REVIEW OF FIBRINOLYTIC THERAPY IN STEMI

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BACKGROUND

- 2 strategies of reperfusion therapy
  - Primary percutaneous coronary intervention (pPCI) or invasive strategy
    - Preferred by clinical practice guideline
    - Higher patency rate
    - Better clinical outcomes
  - Fibrinolytic therapy or conservative strategy

O'Gara PT, et al. J Am Coll Cardiol 2013; 61(4): e78-140.
Steg PG, et al. Eur Heart J 2012; 33(20): 2569-619.

BACKGROUND

- Limitation of pPCI
  - High cost, need of advanced facilities and staffs to perform
    - Insufficient number of PCI-capable hospital
  - Time-relate benefit: 120 minutes from the onset
- Therefore, fibrinolytic therapy remains an important therapeutic modality
  - Especially in the remote area or LMIC

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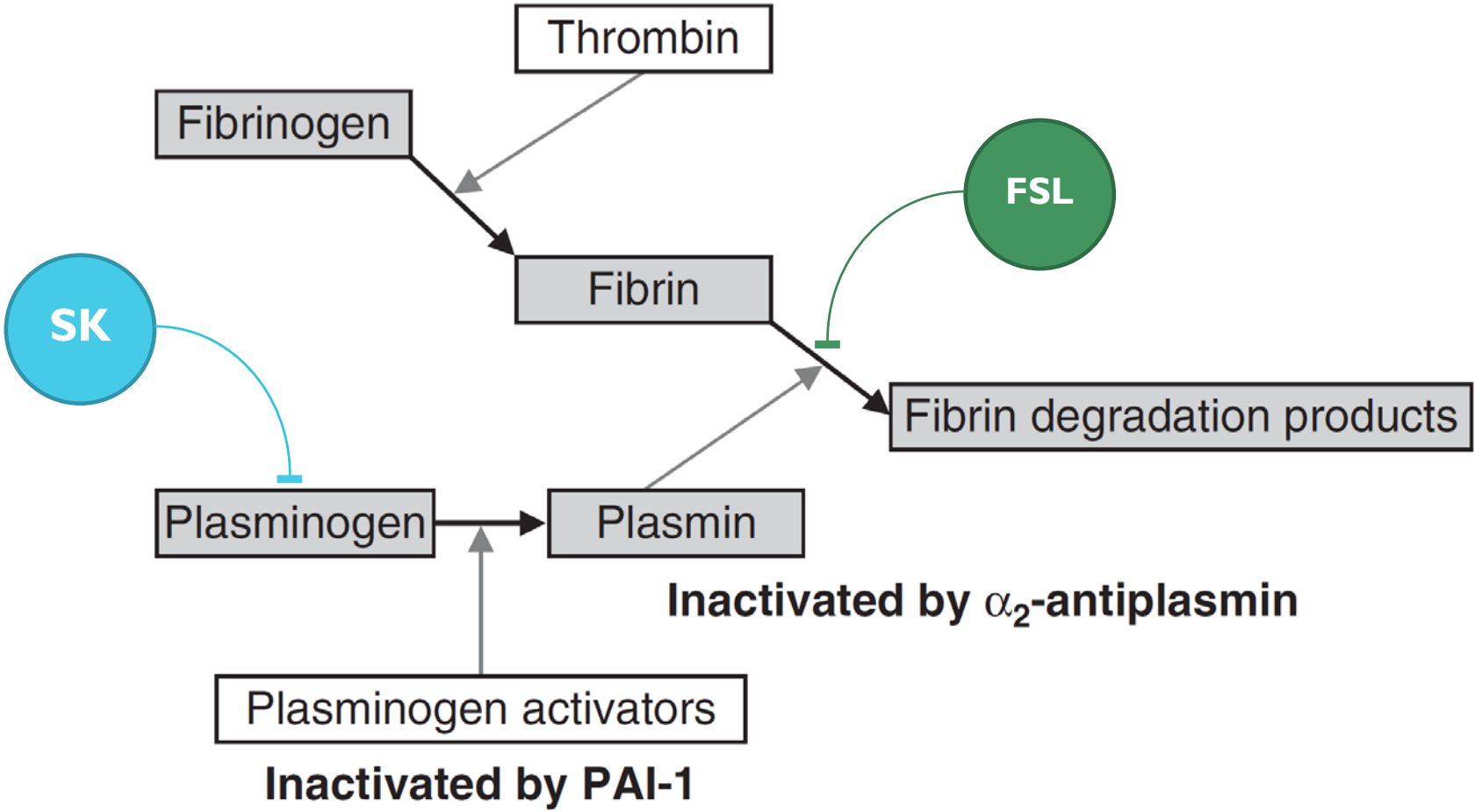
PHARMACOLOGY



