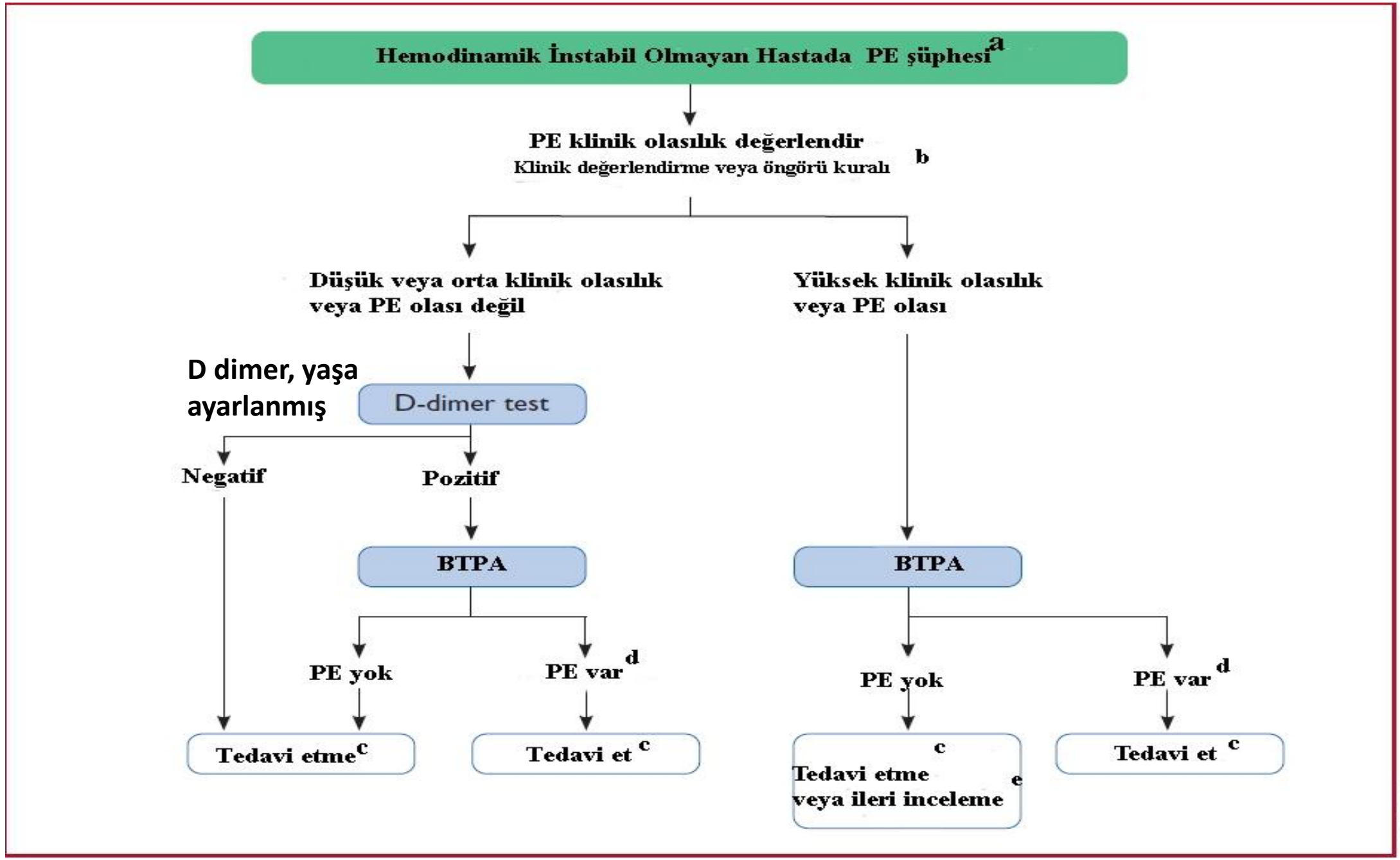
# Pulmoner Emboli: Sorunlar - Çözümler

Dr. Nuri Tutar

Erciyes Üniversitesi Tıp Fakültesi Göğüs Hastalıkları Anabilim Dalı

# Sorun 1: Acile pulmoner emboli şüphesi ile gelen hastada ne zaman ileri inceleme yapmalıyım?

# Pulmoner Emboli Dışlama Kriterleri
# PERC


Hemodinamik İnstabil Olmayan Hastada PE şüphesi[a]
PE klinik olasılık değerlendir
Klinik değerlendirme veya öngörü kuralı [b]
Düşük veya orta klinik olasılık veya PE olası değil
Yüksek klinik olasılık veya PE olası
D dimer, yaşa ayarlanmış
D-dimer test
Negatif
Pozitif
BTPA
BTPA
PE yok
PE var [d]
PE yok
PE var [d]
Tedavi etme[c]
Tedavi et [c]
[c] Tedavi etme veya ileri inceleme [e]
Tedavi et [c]
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# Simplified diagnostic management of suspected pulmonary embolism (the YEARS study): a prospective, multicentre, cohort study

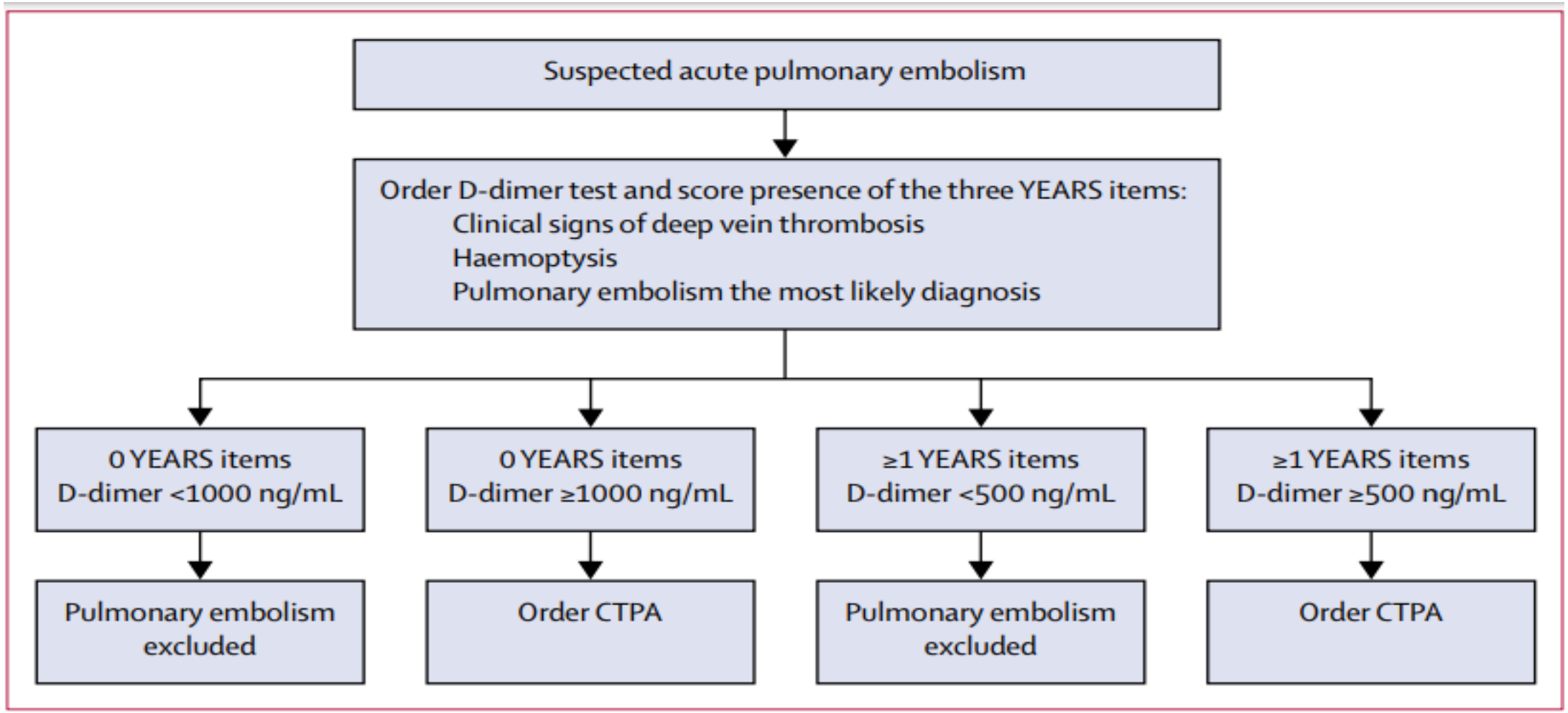
*Tom van der Hulle, Whitney Y Cheung, Stephanie Kooij, Ludo F M Beenen, Thomas van Bemmel, Josien van Es, Laura M Faber, Germa M Hazelaar, Christian Heringhaus, Herman Hofstee, Marcel M C Hovens, Karin A H Kaasjager, Rick C J van Klink, Marieke J H A Kruip, Rinske F Loeffen, Albert T A Mairuhu, Saskia 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**

Acile pulmoner emboli şüphesiyle başvuran ardışık 3465 hasta çalışmaya alınıyor, 456 (%13) hastada emboli saptanıyor.

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

- Pulmoner embolinin dışlandığı 2946 hastada 3 aylık takipte 18 hastada emboli saptanmış, %0.61, fatal emboli %0.20
- Bu protokol %14 oranında kontrastlı BT çekilmesini önlemiş.

