E’ possibile prevenire l’insorgenza della sindrome post-trombotica degli arti inferiori?

No: *Adriana Visonà (Castelfranco Veneto)*

Si: *Paolo Prandoni (Padova)*

Sintesi: *Francesca Falcinelli (Foligno)*

Adriana Visonà

Direttore UOC Angiologia

Azienda ULSS 2 Marca Trevigiana

Past President SIAPAV e ESVM

La sottoscritta Adriana Visonà

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

Alfasigma, Aspen, Amgen, Bayer, Daiichi Sankyo Pfizer, Servier, Sanofi
La sottoscritto dichiara altresì che detti rapporti non sono tali da poter influenzare l'attività di docenza espletata nell'ambito di codesto evento pregiudicando la finalità esclusiva di educazione/formazione di professionisti.

La sottoscritta Adriana Visonà non si trova pertanto in una situazione di conflitto di interessi rispetto all'evento ai sensi e per gli effetti dell'Accordo Stato-Regioni del 05/01/2009.

E’ possibile prevenire la SPT degli arti inferiori? NO

- Definizione e diagnosi
- Fisiopatologia, Fattori di rischio, Score probabilità
- Profilassi del TEV
- Elastocompressione
- Trombolisi farmaco meccanica in acuto

SINDROME POST-TROMBOTICA (SPT)

La più frequente complicazione tardiva del TEV

3/1000/anno popolazione generale

20-50% dopo una TVP

15% dei casi diagnosticati hanno una forma moderata-severa

Un certo grado di disabilità in > 90% dei casi di SPT

2 milioni di giornate lavorative perse ogni anno

Costi medi in USA 7000 $/paziente/anno

Pesavento R, Expert Rev Cardiovasc Ther. 2015

DIAGNOSI SPT

Basata principalmente su criteri clinici

Rilievi strumentali aspecifici

L'ISTH Subcommittee on Control of Anticoagulation **raccomanda** l'uso della **Scala di Villalta** quale più appropriato strumento per la diagnosi e la la valutazione prognostica della SPT

Kahn SR et al J Thromb Haemost 2009

Villalta score

Sintomi	Segni
Tensione	Edema pretibilale
Dolore	Ispessimento della cute
Crampi	Iperpigmentazione
Prurito	Nuove ectasie venose
Parestesie	Rossore
	Dolore alla compressione del polpaccio
	Ulcerazione cutanea

Villalta et al, Haemostasis 1994;

Kahn et al, JTH 2009

Definizione della SPT

Assente	Punteggio ≤ 4
Lieve/Moderata	Punteggio 5-14
Severa	Punteggio ≥ 15 o ulcere

Punteggio 0-3

Villalta et al, Haemostasis, 1994

Kahn et al, Arch Intern Med, 2002

Ragioni per la raccomandazione

- La scala Villalta Scale è comprensiva della presenza e severità sia dei **sintomi** che dei **segni** obiettivabili della SPT
- Validata, responsiva ai **cambiamenti clinici**, buona **riproducibilità** inter-osservatore
- Utilizzabile da **personale** addestrato anche **non- medico**
- Uso puntuale, continuo, a binario
- Applicata in numerosi **studi clinici** sulla SPT in numerosi paesi

Journ Thromb Haemost,2009

Buona pratica clinica

CHI?

Individuare la popolazione maggiormente a rischio di sviluppare PTS (dati strumentali, SOX-PTS score, IDEAL PTS score).

