Il sottoscritto Prof Pasquale Pignatelli dichiara che negli ultimi due anni ha avuto i seguenti rapporti anche di finanziamento con soggetti portatori di interessi commerciali in campo sanitario:

-NOME AZIENDE
-Speaker per le seguenti aziende: Boehringer Ingelheim, Daiichi Sankyo, Bayer, Bristol-Myers Squibb, Pfizer.

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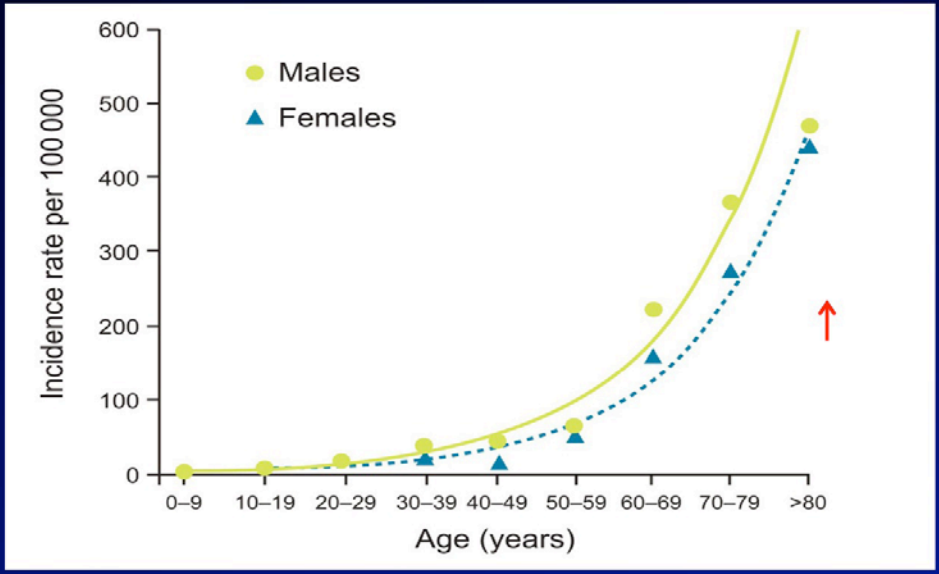
Terapia anticoagulante in paziente con TVP e previsione di terapia breve

Pasquale Pignatelli

Centro di Aterotrombosi - I Clinica Medica -
Dipartimento di Medicina Interna e Specialità
Mediche - Umberto I Policlinico di Roma

Le dimensioni del problema

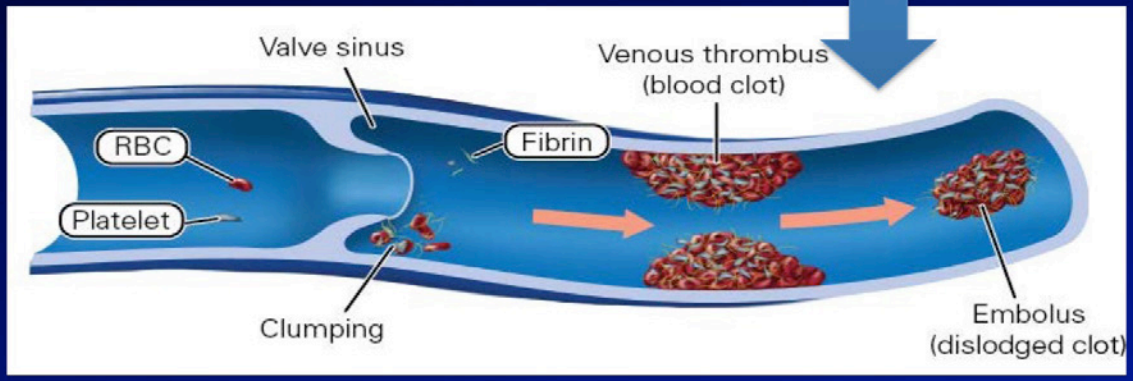
- Incidenza di TVP: 1.5/1000 ab/anno (0.15%)
- Incidenza di EP: 1/1000 ab/anno (0.1%)
- L'incidenza del TEV sale esponenzialmente con l'età, raggiungendo un valore di 5/1000 ab/anno (0.5%) ≥ 80aa