JAMA | Original Investigation

# Effect of a Diagnostic Strategy Using an Elevated and Age-Adjusted D-Dimer Threshold on Thromboembolic Events in Emergency Department Patients With Suspected Pulmonary Embolism

## A Randomized Clinical Trial

Yonathan Freund, MD, PhD; Anthony Chauvin, MD, PhD; Sonia Jimenez, MD; Anne-Laure Philippon, MD; Sonja Curac, MD; Florent Fémy, MD; Judith Gorlicki, MD; Tahar Chouihed, MD, PhD; Hélène Goulet, MD; Emmanuel Montassier, MD, PhD; Margaux Dumont, MD; Laura Lozano Polo, MD; Pierrick Le Borgne, MD; Mehdi Khellaf, MD, PhD; Donia Bouzid, MD; Pierre-Alexis Raynal, MD; Nizar Abdessaied, MD; Saïd Laribi, MD, PhD; Jeremy Guenezan, MD; Olivier Ganansia, MD; Ben Bloom, MD, PhD; Oscar Miró, MD, PhD; Marine Cachanado, MSc; Tabassome Simon, MD, PhD

*JAMA*. 2021;326(21):2141-2149. doi:10.1001/jama.2021.20750

Aranan cevap: PERC Pozitif hastalarda YEARS + yaşa göre ayarlanmış D Dimer ile PE'yi dışlayabilir miyiz?

- Protokole uygun 1217 hasta alınıyor,
- Acilde 100 hastada emboli saptanıyor, 3 aylık takipte de çalışma grubunda 1 hastada, kontrol grubunda 5 hastada emboli saptanıyor (non inferior aralıkta)

- Sonuçta: Acile başvuran PERC pozitif hastalarda YEARS + yaşa göre ayarlanmış D Dimer değeri kullanılması konvansiyonel yöntemlere (BT, v/p sintigrafisine) non inferior çıkmıştır.

# Sorun 2: Pulmoner emboli trombolitik tedavi ne zaman hangi dozda?

- 32 y,
- E
- 5-6 yıldır DM, 2 yıldır hipertansiyon
- BFT bozukluğu saptanınca nefrolojiye gönderiliyor
- BUN:23, Kreat:1.5, proteinüri 1,5 gr
- Sağ böbrek küçülmüş ve parankim kalınlığında artış var, biyopsi amacı ile nefroloji servisine yatırılıyor
- 2 adet bx alınıyor, hemogram düşüşü yok, taburcu ediliyor.
- 3 gün hastane yatışı var.

| | | | |
|---|---|---|---|
| Yaş / Cinsiyeti | 32 / E | Tetkik İsteyen Doktor | AYDIN ÜNAL |
| DosyaNo | 4146235478 | | |
| Numune Türü | Tetkik İstem Zamanı 12.11.2015 14:01 | Numune Kabul Zamanı | 12.11.2015 14:01 |
| | Numune Alma Zamanı 12.11.2015 14:01 | Uzman Onay Zamanı | 24.11.2015 15:01 |
| Eski Biyopsi No | | | |

**KLİNİK BİLGİ:**
Proteinüri (+) BilinenDM + HT hastalıkları mevcut

MAKROSKOPİ :
Kayıtsız tüpte gönderilen 3 adet büyüğü 1,2x0,1x0,1 cm, en küçüğü 0,1x0,1x0,1 cm ölçülerinde bej renkli dokular, 0,3 cm lik kısmı immünoflorasan için ayrıldı. Kalan 2 parça 1 kasette takibe alındı.

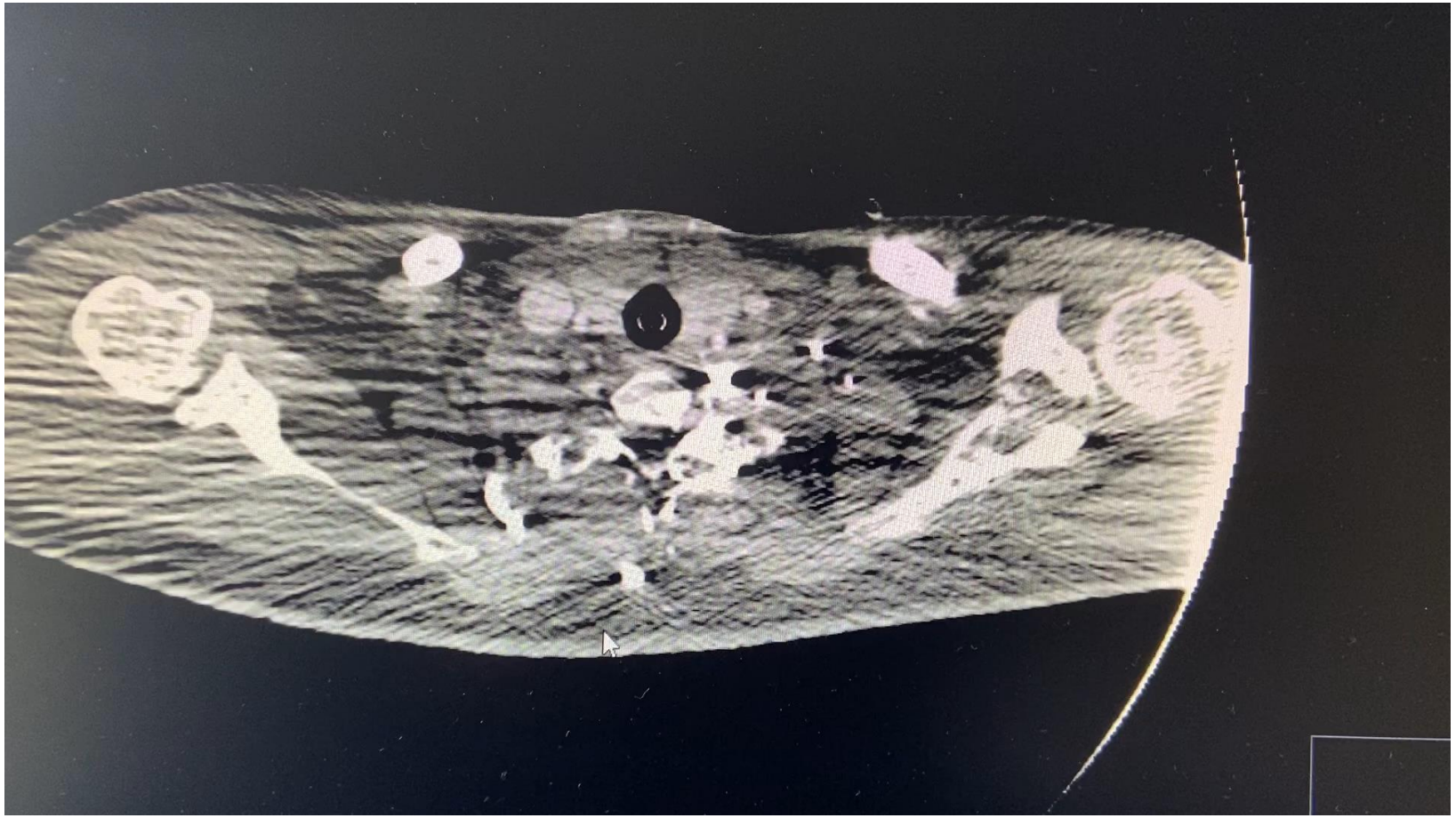
MİKROSKOPİ :
Kesitlerde, böbreğe ait doku parçaları izlendi. Dokunun %80`i korteksten oluşmuştur. Seri kesitlerde en fazla 8 adet glomerül görülmektedir. Glomerüllerden 2 si tamamen sklerotiktir. Diğer 8 glomerülde değişen oranalrada mezengial matriks artışı vardır.
Az sayıda atrofik tüp vardır.
İnterstisyumda hafif şiddette iltihabi mononükleer hücre infiltrasyonu vardır.İki glomerül çevresinde periglomerüler fibrozis görülmektedir.
Damar duvarlarında fibröz intimal kalınlaşma vardır.
Histokimyasal olarak yapılan Kongoı Red boyası ile negatif sonuç elde edildi.
Histokimyasal olarak yapılan PAS ve MT boyaları yukardaki bulguları destekler niteliktedir.
Yapılan immünoflorasan çalışmalarda;
C3 ile glomerül görülmedi. Boyanma izlenmedi.
Ig G ile glomerül görülmedi. Boyanma izlenmedi.
Ig A ile glomerül görülmedi. Boyanma izlenmedi.
Ig M ile glomerül görülmedi. Boyanma izlenmedi.
C4 ile glomerül görülmedi. Boyanma izlenmedi.
C1q ile glomerül görülmedi. Boyanma izlenmedi.
Kappa ile glomerül görülmedi. Boyanma izlenmedi.
Lambda ile glomerül görülmedi. Boyanma izlenmedi.