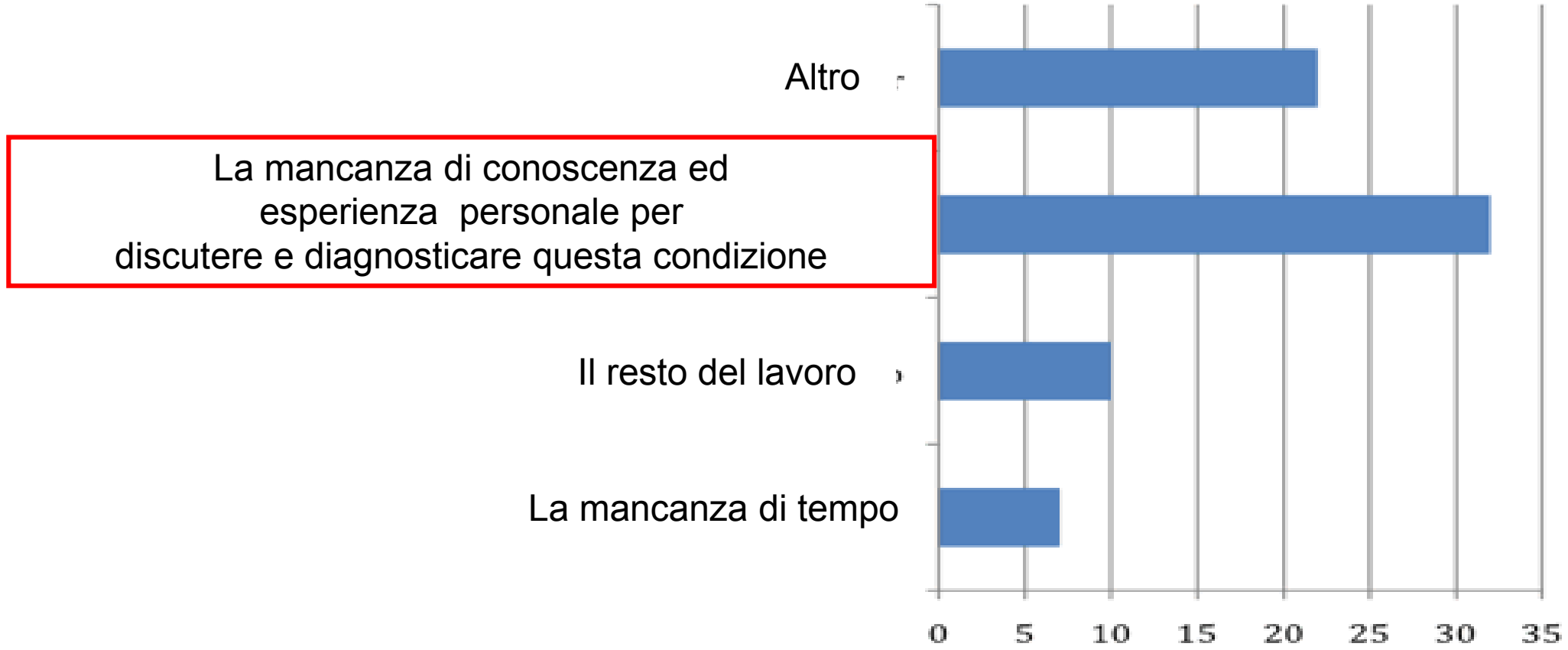
COME?

Segni e sintomi raccolti secondo un idoneo sistema classificativo.

QUANDO?

Non prima di tre mesi dalla DVT. Seguire l'evoluzione nel tempo.

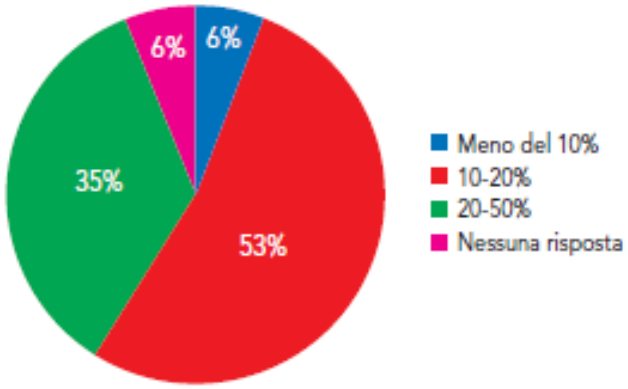
Che cosa ostacola questa pratica clinica ?



