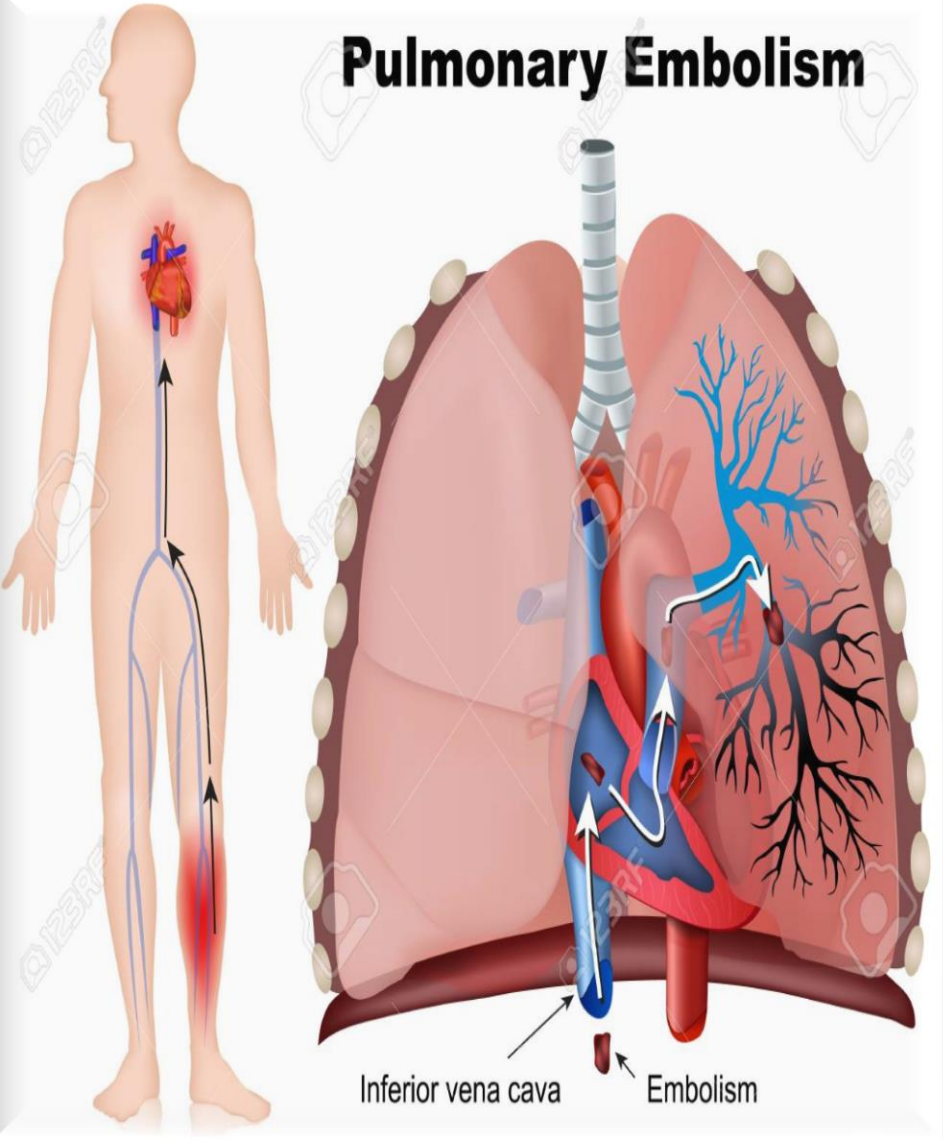
Ο ρόλος της Πυρηνικής Ιατρικής στην Οξεία Πνευμονική Εμβολή

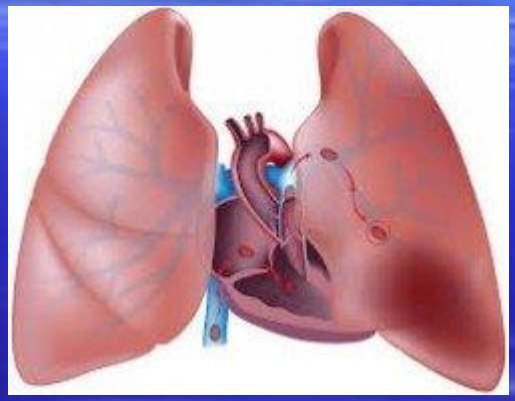


ΜΑΡΙΑ Γ. ΝΤΑΜΠΟΥΔΗ
ΠΥΡΗΝΙΚΟΣ ΙΑΤΡΟΣ
Οκτώβριος 2019

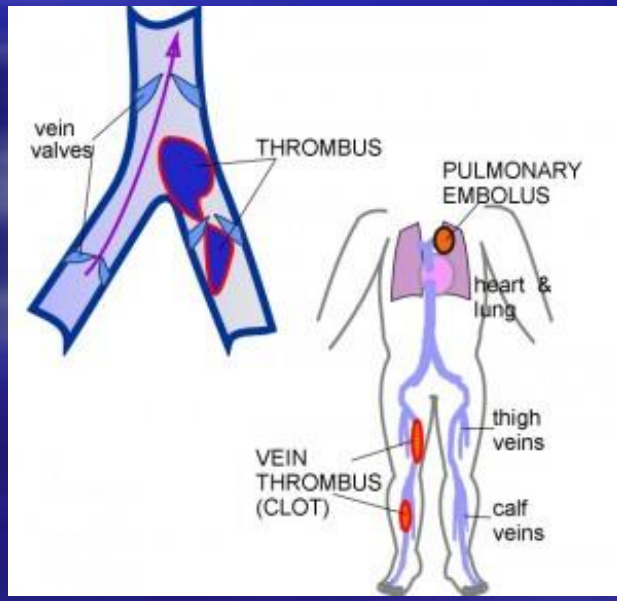
ΟΞΕΙΑ ΠΝΕΥΜΟΝΙΚΗ ΕΜΒΟΛΗ

Η ΠΕ και η ΕΒΦΘ (DVT) αποτελούν εκδηλώσεις μιας νοσολογικής οντότητας της φλεβικής θρομβοεμβολικής νόσου (VTD)

> 90% τα 'εμβολα προέρχονται από τις εν τω βάθει φλέβες της πυέλου και κάτω άκρων.



Η ενσφήνωση θρόμβου εντός της κύριας πνευμονικής αρτηρίας ή κλάδων της. Σπανιότερα επρόκειτο για ενσφήνωση άλλου υλικού (λίπους -αέρα).



Επιδημιολογικά στοιχεία της νόσου

Δυσκολία στην αξιολόγηση

Ασυμπτωματικοί ασθενείς

Τυχαίο εύρημα

Αιφνίδιος θάνατος

Σημαντική αιτία , Θνησιμότητας, Νοσηρότητας και Εισαγωγής στο νοσοκομείο στην Ευρώπη

Επιδημιολογικά στοιχεία της νόσου

Η ΠΕ είναι ή Τρίτη πιο συχνή αιτία καρδιαγγειακού συνδρόμου

Η ετησία επίπτωση της ΠΕ : 39-115 /100 000
Η ετησία επίπτωση της DVT: 53-162 /100 000
>300 000 Θανάτους κάθε χρόνο στις ΗΠΑ

Η **DVT** : 8 φορές πιο συχνή σε άτομα > 80 χρονών
Η συχνότητα εμφάνισης της **ΠΕ** αυξάνεται με το πέρασμα των χρόνων.

8,5 δις υπολογίζονται τα έξοδα για την αντιμετώπιση της ΠΕ στην Ευρώπη.

