Luca Paris

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Shock ostruttivo nella tromboembolia polmonare e gestione della terapia in acuto

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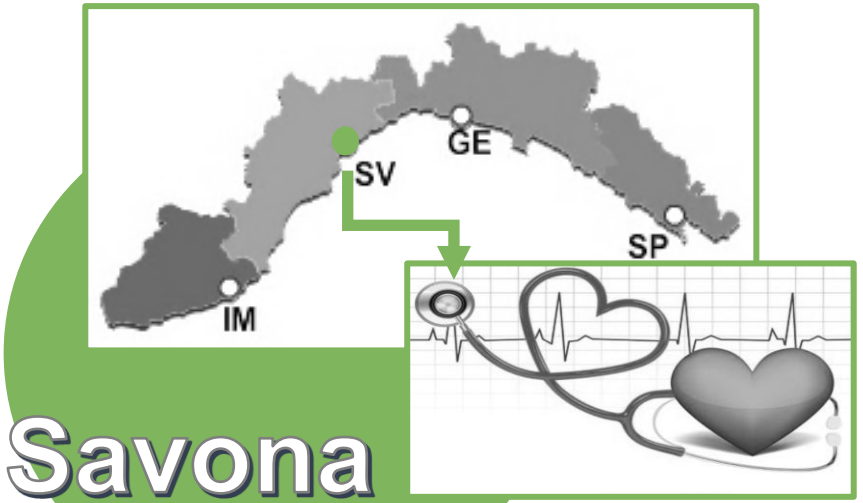

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Review

An Update on the Management of Acute High-Risk Pulmonary Embolism

Romain Chopard [1,2,3,*], Julien Behr [4], Charles Vidoni [1], Fiona Ecarnot [1,2] and Nicolas Meneveau [1,2,3]

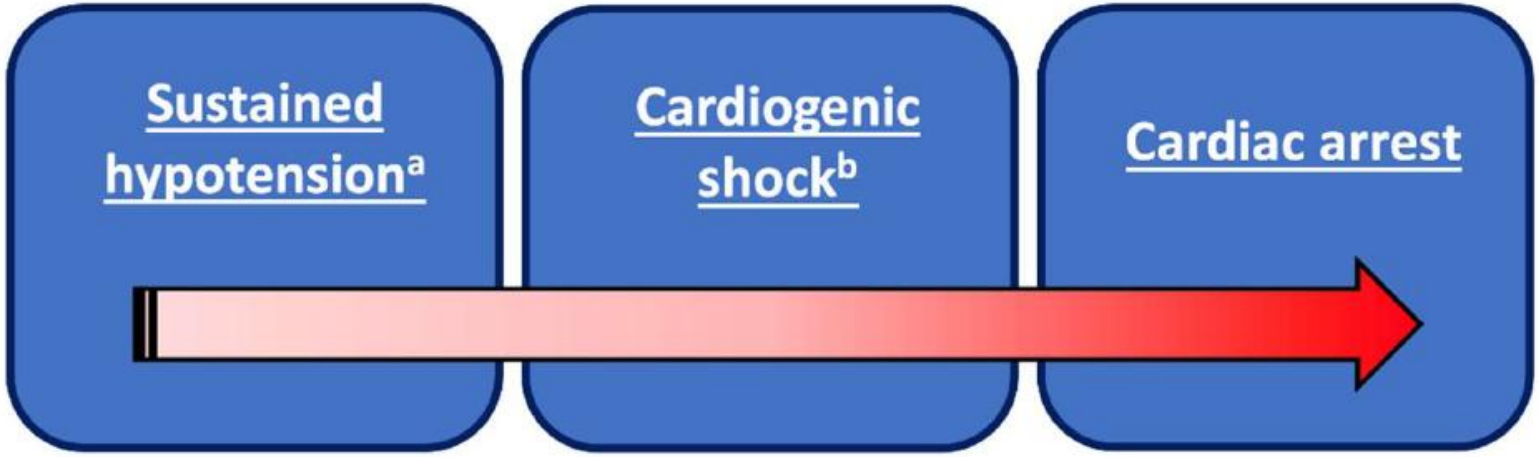

Figure 1. Clinical spectrum of high-risk pulmonary embolism. (a) Systolic blood pressure (BP) < 90 mmHg or systolic BP drop ≥ 40 mmHg, lasting longer than 15 min, and not caused by new-onset arrhythmia, hypovolemia, or sepsis; (b) systolic BP < 90 mmHg or vasopressors required to achieve a BP ≥ 90 mmHg despite adequate filling status and end-organ hypoperfusion (altered mental status; cold, clammy skin; oliguria/anuria; increased serum lactate > 2.4 mmol/L).

An Update on the Management of Acute High-Risk Pulmonary Embolism. *J. Clin. Med.* 2022, *11*, 4807.