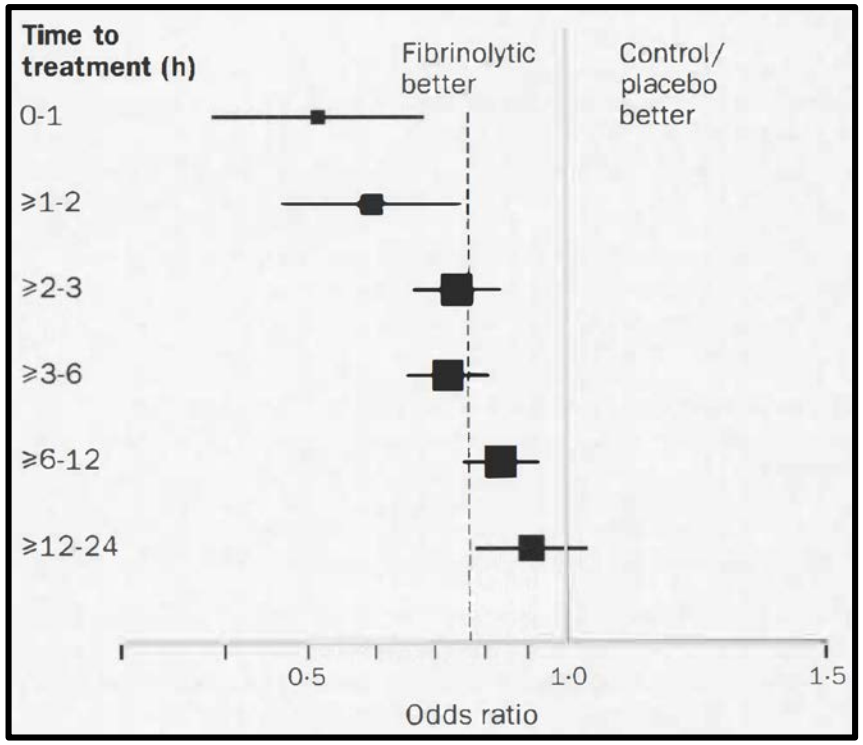
Morse MA, et al. Drugs 2009;69(14):1945-1966.

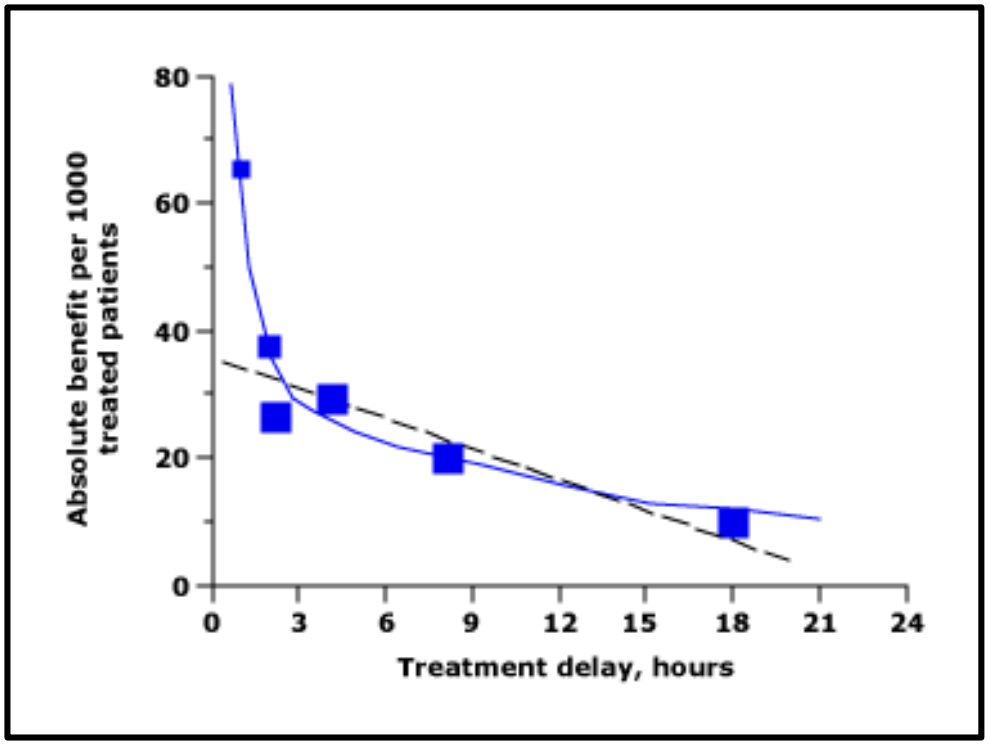
FIBRINOLYTICS

- Indicated in STE ACS who present within 12 hours of onset of chest discomfort when primary PCI can not be performed within 120 mins (Class I)
  - Class IIa in patients presenting between 12 and 24 hrs.