Anderson et al. Arch Int Med 1991. 151: 953
White RH et al. Circulation 2003; 107 (23 Suppl 1): I-4-I-8

DVT formation

- trauma
- Immobilità
- Intervento chirurgico

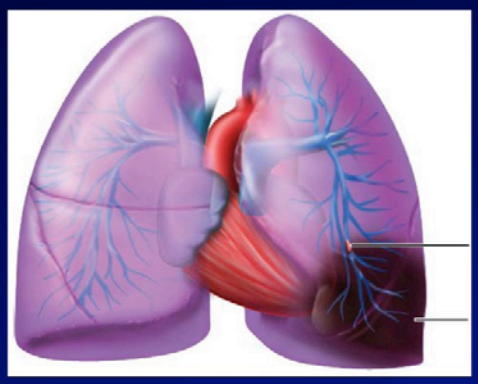


Begins with combination of changes in Virchow's triad

Gay SE. Nurse Pract 2010;35:32-9; Mackman N. J Clin Invest 2012;122:2331-6

PE formation

- Embolus travels in blood stream to heart and then to lungs
- Embolus reaches a point in the pulmonary arterial system through which it cannot pass – result is PE
- DVT cannot cause a stroke



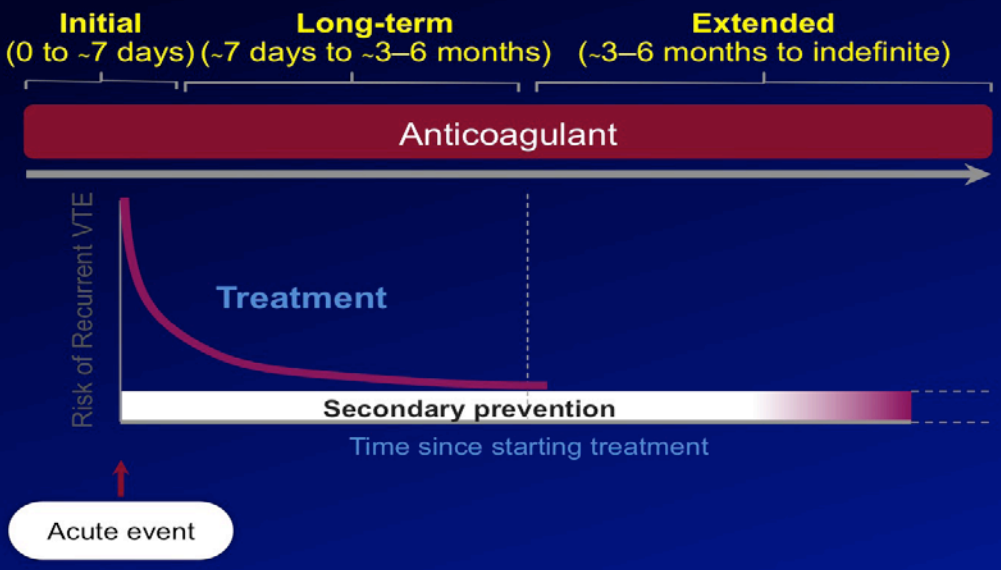
PE

Area of tissue damage

Embolus that travels to the lungs and blocks a pulmonary artery

Gay SE. Nurse Pract 2010;35:32-9

Phases of anticoagulation treatment for DVT and PE



Ad. Kearon et al. Chest 2012;141(2 Suppl):e419s–e494s;
Ad. Kearon. J Thromb Haemost 2012;10:507–511.

ACCP 2016 Treatment of VTE (Duration)

In patients with proximal DVT of the leg or PE provoked by surgery, we recommend treatment with anticoagulation for 3 months (Grade 1B)

In patients with proximal DVT of the leg or PE provoked by a nonsurgical transient risk factor, we recommend treatment with anticoagulation for 3 months (Grade 1B).

We suggest treatment with anticoagulation for 3 months over extended therapy if there is a low or moderate bleeding risk (Grade 2B).

