UNIVERSITAS INDONESIA

2019

EMBOLI PARU

MODUL HEMATOLOGI-ONKOLOGI

NARATOR

DR. FIKRI ICHSAN WIGUNA

NARASUMBER

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Tujuan Pembelajaran

- Peserta didik mampu menjelaskan tentang definisi, patogenesis, dan patofisiologi dari emboli paru
- Peserta didik mampu menjelaskan mengenai cara menegakkan diagnosis emboli paru melalui tanda dan gejala klinis, berbagai sistem skoring, dan pemeriksaan-pemeriksaan penunjang
- Peserta didik mampu menjelaskan mengenai cara menentukan prognosis pasien emboli paru
- Pesrta didik mampu menjelaskan penatalaksanaan farmakologis dan non-farmakologis untuk emboli paru

Daftar isi

DEFINISI - EPIDEMIOLOGI

Penyakit Kardiovaskular
Tersering ketiga[2]

Insidensi
100-200/100.000 penduduk[2]

Tromboemboli Vena[1,2]

Trombosis Vena Dalam

Emboli Paru

Sumber:
1. Sudoyo A. Trombosis vena dalam: pendekatan klinis. In: Kumpulan naskah pertemuan ilmiah nasional XII PB PAPDI. Jakarta: Interna Publishing;
2. Konstantinides S V, Germany C, France ND, Uk DF, Galie N, Uk JSRG, et al. 2014 ESC Guidelines on the diagnosis and management of acute pulmonary embolism The Task Force for the Diagnosis and Management of Acute Pulmonary Embolism of the European Society of Cardiology (ESC) Endorsed by the European Respiratory Society (ERS). 2014;3033–80.

- Obstruksi sebagian atau total sirkulasi arteri pulmonalis/percabangannya akibat emboli trombus atau emboli yang lain

- 30% pasien tromboemboli vena akan mengalami emboli paru.

Emboli Paru

- Mortalitas dalam 3 bulan setelah diagnosis : 15%.

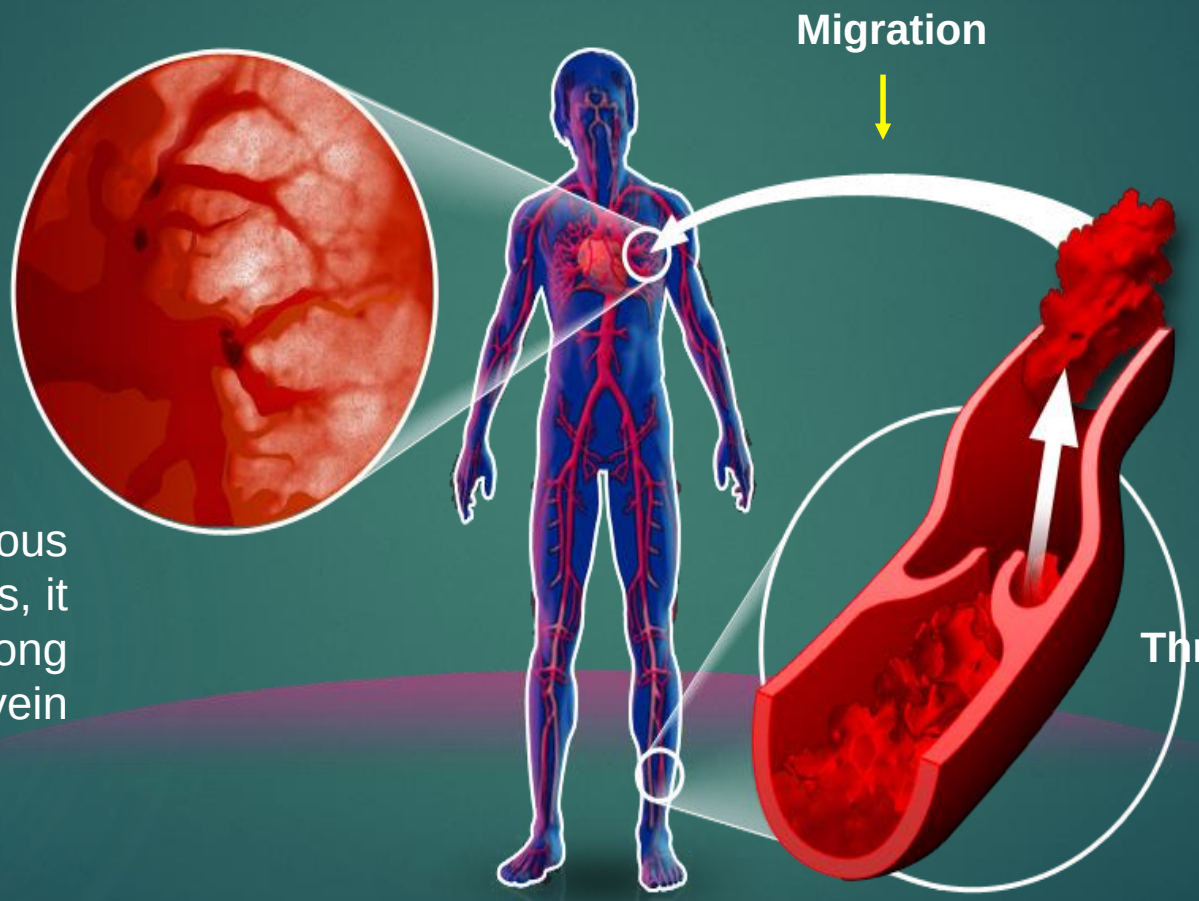
- 80-95% berasal dari trombus di tungkai

Sumber:
2. Konstantinides S V, Germany C, France ND, Uk DF, Galie N, Uk JSRG, et al. 2014 ESC Guidelines on the diagnosis and management of acute pulmonary embolism The Task Force for the Diagnosis and Management of Acute Pulmonary Embolism of the European Society of Cardiology (ESC) Endorsed by the European Respiratory Society (ERS). 2014;3033–80.
3. Wilbur J, Shian B. Deep venous thrombosis and pulmonary embolism: current therapy. Am Fam Physician. 2017;95:296–304

PATOGENESIS – PATOFISIOLOGI

Patogenesis

PE occurs when parts of the clot detach and travel in the blood to block vessels in the lungs

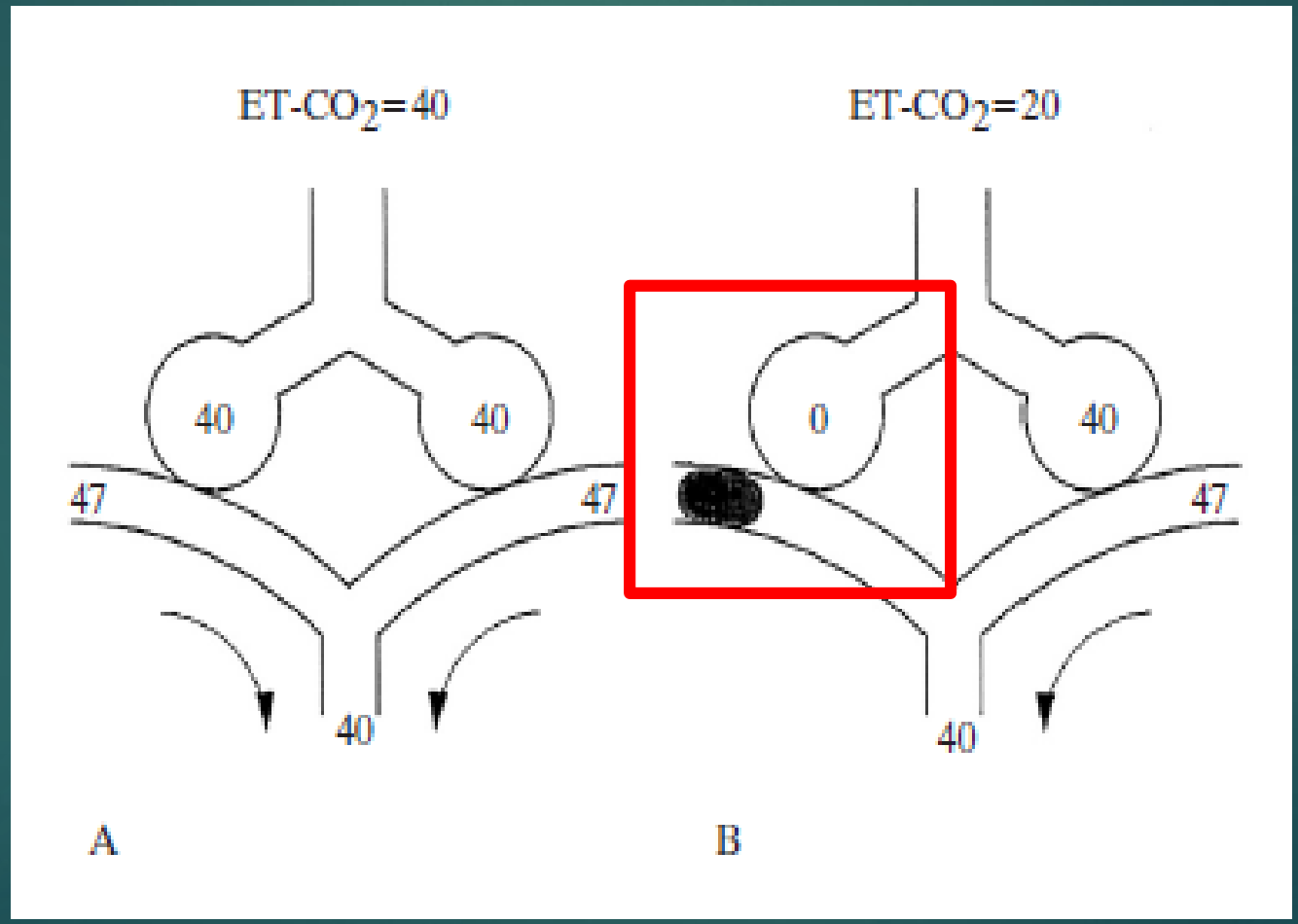


As the venous clot grows, it extends along the vein

Sumber:
3. Wilbur J, Shian B. Deep venous thrombosis and pulmonary embolism: current therapy. Am Fam Physician. 2017;95:296–304
4. Anderson FA, *et al*. Center for Outcomes Research, University of Massachusetts Medical Center; 1998
5. Riyanto B. Nyeri dada non kardiak. In: Kumpulan naskah pertemuan ilmiah nasional XII PB PAPDI. Jakarta: Interna Publishing; p. 301–24
6. Goldhaber SZ. *J Am Coll Cardiol* 1992;19:246–247

Patofisiologi

Emboli paru menyebabkan gangguan pada sirkulasi pulmoner dan pertukaran gas di paru