Consapevolezza rischio SPT

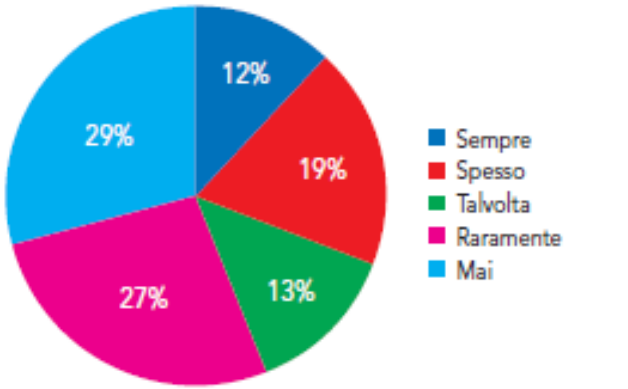
Risultati dei questionari

"Quale percentuale di pazienti con TVP sviluppa Sindrome Post-Trombotica"



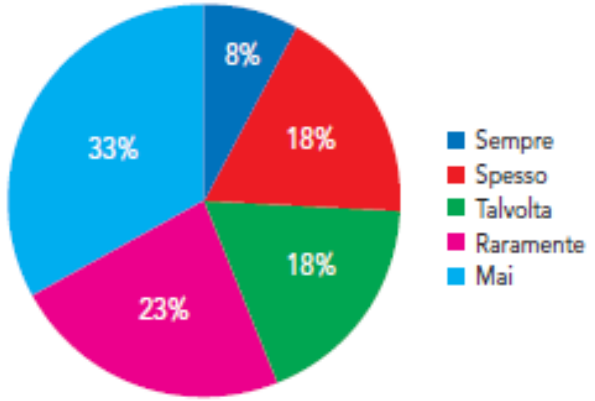
Conclusione: gli intervistati sottostimano l'incidenza della SPT (risposta corretta: 20-50%)

"Con quale frequenza affronta con il paziente il rischio SPT"



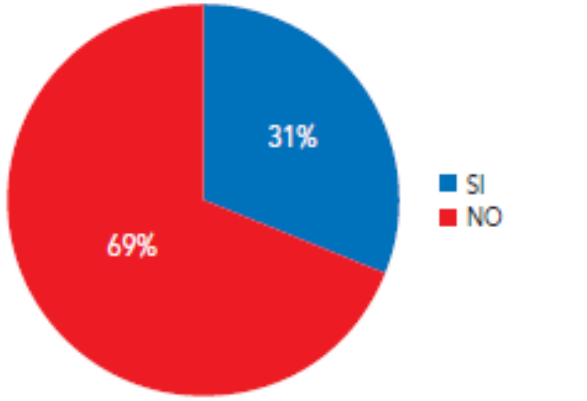
Conclusione: Solo 1/3 degli intervistati discute affronta regolarmente il rischio della SPT con i pazienti

Con quale frequenza valuta i sintomi ed i segni di SPT dopo una TVP?