Global burden of thrombosis: epidemiologic aspects. Circ Res 2016;118:1340?1347

Predisposing factors for venous thromboembolism

Strong risk factors (odds ratio >10)
Fracture of lower limb
Hospitalization for heart failure or atrial fibrillation/flutter (within previous 3 months)
Hip or knee replacement
Major trauma
Myocardial infarction (within previous 3 months)
Previous venous thromboembolism
Spinal cord injury
Moderate risk factors (odds ratio 2-9)
Arthroscopic knee surgery
Auto-immune diseases
Blood transfusion
Central venous lines
Chemotherapy
Congestive heart or respiratory failure
Erythropoiesis-stimulating agents
Hormone replacement therapy (depends on formulation)
In vitro fertilization

www.escardio.org/guidelines

European Heart Journal (2014):doi:10.1093/eurheartj/ehu283

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Predisposing factors for VTE (cont'd)

Infection (specifically pneumonia, urinary tract infection and HIV)
Inflammatory bowel disease
Cancer (highest risk in metastatic disease)
Oral contraceptive therapy
Paralytic stroke
Postpartum period
Superficial vein thrombosis
Thrombophilia
Weak risk factors (odds ratio <2)
Bed rest >3 days
Diabetes mellitus
Hypertension
Immobility due to sitting (e.g. prolonged car or air travel)
Increasing age
Laparoscopic surgery (e.g. cholecystectomy)
Obesity
Pregnancy
Varicose veins

www.escardio.org/guidelines

European Heart Journal (2014):doi:10.1093/eurheartj/ehu283

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What is new in the ESCARDIO Guidelines 2019?

Diagnosis

D-dimer cut-off values adjusted for age or clinical probability can be used as an alternative to the fixed cut-off value.

Updated information is provided on the radiation dosage when using CTPA and a lung scan to diagnose PE

Risk assessment

A clear definition of haemodynamic instability and high-risk PE is provided.

PE in pregnancy

A dedicated diagnostic algorithm is proposed for suspected PE in pregnancy

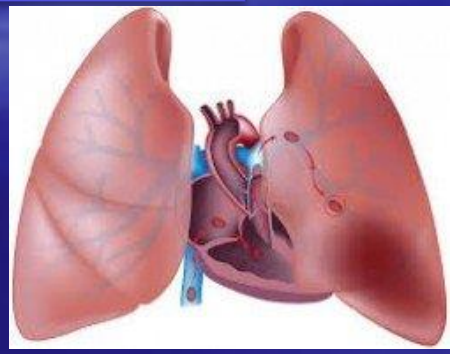
Updated information is provided on radiation absorption related to procedures used for diagnosing PE in pregnancy.

Διάγνωση ΠΕ

Ο κλινικός ιατρός υποψιάζεται πολύ πιο εύκολα την ΠΕ (παγκοσμίως) λόγω της ευαισθητοποίησης για την VTE και της εύκολης διαθεσιμότητας των μη επεμβατικών διαγνωστικών μεθόδων.

Τα τελευταία χρόνια στην Β. Αμερική η ΠΕ επιβεβαιώνεται μόνο στο 5% των ασθενών που υποβάλλονται σε έλεγχο για ΠΕ.

Το **1980** η ΠΕ επιβεβαιωνόταν στο 50% των ασθενών με υποψία ΠΕ.



Διάγνωση

Πολυπαραγοντική

1. Κλινική εικόνα
2. Αξιολόγηση της κλινικής πιθανότητας (pre test propability)
3. Ο ρόλος των d-dimers
4. Απεικονιστικές εξετάσεις
5. Στρατηγική διάγνωσης.

1.Κλινική συμπτωματολογία

Τα κλινικά συμπτώματα και σημεία δεν βοηθούν ιδιαίτερα και είναι μη ειδικά .

Δύσπνοια
Πλευριτικό θωρακικό 'αλγος
Βήχας
Υποξιφοειδικό θωρακικό άλγος
Πυρετός
Αιμόπτυση
Συγκοπή
Μονόπλευρο άλγος κάτω άκρου
Συμπτώματα DVT (μονόπλευρο οίδημα κάτω άκρου)

80% των ασθενών με ΠΕ έχουν σημεία ΕΒΦΘ, και περίπου 50% των ασθενών με επιβεβαιωμένη ΕΒΦΘ έχουν ΠΕ.
Κανένα από τα παραπάνω συμπτώματα δεν είναι ειδικά για την διάγνωση της ΠΕ.

2.Εκτίμηση κλινικής πιθανότητας για οξεία ΠΕ

Wells score

Assessment of pre-test probability

Clinical prediction rules for pulmonary embolism		
	Clinical decision rule points	
Wells rule	**Original version**	**Simplified version**
Previous PE or DVT	1.5	1
Heart rate ≥100 b.p.m.	1.5	1
Surgery or immobilization within the past 4 weeks	1.5	1
Haemoptysis	1	1
Active cancer	1	1
Clinical signs of DVT	3	1
Alternative diagnosis less likely than PE	3	1
Clinical probability		
Three-level score		
Low	0-1	N/A
Intermediate	2-6	N/A
High	≥7	N/A
Two-level score		
PE unlikely	0-4	0-1
PE likely	≥5	≥2

www.escardio.org/guidelines

European Heart Journal (2014):doi:10.1093/eurheartj/ehu283

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2.Εκτίμηση κλινικής πιθανότητας για οξεία ΠΕ

Geneva score

Assessment of pre-test probability (cont'd)

Clinical prediction rules for pulmonary embolism (cont.)		
	Clinical decision rule points	
Revised Geneva score	**Original version**	**Simplified version**
Previous DVT or PE	3	1
Heart rate 75-94 b.p.m. ≥95 b.p.m.	 3 5	 1 2
Surgery or fracture within the past month	2	1
Haemoptysis	2	1
Active cancer	2	1
Unilateral lower limb pain	3	1
Pain on lower limb deep venous palpation and unilateral oedema	4	1
Age >65 years	1	1
Clinical probability		
Three-level score		
Low	0-3	0-1
Intermediate	4-10	2-4
High	≥11	≥5
Two-level score		
PE unlikely	0-5	0-2
PE likely	≥6	≥3

www.escardio.org/guidelines

European Heart Journal (2014):doi:10.1093/eurheartj/ehu283

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Three levels classification : low / medium / high clinical probability for PE or two levels classification : unlikely / likely for PE

Three levels classification

PE is confirmed in 10% of Low clinical probability
PE is confirmed in 30% of Medium clinical probability
PE is confirmed in 65% of High clinical probability

Two levels classification

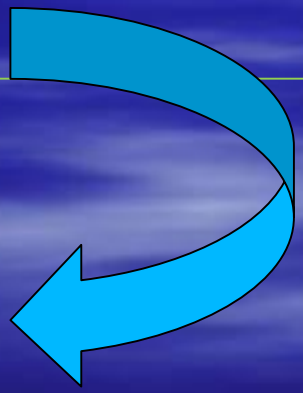
PE is confirmed in 12 % of unlikely
PE is confirmed in 30% of likely.

Avoiding overuse of diagnostic tests for pulmonary embolism

Pulmonary Embolism Rule-out Criteria (PERC) were developed for emergency department patients with the purpose of selecting, on clinical grounds, patients whose likelihood of having PE is so **low** that diagnostic workup should not even be initiated.

1) age < 50 years
2) pulse < 100 beats per minute
3) SaO 2 >94%
4) no unilateral leg swelling
5) no haemoptysis
6) no recent trauma or surgery
7) no history of VTE
8) no oral hormone use

safe exclusion of PE in patients with low clinical probability who, in addition, met all criteria of the PERC rule.



The risk of DVT in patients with low or intermediate possibility for PE ,who were untreated, was <1%

3.Ο ρόλος των D-dimers

Είναι προϊόντα αποδομής του Ινώδους.

Ευαισθησία ?

Ειδικότητα ?

Διάφορες μέθοδοι αξιολόγησης. (rapid elisa, latex, simply red)

Μόνο σε ασθενείς χαμηλού ή ενδιάμεσου κινδύνου για ΠΕ.

Μόνο η μέθοδος με rapid elisa μπορεί να αποκλείσει την ΟΠΕ σε ασθενείς χαμηλού ή ενδιάμεσου κινδύνου για ΠΕ.

Age-adjusted D-dimer cut-offs

Guidelines 2019

The specificity of D-dimer in suspected PE decreases steadily with age to ~10% in patients >80 years of age.

(age x 10 μg/L, for patients aged >50 years)

Μελέτη με 3346 ασθενείς

The use of age-adjusted cut-offs may **improve** the performance of D-dimer testing in the elderly.

Among the **766** patients who were **>75 years of age**, **673** had a non-high clinical probability. Use of the age-adjusted (instead of the 'standard' 500 μg/L) D-dimer cut-off increased the number of patients in whom PE could be excluded from **6.4% to 30%,without additional false-negative findings**.

Age-adjusted D-dimer cutoff levels to rule out pulmonary embolism: the ADJUST-PE study.JAMA 2014;311:1117?1124.