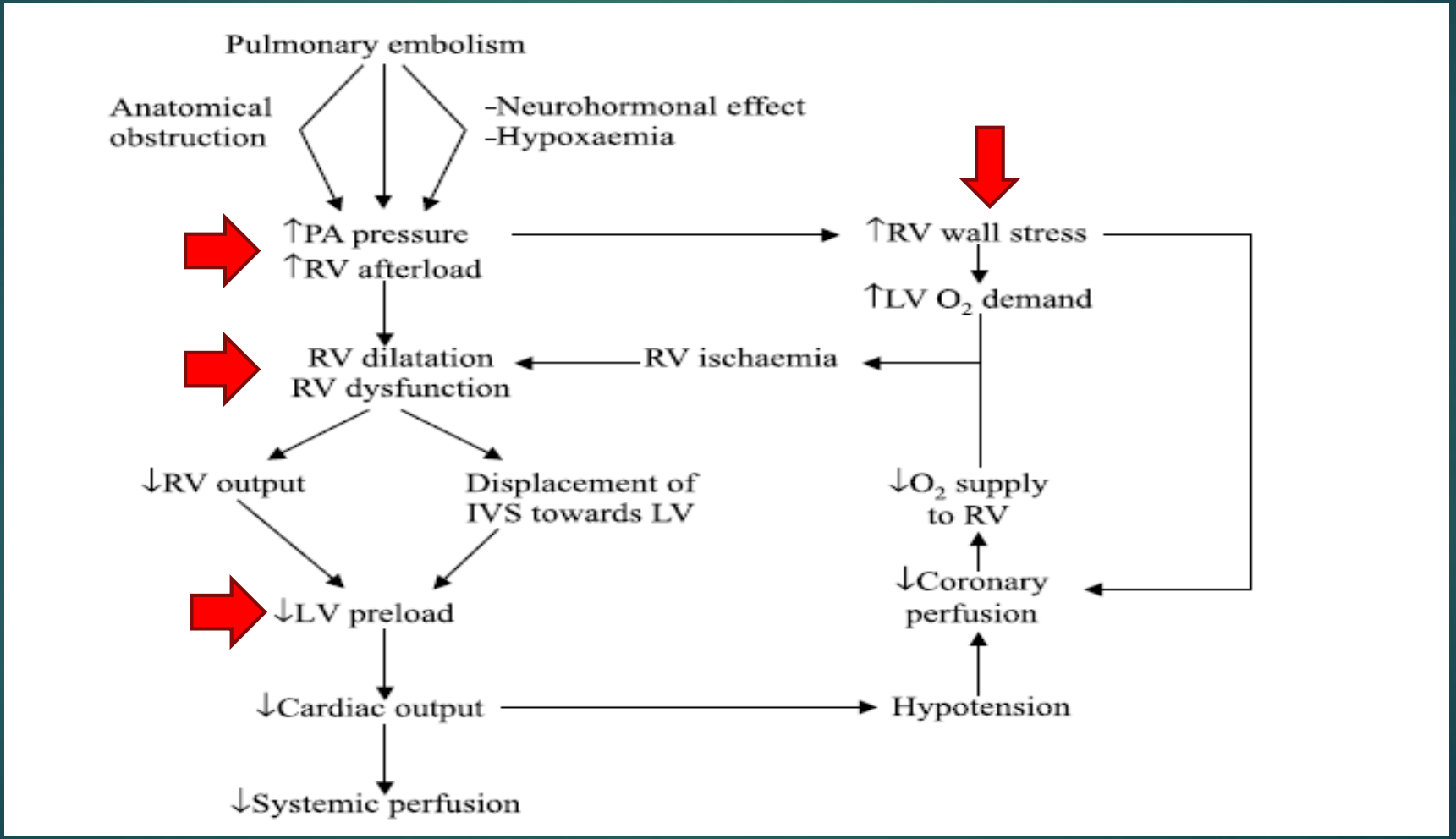


Sumber:

7. Kostadima E, Zakhynthinos E. Pulmonary embolism : pathophysiology, diagnosis, treatment. Hell J Cardiol. 2007;48:94–107.

Patofisiologi

Emboli paru menyebabkan penurunan curah jantung dan berujung pada gangguan gangguan perfusi sistemik



Sumber:

7. Kostadima E, Zakhynthinos E. Pulmonary embolism : pathophysiology, diagnosis, treatment. Hell J Cardiol. 2007;48:94–107.

DIAGNOSIS

Diagnosis

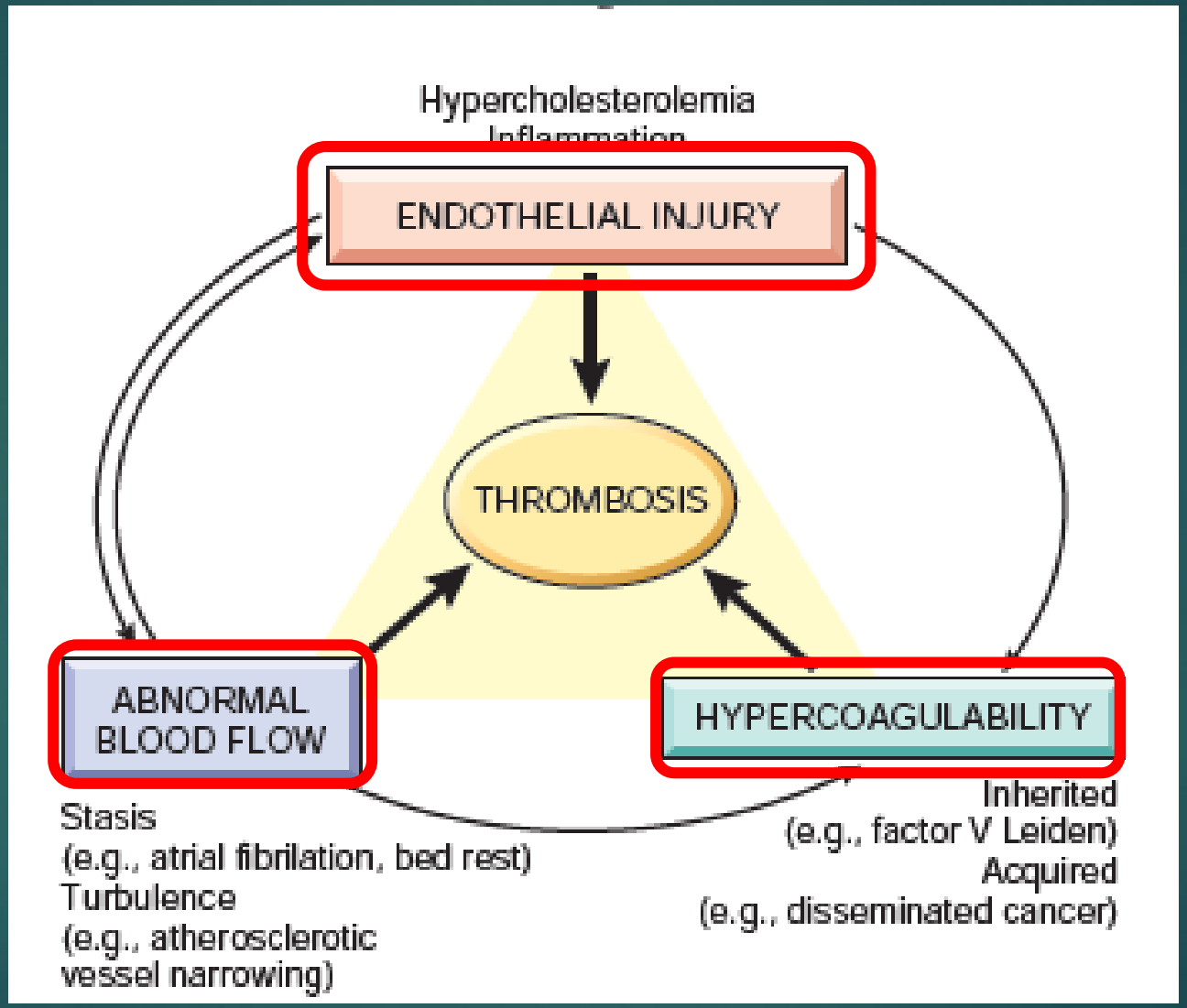
- Membutuhkan kepekaan terhadap **tanda klinis!**
  - Selalu kenali **Trias Virchow's** pada setiap pasien
  - Tanda dan gejala tidak sensitif dan spesifik, sebanyak 70% kasus asimtomatik

- Trias klasik emboli paru :

  - Bisa langsung tidak sadarkan diri atau henti jantung tanpa gejala sesak napas sebelumnya.

Sumber:
7. Kostadima E, Zakhynthinos E. Pulmonary embolism : pathophysiology, diagnosis, treatment. Hell J Cardiol. 2007;48:94–107

Trias Virchow's



Sumber:
8. Kumar V, Abbas A, editors. Hemodynamic disorders, thromboembolic disease and shock. In: Robbins and Cotrans Pathologic Basis of Disease. Elsevier; 2015. p. 113–35.

Etiologi Hiperkoagulabilitas

Primer

- **Umum**
  - Mutasi factor V
  - Mutasi protrombin
  - ⬆ Faktor VIII, IX, XI dan fibrinogen
- **Jarang**
  - Defisiensi antitrombin III / protein C / protein S
- **Sangat Jarang**
  - Defek fibrinolysis
  - Homosistinuria homozigot

Sekunder

- **Risiko tinggi trombosis**
  - Imobilisasi jangka panjang
  - Infark miokard
  - Fibrilasi atrium
  - Katup jantung prostetik
  - Kerusakan jaringan
  - Kanker
  - Koagulasi intravaskular diseminata
  - Trombositopenia terinduksi heparin
  - Sindrom antibodi antifosfolipid
- **Risiko rendah thrombosis**
  - Kardiomiopati
  - Sindrom nefrotik
  - Hiperestrogenik
  - Kontrasepsi oral
  - Anemia sel sabit
  - Merokok

Sumber:
8. Kumar V, Abbas A, editors. Hemodynamic disorders, thromboembolic disease and shock. In: Robbins and Cotrans Pathologic Basis of Disease. Elsevier; 2015. p. 113–35.

Karakteristik Klinis Pasien EP di Emergensi Unit

Feature	PE confirmed (*n* = 1880)	PE not confirmed (*n* = 528)
Dyspnoea	50%	51%
Pleuritic chest pain	39%	28%
Cough	23%	23%
Substernal chest pain	15%	17%
Fever	10%	10%
Haemoptysis	8%	4%
Syncope	6%	6%
Unilateral leg pain	6%	5%
Signs of DVT (unilateral extremity swelling)	24%	18%

Sumber:

2. Konstantinides S V, Germany C, France ND, Uk DF, Galie N, Uk JSRG, et al. 2014 ESC Guidelines on the diagnosis and management of acute pulmonary embolism The Task Force for the Diagnosis and Management of Acute Pulmonary Embolism of the European Society of Cardiology (ESC) Endorsed by the European Respiratory Society (ERS). 2014;3033–80.

ESC, guideline 2014.

Pemeriksaan Fisis

- Tanda disfungsi ventrikel kanan dan hipertensi pulmoner
  - P2 mengeras

    Auskultasi di area pulmonal. Komponen P2 dianggap mengeras jika terdengar lebih keras dari A2 di area pulmonal
  - Heave di ventrikel kanan
  - Peningkatan JVP

Diagnosis Diferensial

- Infark Miokard Akut
- Diseksi Aorta
- Gangguan muskuloskeletal
- PPOK Eksaserbasi akut
- Asma
- Pneumonia
- Pneumotoraks

Sumber:
9. Limantoro C. Emboli paru akut. In: Setiyohadi B, Nasution S, Arsana P, editors. EIMED PAPDI : kegawatdaruratan penyakit dalam (emergency in internal medicine). 2nd ed. Jakarta: Interna Publishing; 2016. p. 165–72.

Diagnosis Emboli Paru: Penggunaan Wells' Criteria untuk *Pre-Test Probability*

Wells' Criteria

- Tanda dan gejala klinis dari DVT– 3
- Laju nadi ≥ 100x/ menit – 1.5
- Imobilisasi (untuk ≥ 3 hari berturut-turut) – 1.5
- Riwayat operasi dalam 4 minggu terakhir – 1.5
- Hemoptisis – 1.0
- Riwayat kanker (dalam pengobatan atau pengobatan dalam 6 bulan terakhir atau paliatif) – 1.0
- Diagnosis emboli paru sangat mungkin dibanding diagnosis lainnya – 3.0

Probabilitas rendah <2.0

Probabilitas sedang = 2.0-6.0

Probabilitas Tinggi ≥ 7.0

Kemungkinan bukan emboli paru = 0-4.0

Kemungkinan emboli paru ≥ 5.0

Sumber:
10.Mazzolai L, Aboyans V, Ageno W, Agnelli G, Alatri A, Bauersachs R, et al. Diagnosis and management of acute deep vein thrombosis : a joint consensus document from the European Society of Cardiology working groups of aorta and peripheral vascular diseases and pulmonary circulation and right ventricular function. 2018;4208–18.

