให้ระดับ MAP ถึงค่า โดยอาจจำเป็นต้องให้ vasopressor เช่น Levophed ช่วย

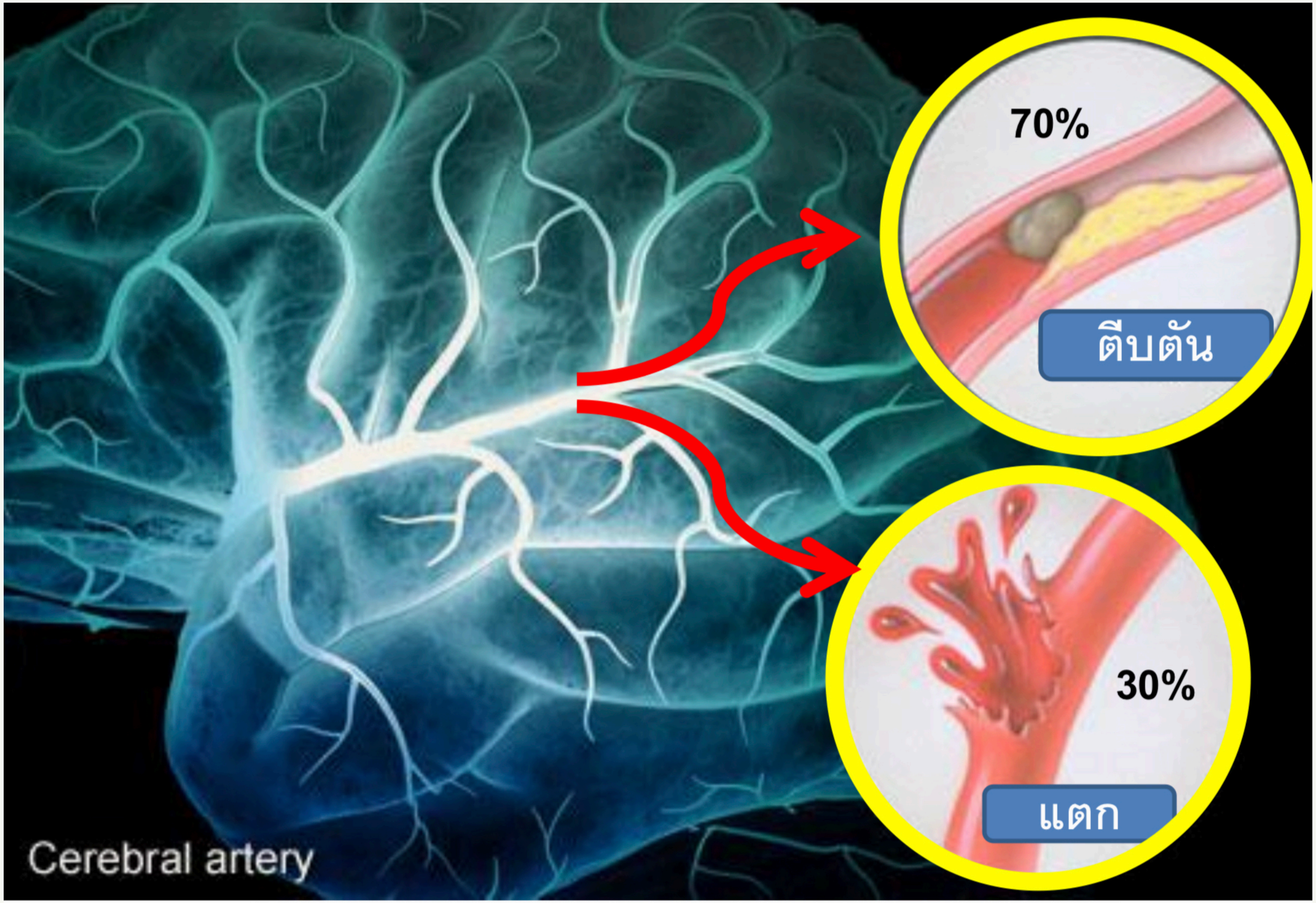
3.ScVO2 > 70% หลังจาก MAP ถึงเป้าแล้ว ต้องเพิ่มให้ระดับ central vein oxygen saturation ถึง goal ด้วย โดยดูว่า Hct > 30% หรือยัง ถ้ายังให้เติมเลือด ถ้าถึงแล้วให้พิจารณาให้ Dobutamine

