L'antiaggregante nella prevenzione secondaria del tromboembolismo venoso

CONTROVERSIE SULL'USO DEI FARMACI ANTITROMBOTICI

7-8 ottobre 2016 - Hotel Lloyd's Baia - Via Enrico de Marinis, 2 - 84019 Vietri sul Mare

7 OTTOBRE 2016

15.00 Apertura segreteria

I SESSIONE: TROMBOSI VENOSE E FIBRILLAZIONE ATRIALE Moderatori: **A.Ciampa, M.Spina**

Trattamento anticoagulante orale nella fibrillazione atriale non valvolare

15.30 AVK..... meglio di NOA: **G. Rescigno**
15.50 NOA .....meglio di AVK: **F. Marongiu**

Terapia anticoagulante orale nel trattamento e nella prevenzione del Tromboembolismo venoso

16.10 AVK .....meglio di NOA **N.Ciavarella**
16.30 NOA .....meglio di AVK **S. Pezzella**
16.50 Aggiornamento bibliografico **V. Marottoli**
17.00 Discussione
17.20 17.40 Coffee break
17.40 L'Antiaggregante nella prevenzione secondaria del tromboembolismo venoso **S.Vivolo**
18.00 Ruolo delle EBPM e del fondaparinux nell'era dei NOA **M. Frigino**
18.30 Tavola rotonda: AVK, EBPM, Pentasaccaride, Eparina Sodica, Nao: Criteri di Scelta
Moderatori: **F.Marongiu, S. Pezzella**
Discussant: **N. Ciavarella, M. Frigino, G. Rescigno**

8 OTTOBRE 2016

9.00 Apertura segreteria

II SESSIONE: LABORATORIO E NOA Moderatori: **M.R. Lupone, C. Salapete**

Monitoraggio di laboratorio dei NOA

9.05 Si - **S. Testa**
9.25 No - **D. Poli**
9.50 Aggiornamento bibliografico **V. Marottoli**
10.00 Discussione
10.15 10.30 Coffee break

III SESSIONE: ARTERIOPATIE PERIFERICHE Moderatori: **M. Frigino, A. Niglio**

10.40 Le Arteriopatie Periferiche - **A. Niglio**
11.00 Le arteriopatie neurologiche - **D. Spitaleri**
11.20 I percorso terapeutico nel paziente con arteriopatia periferica **M. Amitrano**
11.40 L'Acidoacetilsalicilico nella prevenzione cardio-oncologica: fatti e misfatti **P.A. Modesti**
12.00 Trattamento delle arteriopatie periferiche: AVK versus Antiaggregante **M. Moia versus A.Falanga**
12.40 Aggiornamento bibliografico **V. Marottoli**
12.50 Discussione
13.10 Tavola Rotonda: AVK, EBPM, Pentasaccaride, Eparina Sodica, Nao: Gestione Delle Complicanze Emorragiche
Moderatori **A. Falanga, M. Moia**
Discussant **N. Ciavarella, M. Frigino, G. Rescigno**
13.30 ... e ora due conti sul costo della terapia antitrombotica... **A. Ciampa**
14.00 Compilazione questionario ECM

SEDE
Hotel Lloyd's Baia
Via Enrico de Marinis, 2 - 84019 Vietri sul Mare

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ACCREDIMENTO E.C.M.
Il Corso è stato inserito nel Piano Formativo 2016 per la Formazione Continua in Medicina (ECM).
Il Corso ha ottenuto i seguenti crediti: n. 8,5

ISCRIZIONI
L'iscrizione al corso avrà un costo di 50 euro e dovrà essere effettuata on line al seguente indirizzo: **www.elleventi.it**

Dott.ssa Sabrina Vivolo

Vietri, 07/10/16

emostasi:

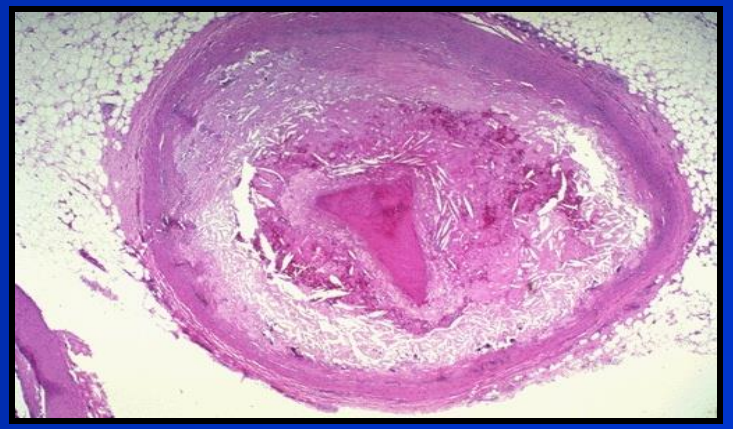
insieme di processi attraverso i quali:

1) si forma un coagulo efficace a livello di una lesione vascolare

2) l'estensione del coagulo viene limitata alla sede della lesione

3) il coagulo viene successivamente lisato;

emorragia ⟷ **trombosi**



… LA TROMBOSI…

- COS’E’ ?

TROMBOSI

- **E’ un processo che determina la formazione di una massa semisolida chiamata TROMBO formata dai costituenti del sangue, all’interno del sistema vascolare.**
- **Tale massa aderisce alla parete del vaso almeno in un punto e si forma quando l’individuo è ancora in vita.**
- **Rappresenta l’estensione patologica del normale processo emostatico.**

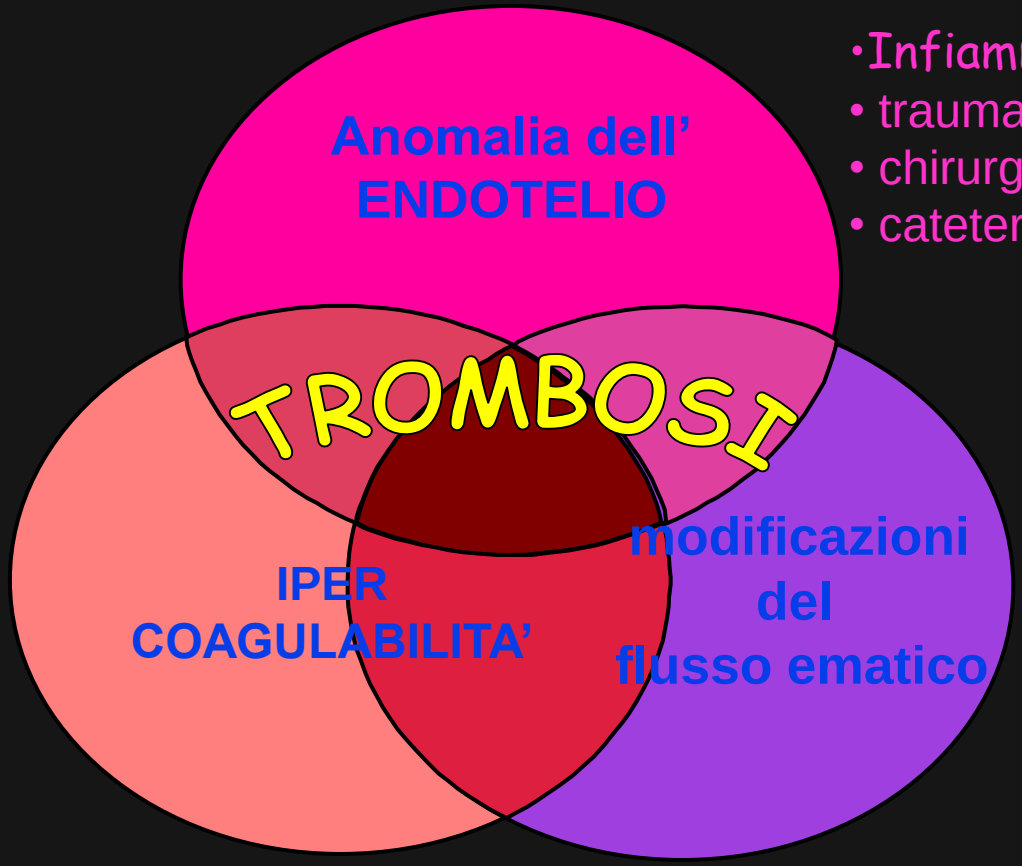
DALLA PATOGENESI ALLA TRASVERSALITA' DELLA TROMBOSI

Virchow, 1856

LA TROMBOSI

E' UN FENOMENO PATOLOGICO RISULTANTE DA UNA INAPPROPRIATA RISPOSTA EMOSTATICA

Virchow's triade 1856

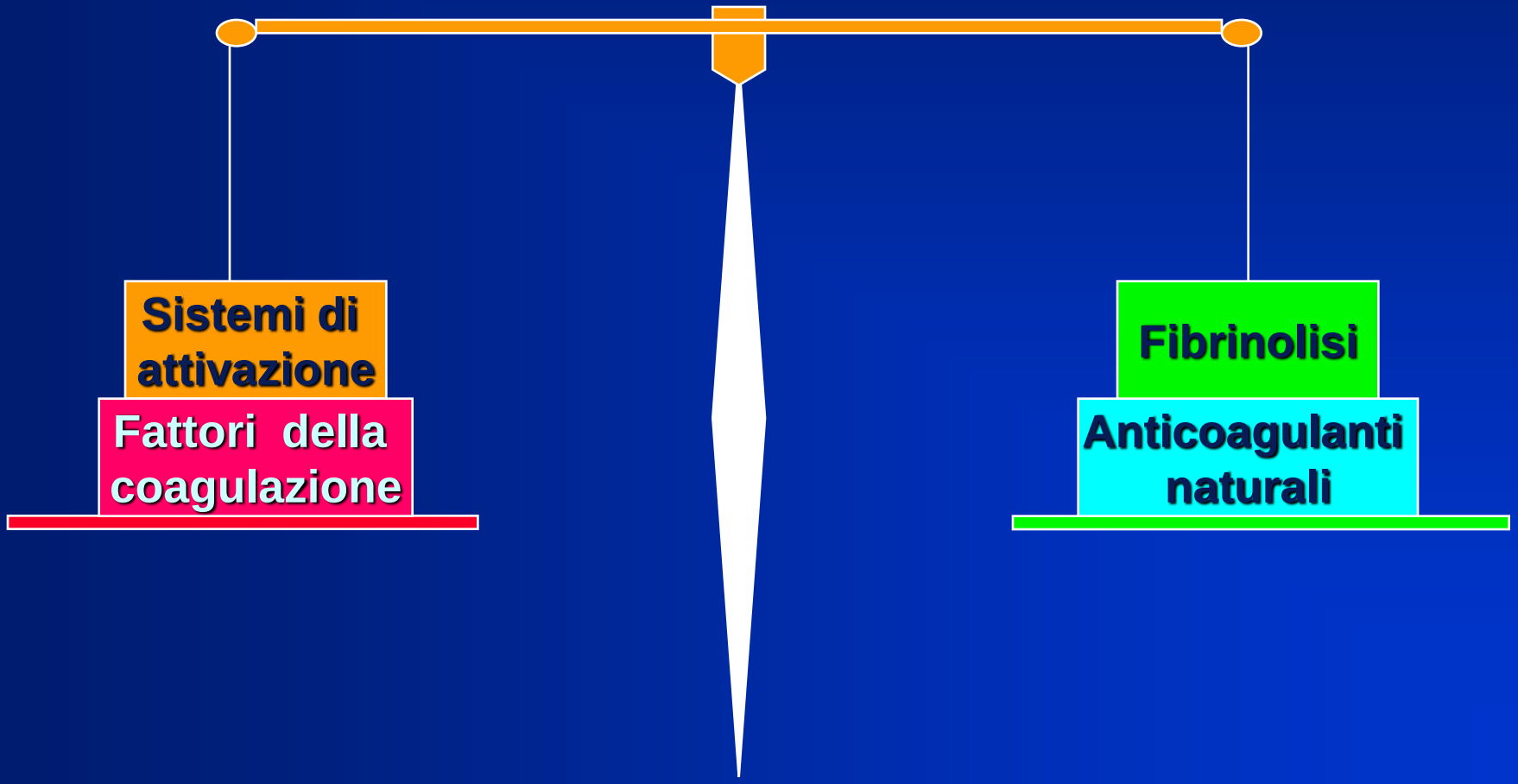


- Infiammazione
- trauma
- chirurgia
- catetere etc..