Mendiagnosis Emboli Paru: Penggunaan Wells' Criteria untuk *Pre-Test Probability*

Simplified Wells' Criteria

- Tanda dan gejala klinis dari DVT– 1
- Laju nadi ≥ 100x/ menit – 1
- Imobilisasi (untuk ≥ 3 hari berturut-turut) – 1
- Riwayat operasi dalam 4 minggu terakhir – 1
- Hemoptisis – 1
- Riwayat kanker (dalam pengobatan atau pengobatan dalam 6 bulan terakhir atau paliatif) – 1
- Diagnosis emboli paru sangat mungkin dibanding diagnosis lainnya – 1

Kemungkinan bukan emboli paru <2

Kemungkinan Emboli Paru ≥ 2

Sumber:
10. Mazzolai L, Aboyans V, Ageno W, Agnelli G, Alatri A, Bauersachs R, et al. Diagnosis and management of acute deep vein thrombosis : a joint consensus document from the European Society of Cardiology working groups of aorta and peripheral vascular diseases and pulmonary circulation and right ventricular function. 2018;4208–18.

Mendiagnosis Emboli Paru: Penggunaan Geneva Criteria untuk *Pre-Test Probability*

Geneva Criteria

- Tanda dan gejala klinis DVT – 3
- Laju nadi
  - 75-94 x/menit– 3
  - ≥ 95 x/menit - 5
- Usia > 65 tahun- 1
- Riwayat operasi dalam 4 minggu terakhir – 2
- Hemoptisis – 2
- Riwayat kanker (dalam pengobatan atau pengobatan dalam 6 bulan terakhir atau paliatif) – 2
- Nyeri pada satu sisi tungkai – 3

Probabilitas rendah 0-3

Probabilitas sedang: 4-10

Probabilitas tinggi ≥ 11

Kemungkinan bukan emboli paru 0-5

Kemungkinan emboli paru ≥ 6

Sumber:
10. Mazzolai L, Aboyans V, Ageno W, Agnelli G, Alatri A, Bauersachs R, et al. Diagnosis and management of acute deep vein thrombosis : a joint consensus document from the European Society of Cardiology working groups of aorta and peripheral vascular diseases and pulmonary circulation and right ventricular function. 2018;4208–18.

Predicting Pre-test probability for PE

Simplified Geneva Criteria

- Tanda dan gejala klinis DVT – 1
- Laju nadi
  - 75-94 x/menit– 1
  - ≥ 95 x/menit - 2
- Usia > 65 tahun- 1
- Riwayat operasi dalam 4 minggu terakhir – 1
- Hemoptisis – 1
- Riwayat kanker (dalam pengobatan atau pengobatan dalam 6 bulan terakhir atau paliatif) – 1
- Nyeri pada satu sisi tungkai – 1

Probabilitas rendah 0-1

Probabilitas sedang : 2-4

Probabilitas tinggi ≥ 5

Kemungkinan bukan emboli paru 0-2

Kemungkinan emboli paru ≥ 3

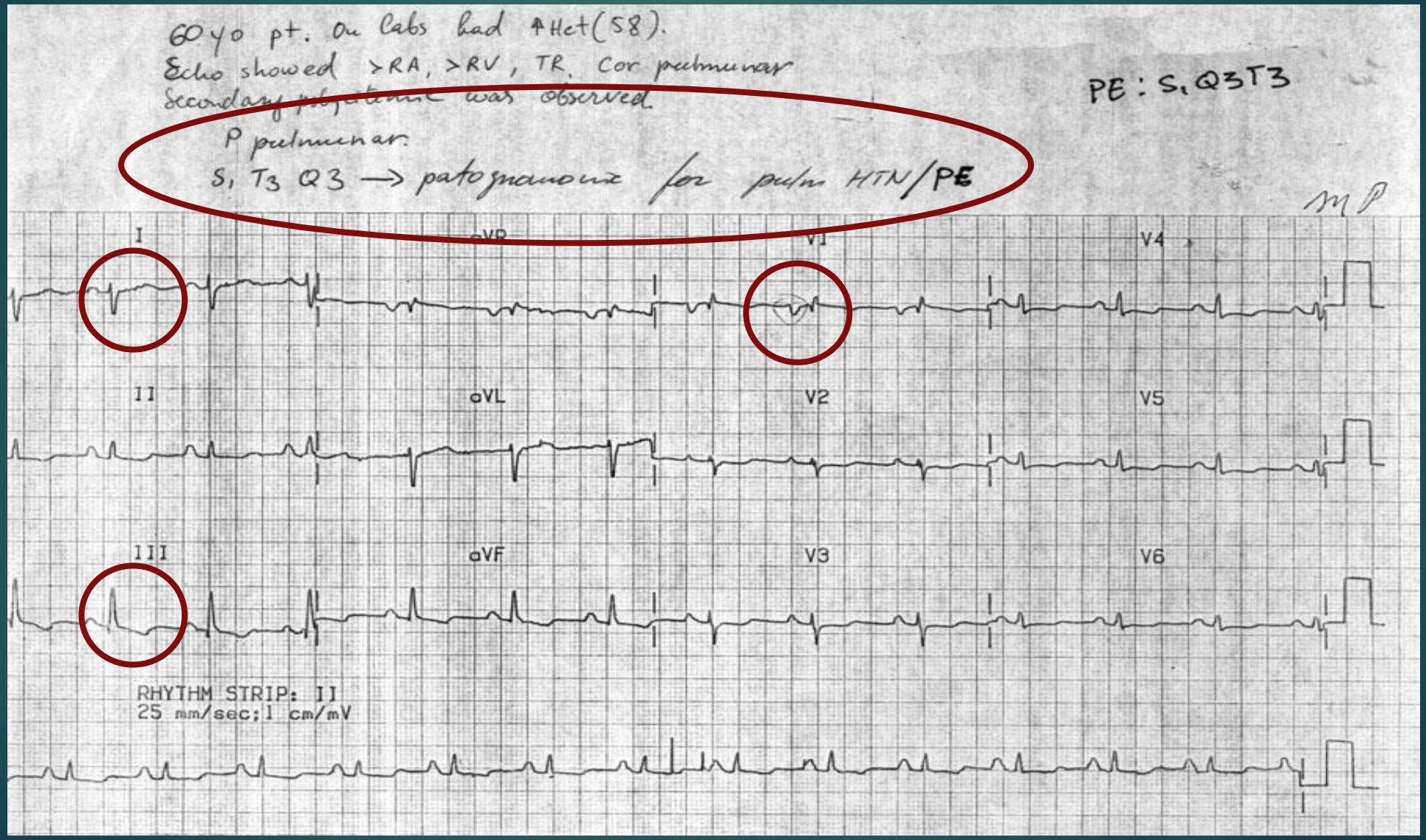
Sumber:
10. Mazzolai L, Aboyans V, Ageno W, Agnelli G, Alatri A, Bauersachs R, et al. Diagnosis and management of acute deep vein thrombosis : a joint consensus document from the European Society of Cardiology working groups of aorta and peripheral vascular diseases and pulmonary circulation and right ventricular function. 2018;4208–18.

Pemeriksaan penunjang sederhana untuk diagnosis emboli paru

- Analisis Gas Darah: Hipoksemia (tidak selalu), Hipokapnia
- X-ray Dada: temuan abnormal yang tidak spesifik, berguna untuk eksklusi diagnosis banding
- EKG: Gambaran RV strain: inversi gelombang T pada V1-V4, Gambaran QR pada V1, **gambaran S1Q3T3**, RBBB inkomplit → gambaran muncul pada kasus-kasus berat. Pada kasus ringan hanya sinus takikardia.
- Fibrilasi atrium dihubungkan dengan emboli paru akut

Sumber:
10. Mazzolai L, Aboyans V, Ageno W, Agnelli G, Alatri A, Bauersachs R, et al. Diagnosis and management of acute deep vein thrombosis : a joint consensus document from the European Society of Cardiology working groups of aorta and peripheral vascular diseases and pulmonary circulation and right ventricular function. 2018;4208–18.

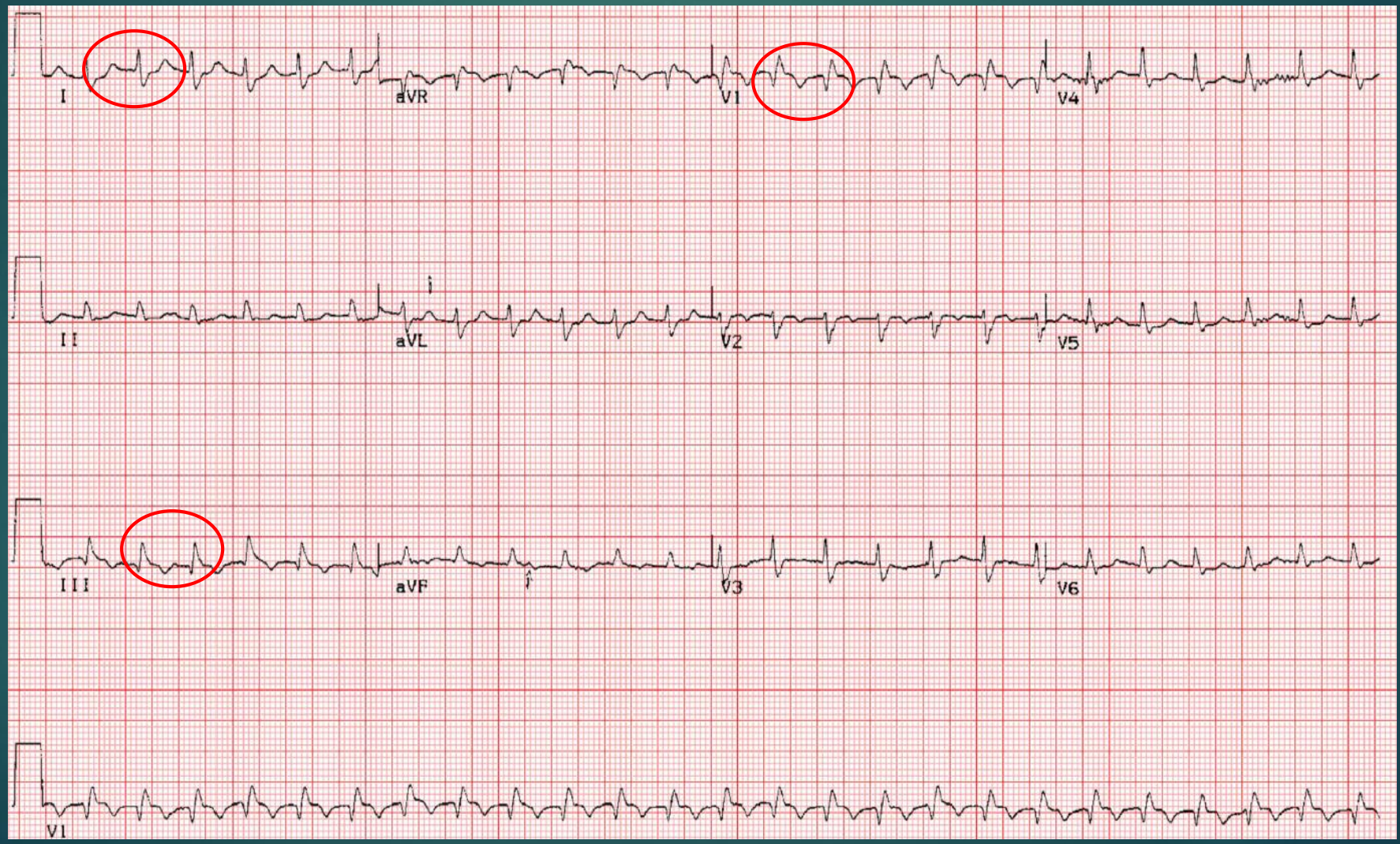
Elektrocardiography:



Wanita , 40 thn KU: pleuritic chest pain

S1Q3T3; prominent S lead I, gel.Q & inverted T lead III, ST,

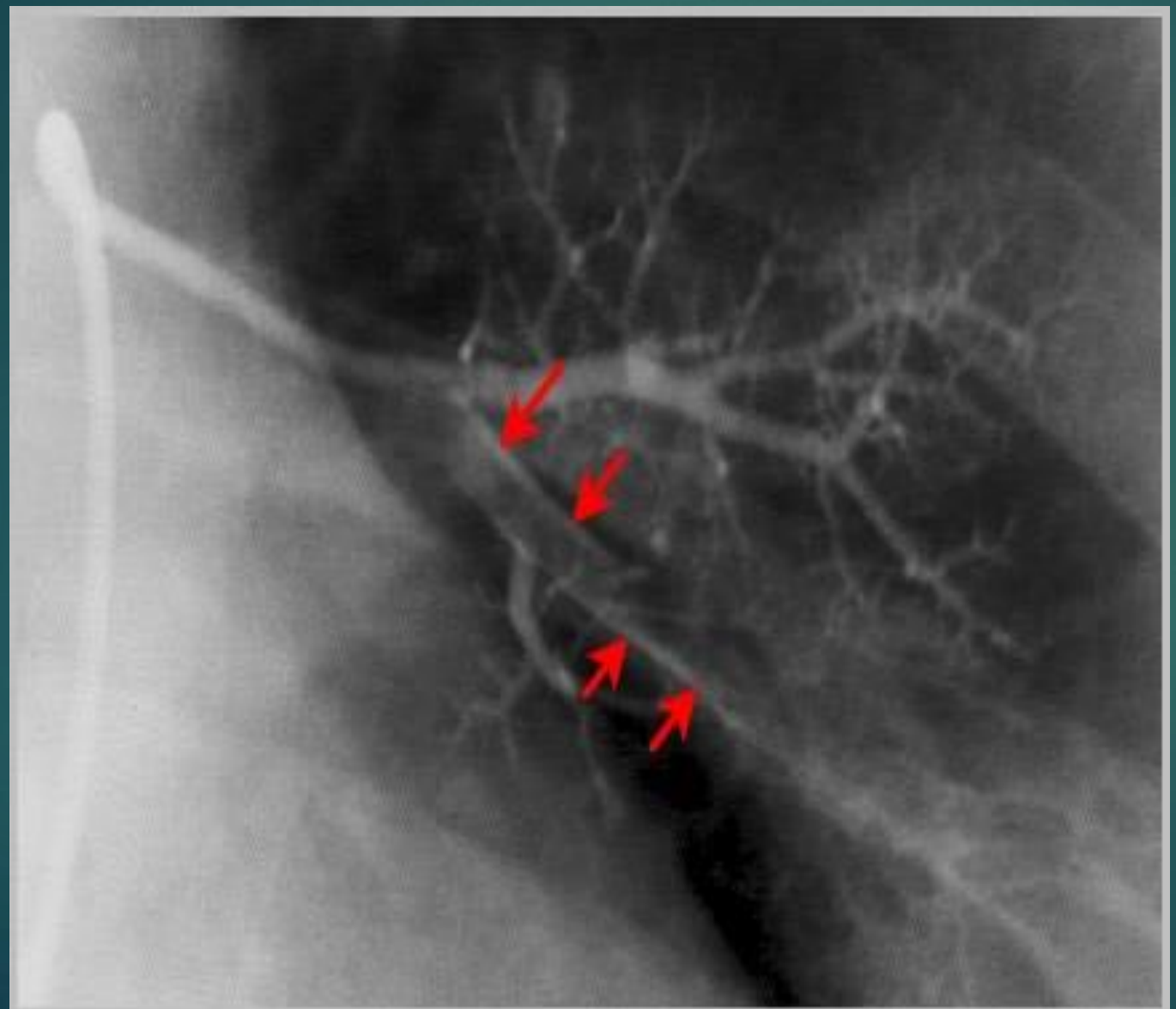
T inverted: leads V1 - V3, RBBB, defleksi amplitudo rendah



Pemeriksaan D-dimer

- D-dimer meningkat di plasma karena adanya aktivitas koagulasi dan fibrinolisis secara terus menerus
- NPV tinggi , tetapi PPV rendah → tidak berguna untuk konfirmasi diagnosis emboli paru
- *ELISA-derived assays* → sensitivitas ≥ 95% → digunakan untuk mengeksklusi emboli paru pada pasien dengan *pre-test probability* rendah atau sedang
- *Quantitative latex-derived assays* dan *whole-blood agglutination assays* → sensitivitas < 95% → masih aman untuk mengeksklusi emboli paru pada pasien dengan probabilitas rendah
- Nilai titik potong: 500 ug/L atau sesuai usia (usia x 10 ug/L di atas 50 tahun). Nilai yang sesuai usia lebih baik spesifisitasnya

Pemeriksaan Penunjang
Pulmonary Angiography (Gold Standard)

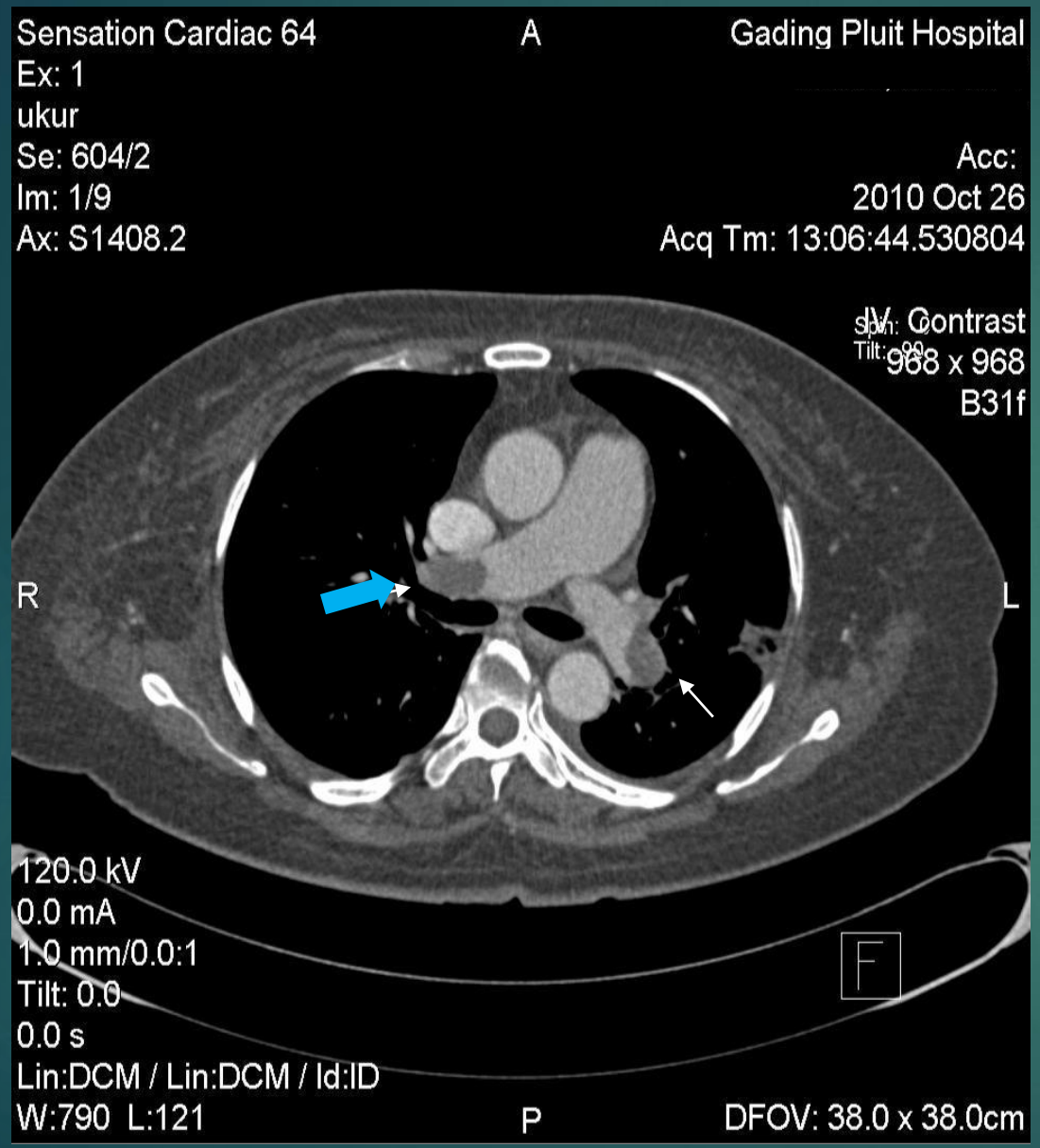


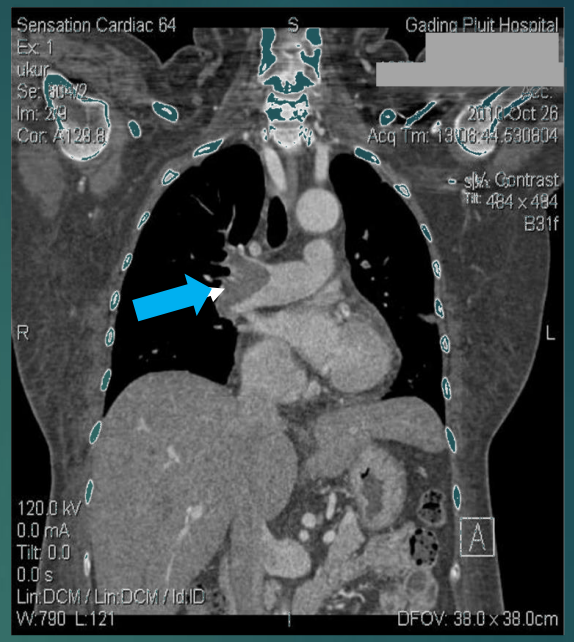
“Gold” standard

Kekurangan:
- **Invasive**
- **Contrast dye**
- **Availability**
- **Adverse effect (mortality 0,5%)**

Pemeriksaan penunjang: Computed Tomography Pulmonary Angiography (CTPA)

- PIOPED II trial: Sensitivitas 83% dan spesifisitas 96%
- Pada pasien probabilitas rendah dan sedang → NPV tinggi (96% dan 89%, berturut-turut) → dapat mengeksklusi emboli paru
- Pada pasien probabilitas tinggi dan sedang → PPV tinggi (92-96%)
- Akan tetapi signifikansi CT angiografi pada emboli paru sub-segmental terisolasi rendah → penggunaan ultrasonografi untuk memastikan apakah ada DVT atau tidak dapat dilakukan
- Pemeriksaan CT thorax biasa dapat mengidentifikasi emboli paru tanpa gejala pada pasien-pasien dengan faktor risiko seperti kanker, fibrilasi atrium, atau gagal jantung (1-2% kasus)


Sensation Cardiac 64
A
Gading Pluit Hospital
Ex: 1
ukur
Se: 604/2
Im: 1/9
Ax: S1408.2
Acc:
2010 Oct 26
Acq Tm: 13:06:44.530804
IV Contrast
Tilt: 0.0
968 x 968
B31f
R
L
120.0 kV
0.0 mA
1.0 mm/0.0:1
Tilt: 0.0
0.0 s
Lin:DCM / Lin:DCM / Id:ID
W:790 L:121
P
DFOV: 38.0 x 38.0cm


Sensation Cardiac 64
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Im: 2/9
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IV Contrast
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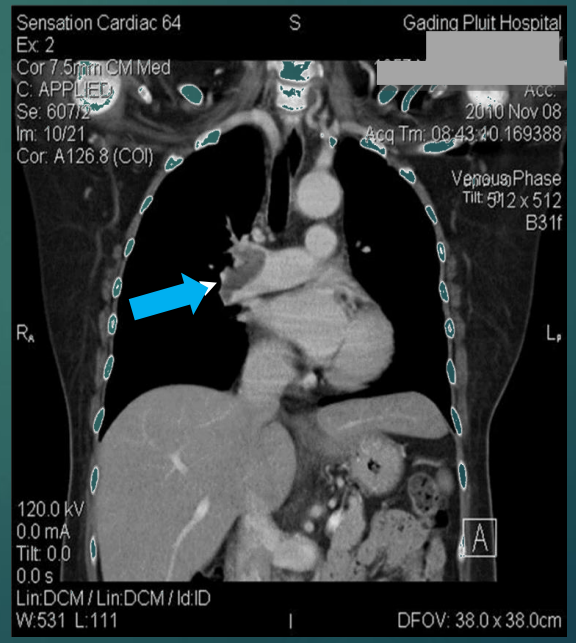
DFOV: 38.0 x 38.0cm