FISIOPATOLOGIA EMBOLIA POLMONARE ALTO RISCHIO

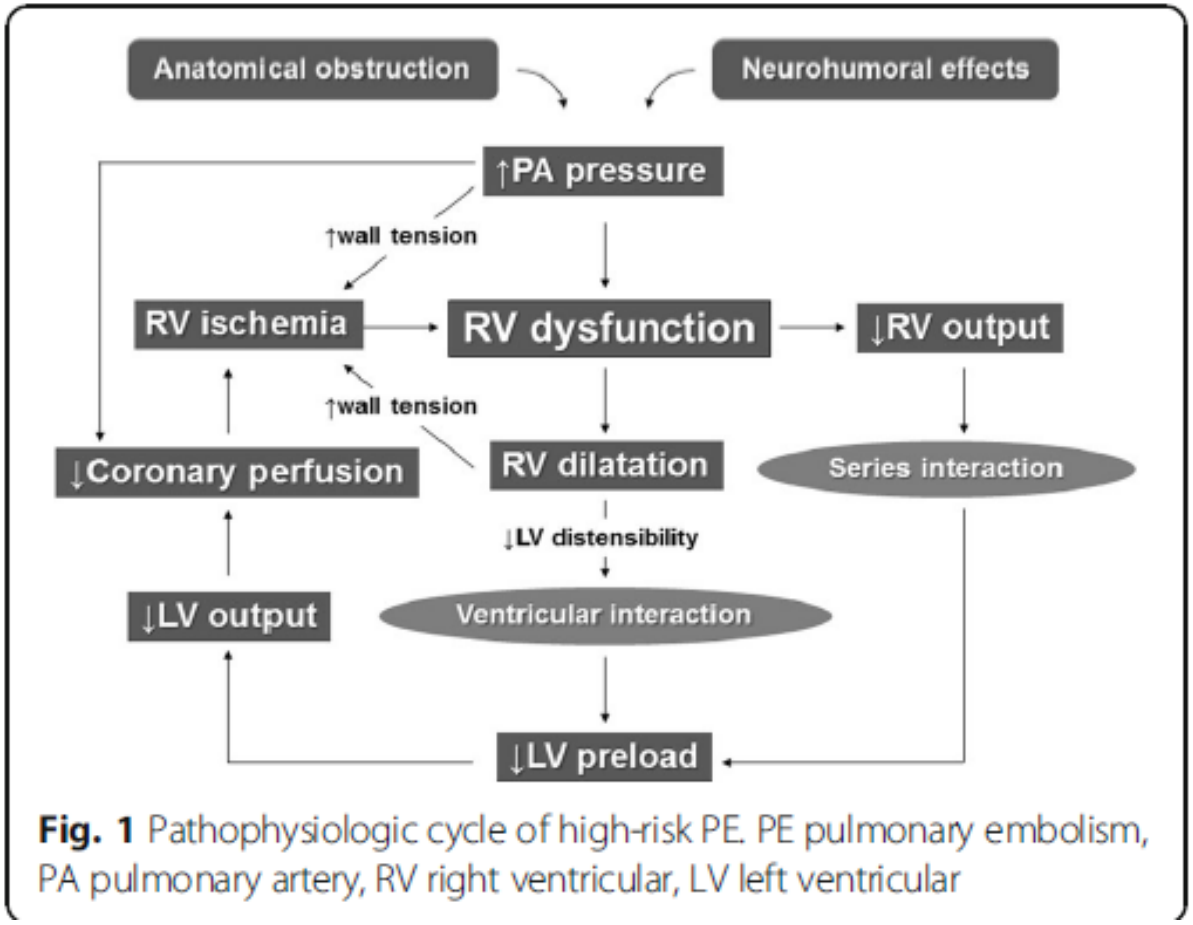

Fig. 1 Pathophysiologic cycle of high-risk PE. PE pulmonary embolism, PA pulmonary artery, RV right ventricular, LV left ventricular

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Epidemiologia EMBOLIA POLMONARE

-Incidenza 39-115 casi/100000

-incidenza aumenta in modo significativo con aumentare età

- soggetti >80 anni hanno incidenza 8 volte superiore rispetto a quelli di 40-50 anni

Keller K, et al Eur Heart Journal 2020;41:522-9
Wendelboe AM, et al Circ Res 2016; 118:1340-7

-incidenza annuale età correlata è più alta uomini rispetto alle donne (130 casi/100000 VS 110 casi/100000)

