Pulmoner Emboli: Zor Olgular, Zor Kararlar

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Erciyes Üniversitesi

OLGU 1

- 67 Yaş, E, çiftçi, Sarız/Kayseri

- Şikayet: Nefes Darlığı, Öksürük –1 aydır—

- Hikaye: Kronik hastalık öyküsü yok

Sigara: 50 p/yıl (halen)

İki ay önce sağ kolunda istemsiz hareketler olup, intrakranial kitle öntanısı ile biyopsi alınmış.

Kullandığı ilaç: Levetirasetam (keppra), deksametazon (2 aydır alıyor)

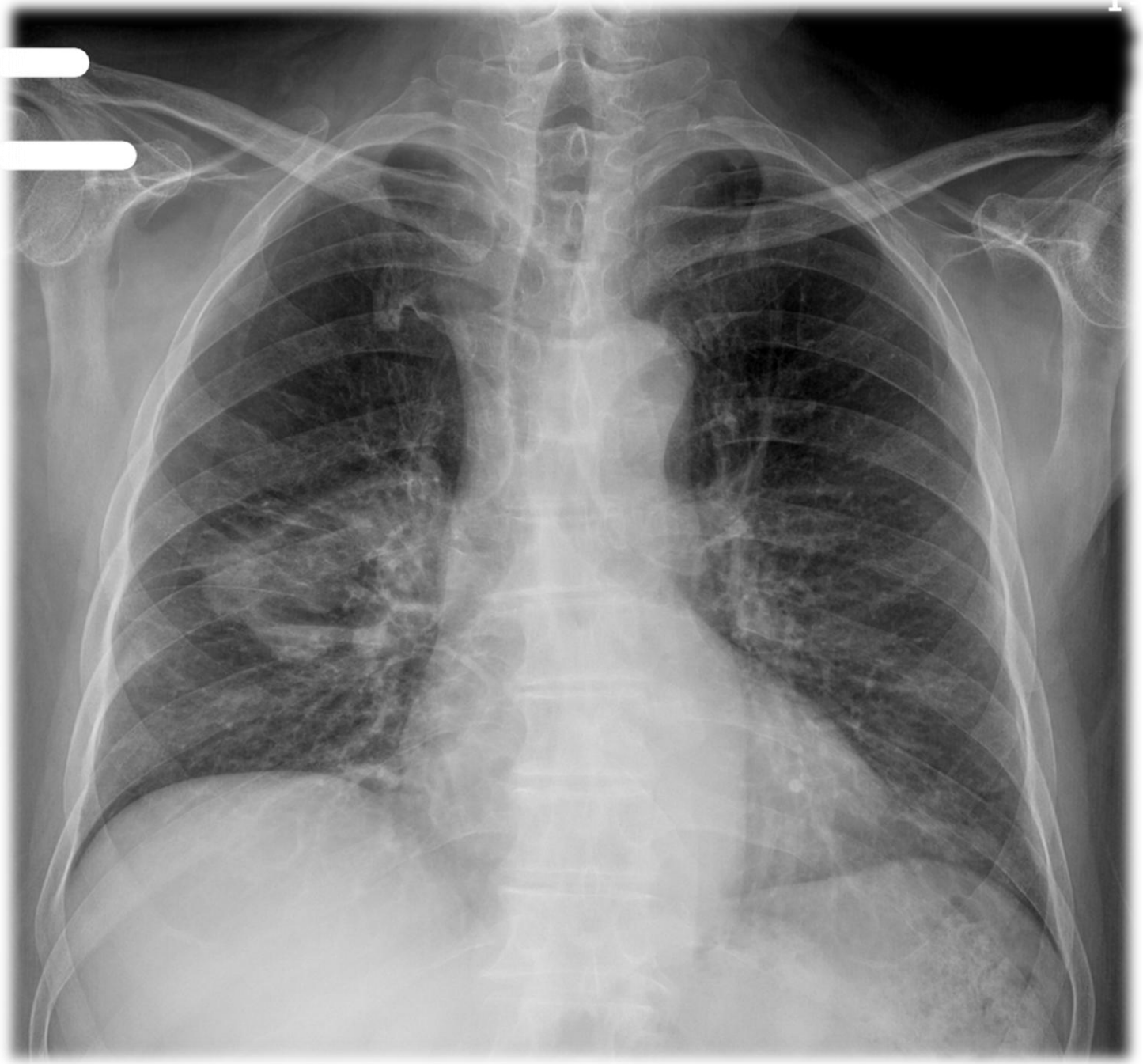
- Fizik muayene:

Genel durumu orta-iyi, koopere, oryante

SPO2: 93 (OH) Nabız: 73

Solunum sistemi ve Kardiyovasküler sistem muayenesinde anlamlı patoloji görülmedi.

Hastanın yakın zamanda çekilen dış merkezli Toraks görüntülemesinde kavite olması üzerine oral antibiyotik verildiği öğrenildi.



Laboratuvar:

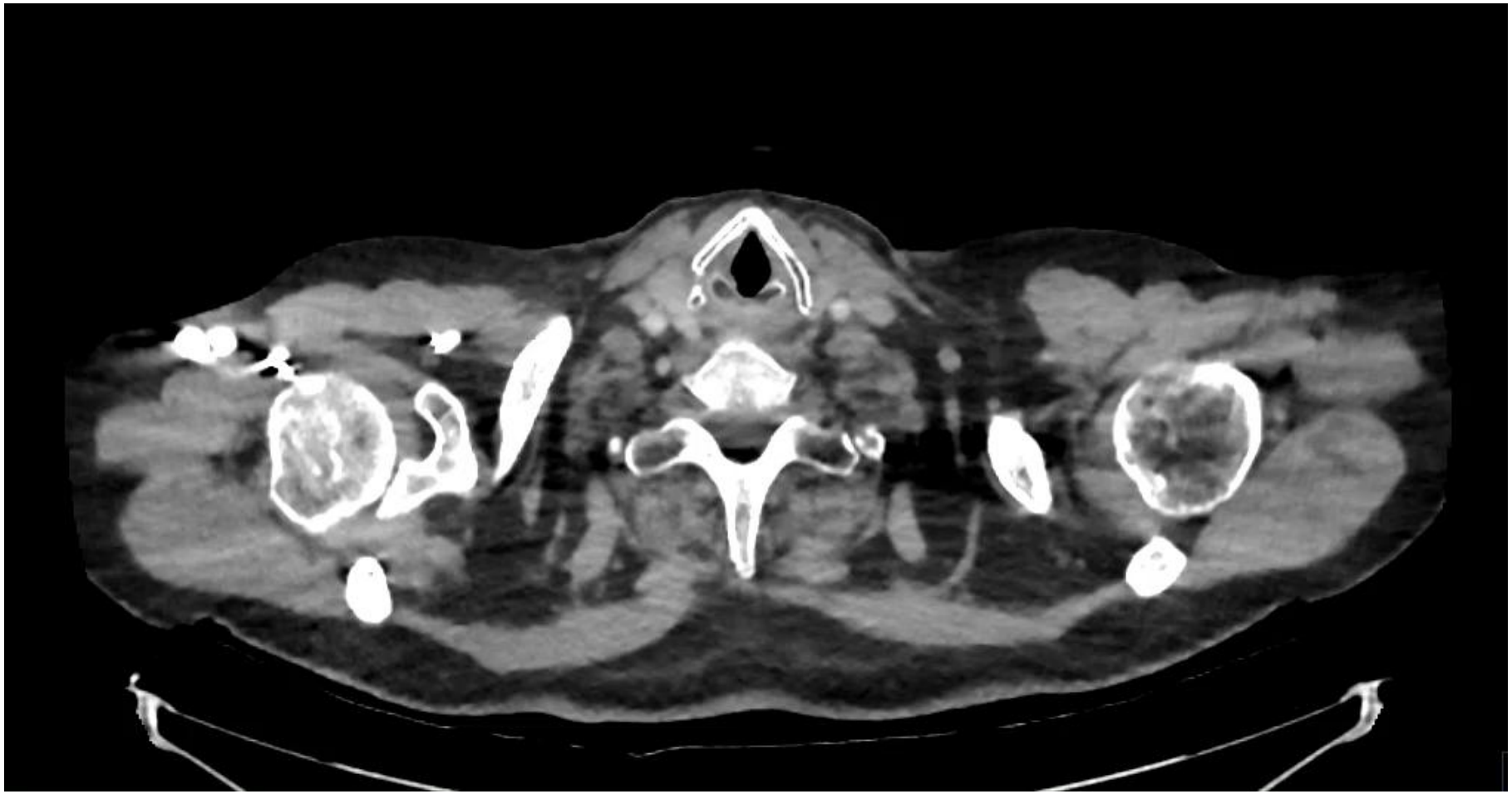
WBC: **12990** /µL
Nötrofil: 7480 /µL
Lenfosit: 4610 /µL
Platelet: 206.000 /µL
Hgb: **13.6** g/dL
BUN / Kreatinin: 21 / 0.96 mg/dL
GFR: 82
Na / K: 141 / 4.34 mmol/L
Ca / P: 9.95 / 2.56 mg/ dL
AST / ALT: 15 / 25 u/L
T. Protein / albümin: 6.5/3.6 g/dL
CRP: **19.27** mg/L
Prokalsitonin: 0.04 ng /mL
Sedimentasyon: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

- Hasta bana danışıldı, Nekrotizan Pnömoni? Akciğer Absesi? Malignite? ön tanıları ile Göğüs Hastalıkları Servisine yatırıldı.

- Balgam çıkaramayan hastaya bronkoskopi planlandı.

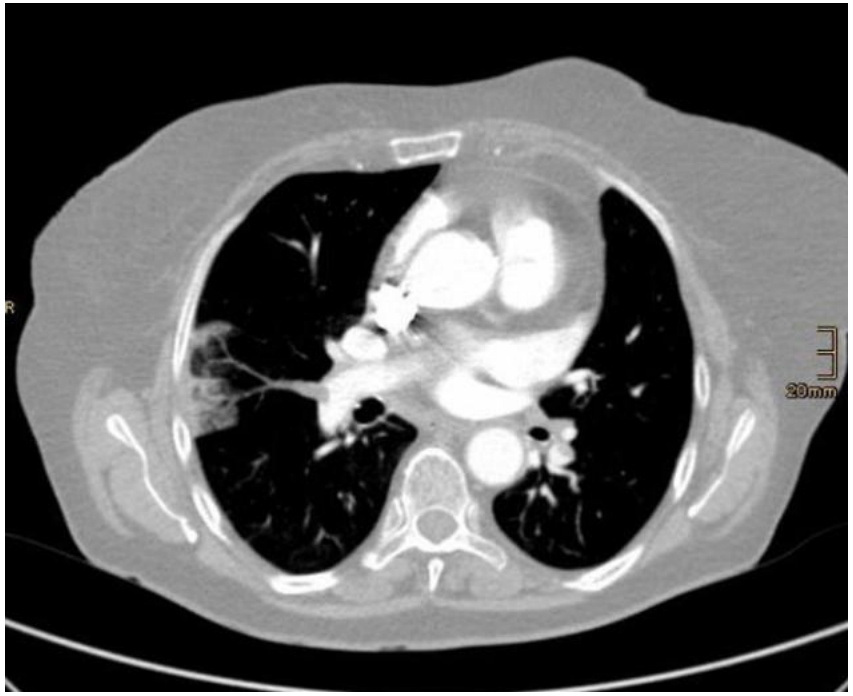
- D-dimer: **8890 µg/L**
- Troponin: 19.6 ng/ L
- Pro BNP: 270 pg/ mL

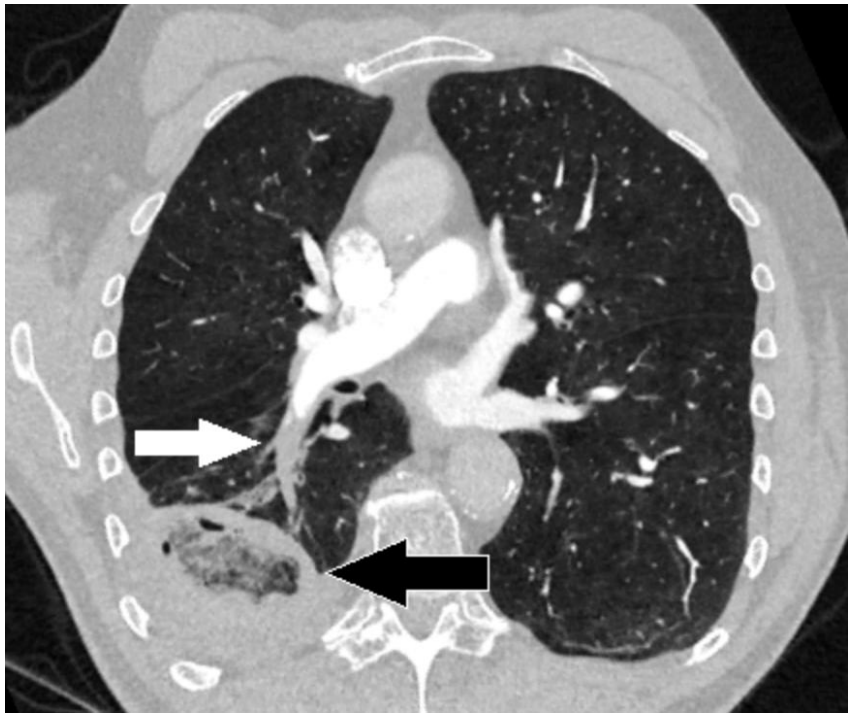
- Burcu hoca☺
- CT anjiografi planlanıyor.