D-dimer cut-offs adapted to clinical probability

YEARS' clinical decision rule:
Three clinical items of the "Wells score" : signs of DVT, haemoptysis, and PE more likely than an alternative diagnosis—plus D-dimer concentrations.

Guidelines 2019

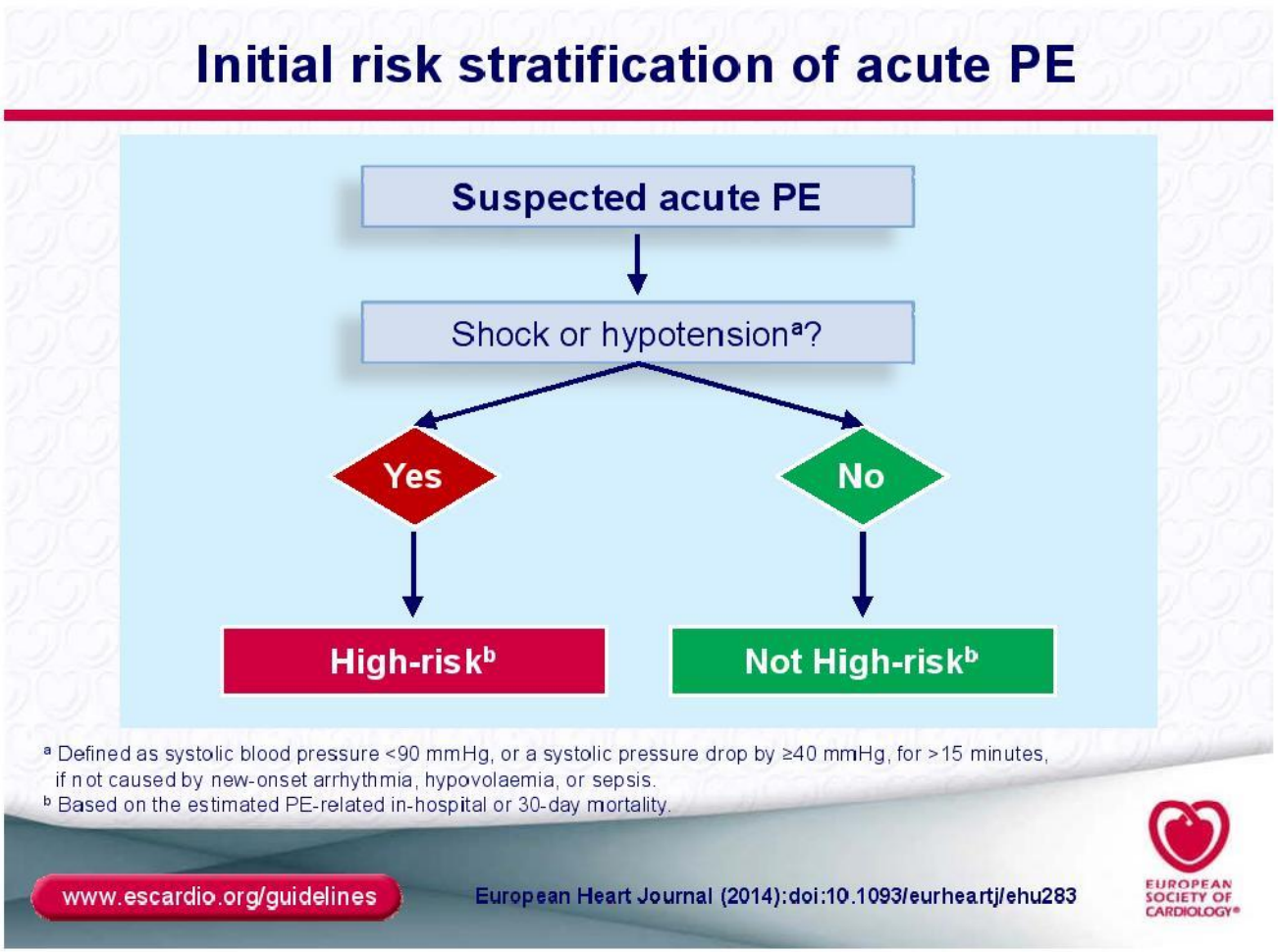
PE was considered to be excluded in patients without clinical items and D-dimer levels <1000 ng/mL

or in patients with
one or more clinical items and D-dimer levels <500 ng/mL

Of the 2946 patients **(85%)** in whom PE was ruled out at baseline and who were left untreated, **18** were diagnosed with symptomatic VTE during the 3 month follow-up. ***CTPA was avoided in 48%*** of the included patients using this algorithm, compared to 34% if the Wells rule and a fixed D-dimer threshold of 500 ng/ml would have been applied.

Simplified diagnostic management of suspected pulmonary embolism (the YEARS study): a prospective, multicentre, cohort study.
Lancet 2017;390:289?297.

Clinical classification of PE severity



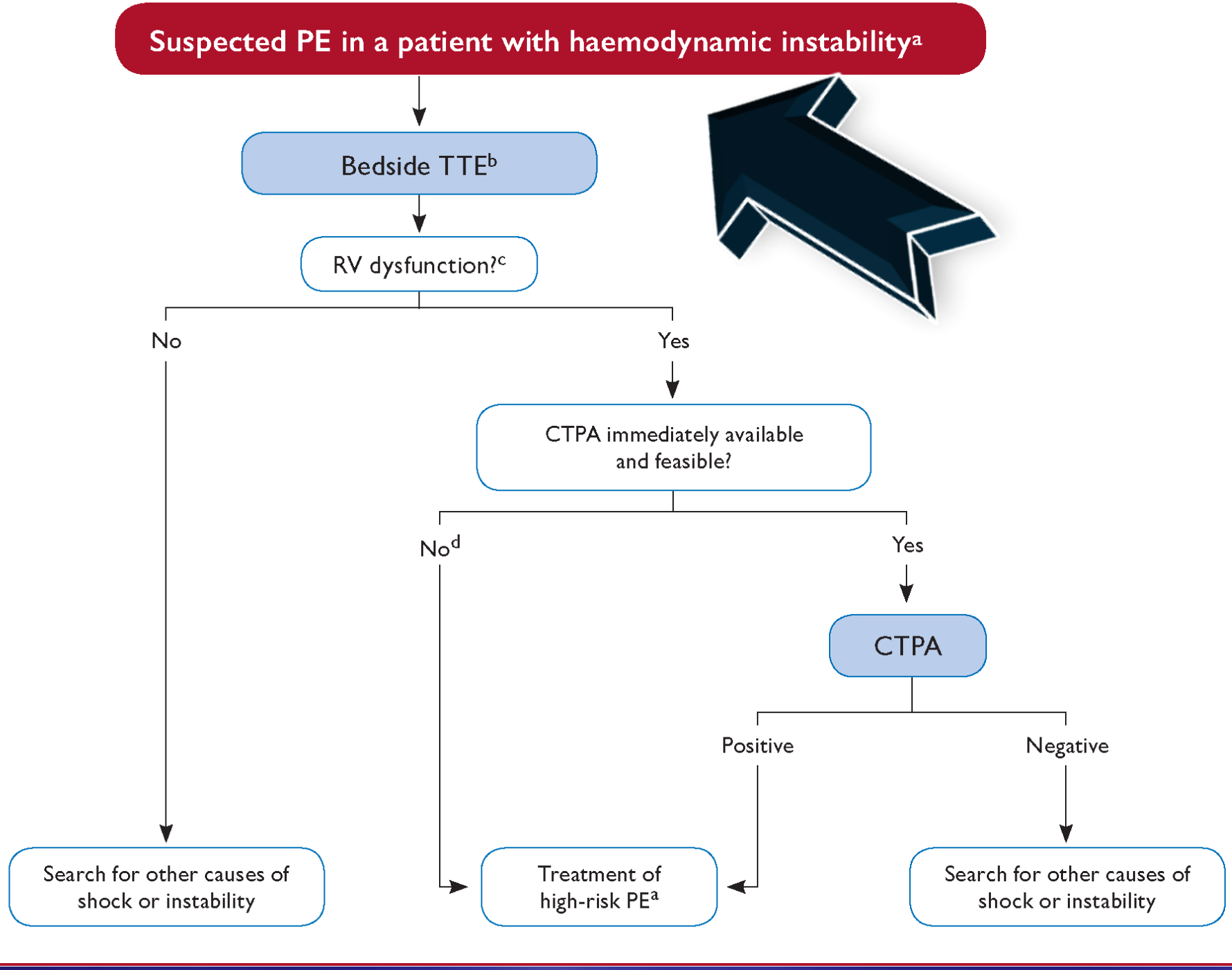
Definition of haemodynamic instability, which delineates acute high-risk pulmonary embolism