- gravidanza
- Tumore
- estrogeni
- trauma
- chirurgia etc..

- Immobilizz.
- CHF
- AF
- insuff. Venosa etc..

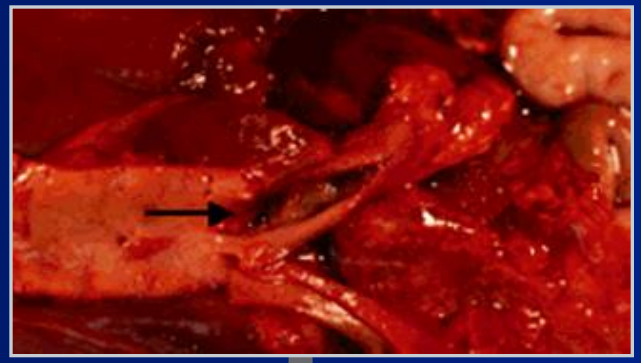
IL BILANCIO DEL SISTEMA EMOSTATICO



Le diverse sedi della Trombosi

Trombosi

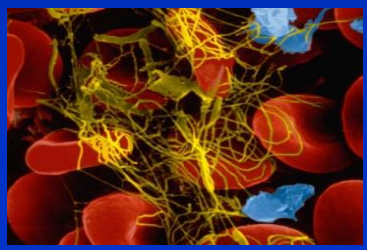
Arteriosa



Piastrine e coagulazione

TROMBI ARTERIOSI	TROMBI VENOSI
-Si formano di solito su superfici endoteliali lese (soprattutto per processi aterosclerotici o vasculitici)	-Si formano di solito in condizioni di stasi ematica
-Si presentano come masse friabili	-Si presentano come masse rosse (fibrina che trattiene globuli rossi)
-Nel cuore e nell'aorta hanno l'aspetto di trombi variegati (strie di Zahn rosse e gialle)	-Si formano spesso a livello delle valvole venose, dove il sangue ristagna facilmente
-Nelle arterie di piccolo calibro si presentano come trombi bianchi (piastrine)	-Interessano quasi sempre (90%) le vene degli arti inferiori
-Possono essere murali o occlusivi	-Sono sempre occlusivi

Venosa

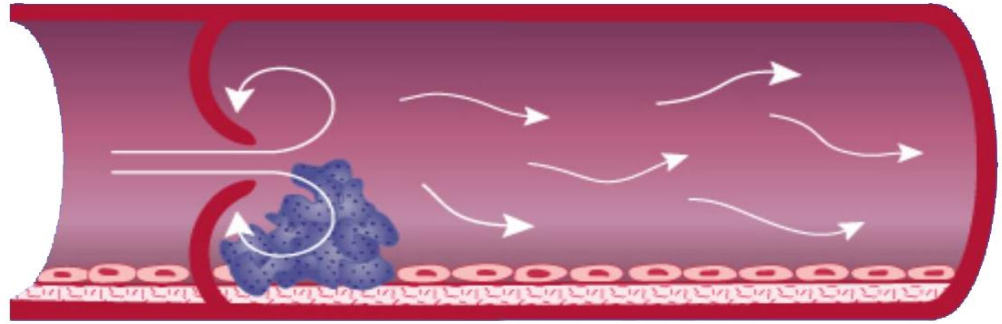


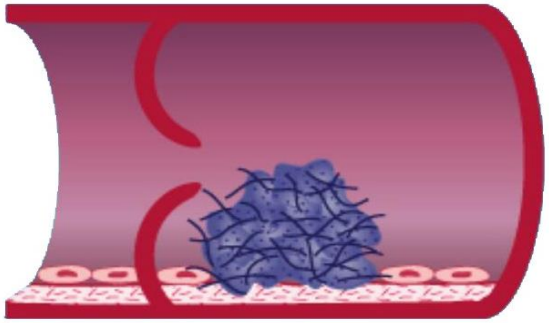
Coagulazione

Trombosi venosa

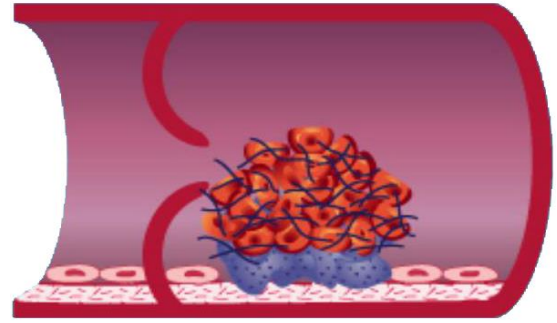
Formazione di un coagulo nel lume venoso

1 Il flusso rallentato e turbolento nelle vene induce stasi e promuove la coagulazione





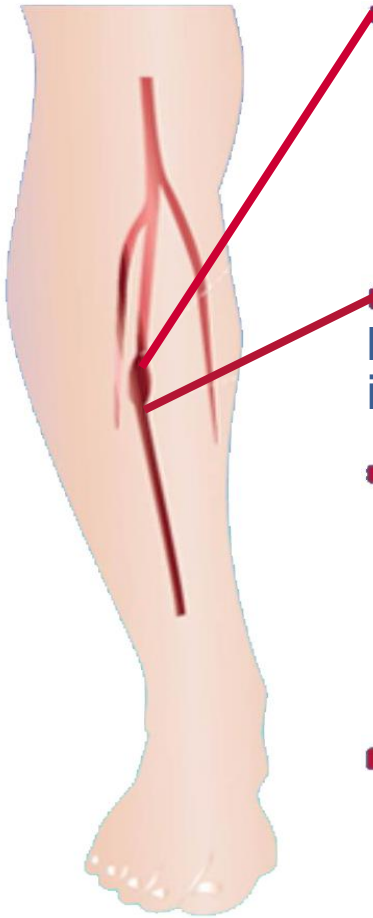
2 La polimerizzazione della fibrina stabilizza il coagulo

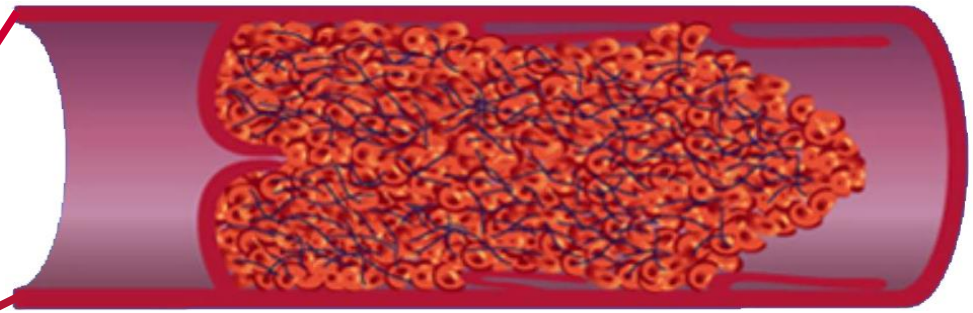


3 Crescita del coagulo

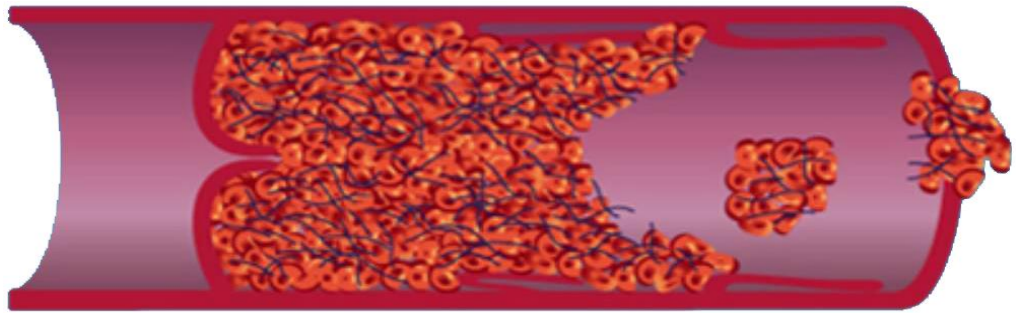
Trombosi venosa

Patogenesi e conseguenze cliniche





La crescita del trombo avviene
in progressione prossimale lungo la vena

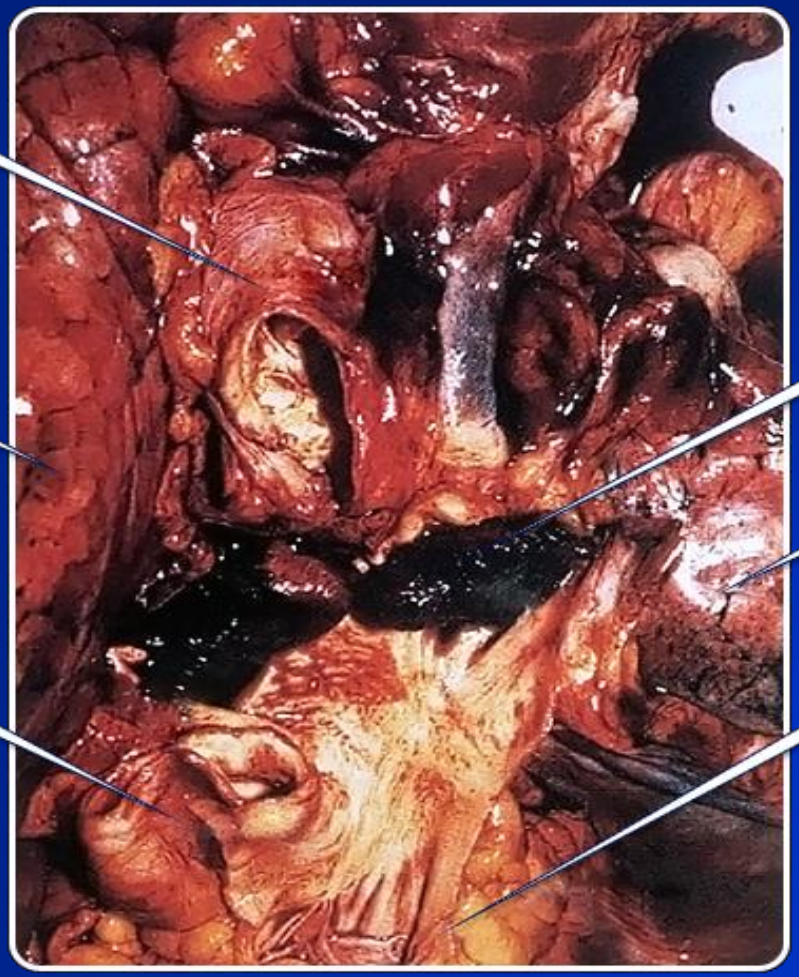


Trombosi venosa profonda → Danneggiamento delle vene (SPT)

→ Embolia polmonare

Prandoni P, et al. Haematologica 1997; 82: 423–428

Embolia polmonare fatale



Tromboembolismo venoso (TEV): una patologia frequente, spesso silente e potenzialmente mortale

