Pulmonary Embolism: Case Discussion

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CASE 1

- 67 years old, male, farmer,

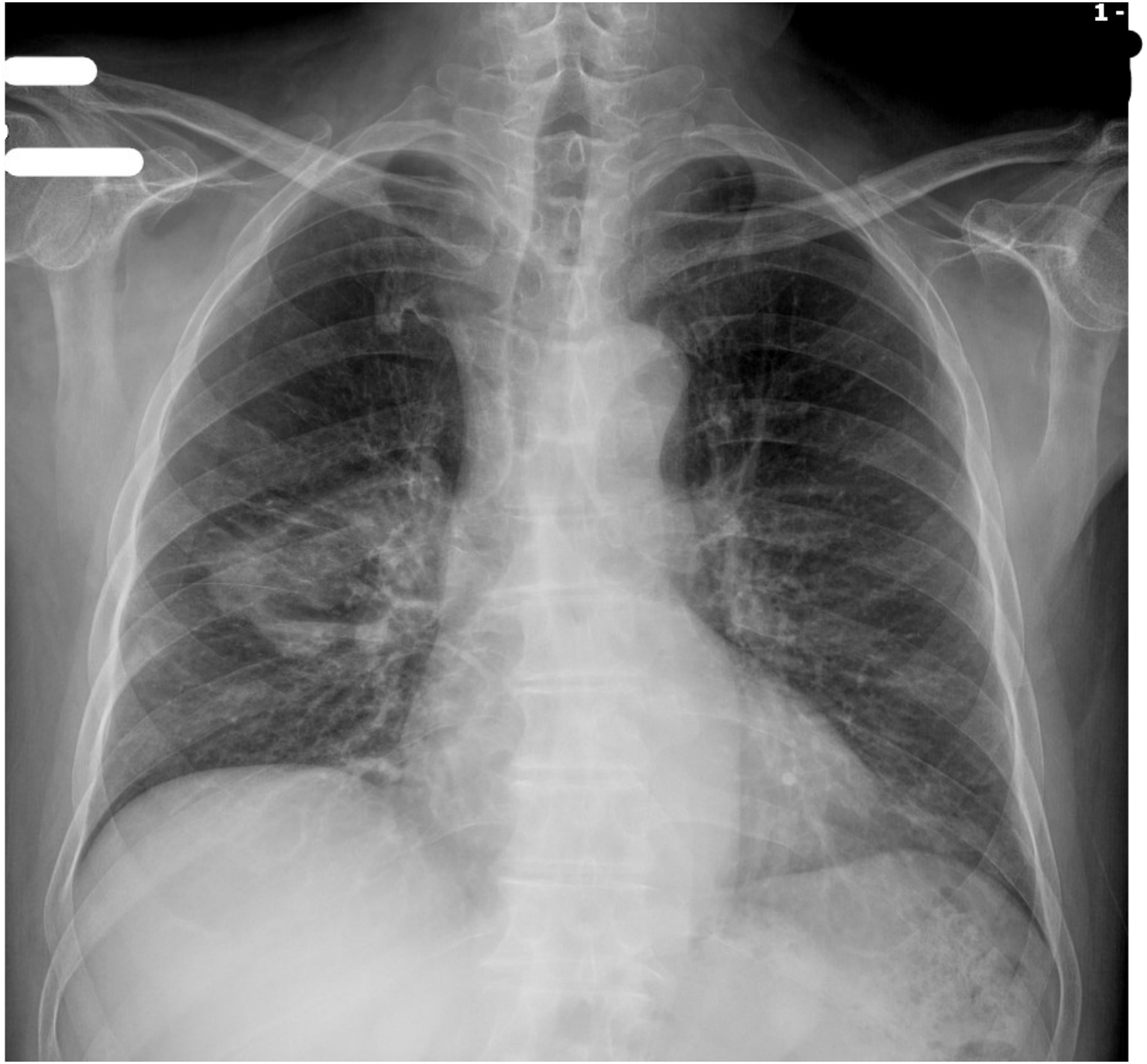
- Complaints: Dyspnea, Chough– for one year—

- Anamnesis: No history of chronic diseases

Smoking: 50 p/years

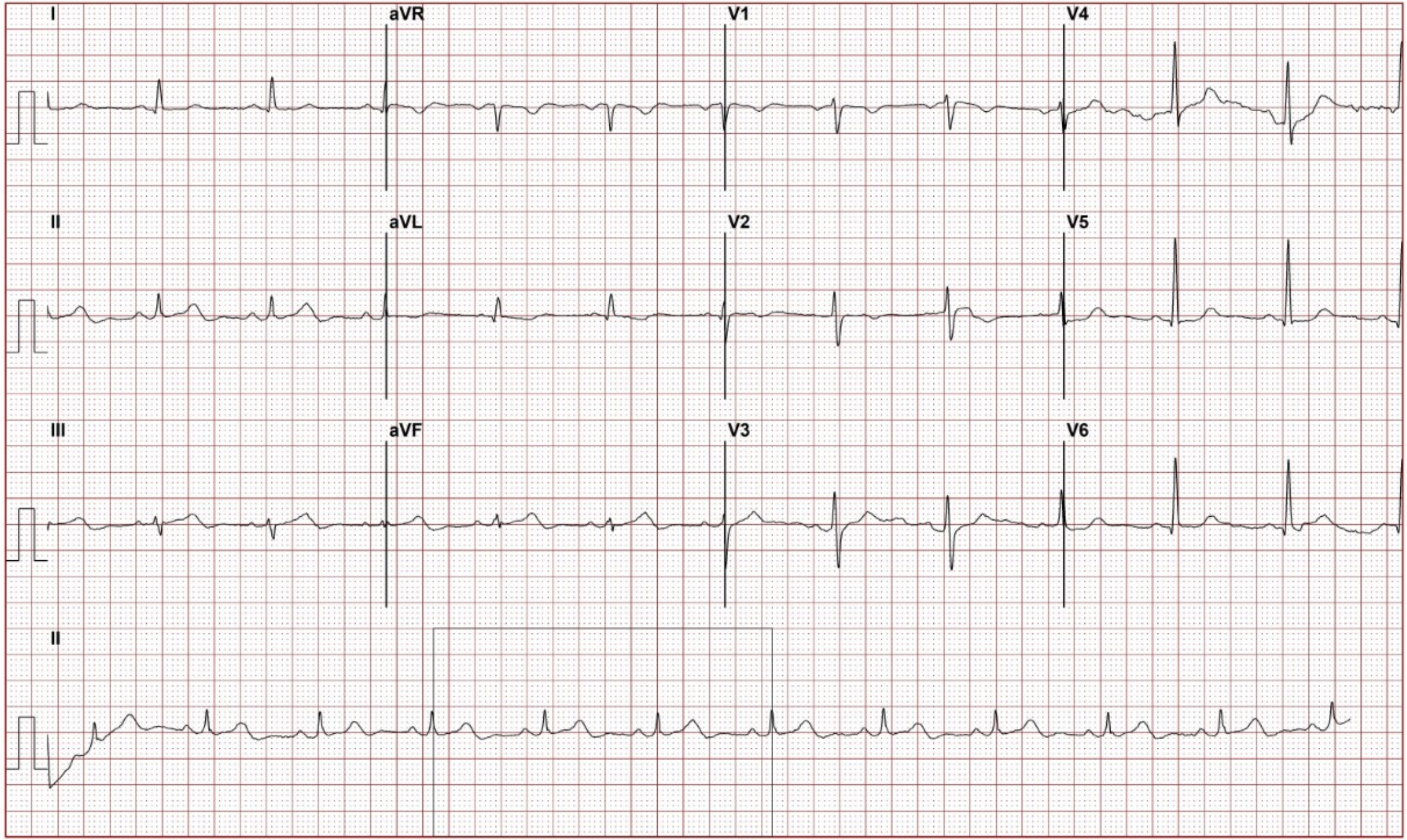
- Two months ago, he had involuntary movements in his right arm and a biopsy was taken with the preliminary diagnosis of an intracranial mass.
- Medication used: Levetiracetam, dexamethasone (taking it for 2 months)

- Physical Examination:
- His general condition is fair-good, cooperative, oriented.
- SPO2: 93 (room air) Pulse: 73 min
- No significant pathology was observed in the respiratory system and cardiovascular system examination.
- It was learned that the patient took oral antibiotics as there was a cavity in the recent chest imaging.

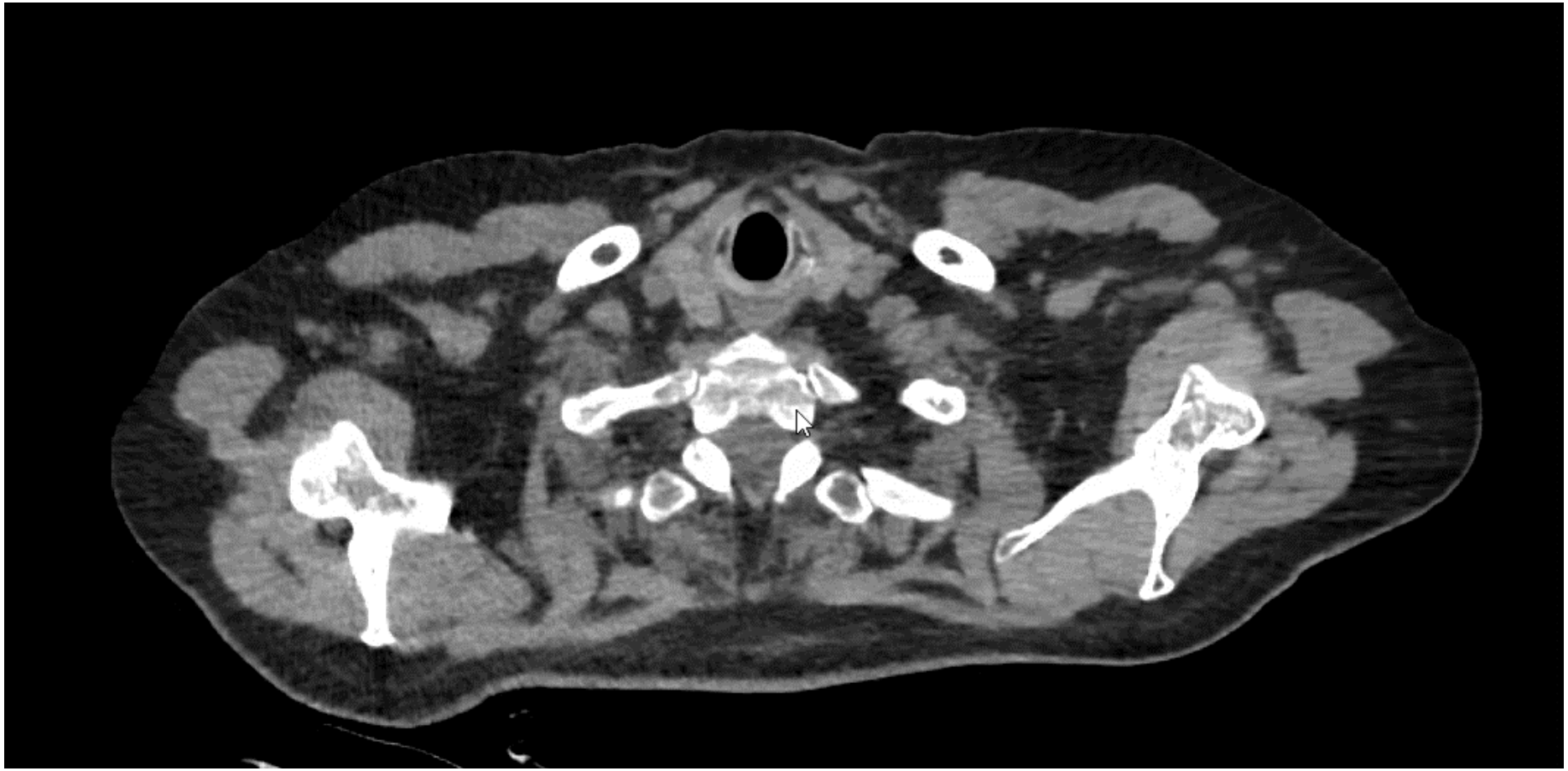


Laboratory:

WBC: **12990** /µL
Neutrophil: 7480 /µL
Lymphcyte: 4610 /µL
Platelet: 206.000 /µL
Hgb: **13.6** g/dL
BUN / Kreatinin: 21 / 0.96 mg/dL
GFR: 82
Na / K: 141 / 4.34 mmol/L
Ca / P: 9.95 / 2.56 mg/ dL
AST / ALT: 15 / 25 u/L
T. Protein / albumin: 6.5/3.6 g/dL
CRP: **19.27** mg/L
Procalcitonin: 0.04 ng /mL
Sedimentation: **53** mm/s



WinEkg ver 5.0.08, Kardinero © 2016-2017 25 mm/sec 10 mm/mV Filtreler(Taban çizgisi:0.67Hz EMG:22Hz Line:50Hz)