Kearon et al. Chest 2016

ACCP 2016 Treatment of acute VTE

For VTE and no cancer, as long-term anticoagulant therapy, we suggest
dabigatran (Grade 2B)
rivaroxaban (Grade 2B)
apixaban (Grade 2B)
edoxaban (Grade 2B)
over VKA therapy,
and suggest VKA therapy over LMWH (Grade 2C).

For VTE and cancer, we suggest LMWH over VKA (Grade 2B), dabigatran (Grade 2C), rivaroxaban (Grade 2C), apixaban (Grade 2C) or edoxaban (Grade 2C).

Kearon et al. Chest 2016

Fasi del trattamento della DVT-PE

Time[1]

- Acute (first0-7 days)
- Long term (from end of acute treatment to 3-6 months)
- Extended (beyond 3-6 months).

Who?

- Acute (first5-10 days) All patients
- Long term(from end of acute treatment to 3-6 months) All patients (according to resolution)
- Extended (beyond 3-6 months). un-provoked (first VTE occurs without any identifiable thrombotic risk factor) and High risk for recurrence[1]

Risk factors

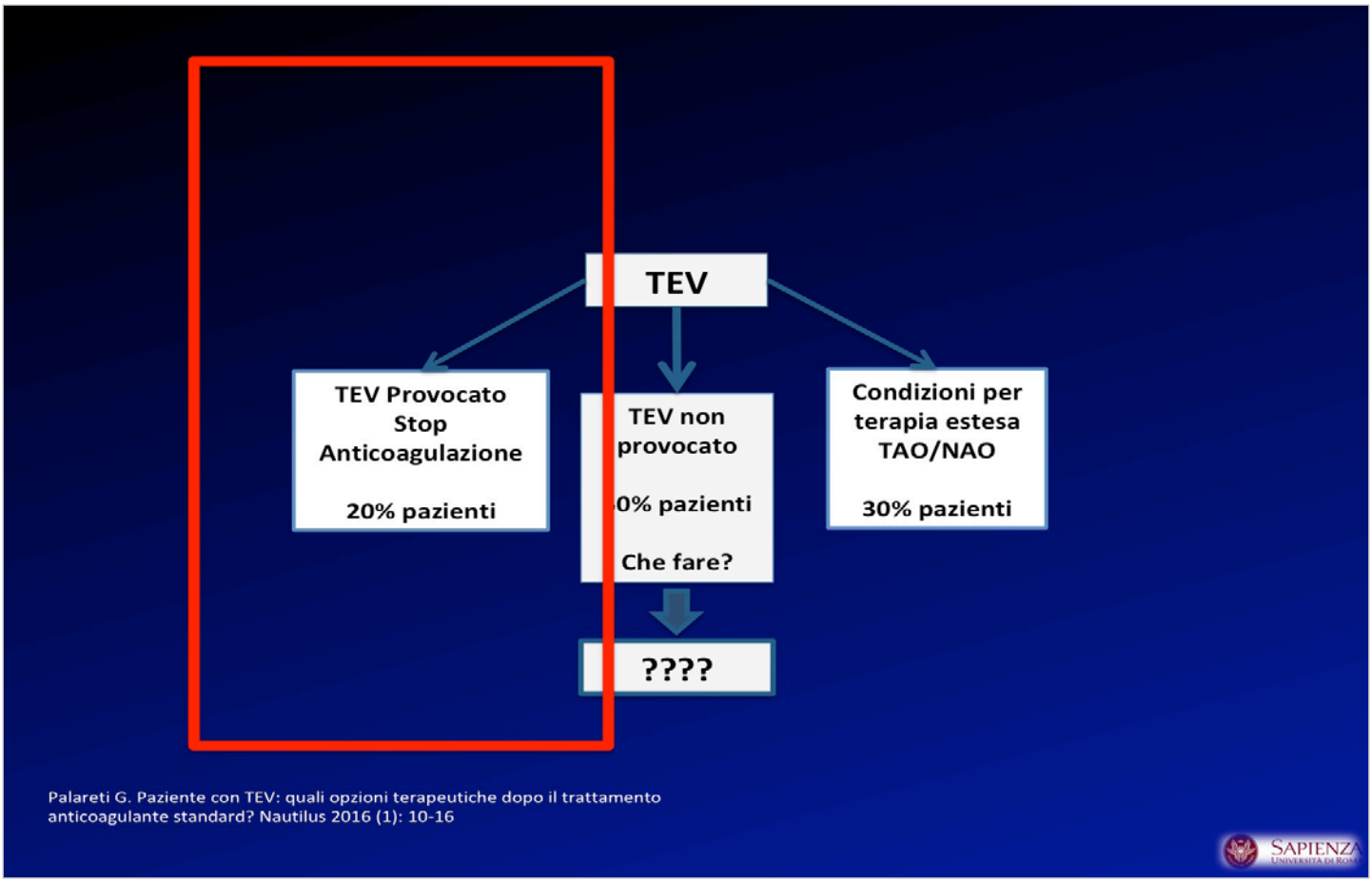
1) Kearon C et al. Chest 2012;141:e419S–94S.

