XXIX CONGRESSO NAZIONALE ANCE

SORRENTO 10-13 OTTOBRE 2019

ESC European Society of Cardiology

ATTUALITA' CLINICO TERAPEUTICHE NEL TROMBOEMBOLISMO VENOSO

RELATORE
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Declaration of Interest

-Consulting/ Royalties/ Owner / Stockholder, of a healthcare company (Personal consulting and lecture fees for Bayer *AG1* Boehringer Ingelheim1 MSD1 BTG, Actelion, Pfizer-Bristol Myers Squibb)

- Research contracts (Research grants to my institution by Bayer AG, Boehringer Ingelheim., Daiiichi-Sankyo., Actelion., BTG),
- Others (Travel support: Leo Pharma Stago, BMS-Pfizer)
- Research contracts (Leo Pharma, Boehringer -Ingelheim, Stago)

2019 ESC Guidelines on the diagnosis and management of acute pulmonary embolism

The Task Force for the Diagnosis and management of Acute Pulmonary Embolism of the European Society of Cardiology (ESC).

Developed in collaboration with the European Respiratory Society (ERS)

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[1] Representing the European Respiratory Society (ERS)

2019 PE Guidelines: What has changed? What is new?

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- Haemodynamic instability and high-risk pulmonary embolism
- Risk-adapted diagnostic algorithms
- New recommendations for diagnosis
- Prognostic importance of right ventricular dysfunction
- Integrated management algorithm
- Indications for extended treatment after acute pulmonary embolism
- Cancer-associated pulmonary embolism
- Diagnosis and management of pulmonary embolism in pregnancy
- Long-term follow-up and search for late sequelae

GENEVE CRITERIA /WELLS SCORE:
l' importanza della probabilità pre-test

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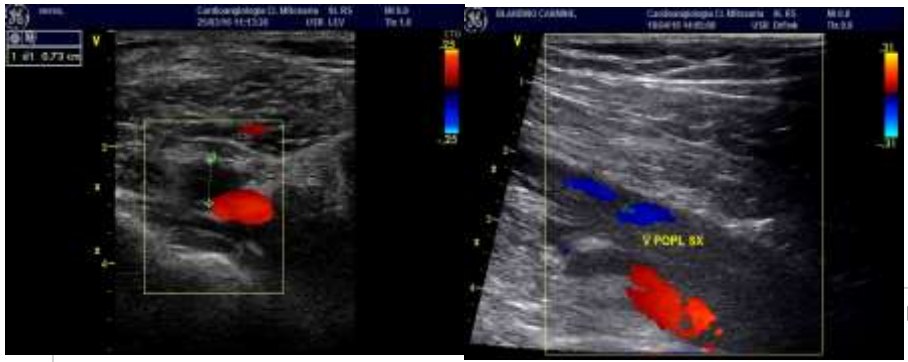
ITEMS	POINTS
PRECEDENTE TEV	1
F.C. 75-94	1
F.C. >95	2
CHIRURGIA O FRATTURA	1
EMOTTISI	1
NEOPLASIA	1
DOLORE UNILATERALE ARTO INF	1
DOLORE ED EDEMA ARTO INF	1
ETA' >65	1
SCORE DA 0 A 2 PE IMPROBABILE BASSA PROBABILITA'	SCORE DA 0-1
SCORE >3 PE PROBABILE INTERMEDIA	SCORE DA 2-4
ALTA	SCORE >5

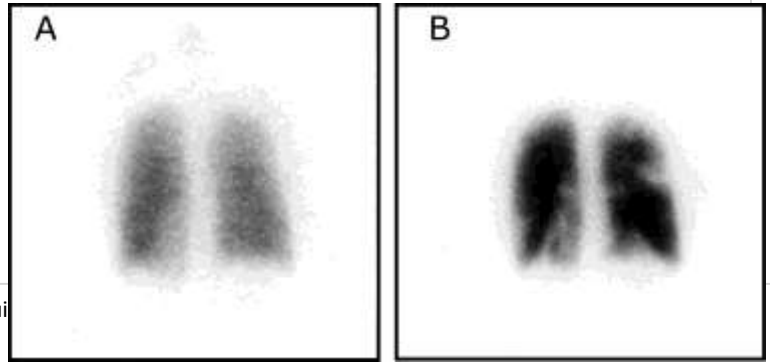
Punteggio di Wells

Punteggio clinico per Embolia Polmonare		
	Punteggio clinico	
Punteggio di Wells	***Vers. originale***	***Vers. semplificata***
Precedente EP o TVP	1.5	1
FC ≥ 100/m'	1.5	1
Chirurgia o immobilizzazione prec. 4 sett.	1.5	1
Emottisi	1	1
Cancro attivo	1	1
Segni clinici di TVP	3	1
Diagnosi alternativa meno probabile di EP	3	1
Probabilità Clinica		
Punteggio a tre livelli		
basso	0-1	ND
intermedio	2-6	ND
alto	≥7	ND
Punteggio a due livelli		
EP improbabile	0-4	0-1
EP probabile	≥5	≥2

Main NEW recommendations for PE diagnosis

Diagnosis	
D-dimer test using an age-adjustedcut-off, or adapted to clinical probability, should be considered as an alternative to the fixed cut-off level.	IIa
If a positive proximal CUS is used to confirm PE, risk assessment should be considered to guide management.	IIa
V/Q SPECT may be considered for PE diagnosis.	IIb





Main NEW recommendations for PE diagnosis

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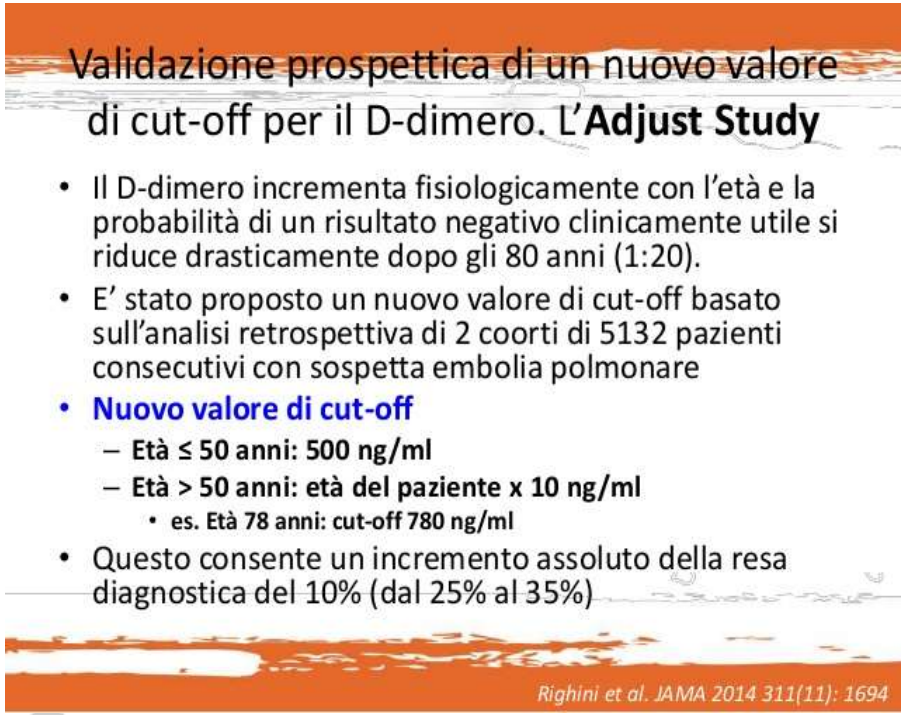
D-Dimer age –adjust cut-off