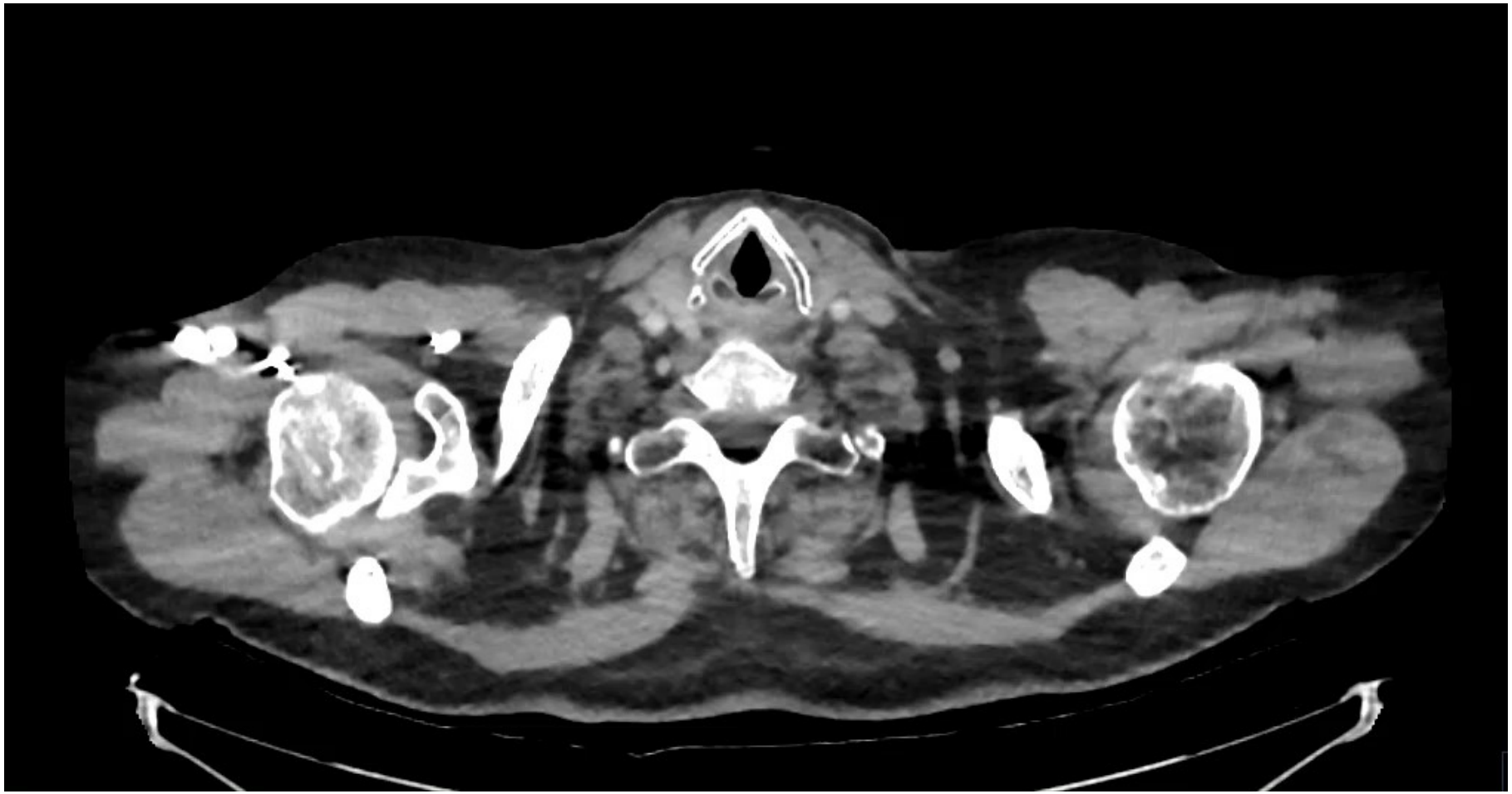


- He was admitted to the Pulmonology Clinic with a preliminary diagnosis of Necrotizing Pneumonia? Lung Abscess? Malignancy?

- Bronchoscopy was planned for the patient who could not expectorate sputum.

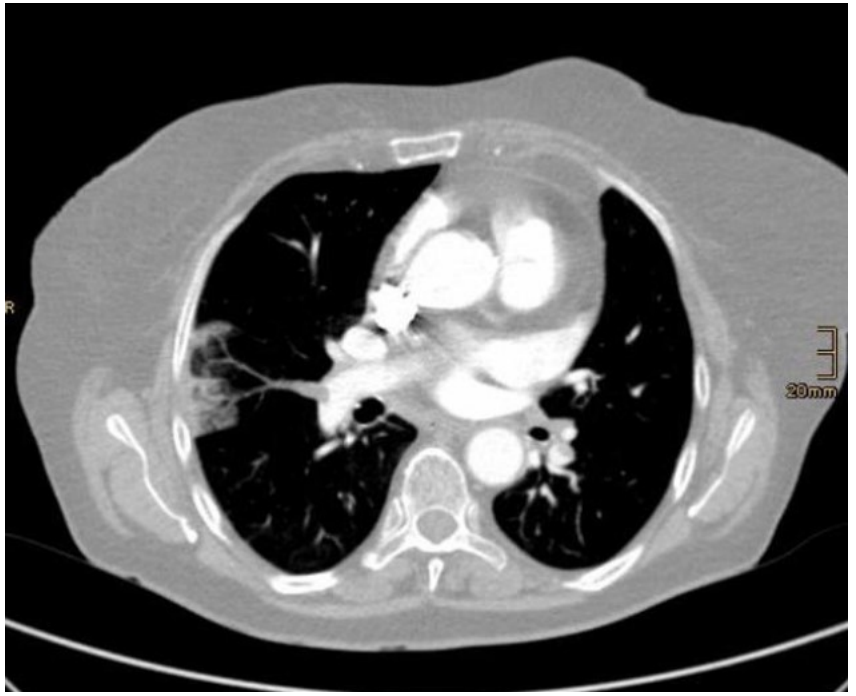
- D-dimer: **8890 µg/L**
- Troponin: 19.6 ng/ L
- Pro BNP: 270 pg/ mL

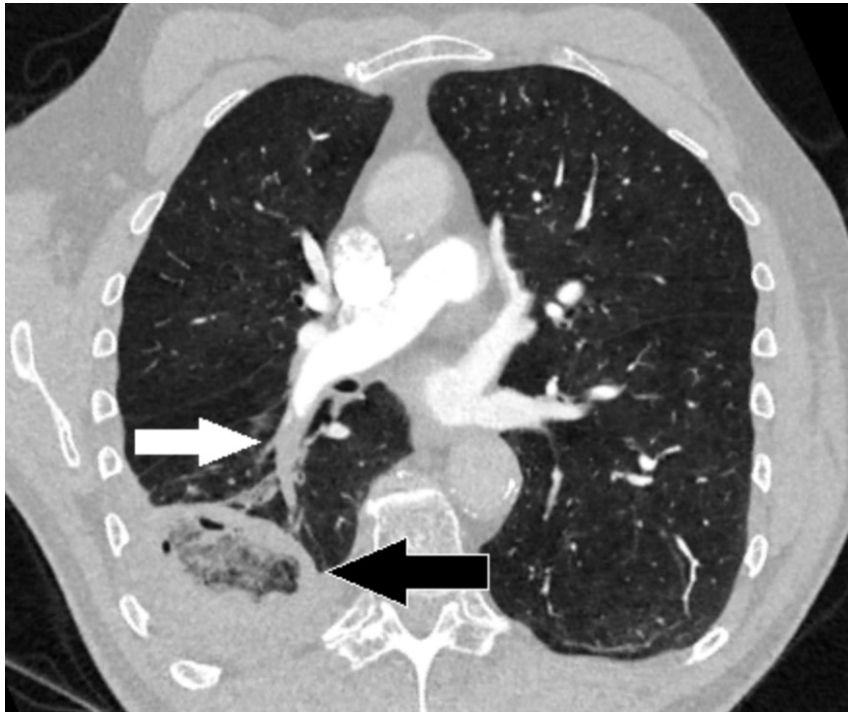
- Pulmonary CT angiography was performed with suspicion of PTE.

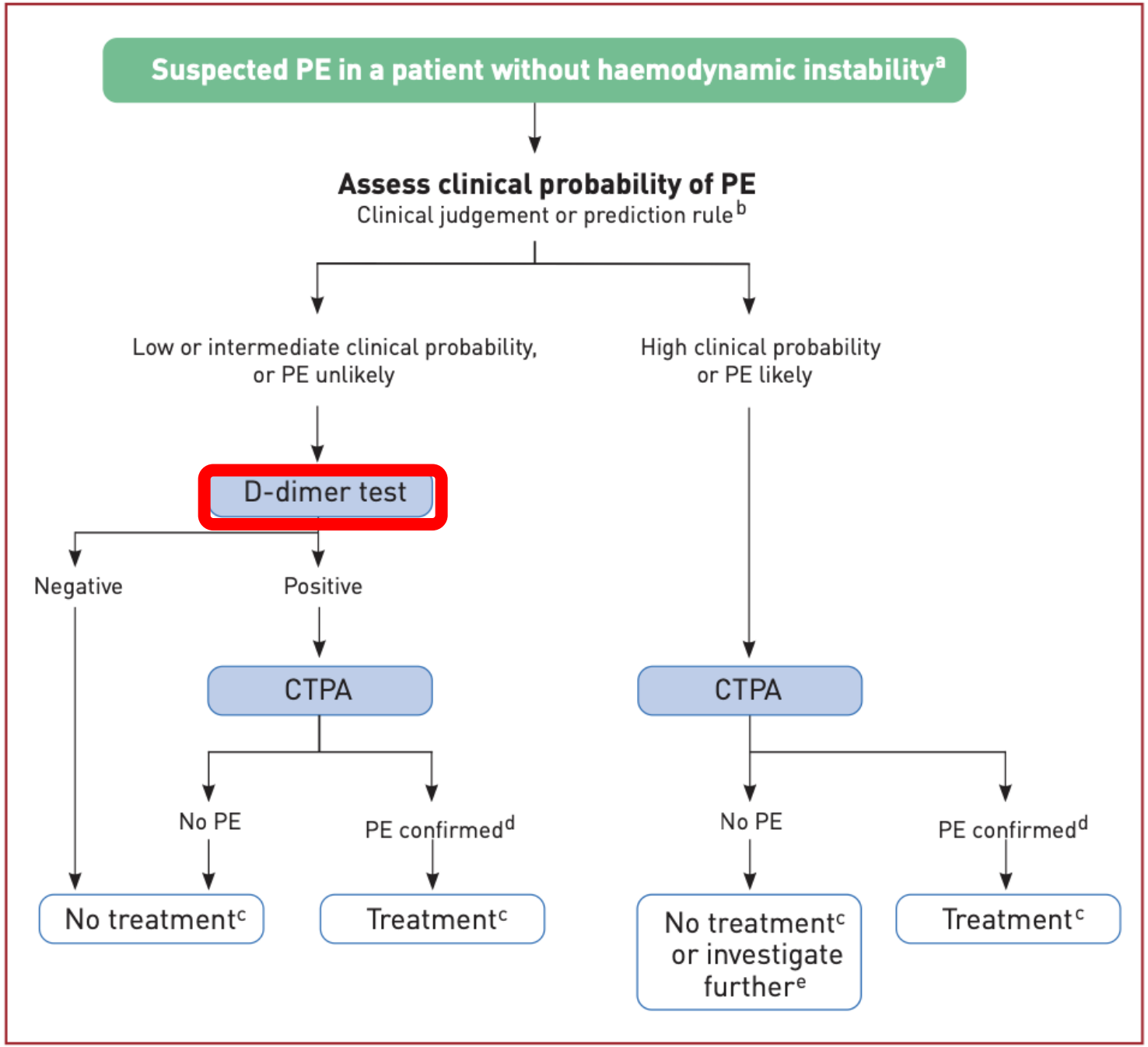


Pulmonary Infarction in PTE

- Occlusion of the distal pulmonary arteries causes ischemia, hemorrhage and eventually necrosis in the lung parenchyma.
- It is most commonly caused by acute pulmonary embolism and its incidence has been reported to be approximately 30%.
- Following pulmonary artery occlusion, the bronchial arteries become the primary source of perfusion of the pulmonary capillaries.
- Relatively higher blood pressure in the bronchial circulation causes an increase in capillary blood flow, leading to extravasation of erythrocytes (alveolar hemorrhage). If this bleeding is not resorbed, it will result in tissue infarction and necrosis.







D dimer
Age X10 = Upper limit

Simplified diagnostic management of suspected pulmonary embolism (the YEARS study): a prospective, multicentre, cohort study

*Tom van der Hulle, Whitney Y Cheung, Stephanie Kooij, Ludo F M Beenen, Thomas van Bemmel, Josien van Es, Laura M Faber, Germa M Hazelaar, Christian Heringhaus, Herman Hofstee, Marcel M C Hovens, Karin A H Kaasjager, Rick C J van Klink, Marieke J H A Kruip, Rinske F Loeffen, Albert T A Mairuhu, Saskia Middeldorp, Mathilde Nijkeuter, Liselotte M van der Pol, Suzanne Schol-Gelok, Marije ten Wolde, Frederikus A Klok, Menno V Huisman, for the YEARS study group**