- Patologia vascolare frequente
- Debilitante e costosa
- Spesso silente e potenzialmente mortale
- Una popolazione molto ampia a rischio
- Incidenza molto elevata in chirurgia ortopedica

Dimensione del problema

- 80% delle TVP non ha segni premonitori[1]
- EP è la causa di morte più comune nel paziente ospedalizzato[2]
- 70% delle EP fatali è diagnosticato post mortem[3,4]
- In Italia, 100 nuovi casi per anno/100.000[5*]
- La terapia è ancora fortemente sottoutilizzata[2]

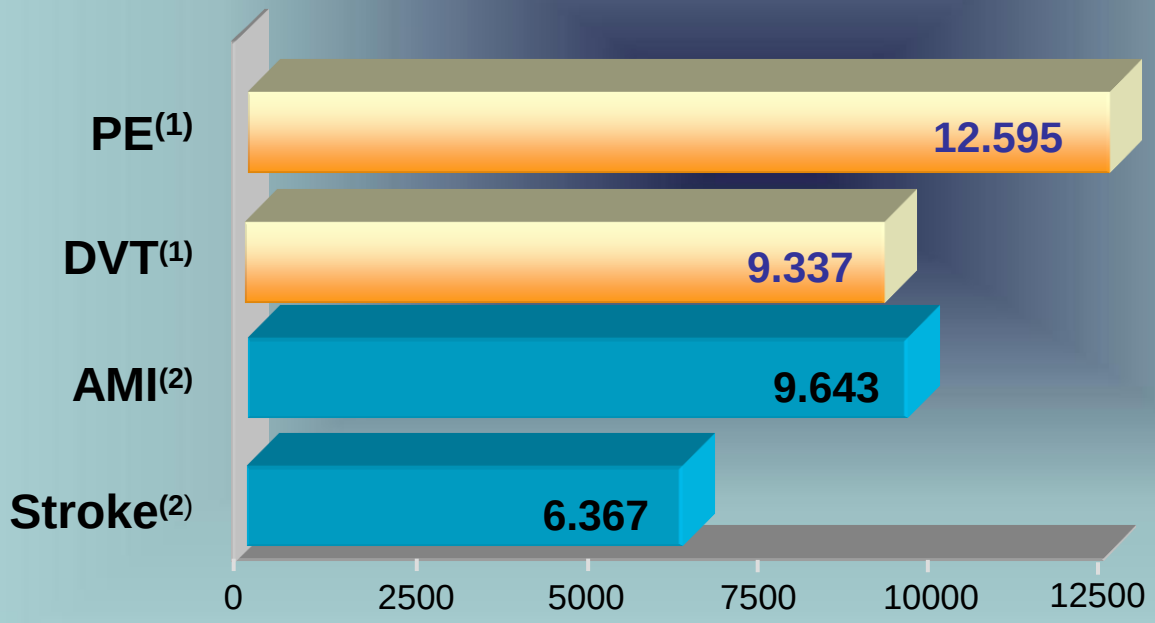
* Il dato del lavoro 5 è riferito all'azienda ospedaliera di Pisa, dove il numero di soggetti con diagnosi di EP (circa 250/anno) è stato rapportato alla popolazione vivente nel bacino di provenienza (circa 250.000 persone).

1. Lethen H et al. Am J Cardiol 1997;80(8):1066-9 — 2. Stratton MA et al. Arch Intern Med 2000;160:334-40
3. Sandler DA et al. J R Soc Med 1989;82(4):203-5 — 4.Stein PD, Henry PD. Chest 1995;108(4):978-81
5. Giuntini C et al. Chest 1995;107:3S-9S

VTE: costs

In-hospital direct costs of VTE comparable to those of AMI or stroke [1,2]

Further long-term medical costs of DVT: 75% of the initial cost [3]



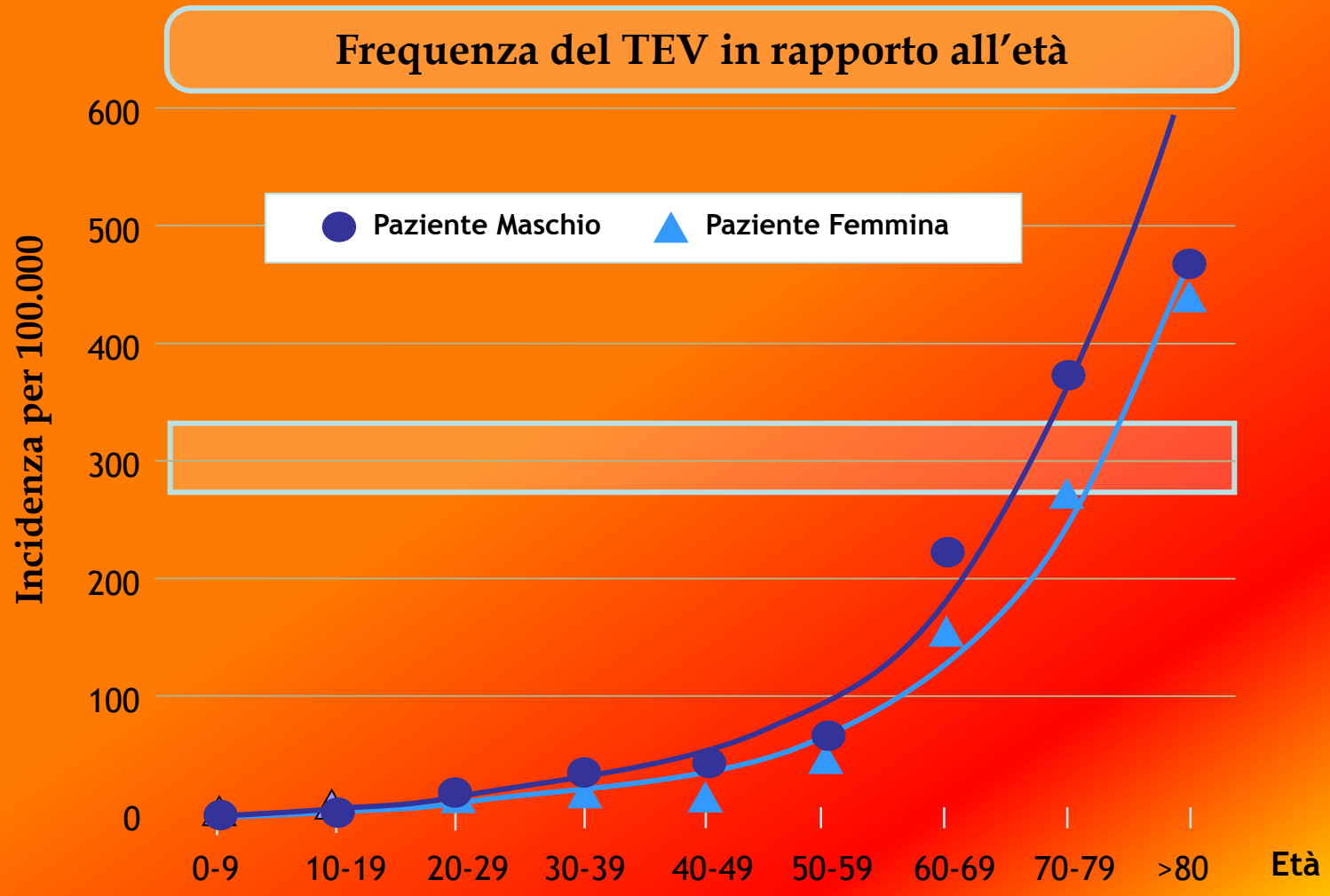
Mean cost (USA) for admissions ($)

Bick RL. *Clin Appl Thromb Hemost.* 1999;5(1):2–9

2. *Medicare & DRG.* 1996

3. Bergqvist D, *et al. Ann Intern Med.* 1997;126:454–457

INCIDENZA DI TEV IN BASE ALL'ETA' E AL SESSO



Anderson FA et al. Arch Intern Med 1991; 151: 933-38.

Fattori di rischio acquisiti per TEV

- Età avanzata
- Pregresso episodio tromboembolico
- Neoplasia
- Frattura o chirurgia recente
- Infarto miocardico acuto
- Scompenso cardiaco
- Ictus ischemico
- Immobilizzazione prolungata per patologia internistica
- Gravidanza/puerperio
- Terapia ormonale
- Sindrome da anticorpi antifosfolipidi

Fattori di rischio congeniti per TEV

- Deficit di antitrombina
- Deficit di Proteina C
- Deficit di Proteina S
- Fattore V Leiden
- Mutazione G20210A della protrombina
- Iperomocisteinemia
- Elevati livelli di VIII-IX-XI

Fattori di rischio per TEV

Alto	Intermedio	Basso
≥75 anni	60-75 anni	40-60 anni
Pregresso TEV	Familiarità per TEV	Sesso maschile
Pregressa tromboflebite	Fumo (>15 sigarette/die)	Gruppo non 0
Trombofilia	Gravidanza	Arteriopatia
Puerperio	Abortività	Diabete
Chirurgia maggiore*	Estroprogestinici	BPCO
Chirurgia ortopedica*	Obesità	TIA (in terapia)
Traumi*	Malattia infett. intest. cron.	Antipsicotici
Neoplasie	Insuff. resp. cronica	
M. autoimmunitarie	Iperomocisteinemia	
Scompenso cardiaco (III-IV NYHA)	S. mieloproliferative	
Ictus	Scompenso cardiaco (I-II NYHA)	
Paralisi	Broncopatia acuta	
Immobilizzazione*	Recente ricovero (>10 gg)	
Ricovero in terapia intensiva	Sepsi	

* entro 3 mesi

FATTORI DI RISCHIO CHE PREDISPONGONO A TEV

I mezzi terapeutici e di profilassi disponibili

FARMACOLOGICI

- EBPM
- ENF
- AVK
- Pentasaccaride
- NUOVI AO

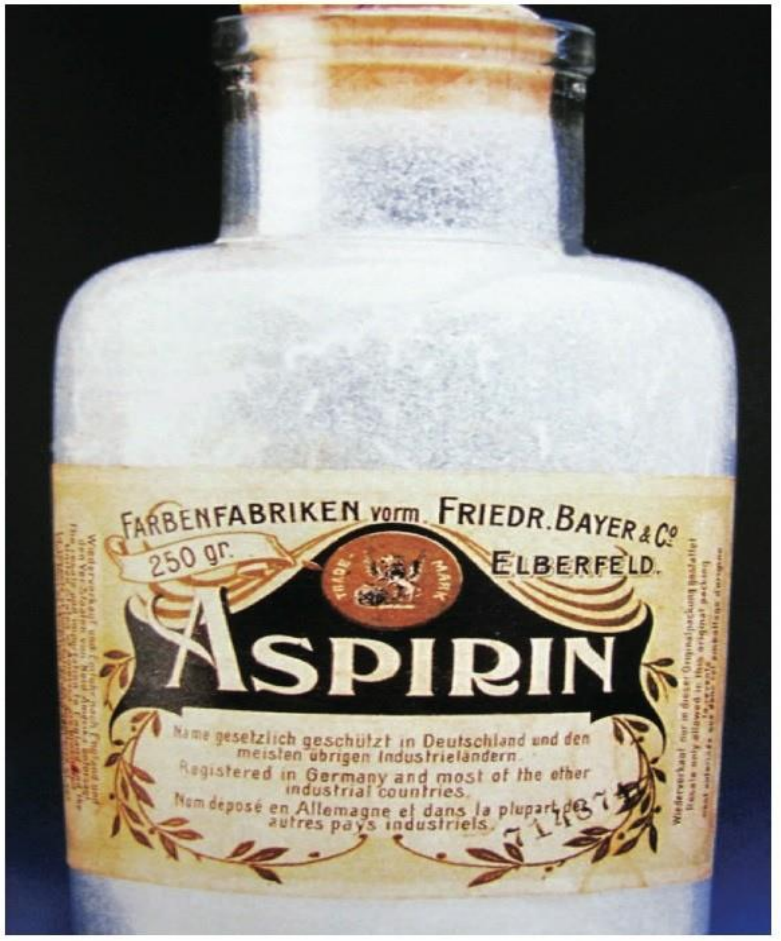
MECCANICI

- Calze elastiche
- Compressione Pneumatica Intermittente

Recommended Long-Term Anticoagulation Therapy for Patients with Thromboembolic Episode(s).[11]