D-Dimer cut off adapted to clinical propability

-segni di DVT
-emottisi
-PE + probabile di altra diagnosi

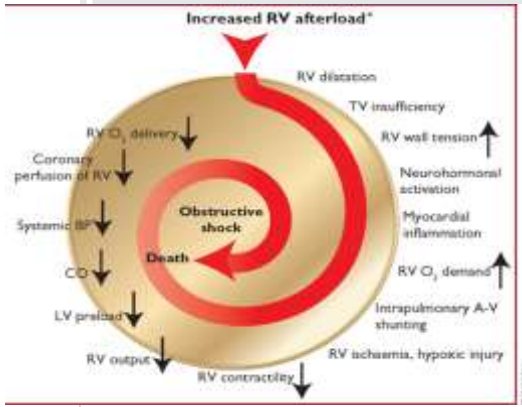
DD>1000 ng/ml ..0 segni

→ **PE esclusa**

1-2 segni DD <500 ng/ml

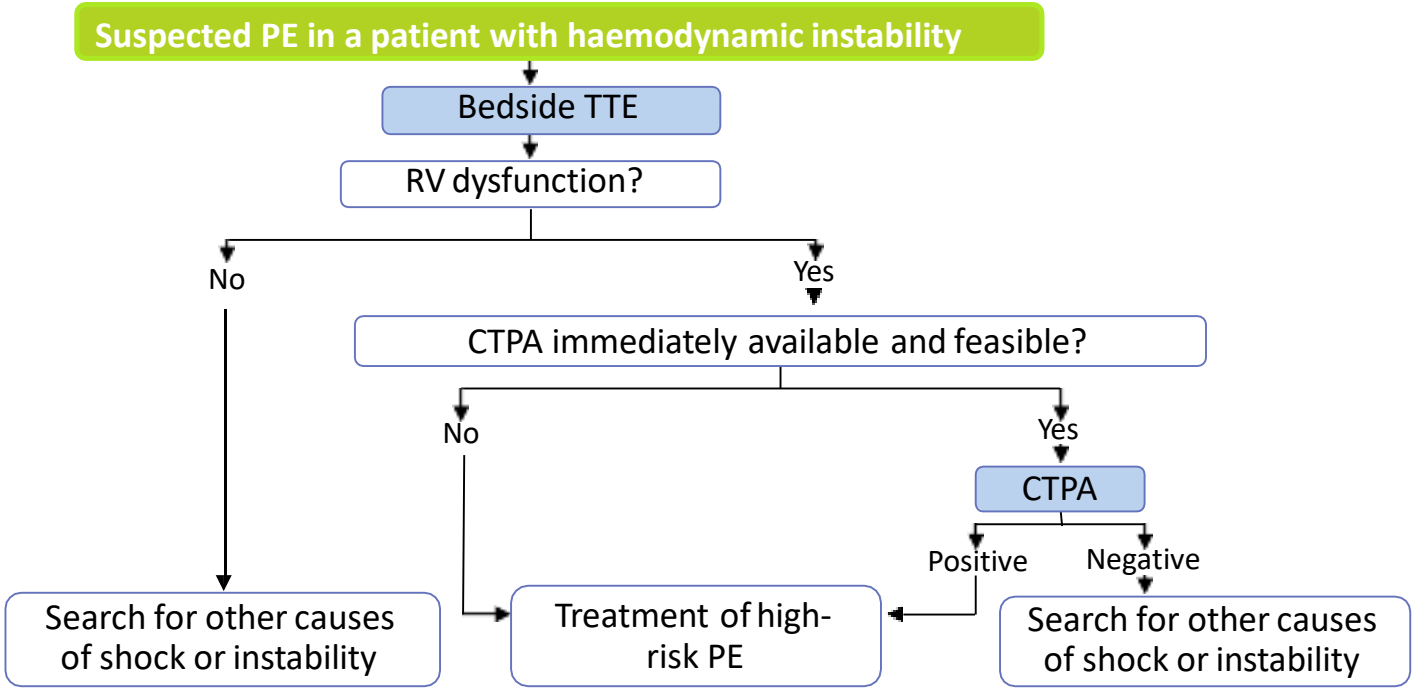
Definition of haemodynamic instability and high-risk PE

(1) Cardiac arrest	(2) Obstructive shock	(3) Persistent hypotension
Need for cardiopulmonary resuscitation	Systolic BP <90 mmHg, or vasopressors required to achieve a BP ≥90 mmHg despite adequate filling status ***And*** End-organ hypoperfusion (altered mental status; cold, clammy skin; oliguria/anuria; increased serum lactate)	Systolic BP <90 mmHg, or systolic BP drop ≥40 mmHg, either lasting longer than 15 minutes and not caused by new-onset arrhythmia, hypovolaemia, or sepsis



2019 ESC Guidelines on the diagnosis and management of acute pulmonary embolism (European Heart Journal 2019 - doi/10.1093/eurheartj/ehz405)

Diagnostic algorithm for suspected *high-risk* PE



CTPA = computed tomography pulmonary angiography; RV = right ventricular; TTE = transthoracic echocardiography

QUALI SONO I SEGNI ECOCARDIOGRAFICI DI DISFUNZIONE DEL VD?

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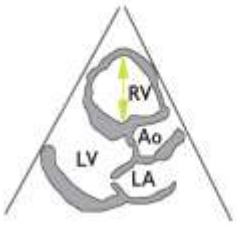
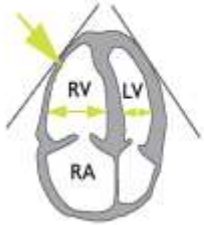
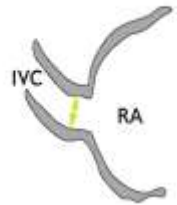


A. Enlarged right ventricle, parasternal long axis view

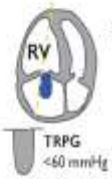


B. Dilated RV with basal RV/LV ratio >1.0, and McConnell sign (arrow), four chamber view

C. Flattened intraventricle septum (arrows) parasternal short axis view

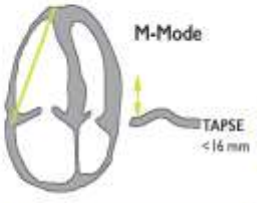


D. Distended inferior vena cava with diminished inspiratory collapsibility, subcostal view

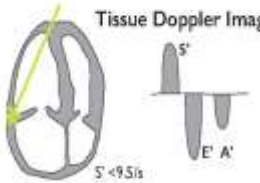


E. 60/60 sign: coexistence of acceleration time of pulmonary ejection <60 ms and midsystolic "notch" with mildy elevated (<60 mmHg) peak systolic gradient at the tricuspic valve