-Età 16-44 anni più frequente nelle donne

Engbers MJ, et al Thromb Haemost 2010; 8:2105-12

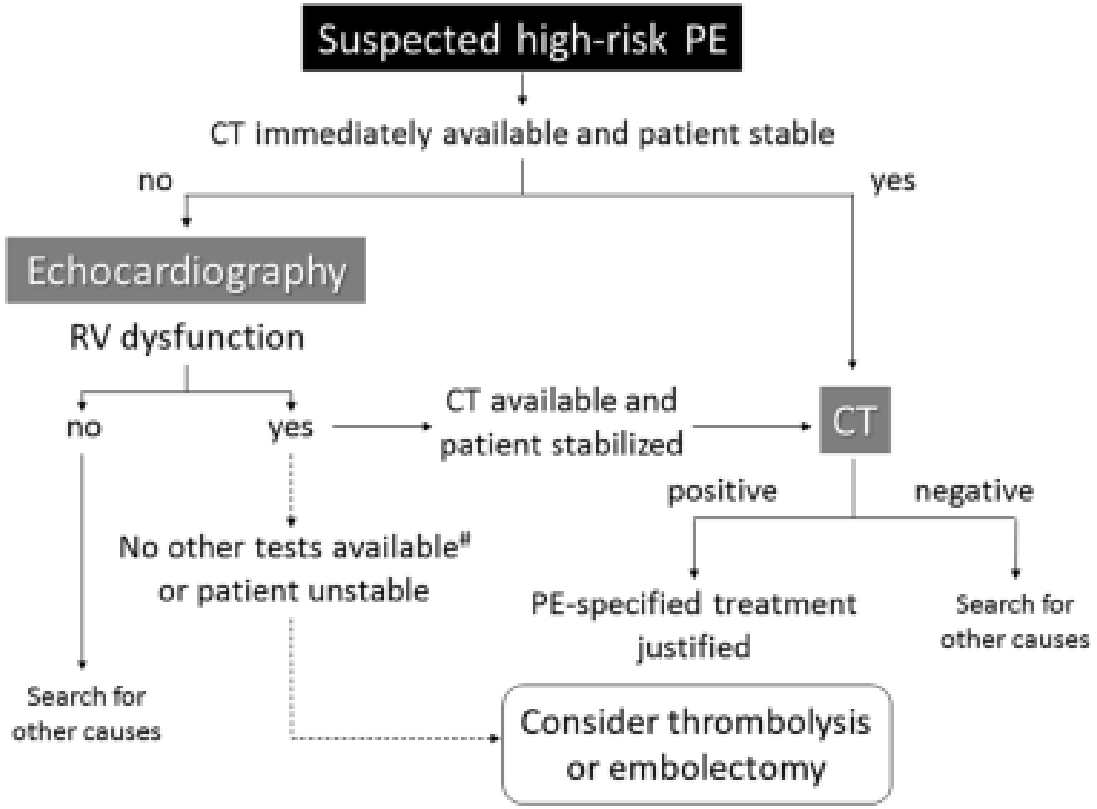

Fig. 2 Proposed diagnostic algorithm for patients with suspected high-risk PE. #Apart from the diagnosis of RV dysfunction, bedside transthoracic echocardiography may, in some cases, directly confirm PE by visualizing mobile thrombi in the right heart chambers. Ancillary bedside imaging tests include transesophageal echocardiography, which may detect emboli in the pulmonary artery and its main branches, and bilateral compression venous ultrasonography, which may confirm deep vein thrombosis and thus be of help in emergency management decisions. PE pulmonary embolism, RV right ventricular

ALGORITMO DIAGNOSTICO EMBOLIA POLMONARE ALTO RISCHIO

Review

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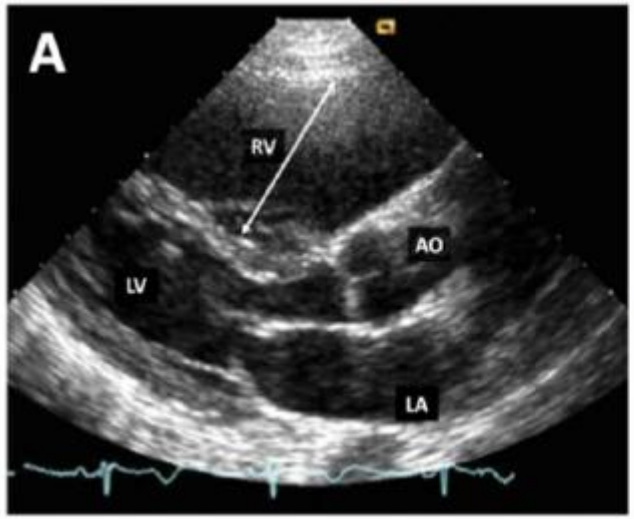
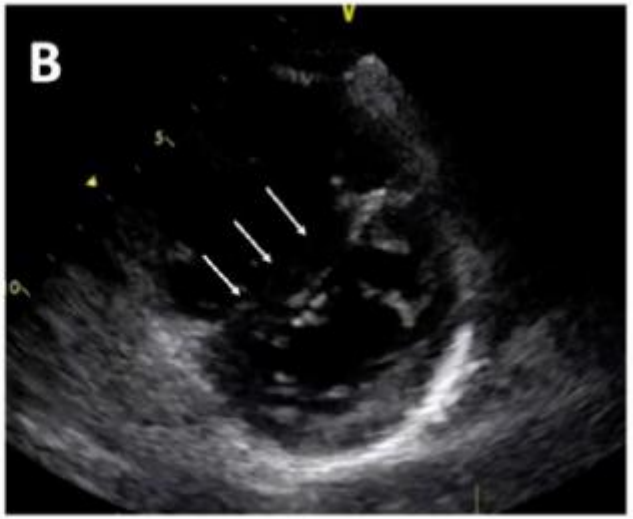
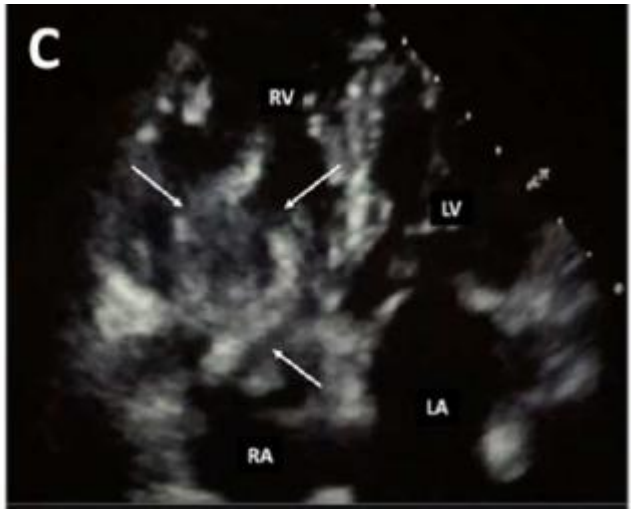
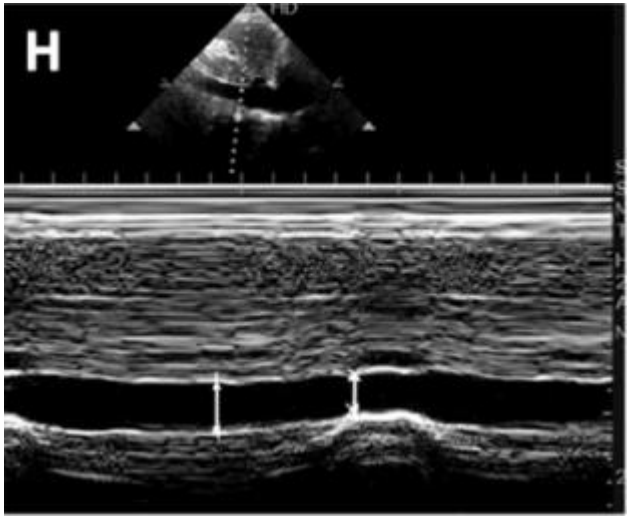




An Update on the Management of Acute High-Risk Pulmonary Embolism. *J. Clin. Med.* 2022, *11*, 4807.