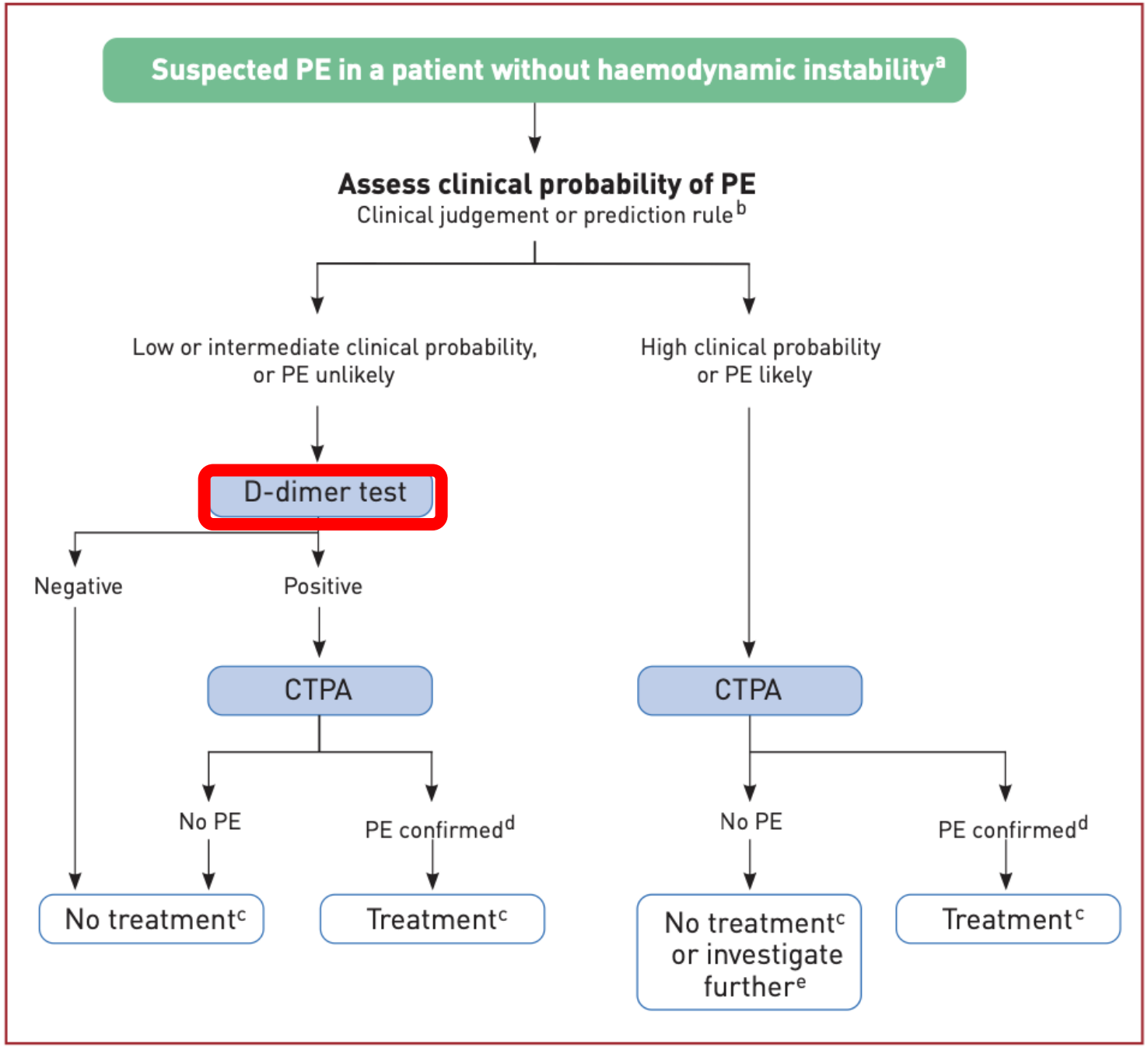


PTE de pulmoner enfarktüs

- Distal pulmoner arterlerin tıkanması sonucu akciğer parankiminde iskemi, hemoraji ve nihayetinde nekroza yol açar.
- En sık akut pulmoner emboliden kaynaklanır ve insidansı yaklaşık %30 olarak bildirilmiştir.
- Pulmoner arterin tıkanmasını takiben, bronşiyal arterler pulmoner kapillerlerin birincil perfüzyon kaynağı olarak devreye girer.
- Bronşiyal dolaşımdaki nispeten daha yüksek kan basıncı, kapiller kan akışında artışa neden olarak eritrositlerin ekstravazasyonuna (alveolar hemoraji) yol açar. Bu kanama rezorbe olmazsa doku nekrozu ve enfarktüs ile sonuçlanır.







D dimer
Yaş X10 = Üst Sınır

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

YEARS kriterlerine göre

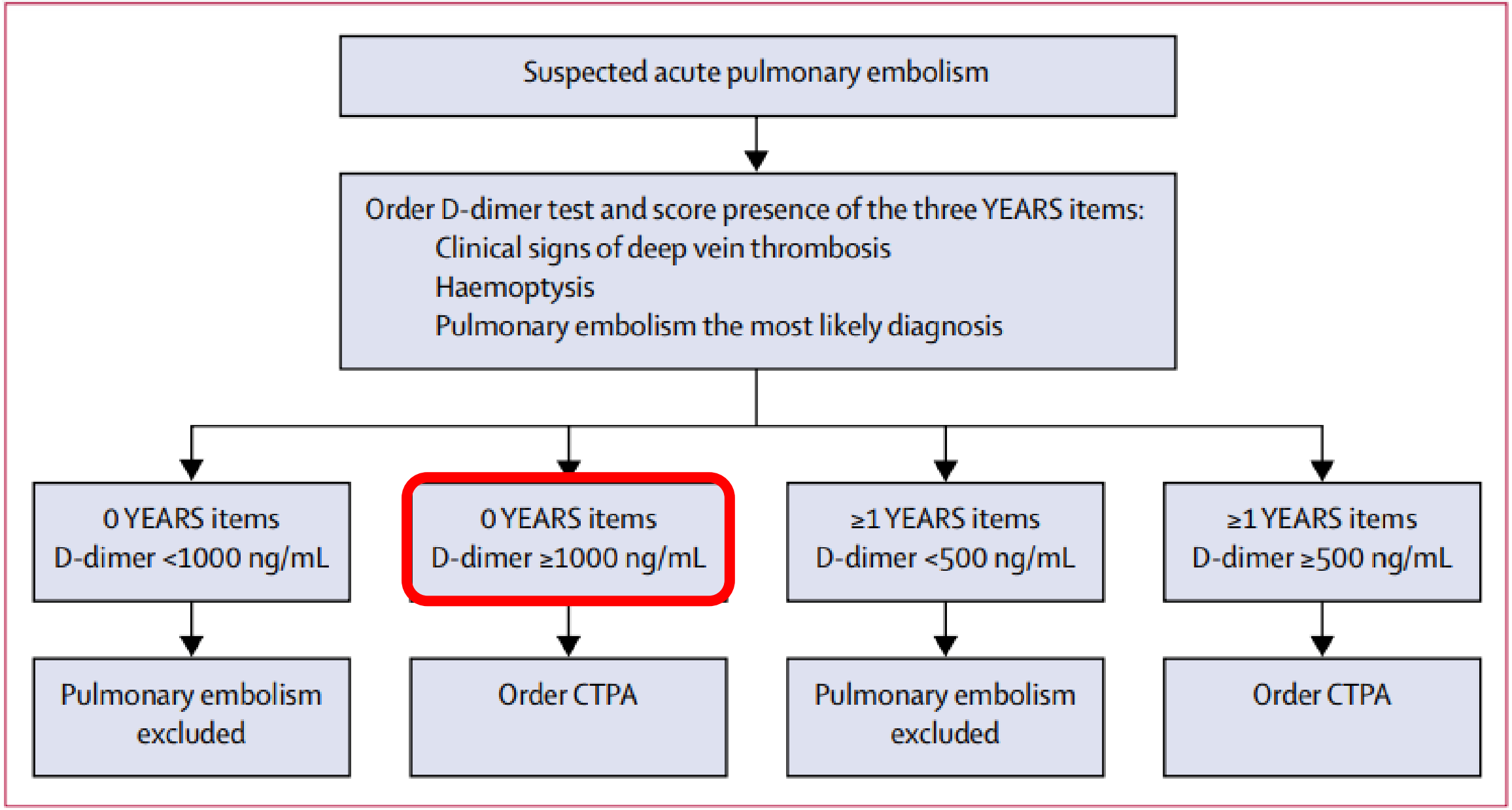
1- DVT bulguları varlığı

2- Hemoptizi

3- Pulmoner emboli en olası tanı olması

YEARS kriterinin hiçbiri yok + D DİMER <1000, veya

YEARS dan biri veya daha fazlası var + D DİMER<500 ise **emboli dışlanıyor**


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

D-Dimer thresholds for diagnosis of pulmonary embolism based on a single question: is it the most likely diagnosis? A prospective, multicentre, open-label, single-arm interventional study

Mélanie Roussel, Héloïse Bannelier*, Soufiane Lebal, Christian Kassasseya, Donia Bouzid, Olivier Peyrony, Aurélien Baud, Anthony Chauvin, Agathe Beauvais, Nicolas Javaud, Judith Gorlicki, Jennifer Truchot, Pierrick Le Borgne, Richard Chocron, Tabassome Simon, Yonathan Freund*

Summary

Background Validated diagnostic strategies for pulmonary embolism allow raising the D-dimer threshold to 1000 ng/mL in selected patients with a low probability of pulmonary embolism, but adherence to this strategy in routine practice remains poor. Retrospective studies suggest that these rules could be replaced by a single clinical question as to whether pulmonary embolism is the most likely diagnosis. We aimed to assess the safety of a simplified approach that applies a 1000 ng/mL threshold when pulmonary embolism is unlikely and an age-adjusted threshold otherwise, including patients at a high probability for pulmonary embolism.

Lancet Respir Med 2025
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October 21, 2025
https://doi.org/10.1016/S2213-2600(25)00292-9
See Online/Comment
https://doi.org/10.1016/

Çözülmesi gereken sorun, acilde emboliyi dışlamak için çok fazla BT anjio çekiliyor.
Hastaları acilde değerlendirmek için bir çok klinik skorlama var.

Ancak bu çalışmada doktora tek bir soru soruluyor: **PE en olası tanı mı?**
Hayır ise **D Dimer eşik değeri 1000 ng/mL**
Evet ise Yaşa uyarlanan D Dimer **(50 yaş üstü için Yaş x10)**

Bu basit sınıflama kullanılırsa
Tanı hata oranı %0.00
%20-40 arası Bt anjio isteminde azalma

📌 2. Kritik Analiz – Çalışmanın Getirdiği Yenilikler

🔹 A) "Tek soru" ile pretest probability belirleme

YEARS veya Wells gibi çok maddeli CDR yerine **tek bir subjektif soru** kullanılıyor:

> **"Pulmoner emboli en olası tanı mı?"**

Avantaj: pratik, hızlı
Dezavantaj: subjektiflik, deneyim gereksinimi
→ Yazar, özellikle **deneyimsiz hekimlerde önyargı ve karar hatalarına** açık olabileceğini vurguluyor (Kahneman'ın "heuristic bias" çalışmalarıyla destekliyor). D-dimer thresholds in pulmonary...

🔹 B) Yüksek olasılıklı hastalarda D-dimer kullanılması

Bu çok önemli çünkü klasik algoritmalarda:

- **Yüksek Wells/YEARS skoru → direkt CTPA**

Fakat Roussel çalışması gösteriyor ki:

- Yüksek olasılık grubundaki hastaların **%39'unda D-dimer PE'yi ekarte etmek için yeterli**, CTPA gerekmiyor.

Bu, yıllardır geçerli olan kuralı sorgulayan güçlü bir bulgu.