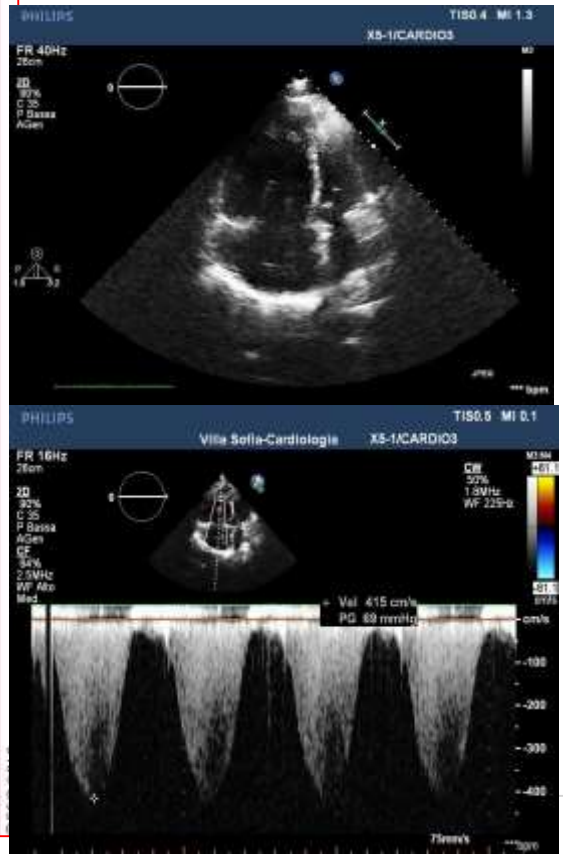
F. Right heart mobile thrombus detected in right heart cavities (arrow)



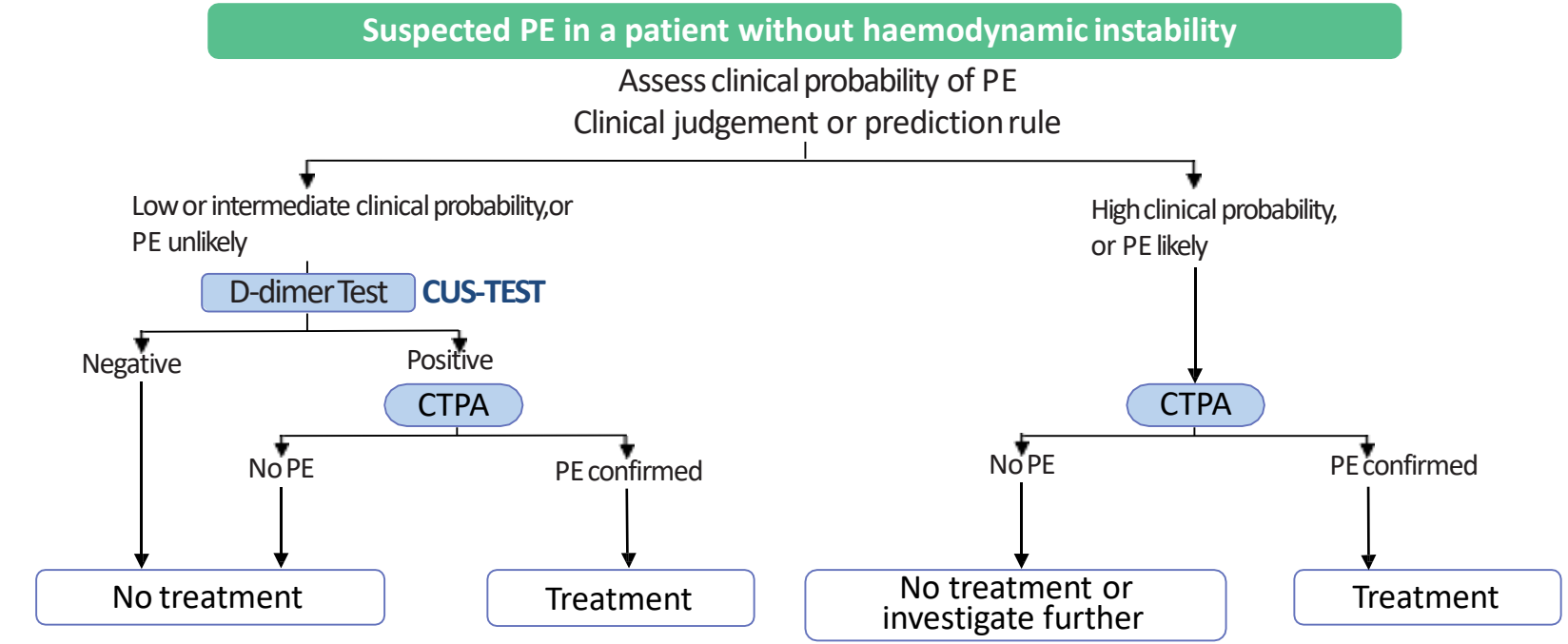
G. Decreased tricuspid annular plane systolic excursion (TAPSE) measured with M-Mode (<16 mm)



H. Decreased peak systolic (S') velocity of tricuspid annulus (<9.5 cm/s)



Diagnostic algorithm for suspected PE *without* haemodynamic instability



CTPA = computed tomography pulmonary angiography

Main NEW recommendations for risk assessment

Risk assessment	
Assessing the RV by imaging or laboratory biomarkers should be considered even in the presence of a low PESI or a s PESI of 0.	IIa
Validated scores combining clinical, imaging and laboratory prognosticfactors may be considered to further stratify PE severity.	IIb