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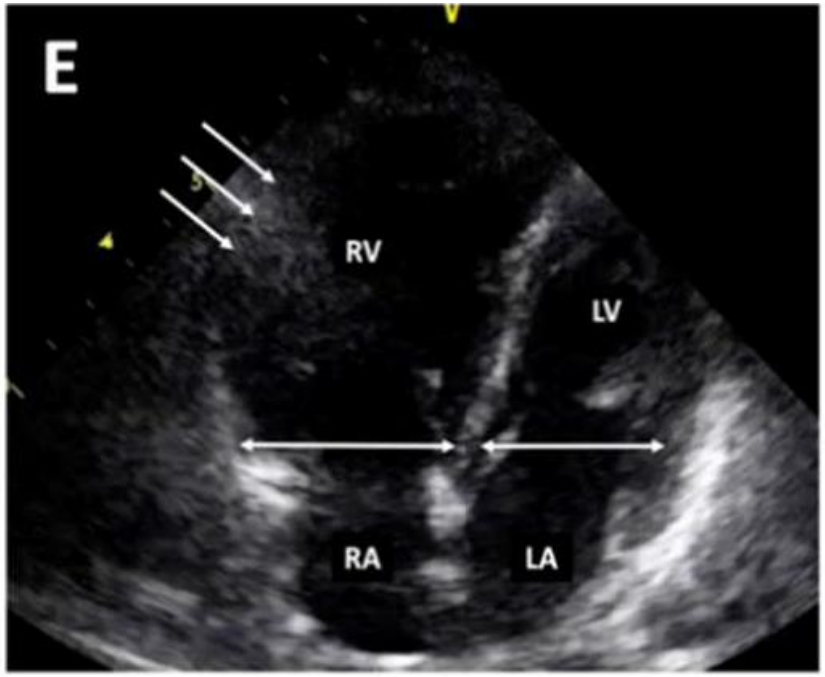
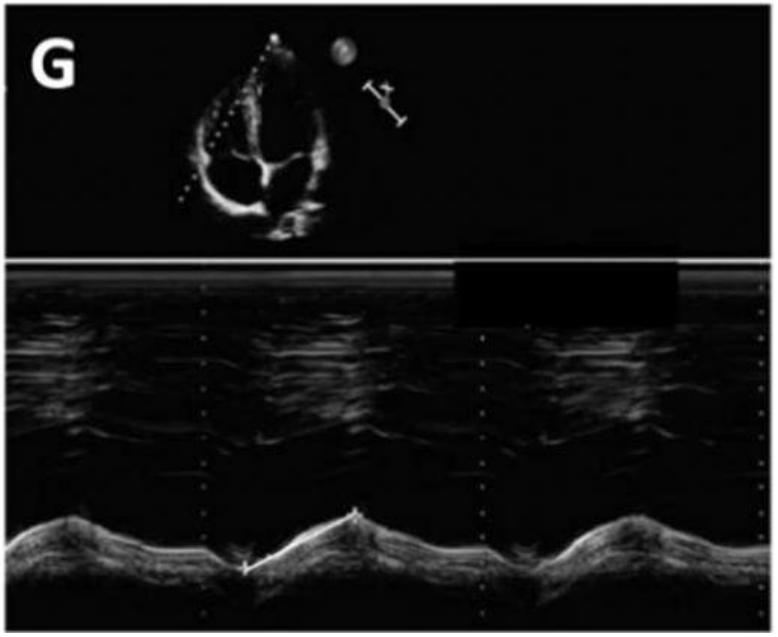


Mc Connel sign



TAPSE< 16 mm

An Update on the Management of Acute High-Risk Pulmonary Embolism. *J. Clin. Med.* 2022, *11*, 4807.

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EMBOLIA POLMONARE: stratificazione rischio e gestione

BOVA-score

1-FC ≥ 110 bpm (+1)

2- PA sistolica 90-100 bpm (+2)

3- alti livelli di troponina I (+2)

4-segni di disfunzione Vdx a ecocardio o angio-TC (+2)

Bova score > 4 punti → mortalità EP correlata a 1 mese del 15,5%

Bova C, Sanchez O, Prandoni P, et al Eur Repir J 2014; 44 (3):694-703

eBOX 1

HESTIA criteria (modified from [27])

HESTIA criteria for exclusion of out-of-hospital care of a patient with PE. If one or more of these criteria are fulfilled, treatment outside the hospital setting is not recommended.