TANI :
DİFFÜZ GLOMERÜLOSKLEROZ, BÖBREK İĞNE BİYOPSİSİ

ARŞ.GÖR.ŞERİFE SEÇİL BARATALI
Dipl Tescil No 155202

PROF.DR.HÜLYA AKGÜN
Dipl Tescil No 76108

- Hasta hastaneden çıkıp otobüs durağına yürüyerek gidiyor,
- Orada nefes darlığı ve göğüs ağrısı gelişiyor,
- Tekrar hastaneye dönerek acile başvuruyor,
- Acile başvuruda hastanın Genel durumu orta, takipnesi var,
- Birkaç dakika sonra solunumu yüzeyelleşiyor ve hasta entübe ediliyor.
- Sonra kardiyak arrest, CPR ile geri dönüyor
- Kontrastlı BT çekiliyor
- Bu esnada D Dimer sonucu çıkıyor = **190**



ELSEVIER

Thrombosis Research

Volume 120, Issue 2, 2007, Pages 195-200

REGULAR ARTICLE

# Diagnostic value of D-dimer in patients with suspected pulmonary embolism: Results from a multicentre outcome study ☆

Florence Parent [a], Sophie Maître [a], Guy Meyer [c], Chantal Raherison [d], Hervé Mal [e], Rémi Lancar [f], Francis Couturaud [g], Dominique Mottier [g], Philippe Girard [b], Gérald Simonneau [a], Christophe Leroyer [g] ✉

## Results

Three hundred and fifty two patients were included in 4 centres. Prevalence of PE was 38.6%. PCP was low in 82 (23.3%), intermediate in 176 (50%) and high in 94 (26.7%) patients. Sensitivity of D-dimer was 96.3% (95% CI: 93–99) and negative predictive value reached 94.4% (95% CI: 90–99). Five patients with a confirmed PE had a D-dimer level below 500 ng/ml (two patients with a high PCP). Among 258 patients with low or intermediate PCP, 80 (31%) had a negative D-dimer test result; three of them had a false negative result and the number needed to test was 3.3. Among 94 patients with a high PCP, 9 had a negative D-dimer test result; two of them had a false negative result and the number needed to test was 13.5.

## Conclusion

These results confirm that rapid assays used in this study can safely exclude PE in first-line testing only in non-high CP patients.

# Risk factors of venous thromboembolism in focal segmental glomerulosclerosis with nephrotic syndrome

Shi-jun Li [1], Yuan-Mao Tu [2], Chang-sheng Zhou [3], Li-Hua Zhang [2], Zhi-hong Liu [2]

Affiliations + expand

PMID: 26220221 DOI: 10.1007/s10157-015-1149-4

## Abstract

**Background:** Venous thromboembolism (VTE) is an important and potentially life-threatening complication in focal segmental glomerulosclerosis (FSGS). The aim of this study was to investigate the prevalence and predisposing risk factors of venous thromboembolism in patients with FSGS with nephrotic syndrome.

**Methods:** A total of 120 FSGS patients with nephrotic syndrome were enrolled in this study. Venous thromboembolism was confirmed by contrast-enhanced dual-source computed tomography angiography or magnetic resonance venography. Potential clinical and laboratory risk factors for VTE were screened.

**Results:** Venous thrombosis was demonstrated in 12 (10 %) patients. Venous thrombosis occurred during the first episode of nephrotic syndrome in 3 patients and during a relapse in 9 patients. Eight patients had a pulmonary embolism, four had a renal vein thrombosis, three had a lower limb deep vein thrombosis, one had a cerebral sinovenous thrombosis, and one had a portal vein thrombosis. The positive predictive value for the D-dimer level was 22.4 % in the patients with FSGS, and the negative predictive value for the D-dimer level was 100 %. Of the screened risk factors, higher hematocrit and relapse of nephrotic syndrome were risk factors for VTE. Other risk factors, such as proteinuria, hypoalbuminemia, platelet count, fibrinogen level, and antithrombin III level, were not risk factors for VTE in patients with FSGS.

- Hastaya hangi dozda trombolitik verilir?
- A- 100 mgr TPA 2 saatte
- B- 50 mgr TPA 2 saatte
- C- 50 mgr TPA 15 dk da
- D- 100 mgr TPA 30 dk da

- Hastaya hangi dozda trombolitik verilir?
- A- 100 mgr TPA 2 saatte
- B- 50 mgr TPA 2 saatte
- C- 50 mgr TPA 15 dk da
- D- 100 mgr TPA 30 dk da

- 100 mgr TPA 2 saatte veriliyor
- Hb düşüşü oluyor
- 2 ünite ES veriliyor
- Tekrar arrest ve exitus oluyor

# Reperfüzyon tedavisi

- PE de trombolitik tedavi ile pulmoner obstrüksiyon, pulmoner arter basıncı ve pulmoner vasküler rezisdansta UFH ne göre çok daha hızlı düzelme sağlanır.
- İlk 48 saatte en yüksek etkiyi gösterir ama 6-14 güne kadar etkilidir.
- Metaanalizde **%9.9** ciddi kanama yaptığı ve **%1.7** intrakranial kanama yaptığı gösterilmiştir.
- Yüksek riskli PE hastalarında Kanıt 1B olarak önerilmektedir.

| Molecule | Regimen | Contraindications to fibrinolysis |
|---|---|---|
| rtPA | 100 mg over 2 h | **Absolute** |
| | 0.6 mg/kg over 15 min (maximum dose 50 mg)[a] | History of haemorrhagic stroke or stroke of unknown origin |
| Streptokinase | 250 000 IU as a loading dose over 30 min, followed by 100 000 IU/h over 12–24 h | Ischaemic stroke in previous 6 months |
| | Accelerated regimen: 1.5 million IU over 2 h | Central nervous system neoplasm |
| Urokinase | 4400 IU/kg as a loading dose over 10 min, followed by 4400 IU/kg/h over 12–24 h | Major trauma, surgery, or head injury in previous 3 weeks |
| | Accelerated regimen: 3 million IU over 2 h | Bleeding diathesis |
| | | Active bleeding |
| | | **Relative** |
| | | Transient ischaemic attack in previous 6 months |
| | | Oral anticoagulation |
| | | Pregnancy or first post-partum week |
| | | Non-compressible puncture sites |
| | | Traumatic resuscitation |
| | | Refractory hypertension (systolic BP >180 mmHg) |
| | | Advanced liver disease |
| | | Infective endocarditis |
| | | Active peptic ulcer |





BP = blood pressure; IU = international units; rtPA, recombinant tissue-type plasminogen activator.

[a]This is the accelerated regimen for rtPA in pulmonary embolism; it is not officially approved, but it is sometimes used in extreme haemodynamic instability such as cardiac arrest.

# KONTRENDİKASYONLAR

**Web Table 4 Contraindications to thrombolytic therapy (adapted from ref. 312)**

**Absolute contraindications:**[a]

- Haemorrhagic stroke or stroke of unknown origin at any time
- Ischaemic stroke in the preceding 6 months
- Central nervous system damage or neoplasms
- Recent major trauma/surgery/head injury in the preceding 3 weeks
- Gastrointestinal bleeding within the last month
- Known bleeding risk

**Relative contraindications**

- Transient ischaemic attack in the preceding 6 months
- Oral anticoagulant therapy
- Pregnancy, or within one week postpartum
- Non-compressible puncture site
- Traumatic resuscitation
- Refractory hypertension (systolic blood pressure >180 mm Hg)
- Advanced liver disease
- Infective endocarditis
- Active peptic ulcer