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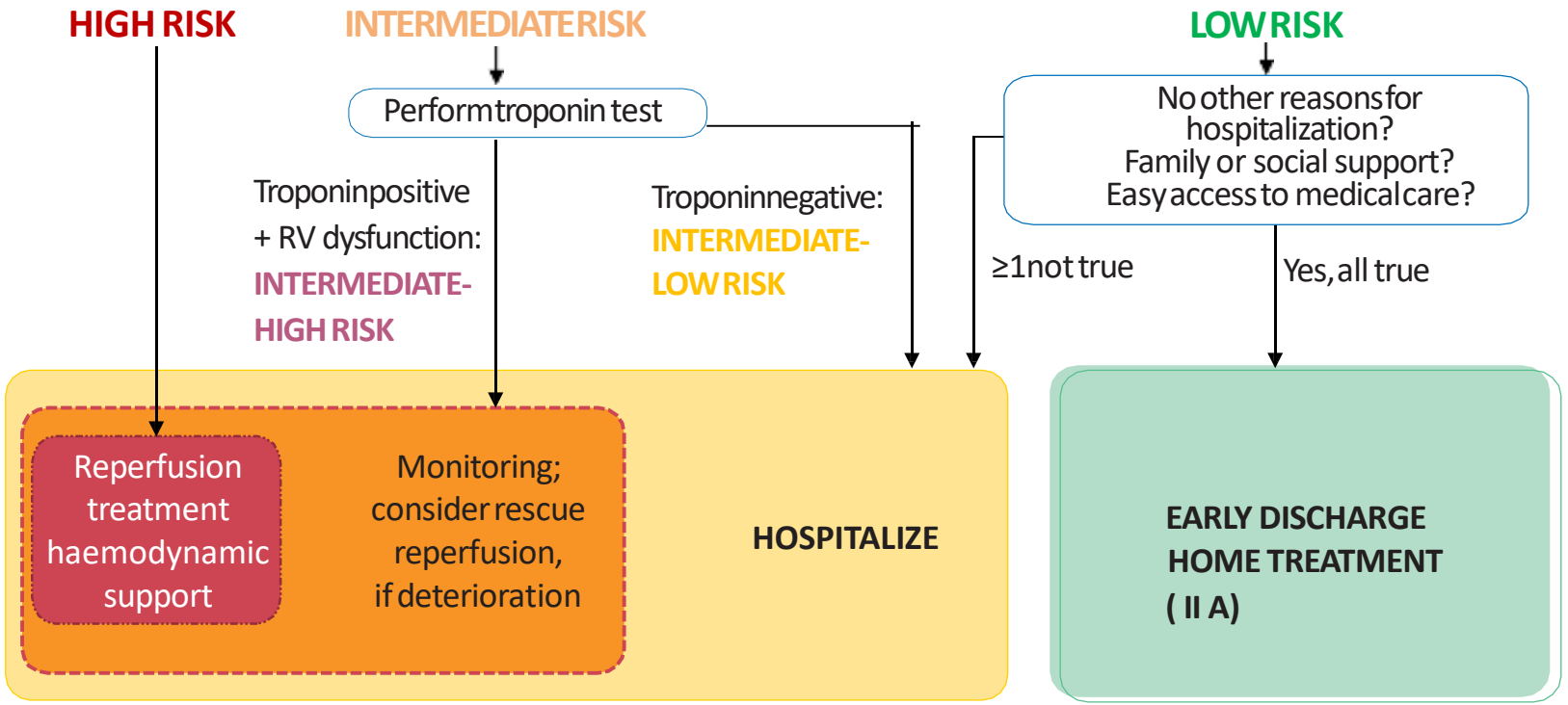
Classification of pulmonary embolism severity and the risk of early death

Early mortality risk		Indicators of risk			
		Haemodynamic instability[a]	Clinical parameters of PE severity and/or comorbidity: PESI class III–V or sPESI ≥1	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

Risk-adjusted management strategy for acute PE



CTPA = computed tomography pulmonary angiography; PESI = Pulmonary Embolism Severity Index; RV = right ventricular; TTE = transthoracic echocardiography.

ACUTE PHASE TREATMENT FOR HIGH RISK PE

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Recommendations	Class[b]	Level[c]
It is recommended that anticoagulation with UFH, including a weight-adjusted bolus injection, be initiated without delay in patients with high-risk PE.	I	C
Systemic thrombolytic therapy is recommended for high-risk PE. [282]	I	B
Surgical pulmonary embolectomy is recommended for patients with high-risk PE, in whom thrombolysis is contraindicated or has failed.[d] [281]	I	C
Percutaneous catheter-directed treatment should be considered for patients with high-risk PE, in whom thrombolysis is contraindicated or has failed.[d]	IIa	C
Norepinephrine and/or dobutamine should be considered in patients with high-risk PE.	IIa	C
ECMO may be considered, in combination with surgical embolectomy or catheter-directed treatment, in patients with PE and refractory circulatory collapse or cardiac arrest.[d] [252]	IIb	C

CHANGE IN RACCOMANDATIONS 2014-2019

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RECCOMANDATIONS	2014	2019
RESUE THROMBOLITIC THERAPY IS RECOMMENDED FOR PATIENTS WHO DETERIORATE HAEMODINAMICALLY	II a	I
SURGICAL EMBOLECTOMY OR CATHETER-DIRECTED TREATMENT WHEN TROMBOLISIS FAILED OR CONTROINICATED….	II b	II a

Main NEW recommendations for acute-phase treatment in patient without haemodinamic instability

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Treatmentin the acute phase	
When oral anticoagulation is initiated in a patient with PE who is eligible for a NOAC (apixaban,dabigatran, edoxaban, or rivaroxaban), a NOAC is the recommended form of anticoagulant treatment.	I

Recommendation	Class[a]	Level[b]
Set-up of a multidisciplinary team and a programme for the management of high- and (in selected cases) intermediate-risk PE should be considered, depending on the resources and expertise available in each hospital.	IIa	C

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PULMUNOLGY

CARDIOLOGY

INTERVENTIONAL RADIOLOGY

MULTIDISCIPLINARY PULMONARY EMBOLISM TEAMS

CARDIOTHORACIC SURGERY

HAEMATOGY

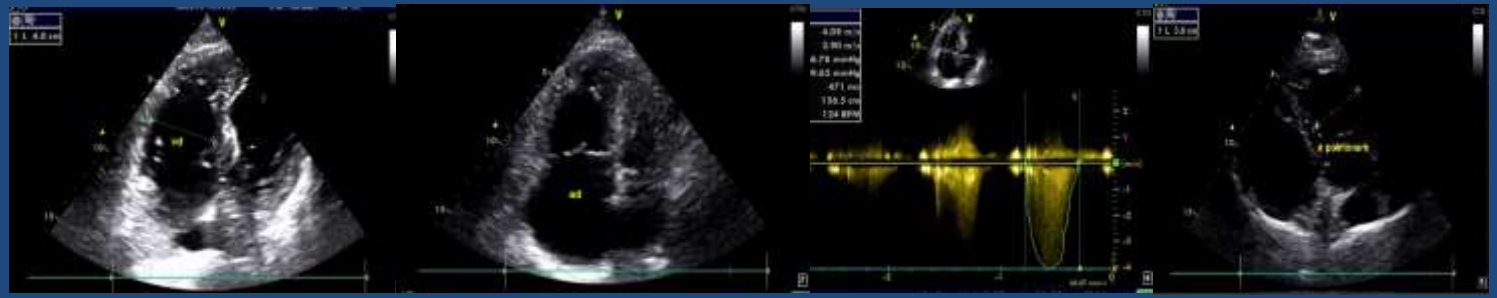
ANAESTESIOLOGY/ INTENSIVE CARE

VASCULAR MEDICINE

DALLE «GUIDELINES» ALLA REAL -LIFE

B.G. ANNI 90
DISPNEA, DOLORE TORACICO
SO2 82%, PA 100/60 MMHG
Segni ecg di sovraccarico dx .