www.thelancet.com Vol 390 July 15, 2017

According to **YEARS criteria**

1- Presence of DVT findings

2- Hemoptysis

3- Pulmonary embolism is the most likely diagnosis

None of the YEARS criteria + D DIMER <1000, or

If there is one or more of YEARS + D DIMER<500, embolism is excluded

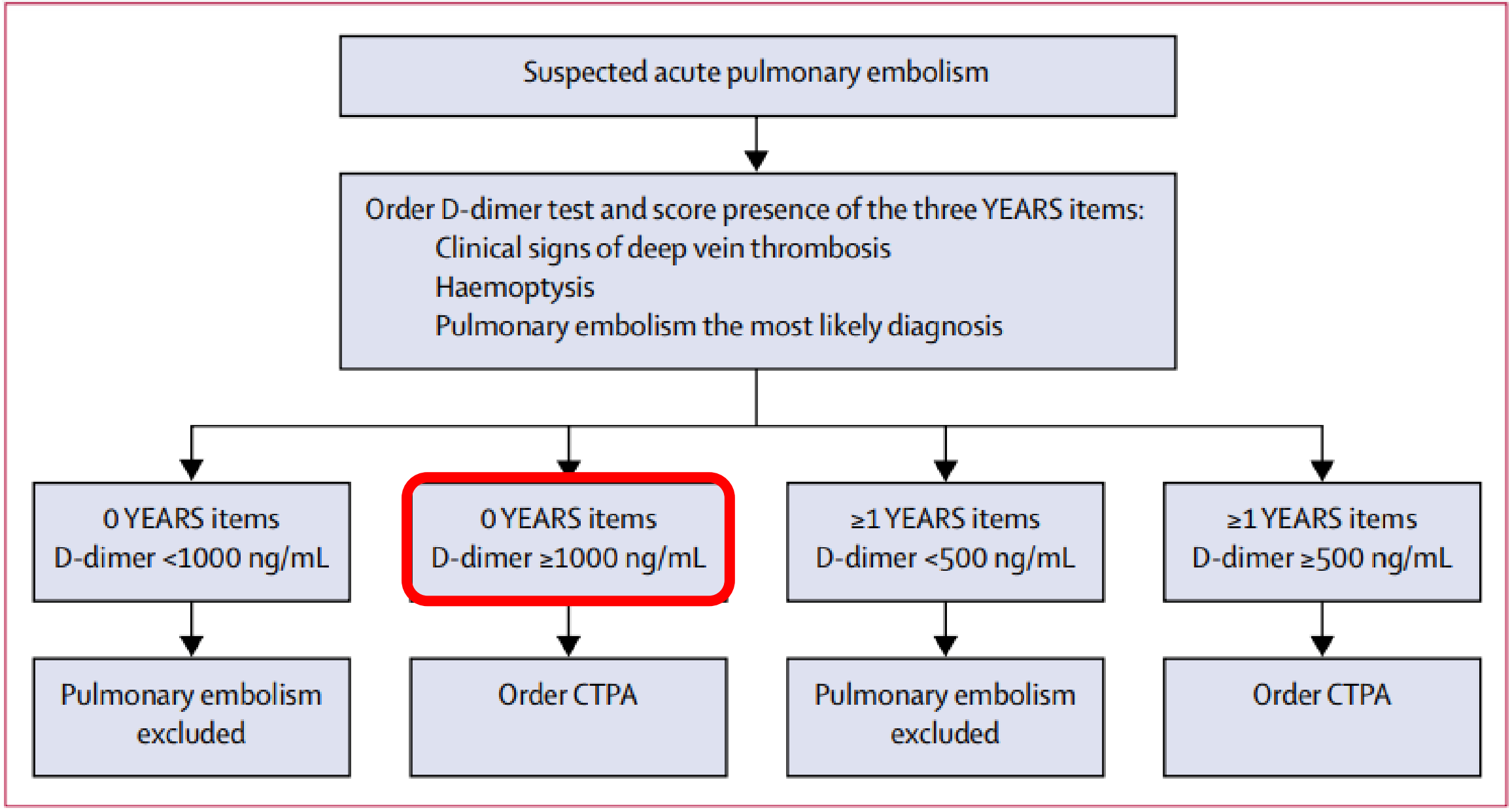
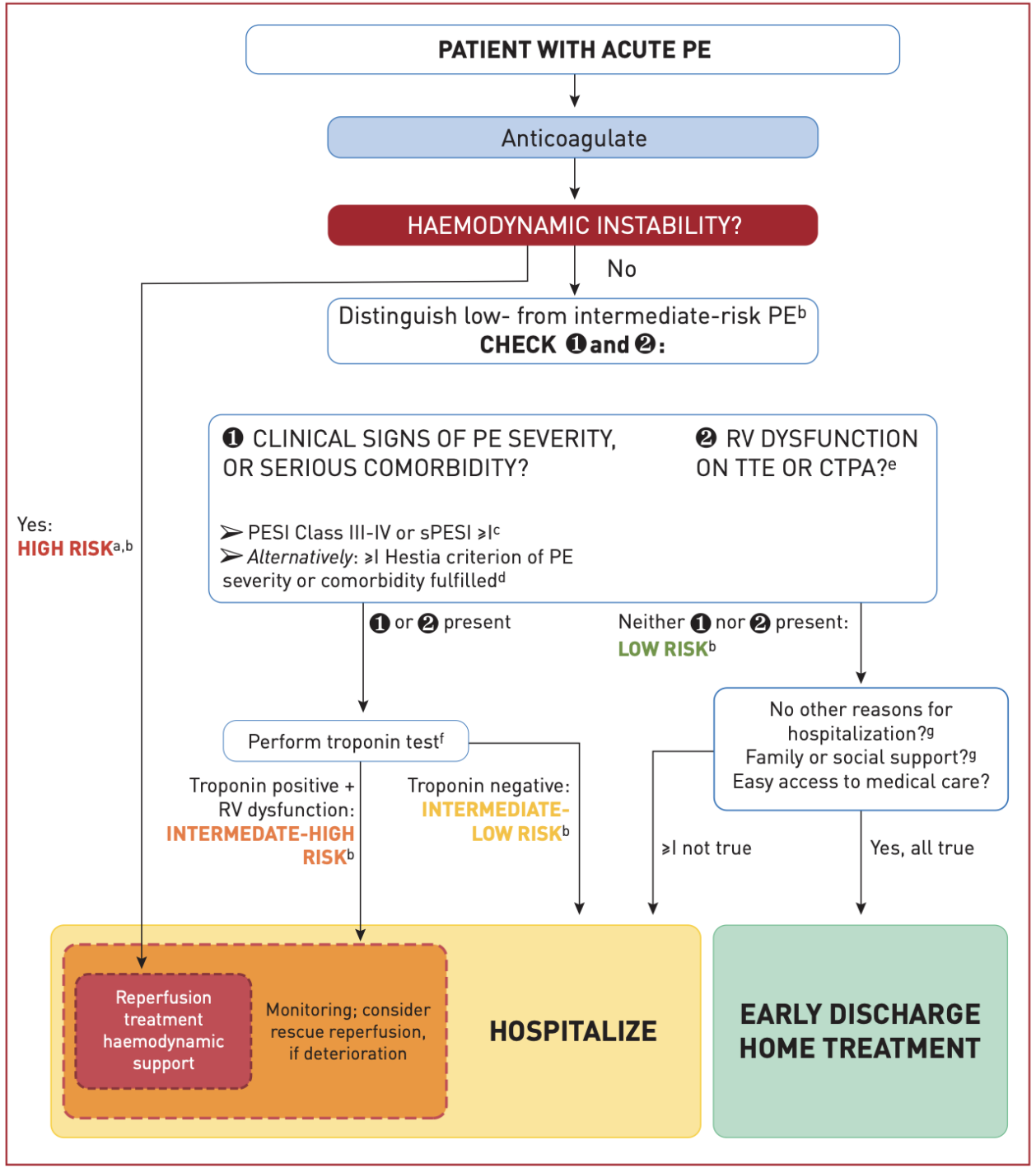

Suspected acute pulmonary embolism
Order D-dimer test and score presence of the three YEARS items:
Clinical signs of deep vein thrombosis
Haemoptysis
Pulmonary embolism the most likely diagnosis
0 YEARS items
D-dimer <1000 ng/mL
0 YEARS items
D-dimer ≥1000 ng/mL
≥1 YEARS items
D-dimer <500 ng/mL
≥1 YEARS items
D-dimer ≥500 ng/mL
Pulmonary embolism excluded
Order CTPA
Pulmonary embolism excluded
Order CTPA

Table 8 Classification of pulmonary embolism severity and the risk of early (in-hospital or 30 day) death

Early mortality risk		Indicators of risk			
		Haemodynamic instability[a]	Clinical parameters of PE severity and/or comorbidity: PESI class III–V or sPESI ≥I	RV dysfunction on TTE or CTPA[b]	Elevated cardiac troponin levels[c]
High		+	(+)[d]	+	(+)
Intermediate	Intermediate–high	-	+[e]	+	+
	Intermediate–low	-	+[e]	One (or none) positive	
Low		-	-	-	Assesment optional; if assessed, negative

sPESI = 1


PATIENT WITH ACUTE PE
Anticoagulate
HAEMODYNAMIC INSTABILITY?
No
Distinguish low- from intermediate-risk PE[b]
CHECK ❶ and ❷:
Yes:
HIGH RISK[a,b]
❶ CLINICAL SIGNS OF PE SEVERITY, OR SERIOUS COMORBIDITY?
➢ PESI Class III-IV or sPESI ⩾I[c]
➢ Alternatively: ⩾I Hestia criterion of PE severity or comorbidity fulfilled[d]
❷ RV DYSFUNCTION ON TTE OR CTPA?[e]
❶ or ❷ present
Neither ❶ nor ❷ present:
LOW RISK[b]
Perform troponin test[f]
Troponin positive + RV dysfunction:
INTERMEDATE-HIGH RISK[b]
Troponin negative:
INTERMEDIATE-LOW RISK[b]
No other reasons for hospitalization?[g]
Family or social support?[g]
Easy access to medical care?
⩾I not true
Yes, all true
Reperfusion treatment haemodynamic support
Monitoring; consider rescue reperfusion, if deterioration
HOSPITALIZE
EARLY DISCHARGE
HOME TREATMENT

- **Bilateral lower extremity ven**
  the left main and superficial fe
  to be completely thrombosed.
- The patient was started on Enc

We planned rebiopsy

KLİNİK BİLGİ:
SAĞ FRONTAL KİTLE

MAKROSKOPİ:
Kayıtsız kapta gönderilen büyüğü 1x0,1x0,1 cm küçüğü 0,3x0,1x0,1 cm ölçülerinde 6 adet dokuların tamamı 1,2,2 kasette takibe alındı.fs/ sd

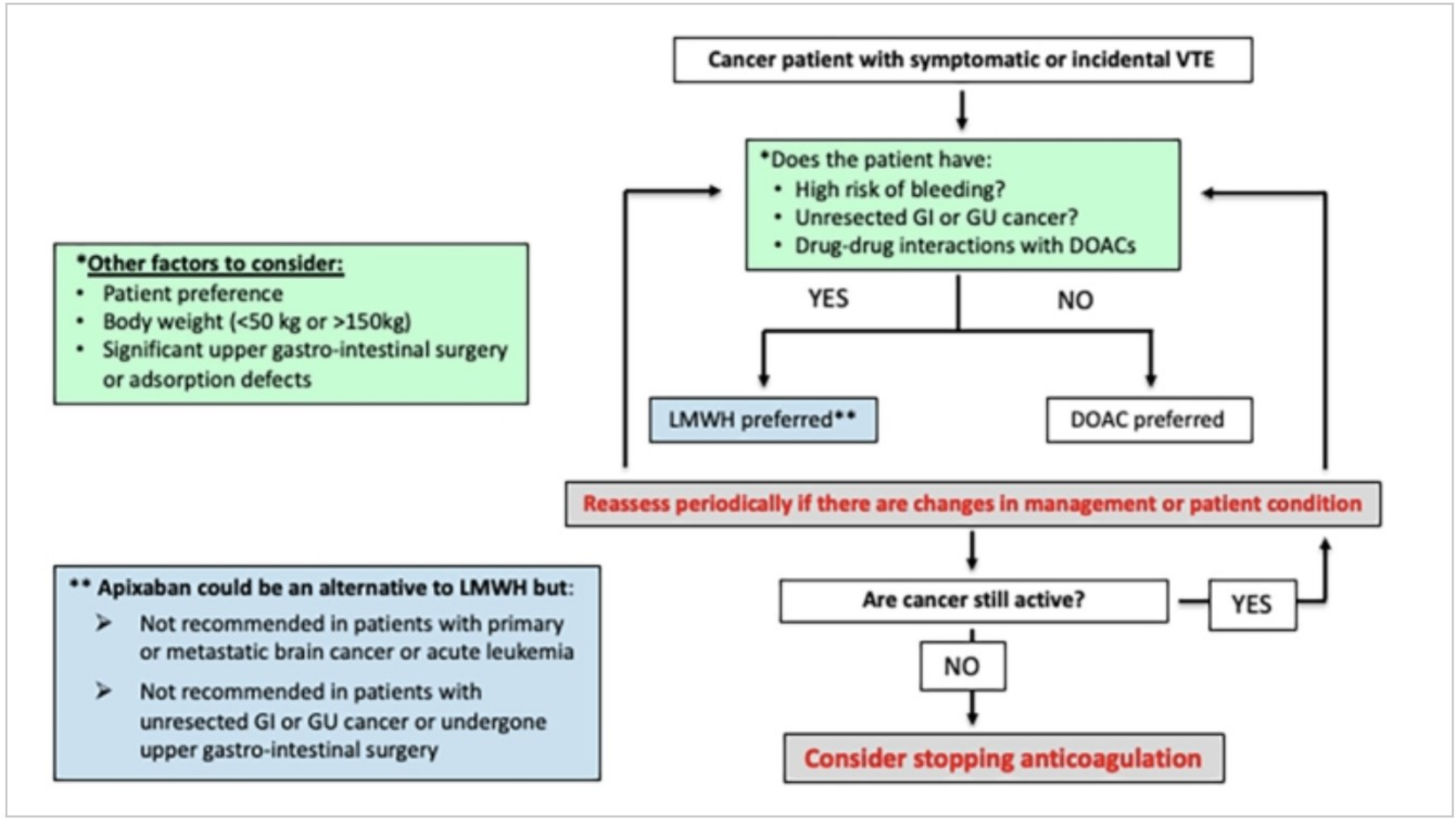
MİKROSKOPİ:
Kesitlerde küçük parçalar halinde nöroglial doku örneği görülmüştür.Normal histolojiden belirgin selüler ve belirign vasküler artış gösteren dokuda GFAP ile yaygın pozitif boyanma görüldü.CD34 ile kapiller artış görülmüş olup endotelyal proliferasyon sınırlı ve şüpheli izlenmiştir.Dokuda belirgin CD163 pozitif mikroglialar mevcuttur.Bu lezyonda IDH1 pozitif, ATRX kaybı yok ve P53 minimal %5 oranında değerlendirilmiştir.Kİ67 proliferasyon indeksi %10 civarındadır, ancak bu artışın mikroglialara bağlı olabileceği de düşünülmüştür.H3K27M ile zayıf, şüpheli bir boyanma görülmüştür.Bulgular astrositik neoplazmı desteklemektedir.Dereceleme ve tiplendirme açısından muhtemel örneklemeye bağlı olarak daha ileriye gidilememiştir.

TANI (ICD-O kodları)
ASTROSİTİK NEOPLAZM, SAĞ FRONTAL BÖLGE, STEREOTAKTİK BİYOPSİSİ

Neoplazm lehine bulgu izlenmemiştir.

TANI (ICD-O kodları)
REAKTİF DEĞİŞİKLİKLER GÖSTEREN NÖROGLİAL DOKU, SOL TALAMİK BÖLGE, VARİOGUİDE BİYOPSİ MATERYALİ

Figure 1. Algorithm for the treatment of cancer-associated venous thromboembolism.



ESC European Society of Cardiology

DOAC: direct oral anticoagulants; GI: gastrointestinal; GU: genitourinary; LMWH: low-molecular-weight heparin; VTE: venous thromboembolism

Table 3 Guideline Recommendations for the Treatment of Cancer-Associated VTE

Guideline	Recommendations	
	Initial Treatment	**Treatment Duration**

ACCP[a]	• Apixaban, edoxaban or rivaroxaban (strong recommendation)
	  ○ Apixaban or LMWH may be preferred in luminal GI malignancies.
		• Extended-phase DOAC therapy (>3 months)
		  ○ Reassess periodically.

	• DOAC (apixaban or rivaroxaban) or LMWH (conditional recommendation)
	  ○ Caution with DOACs in GI cancers.
		• Treat for 3–6 months with a DOAC (apixaban, edoxaban or rivaroxaban) over LMWH or VKA (conditional recommendations).
		• Treat for >6 months rather than short term (3–6 months) in patients with active cancer (conditional recommendation).
		  ○ Suggest continuing indefinitely rather than stopping after completion of a definitive period of anticoagulation (conditional recommendation).
		  ○ Use a DOAC or LMWH (conditional recommendation).

NCCN[a]	• Apixaban (category 1), edoxaban after ≥5 days of parenteral anticoagulation (category 1) or rivaroxaban (category 2A) preferred for patients without gastric or gastroesophageal lesions ○ Caution in GU tract lesions • LMWH preferred for patients with gastric or gastroesophageal lesions (category 1). • Dabigatran if above regimens are not appropriate or unavailable.	• ≥3 months or as long as active cancer or cancer therapy.