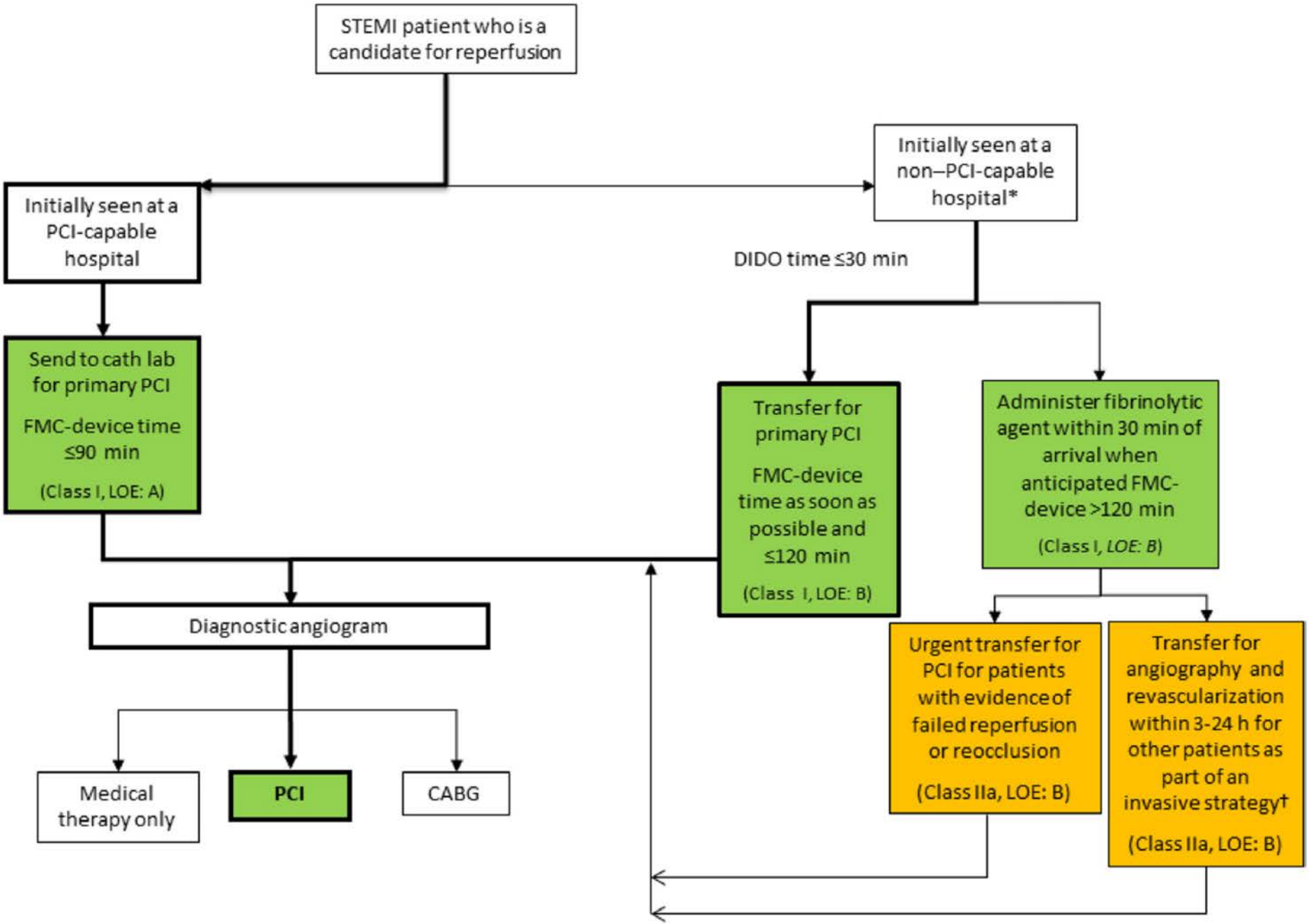
* แม้ประสิทธิภาพของ streptokinase อาจไม่ได้เป็นยาที่มีประสิทธิภาพสูงสุด of แต่คณะกรรมการ ฯ มีความเห็นว่ามีความเหมาะสมกับประเทศไทย ในกรณีที่เคยได้ streptokinase มาก่อน เกรงว่าความดันโลหิตจะลดต่ำลงจากยา streptokinase หรือต้องการประสิทธิภาพการเปิดเส้นเลือดหัวใจเพิ่มขึ้น อาจเลือกใช้ alteplase หรือ tenecteplase แต่จะมีค่าใช้จ่ายเพิ่มขึ้นมาก

TIME-RELATE BENEFIT OF FIBRINOLYTIC THERAPY





Boersma E, et al. Lancet 1996;348:771-75.