ECOCOLORDOPPLER CARDIACO 2 D



DILATAZIONE SEZIONI DX

PAPS STIMATA 80 mmHG

DILATAZIONE A.POLMONARE

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RISK ASSESMENT

PESI II CLASSE (PUNTEGGIO 85)
SEGNI DI DISFUNZIONE VD +
TROPONINA I 102 pg/ml
-DDimero 1882 ng/ml

PAZIENTE NELLA CATERGORIA DI RISCHIO INTERMEDIO ALTO

DALLE «GUIDELINES» ALLA REAL-LIFE

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ENOXAPARINA 6000 FL 1 FL SC 2 VOLTE AL GIORNO
(DOSAGGIO DI 1 MG/KG 2 VOLTE AL GIORNO)

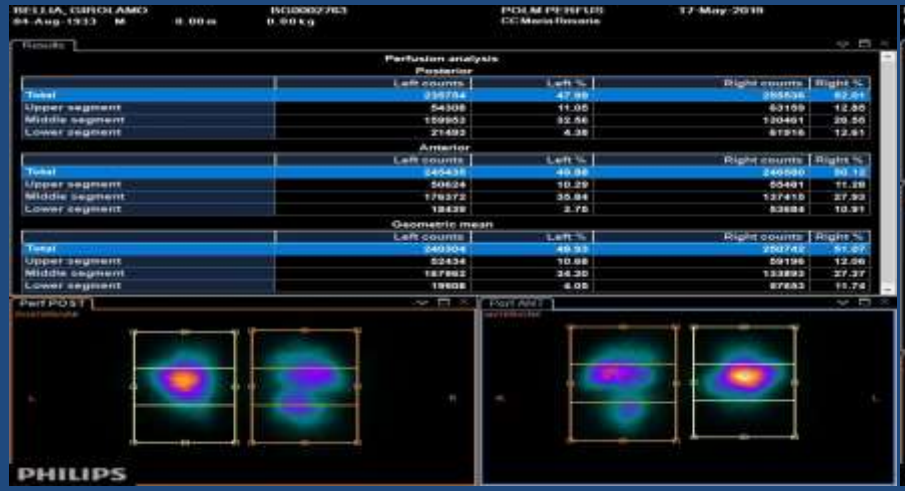
PER 2 GG

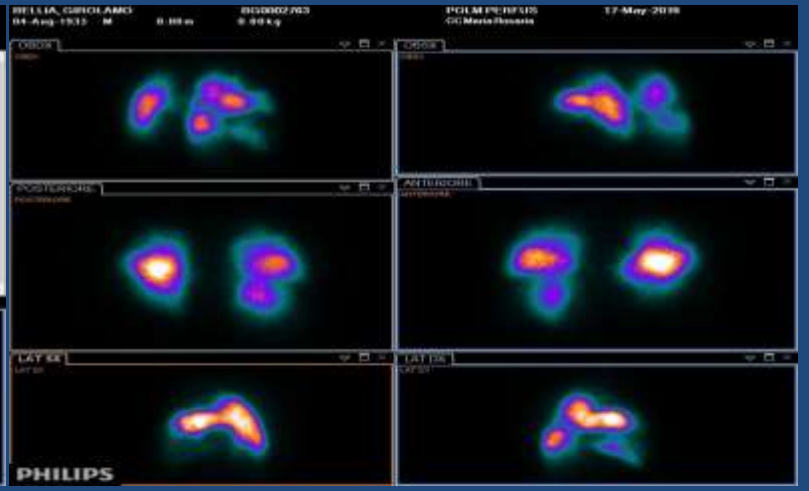
INIZIO TERAPIA CON RIVAROXABAN 15 MG/BIS DIE PER 21 GG

A SEGUIRE 15 MG/DIE

BUONO IL DECORSO CLINICO

DALLE «GUIDELINES» ALLA REAL-LIFE





V/Q SCAN :

«…lo studio con radioisotopo..ha messo in evidenza multiple aree di ipoperfusione a carico di entrambi i polmoni»

CHRONIC TREATMENT AND PREVENTION OF RECURRENCE
CATEGORY RISK

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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 (3–8% per year)	Transient or reversible factors associated with ≤10-fold increased risk for **first** (index) VTE	• Minor surgery (general anaesthesia for <30 min) • Admission to hospital for <3 days with an acute illness • Oestrogen therapy/contraception • Pregnancy or puerperium • **Confined** to bed out of hospital for ≥3 days with an acute illness • Leg injury (without fracture) associated with reduced mobility for ≥3 days • Long-haul **flight**
	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

Main NEW recommendations for chronic/extended treatment

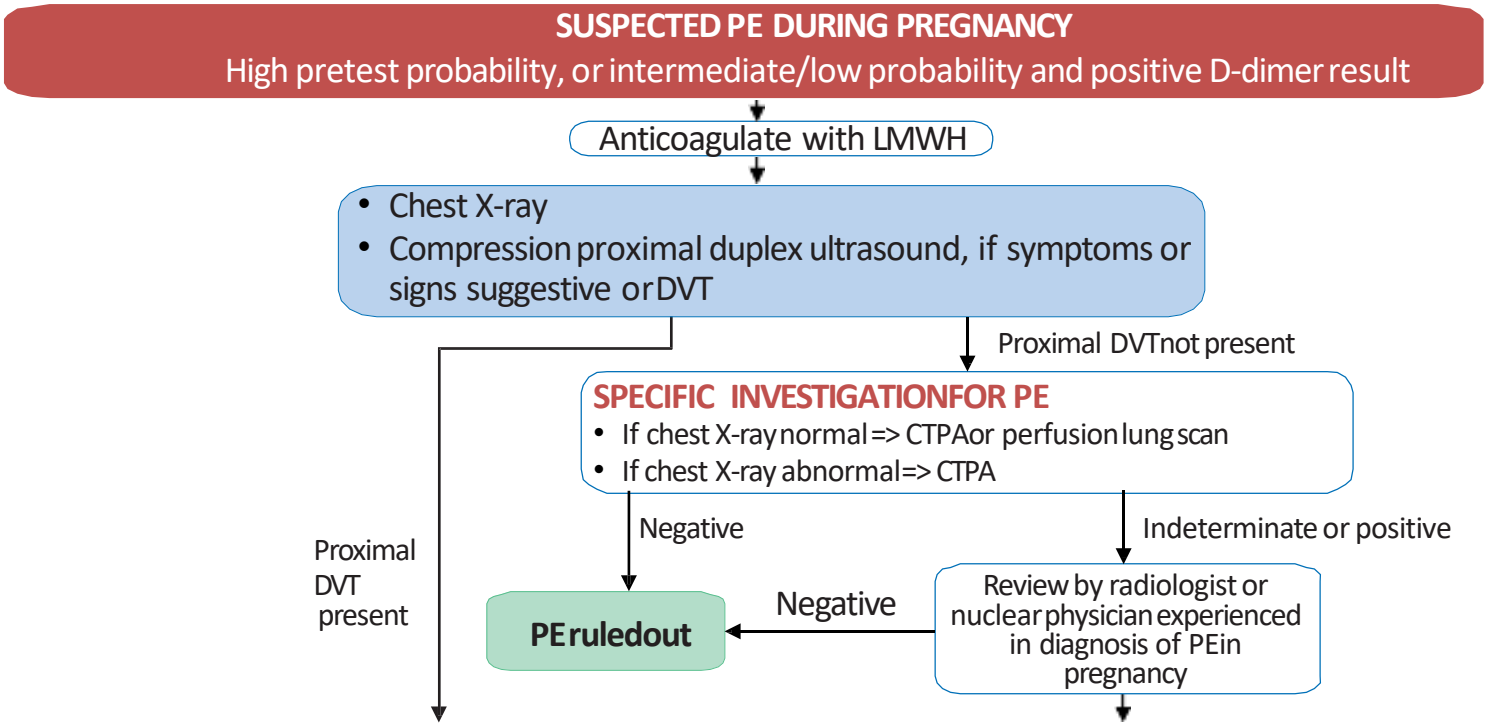
Chronic treatment and prevention of recurrence in patients without cancer	
Indefinite treatment with a VKA in patients with the antiphospholipid antibody syndrome.	I
Extended anticoagulation for patients with no identifiable risk factor for the index PE event.	IIa
Extended anticoagulation for patients with a persistent risk factor other than the antiphospholipid antibody syndrome.	IIa
Extended anticoagulation for patients with a minor transient/reversible risk factor for the index PE event.	IIa
Reduced dose of apixaban or rivaroxaban after the first 6 months.	IIa
Pulmonary embolism in patients with cancer	
Edoxaban or rivaroxaban as an alternative to LMWH, with the exception of patients with gastro intestinal cancer.	IIa