ASCO[b]	• LMWH, UFH, fondaparinux, rivaroxaban, or apixaban
	  ○ For long-term anti-coagulation, LMWH, edoxaban, rivaroxaban, or apixaban for at least 6 months are preferred over VKAs. Caution with direct factor Xa inhibitors in patients with GI and GU cancers or other high-risk settings.
		• Offer LMWH, DOACs or VKAs beyond the initial 6 months to select patients with active cancer, such as those with metastatic disease or those receiving chemotherapy.
		  ○ LMWH, edoxaban or rivaroxaban preferred.
		  ○ LMWH preferred in settings with increased bleeding risk.
		• Assess intermittently to ensure a continued favorable risk-benefit profile.
		• Patients needing extended pharmacologic antithrombotic prophylaxis post cancer surgery
		  ○ Prophylactic doses of LMWH

ESC[b]	• PE and cancer: LMWH for the first 3–6 months (IIa. A) • Edoxaban (IIa. B) or rivaroxaban (IIa. C) may be used except in GI cancer patients.	• Extend indefinitely or until the cancer is cured (IIa. B). • Consider LMWH, DOAC or VKA.
ITAC[b]	• LMWH when CrCl ≥30 mL/min (grade 1A). • Apixaban or rivaroxaban (first 10 days) or edoxaban (started after initial LMWH/UFH for 5 days) can be used for initial treatment if CrCl ≥30 mL/min and patient is not at high risk of GI or GU bleeding (grade 1 A).	• LMWH or DOACs for ≥6 months (grade 1 A) ○ DOACs when CrCl ≥30 mL/min if no impairment in GI absorption or strong DDIs (grade 1 A), but caution advised in GI malignancies, especially upper GI tract. • After 6 months, termination or continuation of anticoagulation based on benefit–risk ratio, tolerability, drug availability, patient preference and cancer activity (guidance).
ISTH[b]	• Patients with low bleeding risk and no DDIs: edoxaban or rivaroxaban; LMWHs are acceptable alternatives. • Patients with high bleeding risk[c]: LMWH; edoxaban or rivaroxaban as an alternative if no potential DDI.	• No specific recommendation.

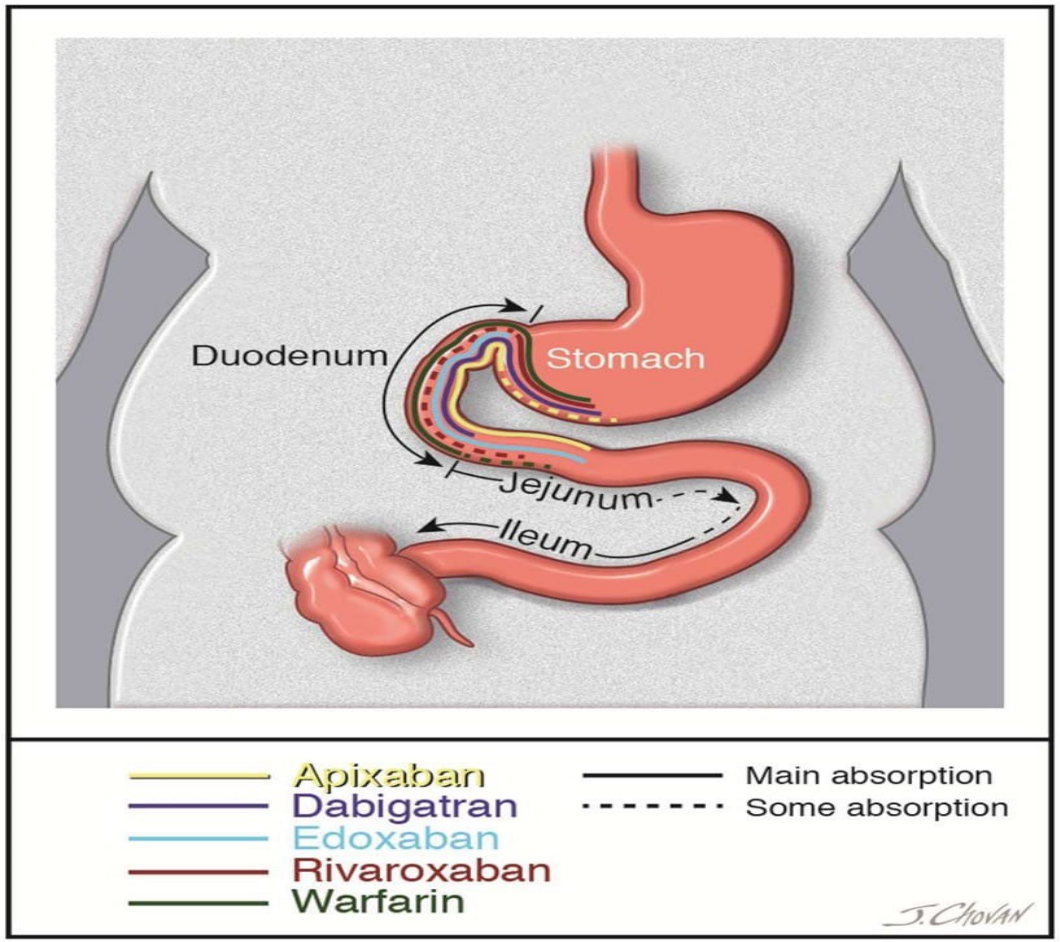
(*Continued*)

Table 3 (Continued).

Guideline	Recommendations
NICE[b]	linical need.
ESMO	is e preferred ncer (II, B), werful indu-) LMWH is an, rivarox- l, B) tion therapy

Notes: This tab
[a]Recommendati
trial results. [c]Hig
or nephrostomy
Abbreviations
DDI, drug–drug
genitourinary; IS
NICE, National
unfractionated h

able since then.
and SELECT-D
y tract, bladder,
ome P450 3A4;
ointestinal; GU,
weight heparin;
mbolism; UFH,



J Blood Med. 2024; 15: 171–189.

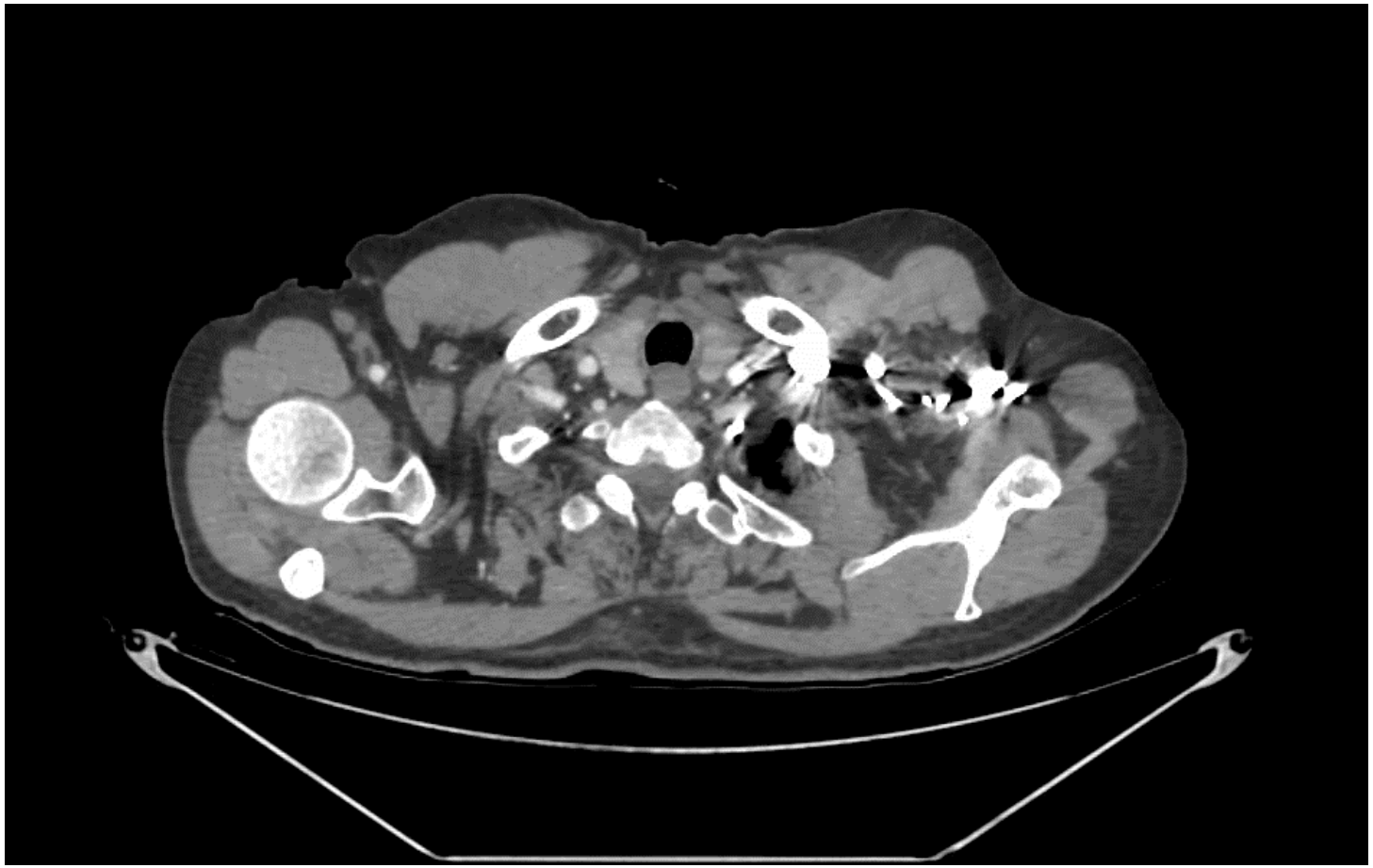
In the treatment of cancer-related VTE;

- Individualized treatment (drug interaction, risk of bleeding)
- Monotherapy (rather than combined antithrombotics)
- Treatment for 3-6 months, but continuing treatment as long as there is active cancer

In the treatment of cancer-related VTE;

- **Conditions with a high risk of bleeding;**
- GI or GU cancers
- Brain cancer
- Recent surgery or life-threatening bleeding
- Concomitant cancer therapy associated with increased risk of bleeding (e.g., bevacizumab, agents that induce GI mucosal toxicity)
- Severe thrombocytopenia (<50,000)
- Kidney or liver failure
- Concomitant antiplatelet therapy

After 3 months of anticoagulant (LMWH) treatment



Should imaging methods (such as CT angiography or V/P scintigraphy) be performed to show that thromboembolism has disappeared after PTE treatment?

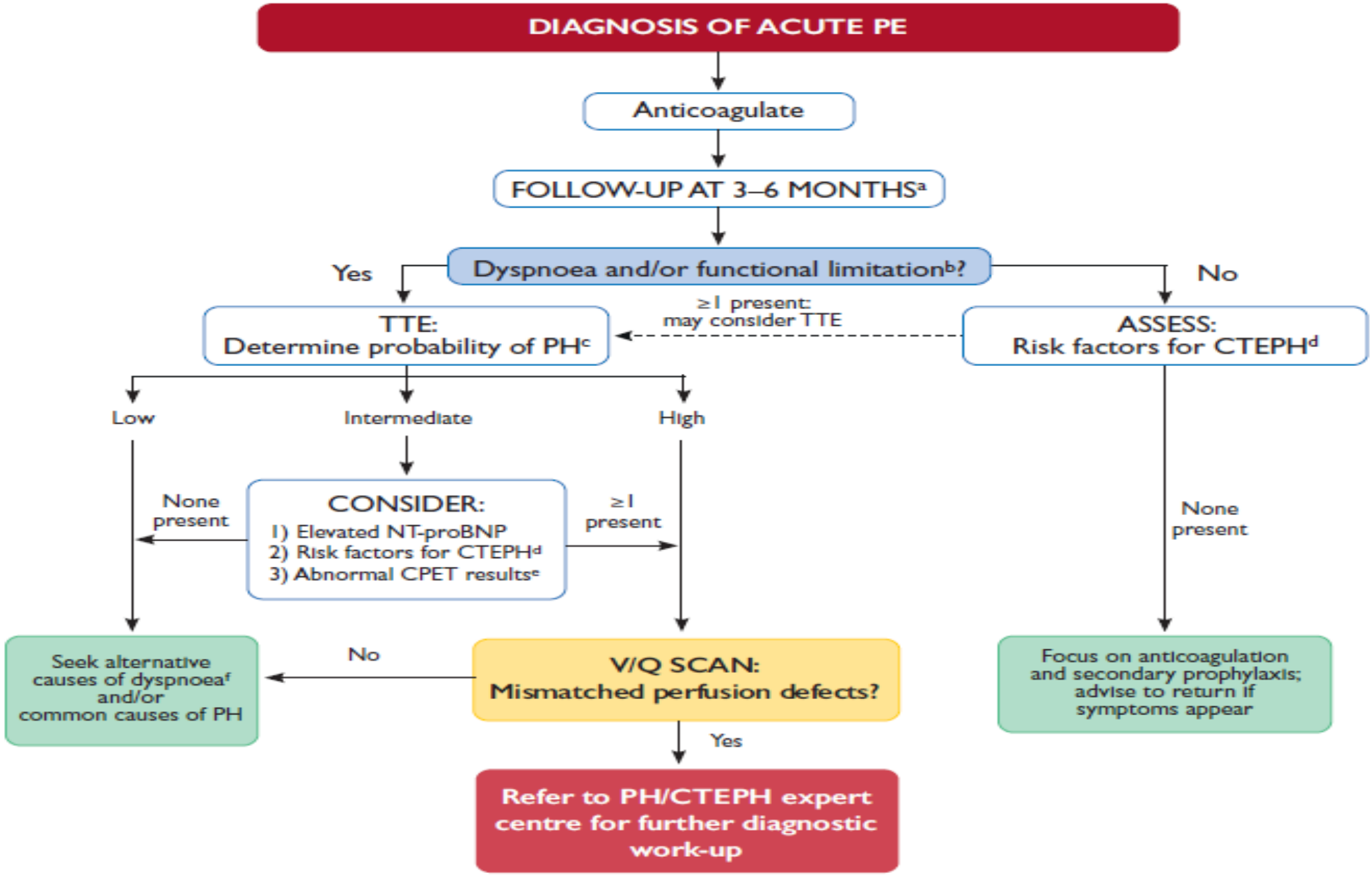

DIAGNOSIS OF ACUTE PE
Anticoagulate
FOLLOW-UP AT 3–6 MONTHS[a]
Dyspnoea and/or functional limitation[b]?
Yes
No
≥1 present: may consider TTE
TTE: Determine probability of PH[c]
ASSESS: Risk factors for CTEPH[d]
Low
Intermediate
High
None present
CONSIDER:
1) Elevated NT-proBNP
2) Risk factors for CTEPH[d]
3) Abnormal CPET results[e]
≥1 present
None present
Seek alternative causes of dyspnoea[f] and/or common causes of PH
No
V/Q SCAN: Mismatched perfusion defects?
Yes
Refer to PH/CTEPH expert centre for further diagnostic work-up
Focus on anticoagulation and secondary prophylaxis; advise to return if symptoms appear