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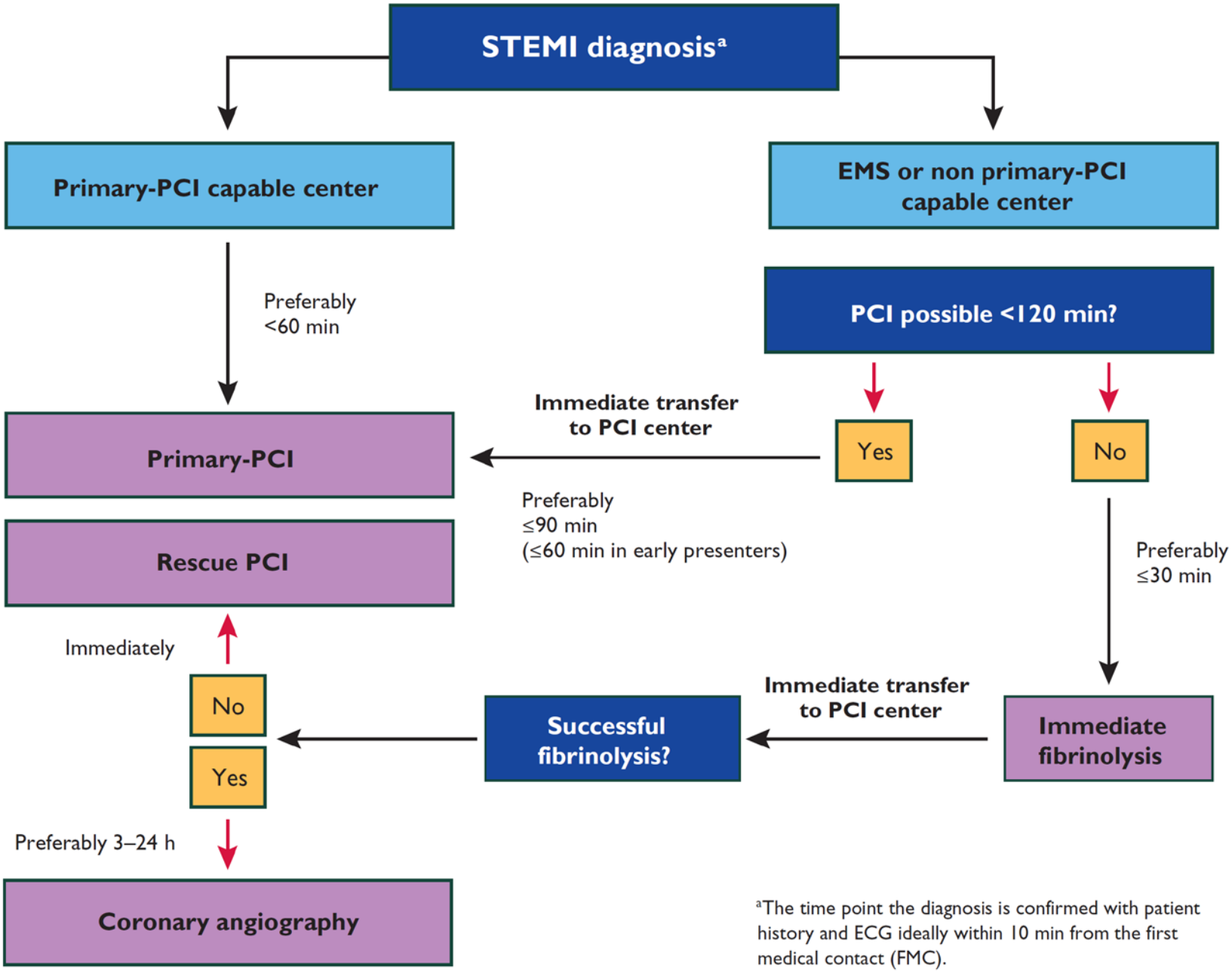