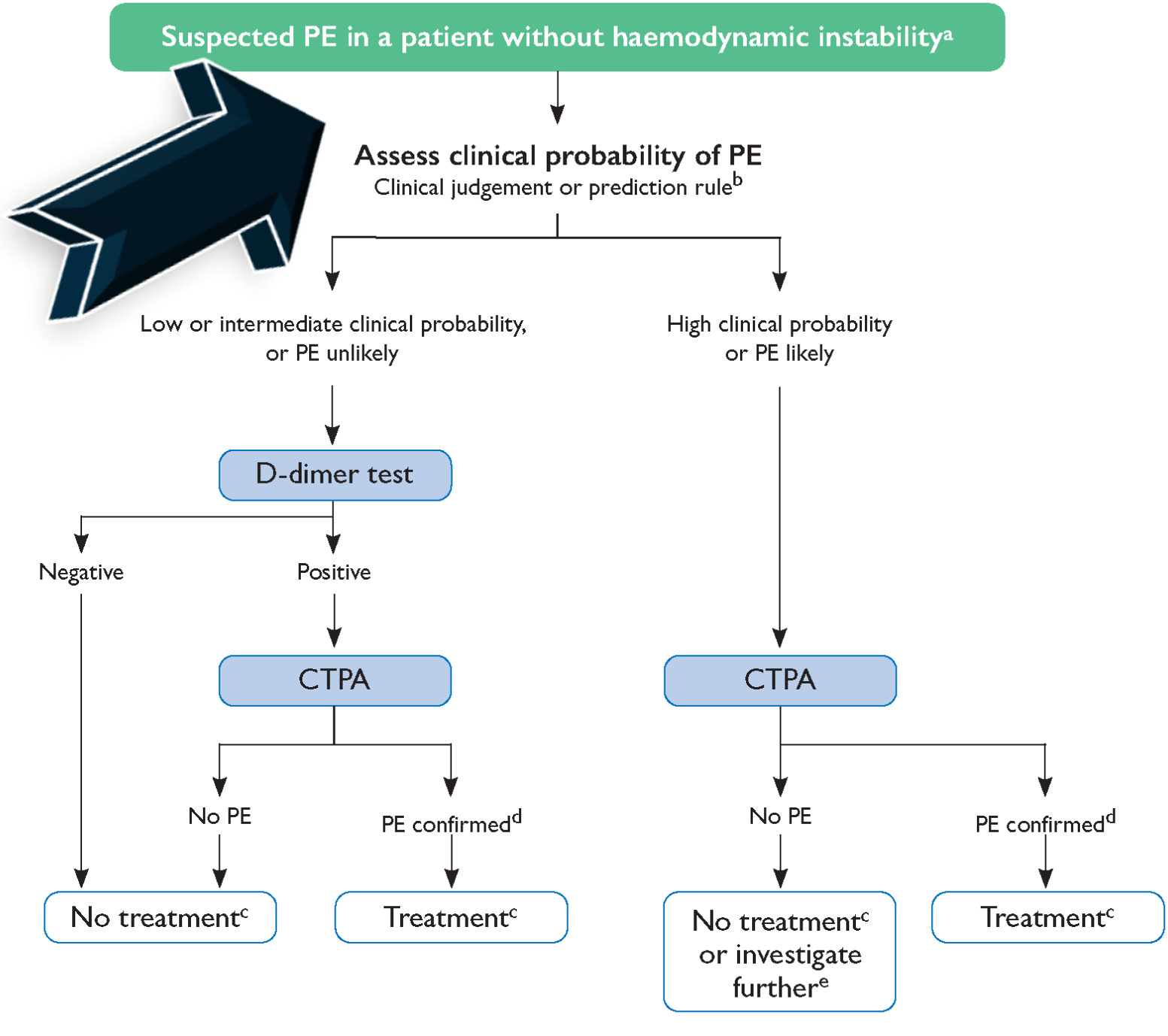
Guidelines 2019

(1) Cardiac arrest
Need for cardiopulmonary resuscitation

(2) Obstructive shock
Systolic BP < 90 mmHg or vasopressors required to achieve a BP >_90 mmHg despite adequate filling status
end organ hypoperfusion (altered mental status; cold, clammy skin; oliguria/anuria; increased serum lactate)

(3) Persistent hypotension
Systolic BP < 90 mmHg or systolic BP drop >40 mmHg, lasting longer than 15 min and not caused by new-onset arrhythmia, hypovolaemia, or sepsis


Suspected PE in a patient with haemodynamic instability[a]
Bedside TTE[b]
RV dysfunction?[c]
No
Yes
CTPA immediately available and feasible?
No[d]
Yes
CTPA
Positive
Negative
Search for other causes of shock or instability
Treatment of high-risk PE[a]
Search for other causes of shock or instability


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
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]

ΣΠΙΝΘΗΡΟΓΡΑΦΗΜΑ ΑΙΜΑΤΩΣΗΣ ΠΝΕΥΜΟΝΩΝ

Validated Diagnostic Test
ESC guidelines 2019

Διαθεσιμότητα

CTPA 10-50mGY
SCAN 0,28mGY

In patients with
Severe renal impairment and iodinated allergy!!

First line imaging
in pregnant and younger patients.

A V/Q scan indicating a high probability of PE provides sufficient evidence for the initiation of treatment but a low probability scan does not rule out PE – further diagnostic tests may be required

ΣΠΙΝΘΗΡΟΓΡΑΦΗΜΑ ΑΙΜΑΤΩΣΗΣ ΠΝΕΥΜΟΝΩΝ

Ραδιοφάρμακο : Tc 99m-Macroaggregated Albumin
Δοσολογία : 2-5 mCi (iv), 200.000-500.000 σωματίδια

Πνευμονική Υπέρταση : μείωση των σωματιδίων σε 100.000 – 250.000 σωματίδια

Έγκυες γυναίκες : μικρότερη ακτινοβολία και τουλάχιστον 100.000 σωματίδια.

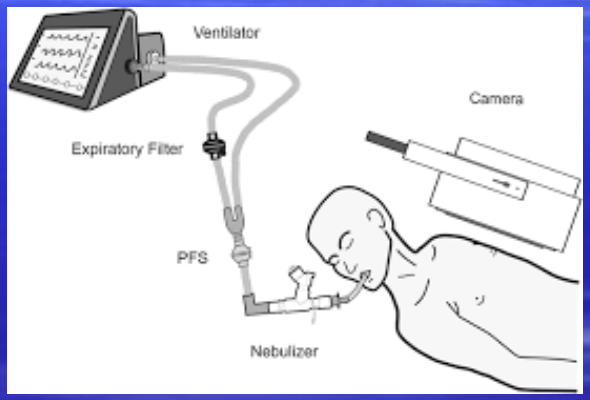
Ιδιαίτερη προσοχή

Κατευθυντήρας : χαμηλής ενέργειας-παραλλήλων οπών
Κρούσεις : 500-750 χιλ κρούσεις / ανά εικόνα
Λήψεις : πρόσθια, οπίσθια, πλάγιες και οπίσθια λοξές άμφω
Ο ασθενής είναι σε ύπτια θέση

ΣΠΙΝΘΗΡΟΓΡΑΦΗΜΑ ΑΕΡΙΣΜΟΥ ΠΝΕΥΜΟΝΩΝ

Ραδιοφάρμακα : Xe 133, Xe 127,Kr81m
ή Tc 99m-DTPA (αεροσόλη)

Δοσολογία : 30mCi Tc 99m-DTPA στον νεφελοποιητή



Κατευθυντήρας : χαμηλής ενέργειας-παραλλήλων οπών
Κρούσεις : 300-500 χιλ κρούσεις / ανά εικόνα
Λήψεις : πρόσθια, οπίσθια, πλάγιες και οπίσθια λοξές άμφω
Ο ασθενής είναι σε ύπτια θέση

Scanning αιμάτωσης πνευμόνων
Ερμηνεία των σπινθηρογραφικών ευρημάτων

Modified PIOPED Criteria

High Probability

- >= 2 Large segmental perfusion defects (SPD).
- 1 Large SPD and >= 2 Moderate SPD.
- >= 4 Moderate SPD.