4.Urine output > 0.5 ml/kg/hour หรือ Urine output ออกเท่า Body weight/2 ต่อชั่วโมงเป็นอย่างน้อย

ต้องให้ Empirical Antibiotic ให้เร็วที่สุดภายใน 1 ชั่วโมงตั้งแต่ Dx

Stroke

Smart refer


70%
ตีบตัน
30%
แตก
Cerebral artery

Assessment

F=Faceปากเบี้ยว

A = Arms แขนขาอ่อนแรง

S = Speech ลิ้นแข็ง พูดไม่ชัด พูดลำบาก

T = Time ระยะเวลาเกิดอาการ

อย่าลืมเจาะดูน้ำตาลในเลือดเพื่อ exclude hypo-/hyperglycemia ที่อาจจะ mimic stroke ได้

MANAGEMENT OF ACUTE ISCHEMIC STROKE

Suspected acute stroke
(from history & physical examination)

- Non-contrast CT or MRI brain to exclude ICH
- Blood glucose to exclude hypo-/hyperglycemia

Onset ≤ 4.5 hrs

CONTRAINDICATIONS TO IV FIBRINOLYTICS

- Previous ischemic stroke within 3 months
- Mild, non-disabling stroke (NIHSS 0-5)
- Severe head trauma within 3 months
- Intracranial or intraspinal surgery within 3 months
- Hx of intracranial hemorrhage
- GI malignancy or GI hemorrhage within 21 days
- Coagulopathy (Plt < 100,000/mm^3, INR > 1.7, PTT > 40 s, PT > 15 s)
- Receiving LMWH within 24 hrs
- Taking DOAC within 48 hrs (with normal renal function) unless associated lab assays are normal
- Aortic dissection
- Infective endocarditis
- Intra-axial intracranial neoplasm

No contraindication → **1 Additional recommendations for IV alteplase** → **IV alteplase**

Has contraindication(s) → **No fibrinolytic indicated**

Wake-up stroke or unclear onset (> 4.5 hrs)

DW-MRI shows a lesion smaller than 1/3 of MCA territory and no visible signal change on FLAIR *(WAKE-UP)*

YES → **IV alteplase**

NO → **No fibrinolytic indicated**

Onset 6 - 24 hrs

CTA with CTP or
MRA with DW-MRI ± MR perfusion

6 - 16 hrs *(DAWN or DEFUSE 3)*

16 - 24 hrs *(DAWN)*

DAWN Clinical-Imaging Mismatch Criteria

ONE of the following :
1. Age < 80 + NIHSS ≥ 10 + infarct core 0 - 30 ml
2. Age < 80 + NIHSS ≥ 20 + infarct core 31 - 51 ml
3. Age ≥ 80 + NIHSS ≥ 10 + infarct core 0 - 20 ml

DEFUSE 3 Persistent Target Mismatch Criteria

ALL of the following :
1. Infarct core volume < 70 ml
2. Mismatch volume > 15 ml (T_{max} > 6 sec)
3. Penumbra/core mismatch ratio > 1.8

Criteria not fulfilled → **No fibrinolytic indicated**

Criteria fulfilled → **Mechanical Thrombectomy**

- **2 General and emergency management**
- **3 Management during and after IV alteplase**
- **4 Consider mechanical thrombectomy if eligible**
- **5 Intrahospital care**
- **6 Secondary stroke prevention**

- **2 General and emergency management**
- **5 Intrahospital care**
- **6 Secondary stroke prevention**

INTRAHOSPITAL MANAGEMENT OF STROKE (1)

1 Additional recommendations for IV alteplase

- Pre-existing disability : mRS ≥ 2 may be associated with less neurological improvement.
  Take into considerations : QoL, caregiver, residence, families & patients' preferences, goals of care, life expectancy, and premorbid level of function before administering IV alteplase.
- IV alteplase is likely to be beneficial under the following settings (class IIa recommendation) :
  - Concurrent menstruation without history of menorrhagia
  - Unruptured intracranial aneurysm < 10 mm
  - Concurrent acute MI (Rx IV alteplase then PCI if indicated)
  - Recent NSTEMI < 3 months
  - Recent STEMI of right or inferior myocardium < 3 months
  - Sickle cell disease
  - Extra-axial intracranial neoplasm
  - Diabetic hemorrhagic retinopathy and other hemorrhagic ophthalmic conditions
- IV alteplase may be beneficial under the following settings (class IIb recommendation) :
  - Dural puncture within preceding 7 days
  - Previous GI bleeding > 21 days
  - Previous GU bleeding
  - Major surgery within preceding 14 days
  - Intracranial AVM with severe stroke that outweighs anticipated risk of ICH
  - History of menorrhagia without clinically significant anemia or hypotension
  - Recent STEMI of left myocardium < 3 months
  - Acute pericarditis with stroke likely to produce severe disability
  - Pregnancy
  - Systemic malignancy with life expectancy > 6 months without other contraindications (e.g. coagulopathy, recent Sx, systemic bleeding, etc.)

