The PREP score

The PREP score is an abridged version of the PESI score and is based on only three clinical variables, namely presence of altered mental status, cardiogenic shock and cancer, as well as echocardiographic and biochemical variables. Patients are categorised as having a low or a high risk of death according to their PREP score.

These prediction rules can be used to provide guidance for the most appropriate treatment intervention and also for identifying low-risk patients for whom home treatment may be suitable. According to the European Society of Cardiology (ESC) guidelines, patients with an intermediate risk of mortality of 3–15% should be admitted to hospital, whereas patients with a mortality risk of <1% can be considered for home treatment.

Geneva Prognostic Score (GPS)

Facteur de prédiction	Points
Cancer	+2
Insuffisance cardiaque	+1
Anamnèse de TVP	+1
Tension artérielle systolique < 100 mm Hg	+2
TVP proximale à l'US	+1
PaO2 <60 mm Hg (8 kPa) à l'air ambiant	+1

Points	Risque	Complications à 3 mois*
0-2	Bas	2.2%
≥3	Elevé	26.1%

*Mortalité, récidive ou hémorragie majeure

Wicki, Thromb Haemost 2000

International Winter Meeting on Coagulation

La gestione del rischio

A. D'Angelo & F. Piovella, Cortina D'Ampezzo, La Thuile, Bormio 1994-2013

Schemi raccomandati per la terapia trombolitica

	Dose di carico	Dose di mantenimento
Streptochinasi	250.000 UI	100.000 UI/h per 24 ore
Streptochinasi		100.000 IU/h per 12 ore
Streptochinasi		1.500.000 UI in 2 ore
Urochinasi	4.400 UI/Kg	4.400 UI/Kg/h per 12 ore*
Urochinasi		3.000.000 UI in 2 ore
Urochinasi		2.000 UI/Kg/h per 24 ore
+		eparinoterapia
Alteplase	10 mg	90 mg in 2 ore ± eparinoterapia

Thrombolytic and interventional treatment for acute venous thromboembolism

Catheter directed therapy (CDT) may be used in patients with acute PE at increased risk of bleeding as a lower dose of a thrombolytic agent is infused directly into the pulmonary artery via a catheter.

CDT is also effective in lowering pulmonary arterial pressure and improving RV function.

In a randomized controlled trial of 59 patients with acute intermediate risk PE, ultrasound-assisted catheter-directed thrombolysis followed by heparin was compared to treatment with heparin alone. At 24 h, CDT improved the hemodynamics compared to anticoagulation. At 90 days of follow-up, there was no difference in mortality or major bleeding between the two groups. Most of the evidence is limited by small sample size and of low quality compared to the available evidence for systemic thrombolysis. Systemic thrombolysis is therefore currently recommended over CDT in patients with acute PE who are candidates for thrombolysis.

New Guidelines

Evidence-based guidelines for anticoagulation treatment of acute PE have been published by the European Society of Cardiology ESC and the American College of Chest Physicians (ACCP). The treatment approach for acute PE is dependent on risk stratification of the individual patient.

In haemodynamically stable patients, anticoagulation with dual-drug strategies, involving acute phase parenteral anticoagulation (with low molecular weight heparin, fondaparinux or unfractionated heparin [UFH]), overlapping with and followed by VKA therapy, is recommended.

Dabigatran is recommended as an alternative to VKA treatment.

As an alternative to dual-drug therapy, single-drug therapy with apixaban or rivaroxaban is recommended with an initial intensified treatment regimen; this approach avoids the need for parenteral administration, which is considered to be inconvenient in some patients.