Fasi del trattamento della DVT-PE

Risk factors[2]

- Malignancy
- APL syndrome (29% of recurrence after therapy cessation)
- Lupus (risk ratio of 2.88 for recurrence)
- Thrombophilia (protein C, protein S, antithrombin deficiency, and homozygous factor V Leiden or pro- thrombin gene defect)
- A second unprovoked VTE
- Male sex[3]
- Elevated D-Dimer after discontinuation[3]

1) Kearon C et al. Chest 2012; 141:e419S–94S. 2) Wells PS et al. Jama 2014 *3) Kearon et al. Chest 2016*


TEV
TEV Provocato
Stop
Anticoagulazione
20% pazienti
TEV non
provocato
0% pazienti
Che fare?
????
Condizioni per
terapia estesa
TAO/NAO
30% pazienti
Palareti G. Paziente con TEV: quali opzioni terapeutiche dopo il trattamento anticoagulante standard? Nautilus 2016 (1): 10-16
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Fattori di rischio per recidiva
INCREMENTO RISCHIO DI TROMBOSI
MAGGIORE DURATA DELLA TERAPIA ANTICOAGULANTE
POST CHIRURGIA
PROVOCATA NON POST-CHIRURGIA
NON PROVOCATA DONNE
NON PROVOCATA UOMINI
Data from ACCP 2016 : rappresentazione grafica
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CHEST (2016): Rischio Emorragico

TABLE 11] Risk Factors for Bleeding with Anticoagulant Therapy and Estimated Risk of Major Bleeding in Low-, Moderate-, and High-Risk categories[a]

Risk Factors[b]
Age >65 y[184-193]
Age >75 y[184-188,190,192,194-202]
Previous bleeding[185,191-193,198,201-204]
Cancer[187,191,195,198,205]
Metastatic cancer[181,204]
Renal failure[185,191-193,196,199,201,206]
Liver failure[186,189,195,196]
Thrombocytopenia[195,204]
Previous stroke[185,192,195,207]
Diabetes[185,186,196,200,202]
Anaemia[185,189,195,198,202]
Antiplatelet therapy[186,195,196,202,208]
Poor anticoagulant control[189,196,203]
Comorbidity and reduced functional capacity[191,196,204]
Recent surgery[189,209,c]
Frequent falls[195]
Alcohol abuse[191,192,195,202]
Nonsteroidal anti-inflammatory drug[210]