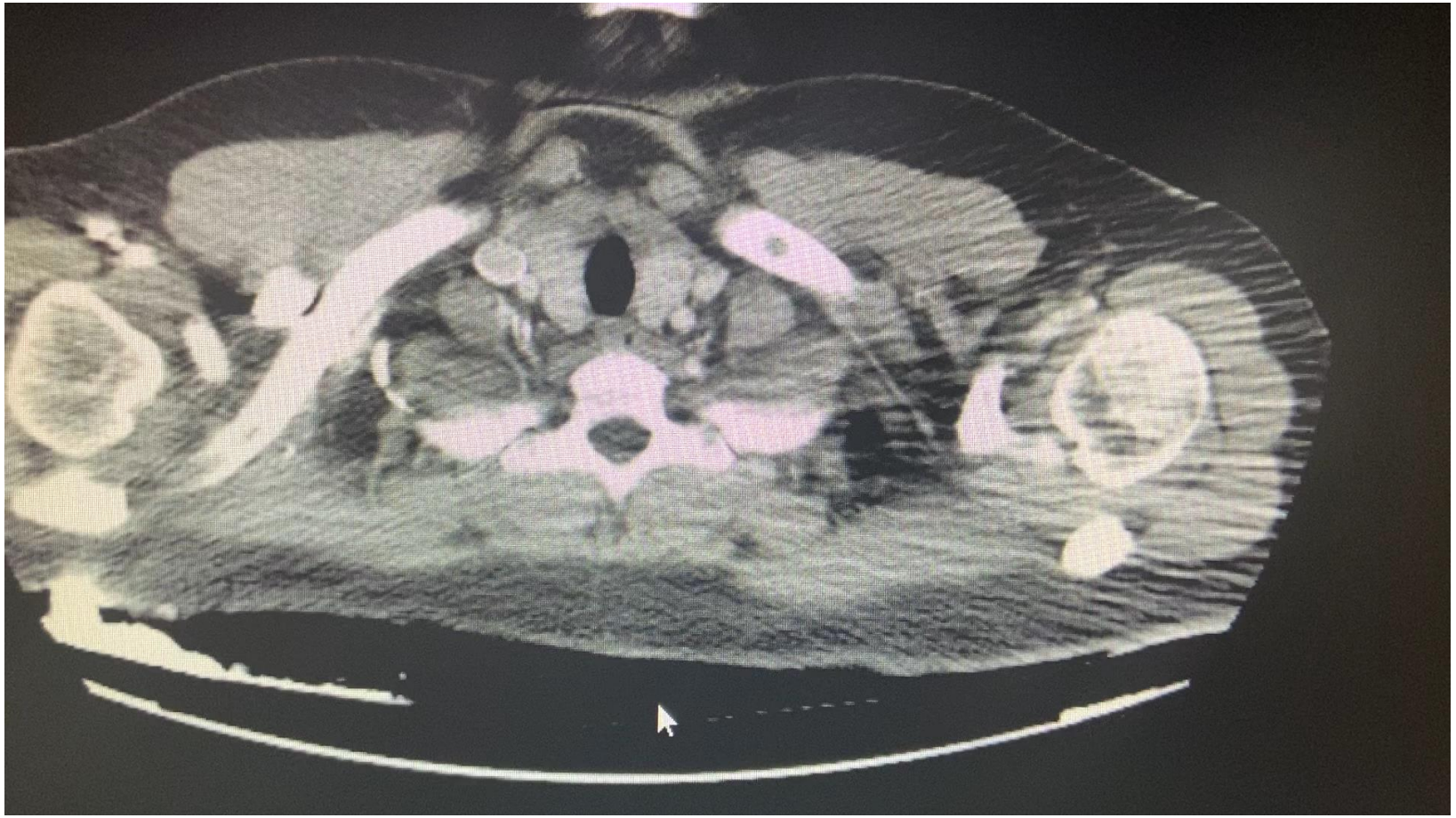
ESC 2014, European Heart Journal

## Absolute contraindications:[a]

[a]Absolute contraindications to thrombolysis might become relative in a patient with immediately life-threatening high-risk PE.

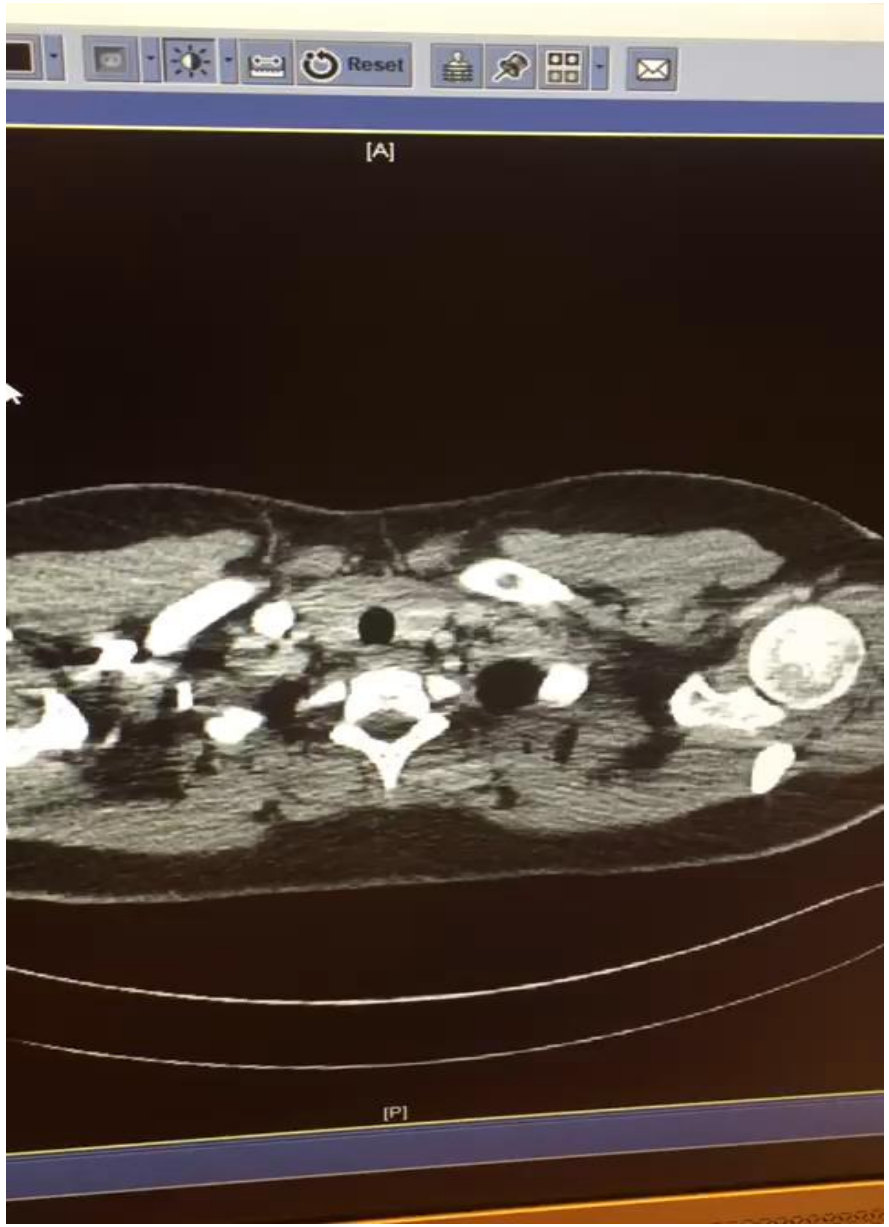
# Olgu 2

- 24 y
- Erkek hasta
- Hemoptizi, göğüs ağrısı ve ateş şikayeti ile geliyor,
- D Dimer 3860
- Troponin negatif



- Antibiyotik veriliyor,
- Poliklinik kontrol öneriliyor

- Sabah tekrar polikliniğe geliyor,
- Solunum sayısı: 40
- Nabız:122
- KB:140/70
- SPO2:85
- Tekrar BT


Reset
[A]
[P]

- YBÜ yatış,
- Solunum sayısı=48
- Nazal kanülden 4 lt/dk dan oksijen alırken spo2:90-91, NIMV ye alınıyor= 40 soluyor
- Troponin +
- Yatak başı EKO yapılamıyor ancak BT de RV/LV oranı 1.

- 1- Hasta hangi grupta?

# sPESI

- 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

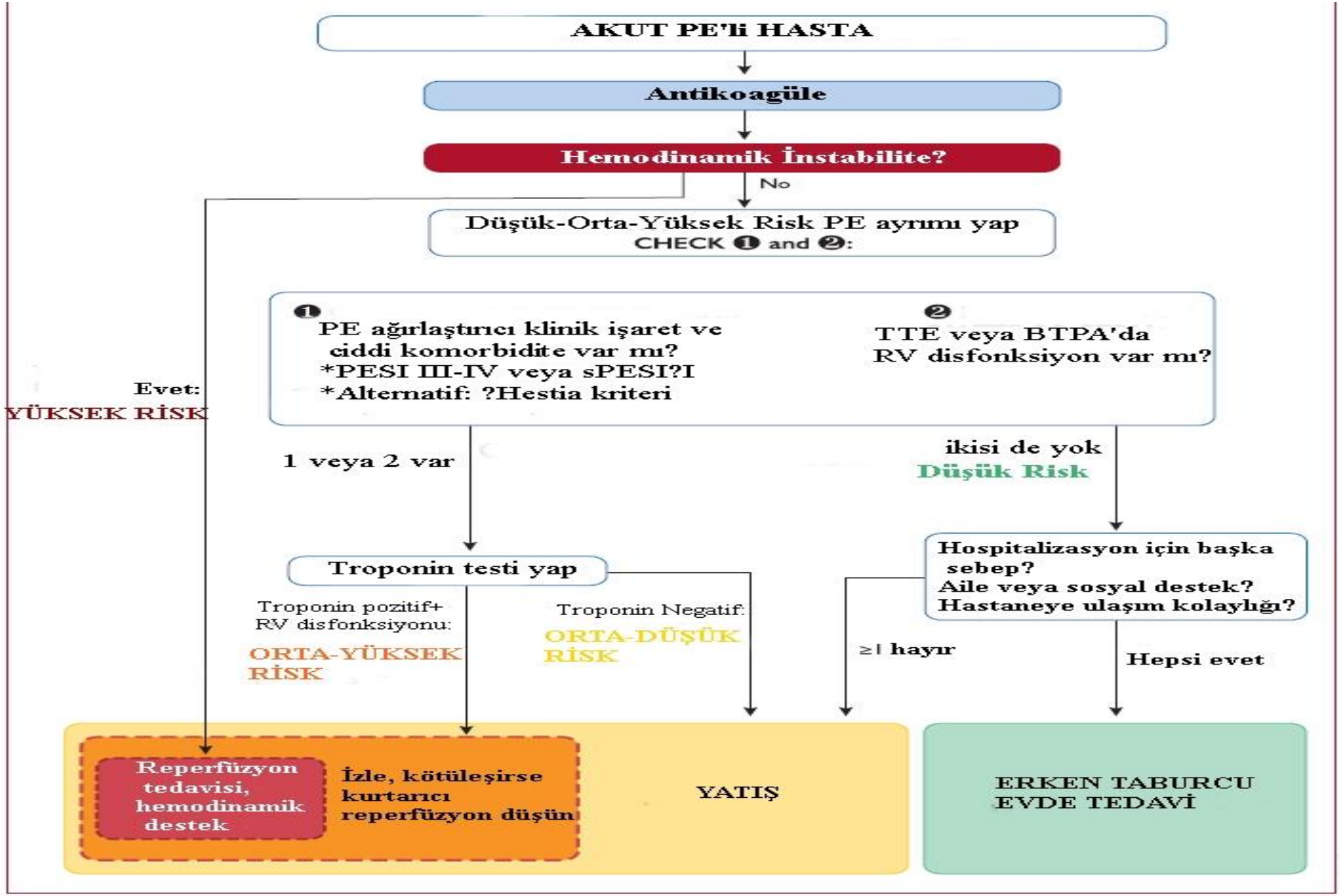
**PESI Class III to V indicates moderate to very high 30-day mortality risk; sPESI ≥1 point(s) indicate high 30-day mortality risk.**

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

# 2019

| 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 |

- 1- Hasta hangi grupta?
- intermediate high
- 2- Hastaya tedavi planı ne olmalı?