Thrombolytic and interventional treatment for acute venous thromboembolism

Systemic thrombolysis is a widely accepted treatment for PE in patients with persistent hypotension (e.g., systolic blood pressure <90 mmHg for 15 min) and not at high risk of bleeding

Three recently published trials have examined the role of systemic thrombolysis in intermediate risk patients

In the Moderate Pulmonary Embolism Treated Thrombolysis (MOPETT) trial, 121 patients were randomly assigned to receive heparin (unfractionated or LMWH) alone or the combination of tissue type plasminogen activator (tPA) plus heparin. Compared to the heparin group, treatment with tPA resulted in lower rates of pulmonary hypertension and significantly lower pulmonary artery systolic pressures at 28 months. The rates of bleeding, recurrent PE, and mortality was similar in both groups

Sharifi M, Bay C, Skrocki L, et al. (for the "MOPETT" Trial Investigators) Am J Cardiol. 2013;111:273–7.

In another trial comparing the combination of LMWH plus an intravenous bolus of tenecteplase versus LMWH alone in intermediate risk PE patients, those treated with tenecteplase had fewer adverse outcomes and better functional capacity at 90 days.

Kline JA, Nordenholz KE, Courtney DM, et al. J Thromb Haemost. 2014;12:459–68.

Thrombolytic and interventional treatment for acute venous thromboembolism

In a large multicenter randomized trial (PEITHO), 1005 intermediate risk patients with PE were randomized to tenecteplase and heparin or to heparin therapy alone. Thrombolysis therapy led to reduction in the primary composite outcome of death or cardiovascular collapse at seven days after randomization although it increased major bleeding (including intracranial bleeding) with no overall gained benefit from thrombolysis.

Meyer G, Vicaut E, Danays T et al., N Engl J Med 2014;370:1402-11

A meta-analysis of 16 trials comprising 2115 intermediate risk patients reported that 59 patients would need to be treated with thrombolysis to prevent one death, while a major bleeding occurs with every 18 patients treated. Further studies are needed to identify subgroups of intermediate risk patients who will benefit from systemic thrombolytic therapy.

The PEITHO Study

- A randomized, double-blind trial, comparing tenecteplase plus heparin with placebo plus heparin in normotensive patients with intermediate-risk pulmonary embolism.
- Eligible patients had right ventricular dysfunction on echocardiography or computed tomography, 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 randomization.
- The main safety outcomes were major extracranial bleeding and ischemic or hemorrhagic stroke within 7 days after randomization.

The PEITHO Study

Of 1006 patients who underwent randomization, 1005 were included in the intentionto-treat analysis.

Death or hemodynamic decompensation occurred in 13 of 506 patients (2.6%) in the tenecteplase group as compared with 28 of 499 (5.6%) in the placebo group (odds ratio, 0.44; 95% confidence interval, 0.23 to 0.87; P=0.02). Between randomization and day 7, a total of 6 patients (1.2%) in the tenecteplase group and 9 (1.8%) in the placebo group died (P=0.42).

Extracranial bleeding occurred in 32 patients (6.3%) in the tenecteplase group and 6 patients (1.2%) in the placebo group (P<0.001). Stroke occurred in 12 patients (2.4%) in the tenecteplase group and was hemorrhagic in 10 patients; 1 patient (0.2%) in the placebo group had a stroke, which was hemorrhagic (P=0.003).

By day 30, a total of 12 patients (2.4%) in the tenecteplase group and 16 patients (3.2%) in the placebo group had died (P=0.42). 33

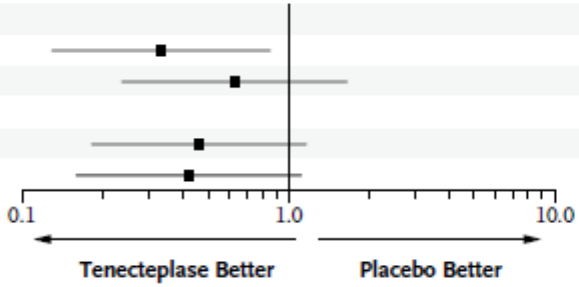
The PEITHO Study

Guy Meyer, M.D., Eric Vicaut, M.D., Thierry Danays et al., N Engl J Med 2014;370:1402-11