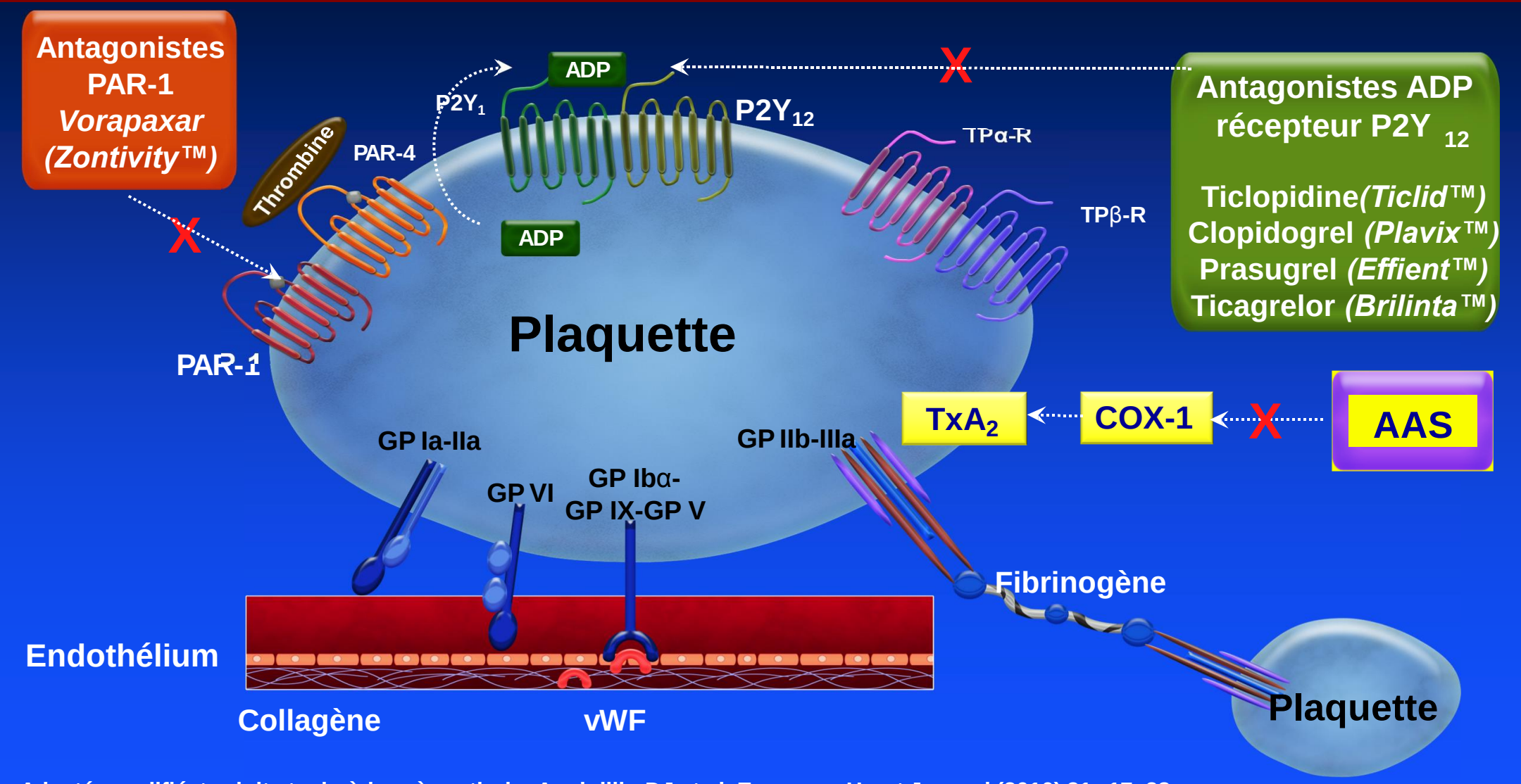
First Episode Related to a Major Reversible Event	Unprovoked / Recurrent Episode	Persistent Risk Factors (E.g. Malignancy)
Oral Warfarin should be administered as first line therapy. The standard of care requires Warfarin to overlap with initial anticoagulation therapy for a minimum of 5 days until INR range is > 2.0 for at least 24 hours, and then targeted to an INR of 2.0 to 3.0. Anticoagulation should cease after 3 months.	At least 6 months of anticoagulation should be administered, with the consideration of indefinite period of anticoagulation with frequent reassessment of risks and benefits of continued anticoagulation	Low molecular weight heparin is advised for at least 3 to 6 months, or as long as the malignancy or treatment is ongoing.

Aspirina ?


FARBENFABRIKEN vorm. FRIEDR. BAYER & Co
250 gr.
ELBERFELD.
ASPIRIN
Name gesetzlich geschützt in Deutschland und den meisten übrigen Industrieländern.
Registered in Germany and most of the other industrial countries.
Nom deposé en Allemagne et dans la plupart des autres pays industriels.

Antiplaquettaires oraux 2014 (Canada et USA)

Bloqueurs TxA2, ADP ($P2Y_{12}$) et PAR-1



Adapté, modifié, traduit et mis-à-jour à partir de: Angiolillo DJ et al. European Heart Journal (2010) 31, 17–28

A. Roussin MD

PERO'...

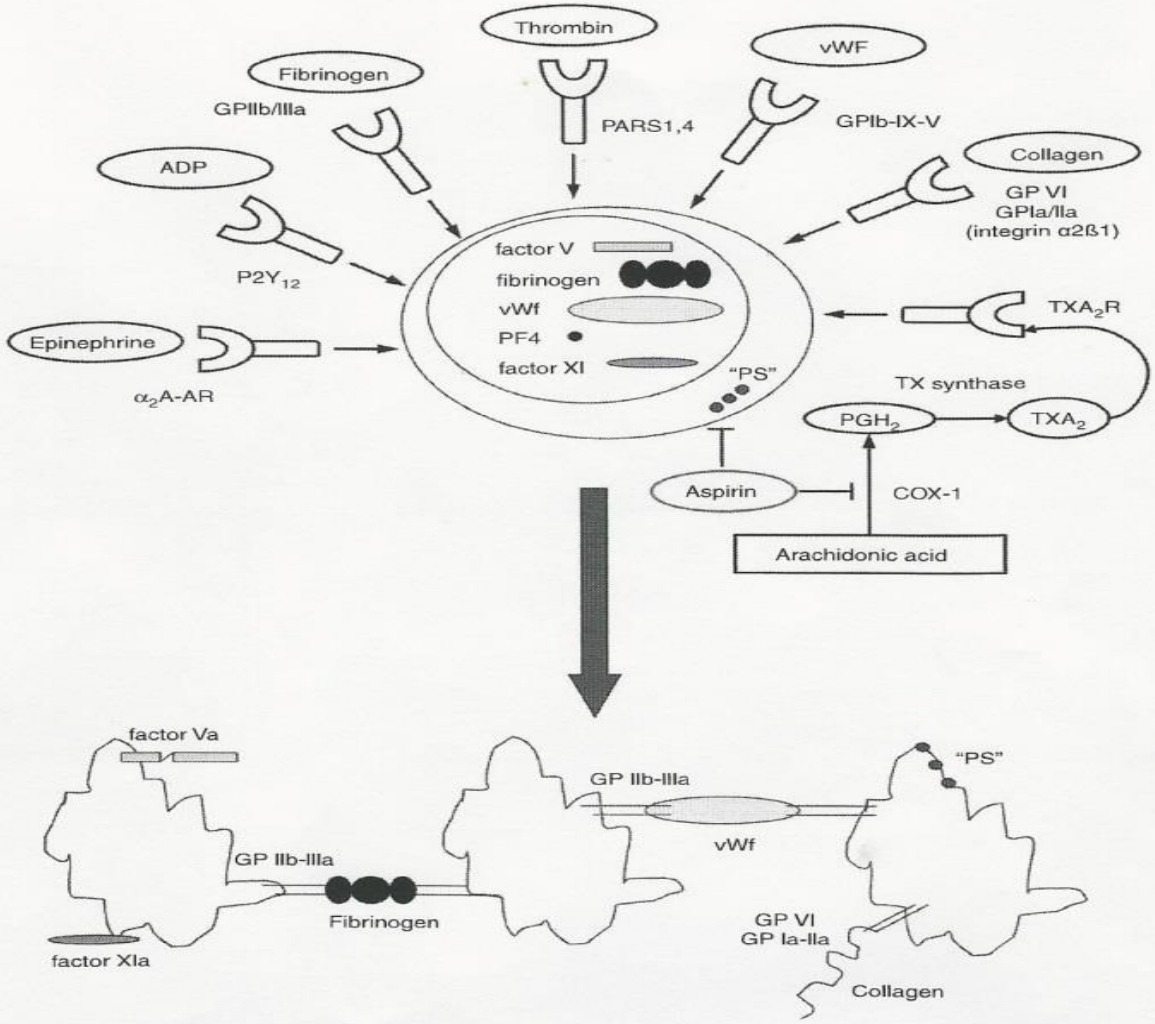
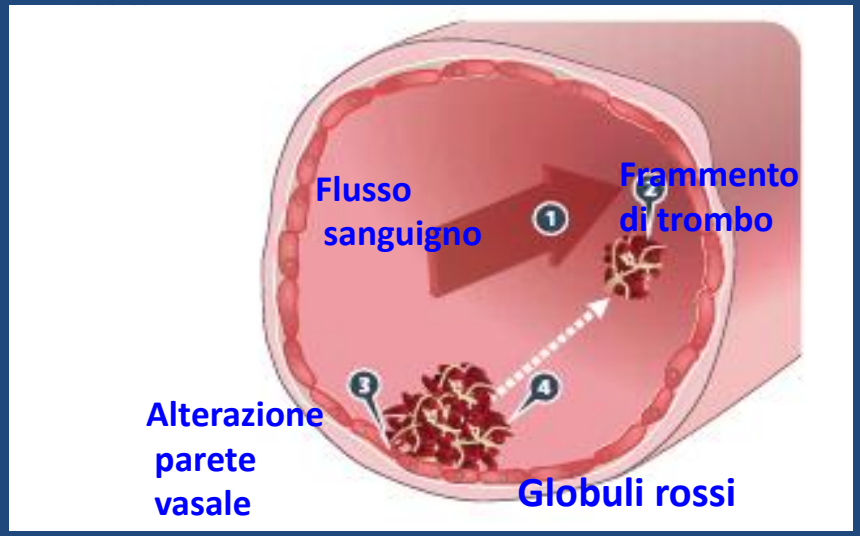


Fig. 1. Major prothrombotic mechanisms of platelet activation that could be affected by aspirin. Platelet adhesion initiated by