www.escardio.org/guidelines

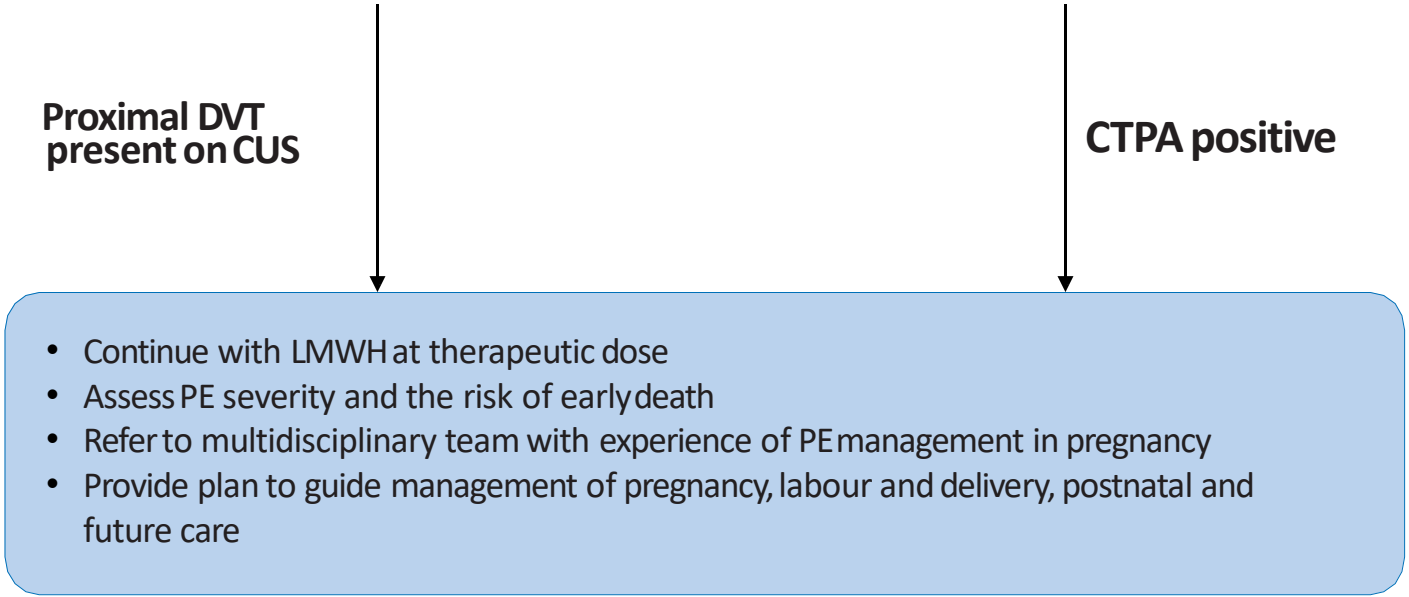
2019 ESC Guidelines on the diagnosis and management of acute pulmonary embolism
(European Heart Journal 2019 - doi/10.1093/eurheartj/ehz405)

Recommendations	Class[a]	Level[b]
Therapeutic anticoagulation for ≥ 3 months is recommended for all patients with PE.[347]	I	A
Patients in whom discontinuation of anticoagulation after 3 months is recommended		
For patients with first PE/VTE secondary to a major transient/reversible risk factor, discontinuation of therapeutic oral anticoagulation is recommended after 3 months.[331,340,341]	I	B
Patients in whom extension of anticoagulation beyond 3 months is recommended		
Oral anticoagulant treatment of indefinite duration is recommended for patients presenting with recurrent VTE (that is, with at least one previous episode of PE or DVT) not related to a major transient or reversible risk factor.[358]	I	B
Oral anticoagulant treatment with a VKA for an indefinite period is recommended for patients with antiphospholipid antibody syndrome.[359]	I	B
Patients in whom extension of anticoagulation beyond 3 months should be considered[c,d]		
Extended oral anticoagulation of indefinite duration should be considered for patients with a first episode of PE and no identifiable risk factor.[330,331,347,351–353]	IIa	A
Extended oral anticoagulation of indefinite duration should be considered for patients with a first episode of PE associated with a persistent risk factor other than antiphospholipid antibody syndrome.[330,352,353]	IIa	C
Extended oral anticoagulation of indefinite duration should be considered for patients with a first episode of PE associated with a minor transient or reversible risk factor.[330,331,352]	IIa	C
NOAC dose in extended anticoagulation[e]		
If extended oral anticoagulation is decided after PE in a patient without cancer, a reduced dose of the NOACs apixaban (2.5 mg b.i.d.) or rivaroxaban (10 mg o.d.) should be considered after 6 months of therapeutic anticoagulation.[352,353]	IIa	A
Extended treatment with alternative antithrombotic agents		
In patients who refuse to take or are unable to tolerate any form of oral anticoagulants, aspirin or sulodexide may be considered for extended VTE prophylaxis.[353–357]	IIb	B
Follow-up of the patient under anticoagulation		
In patients who receive extended anticoagulation, it is recommended that their drug tolerance and adherence, hepatic and renal[f] function, and bleeding risk be reassessed at regular intervals.[359]	I	C

Diagnostic work-up for suspected PE during pregnancy and up to 6 weeks postpartum (1)



Diagnostic work-up for suspected PE during pregnancy and up to 6 weeks postpartum (2)



CTPA = computed tomography pulmonary angiography; CUS = compression venous ultrasound; DVT = deep vein thrombosis; LMWH = low molecular weight heparin.