The NEW ENGLAND JOURNAL of MEDICINE

A Death or Hemodynamic Decompensation

Subgroup	Tenecteplase (N=506) no. of events/total no. (%)	Placebo (N=499) no. of events/total no. (%)	Odds Ratio (95% CI)	P Value for Interaction
Age				0.36
≤75 yr	6/344 (1.7)	17/335 (5.1)	0.33 (0.13–0.85)	
>75 yr	7/162 (4.3)	11/164 (6.7)	0.63 (0.24–1.66)	
Sex				0.90
Male	7/242 (2.9)	14/231 (6.1)	0.46 (0.18–1.16)	
Female	6/264 (2.3)	14/268 (5.2)	0.42 (0.16–1.12)	



B Major Extracranial Bleeding

Subgroup	Tenecteplase (N=506) no. of events/total no. (%)	Placebo (N=499) no. of events/total no. (%)	Odds Ratio (95% CI)	P Value for Interaction
Age				0.09
≤75 yr	14/344 (4.1)	5/335 (1.5)	2.80 (1.00–7.86)	
>75 yr	18/162 (11.1)	1/164 (0.6)	20.38 (2.69–154.53)	
Sex				0.13
Male	11/242 (4.5)	4/231 (1.7)	2.70 (0.85–8.61)	
Female	21/264 (8.0)	2/268 (0.7)	11.49 (2.67–49.53)	

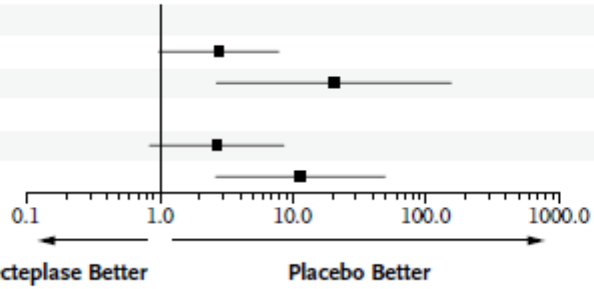


Figure 1. Efficacy and Safety Outcomes in Prespecified Subgroups.

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 PEITHO Study

- In conclusion, in normotensive patients with intermediate-risk pulmonary embolism, the composite primary outcome of early death or hemodynamic decompensation was reduced after treatment with a single intravenous bolus of tenecteplase.
- However, tenecteplase was also associated with a significant increase in the risk of intracranial and other major bleeding.
- Therefore, great caution is warranted when considering fibrinolytic therapy for hemodynamically stable patients with pulmonary embolism, right ventricular dysfunction, and a positive cardiac troponin test.

Thrombolytic and interventional treatment for acute venous thromboembolism

Anticoagulant therapy alone is recommended over thrombolysis for most patients with an acute DVT with exception for those with extensive iliofemoral or proximal DVT at high risk of limb ischemia

Kearon C, Akl EA, Comerota AJ, et al. Chest. 2012;141(2 Suppl):e419S–94
Kearon C, Akl EA, Ornelas J, et al. Chest. 2016;149:315–52.

Thrombolytic therapy (systemic or catheter-directed) increase clot lysis and reduce the incidence of PTS compared to anticoagulation alone

Enden T, Haig Y, Kløw NE, et al. for the CaVenT study investigators. Lancet. 2012;379:31–8.
Watson L, Broderick C, Armon MP. Cochrane Database Syst Rev. 2014;1

However, this is at the expense of higher rate of major bleeding and no difference in rate of recurrent VTE or mortality

Bashir R, Zack CJ, Zhao H et al. JAMA Intern Med. 2014;174:1494

The management of cerebrovascular disease has advanced considerably in 2015

Five randomized control trials have firmly established the role of endovascular thrombectomy for ischemic strokes due to large vessel occlusion, showing benefit in terms of functional outcomes at 90 days.

1. The randomized trial of intraarterial treatment for acute ischemic stroke (MR CLEAN, Berkhemer et al. NEJM 2015;372:11-20) was the first of a series on the topic.