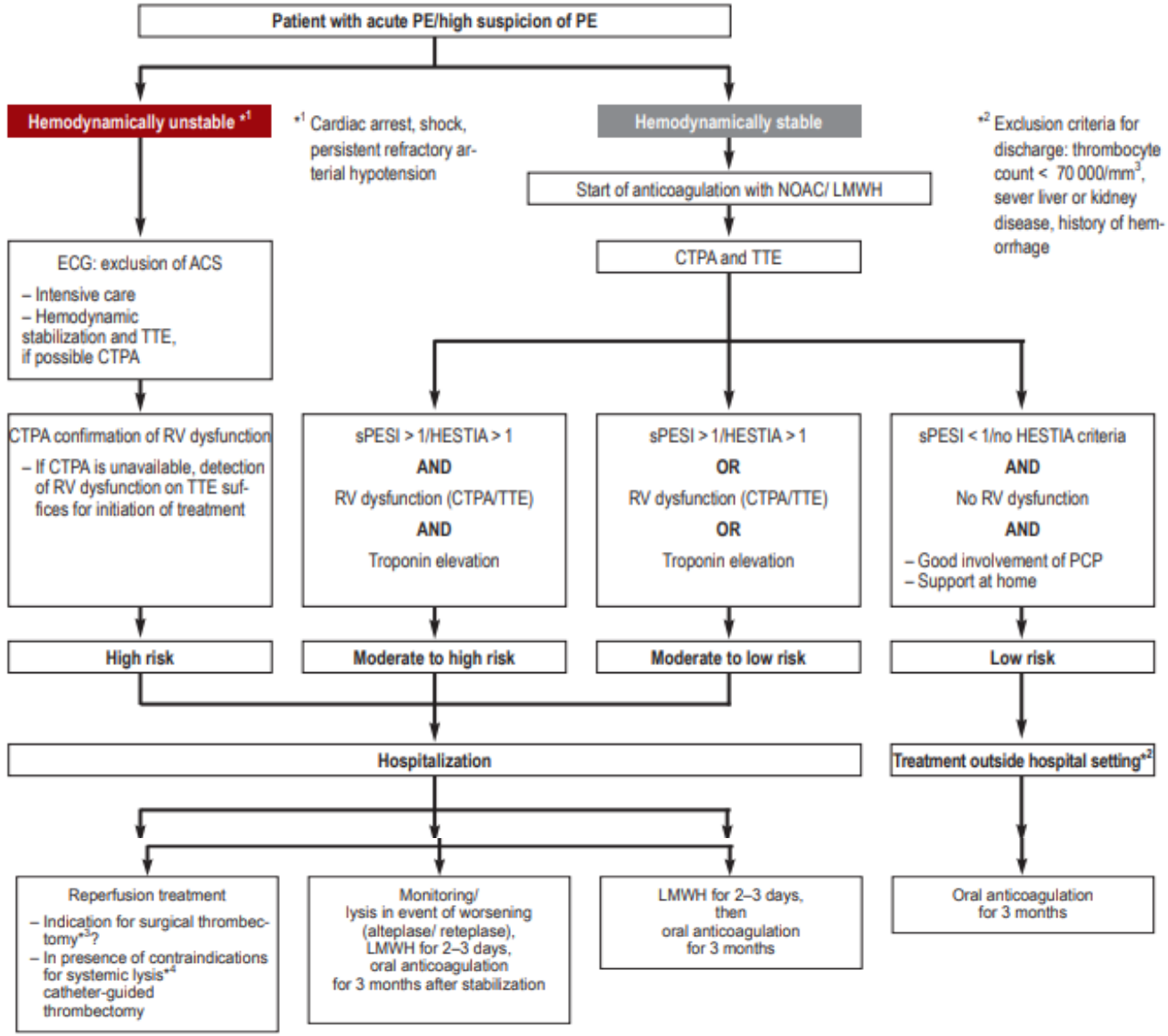
- Hemodynamic instability
- Necessity of thrombolysis or thrombectomy
- Presence of active bleeding or high risk of bleeding
- Need for oxygen therapy ≥ 24 h, $SpO_2 \leq 90$ %
- Diagnosis of PE during ongoing anticoagulation treatment
- Need for intravenous pain treatment ≥ 24 h
- Hospitalization indicated on medical/social grounds
- Creatinine clearance < 30 mL/min
- Severe liver dysfunction
- Pregnancy
- History of HIT (heparin-induced thrombocytopenia)

Contemporary management of acute pulmonary embolism
Trends in Cardiovascular Medicine, July 10 2021;11:48

PE

MANAGEMENT

FIGURE



*3 Massive or submassive PE **AND** one of the following:
- Contraindications to systemic lysis
- Unsuccessful lysis treatment
- Foramen ovale
- Pregnancy
- Right heart failure or cardiogenic shock
- Thrombus visible in right ventricle

*4
- Cerebral hemorrhage in patient's own medical history
- Intracranial tumor or intracranial aneurysm
- Craniocerebral trauma in previous 3 months
- Major surgery in previous 4 weeks
- Surgery in vicinity of brain or spinal cord in previous 2 months

TABLE 2

Criteria of the simplified Pulmonary Embolism Severity Index (sPESI), which enables estimation of the risk of 30-day mortality after diagnosis of PE (5)

Parameter	Score
– Age (if >80 years)	1
– Active tumor disease	1
– Chronic cardiopulmonary disease	1
– Heart rate >100/min	1
– Systolic blood pressure <100 mm Hg	1
– SaO_2 <90%	1

0 points = low (30-day mortality 1%)
≥ 1 point = high (30-day mortality 10.9%)

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GOALS TRATTAMENTO EMBOLIA POLMONARE ACUTA

- STABILIZZAZIONE EMODINAMICA/RESPIRATORIA

-ANTICOAGULAZIONE SISTEMICA

-RIPERFUSIONE ARTERIOSA POLMONARE

Martinez Licha CR, et al Ann Thorac Cardiovasc Surg 2020; 40:902-10

TRATTAMENTO EP ALTO RISCHIO

- Infusione di cristalloidi (500-1000 ml al max): evitare sovvraccarico emodinamico → peggiora la performance Vdx → riduzione del precarico Vsn → riduzione gittata sistolica Vsn

- vasopressori (noradrenalina)

-supporto di ossigeno: meglio ossigenoterapia alti flussi (considerare MOLTA PRUDENZA ventilazione MECCANICA → pressione telesp. plateau < 30 cmH20)

(Konstantinides, Agnelli G, et al ESC 2014, Eur Heart J 2014)

LINEE GUIDA CHEST 2021

Thrombolytic Therapy in Patients With Acute PE

PICO Question: Should systemic thrombolytic therapy vs anticoagulant therapy alone be given to patients with acute pulmonary embolism?:

Guidance statements:

7. In patients with acute PE associated with hypotension (eg, systolic BP < 90 mm Hg) who do not have a high bleeding risk, we suggest systemically administered thrombolytic therapy over no such therapy (weak recommendation, low-certainty evidence).