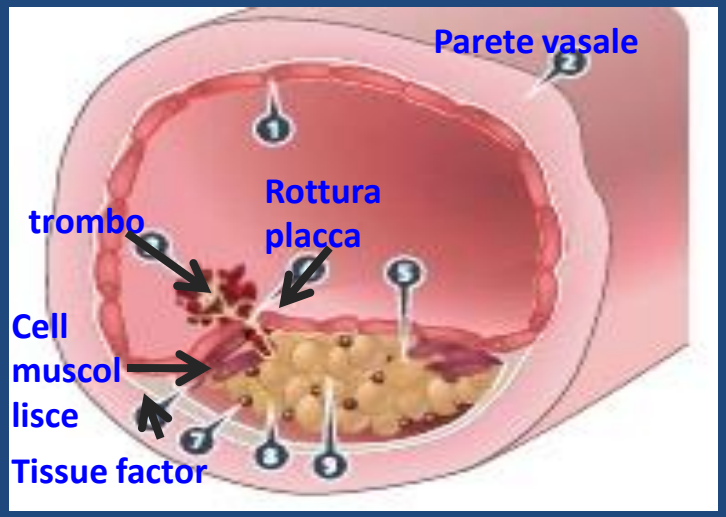
Turpie AGG, Esmon C, Thromb Haemost 2011

TROMBOSI VENOSA



Stasi, ***ipercoagulabilità***, danno endoteliale

TROMBOSI ARTERIOSA



- Rottura placca
- Esposizione core lipidico
- Attivazione piastrinica

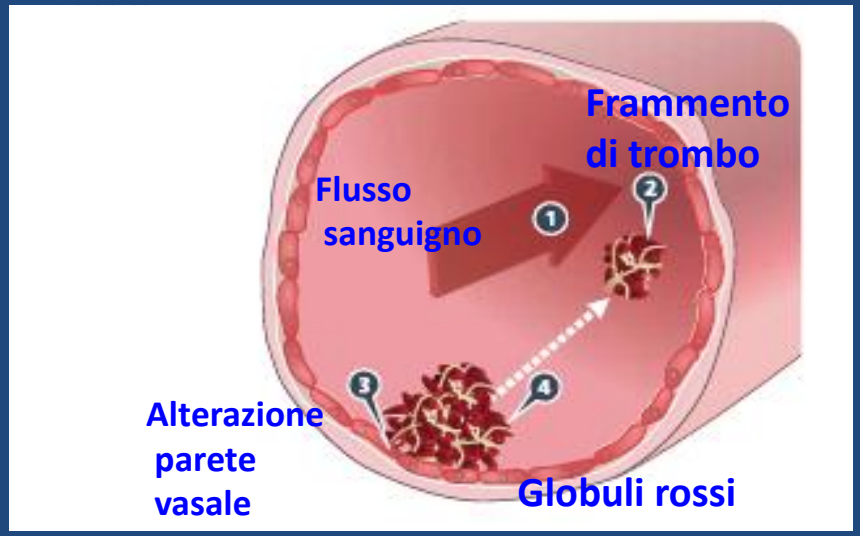
Venous and arterial thrombosis – pathogenesis and the rationale for anticoagulation

Alexander G. G. Turpie[1]; Charles Esmon[2]

[1]Department of Medicine, McMaster University, Hamilton, Ontario, Canada; [2]Oklahoma Medical Research Foundation, Howard Hughes Medical Institute, and Departments of Pathology and Biochemistry & Molecular Biology, University of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma, USA

Thromb Haemost 2011

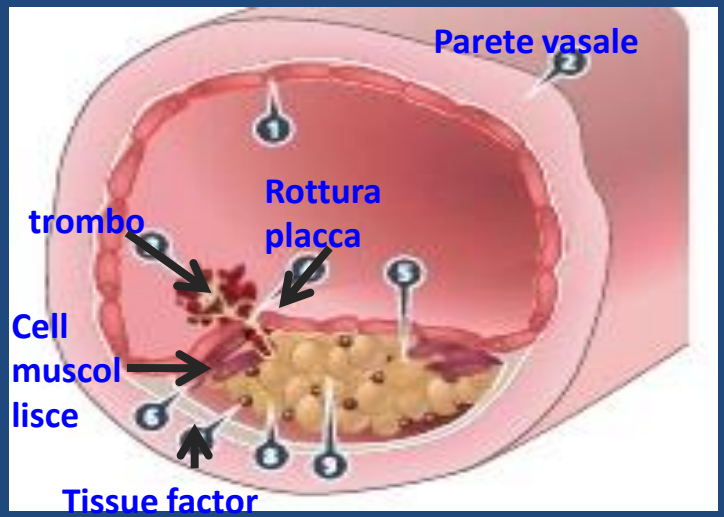
TROMBOSI VENOSA



- Stasi, ***ipercoagulabilità***, danno endoteliale

Attivazione piastrinica

TROMBOSI ARTERIOSA



- Rottura placca
- Esposizione core lipidico
- Attivazione piastrinica

e della coagulazione, con formazione di trombina

ANTIAGGREGANTI

- Acido acetilsalicilico e tienopiridine
- Profilassi e terapia della trombosi arteriosa

Ruolo delle piastrine nella patogenesi della trombosi venosa

Efficacia nella profilassi del TEV?

Does acetyl salicylic acid (ASA) have a role in the prevention of venous thromboembolism?

Ganesan Karthikeyan,[1,2] John W. Eikelboom,[2] Alexander G. G. Turpie[2] and Jack Hirsh[3]

[1]All India Institute of Medical Sciences, New Delhi, India, [2]Hamilton General Hospital, McMaster University, Hamilton, ON, and [3]Henderson Hospital Site, McMaster University, Hamilton, ON, Canada

Br J Haematol 2009

ASA vs placebo

a- APTC 1994 (chir generale e ortopedica, medicina ad alto rischio)

↓ rischio TEV del **26%** (24.8 vs 33.6%9

↓ rischio EP del **63%** (1 vs 2.7%)

↑ trasfusioni (0.4 vs 0.7%), ematomi cutanei, reinterventi

Trials inclusi NON sono blindati!

Dubbie metodologie per diagnosi TEV (I125 < venografia!)

b – PEP trial (Lancet 2000)

chirurgia anca/ginocchio

- ↓ TVP del **28%** e EP del **39%**
- ↑ bleeding postoperatorio, ematemesi e melena (2.7 vs 1.8%)

CONCLUSIONI

↓ rischio vs placebo in pz ad alto rischio

ASA vs altre terapie

NON esistono ampi trials randomizzati o metaanalisi

Table 2

Summary of the largest meta-analyses on the use of antiplatelet agents in venous thromboembolism and anticoagulants in arterial thrombotic diseases

Author [Ref.]	Population	Results
a) Antiplatelet therapy in venous thromboembolic disase		
Antiplatelet Trialists' Collaboration [44]	10,000 surgical or immobilized patients enrolled in 80 randomized trials	Antiplatelet therapy is associated a reduction in the incidence of VTE in high-risk medical or surgical patients
Antithrombotic Trialists' Collaboration [46]	64,535 high-risk patients enrolled in 32 randomized trials	Antiplatelet therapy reduces fatal or non-fatal PE
b) Anticoagulant therapy in arterial thrombotic disease		
Andreotti [50]	25,307 patients with acute coronary syndromes enrolled in 14 randomized trials	Warfarin plus aspirin is superior to aspirin alone in preventing major adverse outcomes, but doubles the risk of major bleeding
Gubitz [55]	21,966 patients in the acute phase of stroke enrolled in 6 randomized trials	Anticoagulants (heparins and vitamin-K antagonist) in the acute phase of stroke do not improve functional outcomes and increase the rate of intracranial bleeding
Aguilar [57]	9598 patients with non-valvular atrial fibrillation enrolled in 8 randomized trials	Oral anticoagulants are superior to antiplatelet therapy in preventing stroke and other major vascular events but increase the risk of intracranial bleeding
WAVE Investigators [59]	4889 patients with PAD enrolled in 9 randomized trials	Oral anticoagulants are not superior to aspirin in preventing graft occlusion or death and increase the risk of major bleeding

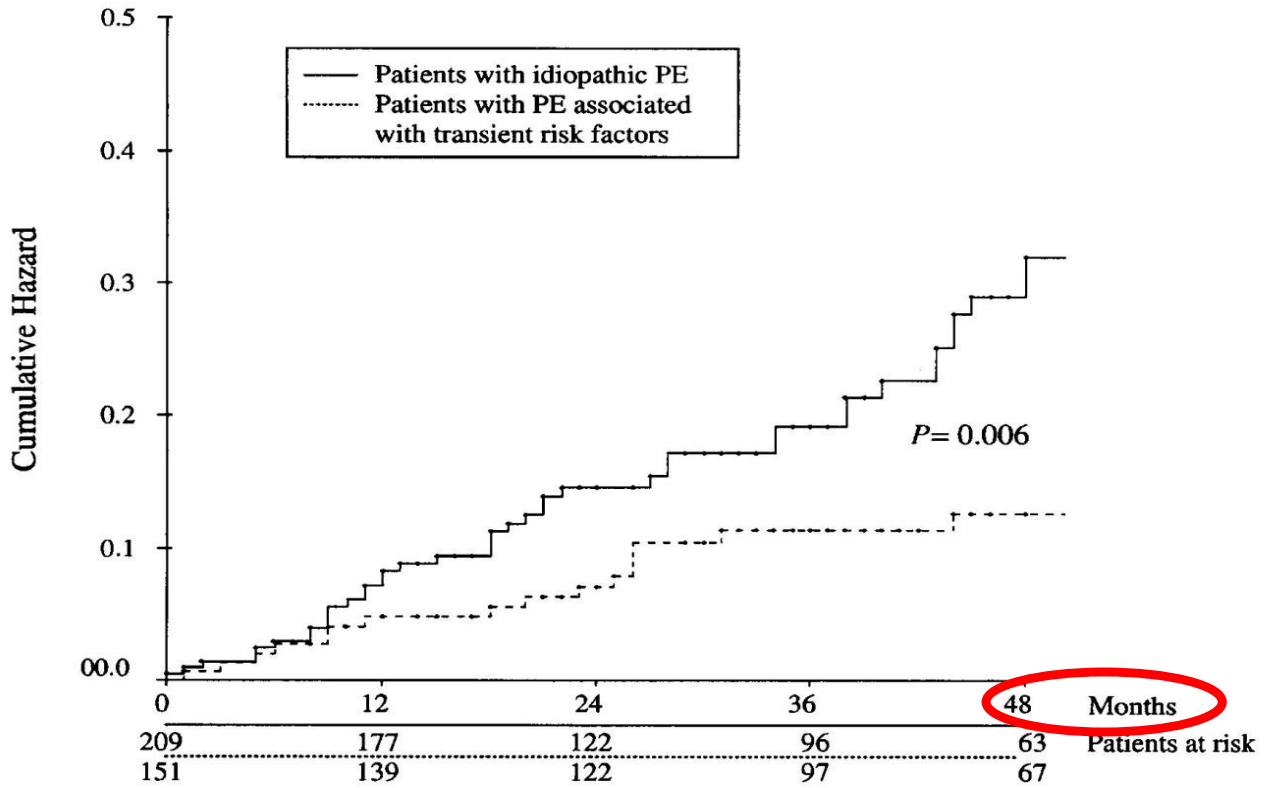
RR, relative risk; VTE, venous thromboembolism; PE, pulmonary embolism; PAD, peripheral artery disease; WAVE, Warfarin Antiplatelet Vascular Evaluation.