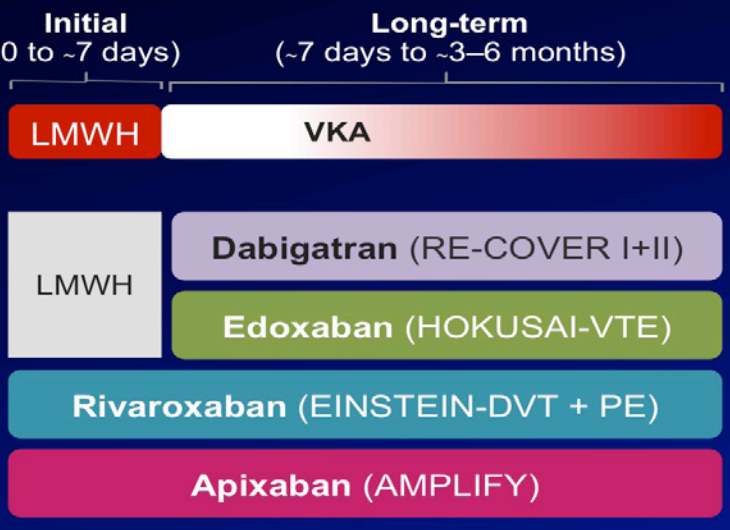
Categorization of Risk of Bleeding[d]	Estimated Absolute Risk of Major Bleeding		
	Low Risk[e] (0 Risk Factors)	Moderate Risk[e] (1 Risk Factor)	High Risk[e] (≥2 Risk Factors)
Anticoagulation 0-3 mo[f]			
Baseline risk (%)	0.6	1.2	4.8
Increased risk (%)	1.0	2.0	8.0
Total risk (%)	1.6[g]	3.2	12.8[h]
Anticoagulation after first 3 mo[f]			
Baseline risk (%/y)	0.3[i]	0.6	≥2.5
Increased risk (%/y)	0.5	1.0	≥4.0
Total risk (%/y)	0.8[j]	1.6[j]	≥6.5

Numerosi sotto i fattori di rischio che possono influenzare il sanguinamento.

Tra i più rilevanti

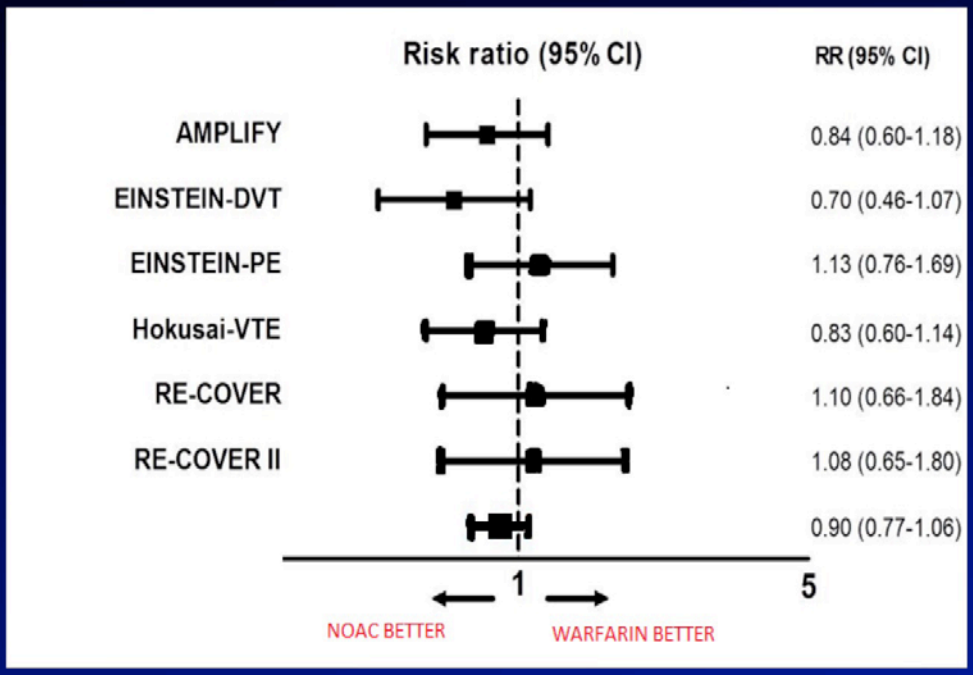
-Primi 3 mesi di terapia
-Basso contollo dei parametri coagulativi
-Età (anziani)
-Storia di precedenti sanguinamenti o ictus
-Insufficienza renale