Remark: Studies of systemically administered thrombolytic therapy have used different agents at varying doses. Due to lack of comparative data between these approaches, the panel does not endorse one agent or dosing strategy over another.

TRATTAMENTO EP ALTO RISCHIO

Trombolisi più EFFICACE se eseguita entro 48 ore

→rapida risoluzione del trombo

→migliora la pressione polmonare

→riduce la disfunzione Vdx

→ effetto emodinamico più RAPIDO vs SOLA ANTIACOAGULAZIONE

Becattini, C.; Agnelli, G. et al Bolus tenecteplase for right ventricle dysfunction in hemodynamically stable patients with pulmonary embolism. Thromb. Res. 2010, 125, e82–e86.

Goldhaber, S ; et al. Alteplase versus heparin in acute pulmonary embolism: Randomised trial assessing right-ventricular function and pulmonary perfusion. Lancet 1993, 341, 507–511. [

TRATTAMENTO EP ALTO RISCHIO

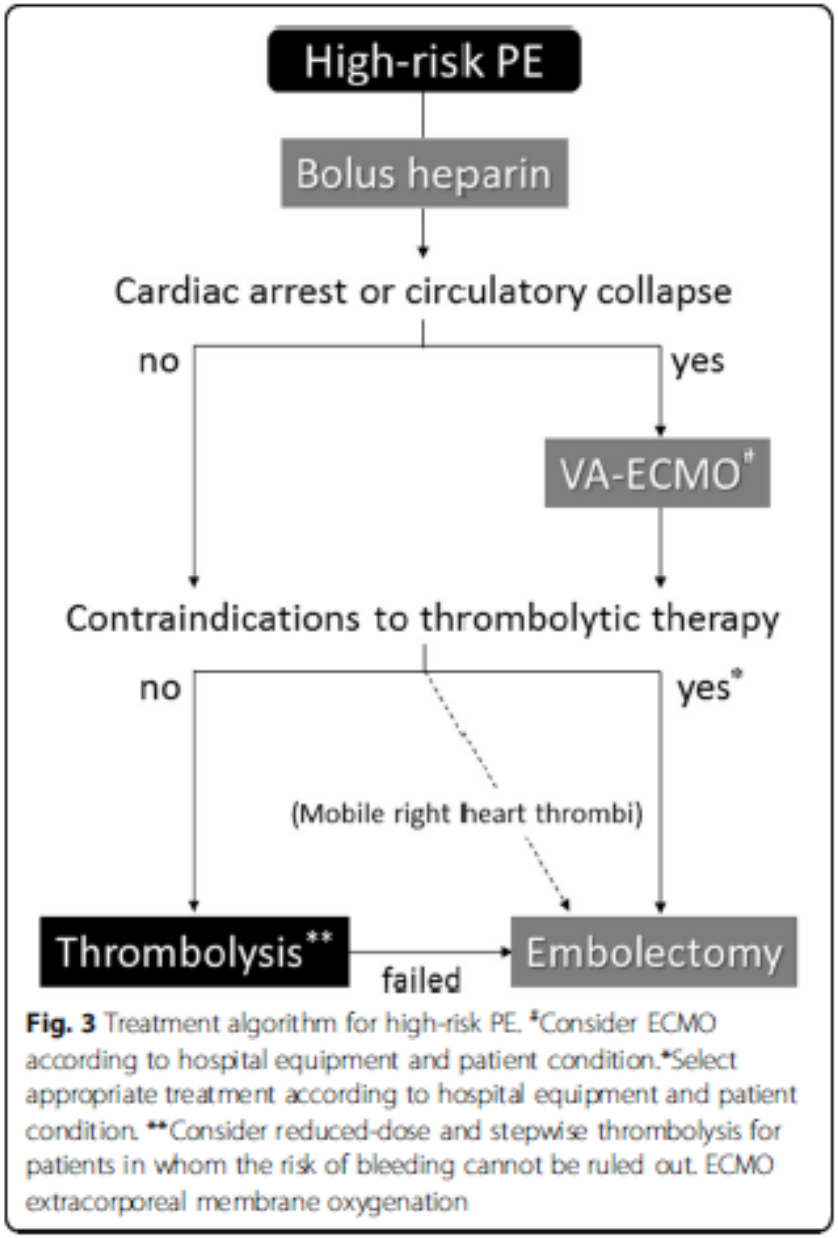

Fig. 3 Treatment algorithm for high-risk PE. #Consider ECMO according to hospital equipment and patient condition. *Select appropriate treatment according to hospital equipment and patient condition. **Consider reduced-dose and stepwise thrombolysis for patients in whom the risk of bleeding cannot be ruled out. ECMO extracorporeal membrane oxygenation

TERAPIE ALTERNATIVE EP ALTO RISCHIO

-TROMBOLISI LOCALE CATETERE DIRETTA

in caso di insuccesso e/o controindicazioni alla trombectomia chirurgica

Kostantinides SV, Meyer G, Becattini C, et al Eur Heart J 2020; 41:543.603

TROMBECTOMIA/EMBOLECTOMIA CHIRURGICA:

mortalità 27,2% in base alla causa di instabilità emodinamica
-arresto cardiaco: 44,4%
-shock: 23,7%
-no shock: 7,9%

Le procedure chirurgiche hanno ridotto la mortalità dal 30 al 70% dal 1960 al 2000