Should weigh bleeding risk and benefit from potential reduction of stroke disability carefully before deciding to give alteplase

- IV alteplase is of uncertain benefit under the following settings :
  - Arterial puncture of noncompressible vessel < 7 days
  - Giant, unruptured intracranial aneursym
  - Intracranial AVM with mild stroke
  - Acute pericarditis with mild stroke
  - Early postpartum period (< 14 days after delivery)

2 General and Emergency Management

- Assess blood sugar (BS) before IV alteplase. Maintain euglycemia (BS 140-180 mg/dl).
- No need to wait for other lab results unless there is a reason to suspect an abnormal test (e.g. in patients taking warfarin).

- If BT > 38°C → give antipyretic and seek cause.

- Airway protection if ↓ LOC or bulbar dysfunction.
- Supplemental O_2 should be given only if SaO_2 ≤ 94%.

- Maintain BP < 185/110 mmHg in patients who :
  - are eligible for IV alteplase
  - have plan for mechanical thrombectomy

  Otherwise keep BP < 220/120 during acute stroke.

INTRAHOSPITAL MANAGEMENT OF STROKE (2)

3 Management during and after IV alteplase

- Dose : 0.9 mg/kg (max 90 mg) IV
  - Initial 10% of dose given as IV bolus over 1 min.
  - Remaining 90% of dose IV drip over 59 min.

- Hyperdense MCA sign and ≤10 cerebral microbleeds (CMBs) are not contraindications for IV alteplase.
- IV alteplase may still be beneficial in patients with >10 CMBs, although there is an associated ↑ risk of symptomatic ICH.

- Follow up CT or MRI 24 hours after IV alteplase before initiating antiplatelet or anticoagulant.

- Monitor for possible complications :
  - **Intracranial hemorrhage**
    - Stop alteplase, emergent non-contrast CT
    - Cryoprecipitate 10 U IV over 10-30 min
    - Tranexamic acid 1,000 mg IV over 10 min
    - Supportive care
    - Consult NeuroSx
  - **Orolingual angioedema**
    - Stop alteplase and ACEI
    - Consider ETT if severe
    - Steroid IV, ranitidine IV, ± epinephrine SC or NB
    - Supportive care

Tenecteplase (class IIb recommendation)
» Dose 0.25 mg/kg (max 25 mg) single IV bolus for patients who are eligible for mechanical thrombectomy *(EXTEND-IA TNK)*
» Dose 0.4 mg/kg single IV bolus as an alternative to alteplase in minor neurological impairment and no major intracranial occlusion

4 Consider mechanical thrombectomy if eligible

- Stent retriever or direct aspiration thrombectomy indicated if all the following criteria are met (class I recommendation) :
  (1) Prestroke mRS 0-1 (2) ICA or MCA M1 occlusion
  (3) Age ≥ 18 (4) NIHSS ≥ 6
  (5) ASPECTS ≥ 6 (6) Groin puncture within 6 hrs of symptom onset
- Stent retriever is of uncertain benefit for occlusions at other sites and for patients with mRS > 1 (class IIb recommendation).
- Keep BP ≤ 180/105 mmHg for 24 hrs after procedure.