🔹 C) Yaşa göre D-dimer ayarlaması (age-adjusted)

≥50 yaş için D-dimer eşik değeri:
Yaş × 10 ng/mL

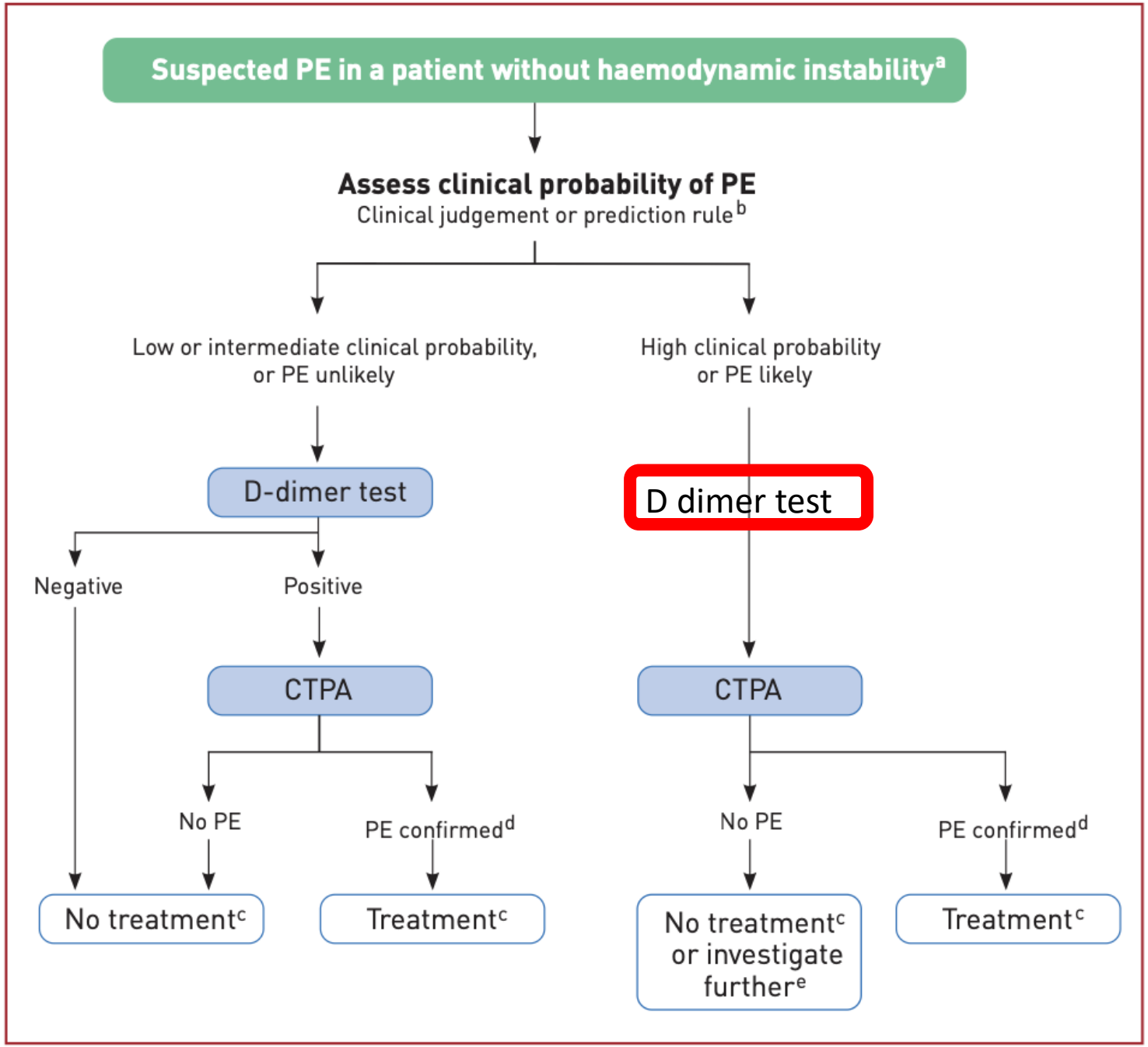
Suspected PE in a patient without haemodynamic instability[a]
Assess clinical probability of PE
Clinical judgement or prediction rule[b]
Low or intermediate clinical probability, or PE unlikely
High clinical probability or PE likely
D-dimer test
D dimer test
Negative
Positive
CTPA
CTPA
No PE
PE confirmed[d]
No PE
PE confirmed[d]
No treatment[c]
Treatment[c]
No treatment[c] or investigate further[e]
Treatment[c]

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]	+	+
sPESI = 1	Intermediate–low	-	+[e]	One (or none) positive	
Low		-	-	-	Assesment optional; if assessed, negative

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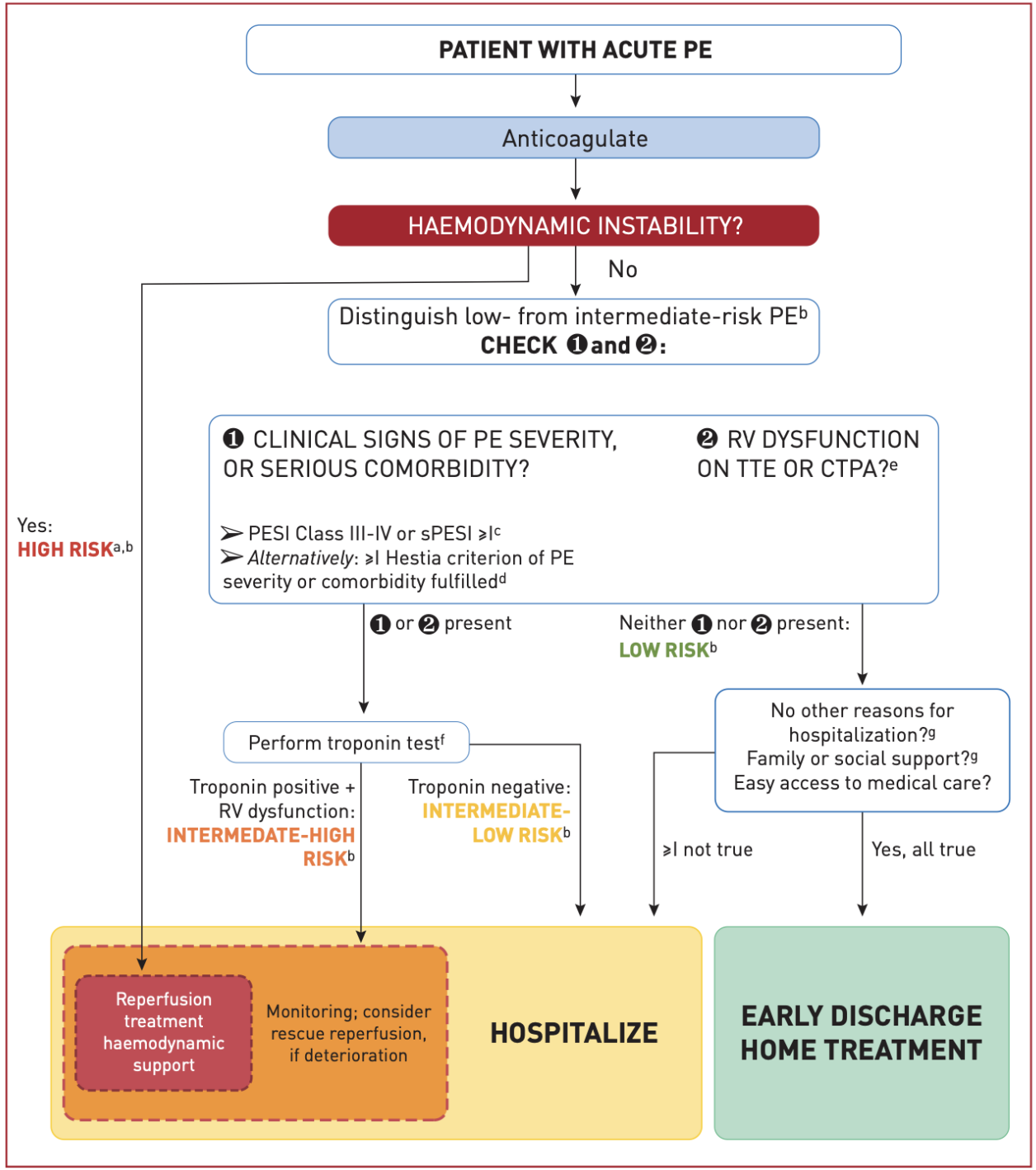
sPESI
(Aynı zamanda hastaneye yatış kriterleri olarak kullanılır)

- 1- 80 Yaş üstü
- 2- 90 saturasyon altı
- 3- 100 sistolik kan basıncı altı
- 4- 110 nabız üstü
- 5- Kronik kardiyopulmoner hastalık
- 6- Malignite
- HERBİRİ 1 PUAN, HERHANGİ BİRİNİN OLMASI YETERLİ

Jimenez D, et al. Arch Intern Med 2010;170:1383-9.


PATIENT WITH ACUTE PE
Anticoagulate
HAEMODYNAMIC INSTABILITY?
No
Yes:
HIGH RISK[a,b]
Distinguish low- from intermediate-risk PE[b]
CHECK ❶ and ❷:
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

- **<u>Bilateral alt ekstremite venöz do</u>**
  femoral ven ayrıca sol popliteal ve
- Hastaya Enoksaparin 2x 0.6 IU baş

Rebiyopsi yapılıyor

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)

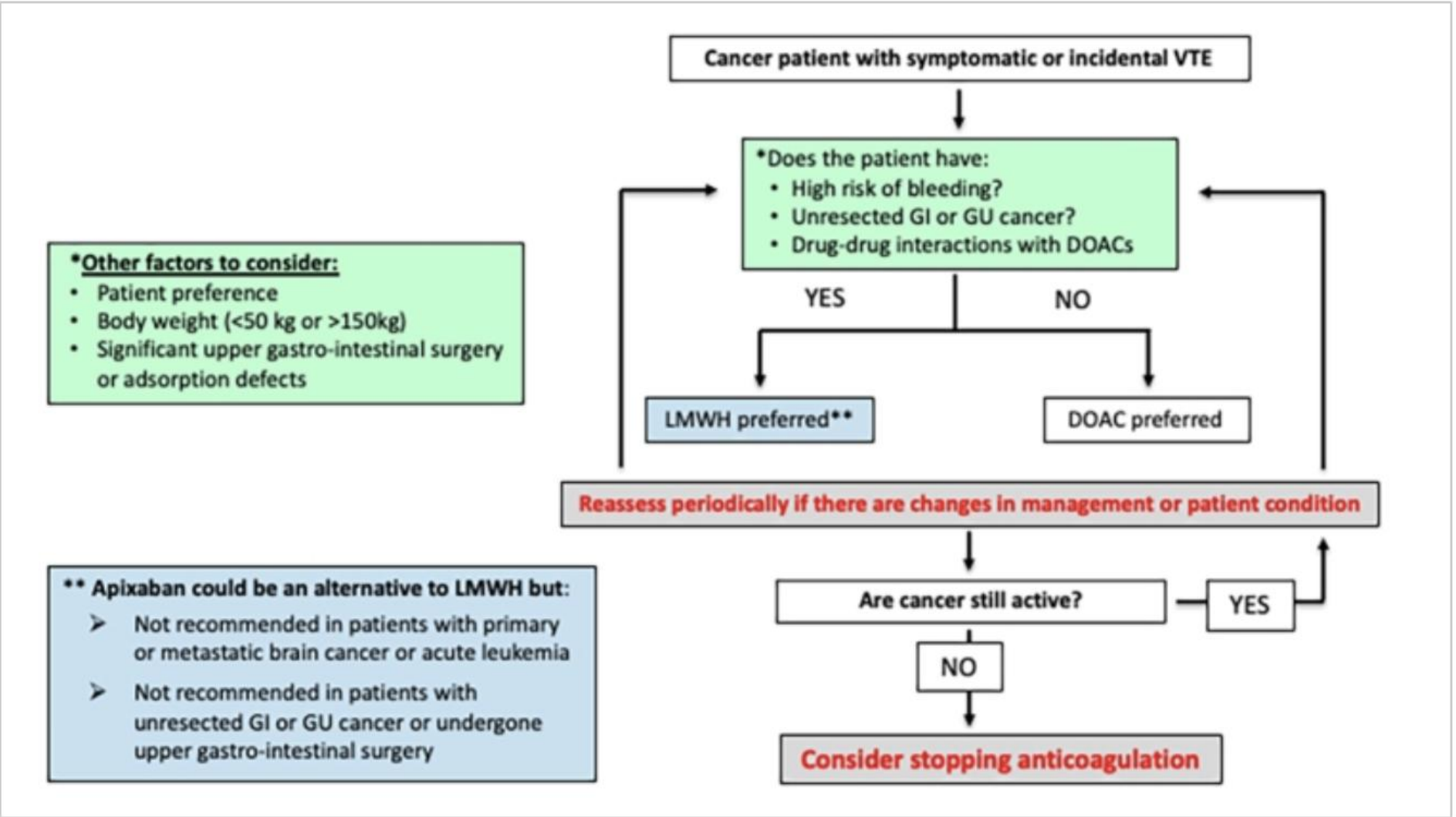
ASTROSİTİK NEOPLAZM, SAĞ FRONTAL BÖLGE, STEREOTAKTİK BİYOPSİSİ

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.