Conclusione: Meno della metà degli intervistati valuta la SPT di routine

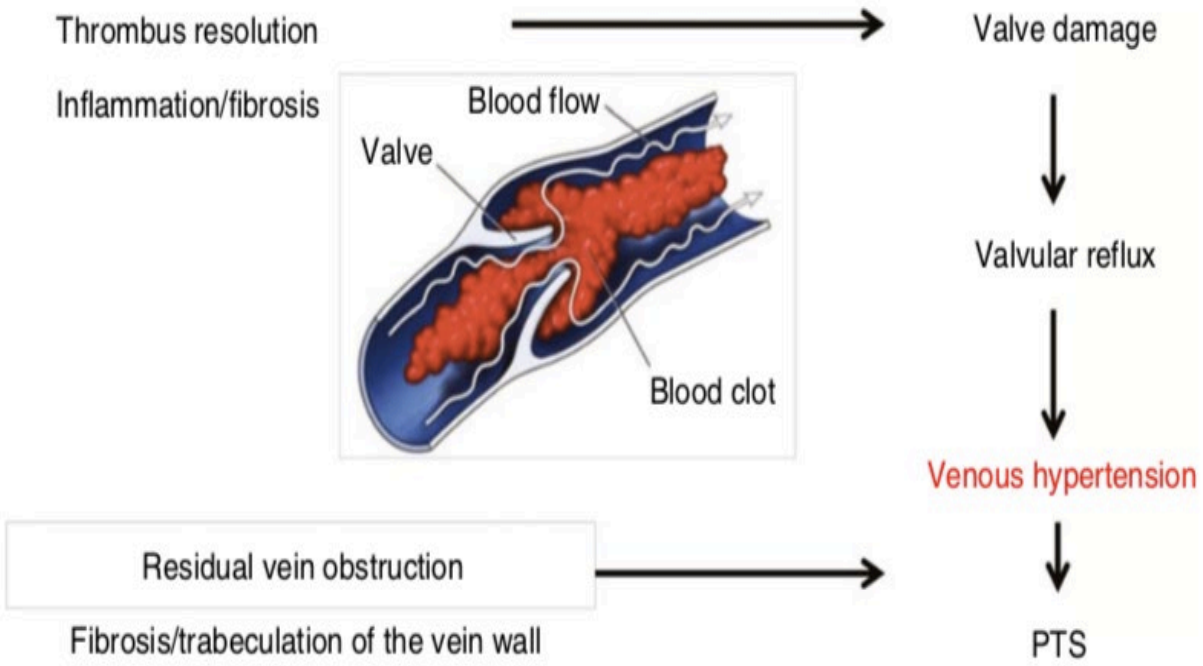
"Ha mai seguito corsi di formazione specifici per la prevenzione e la diagnosi della SPT?"



Conclusione: esiste un gap nella formazione per la prevenzione e la diagnosi della SPT

Kahn SR - Prevent PTS Programme 2012 – Utah University

PERCHE' SI SVILUPPA UNA PTS?



FATTORI DI RISCHIO PER LO SVILUPPO DELLA SPT

Table 2. Risk factors for post-thrombotic syndrome.

Risk factor	Strength of the association with PTS
Older age	Strong
Obesity	Strong
DVT localization	Strong
Primary varicose veins	Strong
Smoking before pregnancy	Strong
Poor INR control	Strong
Ipsilateral DVT recurrence	Strong
RVT	Strong
Residual symptoms and signs at 1 month after DVT	Weak
LMWH versus OAC	Weak
Increased D-dimer levels	Weak
Elevate markers of inflammation	Weak
Gender	Variable
Asymptomatic DVT	Variable
Provoked DVT	Variable
Recent surgery	None
Thrombophilic defects	None
Duration of OAC	None
Physical activity	None

DVT: Deep vein thrombosis; INR: International normalized ratio; LMWHs: Low-molecular-weight heparins; OAC: Oral anticoagulants; PTS: Post-thrombotic syndrome; RVT: Residual venous thrombosis.

EXPERT REVIEWS

Prevention and treatment of the post-thrombotic syndrome and of the chronic thromboembolic pulmonary hypertension

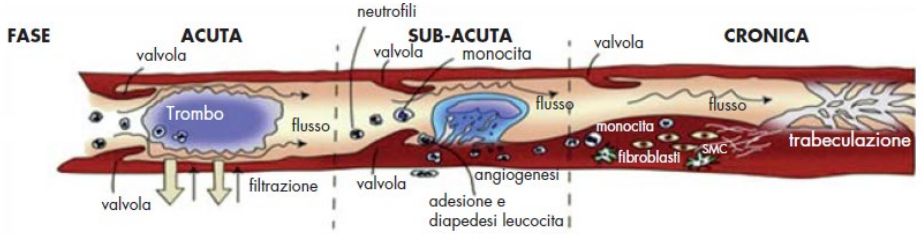
Expert Rev. Cardiovasc. Ther. 13(2), 193–207 (2015)