5 Intrahospital care

- ASA 160-300 mg within 24-48 hrs after onset; if treated with IV alteplase, ASA is delayed until 24 hrs later.
- Dual antiplatelets (ASA + clopidogrel) x 21 days for minor stroke (NIHSS ≤ 3) ↓ recurrence up to 90 days *(CHANCE & POINT)*
- Patients with non-cardioembolic stroke while on ASA, ↑ ASA dose or switching to another antiplatelet is of uncertain benefit.
- Ticagrelor is not superior to ASA for minor stroke (NIHSS ≤ 5 or ABCD2 ≥ 4; *SOCRATES)*, but may be given to patients who have a contraindication to ASA due to their similar safety profiles.
- Isotonic IV fluid, head elevation, maintain BS 140-180 mg/dl
- BP management : If BP above target, aim to lower BP by 15% during the first 24 hrs
  (e.g. nicardipine 5 mg/hr IV. Titrate Δ 2.5 mg/hr q 5-15 min; max dose 15 mg/hr OR labetalol 10-20 mg IV drip in 1-2 min)
  Initiate or re-start oral antihypertensives after 48-72 hrs of stroke onset
- Monitor acute complications e.g. brain edema (Rx osmotic therapy, decompressive craniectomy, ventriculostomy as indicated)
- Dysphagia screening before eating/drinking, intermittent pneumatic compression to prevent DVT, post-stroke depression screening
- Early rehabiliation
- Patient/relative/caregiver education

6 SECONDARY STROKE PREVENTION

DIABETES MELLITUS

- Screen for DM : FBS, HbA1C, or OGTT
- Be aware that plasma glucose level may not be accurate during acute stress/illness.

CARDIAC EVALUATION

- Cardiac monitoring during the first 24 hours of admission to screen for AF and other arrhythmias.
- For AF, initiate anticoagulant (DOAC preferred over warfarin) between 4 and 14 days after stroke onset.
- Routine echocardiography is of uncertain benefit; except in patients with a likely cardioembolic source (e.g. intracardiac thrombus) and in those who meet eligibility criteria of RCTs for mechanical PFO closure.

VASCULAR IMAGING & CAROTID REVASCULARIZATION

- Routine non-invasive imaging of cervical carotid arteries within 24 hrs of admission in patients with minor, non-disabling stroke (mRS 0-2) in carotid territory (class I recommendation).
- Subsequently, CEA or carotid angioplasty & stenting to be performed in such patients between 48 hrs and 7 days of the event (class IIa recommendation).

High-intensity statins	Moderate-intensity statins	Low-intensity statins
Atorvastatin 40-80 mg/day Rosuvastatin[1] 20-40 mg/day	Atorvastatin 10 mg/day Rosuvastatin 10 mg/day Simvastatin 20-40 mg/day Pravastatin 40 mg/day Lovastatin 40 mg/day Fluvastatin 40 mg BID	Pravastatin 10-20 mg/day Lovastatin 20 mg/day

[1] *Max dose of rosuvastatin is 20 mg/day in Asian patients.*

MANAGEMENT OF DYSLIPIDEMIA (AHA/ACC 2018)

Age ≤ 75 → high-intensity statin; target ↓ LDL ≥ 50% (class I recommendation)
→ moderate-intensity statin if contraindicated or cannot tolerate side effects; target ↓ LDL 30-49% (class I recommendation)

Age > 75 → high or moderate-intensity statin as tolerated; evaluate for potential risk reduction, adverse effects, drug-drug interactions, and patient preferences (class IIa recommendation)

Is the patient judged to be very high-risk for future development of ASCVD ?

Very high-risk : Multiple major ASCVD events OR 1 major ASCVD event + multiple high-risk conditions

Major ASCVD events :
- Recent ACS < 12 months
- Hx of MI (other than recent ACS)
- Hx of ischemic stroke
- Symptomatic PAD (Hx of claudication with ABI < 0.85, or previous revascularization or amputation)

High-risk conditions :
- Age ≥ 65 yrs
- Heterozygous familial hypercholesterolemia
- Hx of prior CABG or PCI outside of major ASCVD events
- DM
- HT
- CKD (eGFR 15-59 ml/min)
- Current smoking

Very high-risk and LDL ≥ 70 mg/dl despite on maximally-tolerated statin
→ add ezetimibe (IMPROVE-IT trial) (class IIa recommendation)
→ add PCSK9i after discussing net benefit, safety, and cost (FOURIER, ODYSSEY OUTCOMES trials) (class IIa recommendation)

Not very high-risk and LDL ≥ 70 mg/dl despite on maximally-tolerated statin
→ add ezetimibe (IMPROVE-IT trial) (class IIb recommendation)

ESC 2019 guideline recommends treatment to achieve LDL reduction ≥ 50% from baseline and LDL goal ≤ 55 mg/dl (class I).