Sensation Cardiac 64
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Ex: 2
Cor 7.5mm CM Med
C: APPLIED
Se: 607/2
Im: 10/21
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Venous Phase
Tilt: 0.0
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120.0 kV
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Tilt: 0.0
0.0 s
Lin:DCM / Lin:DCM / Id:ID
W:531 L:111
I
DFOV: 38.0 x 38.0cm

Skintigrafi Paru

- Untuk meningkatkan spesifisitas pada emboli paru akut.
- Skintigrafi Ventilasi-Perfusi (V/Q Scan) mencari V/Q *mismatch* antara ventilasi (normal) pada segmen hipoperfusi.
- Baik digunakan pada pasien rawat jalan, probabilitas rendah, hasil foto thorax normal, usia muda (terutama wanita), riwayat anafilkasis terhadap kontras dan riwayat alergi lain, gagal ginjal, myeloma, dan paraprotenemia

Magnetic resonance angiography dan Echocardiography

Magnetic Resonance Angiography

- Belum dapat digunakan dalam praktik klinis karena senstivitas rendah dan tidak available pada setting gawat darurat

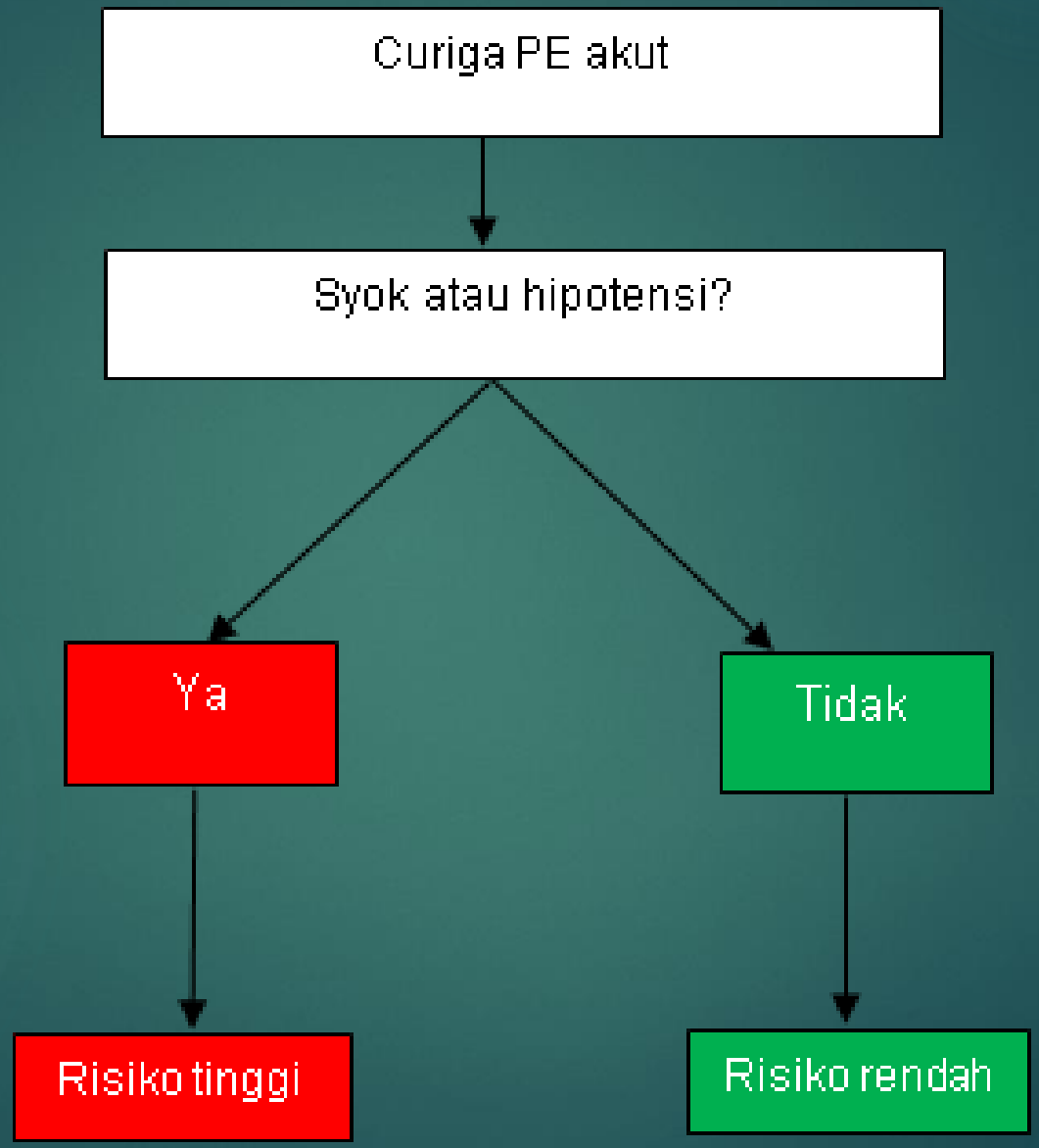
Echocardiography

- Mencari *overload* tekanan dan disfungsi ventrikel kanan
- Dapat mengeksklusi diagnosis banding dari syok
- Pada pasien tidak stabil yang dicurigai emboli paru, tanda-tanda overload tekanan dan disfungsi ventrikel kanan memberikan dasar untuk terapi reperfusi darurat bila CT angiografi tidak tersedia

Compression venous ultrasonography

- Untuk mencari DVT pada pasien Emboli paru → sensitivitas >90% dan spesifisitas 95% pada DVT dengan gejala
- Menunjukkan keberadaan DVT pada 30-50% pasien emboli paru.

Pendekatan Diagnosis



Sumber:

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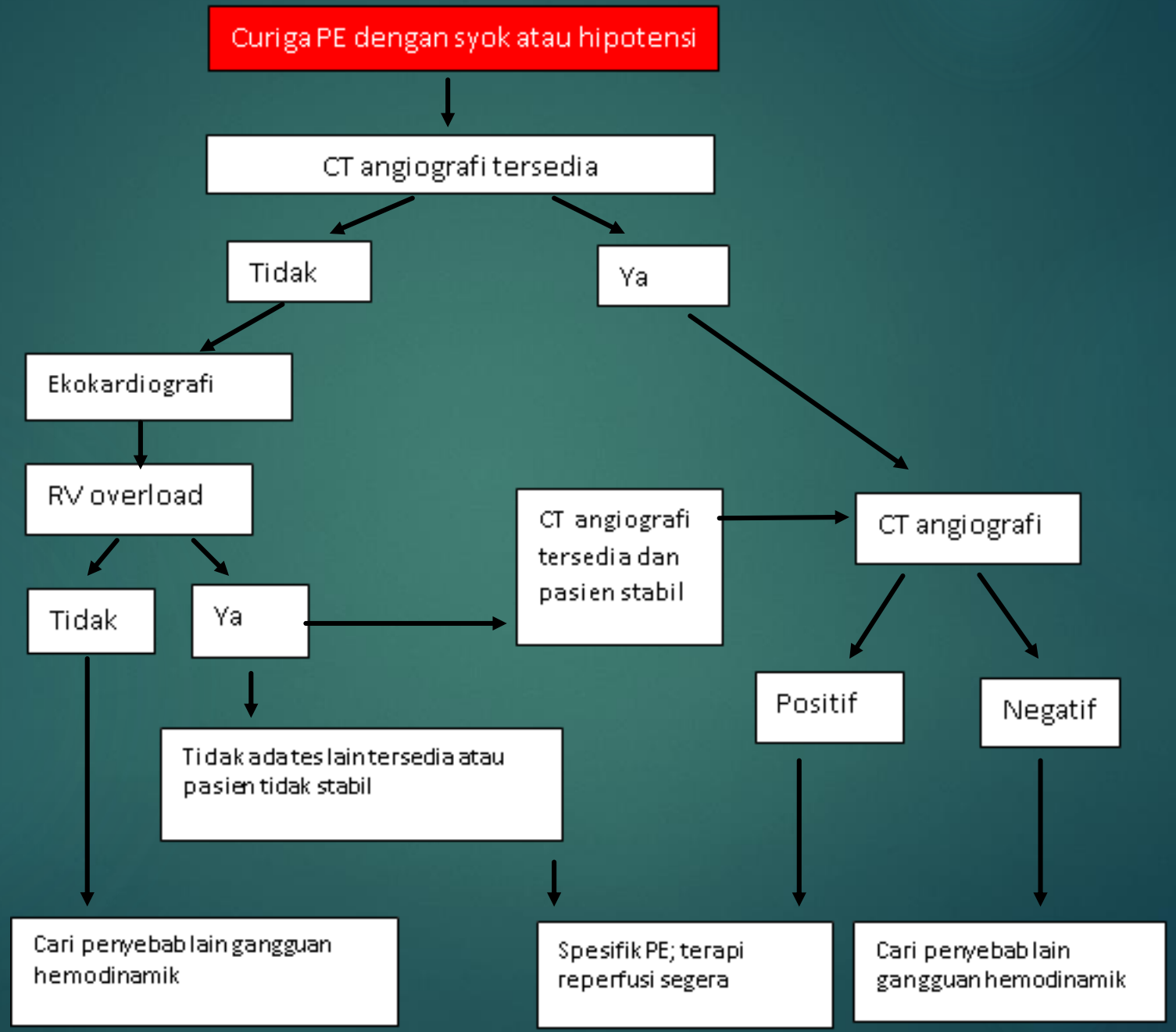
Pendekatan Diagnosis (lanj.)



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Pendekatan Diagnosis (lanj.)

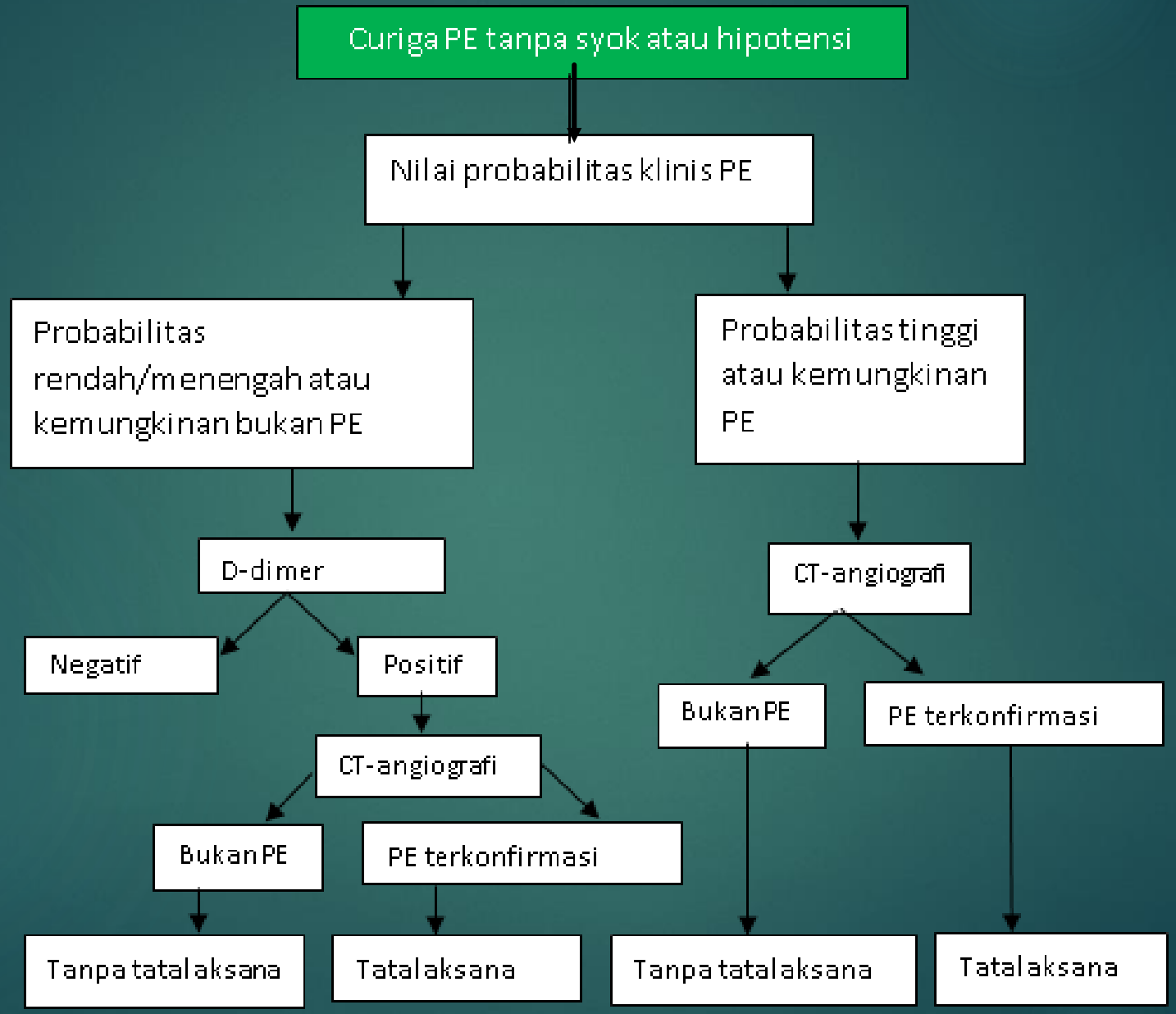

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Table 6 Validated diagnostic criteria (based on non-invasive tests) for diagnosing PE in patients without shock or hypotension according to clinical probability