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

Kanser ilişkili VTE tedavisinde;

- Bireyselleştirilmiş tedavi (ilaç etkileşimi, kanama riski)
- ***Monoterapi (kombine antitrombotiklerdense)***
- İnsidental VTE, nüks riski nedeniyle tedavi edilmesi
- ***3-6 ay tedavi, ancak aktif kanser olduğu sürece tedaviye devam edilmesi***

Outcomes		Major bleeding, %	Recurrent VTE, %	All causes mortality, %
Meyer 2002 (CANTHANOX)	Enoxaparin (n=71)	3m: 7%	3m: 2.8%	31%
	Warfarin (n=75)	3m: 16%	3m: 4%	38.7%
Lee 2003 (CLOT)	Dalteparin (n=338)	6%	9%	38.5%
	VKA (n=338)	4%	17%	40.2%
ONCENOX 2006	Enoxaparin (n=36)	11.1%	6.3%	41.7%
	Warfarin (n=34)	2.9%	10%	32.4%
CATCH 2015	Tinzaparin (n=449)	2.7%	6.9%	33.4%
	Warfarin (n=451)	2.4%	10%	30.6%
SELECT-D 2018	Rivaroxaban (n=203)	6%	4%	25%
	Dalteparin (n=203)	4%	11%	30%
Raskob 2018 (HOKUSAI VTE Cancer)	Edoxaban (n=522)	6.9%	7.9%	39.5%
	Dalteparin (n=524)	4%	11.3%	36.6%*
ADAM VTE 2020	Apixaban (n=150)	0%	0.7%	16%
	Dalteparin (n=150)	1.4%	6.3%	11%
CARAVAGGIO trial 2020	Apixaban (n=576)	3.8%	5.6%	23.4%
	Dalteparin (n=576)	4%	7.9%	26.4%

Kanser Hastalarında Azaltılmış Dozla Uzun Süreli Tedavi

The NEW ENGLAND JOURNAL of MEDICINE

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Extended Reduced-Dose Apixaban for Cancer-Associated Venous Thromboembolism

I. Mahé,[1-4] M. Carrier,[5] D. Mayeur,[6,7] J. Chidiac,[1] E. Vicaut,[2,8] N. Falvo,[4,9] O. Sanchez,[2-4,10] C. Grange,[4,11] M. Monreal,[12-14] J.J. López-Núñez,[12,13,15] R. Otero-Candelera,[15,16] G. Le Gal,[5] E. Yeo,[17] M. Righini,[18] H. Robert-Ebadi,[18] M.V. Huisman,[19] F.A. Klok,[19] P. Westerweel,[20] G. Agnelli,[21] C. Becattini,[21] A. Bamias,[22] K. Syrigos,[23] S. Szmit,[24,25] A. Torbicki,[24] P. Verhamme,[26] A. Maraveyas,[27] A.T. Cohen,[28] C. Ay,[29] C. Chapelle,[30,31] G. Meyer,[2,4*] F. Couturaud,[4,32,33] P. Mismetti,[4,31,34,35] P. Girard,[4,36] L. Bertoletti,[4,31,34,35] and S. Laporte,[4,30,31] for the API-CAT Investigators†

ABSTRACT

- **Apixaban** 2.5 mg 2x1 ile, 5 mgr 2x1 karşılaştırılıyor.
- **En az 6 ay** DMAH-DOAK-Warfarin alan hastalar çalışmaya alınıyor.
- Nüks VTE birincil sonlanım noktası olarak belirlenmiş.
- **1766 hasta** çalışmaya alınmış.

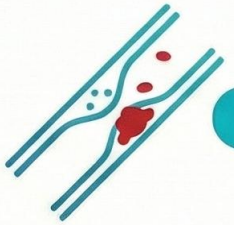
Outcome	Reduced-Dose Apixaban (N=866)	Full-Dose Apixaban (N=900)	Treatment Effect (95% CI)	P Value
	number (percent)			
Primary efficacy outcome: recurrent venous thromboembolism†	18 (2.1)	24 (2.8)	0.76 (0.41–1.41)	0.001
Recurrent symptomatic venous thromboembolism	17 (2.0)	18 (2.1)	0.97 (0.50–1.88)	—
Lower-limb deep-vein thrombosis‡	8 (0.9)	6 (0.7)	—	
Pulmonary embolism	9 (1.1)	10 (1.2)	—	
Fatal pulmonary embolism	0	0	—	
Unexplained sudden death§	3 (0.4)	2 (0.3)	—	
Upper-limb deep-vein thrombosis	1 (0.1)	3 (0.4)	—	
Central venous catheter–related thrombosis	1 (0.1)	2 (0.2)	—	
Incidental venous thromboembolism¶	1 (0.1)	6 (0.7)	—	
Recurrent major venous thromboembolism‖	17 (2.0)	21 (2.4)	0.83 (0.44–1.57)	—
Key secondary safety outcome: major or clinically relevant nonmajor bleeding**	102 (12.1)	136 (15.6)	0.75 (0.58–0.97)	0.03
Major bleeding	24 (2.9)	37 (4.3)	0.66 (0.40–1.10)	—
Fatal bleeding	2 (0.2)	2 (0.2)	—	
Major gastrointestinal bleeding	12 (1.4)	25 (2.9)	—	
Upper gastrointestinal bleeding	6 (0.7)	13 (1.5)	—	
Lower gastrointestinal bleeding	7 (0.8)	13 (1.5)	—	
Clinically relevant nonmajor bleeding	84 (10.0)	107 (12.3)	0.79 (0.59–1.05)	

- Bu çalışma şunları göstermektedir:
- Aktif kanserli hastalarda tekrarlayan venöz tromboembolizmin önlenmesinde, düşük doz apixaban ile uzun süreli antikoagülasyon, tam doz apixaban ile karşılaştırıldığında **daha düşük etkili değildir.**
- Düşük doz, tam doza kıyasla klinik olarak **anlamlı kanama komplikasyonlarının daha düşük insidansına** yol açmıştır.

Apixaban for Cancer-Associated Blood Clots: Finding the Right Balance

Reduced Dose is **Equally Effective for Prevention**

The 2.5 mg dose was proven **noninferior** to the full 5.0 mg dose.



Recurrent Blood Clots

2.1%

2.8%
Full Dose
(5.0 mg)

Reduced Dose is **Significantly Safer**

It led to a statistically lower incidence of clinically relevant bleeding complications.

12.1%
Clinically Relevant Bleeding

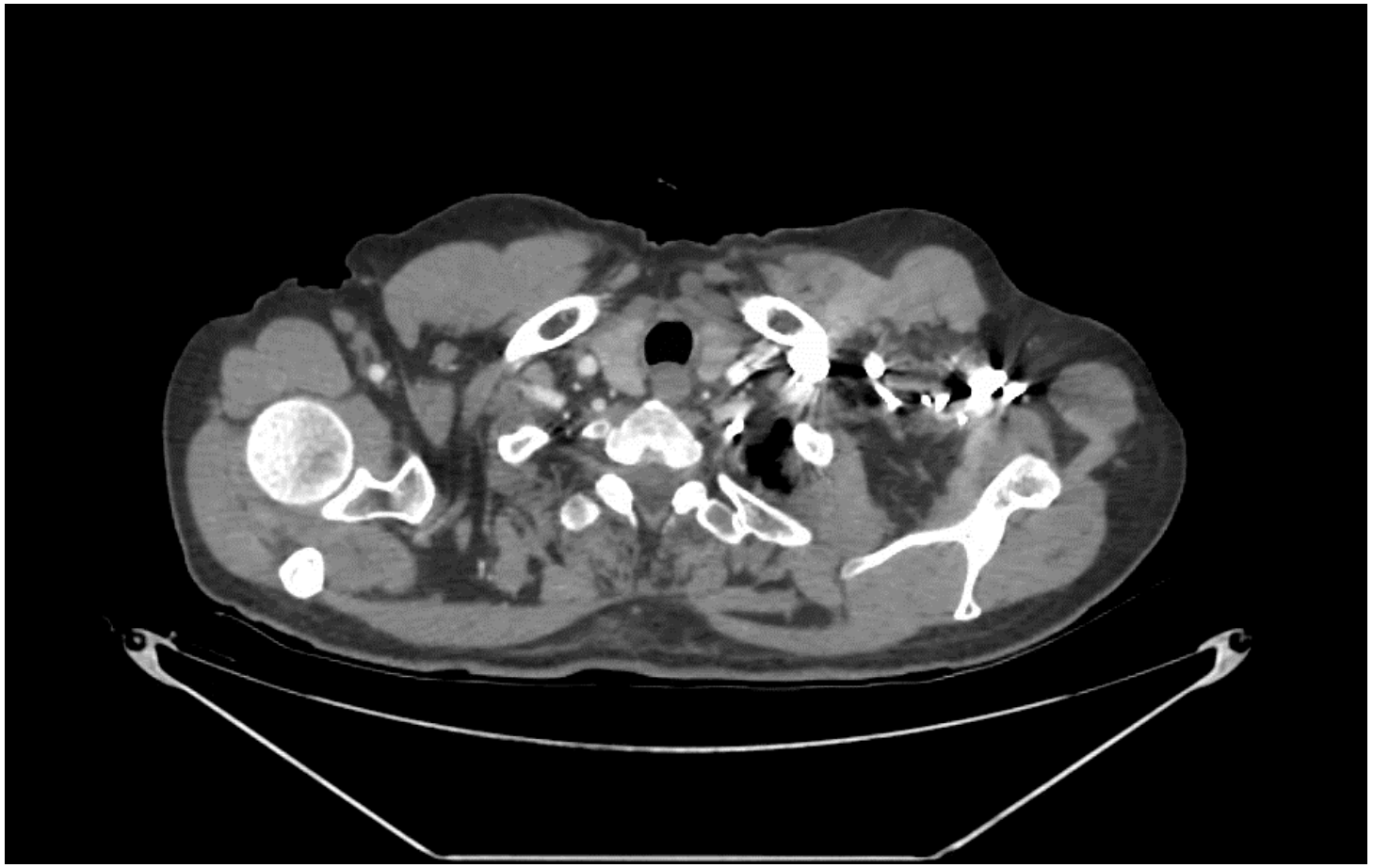
15.6%

2.9%
Major Bleeding

4.3%
Full Dose (5.0 mg)

NotebookLM

3 aylık DMAH tedavisi sonrası kontrol BT



PTE tedavisi sonrası tromboembolinin ortadan kalktığını göstermek için görüntüleme yöntemleri (BT anjiyografi veya V/P sintigrafisi gibi) yapılmalı mıdır?

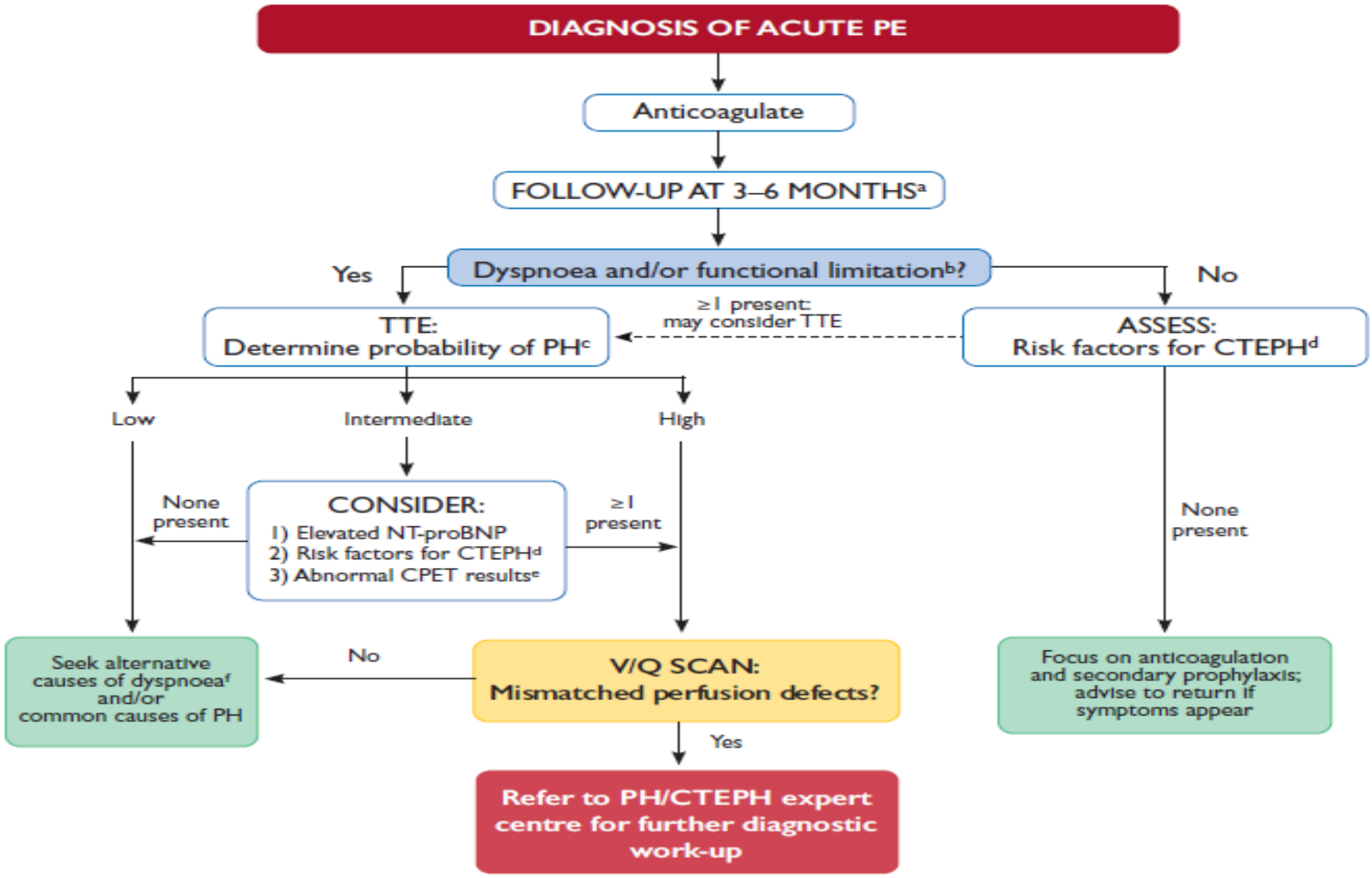

DIAGNOSIS OF ACUTE PE
Anticoagulate
FOLLOW-UP AT 3–6 MONTHS[a]
Dyspnoea and/or functional limitation[b]?
Yes
No
≥1 present: may consider TTE
TTE: Determine probability of PH[c]
ASSESS: Risk factors for CTEPH[d]
Low
Intermediate
High
None present
CONSIDER:
1) Elevated NT-proBNP
2) Risk factors for CTEPH[d]
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

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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

© ESC 2019

Vaka 2

- 18 yaş, E, Nevşehir, Öğrenci
- Horlama nedeniyle KBB muayenesi olan hastanın, burunda yara ve CRP yüksekliği olması üzerine hastaya sefuroksim aksetil başlanmış.
- Hasta antibiyotik alırken evde öksürmekle birlikte ağızdan kan gelme şikayeti ile Nevşehir DH Acil servise başvurmuş. Hastanın 5-6 kere taze kırmızı, toplamda 1 fincan kadar hemoptizisi olmuş.