AKUT PE'li HASTA
Antikoagüle
Hemodinamik İnstabilite?
No
Düşük-Orta-Yüksek Risk PE ayrımı yap
CHECK ❶ and ❷:
❶
PE ağırlaştırıcı klinik işaret ve ciddi komorbidite var mı?
*PESI III-IV veya sPESI?I
*Alternatif: ?Hestia kriteri
❷
TTE veya BTPA'da RV disfonksiyon var mı?
Evet:
YÜKSEK RİSK
1 veya 2 var
ikisi de yok
Düşük Risk
Troponin testi yap
Troponin pozitif+ RV disfonksiyonu:
ORTA-YÜKSEK RİSK
Troponin Negatif:
ORTA-DÜŞÜK RİSK
Hospitalizasyon için başka sebep?
Aile veya sosyal destek?
Hastaneye ulaşım kolaylığı?
≥I hayır
Hepsi evet
Reperfüzyon tedavisi, hemodinamik destek
İzle, kötüleşirse kurtarıcı reperfüzyon düşün
YATIŞ
ERKEN TABURCU
EVDE TEDAVİ
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- 2- Hastaya tedavi planı ne olmalı?
- Rehbere göre antikoagülan

- Takipnesi kırılmaması nedeniyle trombolitik veriliyor,
- 100 mgr 2 saatte,
- Genel durumu 1 gün sonra düzeliyor,
- Solunum sayısı O2 le 20 lere düşüyor,
- Takip eden günlerde servis devri ve tab ediliyor

# Intermediate high risk hastalarda trombolitik verelim mi?

- Evet
- Hayır

# INTERMEDIATE RİSKTE (SUBMASİF) TROMBOLİTİK

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

## Fibrinolysis for Patients with Intermediate-Risk Pulmonary Embolism

Guy Meyer, M.D., Eric Vicaut, M.D., Thierry Danays, M.D., Giancarlo Agnelli, M.D.,

**N Engl J Med 2014;370:1402-11.**

- Randomize, çift kör, hipotansiyonu olmayan intermediate yüksek risk hastalarda **tenekteplaz+ heparin** ile **plasebo + heparin** tedavisi karşılaştırılıyor.
- 1. haftada ölüm, hemodinamik bozukluk ve kanama oranları karşılaştırılıyor.
- 1005 hasta

**Table 3. Efficacy Outcomes.***

| Outcome | Tenecteplase (N = 506) | Placebo (N = 499) | Odds Ratio (95% CI) | P Value |
|---|---|---|---|---|
| Primary outcome — no. (%) | 13 (2.6) | 28 (5.6) | 0.44 (0.23–0.87) | 0.02 |
| Death from any cause | 6 (1.2) | 9 (1.8) | 0.65 (0.23–1.85) | 0.42 |
| Hemodynamic decompensation | 8 (1.6) | 25 (5.0) | 0.30 (0.14–0.68) | 0.002 |
| Time between randomization and primary efficacy outcome — days | 1.54±1.71 | 1.79±1.60 | | |
| Recurrent pulmonary embolism between randomization and day 7 — no. (%) | 1 (0.2) | 5 (1.0) | 0.20 (0.02–1.68) | 0.12 |
| Fatal | 0 | 3 (0.6) | | |
| Nonfatal | 1 (0.2) | 2 (0.4) | | |

**Table 4. Safety Outcomes in the Intention-to-Treat Population.***

| Outcome | Tenecteplase (N=506) | Placebo (N=499) | Odds Ratio (95% CI) | P Value |
|---|---|---|---|---|
| | *no. (%)* | | | |
| Bleeding between randomization and day 7 | | | | |
| Major extracranial bleeding | 32 (6.3) | 6 (1.2) | 5.55 (2.3–13.39) | <0.001 |
| Minor bleeding | 165 (32.6) | 43 (8.6) | | |
| Major bleeding† | 58 (11.5) | 12 (2.4) | | |
| Stroke between randomization and day 7 | 12 (2.4) | 1 (0.2) | 12.10 (1.57–93.39) | 0.003 |
| Ischemic stroke | 2 (0.4) | 0 | | |
| Hemorrhagic stroke‡ | 10 (2.0) | 1 (0.2) | | |

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# Impact of Thrombolytic Therapy on the Long-Term Outcome of Intermediate-Risk Pulmonary Embolism

Stavros V. Konstantinides, MD, PhD,[a,b] Eric Vicaut, MD, PhD,[c] Thierry Danays, MD,[d] Cecilia Becattini, MD,[e]

- 709 hasta
- 1 ay ve 24 aylık sonuçlar karşılaştırılıyor

**TABLE 3** Overall and Cause-Specific 30-Day and Long-Term Mortality

| | Tenecteplase (N = 359) | Placebo (N = 350) | p Value |
|---|---|---|---|
| Death from any cause between randomization and day 30 | 8 (2.2) | 10 (2.9) | 0.595 |
| Hemodynamic collapse | 1 (0.3) | 1 (0.3) | |
| Stroke (ischemic or hemorrhagic) | 4 (1.1) | 0 (0.0) | |
| Recurrent pulmonary embolism | 0 (0.0) | 2 (0.6) | |
| Respiratory failure | 0 (0.0) | 2 (0.6) | |
| Extracranial bleeding | 1 (0.3) | 0 (0.0) | |
| Sudden unexplained death | 0 (0.0) | 2 (0.6) | |
| Other | 2 (0.6) | 3 (0.9) | |
| Death from any cause between day 30 and long-term follow-up | 65 (18.1) | 53 (15.1) | |
| Stroke | 1 (0.3) | 2 (0.6) | |
| Acute myocardial infarction | 0 (0.0) | 1 (0.3) | |
| Respiratory failure | 2 (0.6) | 1 (0.3) | |
| Sudden unexplained death | 2 (0.6) | 0 (0.0) | |
| Cancer | 8 (2.2) | 9 (2.6) | |
| Bleeding | 0 (0.0) | 1 (0.3) | |
| Chronic heart failure | 1 (0.3) | 0 (0.0) | |
| Other | 19 (5.3) | 4 (1.1) | |
| Unknown cause | 32 (8.9) | 35 (10.0) | |
| Death from any cause between randomization and long-term follow-up | 73 (20.3) | 63 (18.0) | 0.430 |

**TABLE 4 Findings in Patients With Echocardiographic Long-Term Follow-Up**

| | Tenecteplase (N = 144) | Placebo (N = 146) | p Value |
|---|---|---|---|
| Right ventricular end-diastolic diameter >30 mm | 34 (23.6) | 22 (15.1) | 0.058 |
| Missing data | 12 (8.3) | 11 (7.5) | |
| Right/left ventricular end-diastolic diameter >0.9 | 34 (23.6) | 22 (15.1) | 0.834 |
| Missing data | 12 (8.3) | 11 (7.5) | |
| Hypokinesia of the right ventricular free wall (any view) | 6 (4.2) | 5 (3.4) | 0.740 |
| Missing data | 4 (2.8) | 4 (2.7) | |
| Tricuspid annulus plane systolic excursion reduced | 14 (9.7) | 7 (4.8) | 0.107 |
| Mean, mm Hg | 23.6 ± 4.8 | 23.9 ± 3.6 | |
| Median, mm Hg | 24.0 (20.0–27.0) | 24.0 (21.0–26.0) | 0.551 |
| Missing data, | 19 (13.2) | 18 (12.3) | |
| Tricuspid systolic velocity >2.6 m/s | 22 (15.3) | 27 (18.5) | 0.412 |
| Missing data | 11 (7.6) | 14 (9.6) | |
| Systolic pulmonary artery pressure, mm Hg | | | |
| Mean | 31.6 ± 12.3 | 30.7 ± 10.2 | 0.527 |
| Median | 30.0 (24.0–35.0) | 30.0 (25.0–35.0) | |
| Missing data | 33 (22.9) | 39 (26.7) | |

## CONCLUSIONS

In a large, prospective randomized controlled trial of patients with intermediate- to high-risk PE, thrombolytic treatment with tenecteplase did not affect long-term mortality rates, and it did not appear to reduce residual dyspnea, functional limitation, or persisting RV dysfunction, which were mostly mild in both treatment arms. These results suggest that

# Trombolitik tedavi dozu ne olmalı (tam doz? Yarı doz?)

- A- 100 mgr
- B- 50 mgr

# Hangi trombolitik dozu?

## Efficacy and Safety of Low Dose Recombinant Tissue-Type Plasminogen Activator for the Treatment of Acute Pulmonary Thromboembolism

### A Randomized, Multicenter, Controlled Trial

*Chen Wang, MD, PhD, FCCP; Zhenguo Zhai, MD, PhD; Yuanhua Yang, MD; Qi Wu, MD,*

*Background:* Optimal dosing of the recombinant tissue-type plasminogen activator (rt-PA) is important in treating pulmonary thromboembolism (PTE). The aim of this study was to compare the efficacy and safety of a 50 mg/2 h rt-PA regimen with a 100 mg/2 h rt-PA regimen in patients with acute PTE.