Table 13 Risk factors and predisposing conditions for chronic thromboembolic pulmonary hypertension[447–449]

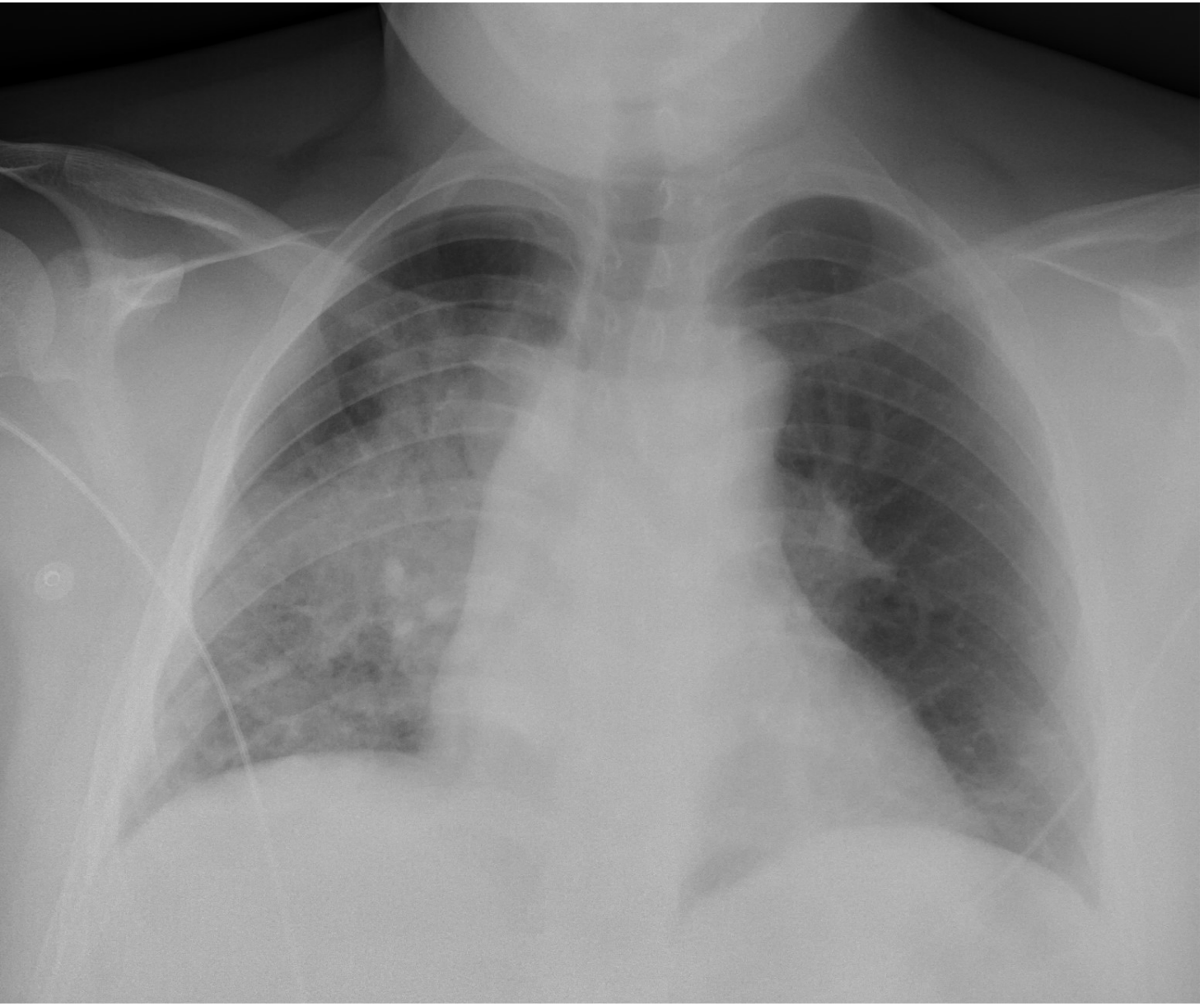
Findings related to the acute PE event (obtained at PE diagnosis)	Concomitant chronic diseases and conditions predisposing to CTEPH (documented at PE diagnosis or at 3–6 month follow-up)
Previous episodes of PE or DVT	Ventriculo-atrial shunts
Large pulmonary arterial thrombi on CTPA	Infected chronic i.v. lines or pacemakers
Echocardiographic signs of PH/RV dysfunction[a]	History of splenectomy
CTPA findings suggestive of pre-existing chronic thromboembolic disease[b]	Thrombophilic disorders, particularly antiphospholipid antibody syndrome and high coagulation factor VIII levels
	Non-O blood group
	Hypothyroidism treated with thyroid hormones
	History of cancer
	Myeloproliferative disorders
	Inflammatory bowel disease
	Chronic osteomyelitis

Case 2

- 18 yo, male, student
- The patient, who had an ENT examination due to snoring, had a sore in the nose and high CRP, and was started on cefuroxime axetil.
- While taking antibiotics, the patient applied to Emergency Department of Local Hospital with the complaint of coughing and hemoptysis at home. The patient had 5-6 fresh red hemoptysis, approximately 1 cup in total.

- Since the patient also had hypoxemia, he was admitted to the Anesthesia ICU and empiric antibiotic therapy and methylprednisolone 100 mg were administered. The patient was admitted to our ICU on the same day due to increased respiratory distress and the need for high flow.
- **Complaint:** Hemoptysis, shortness of breath and palpitations
- **Background:** VSD closure in childhood
- No chronic diseases, no smoking or any other habit

- Physical Examination:
- General condition is moderate-poor, GCS: 15, dyspneic
- SS: ral+ in places in the right middle-lower zone,
- CVS: rhythmic, tachycardic Pulse: 110 / min
- No significant pathology was observed in other system examinations.



Laboratory:

WBC: **17090** /µL

Neutrophil: **15660** - Lymphocyte: 1020 /µL

Platelet: 50.000 /µL

Hgb: **15.1** g/dL

BUN / Kreatinin: 13.9 / 0.84 mg/dL

GFR: 127

Na / K: 142 / 4.36 mmol/L

Ca / P: 9.23 / 2.7 mg/ dL

AST / ALT: 22 / **62** u/L

t. Bil / d. Bil : 0.57 / 0.23 mg/dL

T. Protein / albumin: 7.4 / 4.5 g/dL

CRP: **73.8** mg/L

Procalcitonin: 0.07 ng /mL

Sedimentation: **53** mm/s

Pro-BNP: **411** pg/mL,

troponin: 30 ng/L

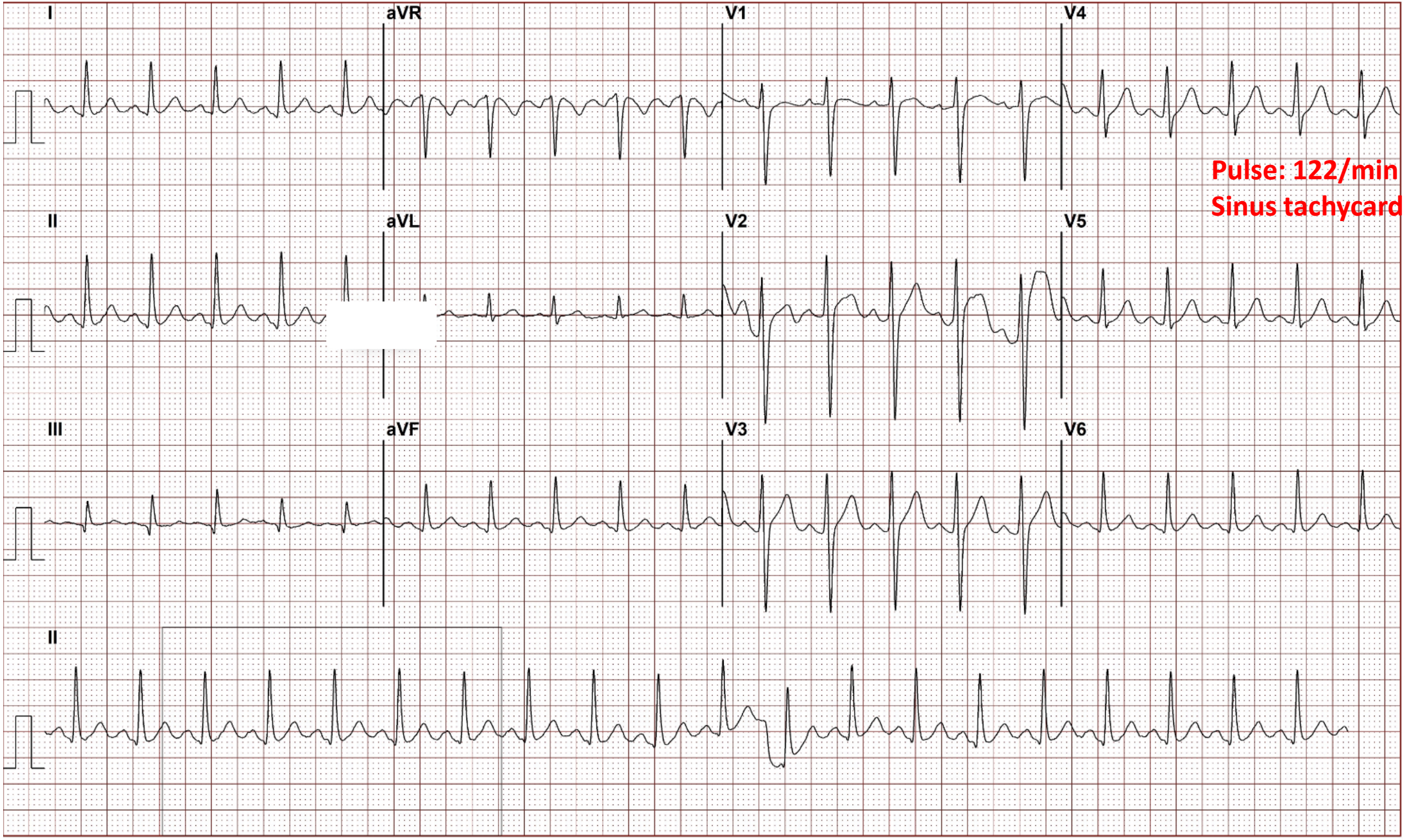
D-dimer: **2860** µg/L

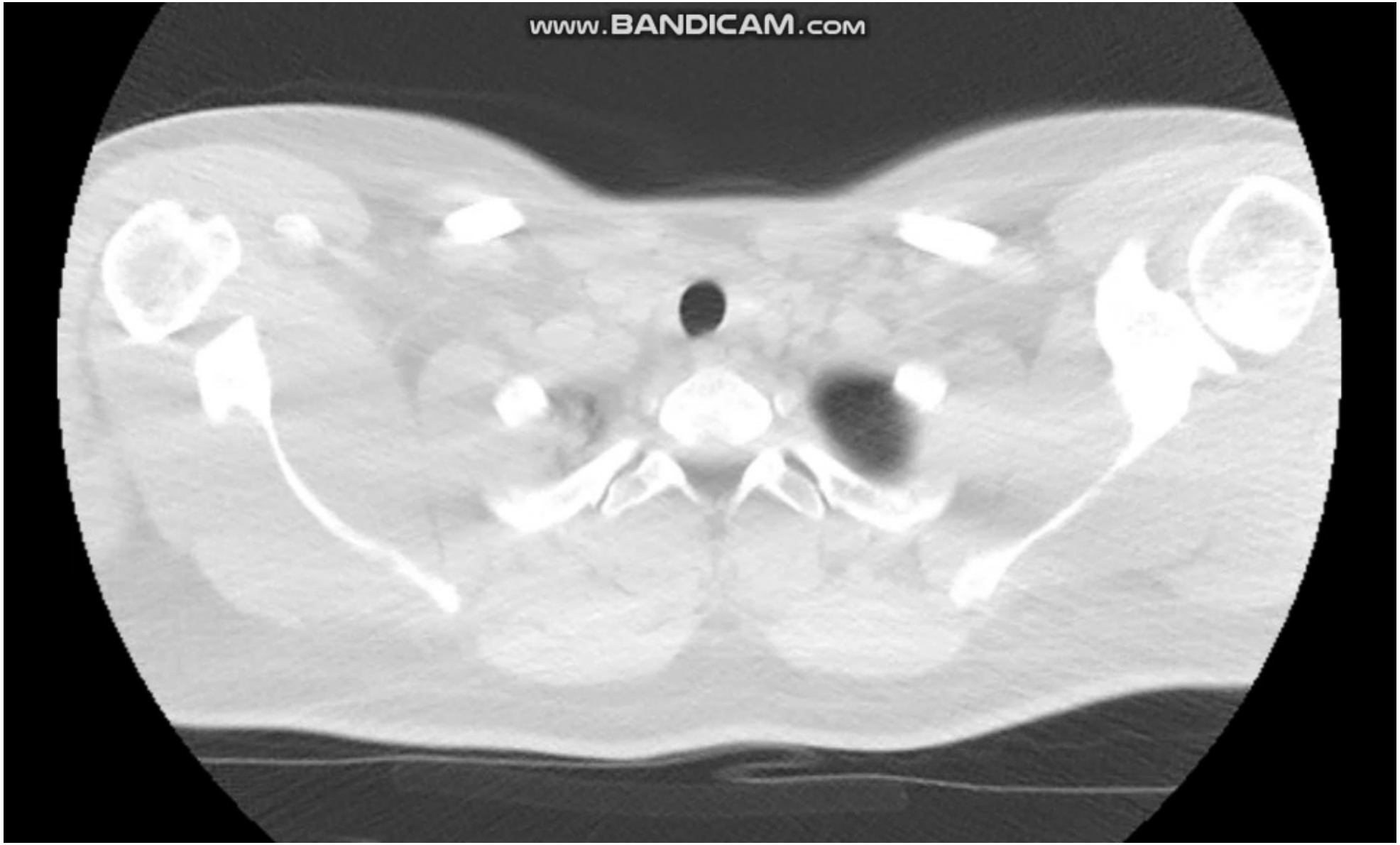
Urinalysis: Blood:25 leukocyte: 100

pH: 6.5. eritrosit: 10, nitrit:-

Urine microprotein/creatinine

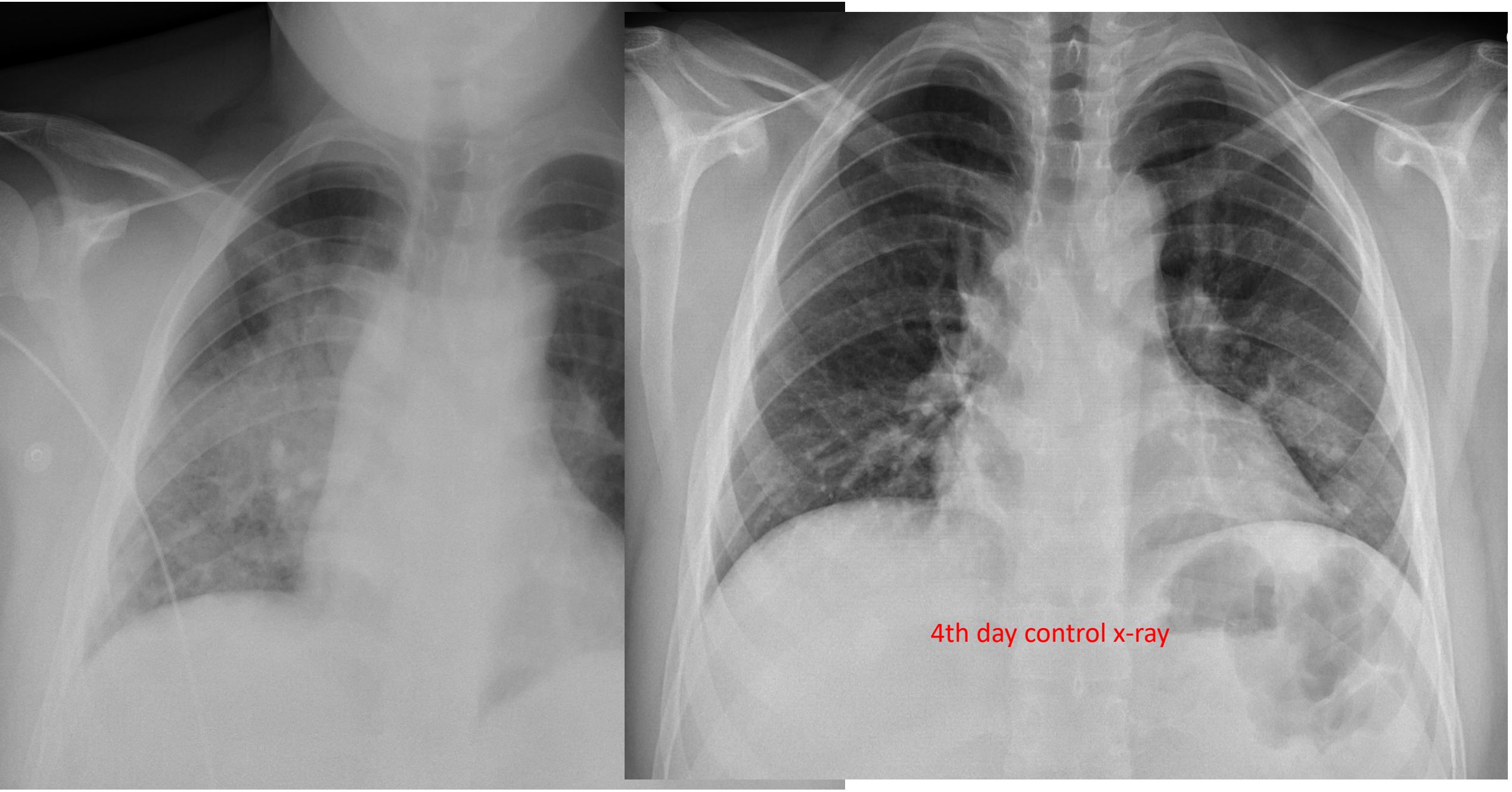
: 47 / 265 mg/dL


I
aVR
V1
V4
II
aVL
V2
V5
III
aVF
V3
V6
II
Pulse: 122/min
Sinus tachycardia
WinEkg ver 5.0.08 Kardiyero © 2016-2017 25 mm/sec 10 mm/mV Filtreler(Tahan cizgisi:0.67Hz, EMG:22Hz,)


www.BANDICAM.com

- The patient was consulted to Hematology due to thrombocytopenia.
- ► Peripheral smear compatible with 50,000 /µL, no atypical cells
- ► Abdominal USG: The liver is of normal size, with smooth contours (Grade 2 steatosis), the spleen is normal, and no pathological findings were found in other organs.
- ► Serological blood samples were sent.
- Cardiology was consulted. EF: 65, normal echo findings, no additional recommendations.

- Vasculitis was considered the primary diagnosis because the patient was young, had hemoptysis, alveolar hemorrhage (high flow requirement), and microscopic hematuria upon arrival.
- Pulse steroids (1 g/day) and empiric antibiotics were given for 3 days.
- The patient's hemoptysis regressed, his need for oxygen decreased, and the clinic recovered.
- CRP became negative.

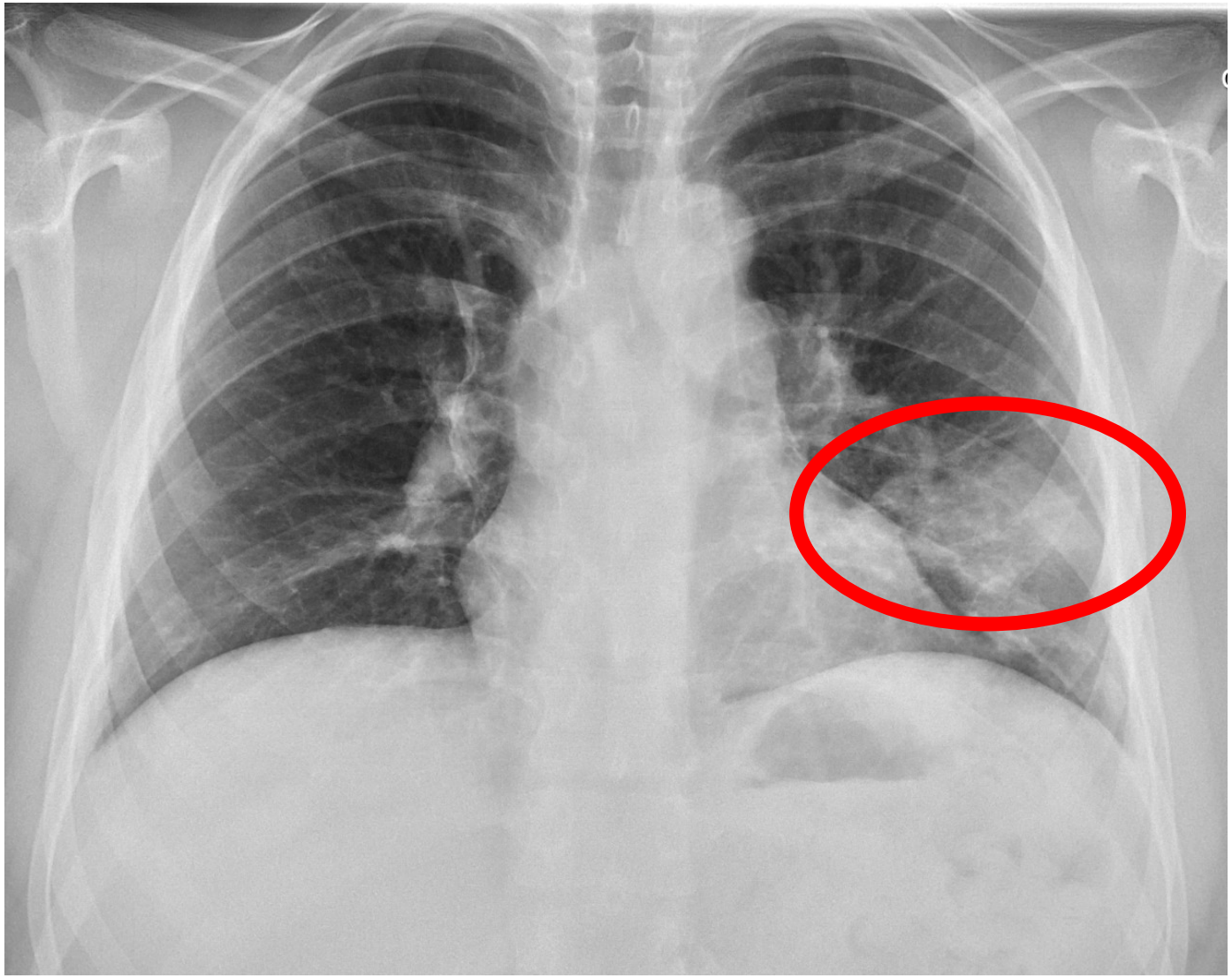

4th day control x-ray

Serological findings

- **Lupus anticoagulant: positive**
- BETA-2 MICROGLOBULIN: N
- ACA- Ig M: negative**, ACA- Ig G: pos**
- **Anti-phosphatidylserine IgG > 120**
- **ANA IFAT: 1/1000 GRANULAR PATT**
- **Anti-ds DNA: 261.46 (positive)**
- ANCA: negative

The patient was consulted to Rheumatology: Systemic Lupus Erythematosis (SLE)

- The platelet level of the patient was around 40-80.000. During this period, no prophylactic anticoagulant treatment was given except **compression stockings.**
- On the 6th day of hospitalization, severe chest pain and tachycardia developed.



What do we do now?

- Would it help to look for a D-dimer?
- Patient's baseline D-dimer was 2860 µg/L
- Would you give a prophylactic dose of anticoagulant on arrival?

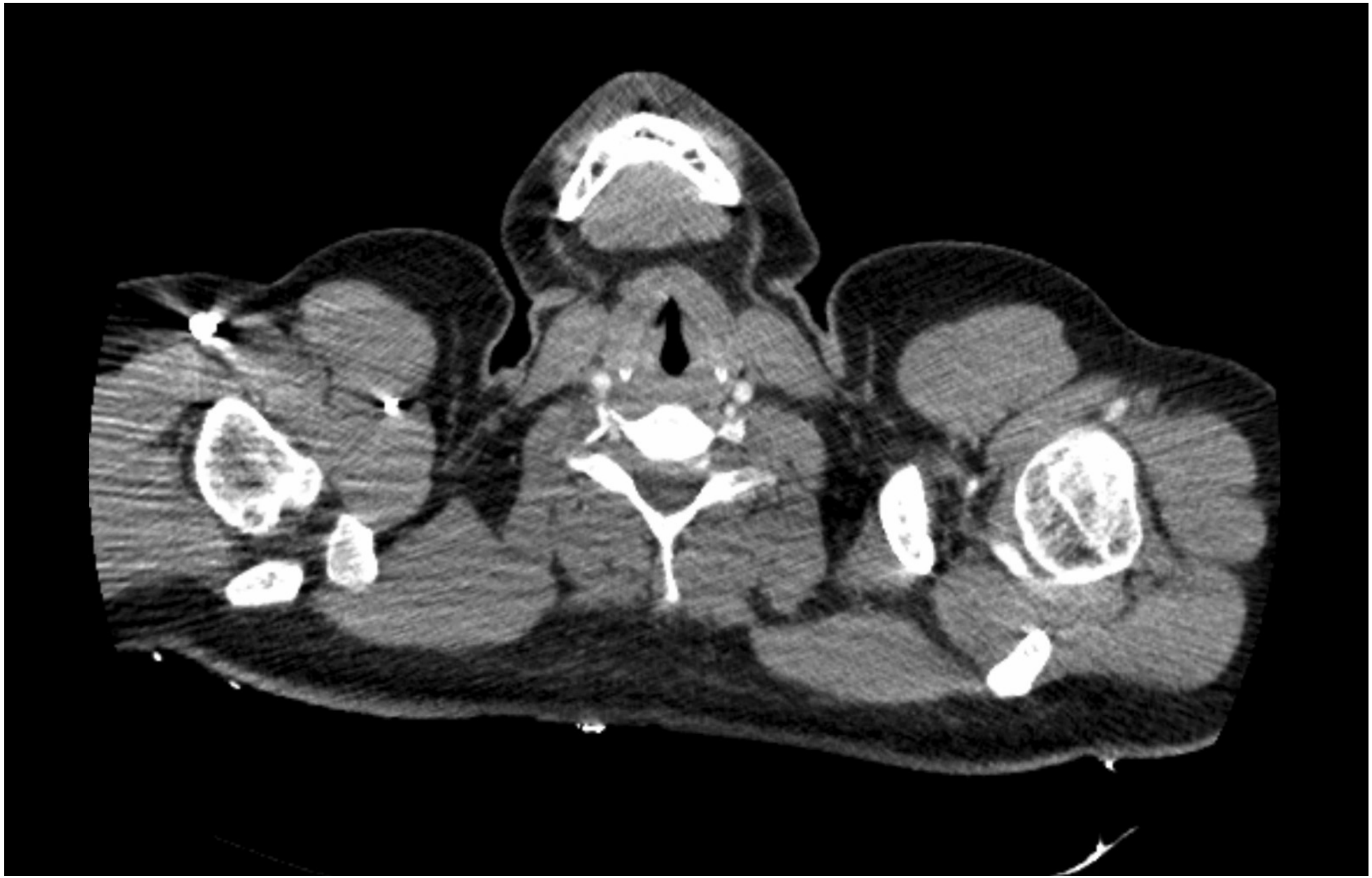
Padua Prediction Score.