- Hasta hipoksemisi de olması üzerine Anestezi YBÜ ye yatırılarak, ampirik antibiyoterapi ve metilprednizolon 100 mg verilmiş. Hastanın takibinde solunum sıkıntısı artması ve high flow ihtiyacı olması üzerine aynı gün ERÜTF GHYBÜ ne kabul edildi.
- Şikayet: Ağızdan öksürmekle kan gelmesi, nefes darlığı ve çarpıntı
- Özgeçmiş: Çocukluğunda VSD kapatılması

Kronik hastalık yok, sigara veya herhangi bir alışkanlığı yok

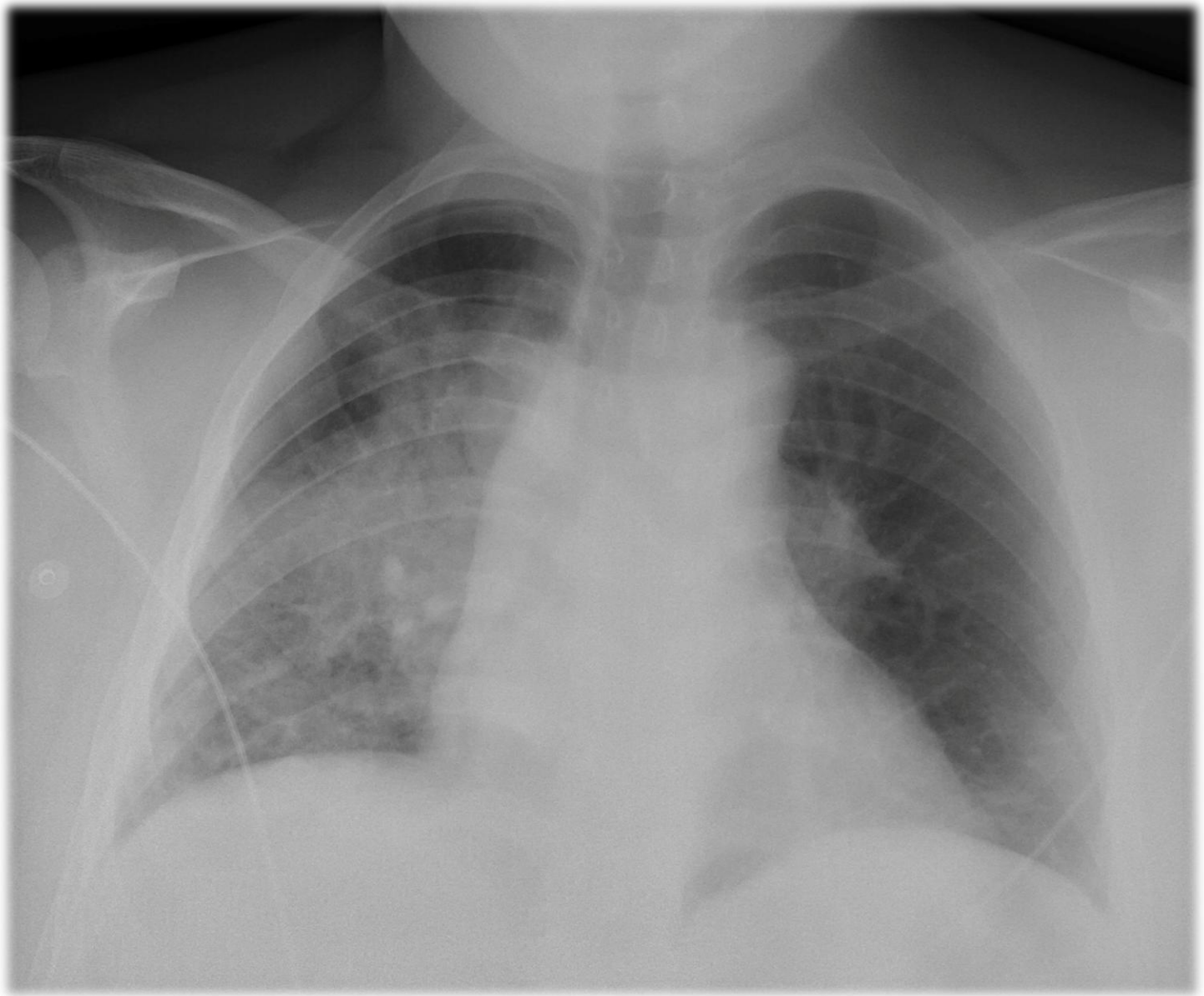
- Fizik muayene:

Genel durumu orta-kötü, GKS:15, dispneik

SS: sağ orta-alt zonda yer yer ral+,

KVS: ritmik, taşikardik Nbz: 110 /dk

Diğer sistem muayenelerinde anlamlı patoloji izlenmedi



Laboratuvar:

WBC: **17090** /µL

Nötrofil: **15660** - Lenfosit: 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 / albümin: 7.4 / 4.5 g/dL

CRP: **73.8** mg/L

Prokalsitonin: 0.07 ng /mL

Sedimentasyon: **53** mm/s

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

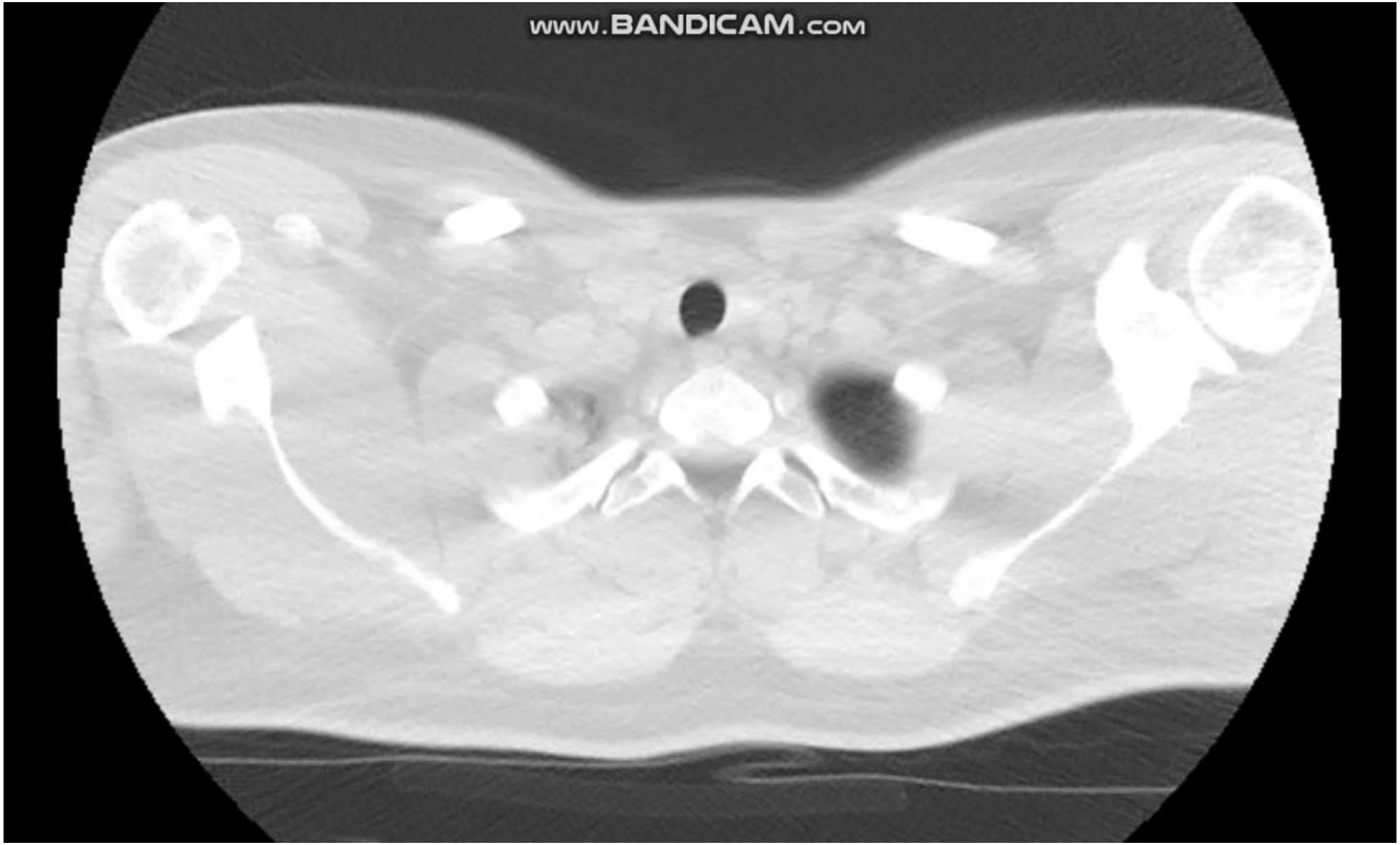
troponin: 30 ng/L

D-dimer: **2860** µg/L

TİT: Kan:25 lökosit: 100 pH: 6.5.

eritrosit: 10, nitrit:-

İdrar mikroprotein/kreatinin: 47 / 265 mg/dL


www.BANDICAM.com

- Hasta trombositopeni? nedeni ile **Hematolojiye** konsülte edildi.

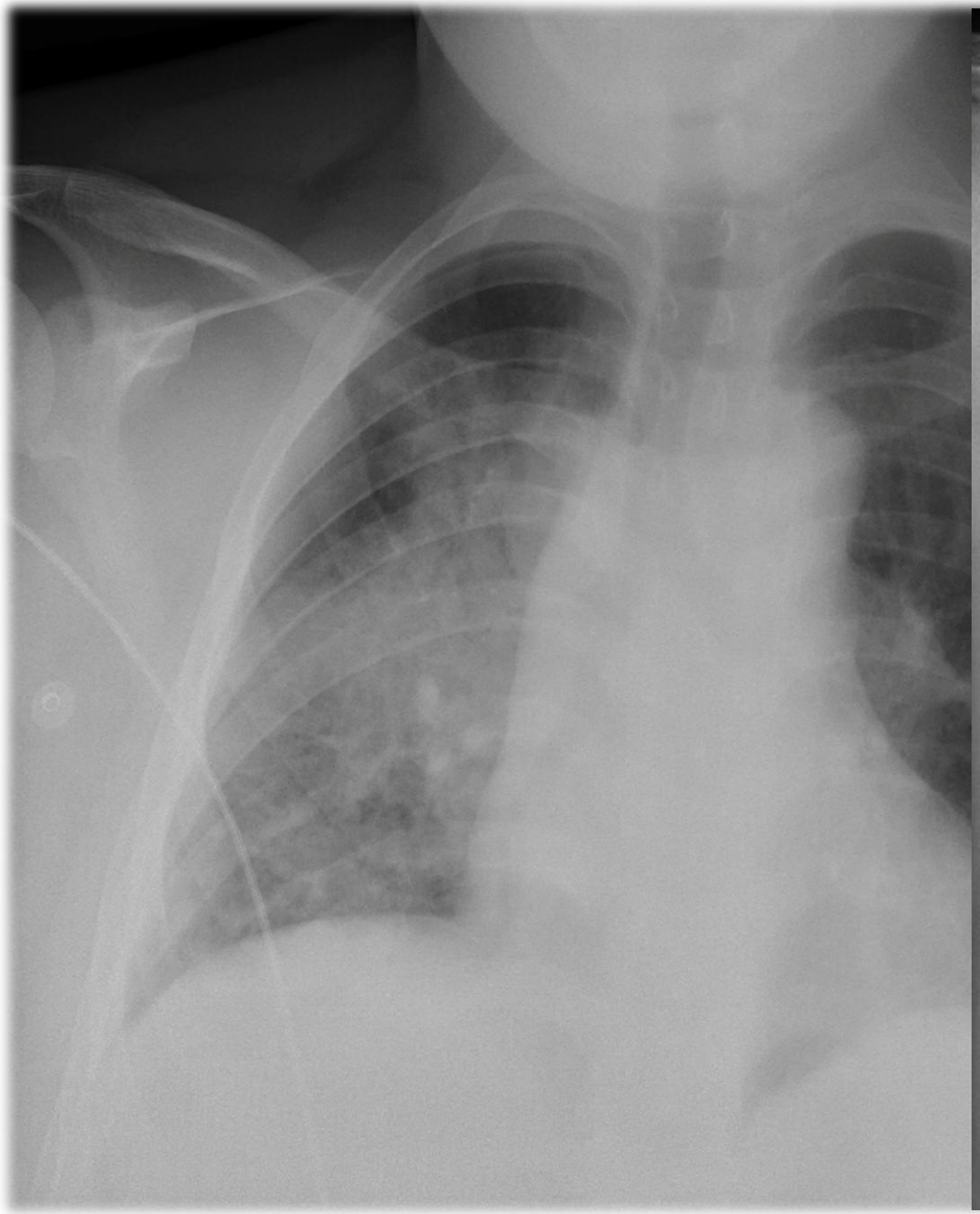
► Periferik yayma 50.000 /µL ile uyumlu, atipik hücre yok