*Methods:* A prospective, randomized, multicenter trial was conducted in which 118 patients with acute PTE and either hemodynamic instability or massive pulmonary artery obstruction were randomly assigned to receive a treatment regiment of either rt-PA at 50 mg/2 h (n = 65) or 100 mg/2 h (n = 53). The efficacy was determined by observing the improvements of right ventricular dysfunctions (RVDs) on echocardiograms, lung perfusion defects on ventilation perfusion lung scans, and pulmonary artery obstructions on CT angiograms. The adverse events, including death, bleeding, and PTE recurrence, were also evaluated.

*Results:* Progressive improvements in RVDs, lung perfusion defects, and pulmonary artery obstructions were found to be similarly significant in both treatment groups. This is true for patients with either hemodynamic instability or massive pulmonary artery obstruction. Three (6%) patients in the rt-PA 100 mg/2 h group and one (2%) in the rt-PA 50 mg/2 h group died as the result of either PTE or bleeding. Importantly, the 50 mg/2 h rt-PA regimen resulted in less bleeding tendency than the 100 mg/2 h regimen (3% vs 10%), especially in patients with a body weight < 65 kg (14.8% vs 41.2%, $P = .049$). No fatal recurrent PTE was found in either group.

*Conclusions:* Compared with the 100 mg/2 h regimen, the 50 mg/2 h rt-PA regimen exhibits similar efficacy and perhaps better safety in patients with acute PTE. These findings support the notion that optimizing rt-PA dosing is worthwhile when treating patients with PTE.

*Trial registration:* clinicaltrials.gov; Identifier: NCT00781378

# Moderate Pulmonary Embolism Treated With Thrombolysis (from the "MOPETT" Trial)

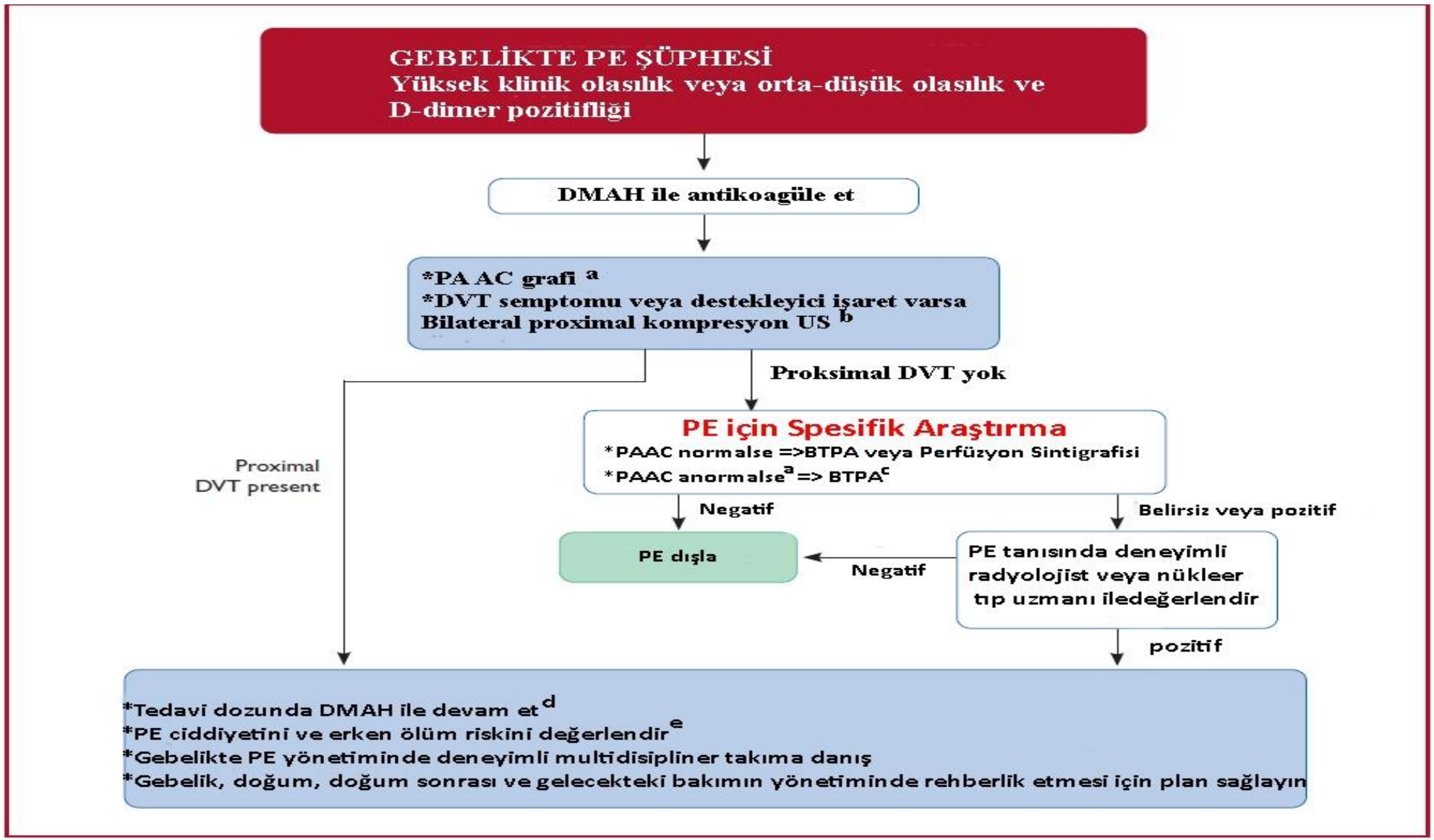
Mohsen Sharifi, MD[a,b,*], Curt Bay, PhD[b], Laura Skrocki, DO[a], Farnoosh Rahimi, MD[a], and Mahshid Mehdipour, DMD[a,b], "MOPETT" Investigators

The role of low-dose thrombolysis in the reduction of pulmonary artery pressure in moderate pulmonary embolism (PE) has not been investigated. Because the lungs are very sensitive to thrombolysis, we postulated that effective and safe thrombolysis might be achieved by a lower dose of tissue plasminogen activator. The purpose of the present study was to evaluate the role of this "safe dose" thrombolysis in the reduction of pulmonary artery pressure in moderate PE. During a 22-month period, 121 patients with moderate PE were randomized to receive a "safe dose" of tissue plasminogen activator plus anticoagulation (thrombolysis group [TG], n = 61 patients) or anticoagulation alone (control group [CG], n = 60). The primary end points consisted of pulmonary hypertension and the composite end point of pulmonary hypertension and recurrent PE at 28 months. Pulmonary hypertension and the composite end point developed in 9 of 58 patients (16%) in the TG and 32 of 56 patients (57%) in the CG ($p < 0.001$) and 9 of 58 patients (16%) in the TG and 35 of 56 patients (63%) in the CG ($p < 0.001$), respectively. The secondary end points were total mortality, the duration of hospital stay, bleeding at the index hospitalization, recurrent PE, and the combination of mortality and recurrent PE. The duration of hospitalization was $2.2 \pm 0.5$ days in the TG and $4.9 \pm 0.8$ days in the CG ($p < 0.001$). The combination of death plus recurrent PE was 1 (1.6%) in TG and 6 (10%) in the CG ($p = 0.0489$). No bleeding occurred in any group, and despite a positive trend in favor of a "safe dose" thrombolysis, no significant difference was noted in the rate of individual outcomes of death and recurrent PE when assessed independently. In conclusion, the results from the present prospective randomized trial suggests that "safe dose" thrombolysis is safe and effective in the treatment of moderate PE, with a significant immediate reduction in the pulmonary artery pressure that was maintained at 28 months.  (Am J Cardiol 2013;111:273—277)

# Sorun 3: Kanser ve embolide yaklaşım ne olmalı

- 1- **İlk 6 ay**, warfarin yerine **DMAH** önerilir. (Kanıt 2aA)
- 2- GIS kanseri **olmayan** hastalarda DMAH yerine EDOXABAN kullanılabilir (Kanıt 2aB)
- 3- GIS kanseri **olmayan** hastalarda DMAH yerine RİVAROKSABAN kullanılabilir (Kanıt 2aC)
- 4- Kanser hastalarında **malignitede kür saptanana kadar ya da süresiz** antikoagülasyon önerilir (Kanıt 2aB)

# Sorun 4: Gebelik ve emboli



The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

# Pregnancy-Adapted YEARS Algorithm for Diagnosis of Suspected Pulmonary Embolism

N ENGL J MED 380;12 NEJM.ORG MARCH 21, 2019

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

510 hasta, ilk başta 20 hastada emboli saptanmış
Kriterlerin dışladığı Sadece 1 hastada takipte DVT gelişiyor
Hastaların farklı trimestere göre %32-65 inde Pulmoner BT anjiografi çekilmesini önlemiş

- Gebelikte PE’de **DMAH** tercih edilmelidir çünkü VKA ve YOAK’ların aksine plasentayı geçmez, fötal hemoraji ve teratojenik etkisi yoktur.
- Her ne kadar minör transplasental geçiş bildirilip yeterli veri mevcut değilse de eğer bir allerji veya advers reaksiyon gelişirse **fondaparinux** tercih edilebilir.
- Tedavi alan gebede **epidural veya spinal anesteziden 24 saat önce** DMAH kesilmelidir.
- Yüksek riskli durumlarda, örneğin yakın zamanda PE'li hastalarda, DMAH'nin doğumdan> 36 saate önce UFH dönüştürülmesi önerilir.
- Antikoagülan tedavi **doğumdan sonra > 6 hafta** ve **en az 3 ay tedavi** süresinde uygulanmalıdır. **Emziren annelere DMAH ve warfarin verilebilir;** YOAK kullanımı tavsiye edilmez.