Baseline features
Active cancer (local or distant metastases; chemotherapy and/or radiother
Previous VTE (with exclusion of superficial vein thrombosis)
Reduced mobility (bedrest with bathroom privileges for at least 3 days)
Already known thrombophilia
Recent trauma and/or surgery in the last month
Age ≥ 70
Heart and/or respiratory failure
Acute myocardial infarction or ischemic stroke
Acute infection and/or rheumatologic disorder
Obesity (BMI ≥ 30)
Ongoing hormonal treatment

≥ 4 , high risk

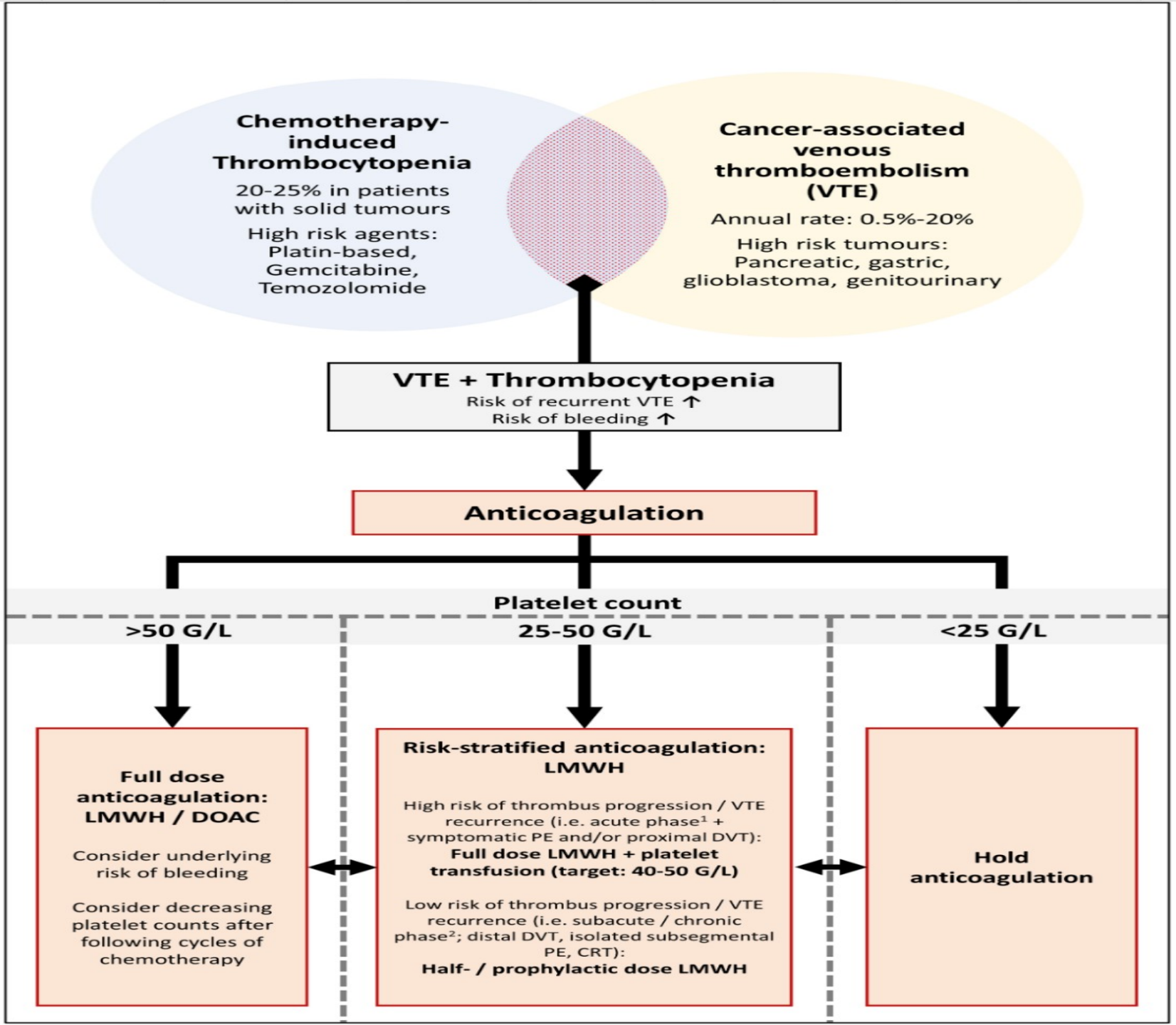
IMPROVE bleeding RAM: score ≥7 indicates high bleeding risk¶	
Renal failure (GFR 30-59 vs ≥60 mL/min per m^2)	1
Male vs female	1
Age 40-80 vs <40 y	1.5
Current cancer	2
Rheumatic disease	2
Central venous catheter	2
ICU/Critical Care Unit stay	2.5
Renal failure (GFR <30 vs ≥60 mL/min per square meter)	2.5
Hepatic failure (INR > 1.5)	2.5
Age ≥85 y vs <40 y	3.5
Platelet count $<50 \times 10^9$/L	4
Bleeding in 3 mo before admission	4
Active gastroduodenal ulcer	4. 5

American Society of Hematology 2018 guidelines for management of venous thromboembolism: prophylaxis for hospitalized and nonhospitalized medical patients



- Enoxaparin 2x0.8 IU/kg was started. Daily platelet count (whole blood) and hemoptysis were monitored.
- Lower Extremity Venous doppler US: Clear
- New ECHO: 1 TY, PAB NOT MEASURED, RIGHT DIAMETER 4.7 -4.8, MINIMAL D FINDING+ SEPTAL BOUNCE+ MCCONEL-

- On the 3rd day of LMWH treatment, platelet count decreased to 33.000 /µL.
- No active bleeding sign was observed.
- LMWH was stopped ---- Fondaparinux 1x7.5 mg SC was started.
  + Concurrent vitamin K antagonist



Thrombosis Research, 2021, March, 38-42

- The use of prophylactic or therapeutic dosage of anticoagulant therapy in patients with moderate to severe thrombocytopenia (<50 × 109/L) is risky.
- Expert opinion recommends **low-dose DMAH** for those with platelet counts between 25-50 × 109/L and no anticoagulation for those with platelet counts <25 × 109/L.

Summary of recommendations for the expert guideline on pharmaceutical practice for fondaparinux.

Recommendations	Recommended intensity	Quality of evidence
Recommendation 1: The Caprini score is advised for surgery, the Padua score is recommended for internal medicine, and the Khorana score is recommended for oncology patients when assessing thrombus risk in hospitalized patients. Particularly in emergency patients, fondaparinux may be used for thromboprophylaxis in hospitalized patients with an elevated risk of thrombosis and a comparatively low risk of bleeding	Strong recommendation	B
Recommendation 2: Fondaparinux can be administered during the first five to 10 days of deep vein thrombosis (DVT), particularly to patients for whom unfractionated heparin (UFH)/low molecular weight heparin (LMWH) treatment is contraindicated. For DVT treatment, the recommended daily dose is 7.5 mg, and if the patient weighs more than 100 kg, this can be increased to 10 mg; if the patient weighs less than 50 kg, the dose can be lowered to 5 mg	Strong recommendation	B
Recommendation 3: In addition to UFH and LMWH, fondaparinux may be chosen for short-term anticoagulation during the initial anticoagulation of patients with hemodynamically stable pulmonary thromboembolism (PE)	Strong recommendation	A
Recommendation 4: Fondaparinux 2.5 mg once daily, which is superior to other anticoagulant regimens, is recommended for superficial vein thrombosis (SVT) that is ≥3 cm from the deep vein junction and ≥5 cm in length. Anticoagulation should be administered for 45 days	Strong recommendation	B

Front Pharmacol. 2024

JAHA
Journal of the American Heart Association

CURRENT ISSUE

RESEARCH ARTICLE | Originally Published 10 October 2023 |

Thrombocytopenia as a Bleeding Risk Factor in Atrial Fibrillation and Coronary Artery Disease: Insights From the AFIRE Study

Raisuke Iijima, MD, PhD, Masahide Tokue, MD, PhD, Masato Nakamura, MD, PhD, Satoshi Yasuda, MD, PhD, Koichi Kaikita, PhD, Masaharu Akao, MD, PhD, Junya Ako, MD, PhD, ... SHOW ALL ... the AFIRE Investigators | AUTHOR INFO & AFFILIATIONS

Journal of the American Heart Association • Volume 12, Number 20 • https://doi.org/10.1161/JAHA.123.031096

- This study evaluated the AFIRE (Atrial Fibrillation and Ischemic Events With **Rivaroxaban** in Patients With Stable Coronary Artery Disease) trial. Thrombocytopenia was defined as platelet count **<100 000/mm3** level at enrollment. A total of **2133 patients** were classified into the **thrombocytopenia (n=70**) and non-thrombocytopenia (n=2063) groups.
- Major bleeding was significantly higher in the thrombocytopenia group than in the non-thrombocytopenia group **(10.0% versus 4.1%, *P*=0.027).**
- CONCLUSIONS: Among patients with atrial fibrillation and chronic coronary syndrome, thrombocytopenia was significantly associated with increased risk of major bleeding. **Selecting drugs for patients with thrombocytopenia continuing antithrombotic therapy should be given special consideration.**

JOURNAL ARTICLE

The efficacy and safety of direct oral anticoagulants in the treatment of the acute phase of heparin–induced thrombocytopenia: A systematic review

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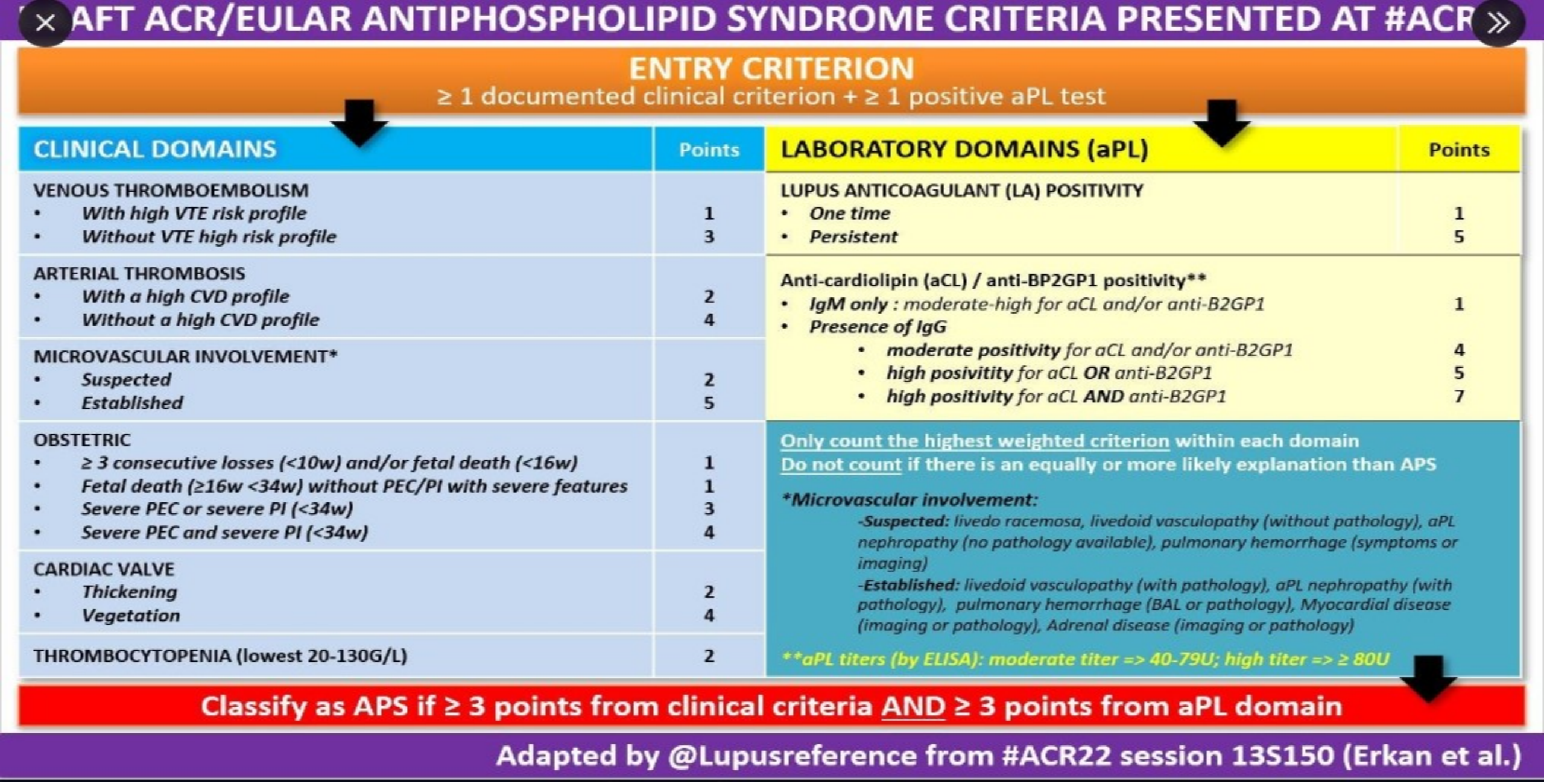
Cooper Sadowski, PharmD, Justin P Reinert, PharmD, MBA, BCCCP

American Journal of Health-System Pharmacy, Volume 81, Issue 19, 1 October 2024, Pages e584–e593, https://doi.org/10.1093/ajhp/zxae109

Published: 23 April 2024 **Article history**

- Rivaroxaban was the most-utilized DOAC (28 patients), followed by apixaban (7 patients) and dabigatran (1 patient). One patient developed a deep venous thrombosis with no other new or recurrent thromboses. There were no reported clinically significant adverse events in any patient
- Argatroban and bivalirudin require intravenous infusion and require close aPTT monitoring and dose adjustment. Fondaparinux requires injection and is contraindicated with body weight <50kg. DOACs would offer the novel ability for an oral treatment in the treatment of the acute phase HIT and allow for minimal monitoring and consistent dosing strategies. **Therefore, DOACs are an intriguing choice for the treatment of the acute phase of HIT.**

- The patient is being followed up in Rheumatology with the diagnoses of SLE and AFAS.
- He is using plaquenil, mycophenolate mofetil, methylprednisolone, warfarin



The 2023 ACR/EULAR APS classification criteria, Arthiritis Rheumatol, 2023 Oct;75(10):1687-1702

Anticoagulant treatment continues with Warfarin.
Duration of treatment?