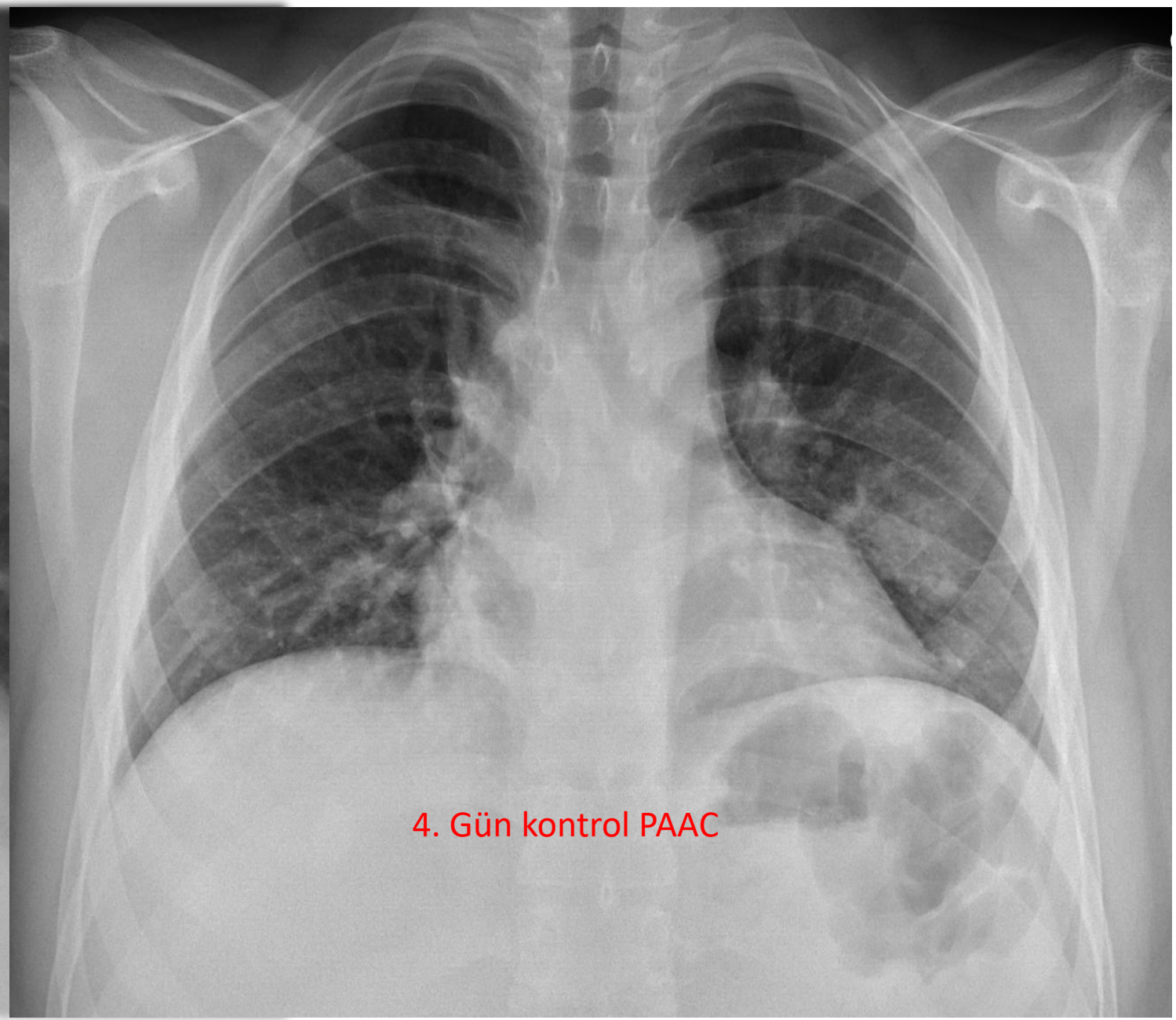
► Batın USG: Karaciğer normal boyutlarda, düzgün konturlu (Grade 2 steatoz) , dalak normal, diğer organlarda da patolojik bulguya rastlanmadı.

► Seroloji istendi.

Kardiyoloijye konsülte edildi. EF: 65 , normal eko bulguları, ek öneri olmadı.

- Hastanın yaşının genç olması, gelişinde hemoptizi, alveolar hemoraji (high flow ihtiyacı), mikroskobik hematüri olması nedeniyle vaskülit? öncelendi.
- 3 gün pulse steroid (1 gr /gün) ve ampirik antibiyoterapi verildi.
- Hastanın hemoptizisi geriledi, oksijen ihtiyacı azaldı, kliniği toparladı.
- CRP negatifleşti.




4. Gün kontrol PAAC

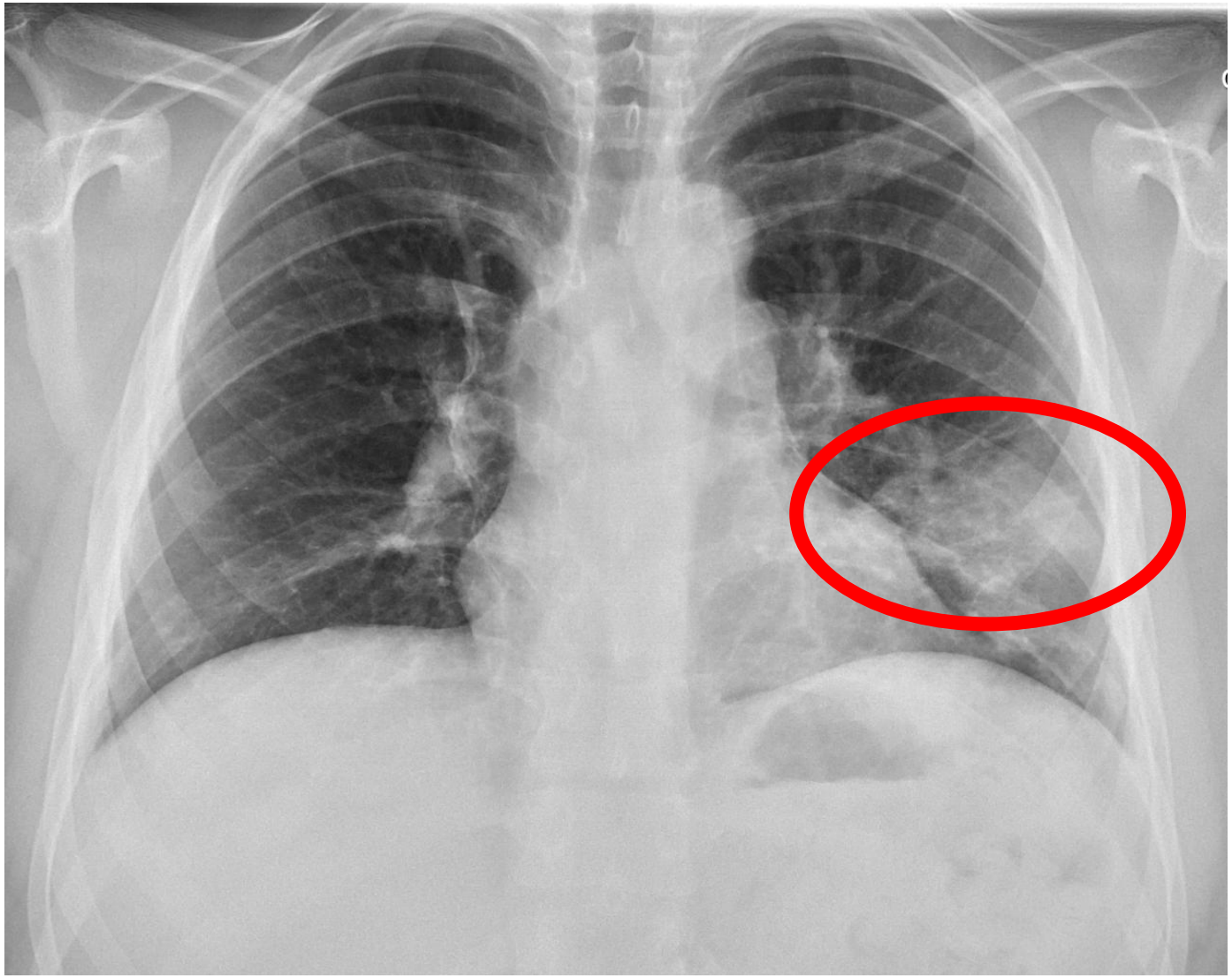
Olgu 2 –Seroloji

- BETA-2 M
- ACA- Ig M
- **Anti-fofa**
- **ANA IFAT**
- **Anti-ds D**
- ANCA: ne

Hasta Romatolojiye konsülte edildi: Sistemik Lupus Eritematozis (SLE)

- Taburculuğu planlanan hastanın Platelet seviyesi 40-80.000 civarında seyretti. Bu süreçte varis çorabı dışında profilaktik antikoagülan tedavi verilmedi.

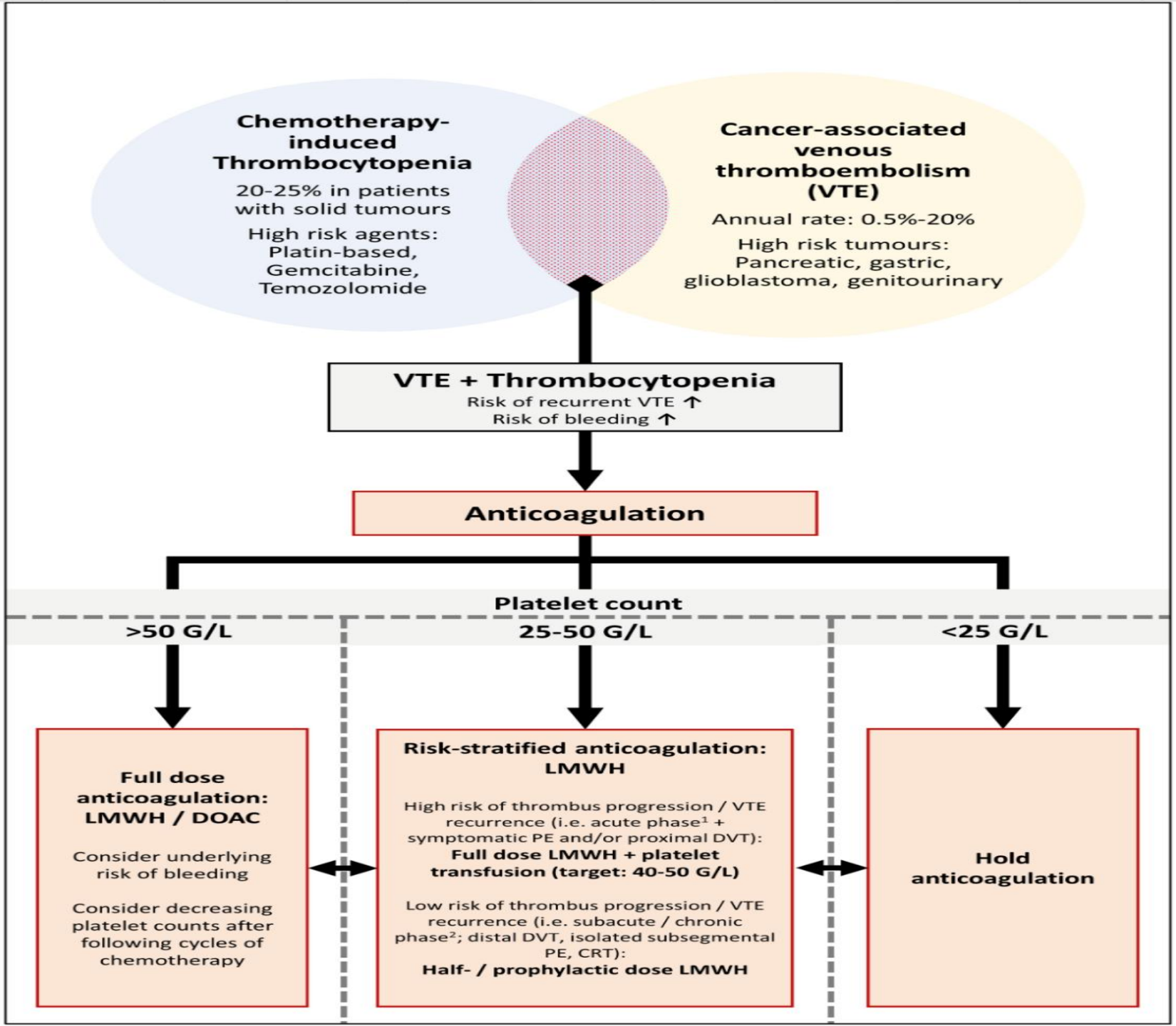
- Yatışının 6. gününde şiddetli göğüs ağrısı ve taşikardi gelişti.