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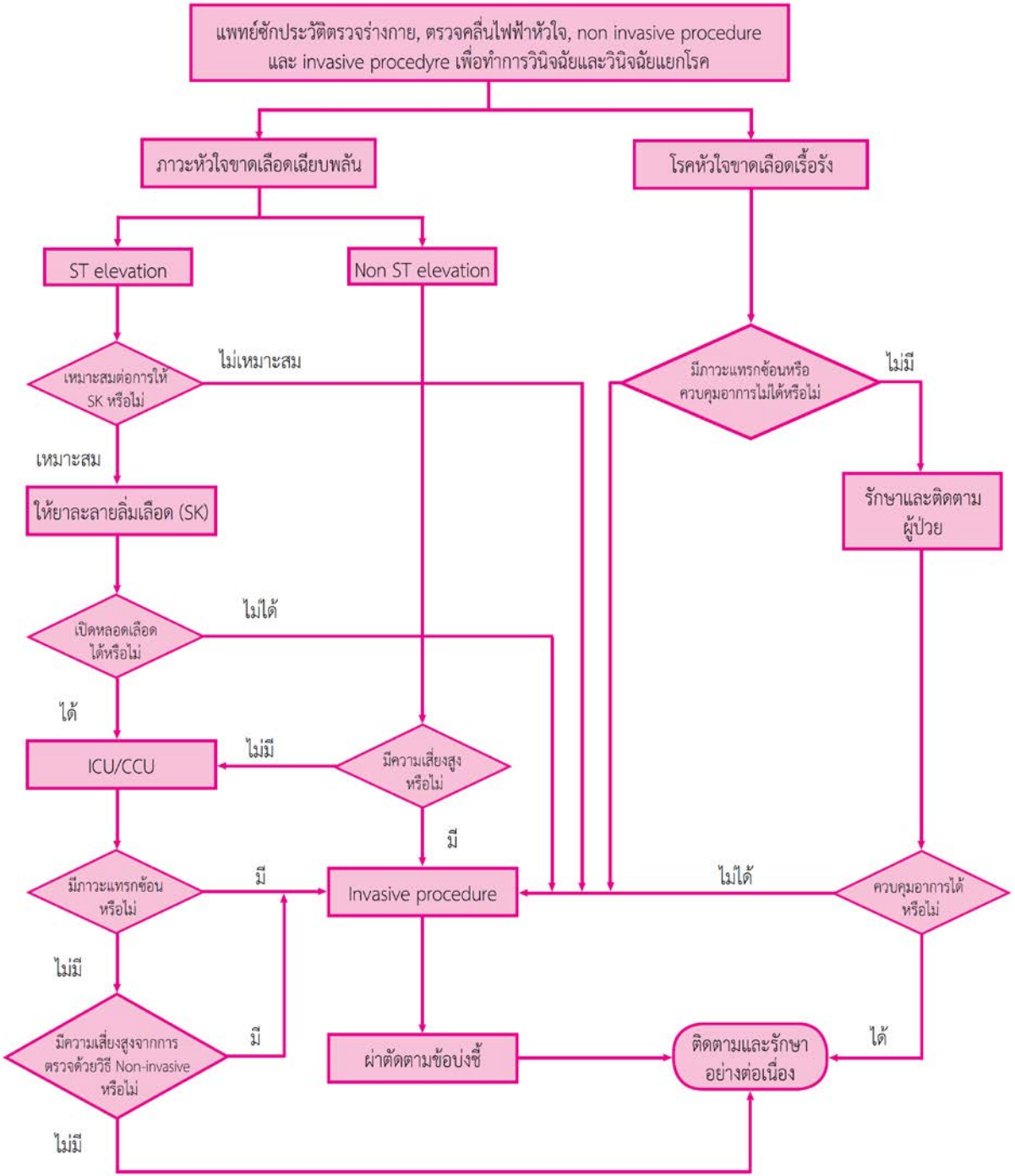

แนวทางเวชปฏิบัติในการดูแลผู้ป่วย โรคหัวใจขาดเลือดในประเทศไทย ฉบับปรับปรุง ปี 2557

FIBRINOLYTICS

- Contraindication
  - Any prior intracranial hemorrhage
  - Known structural cerebrovascular lesions, such as an arterial venous malformation
  - Known intracranial malignant neoplasm
  - Ischemic stroke within 3 months
  - Active bleeding (excluding menses)
  - Significant closed head or facial trauma within 3 months

ADJUNCTIVE ANTITHROMBOTICS

- Antiplatelet
  - ASA 160-325 mg, then 75-325 mg/day
  - P2Y12: No evidence support the use of novel P2Y12
    - Clopidogrel is more preferred
      - 300 mg LD, then 75 mg/day (no LD for age >75 years)
      - Doubtful for giving with SK!
- Anticoagulants
  - UFH, LMWH, or fondaparinux
- GPIIb/IIIa should not given

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AVAILABLE CHOICE OF FIBRINOLYTIC AGENTS