Franchini M, Mannucci PM, 2008

A prospective study on cardiovascular events after acute pulmonary embolism

Cecilia Becattini[1], Giancarlo Agnelli[1*], Paolo Prandoni[2], Mauro Silingardi[3], Rosamaria Salvi[4], Maria Rita Taliani[1], Renzo Poggio[5], Davide Imberti[6], Walter Ageno[8], Enrico Pogliani[7], Ferdinando Porro[9], and Franco Casazza[10]

Eur H J 2005

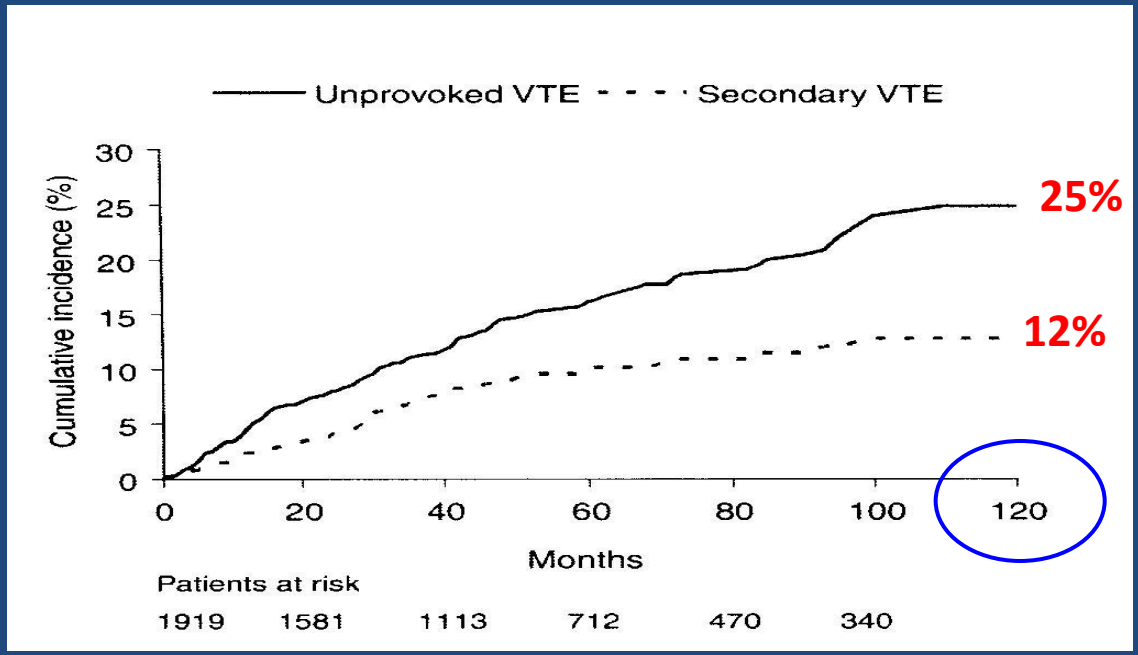


- Gli eventi CV (IMA, stroke) sono più frequenti nei pz con EP "idiopatica" che nei pz con EP associata a fattori di rischio transitori.

Venous thromboembolism and the risk of subsequent symptomatic atherosclerosis

P. PRANDONI,* A. GHIRARDUZZI,† M. H. PRINS,‡ V. PENGO,§ B. L. DAVIDSON,¶ H. SØRENSEN,** R. PESAVENTO,* M. IOTTI,† E. CASIGLIA,†† S. ILICETO,§ A. PAGNAN* and A. W. A. LENSING‡‡

JTH 2006



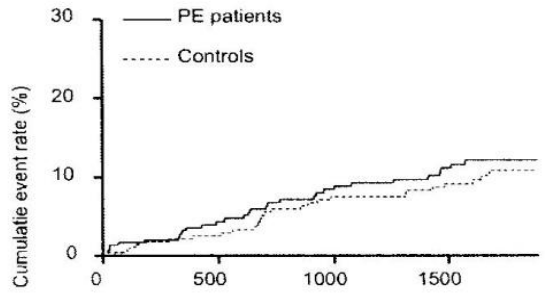
Incidenza aterosclerosi sintomatica in pz con TEV "idiopatico" e "secondario"

Risk of arterial cardiovascular events in patients after pulmonary embolism

Frederikus A. Klok,[1] Inge C.M. Mos,[1] Lisette Broek,[1] Jouke T. Tamsma,[1] Frits R. Rosendaal,[2] Albert de Roos,[3] and Menno V. Huisman[1]

Blood 2009

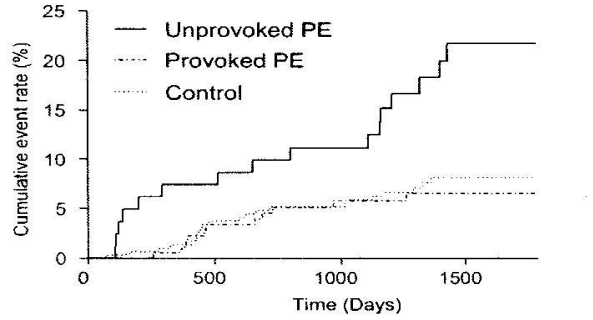
Studies have reported inconsistent evidence for an association between venous thrombosis and arterial cardiovascular events. We further studied the association between both diseases by comparing the occurrence of cardiovascular events in patients diagnosed with acute pulmonary embolism (PE) contrasted to patients with comparable baseline risk characteristics (patients in whom PE was clinically suspected but ruled out). Included were 259 patients with provoked PE, 95 patients with unprovoked PE, and 334 control patients without PE. Patients diagnosed with PE were treated with vitamin K antagonists for 6 months. Median follow-up was 4.2 years. Sixty-three arterial cardiovascular events were registered (incidence, 5.1/100 patient-years). Adjusted hazard ratio was not different between patients with all-cause PE and control patients (1.39, 95% confidence interval [CI], 0.83-2.3) but increased for patients with unprovoked PE versus both patients with provoked PE and control patients without PE (2.18; 95% CI, 1.1-4.5; and 2.62; 95% CI, 1.4-4.9, respectively). This effect was confirmed after redefining the study start date to the moment the vitamin K antagonists were discontinued. Our study underlines the association between unprovoked venous thrombosis and arterial cardiovascular events; however, risk differences between patients with provoked PE and patients in whom PE was clinically suspected but ruled out could not be demonstrated. (Blood. 2009; 114:1484-1488)



At risk:				
Controls	334	291	268	189
Patients	287	247	218	135

Figure 1. Cumulative arterial cardiovascular event rate in pulmonary embolism (PE) patients and control patients without PE.

Eventi arteriosi in pz con EP



At risk:				
Controls	312	279	261	125
Provoked	206	171	146	93
Unprovoked	81	74	69	36

Eventi arteriosi in pz con EP "idiopatica" e "secondaria"

Venous and arterial thrombosis: Different sides of the same coin?

Massimo Franchini [a], Pier Mannuccio Mannucci [b,*]

Eur J Int Med 2008

FATTORI DI RISCHIO
Età avanzata, obesità, ipertensione, diabete, iperlipidemia

Prandoni, Nengl J Med 2003
Becattini, Eur H J 2005
Sorensen, Lancet 2007
Bova, Thromb Haemost 2006

TROMBOSI VENOSA

TROMBOSI ARTERIOSA

Van derHagen, J Thromb Haemost 2006
Reich, J Thromb Haemost 2006

Until recently venous and arterial thrombosis were considered mechanistically distinct entities. However, their separate nature has been challenged by several studies showing that these conditions share a number of risk factors such as age, obesity, infections and the metabolic syndrome. The existence of an association is further supported by the finding that patients with venous thromboembolism are at higher risk of arterial events and vice versa. This review article addresses the association between venous and arterial thrombosis and its clinical and therapeutic implications. We conclude that arterial and venous thrombosis are mechanistically different, but that common risk factors are more relevant and frequent than previously thought.

Cardiovascular Risk Factors and Venous Thromboembolism

A Meta-Analysis

Walter Ageno, MD; Cecilia Becattini, MD; Timothy Brighton, MD;
Rita Selby, MD; Pieter W. Kamphuisen, MD

Circulation 2008

Background—The concept that venous thromboembolism (VTE) and atherosclerosis are 2 completely distinct entities has recently been challenged because patients with VTE have more asymptomatic atherosclerosis and more cardiovascular events than control subjects. We performed a meta-analysis to assess the association between cardiovascular risk factors and VTE.

Methods and Results—Medline and EMBASE databases were searched to identify studies that evaluated the prevalence of major cardiovascular risk factors in VTE patients and control subjects. Studies were selected using a priori defined criteria, and each study was reviewed by 2 authors who abstracted data on study characteristics, study quality, and outcomes. Odds ratios or weighted means and 95% confidence intervals (CIs) were then calculated and pooled using a random-effects model. Statistical heterogeneity was evaluated through the use of χ^2 and I^2 statistics. Twenty-one case-control and cohort studies with a total of 63 552 patients met the inclusion criteria. Compared with control subjects, the risk of VTE was 2.33 for obesity (95% CI, 1.68 to 3.24), 1.51 for hypertension (95% CI, 1.23 to 1.85), 1.42 for diabetes mellitus (95% CI, 1.12 to 1.77), 1.18 for smoking (95% CI, 0.95 to 1.46), and 1.16 for hypercholesterolemia (95% CI, 0.67 to 2.02). Weighted mean high-density lipoprotein cholesterol levels were significantly lower in VTE patients, whereas no difference was observed for total and low-density lipoprotein cholesterol levels. Significant heterogeneity among studies was present in all subgroups except for the diabetes mellitus subgroup. Higher-quality studies were more homogeneous, and significant associations remained unchanged.

Conclusions—Cardiovascular risk factors are associated with VTE. This association is clinically relevant with respect to individual screening, risk factor modification, and primary and secondary prevention of VTE. Prospective studies should further investigate the underlying mechanisms of this relationship. (***Circulation*. 2008;117:93-102.**)

Fattori rischio cardiovascolari (obesità, ipertensione, diabete mellito, fumo, ipercolesterolemia) sono associati ad aumentato rischio di TEV

Risk Factors for Venous Thromboembolism

Results From the Copenhagen City Heart Study

Anders G. Holst, MD; Gorm Jensen, MD, DMSc; Eva Prescott, MD, DMSc

Circulation 2010

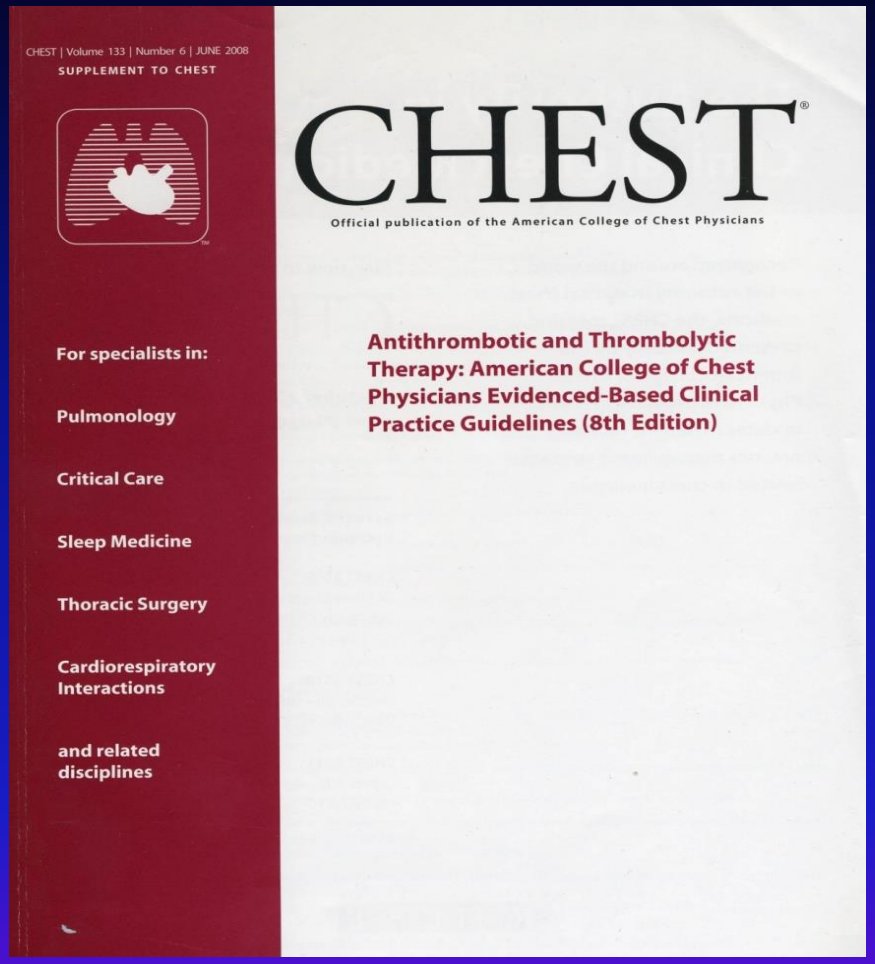
Background—Studies have suggested a link between risk factors for atherosclerotic disease and venous thromboembolism (VTE), but results are heterogeneous. We sought to identify risk factors for VTE with a focus on risk factors for atherosclerotic disease.