Overview of NOAC trials in VTE



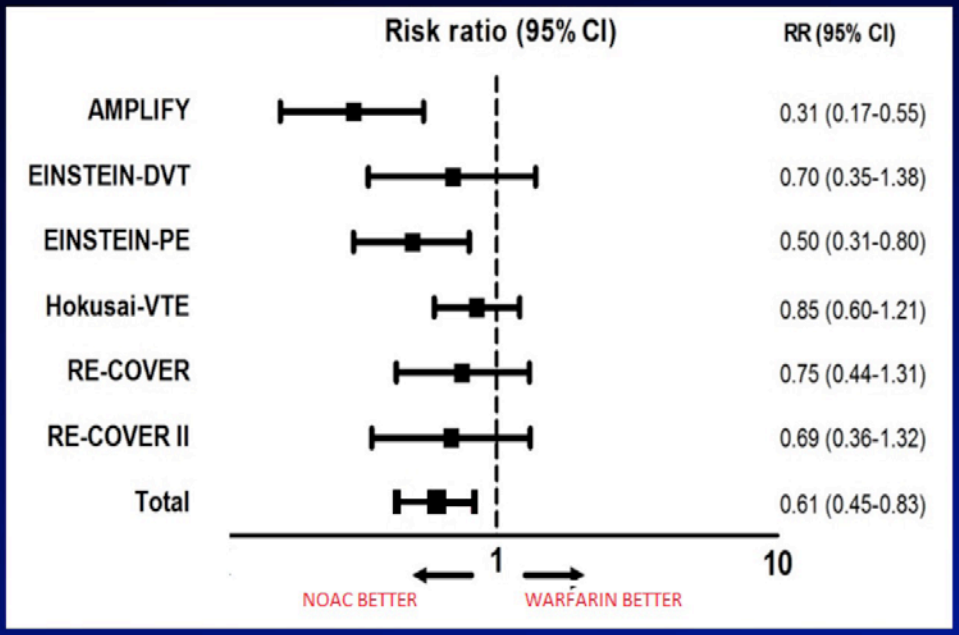
Schulman et al. N Engl J Med 2009;361:2342–2352; Schulman et al. Circulation 2014;129:764–772; Büller HR et al. N Engl J Med. 2013;369:1406-1415; Bauersachs et al. N Engl J Med 2010;363:2499–2510; Büller et al. N Engl J Med 2012;366:1287–1297; Agnelli et al. N Engl J Med 2013;369:799–808.

Meta-analysis of NOAC trials in VTE
Primary efficacy endpoint



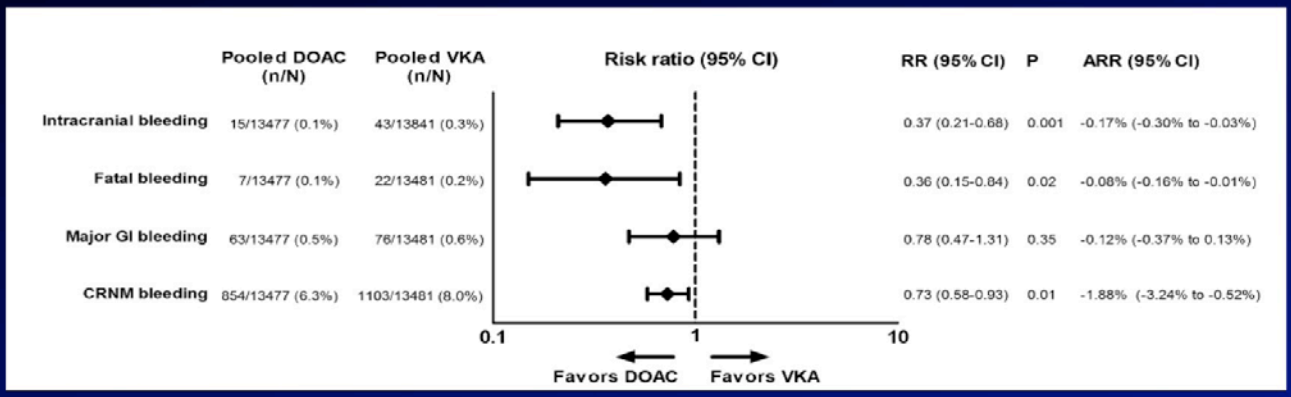
Van Es et al Blood 2014

Meta-analysis of NOAC trials in VTE
Primary safety endpoint



Van Es et al Blood 2014

Intracranial, major gastrointestinal, fatal, and clinically relevant nonmajor bleeding



Van ES et al Blood 2014