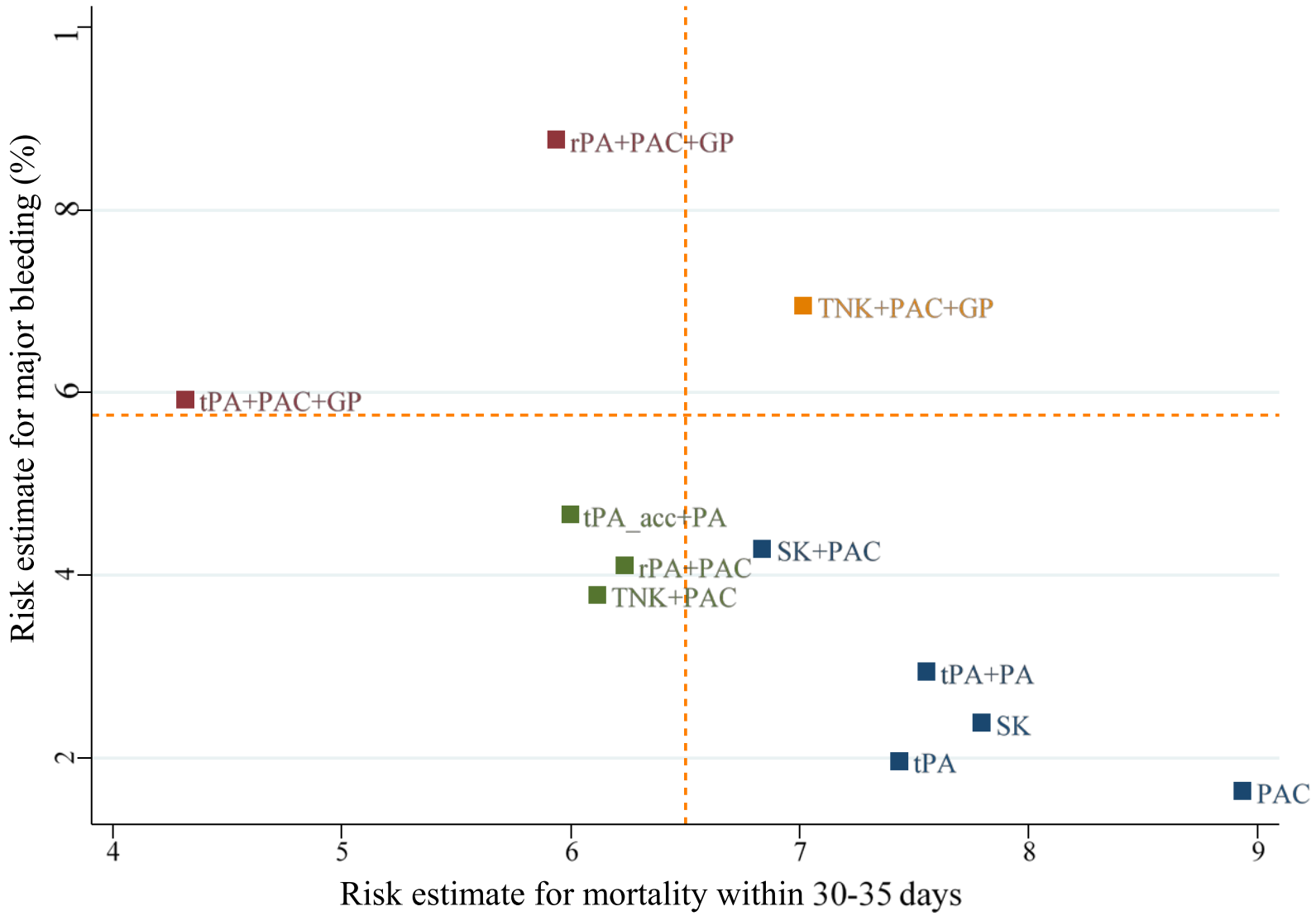
Properties	SK	tPA	rPA	TNK
Product	Derived from β-hemolytic streptococci	Recombinant DNA technology	Recombinant DNA technology	Recombinant DNA technology
Pharmacology	Stable, noncovalent complex with plasminogen	Enhance fibrin-bound plasminogen	Enhance fibrin-bound plasminogen	Enhance fibrin-bound plasminogen
Onset			30-90 mins	
Clearance/ Excretion		Hepatic	Feces and urine	Hepatic
T½ (minute) - Initial - Terminal	23	4-6 3.5 72	18 14-20 98-135	20 11-12 41-138

Adapted from: 1) Tsikouris JP, et al. Pharmacotherapy 2001;21(2):207–217. 2) Morse MA, et al. Drugs 2009;69(14):1945-1966.