Intermediate Probability

- 1 Moderate to < 2 Large SPD.
- Corresponding V/Q defect and CXR opacity in lower lung.
- Single moderately matched V/Q defect.
- Corresponding V/Q defect and small Pleural Effusion.

Low Probability

- Multiple Matching V/Q defects.
- Corresponding V/Q defects and CXR parenchymal opacity in upper or middle lung zone.
- Corresponding V/Q defects and large Pleural Effusion.
- > 3 Small SPD.

Very Low Probability

- <= 3 Small SPD.

Normal

- No perfusion defects and perfusion outlines the shape of the lung seen on CXR

*CXR = Chest Radiograph
**V/Q = Ventilation-Perfusion

MIS-MATCH ΕΥΡΗΜΑΤΩΝ ΑΕΡΙΣΜΟΥ – ΑΙΜΑΤΩΣΗΣ= ΠΕ

Scanning αιμάτωσης πνευμόνων
Ερμηνεία των σπινθηρογραφικών ευρημάτων

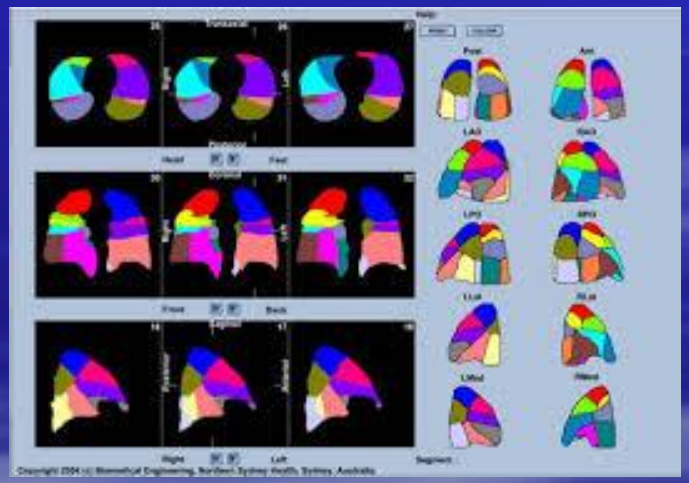
Finding	Modified PIOPED II	PISAPED
PE present	High probability (2 or more segments of perfusion–chest radiograph mismatch)	One or more wedge-shaped perfusion defects
PE absent	Normal perfusion	Normal perfusion
	Very low probability	
	Nonsegmental lesion, for example, prominent hilum, cardiomegaly, elevated diaphragm, linear atelectasis, or costophrenic angle effusion with no other perfusion defect in either lung radiographic lesion	Near normal
	Perfusion defect smaller than radiographic lesion	Contour defect caused by enlarged heart, mediastinum, or diaphragm
	1–3 small segmental defects	Perfusion defect, not wedge-shaped
	Solitary chest radiograph–perfusion matched defect in mid or upper lung zone confined to single segment	
	Stripe sign around perfusion defect (best tangential view)	
	Pleural effusion in at least one third of pleural cavity, with no other perfusion defect in either lung	
Not diagnostic	All other findings	Cannot classify as PE-positive or PE-negative

Guidelines 2019

To facilitate communication with clinicians, a three-tier classification is preferable: normal scan (excluding PE), high-probability scan (considered diagnostic of PE in most patients), and non-diagnostic scan

Scanning αιμάτωσης πνευμόνων
Ερμηνεία των σπινθηρογραφικών ευρημάτων

Αποτέλεσμα scan	Πιθανότητα για ΠΕ
Φυσιολογικό σπινθηρογράφημα	< 5%
Χαμηλής πιθανότητας	5-19%
Μέσης πιθανότητας	20-79%
Υψηλής πιθανότητας	80-100%

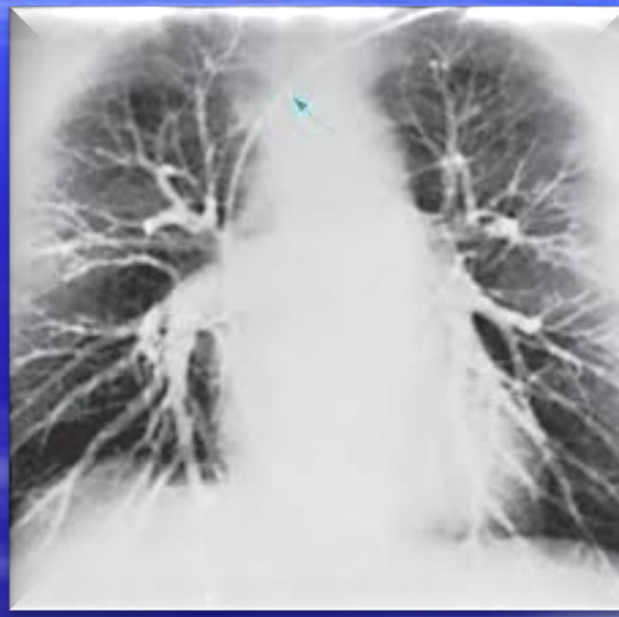


Φυσιολογικό scan αιμάτωσης αποκλείει με ασφάλεια την ΠΕ — **NPV > 95%**

Υψηλής πιθανότητας scan επιβεβαιώνει την ΠΕ — **PPV 85-90%**

ΑΠΕΙΚΟΝΙΣΤΙΚΕΣ ΜΕΘΟΔΟΙ ΔΙΕΡΕΥΝΗΣΗΣ ΠΕ

PULMONARY ANGIOGRAPHY



strengths

Historical gold standard

limitations

- Invasive procedure
- Not readily available in all centres

radiation issues

Highest radiation, effective dose 10-20 mSv

ΑΠΕΙΚΟΝΙΣΤΙΚΕΣ ΜΕΘΟΔΟΙ ΔΙΕΡΕΥΝΗΣΗΣ ΠΕ

Method of choice for imaging

CTPA

strengths

- Readily available in most centres
- Excellent accuracy
- Strong validation in prospective management outcome studies
- Low rate of inconclusive results (3-5%)
- May provide alternative diagnosis if PE excluded
- Short acquisition time

limitations

- Radiation exposure
- Exposure to iodine contrast:
  - limited use in iodine allergy and hyperthyroidism
  - risks in pregnant and breastfeeding women
  - contraindicated in severe renal failure
- Tendency to overuse because of easy accessibility
- Clinical relevance of CTPA diagnosis of subsegmental PE unknown

radiation issues

- **Radiation effective dose 3-10 mSv**
- **Significant radiation exposure to young female breast tissue**

ΑΠΕΙΚΟΝΙΣΤΙΚΕΣ ΜΕΘΟΔΟΙ ΔΙΕΡΕΥΝΗΣΗΣ ΠΕ

Planar V/Q scan

strengths

- Almost no contraindications
- Relatively inexpensive
- Strong validation in prospective management outcome studies

limitations

- Not readily available in all centres
- Interobserver variability in interpretation
- Results reported as likelihood ratios
- Inconclusive in 50% of cases
- Cannot provide alternative diagnosis if PE excluded

radiation issues

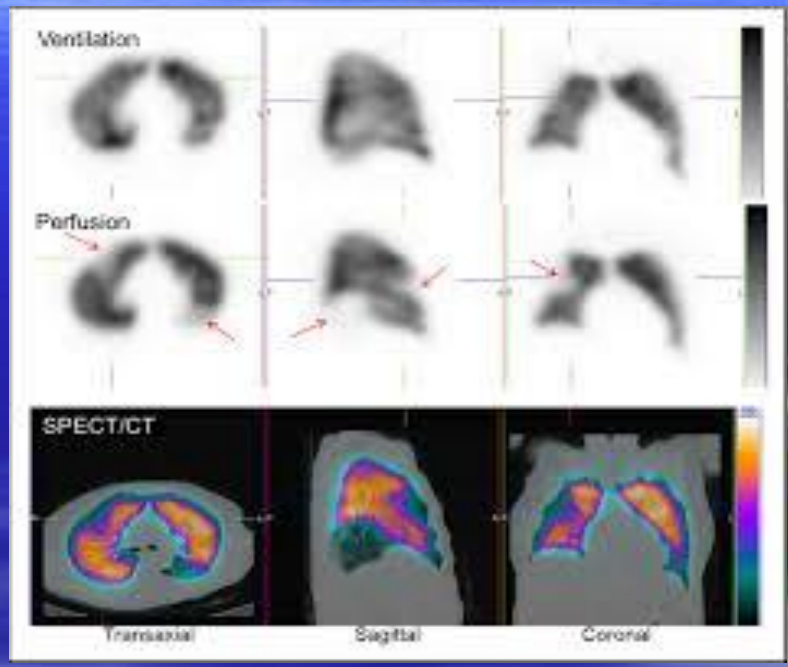
Lower radiation than CTPA, effective dose ~2 mSv