Main NEW recommendations for post PE care

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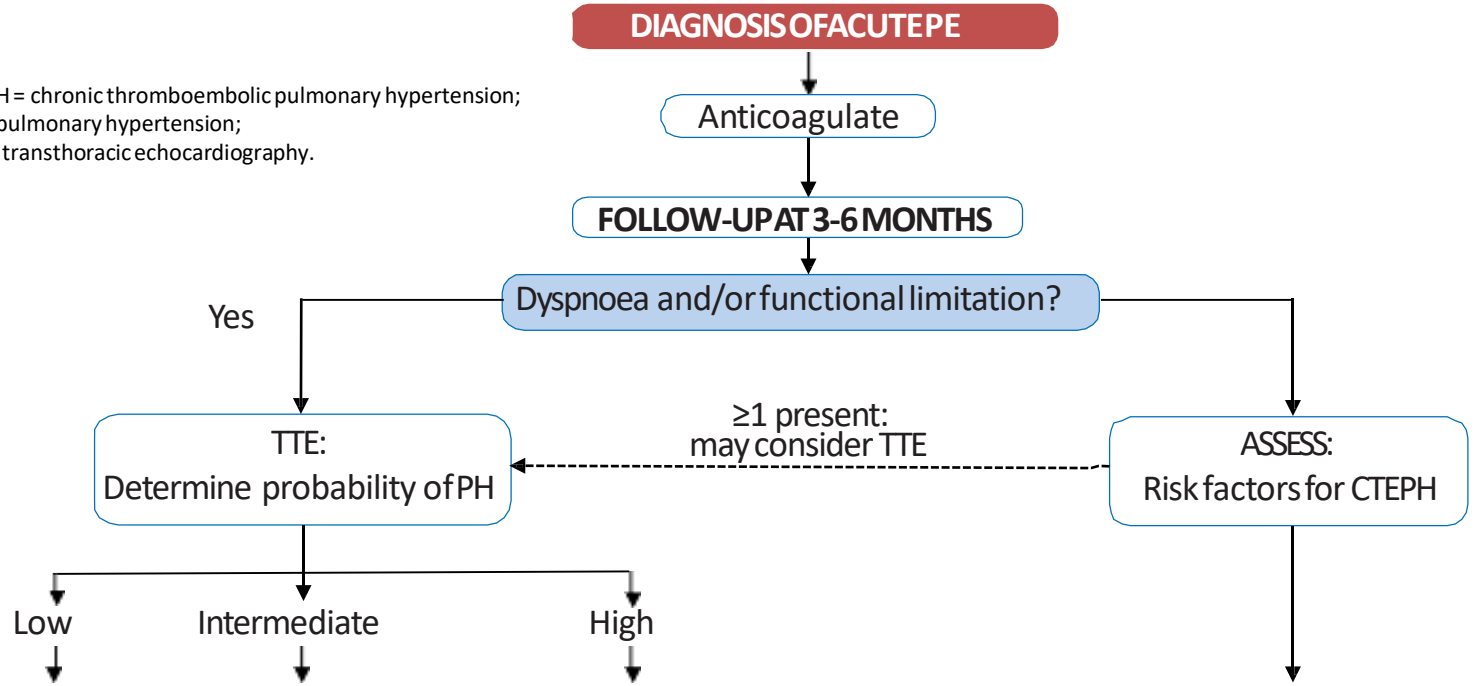
Post-PE care and long-term sequelae	
Routine clinical evaluation is recommended3 to 6 months after acute PE.	I
Integrated model of care is recommended after acute PE to ensure optimal transition from hospital to ambulatory care.	I
It is recommendedto refer symptomatic patients with mismatchedperfusion defects on V/Q scan beyond 3 months after acutePE to a pulmonary hypertension/CTEPH expert centre, taking into account the results of echocardiographyn, natriuretic peptide and/or cardiopulmonary exercise testing.	I

Follow-up strategy and diagnostic work-up for long-term sequelae of PE (1)

CTEPH = chronic thromboembolic pulmonary hypertension;
PH = pulmonary hypertension;
TTE = transthoracic echocardiography.



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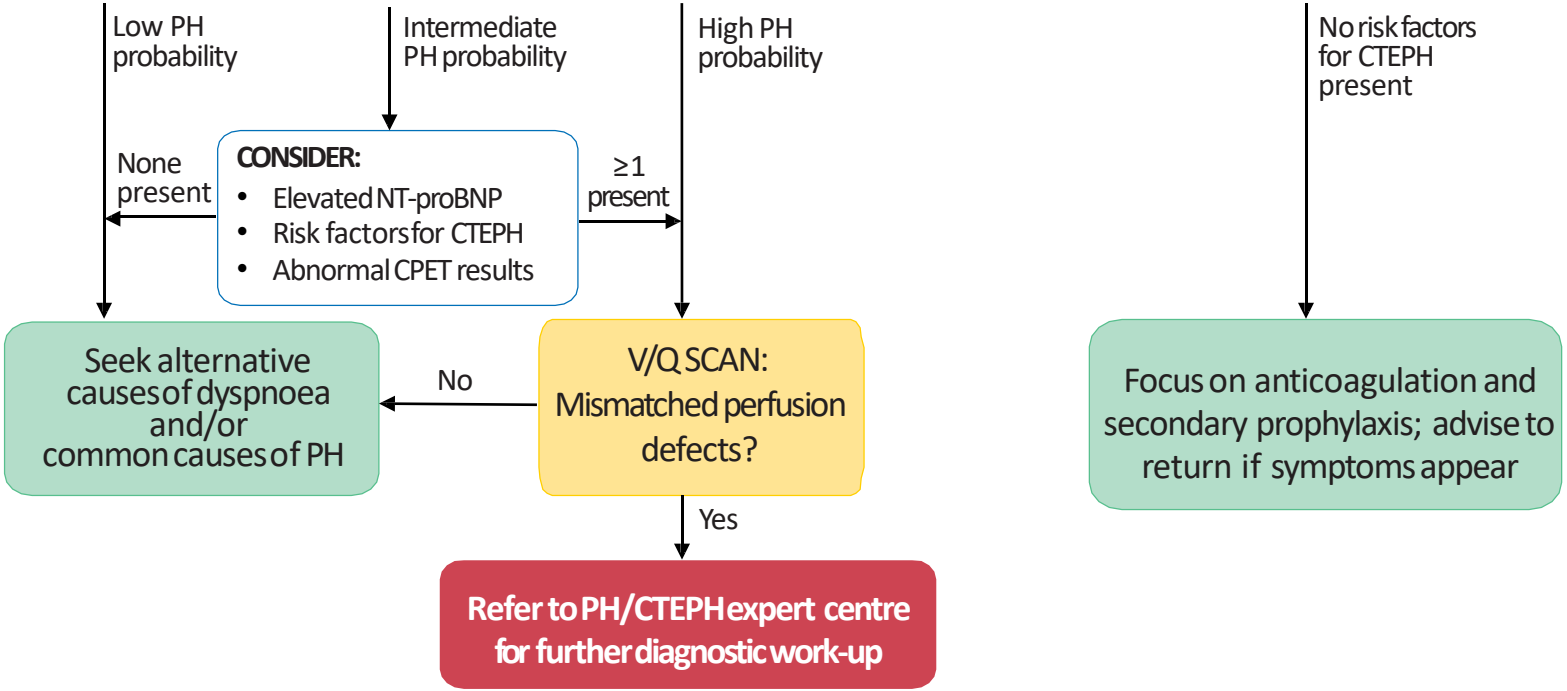
Follow-up strategy and diagnostic work-up for long-term sequelae of PE (2)



CPET = cardiopulmonary exercise testing; CTEPH = chronic thromboembolic pulmonary hypertension; NT-proBNP = N-terminal pro B-type natriuretic peptide; PH = pulmonary hypertension; V/Q = ventilation/perfusion.