Diagnostic criterion	Clinical probability of PE				
	Low	Intermediate	High	PE unlikely	PE likely
Exclusion of PE					
D-dimer					
Negative result, highly sensitive assay	+	+	–	+	–
Negative result, moderately sensitive assay	+	±	–	+	–
Chest CT angiography					
Normal multidetector CT alone	+	+	±	+	±
V/Q scan					
Normal perfusion lung scan	+	+	+	+	+
Non-diagnostic lung scan[a] and negative proximal CUS	+	±	–	+	–
Confirmation of PE					
Chest CT angiogram showing at least segmental PE	+	+	+	+	+
High probability V/Q scan	+	+	+	+	+
CUS showing proximal DVT	+	+	+	+	+

+/green = valid diagnostic criterion (no further testing required); –/red = invalid criterion (further testing mandatory); ±/yellow = controversial criterion (further testing to be considered).

[a]Low or intermediate probability lung scan according to the PIOPED classification.

CT = computed tomographic; CUS = proximal lower limb venous ultrasonography; DVT = deep vein thrombosis; PE = pulmonary embolism; PIOPED = Prospective Investigation of Pulmonary Embolism Diagnosis; V/Q scan = ventilation–perfusion scintigram.

PROGNOSIS

Prognostic Assessment of Patients With Acute PE

	PESI	Simplified PESI
Age	age	1 (if age > 80 years)
Male sex	10	
Cancer	30	1
Chronic HF	10	1
Chronic pulmonary disease	10	
Pulse rate > 110 bpm	20	1
Systolic BP < 100 mm Hg	30	1
Resp rate > 30 breaths per minute	20	
Temperature < 36°C	20	
Altered mental status	60	
Arterial hemoglobin O_2 saturation < 90%	20	1
Risk stratification	Class I-V	≥ 1 point = 10.9% mortality risk

Konstantinides S, et al. *Eur Heart J.* 2014 Aug 29.[1]

Class I: ≤65 points
very low 30-day mortality risk (0–1.6%)
Class II: 66–85 points
low mortality risk (1.7–3.5%)

Class III: 86–105 points
moderate mortality risk (3.2–7.1%)
Class IV: 106–125 points
high mortality risk (4.0–11.4%)
Class V: >125 points
very high mortality risk (10.0–24.5%)

0 points= 30-day mortality risk 1.0%
(95% CI 0.0%–2.1%)

≥1 point(s)= 30-day mortality risk 10.9%
(95% CI 8.5%–13.2%)

Penilaian prognosis dengan Echocardiography dan Biomarker jantung

- Echocardiography: Beberapa kriteria disfungsi ventrikel kanan yang dapat digunakan:
  - Dilatasi ventrikel kanan dan/atau peningkatan rasio end-diastolic RV-LV diameter (0,9-1,0)
  - Hipokinesia dari dinding ventrikel kanan
  - Peningkatan kecepatan regurgitasi tricuspid
- Biomarker yang digunakan:
  - Peningkatan troponin I atau T
  - Peningkatan BNP

Table 9 Classification of patients with acute PE based on early mortality risk

Early mortality risk		Risk parameters and scores			
		Shock or hypotension	PESI class III–V or sPESI ≥1[a]	Signs of RV dysfunction on an imaging test[b]	Cardiac laboratory biomarkers[c]
High		+	(+)[d]	+	(+)[d]
Intermediate	Intermediate–high	–	+	Both positive	
	Intermediate–low	–	+	Either one (or none) positive[e]	
Low		–	–	Assessment optional; if assessed, both negative[e]	

PE = pulmonary embolism; PESI = Pulmonary embolism severity index; RV = right ventricular; sPESI = simplified Pulmonary embolism severity index.

[a]PESI Class III to V indicates moderate to very high 30-day mortality risk; sPESI ≥1 point(s) indicate high 30-day mortality risk.

[b]Echocardiographic criteria of RV dysfunction include RV dilation and/or an increased end-diastolic RV–LV diameter ratio (in most studies, the reported threshold value was 0.9 or 1.0); hypokinesia of the free RV wall; increased velocity of the tricuspid regurgitation jet; or combinations of the above. On computed tomographic (CT) angiography (four-chamber views of the heart), RV dysfunction is defined as an increased end-diastolic RV/LV (left ventricular) diameter ratio (with a threshold of 0.9 or 1.0).

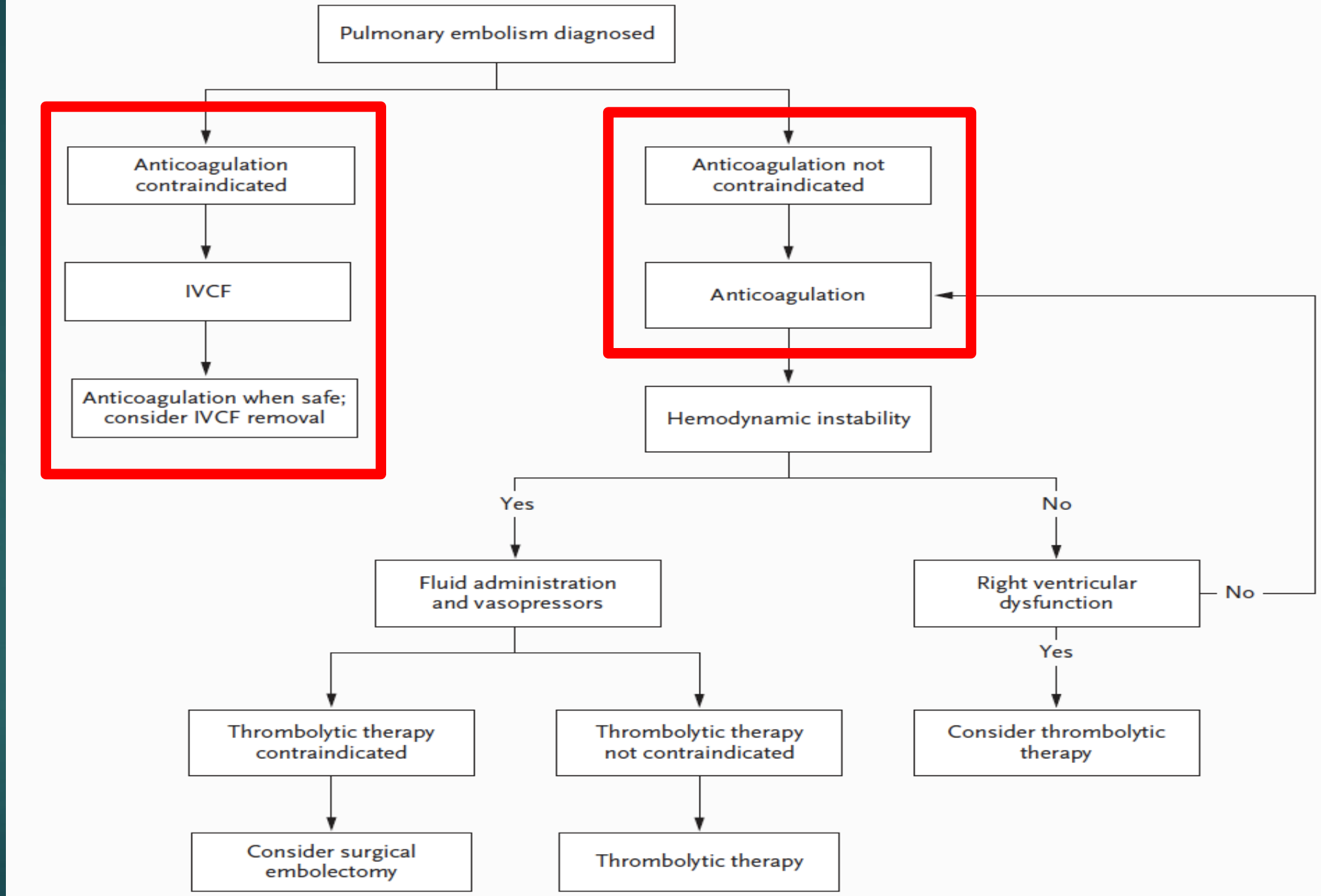
[c]Markers of myocardial injury (e.g. elevated cardiac troponin I or -T concentrations in plasma), or of heart failure as a result of (right) ventricular dysfunction (elevated natriuretic peptide concentrations in plasma).

[d]Neither calculation of the PESI (or sPESI) nor laboratory testing are considered necessary in patients with hypotension or shock.

[e]Patients in the PESI Class I–II, or with sPESI of 0, and elevated cardiac biomarkers or signs of RV dysfunction on imaging tests, are also to be classified into the intermediate-low-risk category. This might apply to situations in which imaging or biomarker results become available before calculation of the clinical severity index.

TATA LAKSANA

Tatalaksana



Tatalaksana

Tatalaksana suportif

- Terapi cairan volume sedang (sekitar 500cc), tidak boleh berlebihan → memperparah fungsi jantung kanan.
- Vasopresor, Inotropik (NE untuk pasien hipotensi, dobutamine/dopamine untuk pasien tidak hipotensi, epinefrin dapat digunakan untuk pasien syok)
- Terapi oksigen untuk pasien hipoksemia (bila perlu ventilasi mekanik, volume tidal 6 mL/kgBB saja)

Sumber:

5. Riyanto B. Nyeri dada non kardiak. In: Kumpulan naskah pertemuan ilmiah nasional XII PB PAPDI. Jakarta: Interna Publishing; p. 301–24.

Tatalaksana

Pemberian antikoagulan

- terapi utama emboli paru untuk mencegah kematian dini, dan berulangnya kejadian tromboemboli vena fatal/simtomatik
- Fase akut : UFH, LMWH, atau fondaparinoux dalam 5-10 hari pertama
- Dilakukan bersamaan dengan VKA atau DOAC. Total masa pemberian antikoagulan adalah tiga bulan

Sumber:

2. Konstantinides S V, Germany C, France ND, Uk DF, Galie N, Uk JSRG, et al. 2014 ESC Guidelines on the diagnosis and management of acute pulmonary embolism The Task Force for the Diagnosis and Management of Acute Pulmonary Embolism of the European Society of Cardiology (ESC) Endorsed by the European Respiratory Society (ERS). 2014;3033–80. Riyanto B. Nyeri dada non kardiak. In: Kumpulan naskah pertemuan ilmiah nasional XII PB PAPDI. Jakarta: Interna Publishing; p. 301–24.