ΑΠΕΙΚΟΝΙΣΤΙΚΕΣ ΜΕΘΟΔΟΙ ΔΙΕΡΕΥΝΗΣΗΣ ΠΕ

V/Q SPECT

strengths

- Almost no contraindications
- Lowest rate of non-diagnostic tests (<3%)
- High accuracy according to available data
- Binary interpretation ('PE' vs. 'no PE')

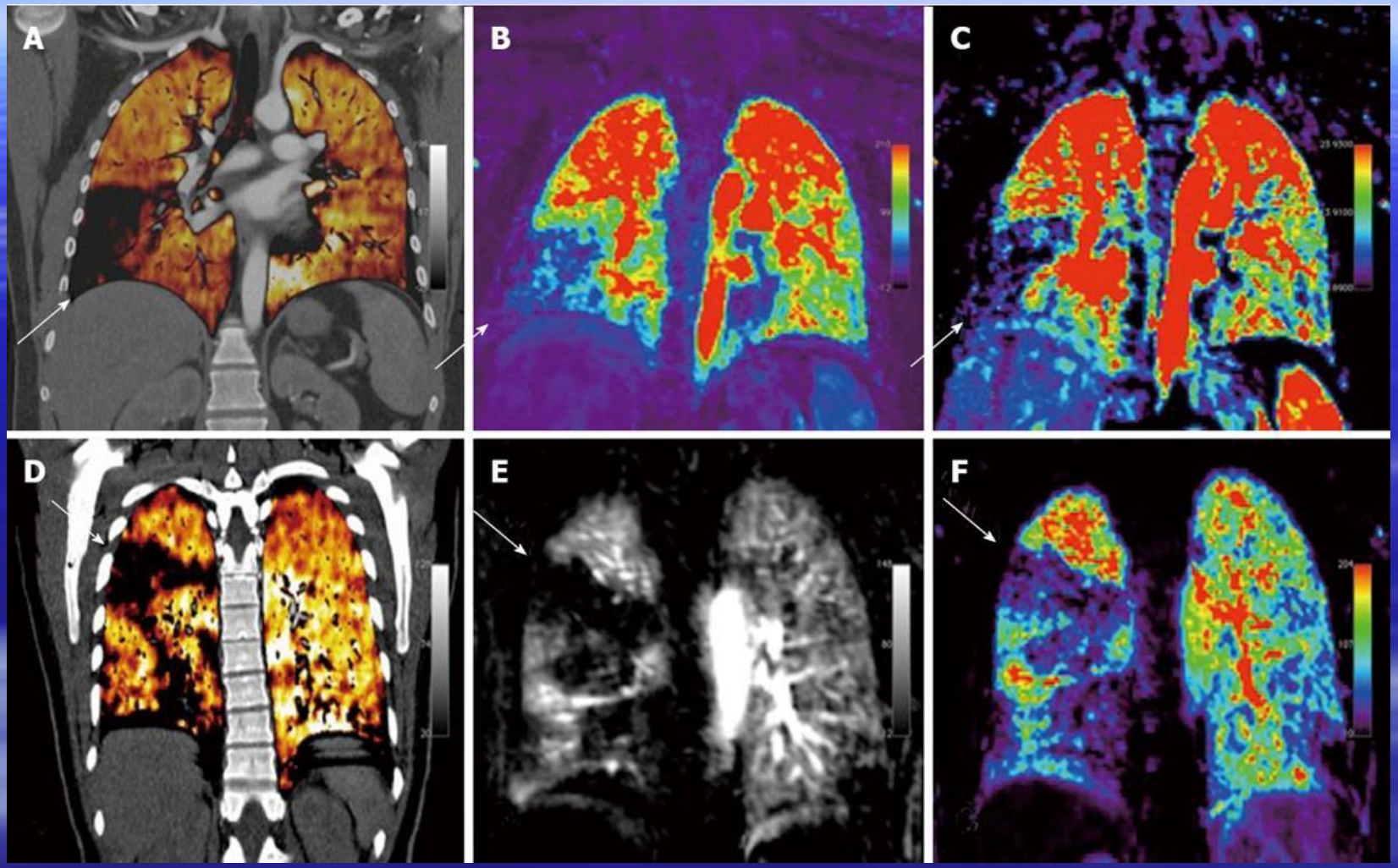


limitations

- Variability of techniques
- Variability of diagnostic criteria
- Cannot provide alternative diagnosis if PE excluded
- No validation in prospective management outcome studies

radiation issues

Lower radiation than CTPA, effective dose ~2 mSv


A
B
C
D
E
F

SUSPECTED PE DURING PREGNANCY : High pretest probability, or intermediate/low probability and positive D-dimer result

Anticoagulate with LMWH

-Chest X-ray
-Compression proximal duplex ultrasound, if symptoms or signs suggestive of DVT

Proximal DVT present

Proximal DVT not present

SPECIFIC INVESTIGATION FOR PE
- If chest X-ray normal => CTPA or perfusion lung scan
- If chest X-ray abnormal a => CTPA

Intermediate or positive

Review by radiologist or nuclear physician experienced in diagnosis of PE in pregnancy