Agnelli G Buller HR, Cohen A, et al J Thromb Haemost 2015; 13:2187-91

AREE DI INCERTEZZA TERAPEUTICA

Early mortality risk		Risk parameters and scores			
		Shock or hypotension	PESI class III-V or sPESI >1[a]	Signs of RV dysfunction on an imaging test[b]	Cardiac laboratory biomarkers[c]
High		+	(+)[d]	+	(+)[d]
Intermediate	Intermediate–high	–	+	Both positive	
	Intermediate–low	–	+	Either one (or none) positive[e]	
Low		–	–	Assessment optional; if assessed, both negative[e]	

Therapeutic strategy for patients at intermediate high risk:

(i)reduced-dose intravenous thrombolysis (SDT) is safe and effective?
(ii)catheter-directed treatment can evolve to become a widely available (and affordable) alternative option

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1006 pz normotensive with intermediate-risk PE (right ventricular dysfunction on echocardiography or TC, as well as myocardial injury as indicated by a positive test for cardiac troponin I or troponin T.)
The primary outcome was death or hemodynamic decompensation (or collapse) within 7 days after RA The main safety outcomes were major extracranial bleeding and ischemic or hemorrhagic stroke within 7 days

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
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)		
Serious adverse events between randomization and day 30	55 (10.9)	59 (11.8)	0.91 (0.62–1.34)	0.63

EFFICACY OUTCOME

SAFETY OUTCOME

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Fibrinolysis for Patients with Intermediate-Risk Pulmonary Embolism

PEITHO

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

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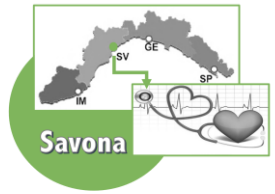

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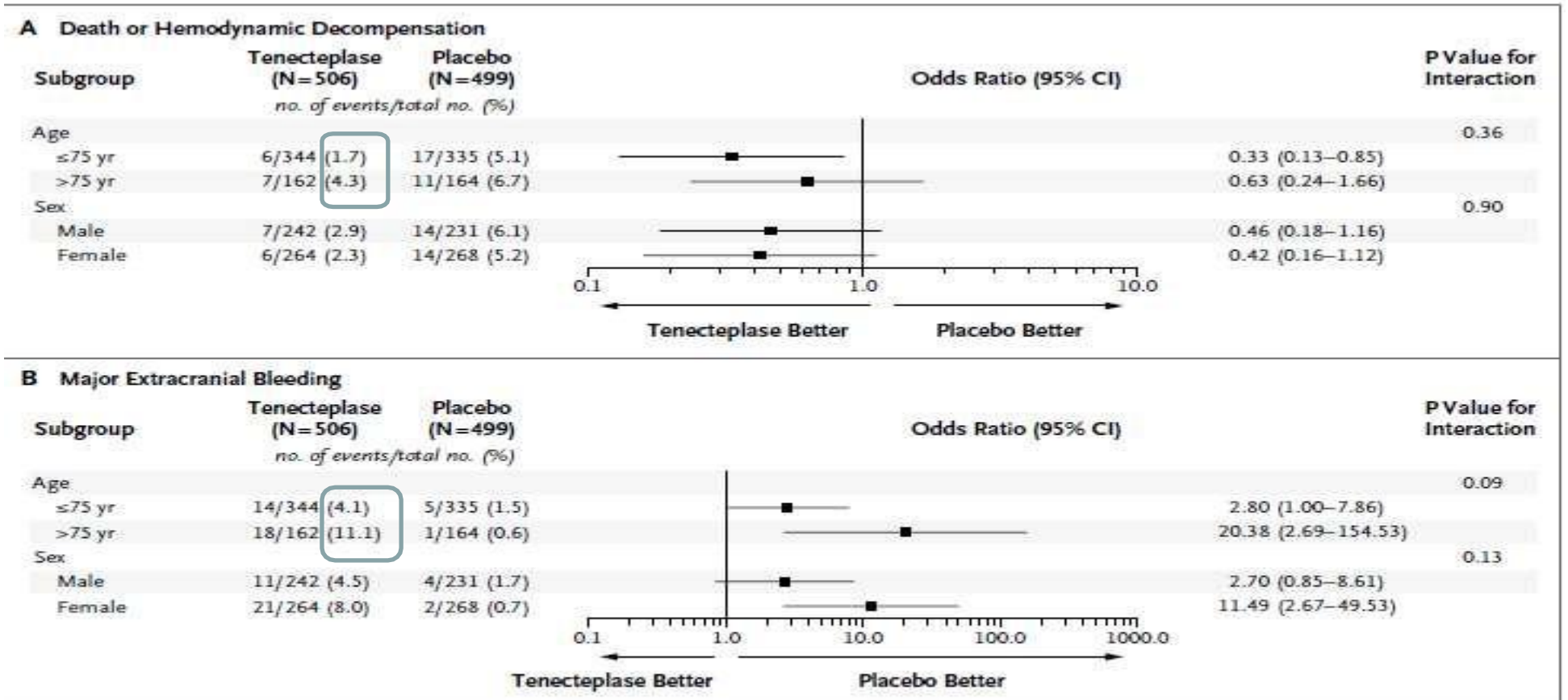

Figure 1. Efficacy and Safety Outcomes in Prespecified Subgroups.
Panel A shows the primary efficacy outcome (death or hemodynamic decompensation), and Panel B shows a safety outcome (major extracranial bleeding), both within 7 days after randomization.

The NEW ENGLAND JOURNAL of MEDICINE

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Contents lists available at ScienceDirect

Thrombosis Research

journal homepage: www.elsevier.com/locate/thromres

Regular Article

Thrombolysis in hemodynamically stable patients with acute pulmonary embolism: A meta-analysis

Antoni Riera-Mestre [a,*], Cecilia Becattini [b], Michela Giustozzi [b], Giancarlo Agnelli [b]

Due to increased risk for MB and ICH with no evidence of reduction in mortality, thrombolysis should not be used for most normotensive PE patients.