FATTORI DI RISCHIO E CONDIZIONI PREDISPONENTI LA *CTEPH*

ELEMENTI LEGATI AD EPISODIO ACUTO	COMORBILITA' E CONDIZIONI CLINICHE PREDISPONENTI
-EPISODIO PRECEDENTE DI TEV -INTERESSAMENTO DEI RAMI PROSSIMALI DELL' A. POLMONARE -SEGNI DI DISFUNZIONE DEL VD	-SEPSI CONCOMITANTE -PREGRESSA SPLENECTOMIA -TROMBOFILIA -IPOTIROIDISMO -PATOLOGIA ONCOLOGICA - DISTURBO INFIAMMATORIO SISTEMICO

«WHAT TO DO AND WHAT NOT TO DO»

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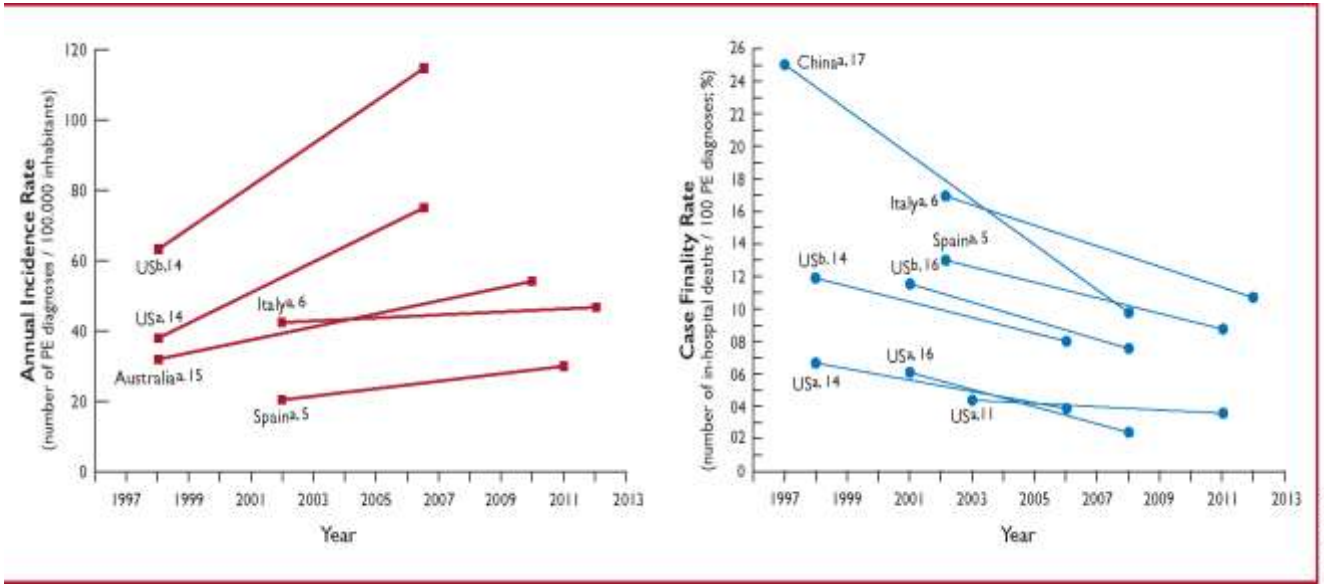
Diagnosis	Class[a]
In suspected high-risk PE, perform bedside echocardiography or emergency CTPA (depending on availability and clinical circumstances) for diagnosis.	I
In suspected high-risk PE, initiate intravenous anticoagulation with UFH without delay, including a weight-adjusted bolus injection.	I
In suspected PE without haemodynamic instability, use validated diagnostic criteria.	I
In suspected PE without haemodynamic instability, initiate anticoagulation in case of high or intermediate clinical probability, while diagnostic workup is in progress.	I
Base the diagnostic strategy on clinical probability, using either clinical judgement or a validated prediction rule.	I
Measure D-dimers in plasma, preferably with a highly sensitive assay, in outpatients/emergency department patients with low or intermediate clinical probability, or who are PE-unlikely.	I
Reject the diagnosis of PE (without further testing) if CTPA is normal in a patient with low or intermediate clinical probability, or if the patient is PE-unlikely.	I
Reject the diagnosis of PE (without further testing) if the perfusion lung scan is normal.	I
Accept the diagnosis of PE if CTPA shows a segmental or more proximal filling defect in a patient with intermediate or high clinical probability.	I
Accept the diagnosis of VTE if CUS shows a proximal DVT in a patient with clinical suspicion of PE.	I
Do not measure D-dimers in patients with high clinical probability, as a normal result does not safely exclude PE.	III
Do not perform CT venography as an adjunct to CTPA.	III
Do not perform MRA to rule out PE.	III
Risk assessment	
Stratify patients with suspected or confirmed PE, based on the presence of haemodynamic instability, to identify those at high risk of early mortality.	I
In patients without haemodynamic instability, further stratify PE into intermediate- and low-risk categories.	I
Treatment in the acute phase	
Administer systemic thrombolytic therapy to patients with high-risk PE.	I
Surgical pulmonary embolectomy for patients with high-risk PE, in whom recommended thrombolysis is contraindicated or has failed.	I
When oral anticoagulation is initiated in a patient with PE who is eligible for a NOAC (apixaban, dabigatran, edoxaban, or rivaroxaban), prefer a NOAC.	I
As an alternative to a NOAC, administer a VKA, overlapping with parenteral anticoagulation until an INR of 2.5 (range 2.0 – 3.0) has been reached.	I
Administer rescue thrombolytic therapy to a patient with haemodynamic deterioration on anticoagulation treatment.	I
Do not use NOACs in patients with severe renal impairment or in those with antiphospholipid antibody syndrome.	III
Do not routinely administer systemic thrombolysis as primary treatment in patients with intermediate- or low-risk PE.	III
Do not routinely use inferior vena cava filters.	III
Chronic treatment and prevention of recurrence	
Administer therapeutic anticoagulation for ≥3 months to all patients with PE.	I
Discontinue therapeutic oral anticoagulation after 3 months in patients with first PE secondary to a major transient/reversible risk factor.	I
Continue oral anticoagulant treatment indefinitely in patients presenting with recurrent VTE (at least one previous episode of PE or DVT) that is not related to a major transient or reversible risk factor.	I
Continue oral anticoagulant treatment with a VKA indefinitely in patients with antiphospholipid antibody syndrome.	I
In patients who receive extended anticoagulation, reassess drug tolerance and adherence, hepatic and renal function, and the bleeding risk at regular intervals.	I
PE in pregnancy	
Perform formal diagnostic assessment with validated methods if PE is suspected during pregnancy or in the post-partum period.	I
Administer therapeutic, fixed doses of LMWH, based on early pregnancy weight, in the majority of pregnant women without haemodynamic instability.	I
Do not insert a spinal or epidural needle within 24 h since the last LMWH dose.	III
Do not administer LMWH within 4 h of removal of an epidural catheter.	III
Do not use NOACs during pregnancy or lactation.	III
Post-PE care and long-term sequelae	
Routinely re-evaluate patients 3 – 6 months after acute PE.	I
Implement an integrated model of care after acute PE, in order to ensure optimal transition from hospital to ambulatory care.	I
Refer symptomatic patients with mismatched perfusion defects on V/Q lung scan beyond 3 months after acute PE to a pulmonary	I

TAKE HOME MESSAGE



Trends in annual incidence rates (left panel) and case fatality rates (right panel) of pulmonary embolism ...

WE CAN DO BETTER !!!!

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THANKS FOR THE ATTENCTION!