- Gebelerde yüksek risk  veya hayatı tehdit eden PE nadirdir.
- Bu durumlarda trombolizis ve embolektomi önerilir (Kanıt 2aC).
- Ancak hayatı tehdit eden durum dışında trombolitik tedavi peri-partum kullanılmamalıdır.

# Sorun 4: Pulmoner tromboembolide tedavi süresi ne kadar?

- Nüks açısından düşük riskli, emboli açısından major risk içeren durumlarda (30 dakikadan uzun anestezi, hastalık nedeniyle 3 günden fazla yatağa bağımlı yaşamak veya kırıklar gelişen travmalarda) **3 aylık** tedavinin yeterli olacağı öneriliyor (Kanıt düzeyi IB).
- Major veya geri döndürülebilir bir risk faktörü olmadan geçirilen **iki VTE atağında sınırsız süre** (indefinite) antikoagülan öneriliyor (Kanıt düzeyi IB).
- Antifosfolipit sendromu olanlarda **WARFARİN ile sınırsız süre** antikoagülan öneriyor (Kanıt düzeyi IB).

# Bunlar düşünülür (considered)

- Sınırsız süreli antikoagülasyon nedeni saptanmayan ilk atakta düşünülebilir (Kanıt düzeyi IIaA).
- Sınırsız süreli antikoagülasyon antifosfolipid antikor sendromu dışında kalıcı risk faktörü varsa ilk atakta düşünülebilir (Kanıt düzeyi IIaC).
- Sınırsız süreli antikoagülasyon minör geçici veya geri döndürülebilir bir risk faktörü varsa ilk atakta düşünülebilir (Kanıt düzeyi IIaC).

# Bunlar düşünülür (considered)

- Eğer kanser hastası dışında bir hastada uzun süreli antikoagülasyon öneriliyor ise, 6 aylık tedaviden sonra azaltılmış dozda **apixaban 2x2.5** mgr veya **rivaroxaban 1x10 mgr** düşünülebilir (Kanıt düzeyi IIaA).

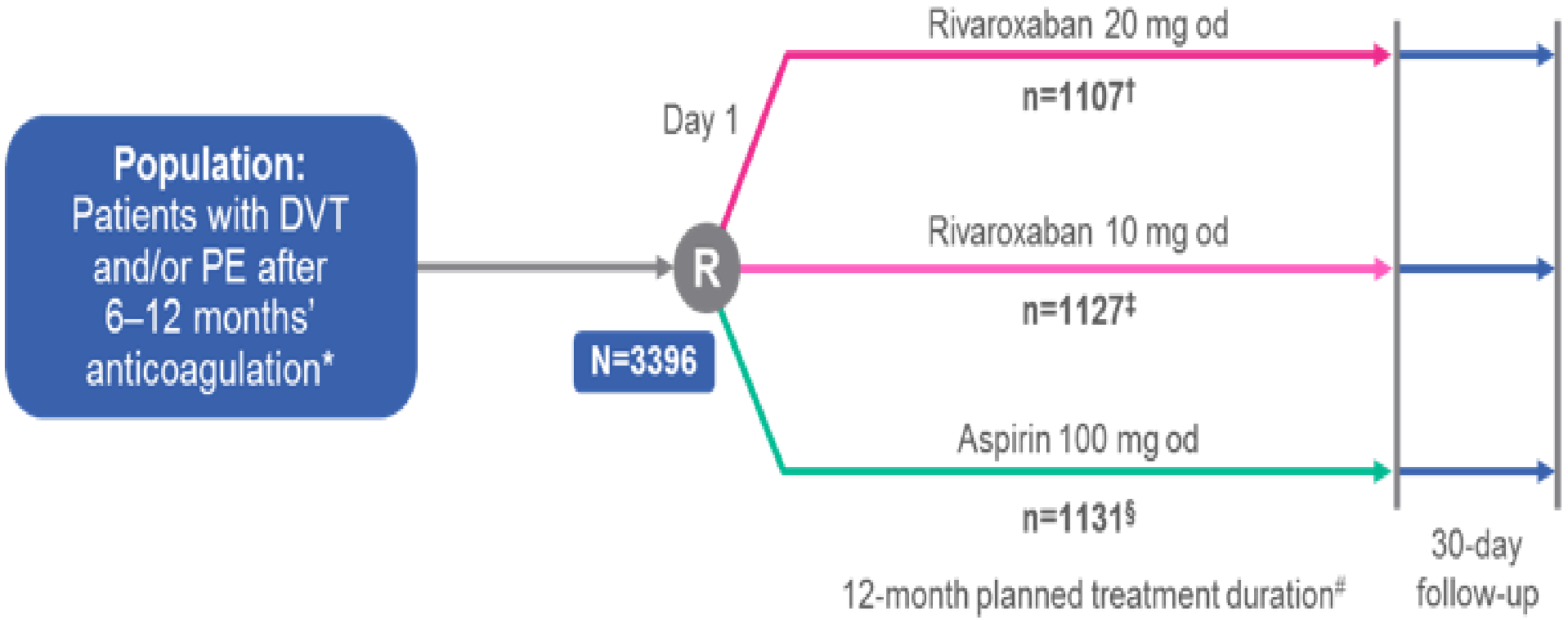
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Mart 2017

# Rivaroxaban or Aspirin for Extended Treatment of Venous Thromboembolism

J.I. Weitz, A.W.A. Lensing, M.H. Prins, R. Bauersachs, J. Beyer-Westendorf,



Supplemental Table S2. Annualized incidence rates of all pre-specified study outcomes.

| Outcome | Rivaroxaban 20 mg (N=1107) | | Rivaroxaban 10 mg (N=1127) | | Aspirin 100 mg (N=1131) | |
|---|---|---|---|---|---|---|
| | Events (n) | % per person year | Events (n) | % per person year | Events (n) | % per person year |
| Primary efficacy outcome | 17 | 1.8 | 13 | 1.4 | 50 | 5.3 |
| **Other efficacy outcomes** | | | | | | |
| Primary efficacy outcome, myocardial infarction, ischemic stroke, or systemic embolism | 19 | 2.0 | 18 | 1.9 | 56 | 6.0 |
| All-cause mortality | 8 | 0.8 | 2 | 0.2 | 7 | 0.7 |
| Primary efficacy outcome or all-cause mortality | 23 | 2.4 | 15 | 1.6 | 55 | 5.8 |
| Primary efficacy outcome or venous thrombosis in other locations | 20 | 2.1 | 16 | 1.7 | 57 | 6.1 |
| Primary efficacy outcome, myocardial infarction, ischemic stroke, systemic embolism or venous thrombosis in other locations | 22 | 2.3 | 21 | 2.2 | 63 | 6.7 |
| **Principal safety outcome** | | | | | | |
| Major bleeding (ISTH) | 6 | 0.7 | 5 | 0.5 | 3 | 0.3 |

Dec
22
2017

# FDA approves low-dose rivaroxaban for long-term PE/DVT prevention

Pulmonary Embolism / DVT / VTE

Add a Comment


The long-term management of recurrent venous thromboembolism continues to evolve with the FDA's approval of once-daily low-dose rivaroxaban, now indicated for patients with recurrent deep venous thrombosis or pulmonary embolism who have completed at least six months of anticoagulation.

FDA approved low-dose rivaroxaban based on data from 3,395 patients in the EINSTEIN-CHOICE study. Both 20 mg and 10 mg daily doses of rivaroxaban appeared equivalent (and better than aspirin) at reducing the risk of recurrent DVT or PE (66% and 74% relative risk reductions, respectively). There was no excess bleeding risk observed.