Methods and Results—Data were taken from the Copenhagen City Heart Study, a prospective cohort study of a random, age-stratified sample of people living in a defined area in Copenhagen, Denmark, started in 1976 with follow-up until 2007. First VTE (deep vein thrombosis and pulmonary embolism) diagnosis was retrieved from electronic national registries from study baseline to 2007. Of 18 954 subjects (median follow-up, 19.5 years) representing 360 399 person-years of follow-up, 969 subjects experienced at least 1 VTE, corresponding to a crude incidence rate of 2.69 (95% confidence interval [CI], 2.52 to 2.86) per 1000 person-years. The variables found to be significantly associated with VTE in a multivariable model adjusted for age and calendar time were as follows: body mass index (hazard ratio [HR] for ≥35 versus <20=2.10 [95% CI, 1.39 to 3.16]); smoking (HR for ≥25 g tobacco per day versus never smoker=1.52 [95% CI, 1.15 to 2.01]); gender (HR for men versus women=1.24 [95% CI, 1.08 to 1.42]); household income (HR for medium versus low=0.82 [95% CI, 0.70 to 0.95]); and diastolic blood pressure (HR for >100 versus <80 mm Hg=1.34 [95% CI, 1.08 to 1.66]). Other cardiovascular risk factors including total/high-density lipoprotein/low-density lipoprotein cholesterol levels, triglyceride levels, and diabetes mellitus were not associated with VTE.

Conclusions—Obesity and smoking were both found to be important risk factors for VTE whereas total/high-density lipoprotein/low-density lipoprotein cholesterol levels, triglyceride levels, and diabetes mellitus were not.

CONCLUSIONI

- Esiste un link tra aterosclerosi (A.S.) e TEV
- A.S. → ipercoagulabilità, Plt, Coagulaz→ T.V. o fattori di rischio comuni?
- L'ipercoagulabilità rappresenta il link tra trombosi arteriosa e venosa
- Alcuni fattori di rischio per aterotrombosi (età, obesità, sindrome metabolica) possono avere un ruolo nel TEV, mentre per altri (fumo, ipertensione e iperlipidemia) l'associazione è meno evidente
- Sono richiesti ulteriori studi per stabilire il beneficio degli antiaggreganti e delle statine nella prevenzione del TEV



- E' controindicato l'utilizzo della sola aspirina per la tromboprofilassi del TEV per qualunque tipo di paziente **grado 1 A**

Journal of Thrombosis and Haemostasis, **8**: 891–897 DOI: 10.1111/j.1538-7836.2010.03777.x

ORIGINAL ARTICLE

Incidence of arterial cardiovascular events after venous thromboembolism: a systematic review and a meta-analysis

C. BECATTINI,* M. C. VEDOVATI,* W. AGENO,† F. DENTALI† and G. AGNELLI*
*Division of Internal and Cardiovascular Medicine & Stroke Unit, University of Perugia; and †University of Insubria, Ospedale di Circolo, Varese, Italy

To cite this article: Becattini C, Vedovati MC, Ageno W, Dentali F, Agnelli G. Incidence of arterial cardiovascular events after venous thromboembolism: a systematic review and a meta-analysis. *J Thromb Haemost* 2010; **8:** 891–7.

The NEW ENGLAND JOURNAL of MEDICINE

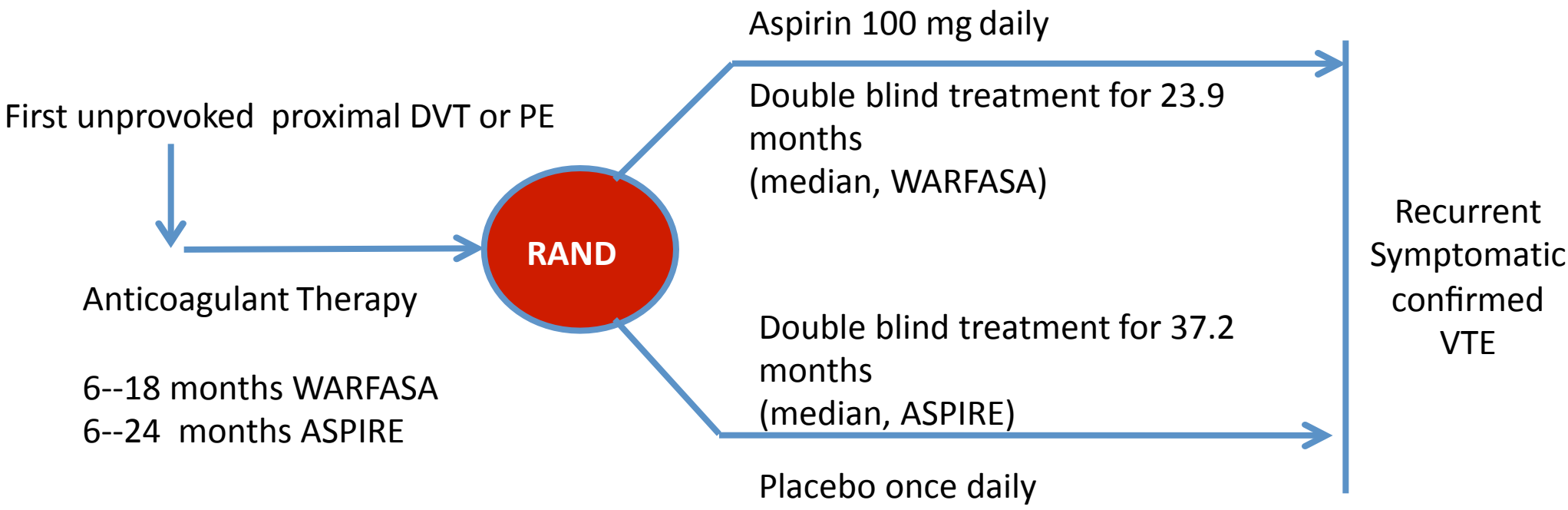
ESTABLISHED IN 1812 NOVEMBER 22, 2012 VOL. 367 NO. 21

Low-Dose Aspirin for Preventing Recurrent Venous Thromboembolism

Timothy A. Brighton, M.B., B.S., John W. Eikelboom, M.B., B.S., Kristy Mann, M.Biostat., Rebecca Mister, M.Sc., Alexander Gallus, M.B., B.S., Paul Ockelford, M.B., Harry Gibbs, M.B., Wendy Hague, Ph.D., Denis Xavier, M.Sc., Rafael Diaz, M.D., Adrienne Kirby, M.Sc., and John Simes, M.D., for the ASPIRE Investigators*

ABSTRACT

ASPIRIN and prevention of VTE
ASPIRE and WARFASA trial design



Becattini C et al NEJM 2012
Brighton TA et al NEJM 2012

WARFASA

- **- IL PRIMARIO METODO DI INCLUSIONE ERA QUELLO DI TESTARE L'EFFICACIA DEL TRATTAMENTO CON ASPIRINA IN PAZIENTI CHE AVEVANO EFFETTUATO TERAPIA ANTICOAGULANTE CON AVK PER 6-18 MESI E POI SOSPESO**
- **- I CRITERI DI INCLUSIONE PREVEDEVANO:**
  PAZIENTI CON UN EPISODIO SINGOLO DI TEV IN ASSENZA DI EVIDENTI FATTORI DI RISCHIO

- **- CRITERI DI ESCLUSIONE ERANO:**

- **-CANCRO**
- **- ACCERTATA TROMBOFILIA**
- **-SANGUINAMENTO IN ATTO**
- **-ALTO RISCHIO DI SANGUINAMENTO**
- **STORIA DI BLEEDING**

DISEGNO DELLO STUDIO

- **- DOPPIO CIECO RANDOMIZZATO MULTICENTRICO IN 403 PAZIENTI DI CUI 203 PAZIENTI TRATTATI CON 100 MG/DIE DI ASPIRINA E 198 PAZIENTI TRATTATI CON PLACEBO.**
- **- END POINT PRIMARIO : RECIDIVA DI TROMBOEMBOLISMO VENOSO**
- **- END POINT SECONDARIO : EVENTI ISCHEMICI ARTERIOSI O MORTE PER QUALSIASI CAUSA**

RISULTATI DELLO STUDIO

- **I pazienti trattati con placebo hanno documentato un'incidenza tromboembolica di 48 casi nei 198 pazienti.**
- **I pazienti trattati con Aspirina hanno documentato un'incidenza tromboembolica di 28 eventi nei 205 pazienti.**

- **Non c’è stata significativa differenza nelle emorragie maggiori o minori, trombocitopenia o altre complicanze tra i gruppi trattati con Aspirina e quello placebo**

VALUTAZIONI GENERALI

- **Lo studio WARFASA ha mostrato una riduzione del 40% delle recidive del TEV nel gruppo dei pazienti trattati con Aspirina rispetto a quelli non trattai senza determinare un significativo incremento dei sanguinamenti maggiori o minori.**

ASPIRE

- Studio multicentrico, randomizzato, doppio cieco che esamina l'efficiacia dell'aspirina nei pazienti che hanno terminato terapia con AVK da 6 settimane a 12 mesi
- Simile al Warfasa ma inizialmente follow up a 4 anni

- **- Non c’è stata significativa differenza nelle emorragie maggiori o minori, trombocitopenia o altre complicanze tra i gruppi trattati con Aspirina e quello placebo**
- **A differenza dello studio Warfasa nn ha dato una significativa riduzione nelle recidive di TEV**
- **Ha però mostrato una significativa riduzione degli aventi cardiovascolari sul circolo arterioso**

ASPIRIN

Recurrent VTE

	Aspirin	Placebo	HR (95% CI)	*p*
WARFASA N= 402	6.6%	11.2	0,58 (0,36--0.93)	.02
ASPIRE N= 822	4.8%	6.5	0,74 (0,52--1.05)	.09
Pooled			0,68 (0,51--0.90)	.007

Major vascular Events (VTE, MI, Stroke, CV death)	HR (95% CI)	
WARFASA	0,67 (0,43--0103)	.06
ASPIRE	0,66 (0,48--0.92)	.01
Pooled	0,66 (0,51--0.86)	.002