Tatalaksana

Filter vena kava

- Indikasi pada pasien emboli paru dengan emboli paru akut yang memiliki kontraindikasi terhadap antikoagulan dan PE rekuren meskipun sudah diberi antikoagulan

Sumber:
2. Konstantinides S V, Germany C, France ND, Uk DF, Galie N, Uk JSRG, et al. 2014 ESC Guidelines on the diagnosis and management of acute pulmonary embolism The Task Force for the Diagnosis and Management of Acute Pulmonary Embolism of the European Society of Cardiology (ESC) Endorsed by the European Respiratory Society (ERS). 2014;3033–80.

Tatalaksana

Trombolisis

- Indikasi pada pasien PE dengan hemodinamik tidak stabil → langsung melisiskan trombus dan mengembalikan perfusi paru lebih cepat dibandingkan dengan antikoagulan

Sumber:
2. Konstantinides S V, Germany C, France ND, Uk DF, Galie N, Uk JSRG, et al. 2014 ESC Guidelines on the diagnosis and management of acute pulmonary embolism The Task Force for the Diagnosis and Management of Acute Pulmonary Embolism of the European Society of Cardiology (ESC) Endorsed by the European Respiratory Society (ERS). 2014;3033–80.

Tatalaksana

Trombektomi

- Merupakan pilihan pada PE dengan risiko tinggi atau PE risiko sedang-tinggi yang memiliki kontraindikasi terhadap trombolitik atau gagal setelah menjalani trombolitik

Sumber:
2. Konstantinides S V, Germany C, France ND, Uk DF, Galie N, Uk JSRG, et al. 2014 ESC Guidelines on the diagnosis and management of acute pulmonary embolism The Task Force for the Diagnosis and Management of Acute Pulmonary Embolism of the European Society of Cardiology (ESC) Endorsed by the European Respiratory Society (ERS). 2014;3033–80.

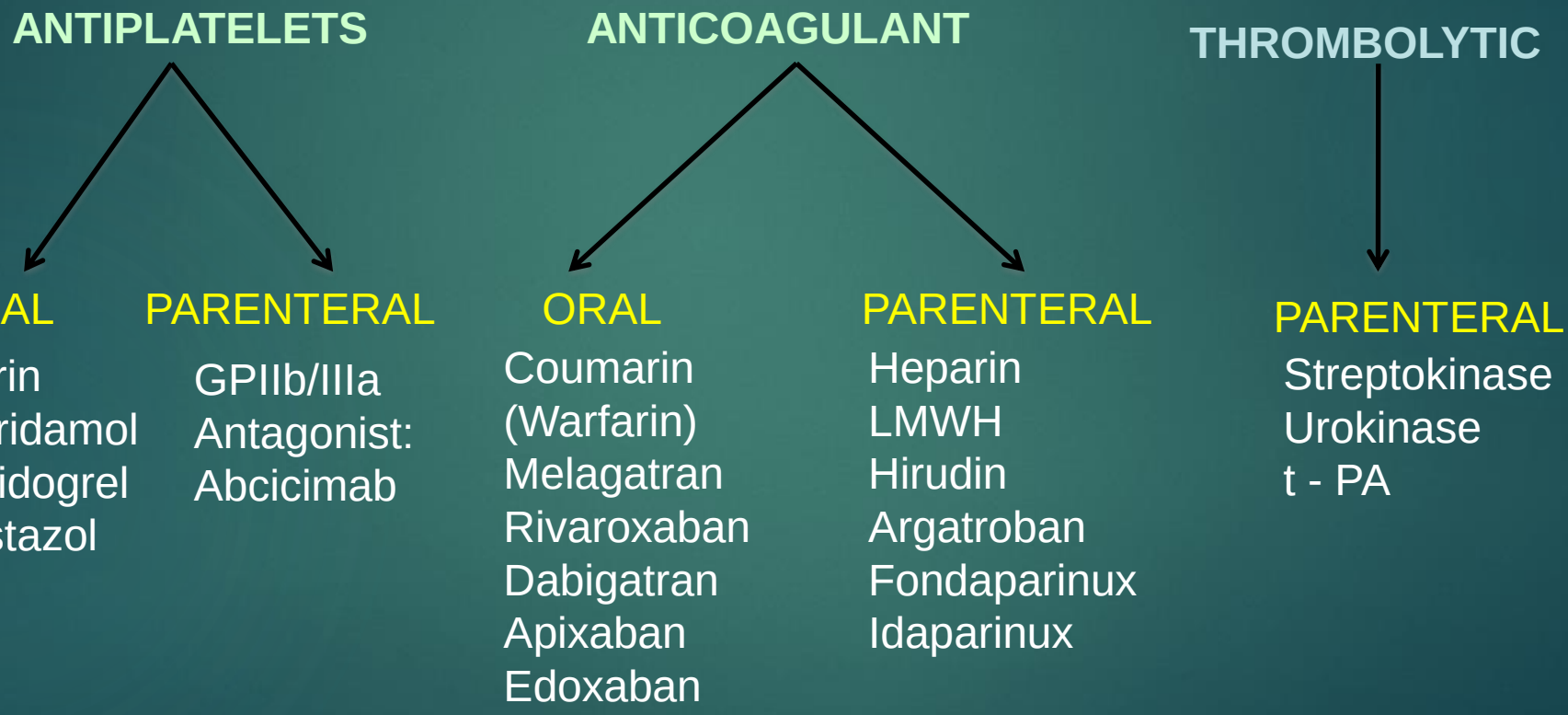
Tatalaksana

Kateterisasi perkutan

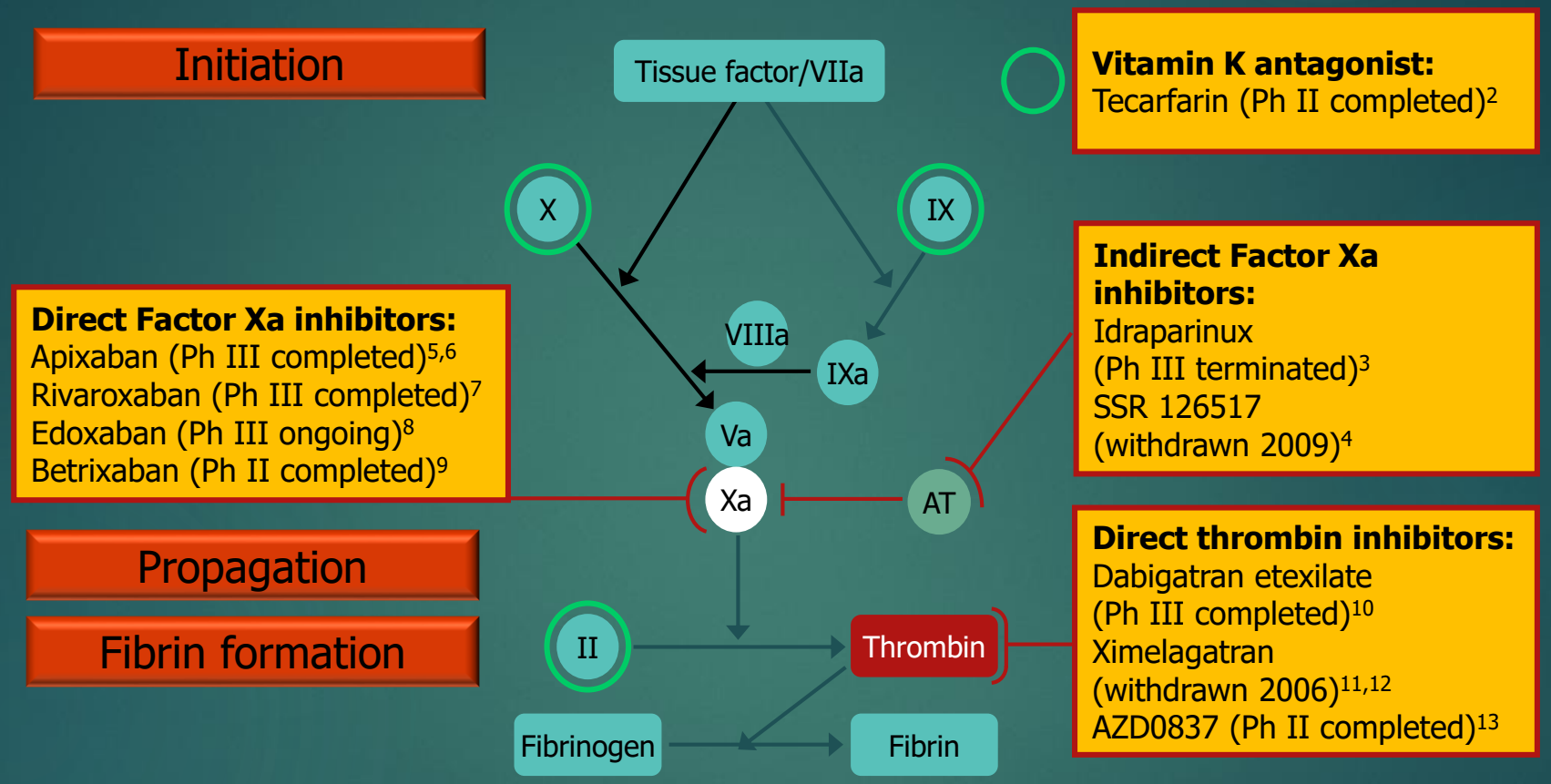
- Indikasi untuk pasien dengan kontraindikasi absolut trombolisis
- Pilihan: fragmentasi trombus dengan pigtail atau balloon catheter, rheolitik trombektmi dengan kateter hidrodinamik, trombektomi suction, trombektomi rotasional

Sumber:
2. Konstantinides S V, Germany C, France ND, Uk DF, Galie N, Uk JSRG, et al. 2014 ESC Guidelines on the diagnosis and management of acute pulmonary embolism The Task Force for the Diagnosis and Management of Acute Pulmonary Embolism of the European Society of Cardiology (ESC) Endorsed by the European Respiratory Society (ERS). 2014;3033–80.

Pilihan Agen
Antiplatelet, Antikoagulan, dan Trombolitik



Target Kerja Agen Antikoagulasi



Sumber:

11. Turpie AG. New oral anticoagulants in atrial fibrillation. Eur Heart J. 2008;29:155–65
12. Ellis DJ et al. The first evaluation of a novel vitamin K antagonist, tecarfarin (ATI-5923), in patients with atrial fibrillation. Circulation 2009;120:1029–35
13. Bousser MG et al. Comparison of idraparinux with vitamin K antagonists for prevention of thromboembolism in patients with atrial fibrillation: a randomised, open-label, non-inferiority trial. Lancet 2008;371:315–21;
14. Connolly SJ et al. Apixaban in patients with atrial fibrillation. N Engl J Med 2011;364:806–17
15. Granger CB et al. Apixaban versus warfarin in patients with atrial fibrillation. N Engl J Med 2011;365:981–92
16. Patel MR et al. Rivaroxaban versus warfarin in nonvalvular atrial fibrillation. N Engl J Med 2011;365:883–91
17. Connolly SJ et al. Dabigatran versus warfarin in patients with atrial fibrillation. N Engl J Med 2009;361:1139–51
18. Olsson SB et al. Ximelagatran was non-inferior to warfarin in preventing stroke and systemic embolism in atrial fibrillation. Lancet 2003;362:1691–8

Direct Oral Anticoagulant

Profil	Rivaroxaban	Apixaban	Dabigatran	Edoxaban
Dosis	2 x 15 mg selama 21 hari , dilanjutkan 20 mg/hari(3-12 bulan)	2x 10 mg selama 7 hari, dilanjutkan 2x5mg selama 6 bulan	LMWH/UFH dahulu selama 5-10 hari, dilanjutkan 2x150 mg selama 6 bulan	LMWH/UFH dahulu selama 5-12 hari, dilanjutkan 1x60 mg/hari selama 3-12 bulan
Efikasi	Noninferior	Noninferior	Noninferior	Noninferior
Perdarahan mayor	↓46%	↓69%	Noninferior	Noninferior
Penyesuaian dosis berdasarkan fungsi ginjal	Hindari bila CrCL< 30ml/min	PK/PD	Hindari bila CrCL<30 ml/min	1 x30 mg jika CrCl 30-50 ml/min, hindari bila CrCl<30 ml/min