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 FEBRUARY 21, 2013 VOL. 368 NO. 8

# Apixaban for Extended Treatment of Venous Thromboembolism

Giancarlo Agnelli, M.D., Harry R. Buller, M.D., Ph.D., Alexander Cohen, M.D., Madelyn Curto, D.V.M., Alexander S. Gallus, M.D., Margot Johnson, M.D., Anthony Porcari, Ph.D., Pharm.D., Gary E. Raskob, Ph.D., and Jeffrey I. Weitz, M.D., for the AMPLIFY-EXT Investigators*

**AMPLIFY-EXT[1]**

- Phase III, randomised, double-blind trial
- 2,482 patients with DVT or PE who completed 6 to 12 months of anticoagulation therapy
- Duration: 12 months

**ELIQUIS® prophylactic dose arm**
**2.5mg BD**
**N=840**

**ELIQUIS® treatment dose arm**
**5mg* BD**
**N=813**

**Placebo arm**
**N=829**

Only ELIQUIS® 2.5mg BD* is licensed for extended treatment

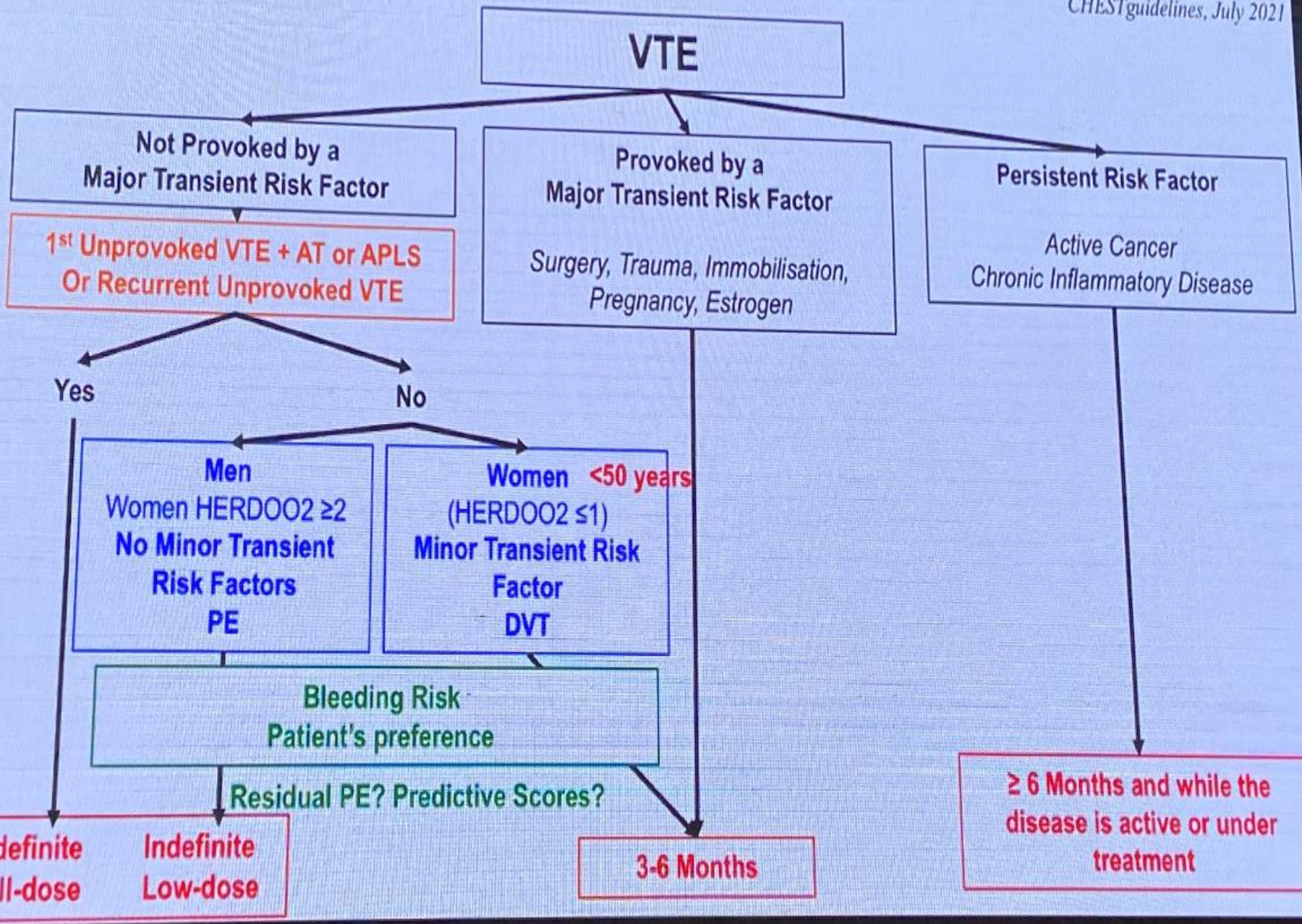
**Table 2. Clinical Outcomes in the Intention-to-Treat Population during the Intended Active Study Period.***

| Outcome | Apixaban, 2.5 mg (N=840) | Apixaban, 5 mg (N=813) | Placebo (N=829) | Relative Risk (95% CI) | | |
|---|---|---|---|---|---|---|
| | | | | Apixaban, 2.5 mg, vs. Placebo | Apixaban, 5 mg, vs. Placebo | Apixaban, 2.5 mg vs. 5 mg |
| | *number (percent)* | | | | | |
| Recurrent VTE or death from any cause — primary efficacy outcome† | 32 (3.8) | 34 (4.2) | 96 (11.6) | 0.33 (0.22–0.48) | 0.36 (0.25–0.53) | NA |
| Recurrent VTE or VTE-related death | 14 (1.7) | 14 (1.7) | 73 (8.8) | 0.19 (0.11–0.33) | 0.20 (0.11–0.34) | 0.97 (0.46–2.02) |
| Non–VTE-related cardiovascular death, myocardial infarction, or stroke | 4 (0.5) | 5 (0.6) | 11 (1.3) | 0.36 (0.11–1.12) | 0.47(0.16–1.33) | 0.77 (0.21–2.88) |
| Recurrent VTE, VTE-related death, myocardial infarction, stroke, or cardiovascular disease–related death | 18 (2.1) | 19 (2.3) | 83 (10.0) | 0.21 (0.13–0.35) | 0.23 (0.14–0.38) | 0.92 (0.48–1.74) |
| Major bleeding | 2 (0.2) | 1 (0.1) | 4 (0.5) | 0.49 (0.09–2.64) | 0.25 (0.03–2.24) | 1.93 (0.18–21.25) |
| Clinically relevant nonmajor bleeding | 25 (3.0) | 34 (4.2) | 19 (2.3) | 1.29 (0.72–2.33) | 1.82 (1.05–3.18) | 0.71 (0.43–1.18) |
| Major or clinically relevant nonmajor bleeding | 27 (3.2) | 35 (4.3) | 22 (2.7) | 1.20 (0.69–2.10) | 1.62 (0.96–2.73) | 0.74 (0.46–1.22) |

- Antitombin eksikliği, protein C veya S eksikliği, homozigot faktör V leiden mutasyonu veya homozigot protrombin G20210A mutasyonu olan hastalarda **ilk atakta da sınırsız süreli antikoagülasyona adaydırlar.**
- Heterozigot faktör V leiden mutasyonu veya heterozigot protrombin G20210A mutasyonu olan hastalarda uzun süreli tedavi için herhangi bir kanıt **bulunmamaktadır.**

# Algorithm

Couturaud et al. French Guidelines. Revue des Maladies Respiratoires (2021) 38, e99—e112
Konstantinides S et al. ESC/ERS guidelines. Eur Heart J 2020
CHESTguidelines, July 2021




# HERDOO2

## HERDOO2 Rule

| | Predictor | Scoring |
|---|---|---|
| **H** | Hyperpigmentation | 1 point total, if any one of these criteria is present |
| **E** | Edema | |
| **R** | Redness of either leg | |
| **D** | D-dimer ≥ 250 µg/L while anticoagulated | 1 |
| **O** | Obesity with BMI ≥ 30 kg/m$^2$ | 1 |
| **O** | Older age, ie, ≥ 65 years | 1 |

| Decision Making: | | |
|---|---|---|
| Women: | 0-1 | Discontinue anticoagulation |
| | ≥2 | Continue anticoagulation |
| All men | | Continue long-term anticoagulation |

Rodger MA, et al. *BMJ*. 2017;356:j1065.

# VTE BLEED SCORE
# (Valide edilmiş (doğrulanmış))

| Factor | Score |
|---|---|
| Active cancer[a] | 2 |
| Male with uncontrolled arterial hypertension[b] | 1 |
| Anaemia[c] | 1.5 |
| History of bleeding[d] | 1.5 |
| Age ≥60 years old | 1.5 |
| Renal dysfunction[e] | 1.5 |
| **Classification of patients with the VTE-BLEED score** | |
| Low bleeding risk | Total score <2 |
| High bleeding risk | Total score ≥2 |

# SONUÇ

- Acile emboli şüphesi ile gelen hastalarda

  YEARS kriterinin hiçbiri yok + D DİMER <1000, veya

  YEARS dan biri veya daha fazlası var + D DİMER<500 ise emboli dışlanır
- Acile emboli şüphesi ile gelen PERC + hastalarda YEARS + Yaşa göre ayarlanmış D Dimer emboliyi dışlar
- Yüksek riskli pulmoner emboli hastası kardiyak arrest gibi akut durumlarda trombolitik dozu 0.6 mg/kg dan 15 dk da olmalıdır
- Orta yüksek riski pulmoner emboli hastalarında yakın takip edilmeli, gerektiğinde 50 mg 2 saatte.

- Gebelikte YEARS+ Ddimer kullanışlı
- Uzun süreli antikoagülasyonda yarı doz YOAK düşünülebilir
- Tedavi kesilmesinde HERDOO2 vs KANAMA skorları kontrol edilmeli

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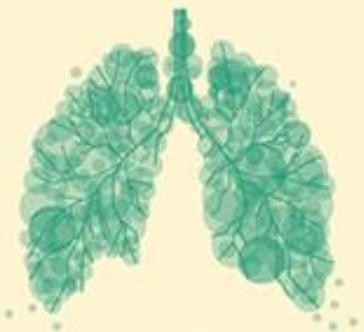
*Sizin Sesiniz, Sizin Kongreniz...*

**UASK 2023**



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