Becattini C et al NEJM 2012
Brighton TA et al NEJM 2012

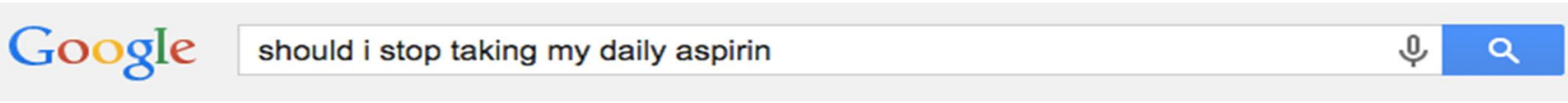
LIMITI NELL'UTILIZZO DELL'ASPIRINA

I FATTORI CHE INCREMENTANO IL RISCHIO DI SANGUINAMENTO SONO:

-ETA’
-USO CONCOMITANTE DI WARFARINA
-USO CONCOMITANTE DI CORTICOSTEROIDI
-ALTE DOSI DI ASPIRINA
-UTILIZZO DI ALTRI FANS COX2 INIBITORI

Table 1. Randomized, placebo-controlled trials of low-dose aspirin (75–325 mg daily dose) for vascular indications that provide information on major gastrointestinal (GI) bleeding outcomes

Study	Population	Aspirin dose (mg)	Double-blind	Major GI bleeding definition	Mean or median follow-up (months)	GI bleeding	
						Aspirin (%)	Placebo (%)
Thrombosis prevention[23]	Men with increased cardiac risk	75	Yes	Fatal/life-threatening that required transfusion or surgery	77	6/1268 (0.47)	2/1272 (0.16)
HOT[24]	Hypertension	75	Yes	'Major' (not defined)	46	77/9399 (0.82)	37/9391 (0.39)
SAPAT[25]	Chronic stable angina	75	Yes	Transfusion, death or 'serious implications'	50	11/1009 (1.09)	6/1026 (0.58)
SALT[26]	50–79 years old with TIA, minor ischaemic stroke, retinal artery occlusion	75	Yes	Severe or causing discontinuation of study drug	29	9/676 (1.33)	4/684 (0.58)
EAFT[27]	TIA or minor ischaemic stroke and atrial fibrillation	300	Yes	Fatal or requiring hospitalization, transfusion or surgery	28	2/404 (0.50)	1/378 (0.26)
PPP[28]	One or more cardiac risk factors	100	No	'Clinically severe'	43	17/2226 (0.76)	5/2269 (0.22)
APRICOT[29]	Post-thrombolytic therapy	325	Yes	Not defined	3	0/102	0/90
Silagy *et al.*[30]	70 years old or older without cardiovascular disease	100	Yes	Required hospitalization	12	1/200 (0.50)	0/200
Physicians' Health[31]	Physicians with no cardiovascular disease	325 every other day	Yes	Required transfusion	60	48/11 037 (0.43)	28/11 034 (0.25)
UK-TIA[32, 33]	TIA or minor ischaemic stroke	300	Yes	Required hospitalization	48	10/810 (1.23)	2/816 (0.25)
Elwood *et al.*[34]	Less than 65 years old with myocardial infarction	300	No	Not defined	12	0/615	0/624
Gavaghan *et al.*[35]	70 years old or less with coronary artery bypass graft surgery	324	Yes	Active ulcer bleeding	12	2/127 (1.57)	0/110
Lewis *et al.*[36]	Unstable angina	324	Yes	Discontinued study drug due to GI bleeding	3	4/625 (0.64)	3/641 (0.47)
ACBS[37]	Carotid stenosis ≥50%	325	Yes	Required hospitalization with transfusion	23	1/188 (0.53)	1/184 (0.54)



Environ 676 000 résultats (0,34 secondes)

An Aspirin a Day? Only If You Have Had a Heart Attack ...

health.clevelandclinic.org/.../an-**aspirin-a-day**-only-if-... ▾ Traduire cette page

12 mai 2014 - At the same time, people taking **aspirin every day** face serious risks. .... I immediately **stopped taking** the **Aspirin** and **will** discuss it with **my** ...

Vous avez consulté cette page le 14-10-21.

Daily aspirin therapy - Mayo Clinic

www.mayoclinic.org/.../**daily-aspirin**.../art-20046797 ▾ Traduire cette page

Subscribe to **our** Heart-Healthy Living e-newsletter to stay up to date on heart-health ... You **should take** a **daily aspirin** only if your doctor advises you to **do** so. ... If you've been **taking daily aspirin** therapy and want to **stop**, it's important to talk to ...

Will I increase my risk of heart attack if I stop taking aspirin ...

www.sharecare.com › ... › Heart Disease › Heart Attack ▾ Traduire cette page

Will I increase **my** risk of heart attack if I **stop taking aspirin**? ... If you need it, take it **every day** and don't stop unless you are experiencing harmful side effects, ...

Aspirin and Your Heart: Many Questions, Some Answers ...

www.health.harvard.edu/.../**aspirin**-and-**your**-heart-m... ▾ Traduire cette page

The benefit of taking a **daily aspirin** to protect against a heart attack is well established, but this ... **Should** I **stop taking my** aspirin before elective surgery?

Vous avez consulté cette page le 14-10-21.

Daily Aspirin - More Benefit Than Risk? - Medical News Today

www.medicalnewstoday.com/articles/243265.php ▾ Traduire cette page

★★★★☆ Note : 3,8 - 17 votes

25 mars 2012 - Many people **take** a low dose of aspirin every day to lower their risk of a further heart ... with the doctor, "In **my** case, doc, **should** I be **taking daily aspirin**?" ...

AAS et récidive de TEV

Efficacité de 32% (aucun consensus ou guide)

BREF:

- **AAS non indiquée en traitement initial**
- **AAS n'est pas aussi efficace qu'un AC**

Becattini C, et al. N Engl J Med. 2012; 366(21):1959-1967. WARFASA
Brighton TA, et al. N Engl J Med. 2012; 367(21):1979-1987. ASPIRE
Simes J, et al. Circulation 2014; on-line 25-08-2014. INSPIRE

AAS et efficacité selon la situation clinique

Situation	RRR	Incidence annuelle: IM + AVC + Mortalité vasc.
Toutes confondues	**25%**	**1 à 10%**
Prévention primaire	**12 à 25%**	**Framingham: < 2%**
SCA	**30%**	**10%**
MCAS après un an	**25%**	**5%**
FA	**22%**	**CHADS: ± 5%**
AIT et AVC aigus	**11%**	**9%**
AIT et AVC long terme	**22%**	**8%**
MAP	**26%**	**5%**
Diabète seul	**7 à 10%**	**3% selon nb. FR**
Récidive TEV long terme	**32% ?**	***5% pour TEV seule***

AAS et récidive de TEV
Efficacité de 32% (aucun consensus ou guide)

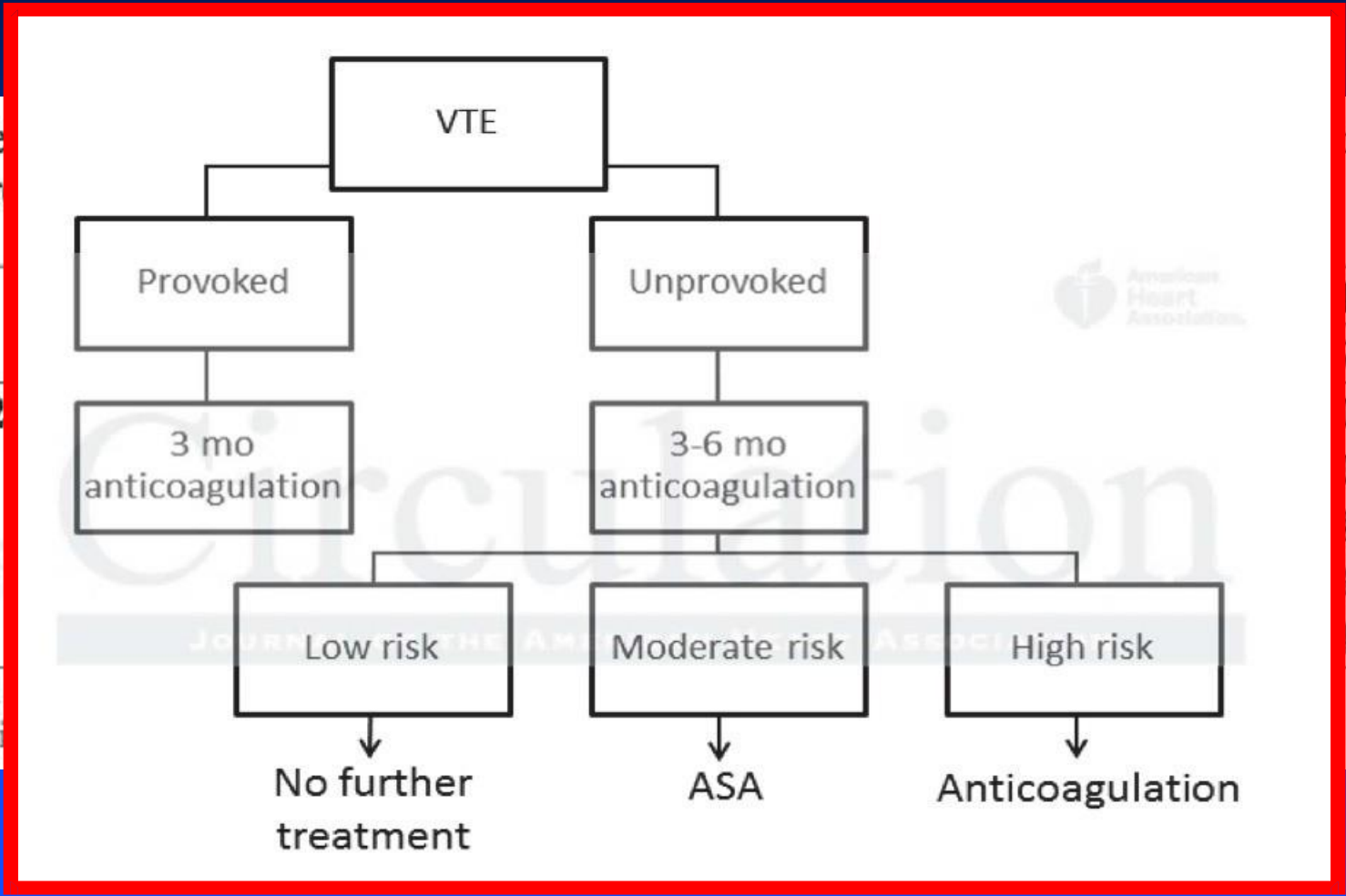
- Deux études comparant AAS au placebo chez pts. avec 1ère TVP idiop. après 6-18 mois d'AC

- Analyse groupée des patients sous AAS:
  - € Réduction de 32% de récidive de TEV (p=0.007)
  - € Réduction de 34 % évén. vasc. majeurs (p=0.002)
  - € Pas d'augmentation des saign. majeurs et clin. signigf.
  - € **Meilleur chez hommes et patients > 65 ans**

Becattini C, et al. N Engl J Med. 2012; 366(21):1959-1967. WARFASA
Brighton TA, et al. N Engl J Med. 2012; 367(21):1979-1987. ASPIRE
Simes J, et al. Circulation 2014; on-line 25-08-2014. INSPIRE

AAS et récidive de TEV

Efficacité comparée et suggestion publiée



Wakefield TW, et al. Circulation 2014; on-line 25-08-2014.

AAS et EP
Recommandations officielles 2014

2014 ESC Guidelines on the diagnosis and management of acute pulmonary embolism

Recommendations for duration of anticoagulation after pulmonary embolism

Recommendations	Class[a]	Level[b]	Ref[c]
In patients who refuse to take or are unable to tolerate any form of oral anticoagulants, aspirin may be considered for extended secondary VTE prophylaxis.	IIb	B	368, 369

Bisogna essere duri senza mai perdere la tenerezza

GRAZIE PER L’ATTENZIONE!!!