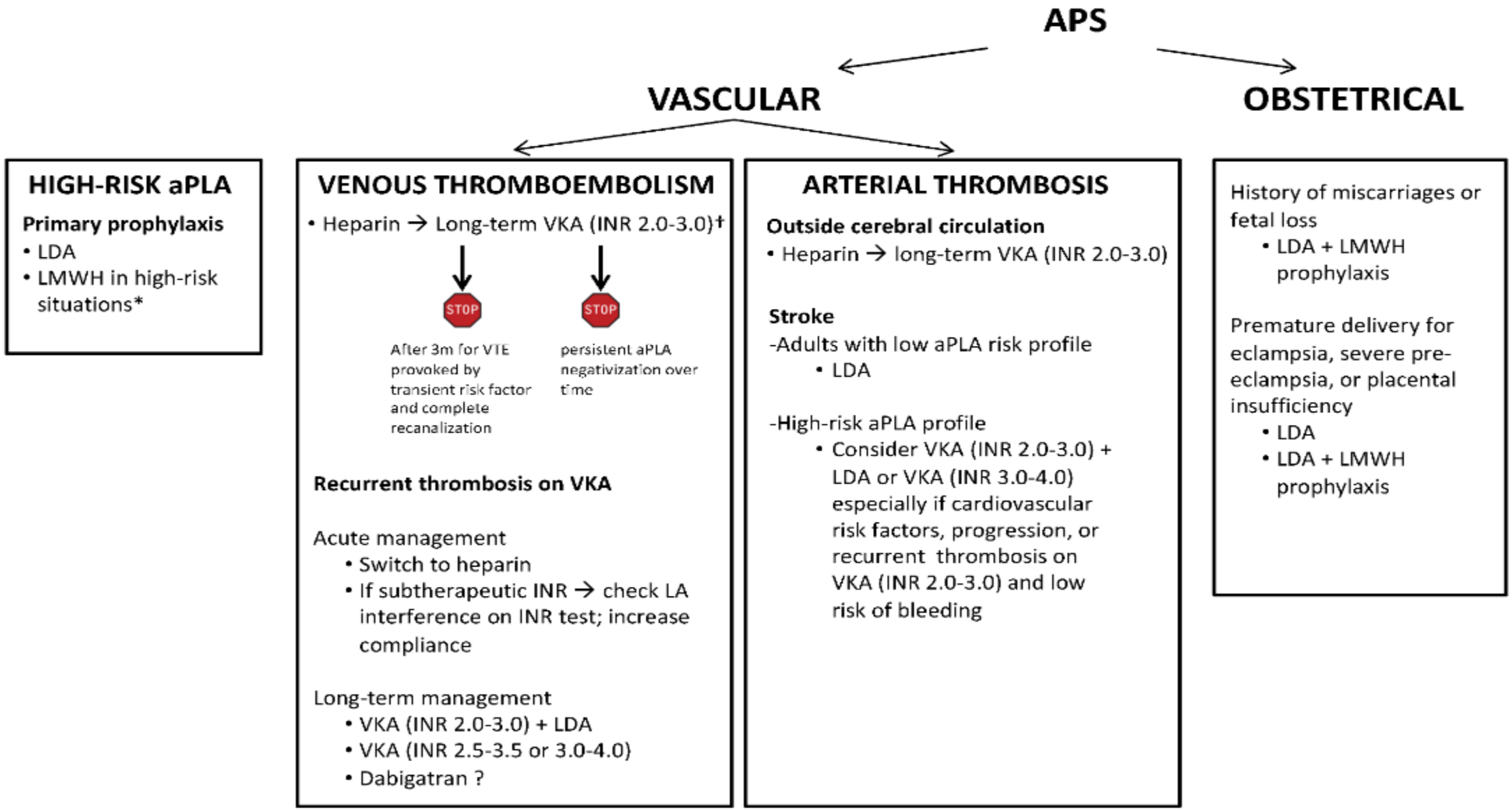


TABLE 11 Categorization of risk factors for venous thromboembolism based on the risk of recurrence over the long-term

Estimated risk for long-term recurrence[a]	Risk factor category for index PE[b]	Examples[b]
Low (<3% per year)	Major transient or reversible factors associated with >10-fold increased risk for the index VTE event (compared to patients without the risk factor)	• Surgery with general anaesthesia for >30 min • Confined to bed in hospital (only "bathroom privileges") for ⩾3 days due to an acute illness, or acute exacerbation of a chronic illness • Trauma with fractures
Intermediate	Non-malignant persistent risk factors	• Inflammatory bowel disease • Active autoimmune disease
	No identifiable risk factor	
High (>8% per year)		• Active cancer • One or more previous episodes of VTE in the absence of a major transient or reversible factor • Antiphospholipid antibody syndrome

Patients in whom extension of anticoagulation beyond 3 months is recommended

Oral anticoagulant treatment of indefinite duration is recommended for patients presenting with recurrent VTE (that is, with at least one previous episode of PE or DVT) not related to a major transient or reversible risk factor [358].

I B

Oral anticoagulant treatment with a VKA for an indefinite period is recommended for patients with antiphospholipid antibody syndrome [359].

I B

Treatment Duration

- Unprovoked
- Without genetic risk factor
- Without additional diseases

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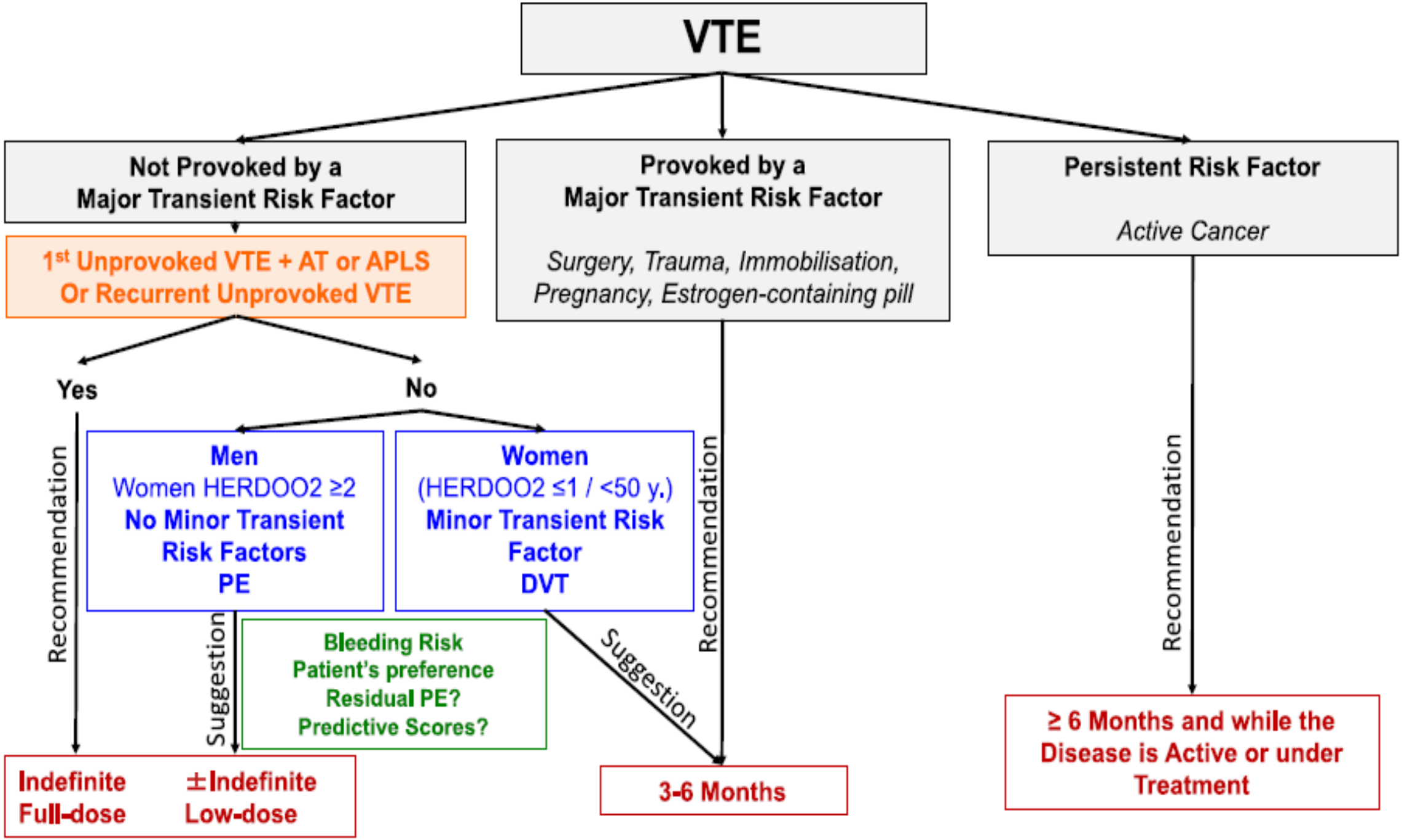
Quarterly Medical Review - Venous thromboembolic disease: a tribute to Professor Guy Meyer

Duration of anticoagulation of venous thromboembolism

Francis Couturaud[a,b,c,*], Nicolas Meneveau[d,e], Marie Antoinette Sevestre[f], Pierre-Emmanuel Morange[g], David Jimenez[h,i,j]


VTE
Not Provoked by a Major Transient Risk Factor
Provoked by a Major Transient Risk Factor
Surgery, Trauma, Immobilisation, Pregnancy, Estrogen-containing pill
Persistent Risk Factor
Active Cancer
1st Unprovoked VTE + AT or APLS
Or Recurrent Unprovoked VTE
Yes
No
Recommendation
Men
Women HERDOO2 ≥2
No Minor Transient Risk Factors
PE
Women
(HERDOO2 ≤1 / <50 y.)
Minor Transient Risk Factor
DVT
Suggestion
Bleeding Risk
Patient's preference
Residual PE?
Predictive Scores?
Recommendation
Suggestion
Recommendation
Indefinite
Full-dose
±Indefinite
Low-dose
3-6 Months
≥ 6 Months and while the Disease is Active or under Treatment

CLINICAL GUIDELINES

blood advances

Check for updates

American Society of Hematology 2023 guidelines for management of venous thromboembolism: thrombophilia testing

Saskia Middeldorp,[1] Robby Nieuwlaat,[2,3] Lisa Baumann Kreuziger,[4] Michiel Coppens,[5,6] Damon Houghton,[7,8] Andra H. James,[9] Eddy Lang,[10] Stephan Moll,[11] Tarra Myers,[12] Meha Bhatt,[2] Chatree Chai-Adisaksopha,[13] Luis E. Colunga-Lozano,[14] Samer G. Karam,[2,3] Yuan Zhang,[1,2] Wojtek Wiercioch,[2,3] Holger J. Schünemann,[2,3,15] and Alfonso Iorio[3]

Case 1: Unprovoked VTE

- 52 year old male
- **Past Medical History:** None
- **Diagnosis:** Unprovoked symptomatic right leg DVT
- **Treatment:** He has been treated with anticoagulation for 3 months without any bleeding concerns

Usual Care

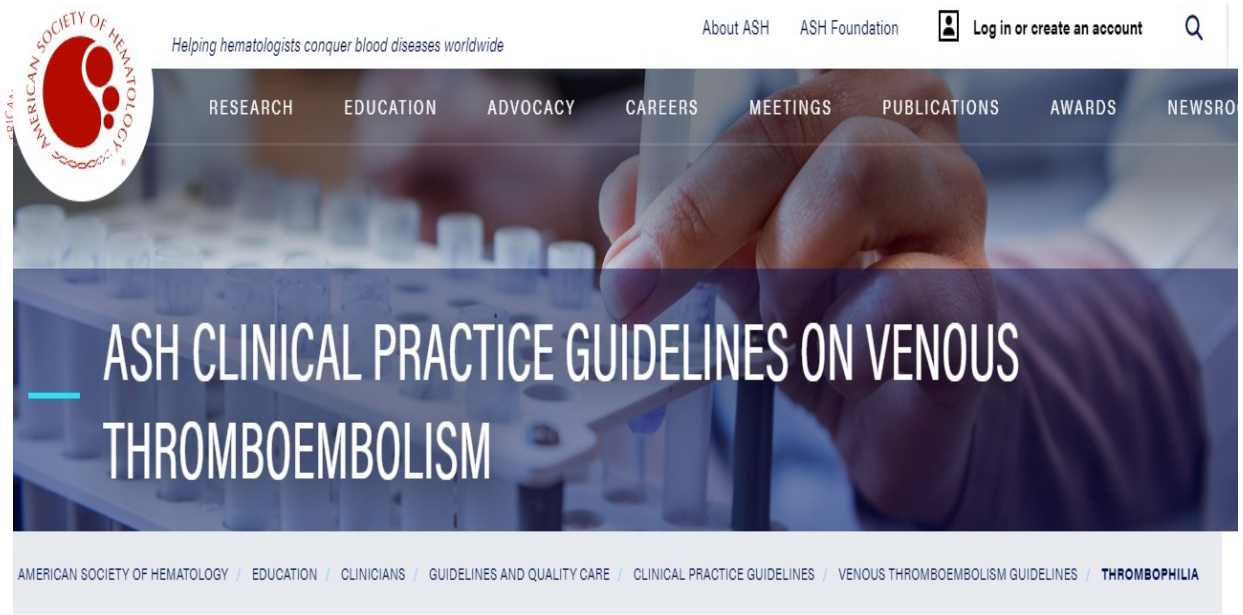
Indefinite antithrombotic therapy is suggested in most individuals with unprovoked VTE (Treatment of VTE ASH guideline)

Thrombophilia testing strategy would mean that patients without thrombophilia would stop anticoagulant therapy (potential for more thrombosis and less bleeding)

What management strategy do you suggest?

a. No thrombophilia testing and indefinite anticoagulation

b. Thrombophilia testing and stop anticoagulation in patients without thrombophilia



ASH VTE Guidelines: Thrombophilia Testing

Thrombophilia testing can be performed in patients with VTE, particularly if they are young, have recurrent episodes, have thrombosis at unusual sites, or have a positive family history of the disease. The purpose of these guidelines is to provide evidence-based recommendations about whether thrombophilia testing and tailoring management based on the test result would improve patient-important outcomes.

Summary of Thrombophilia Testing Strategy for Patients with VTE

	Base Risk of VTE Recurrence (1st year)	Treatment Risk for Major Bleeding	Recommended Strategy for Thrombophilia Testing
Unprovoked	High (10%)	0.5-1.5%	Do Not Test (indefinite anticoagulation in all)
Unusual Site	Intermediate (2.7%-3.8%)		Do Not Test (indefinite anticoagulation in all) OR Test (indefinite anticoagulant therapy in patients with thrombophilia)
Provoked (non-surgical)	Intermediate (5%)		Test (indefinite anticoagulant therapy in patients with thrombophilia)
Provoked (surgical)	Low (1%)		Do Not Test (primary short-term anticoagulation in all)

Intermediate Risk of recurrent thrombosis: **Testing can tip the balance** towards indefinite anticoagulation (thrombophilia positive recurrent VTE risk > bleeding risk)

High or Low Risk of recurrent thrombosis: **Testing does not cross treatment thresholds** (i.e. for unprovoked VTE, recurrent VTE risk > bleeding risk regardless of thrombophilia test results)

Common Types of Thrombophilia[1–3]

Mild Thrombophilia*†	Strong Thrombophilia*†
Heterozygous factor V Leiden (FVL)	Homozygous FVL
Heterozygous factor II G20210A (Prothrombin Gene Mutation -PTGM)	Homozygous factor II G20210A
	Antithrombin deficiency
	Protein C deficiency
	Protein S deficiency
	Antiphospholipid syndrome (APS)
	Combined heterozygous FVL and heterozygous factor II G20210A thrombophilias

It is important to consider the relative and absolute increase in risk associated with thrombophilia testing. For example, the risk of first episode of VTE in the general population is about 1/1000 per year. Heterozygosity for factor V Leiden increases this risk by ~5-fold to 5/1000 per year. Factor V Leiden and PTGM are mild risk factors for recurrent VTE (odds ratio ~1.3). Natural anticoagulant deficiencies are infrequent and usually associated w/strong family history.

* Strong and mild refer to the relative increase in the risk of recurrent VTE w/o anticoagulation.

† Presence of a thrombophilia generally should not impact decisions regarding anticoagulation type or duration, with the exception of high-risk antiphospholipid syndrome (APS; see APS guidance on opposite page).

TEŞEKKÜRLER…