- Hastaya Enoksaparin 2x0.8 IU /kg başlandı. Günlük platelet sayısı (tam kan) ve hemoptizi takibi yapıldı.
- Alt Ekstremite Venöz doppler USG: Açık izlendi.
- Yeni EKO: MY YOK , DEĞERLENDİRİLEBİLDİGİ KADARIYLA 1 TY İZLENDİ PAB ÖLÇÜLEMEDİ, SAĞ ÇAP 4,7 -4,8, MİNİMAL D BULGUSU+ SEPTAL BOUNCE+ MCCONEL-

- DMAH tedavisinin 3. günü trombosit sayısı 33.000 /µL e geriledi.
- Aktif kanama bulgusu izlenmedi.
- DMAH ---- Fondaparinux 1x7.5 mg SC başlandı.

  + Eş zamanlı vitamin K antagonisti



Thrombosis Research, 2021, March, 38-42

JOURNAL ARTICLE

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

Get access >

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**

- En çok kullanılan DOAK (28 hasta) rivaroksaban iken, bunu apixaban (7 hasta) ve dabigatran (1 hasta) takip etti. Bir hastada derin ven trombozu gelişti ve başka yeni veya tekrarlayan tromboz görülmedi. Hiçbir hastada klinik olarak anlamlı advers olay bildirilmedi.
- Argatroban ve bivalirudin intravenöz infüzyon gerektirir ve yakın aPTT takibi ve doz ayarlaması gerektirir. Fondaparinux enjeksiyon gerektirir ve vücut ağırlığı <50 kg olanlarda kontrendikedir. DOAK'lar, akut faz HIT tedavisinde oral tedavi için yeni bir seçenek sunacak ve minimum takip ve tutarlı dozlama stratejilerine olanak tanıyacaktır. **Bu nedenle, DOAK'lar HIT'nin akut fazının tedavisi için ilgi çekici bir seçenektir.**

- Hasta, SLE ve AFAS tanılarıyla Romatoloji bölümünde takip edilmektedir.
- Plaquenil, mikofenolat mofetil, metilprednizolon ve varfarin kullanmaktadır.

DRAFT ACR/EULAR ANTIPHOSPHOLIPID SYNDROME CRITERIA PRESENTED AT #ACR

ENTRY CRITERION

≥ 1 documented clinical criterion + ≥ 1 positive aPL test

CLINICAL DOMAINS	Points
VENOUS THROMBOEMBOLISM	
• *With high VTE risk profile*	1
• *Without VTE high risk profile*	3
ARTERIAL THROMBOSIS	
• *With a high CVD profile*	2
• *Without a high CVD profile*	4
MICROVASCULAR INVOLVEMENT*	
• *Suspected*	2
• *Established*	5
OBSTETRIC	
• *≥ 3 consecutive losses (<10w) and/or fetal death (<16w)*	1
• *Fetal death (≥16w <34w) without PEC/PI with severe features*	1
• *Severe PEC or severe PI (<34w)*	3
• *Severe PEC and severe PI (<34w)*	4
CARDIAC VALVE	
• *Thickening*	2
• *Vegetation*	4
THROMBOCYTOPENIA (lowest 20-130G/L)	2

LABORATORY DOMAINS (aPL)	Points
LUPUS ANTICOAGULANT (LA) POSITIVITY	
• *One time*	1
• *Persistent*	5
Anti-cardiolipin (aCL) / anti-BP2GP1 positivity**	
• ***IgM only** : moderate-high for aCL and/or anti-B2GP1*	1
• ***Presence of IgG***	
• ***moderate positivity** for aCL and/or anti-B2GP1*	4
• ***high posivitity** for aCL **OR** anti-B2GP1*	5
• ***high positivity** for aCL **AND** anti-B2GP1*	7

Only count the highest weighted criterion within each domain
Do not count if there is an equally or more likely explanation than APS

Microvascular involvement:

*-**Suspected:** livedo racemosa, livedoid vasculopathy (without pathology), aPL nephropathy (no pathology available), pulmonary hemorrhage (symptoms or imaging)*

*-**Established:** livedoid vasculopathy (with pathology), aPL nephropathy (with pathology), pulmonary hemorrhage (BAL or pathology), Myocardial disease (imaging or pathology), Adrenal disease (imaging or pathology)*

aPL titers (by ELISA): moderate titer => 40-79U; high titer => ≥ 80U

Classify as APS if ≥ 3 points from clinical criteria AND ≥ 3 points from aPL domain

Adapted by @Lupusreference from #ACR22 session 13S150 (Erkan et al.)

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

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY VOL. 81, NO. 1, 2023
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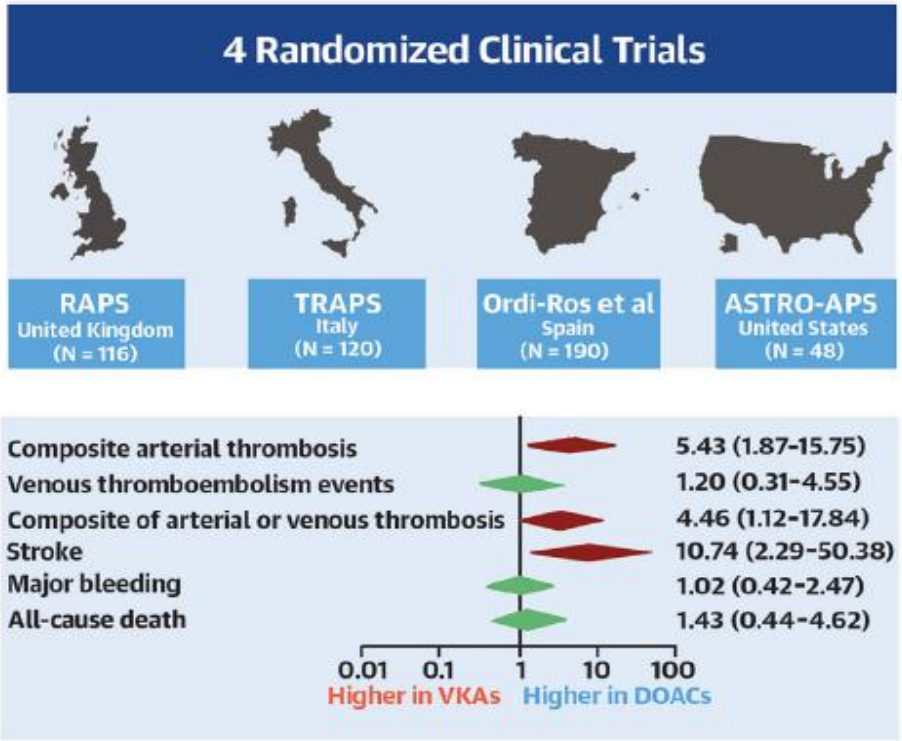
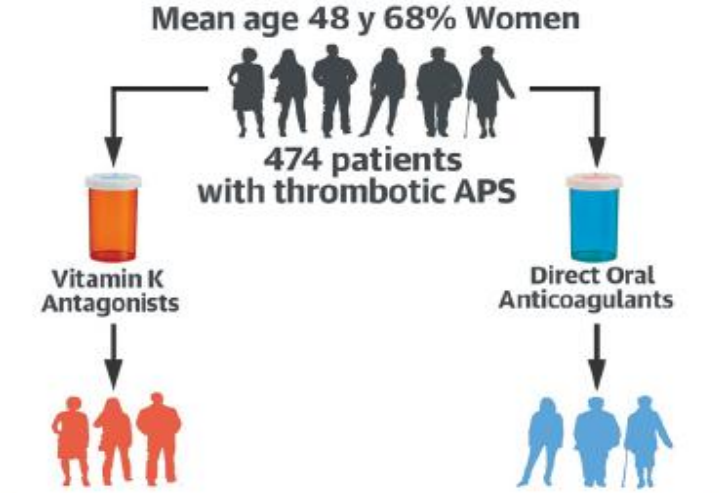
Direct Oral Anticoagulants vs Vitamin K Antagonists in Patients With Antiphospholipid Syndromes

Meta-Analysis of Randomized Trials

CENTRAL ILLUSTRATION Use of Direct Oral Anticoagulants vs Vitamin K Antagonists in Thrombotic Antiphospholipid Syndrome





Use of DOACs Compared With VKAs Was Associated With:

- Increased odds of arterial thrombotic events, especially stroke
- No change in the odds of VTE or major bleeding

Results were consistent within subgroups

Khairani CD, et al. J Am Coll Cardiol. 2023;81(1):16-30.

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].

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

I	B
I	B

Tedavi Süresi

- Provoke olmayan
- Genetik risk faktörü olmayan
- Ek risk faktörü olmayan

Presse Med 53 (2024) 104245

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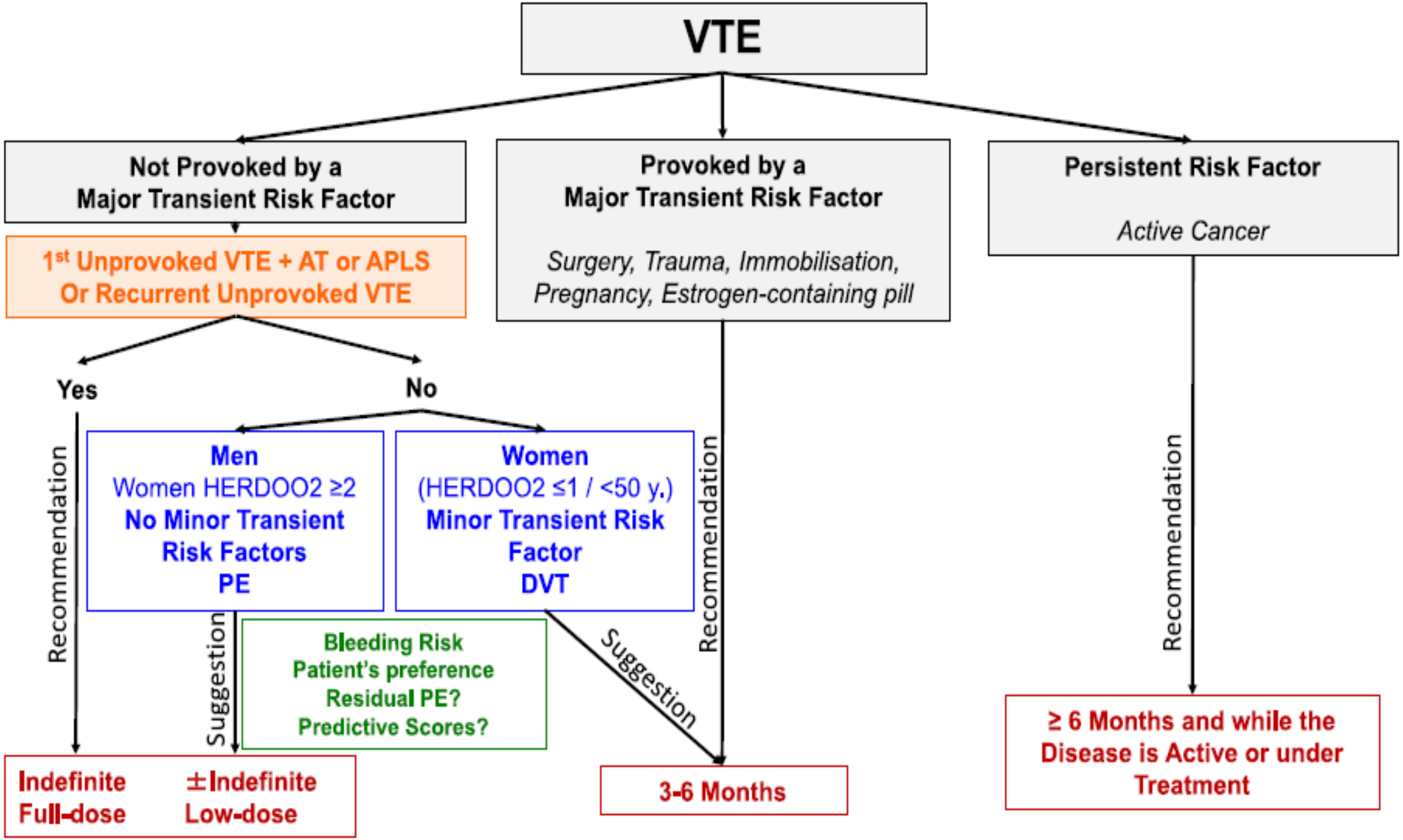
Quarterly Medical Review - Venous thromboembolic disease: a tribute to Professor Guy Meyer

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?
Suggestion
Recommendation
Recommendation
Indefinite Full-dose
±Indefinite Low-dose
3-6 Months
≥ 6 Months and while the Disease is Active or under Treatment

Extended treatment of venous thromboembolism with reduced-dose versus full-dose direct oral anticoagulants in patients at high risk of recurrence: a non-inferiority, multicentre, randomised, open-label, blinded endpoint trial

*Francis Couturaud, Jeannot Schmidt, Olivier Sanchez, Alice Ballerie, Marie-Antoinette Sevestre, Nicolas Meneveau, Laurent Bertoletti, Jérôme Connault, Ygal Benhamou, Joël Constans, Thomas Quemeneur, François-Xavier Lapébie, Gilles Pernod, Gaël Picart, Antoine Elias, Caroline Doutrelon, Claire Neveux, Lina Khider, Pierre-Marie Roy, Stéphane Zuily, Nicolas Falvo, Philippe Lacroix, Joseph Emmerich, Isabelle Mahé, Julien Boileau, Azzedine Yaici, Sylvain Le Jeune, Dominique Stéphan, Pierre Plissonneau-Duquene, Valérie Ray, Marc Danguy des Déserts, Rafik Belhadj-Chaidi, Bouchra Lamia, Yves Gruel, Emilie Presles, Philippe Girard, Cécile Tromeur, Farès Moustafa, Vincent Rothstein, Karine Lacut, Solen Melac, Sophie Barillot, Patrick Mismetti, Silvy Laporte, Dominique Mottier, Guy Meyer, Christophe Leroyer, for the RENOVE Investigators**

Summary

Background In patients with venous thromboembolism at high risk of recurrence for whom extended treatment with direct oral anticoagulants has been indicated, the optimal dose is unknown. We aimed to assess efficacy and safety of reduced-dose versus full-dose direct oral anticoagulants in patients in whom extended anticoagulation has been indicated.