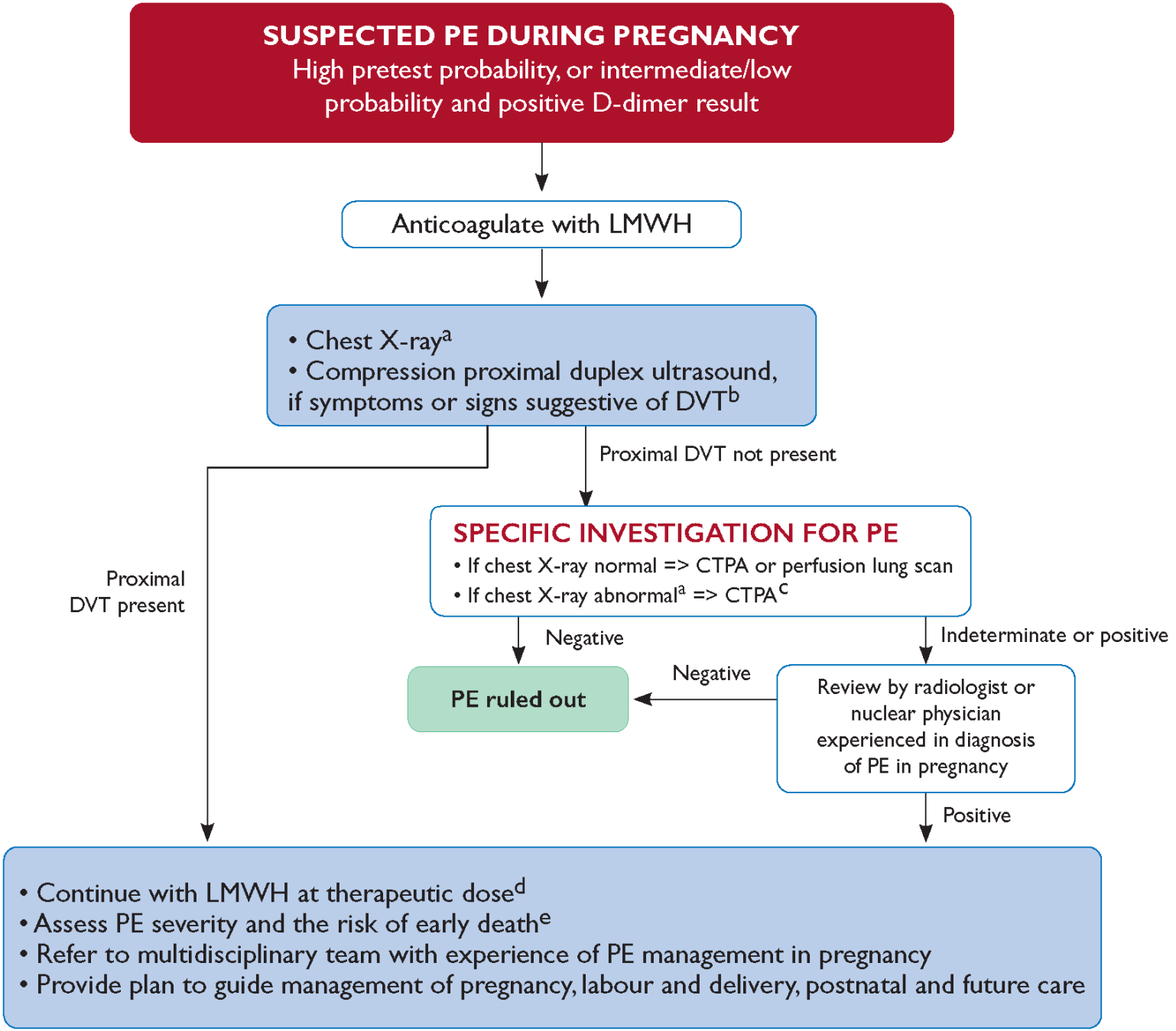
negative

negative

PE ruled out

Continue with LMWH at therapeutic dose
- Assess PE severity and the risk of early death
- Refer to multidisciplinary team with experience of PE management in pregnancy
- Provide plan to guide management of pregnancy, labour and delivery, postnatal and future care

positive


SUSPECTED PE DURING PREGNANCY
High pretest probability, or intermediate/low probability and positive D-dimer result
Anticoagulate with LMWH
• Chest X-ray[a]
• Compression proximal duplex ultrasound, if symptoms or signs suggestive of DVT[b]
Proximal DVT not present
Proximal DVT present
SPECIFIC INVESTIGATION FOR PE
• If chest X-ray normal => CTPA or perfusion lung scan
• If chest X-ray abnormal[a] => CTPA[c]
Negative
Indeterminate or positive
PE ruled out
Negative
Review by radiologist or nuclear physician experienced in diagnosis of PE in pregnancy
Positive
• Continue with LMWH at therapeutic dose[d]
• Assess PE severity and the risk of early death[e]
• Refer to multidisciplinary team with experience of PE management in pregnancy
• Provide plan to guide management of pregnancy, labour and delivery, postnatal and future care

Estimated amounts of radiation absorbed in procedures used to diagnose pulmonary embolism (based on various refer)

Test	Estimated foetal radiation exposure (mGy)	Estimated maternal radiation exposureto breast tissue (mGy)
Chest X-ray	<0.01	<0.1
Perfusion lung scan with Tc-99-labelled albumin Low dose: ~40 MBq High dose: ~200 MBq	**0.02-0.20** 0.20-0.60	**0.16-0.5** 1.2
Ventilation lung scan	0.10-0.30	<0.01
CTPA	**0.05- 0.5**	**3-10**

Conclusions

Suspected PE with haemodynamic instability

Guidelines 2019

In suspected high-risk PE, as indicated by the presence of haemodynamic instability, bedside echocardiography or emergency CTPA is recommended for diagnosis. It is recommended that i.v. anticoagulation with UFH, including a weight-adjusted bolus injection, be initiated without delay in patients with suspected high-risk PE.

Suspected PE without haemodynamic instability

The use of validated criteria for diagnosing PE is recommended.(clinical evaluation-d-dimers)
Initiation of anticoagulation is recommended without delay in patients with high or intermediate clinical probability of PE while diagnostic workup is in progress.

D-dimer measurement **is not recommended** in patients with high clinical probability, as a normal result does not safely exclude PE, even when using a highly sensitive assay.

Conclusions

Guidelines 2019

CTPA

It is recommended to reject the diagnosis of PE (without further testing) if CTPA is normal in a patient with low or intermediate clinical probability, or who is PE-unlikely

It is recommended to accept the diagnosis of PE (without further testing) if CTPA shows a segmental or more proximal filling defect in a patient with intermediate or high clinical probability.

It should be considered to reject the diagnosis of PE (without further testing) if CTPA is normal in a patient with high clinical probability or who is PE-likely.

Further imaging tests to confirm PE may be considered in cases of isolated subsegmental filling defects.

Conclusions

Guidelines 2019

Planar V/Q scan

It is recommended to reject the diagnosis of PE (without further testing) if the perfusion lung scan is normal.

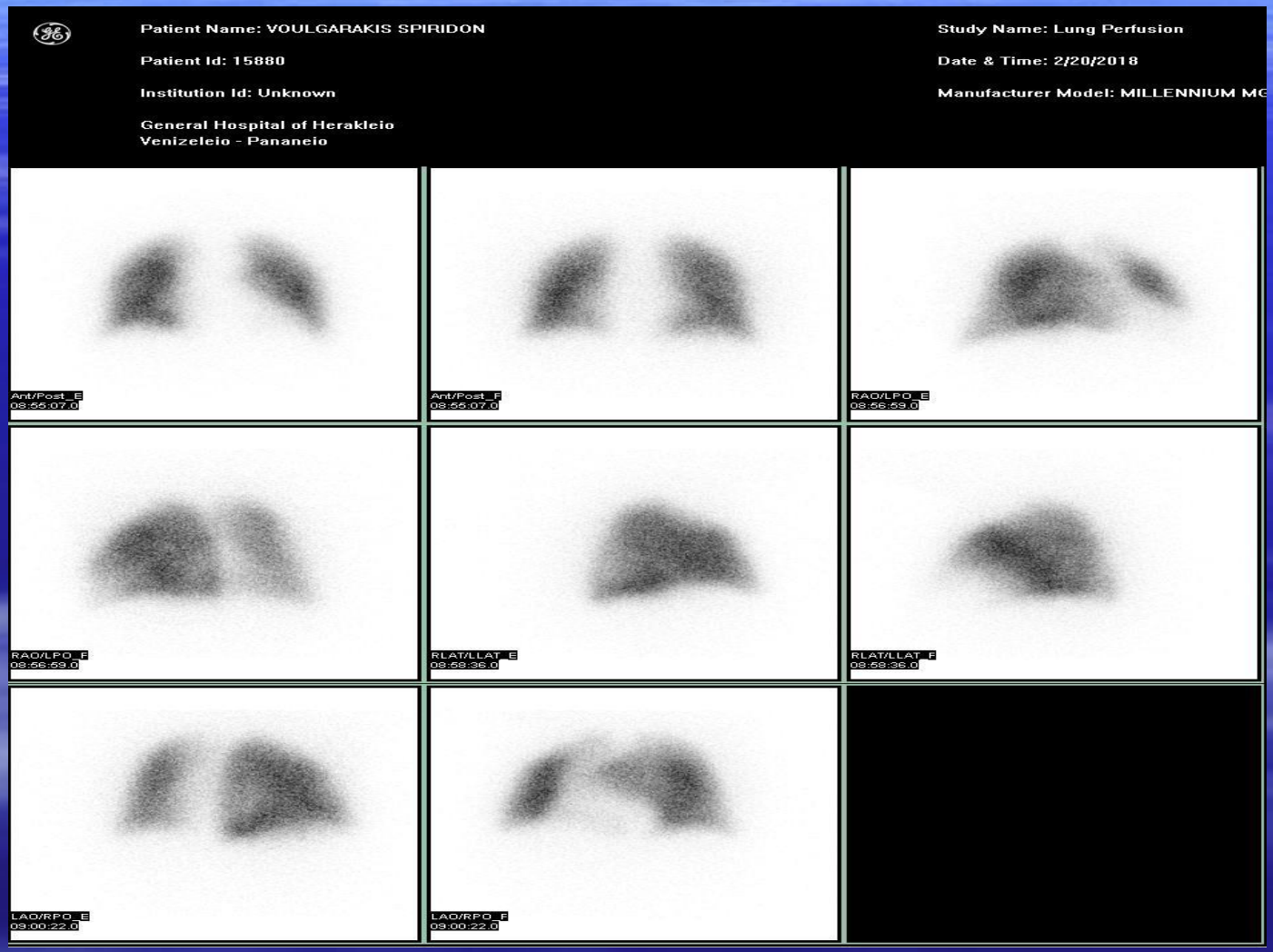
It should be considered to accept that the diagnosis of PE (without further testing) if the V/Q scan yields high probability for PE