2. The Endovascular Therapy for Ischemic stroke with perfusion-imaging selection (EXTENDIA) (Campbell et al. NEJM 2015;372:1009-18)

3. The Randomized assessment of rapid endovascular treatment of ischemic stroke (ESCAPE, Goyal et al. NEJM 2015;372:1019-30) trials

4. The stent-retriever thrombectomy after IV t-PA is t-PA alone in stroke (SWIFT-PRIME, Saver et al. NEJM 2015;372:2285-95)

5. The thrombectomy within 8h after symptom onset in Ischemic stroke (REVASCAT trial, Jovin et al. NEJM 2015; 372:2296-306).

CONCLUSIONS:

Moderate to high quality evidence suggests that:

1. Compared with medical care alone in a selected group of patients,

2. Endovascular thrombectomy as add-on to intravenous thrombolysis performed within six to eight hours after large vessel ischaemic stroke in the anterior circulation,

3. Provides beneficial functional outcomes, without increased detrimental effects.

Rodrigues FB, Neves JB, Caldeira D, Ferro JM, Ferreira JJ, Costa J.
BMJ. 2016 Apr 18;353:i1754.

Intravenous thrombolysis is the standard treatment for acute ischaemic stroke, but the rates for recanalisation are not ideal The use of concomitant endovascular reperfusion techniques, such as adjunctive intra-arterial mechanical thrombectomy, may help to improve clinical outcomes further

This systematic review and meta-analysis of 10 randomised controlled trials provide moderate to high quality evidence suggesting that, in carefully selected patients endovascular treatment, particularly adjunctive intra-arterial mechanical thrombectomy, provided within six to eight hours after ischaemic stroke involving large vessels in the anterior circulation, leads to improved functional outcomes at 90 days without increased mortality or symptomatic intracerebral haemorrhage This evidence supports the need to restructure current neurointerventional resources and to change clinical practice

- Acute ischemic stroke is a major global cause of death, and permanent disability.

- Intravenous tPA has been the only recommended therapy, if given in the time window.

- Intravenous tPA is associated with modest recanalization rates.

- Catheter-based interventions in acute ischemic stroke lagged for several years.

- Stent retrievers emerged as the first effective new therapy in the last 20 years.

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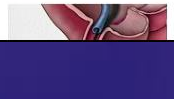

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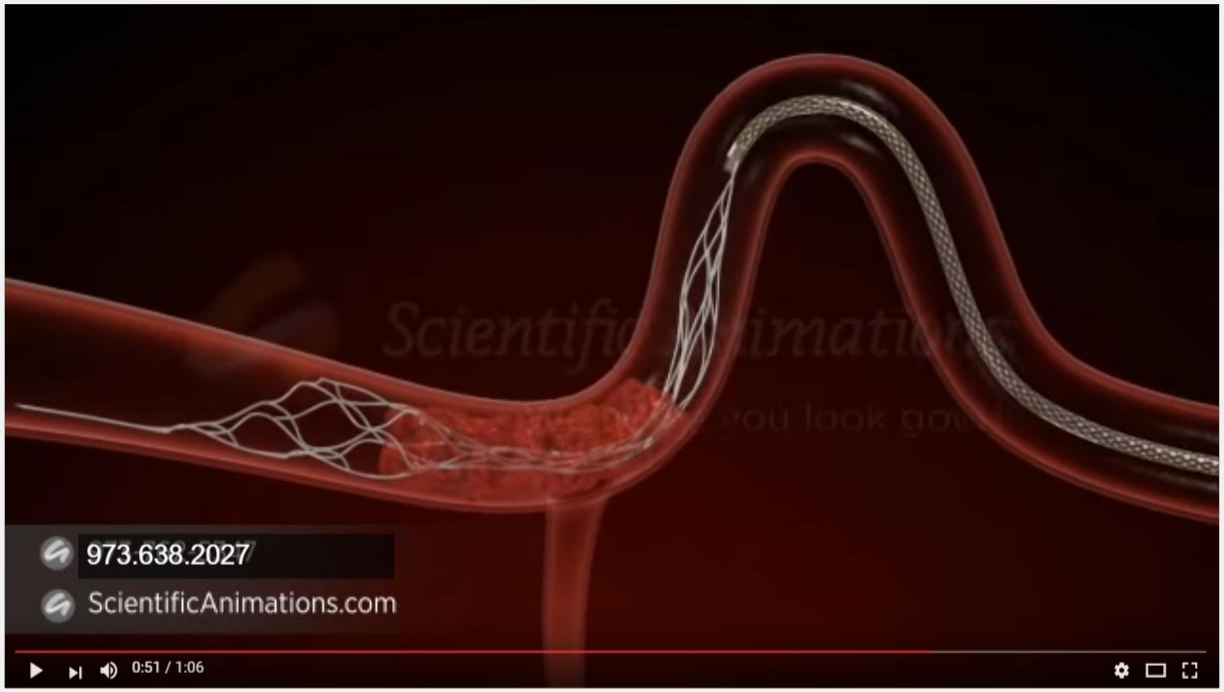