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EMBOLIA POLMONARE SUB-MASSIVA

Submassive PE remains a challenging clinical problem for the hospital physician. The evidence to date does not support the use of routine thrombolysis in this patient group. The benefits of reduced hemodynamic deterioration are outweighed by increased rates of major bleeding, although it is likely a subgroup of patients with severe submassive PE may still derive net gain. Indeed, current definitions of submassive PE are confusing and may not capture a true ‘intermediate-risk’ group, as evidenced by the low rates of mortality

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FUTURO PROSSIMO? LAVORI IN CORSO….

Ultrasound-facilitated, catheter-directed thrombolysis vs anticoagulation alone for acute intermediate-high-risk pulmonary embolism: Rationale and design of the HI-PEITHO study

(Am Heart J 2022;251:43–53.)

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HI-PEITHO study

Abstract

Background Due to the bleeding risk of full-dose systemic thrombolysis and the lack of major trials focusing on the clinical benefits of catheter-directed treatment, heparin antiocoagulation remains the standard of care for patients with intermediate-high-risk pulmonary embolism (PE).

Methods and results The Higher-Risk Pulmonary Embolism Thrombolysis (HI-PEITHO) study (ClinicalTrials.gov Identifier: NCT04790370) is a multinational multicenter randomized controlled parallel-group comparison trial. Patients with: (1) confirmed acute PE; (2) evidence of right ventricular (RV) dysfunction on imaging; (3) a positive cardiac troponin test; and (4) clinical criteria indicating an elevated risk of early death or imminent hemodynamic collapse, will be randomized 1:1 to treatment with a standardized protocol of ultrasound-facilitated catheter-directed thrombolysis plus anticoagulation, vs anticoagulation alone. The primary outcome is a composite of PE-related mortality, cardiorespiratory decompensation or collapse, or non-fatal symptomatic and objectively confirmed PE recurrence, within 7 days of randomization. Further assessments cover, apart from bleeding complications, a broad spectrum of functional and patient-reported outcomes including quality of life indicators, functional status and the utilization of health care resources over a 12-month follow-up period. The trial plans to include 406 patients, but the adaptive design permits a sample size increase depending on the results of the predefined interim analysis. As of May 11, 2022, 27 subjects have been enrolled. The trial is funded by Boston Scientific Corporation and through collaborative research agreements with University of Mainz and The PERT Consortium.

Conclusions Regardless of the outcome, HI-PEITHO will establish the first-line treatment in intermediate-high risk PE patients with imminent hemodynamic collapse. The trial is expected to inform international guidelines and set the standard for evaluation of catheter-directed reperfusion options in the future. (Am Heart J 2022;251:43–53.)

(Am Heart J 2022;251:43–53.)

CONCLUSIONI (1)

-La gestione dell'EMBOLIA POLMONARE ALTO RISCHIO/NON ALTO RISCHIO sta cambiando, vedendo la CO-PARTECIPAZIONE di più specialisti (rianimatori, internisti di Area Critica, cardiologi, pneumologi, radiologi interventisti, cardiochirughi → PERT (Pulmonary Embolism Response Team)

-sono DIVERSE la possibilità terapeutiche nelle VARIE fasi della malattia in base alla RISPOSTA CLINICA

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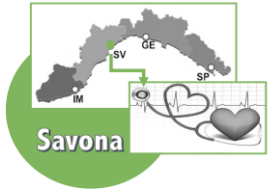

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CONCLUSIONI (2)

Più DIFFICILE ed in CORSO DI STUDIO è la gestione ottimale dell'EMBOLIA POLMONARE SUB-MASSIVA

→valutazione caso per caso, rapporto rischio/beneficio e discussione collegiale

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Shock ostruttivo nella tromboembolia polmonare e gestione della terapia in acuto

Grazie dell'attenzione!!!

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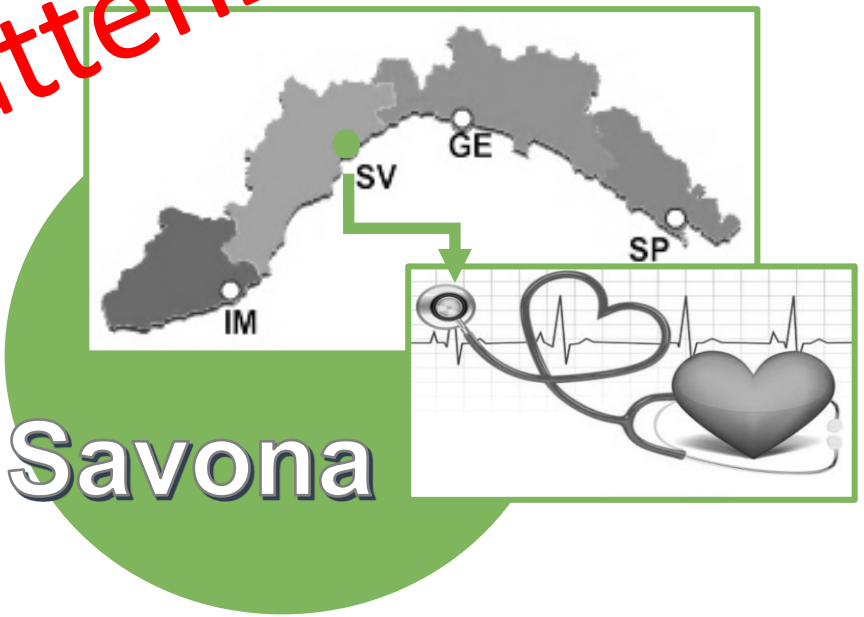

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