Lancet 2025; 405: 725–35

See Comment page 676

*The RENOVE Investigators are listed in the appendix (pp 2–5)

Supplementary methods

Enrolment criteria

Inclusion criteria

- Patients age >18 years
- Patients with indications for long-term anticoagulation after venous thromboembolism (VTE) (ie, symptomatic pulmonary embolism [PE] or proximal deep vein thrombosis [DVT]) initially treated during 6 (–15 days) to 24 months (+3 months):
- Patients with multiple episodes of VTE, or
- Patients with a first episode of unprovoked* VTE
- Patients with VTE associated with persistent risk factor†, or
- Patients for whom clinicians feel that indefinite anticoagulation is warranted‡
- Social security affiliation.

**VTE is defined as unprovoked* if VTE occurred in the absence of major reversible risk factors, such as surgery, trauma of lower limb, prolonged immobilisation in the past three months, oestrogen-containing contraceptive pill or hormonal replacement therapy, pregnancy or delivery from less than 3 months and in the absence of persistent risk factors (see below).

†*Persistent risk factors (not exhaustive list):*

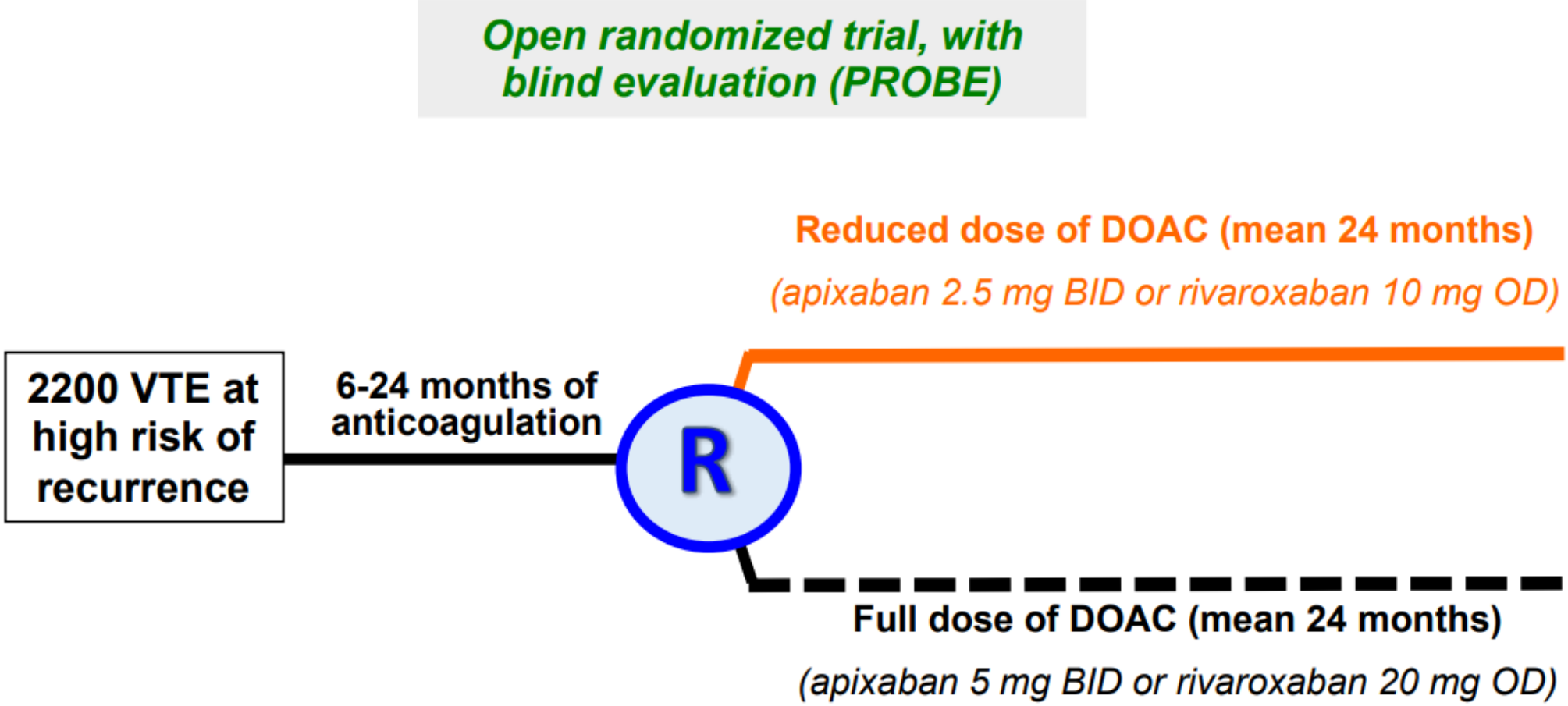
- chronic inflammatory diseases (eg, chronic inflammatory bowel diseases, rheumatoid arthritis, etc.),
- persistent or permanent immobilisation (eg, neurological diseases, or other cause),
- major thrombophilia such as: confirmed protein C, S or antithrombin deficiencies, combined thrombophilia, homozygous Factor V Leiden or homozygous prothrombin gene variant,
- hormonal treatment (eg, for breast and prostate cancer) or other prothrombotic treatment for cancer resolved for more than 6 months before inclusion.

‡Particular situations such as PE at high-risk of death at the acute phase, ilio-vena cava DVT, familial history of fatal PE.

Exclusion criteria

- Known allergy to rivaroxaban and apixaban, allergy to any of the excipients
- Indication for therapeutic dose anticoagulant therapy
- Unable or refusal to give informed consent
- Isolated distal DVT
- HERDOO2 score ≤ 1
- Indication for anticoagulation other than DVT or PE (eg, atrial fibrillation, mechanical valves)
- Treatment with investigational drug in the past 1 month except for patients benefiting from an anticoagulant at therapeutic doses for the initial pathology
- Interruption of anticoagulation for 14 days or more before the inclusion
- Chronic liver disease or chronic hepatitis
- Patient considered at high risk of bleeding (eg, previous gastrointestinal tract bleeding in the past three months, uncontrolled hypertension, etc.)
- Renal insufficiency with creatinine <25 mL per min on Cockcroft and Gault formula
- Antiphospholipid syndrome
- Dual antiplatelet therapy or aspirin at dosage >100 mg per day
- Concomitant use of a strong inhibitor of cytochrome P-450 3A4 (CYP3A4) (eg, a protease inhibitor for human immunodeficiency virus infection or azole-antimycotic drugs ketoconazole, itraconazole, voriconazole, posaconazole) or a CYP3A4 inducer (eg, rifampin, carbamazepine, or phenytoin)
- Active cancer of less than 6 months
- Active pregnancy or expected pregnancy
- No effective contraception in women of childbearing age
- Life expectancy less than 12 months

- Hastalar, tedavi süresince (dahil edilmelerinden çalışma sonuna kadar) ya azaltılmış dozda **apixaban (günde iki kez 2,5 mg)** veya **rivaroxaban (günde bir kez 10 mg)** ya da tam dozda apixaban (günde iki kez 5 mg) veya rivaroxaban (günde bir kez 20 mg) ile oral tedavi aldılar.
- Randomizasyondan sonra **medyan takip süresi 37,1 aydı** (IQR 24,0–48,3).
- 2768 hasta çalışmaya dahil edildi.



DOAC, direct oral anticoagulant; OD, once daily; R, randomisation; VTE, venous thromboembolism.

	Reduced-dose group (n=1383)	Full-dose group (n=1385)	Hazard ratio (95% CI)	p value
Primary outcome				
Symptomatic recurrent venous thromboembolism	19 (2·2% [1·1–3·3])*	15 (1·8% [0·8–2·7])†	1·32 (0·67–2·60)	0·23‡
Symptomatic recurrent pulmonary embolism	11 (1·5% [0·5–2·4])§	13 (1·5% [0·7–2·4])¶	..	..
Fatal pulmonary embolism‖	3 (0·3% [0·0–0·6])	3 (0·3% [0·0–0·7])	..	..
Symptomatic non-fatal pulmonary embolism	8 (1·2% [0·3–2·1])	11 (1·3% [0·5–2·1])	..	..
Symptomatic proximal deep vein thrombosis	9 (1·1% [0·2–2·1])§	2 (0·2% [0·0–0·6])	..	..
Key secondary outcomes				
Clinically relevant non-major bleeding and major bleeding	96 (9·9% [7·7–12·1])	154 (15·2% [12·8–17·6])	0·61 (0·48–0·79)	..
Major bleeding	15 (2·1% [0·7–3·5])**	38 (4·0% [2·7–5·3])††	0·40 (0·22–0·72)	..
Fatal bleeding	2 (0·5% [0·0–1·2])	3 (0·2% [0·0–0·5])	..	..
Non-fatal bleeding	13 (1·7% [0·5–2·9])	35 (3·8% [2·5–5·1])	..	..
Clinically relevant non-major bleeding	84 (8·6% [6·6–10·7])	118 (11·5% [9·3–13·6])	0·70 (0·53–0·93)	..
Net clinical benefit (symptomatic recurrent venous thromboembolism, or major bleeding, or clinically relevant non-major bleeding)	113 (11·8% [9·4–14·3])	166 (16·5% [14·0–19·0])	0·67 (0·53–0·86)	..

- Uzun süreli antikoagülasyon gerektiren venöz tromboemboli hastalarında, doğrudan oral antikoagülan dozunun azaltılması**, non-inferiority kriterlerini karşılamamıştır.**
- Ancak, her iki gruptaki düşük tekrarlama oranları ve **dozun azaltılmasıyla klinik olarak anlamlı kanamaların önemli ölçüde azalması, bu rejimi bir seçenek olarak destekleyebilir**.

VTE Tedavisinde Doz Seçimi: RENOVE Çalışmasının Ana Bulguları

RENOVE klinik çalışmasının temel sonuçlarını özetleyerek, venöz tromboembolizm (VTE) nüks riski yüksek hastalarda uzun süreli antikoagülan tedavisinde düşük doz ile tam doz arasındaki etkinlik ve güvenlik dengesini göstermek.

Etkinlik Karşılaştırması: Pıhtı Tekrarlama Riski

Düşük doz, pıhtılaşmayı önlemede tam doza denkliğini kanıtlayamadı.

Ancak, her iki grupta da pıhtı tekrarlama oranları beklenenden çok düşük bulundu.

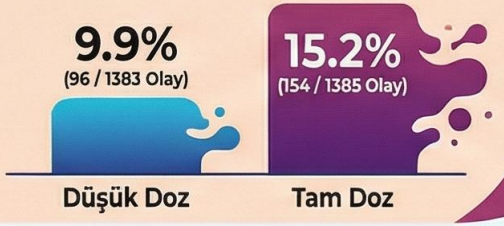
5-yıar VTE rekrarlama oranı

Güvenlik Karşılaştırması: Kanama Riski

Düşük doz, kanama riskini anlamlı ölçüde azalttı.

Majör veya klinik olarak anlamlı kanama olaylarında **%39'luk bir risk azalması** sağladı.

5 yıllık kanama oranı



Genel Sonuç: Risk-Fayda Dengesi

Net klinik fayda düşük doz lehineydi.

Pıhtı, kanama ve ölüm birleşik sonuçları değerlendirildiğinde düşük doz daha avantajlıydı.

> **“Düşük doz, VTE tedavisinde önemli bir seçenek olabilir. Düşük pıhtı riski ve belirgin şekilde daha az kanama avantajı sunmaktadır.”**

NotebookLM

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]

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).

Umarım faydalı olmuştur.

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