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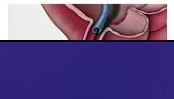

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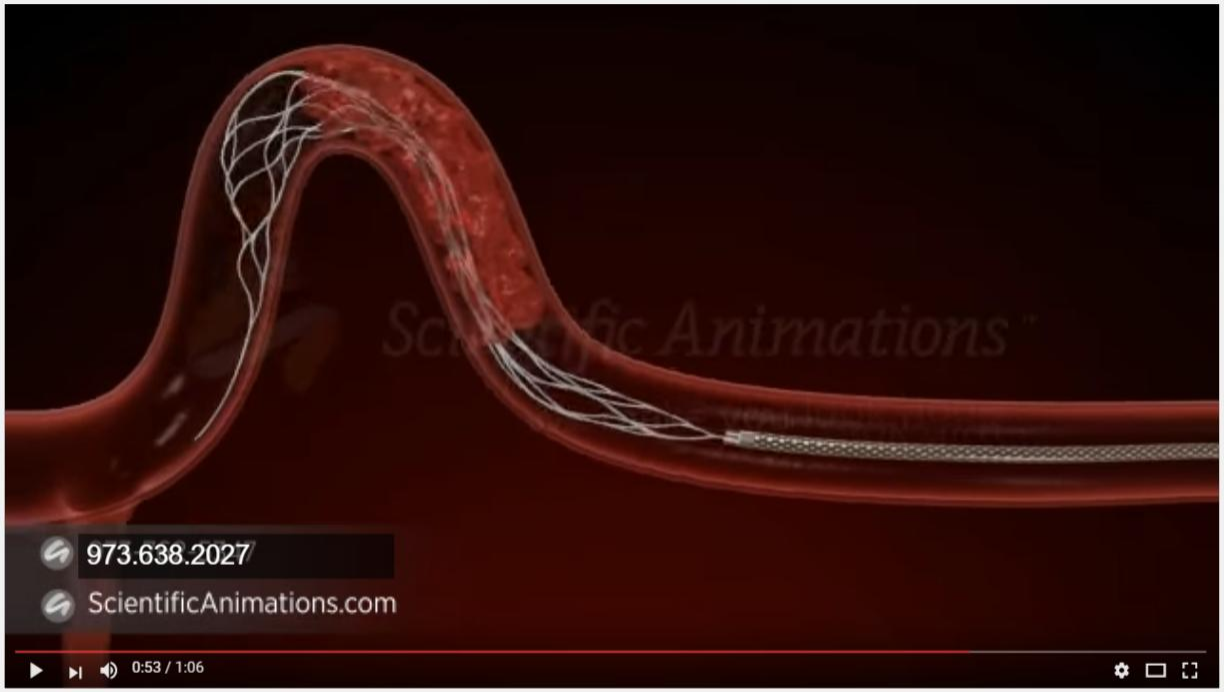

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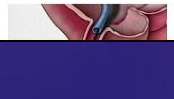

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Chiara Beltrametti
Chiara Picchi
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Diana Iosub
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