AVAILABLE CHOICE OF FIBRINOLYTIC AGENTS

Properties	SK	tPA	rPA	TNK
Fibrin specificity	Non-specific	++	++	++++
Thrombolytic potency	+	++	+++	++++
%TIMI grade 3 flow at 90 min	60-80	73-84	84	85
PAI-1 inhibition		++	+++	+
Antigenicity	+	-	-	-
Dose	1.5 mU in 30-60 mins	15 mg bolus + 85 mg infusion over 90 min	10 mU bolus x 2 30 min apart	Single IV weight-based bolus
Prehospital given			+	+

Adapted from: 1) Tsikouris JP, et al. Pharmacotherapy 2001;21(2):207–217. 2) Morse MA, et al. Drugs 2009;69(14):1945-1966. 3) O'Gara PT, et al. J Am Coll Cardiol 2013; 61(4): e78-140.


Risk estimate for major bleeding (%)
1
2
4
6
8
rPA+PAC+GP
TNK+PAC+GP
tPA+PAC+GP
tPA_acc+PA
SK+PAC
rPA+PAC
TNK+PAC
tPA+PA
SK
tPA
PAC
4
5
6
7
8
9
Risk estimate for mortality within 30-35 days

EVALUATION AFTER FIBRINOLYTIC

- Chest pain resolve
- Reversible of abnormal ECG (within 90-120 mins)
- Normalized cardiac enzyme (within 24-36 hours)
- Hemodynamic stable
- Unobserved VT/VF (within 90 mins)
- **IF NO SIGN OF RESOLUTION → REFER?**

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SPECIFIC POPULATION

- No evidence to support the preferred regimen
- Risk of bleeding should be carefully monitored in
  - Elderly
  - Asian
  - Low body weight

PCI AFTER FIBRINOLYTIC

- 2 options
  - Ischemic guided
  - **Routine early (Pharmacoinvasive strategy)**
    - Within 3 to 24 hours after fibrinolytic therapy
    - Angiographic with PCI when indicated

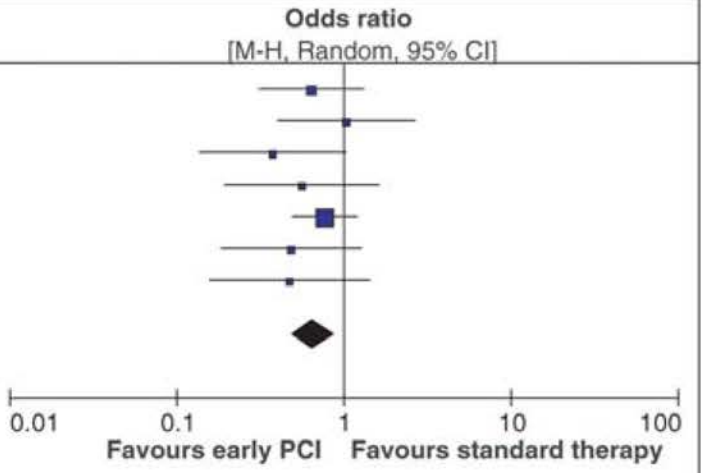
O'Gara PT, et al. J Am Coll Cardiol 2013; 61(4): e78-140.

Early PCI vs. standard therapy

Death-Reinfarction, 30 days

Study	Early PCI Events	Early PCI Total	Standard therapy Events	Standard therapy Total	Weight %	Odds ratio [M-H, Random, 95% CI]
CARESS-IN-AMI	13	299	20	301	16.4	0.64 [0.31, 1.31]
GRACIA-1	9	248	9	251	9.5	1.03 [0.40, 2.65]
CAPITAL-AMI	6	86	14	84	8.3	0.38 [0.14, 1.03]
SIAM-III	6	82	10	81	7.5	0.56 [0.19, 1.62]
TRANSFER-AMI	38	537	47	522	42.4	0.77 [0.49, 1.20]
WEST	7	104	13	100	9.1	0.48 [0.18, 1.27]
NORDISTEMI	5	134	10	132	6.9	0.47 [0.16, 1.42]
Total	**84/1490 (5.6%)**		**123/1471 (8.3%)**		**100.0**	**0.65 [0.49, 0.88]** NNT 37[22-113]