A non-diagnostic V/Q scan should be considered as exclusion of PE when combined with a negative proximal CUS in patients with low clinical probability, or who are PE-unlikely

V/Q SPECT

V/Q SPECT may be considered for PE diagnosis

Φυσιολογικό σπινθηρογράφημα αιμάτωσης πνευμόνων



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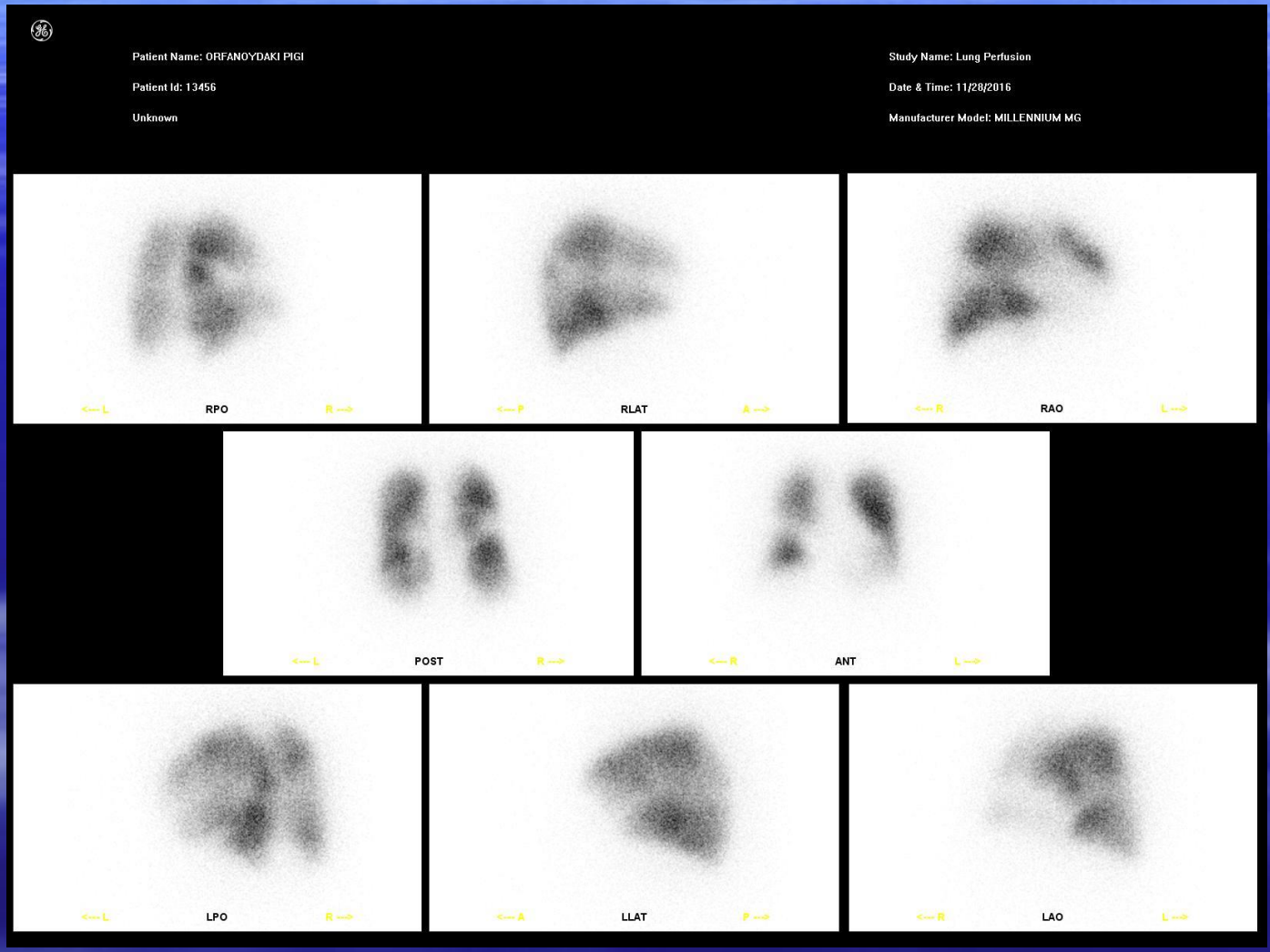

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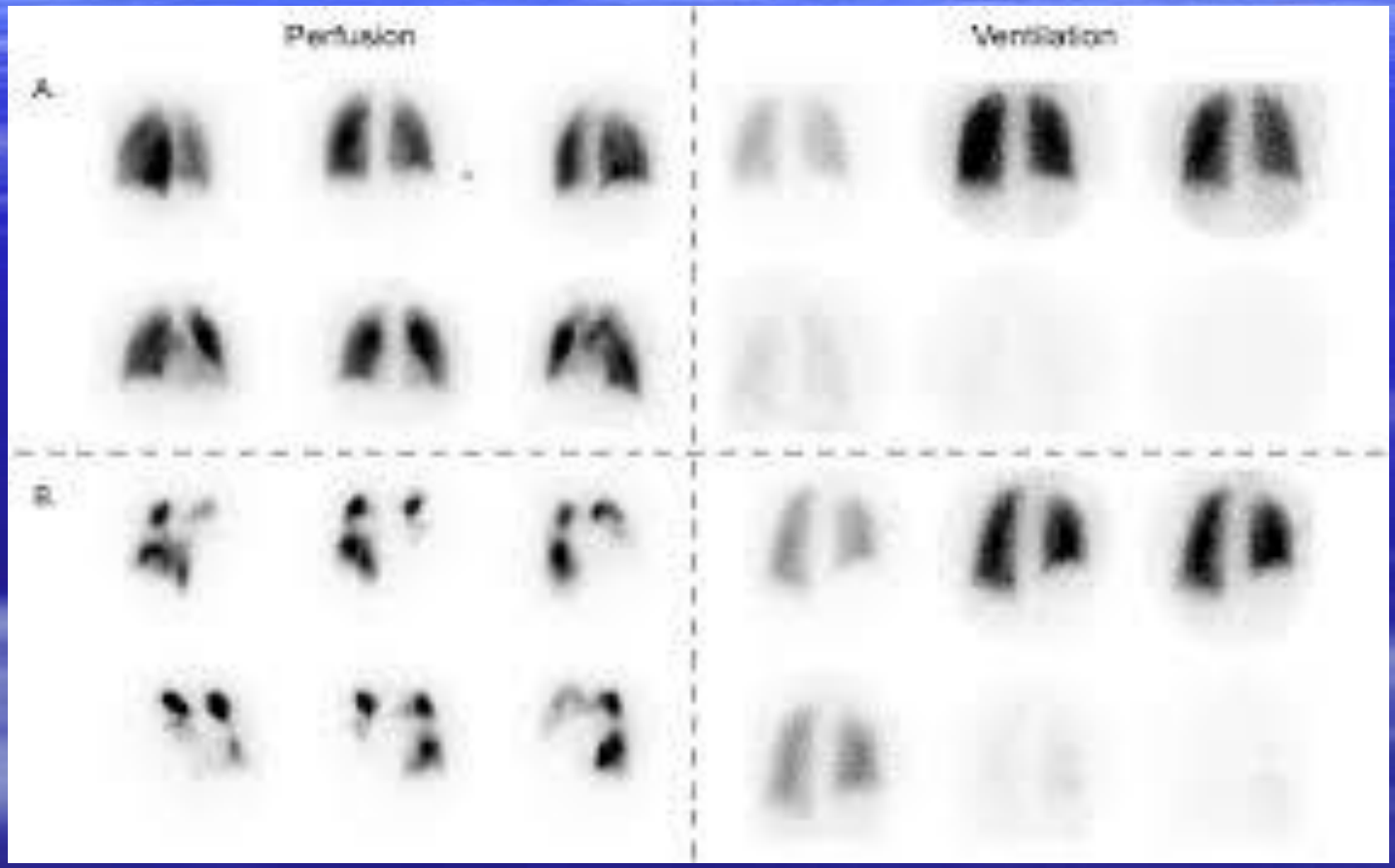

ΕΥΧΑΡΙΣΤΩ ΠΟΛΥ