Evolving Anticoagulation Strategies

Overlapping	LMWH/Warfarin Bridge	UFH/Warfarin Bridge
Switching	LMWH to **Dabigatran** (**RE-COVER**)	LMWH to **Edoxaban** (**HOKUSAI**) (N=8,250)
Oral Monotherapy	**Rivaroxaban** (3 week loading dose) (**EINSTEIN**)	**Apixaban** (1 week load) (**AMPLIFY**)

ESC 2014
PE Anticoagulation Recommendations

- Class I; Level B
  - In parallel to parenteral anticoagulation, treatment with a VKA is recommended, targeting an INR of 2.5 (range 2.0-3.0)
  - Replace combination of parenteral anticoagulation and VKA with anticoagulation and
    - Rivaroxaban (15 mg bid for 3 weeks, followed by 20 mg once daily)

    OR
    - Apixaban (10 mg bid for 7 days, followed by 5 mg bid)
  - Following acute-phase parenteral anticoagulation, replace VKA treatment with
    - Dabigatran (150 mg bid, or 110 mg bid for patients ≥ 80 years of age)

    OR
    - Edoxaban (when approved)

Konstantinides S, et al. *Eur Heart J*. 2014 Aug 29.[1]

Table : Properties of Warfarin, Enoxaparin & Dabigatran

Property	Warfarin	Enoxaparin	Dabigatran
Mechanism of action	Reduced synthesis of prothrombin and other clotting factors	Indirect inhibition of factor Xa	Direct inhibition of thrombin
Administration	Oral	Parenteral	Oral
Dosing	Individualized to each patient and target INR	Fixed dose, dependent on patient's weight	Fixed dose, dependent on indication, creatinine clearance, age, and concomitant use of p-glycoprotein inhibitors
Onset of action	36–72 h	1 h	0.5–2 h
Elimination half-life	20–60 h	4.5–7 h	12–14 h
Duration of action	48–96 h	12 h	24 h
Stable, predictable pharmacokinetics	No	Yes	Yes
Interactions with diet and alcohol	Yes	No	No
Monitoring	INR every 1–4 wk	Not monitored	No routine monitoring required
Dose adjustment	Frequent	Rarely required	Rarely required
Effective anticoagulant	Yes	Yes	Yes (noninferior or superior to enoxaparin and warfarin in phase III studies)
Risk of hemorrhage	Significant	Significant	Similar to or lower than that for enoxaparin and warfarin in phase III studies (RE-LY)
Use in severe liver disease	Problematic	Metabolized by hepatic route	Not studied
Use in severe renal disease	Yes	Yes (dose adjusted)	Not studied in phase III trials
Antidote ★	Rapid reversal with fresh-frozen plasma or PCCs; slow reversal with vitamin K	Protamine sulfate (reverses 60% of enoxaparin)	None available but can be removed by dialysis
Cost	Cheap	Cost-effective for prevention of VTE	Cost-effective for prevention of VTE after TKA and THA[29,30] and prevention of stroke in atrial fibrillation[31]

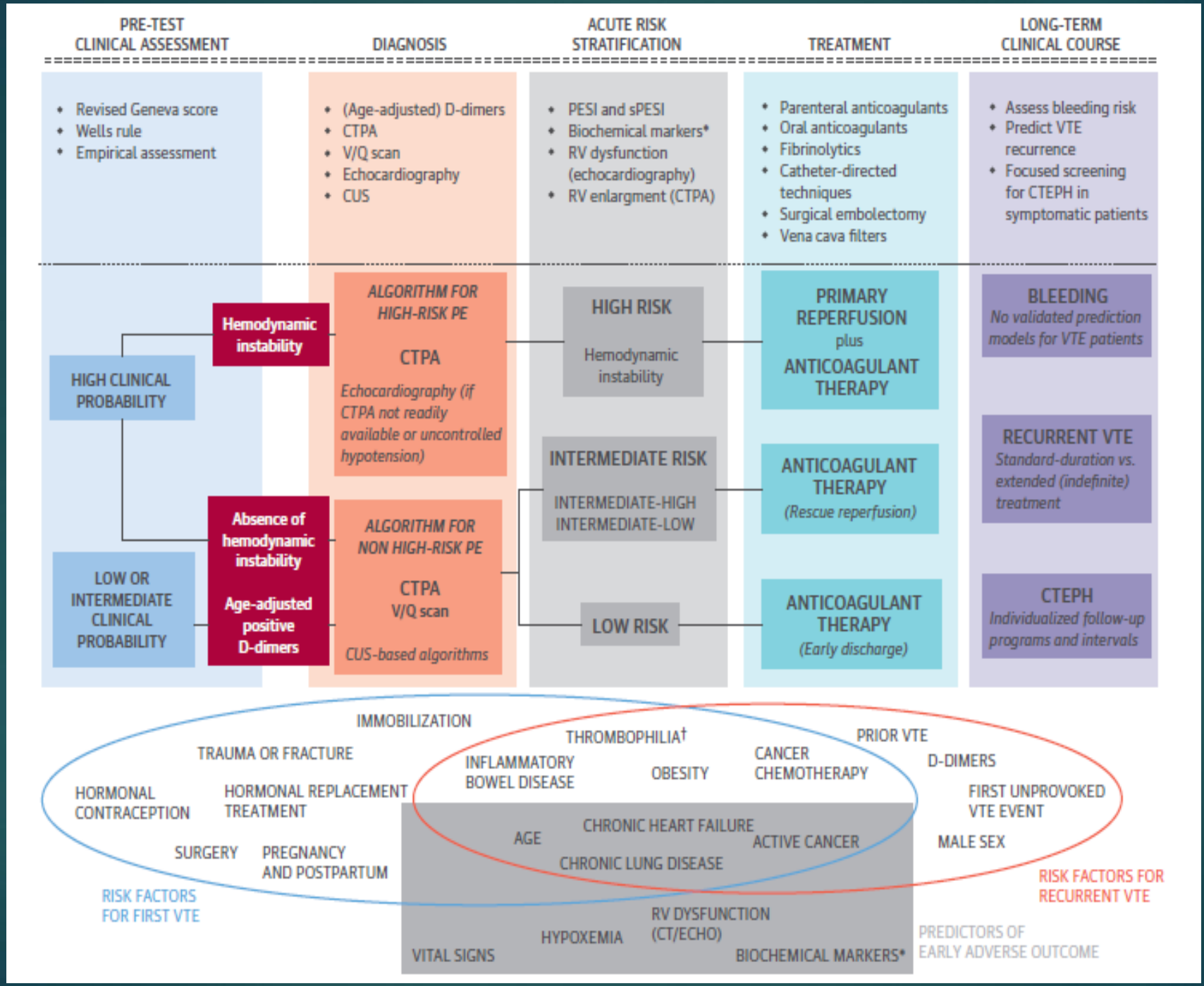
Obat	Dosis	Interval
Enoxaparin	1 mg/kg Atau 1,5 mg/kg	Setiap 12 jam Sekali sehari
Tinzaparin	175 U/kg	Sekali sehari
Dalteparin	100 IU/kg Atau 200 IU/kg	Setiap 12 jam Sekali sehari
Nadroparin	86 IU/kg Atau 171 IU/kg	Setiap 12 jam Sekali sehari
Fondaparinux	BB <50 kg : 5 mg BB 50-100 kg : 7,5 mg BB >100 kg : 10 mg	Sekali sehari

Stratifikasi Risiko Pendarahan

Risiko HAS-BLED	Skor
Hipertensi	1
Fungsi ginjal terganggu	1
Fungsi liver terganggu	1
Stroke	1
Perdarahan	1
INR tidak stabil	1
Usia >65	1
Penggunaan obat-obatan	1
Penggunaan alkohol	1

Risiko ringan (0-1)
Risiko menengah(2)
Risiko tinggi (≥3)

Sumber:
20. Stubss M, Mouyis M, Thomas M. Deep vein thrombosis. BMJ. 2018;360:k351.


PRE-TEST CLINICAL ASSESSMENT
DIAGNOSIS
ACUTE RISK STRATIFICATION
TREATMENT
LONG-TERM CLINICAL COURSE
Revised Geneva score
Wells rule
Empirical assessment
(Age-adjusted) D-dimers
CTPA
V/Q scan
Echocardiography
CUS
PESI and sPESI
Biochemical markers*
RV dysfunction (echocardiography)
RV enlargment (CTPA)
Parenteral anticoagulants
Oral anticoagulants
Fibrinolytics
Catheter-directed techniques
Surgical embolectomy
Vena cava filters
Assess bleeding risk
Predict VTE recurrence
Focused screening for CTEPH in symptomatic patients
HIGH CLINICAL PROBABILITY
Hemodynamic instability
ALGORITHM FOR HIGH-RISK PE
CTPA
Echocardiography (if CTPA not readily available or uncontrolled hypotension)
HIGH RISK
Hemodynamic instability
PRIMARY REPERFUSION plus ANTICOAGULANT THERAPY
BLEEDING
No validated prediction models for VTE patients
LOW OR INTERMEDIATE CLINICAL PROBABILITY
Absence of hemodynamic instability
Age-adjusted positive D-dimers
ALGORITHM FOR NON HIGH-RISK PE
CTPA
V/Q scan
CUS-based algorithms
INTERMEDIATE RISK
INTERMEDIATE-HIGH
INTERMEDIATE-LOW
ANTICOAGULANT THERAPY
(Rescue reperfusion)
RECURRENT VTE
Standard-duration vs. extended (indefinite) treatment
LOW RISK
ANTICOAGULANT THERAPY
(Early discharge)
CTEPH
Individualized follow-up programs and intervals
IMMOBILIZATION
TRAUMA OR FRACTURE
HORMONAL CONTRACEPTION
HORMONAL REPLACEMENT TREATMENT
SURGERY
PREGNANCY AND POSTPARTUM
RISK FACTORS FOR FIRST VTE
THROMBOPHILIA†
INFLAMMATORY BOWEL DISEASE
OBESITY
CANCER CHEMOTHERAPY
PRIOR VTE
D-DIMERS
FIRST UNPROVOKED VTE EVENT
MALE SEX
RISK FACTORS FOR RECURRENT VTE
AGE
CHRONIC HEART FAILURE
ACTIVE CANCER
CHRONIC LUNG DISEASE
HYPOXEMIA
RV DYSFUNCTION (CT/ECHO)
VITAL SIGNS
BIOCHEMICAL MARKERS*
PREDICTORS OF EARLY ADVERSE OUTCOME

Kesimpulan

- Emboli paru merupakan penyakit yang disebabkan oleh obstruksi embolus pada arteri pulmonalis dan percabangannya, yang menyebabkan gangguan perfusi dan ventilasi paru, berujung pada gangguan perfusi sistemik yang menyebabkan kematian
- Tanda dan gejala klinis emboli paru seringkali tidak khas sehingga diperlukan kepekaan terhadap klinis pasien, dibantu dengan sistem skoring wells atau geneva dan pemeriksaan penunjang yang tersedia
- Prognosis emboli paru ditentukan berdasarkan keberadan faktor-faktor prognostk yang dapat dinilai menggunakan sistem skoring PESI/sPESI serta modalitas pemeriksaan penunjang yang ada
- Pemberian antikoagulan merupakan terapi farmakologis wajib pada pasien-pasien tanpa kontraindikasi absolut. Pemberian terapi lain seperti filter vena cava, trombolisis, trombektomi, kateterisasi perkutan, dan terapi suportif diperlukan pada indikasi-indikasi tertentu

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14. Connolly SJ et al. Apixaban in patients with atrial fibrillation. N Engl J Med 2011;364:806–17
15. Granger CB et al. Apixaban versus warfarin in patients with atrial fibrillation. N Engl J Med 2011;365:981–92
16. Patel MR et al. Rivaroxaban versus warfarin in nonvalvular atrial fibrillation. N Engl J Med 2011;365:883–91
17. Connolly SJ et al. Dabigatran versus warfarin in patients with atrial fibrillation. N Engl J Med 2009;361:1139–51
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THANK YOU

Jangan lupa untuk mengerjakan soal latihan ya!!