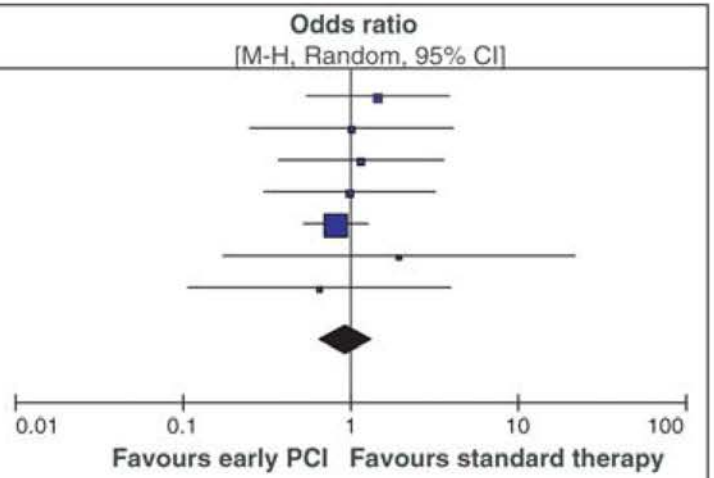
Heterogeneity: $\tau^2 = 0.00$; $\chi^2 = 3.39$, df = 6 ($P = 0.76$); $I^2 = 0\%$
Test for overall effect: $Z = 2.86$ ($P = 0.004$)
Egger`sregression test: P value 0.10



Major Bleeding

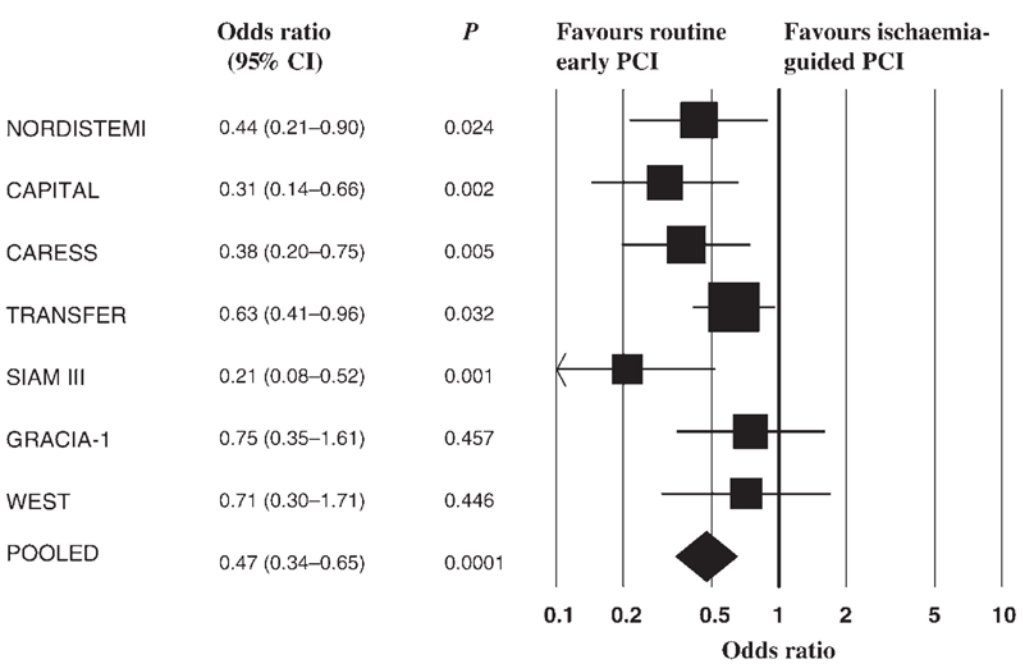
Study	Early PCI Events	Early PCI Total	Standard therapy Events	Standard therapy Total	Weight %	Odds ratio [M-H, Random, 95% CI]
CARESS-IN-AMI	10	299	7	301	12.0	1.45 [0.55, 3.87]
GRACIA-1	4	248	4	251	5.9	1.01 [0.25, 4.09]
CAPITAL-AMI	7	86	6	84	8.9	1.15 [0.37, 3.58]
SIAM-III	6	82	6	81	8.3	0.99 [0.30, 3.20]
TRANSFER-AMI	40	537	47	522	59.4	0.81 [0.52, 1.26]
WEST	2	104	1	100	2.0	1.94 [0.17, 21.7]
NORDISTEMI	2	134	3	132	3.5	0.65 [0.11, 3.96]
Total	**71/1490 (4.9%)**		**74/1471 (5%)**		**100.0**	**0.93 [0.67, 1.31]**

Heterogeneity: $\tau^2 = 0.00$; $\chi^2 = 1.82$, df = 6 ($P = 0.94$); $I^2 = 0\%$
Test for overall effect: $Z = 0.39$ ($P = 0.70$)
Egger`s regression test: P value 0.10



Borgia F, et al. Eur Heart J 2010;31:2156-69.

Routine early PCI vs. ischemic guided



30 days mortality

Major bleeding

D'Souza SP, et al. Eur Heart J 2011;32:972-82.

THANK YOU…