Raffaele Pesavento and Paolo Prandoni*

Department of Cardiothoracic and Vascular Sciences, Vascular Medicine Unit, University of Padua, Via Giustiniani 2, 35128 Padua, Italy
**Author for correspondence:*
Tel.: +39 049 821 2656
Fax: +39 049 821 8731
paoloprandoni@tin.it

Post-thrombotic syndrome (PTS) and chronic thromboembolic pulmonary hypertension (CTEPH) are late complications of venous thromboembolism. The purpose of this review is to present and discuss recently published studies that have improved our knowledge of PTS and CTEPH. The current understanding of the pathophysiology of PTS and CTEPH is discussed as well as the importance of chronic residual venous thrombosis, some polymorphisms of plasminogen activator inhibitor-1, and the current concept of misguided thrombus resolution. The surprising finding that elastic compression stockings may not be effective in preventing PTS and the novel medical treatment in CTEPH are discussed in detail. Novel direct oral anticoagulants show potential for prevention of PTS. No firm conclusions can be drawn on the efficacy of elastic stockings. Novel treatments of CTEPH for inoperable patients and those with persistent pulmonary hypertension after surgery have become available and further research on wider indication for their use is urgently needed.

KEYWORDS: chronic thromboembolic pulmonary hypertension • compression stockings • deep vein thrombosis • post-thrombotic syndrome • pulmonary embolism • pulmonary endarterectomy • stasis ulcer • venous thromboembolism



Sequenza di processi fisiopatologici infiammatori nella vena trombizzata, durante le fasi acuta, subacuta e cronica, che conducono all'esordio della SPT.

Pesavento R, Prandoni P. Expert Rev. Cardiovasc. Ther. 13(2), (2015)
Cate-Hoek AJ et al. Blood Reviews. 2016 (30): 131-137.

Risk factor	Strength of risk association[a]	Potential therapeutic impact/implication[b]
Non-modifiable risk factors		
Extensive proximal DVT	+++	Early thrombus removal (thrombolysis/endovascular interventions/surgery) in selected cases
Ipsilateral DVT recurrence	+++	Individualized AC treatment (drug, dose, duration) to prevent DVT recurrence
Primary venous insufficiency	++	Elastic compression stockings – To treat edema – To prevent worsening of venous insufficiency
Older age	++	None
Residual venous obstruction	++	Venous recanalization in case of established proximal obstruction Early thrombus removal techniques in selected cases with extensive DVT to prevent residual obstruction occurrence

Principal NON MODIFIABLE risk factors for post-thrombotic syndrome and their potential impact on therapeutic management

Galanaud JP, Monreal M, Kahn SR, 2018

Modifiable risk factors		
Anticoagulation		
– Absence	+++	Appropriate (intensity & duration) of AC treatment of DVT
– VKA vs. LMWH	+	Extended LMWH (3 months) in high-risk DVT patients? (requires confirmation in large trials)
– VKA vs. DOAC	+	DOAC (Rivaroxaban) could be more effective than VKA for PTS prevention (requires confirmation in large trials) Frequent and careful INR monitoring for patients on VKA treatment
– Poor INR control	++	
Obesity	++	Weight loss?
Inflammation & fibrinolysis	++/+	LMWH and statin could be effective, but level of evidence is low to date

Principal MODIFIABLE risk factors for post-thrombotic syndrome and their potential impact on therapeutic management

Galanaud JP, Monreal M, Kahn SR, 2018

Fattori predittivi di PTS *all'esordio della TVP*

- Età avanzata
- Presenza di vene varicose
- Obesità
- Interessamento del circolo prossimale e in particolare del tratto femoro-iliaco vs. tvp distale isolata
- Intensità della sintomatologia clinica iniziale

Fattori predittivi di PTS *successivamente all'esordio della TVP*

- Persistenza di sintomatologia clinica intensa a distanza di un mese dall'esordio della TVP
- La persistenza di residuo trombotico valutato con ecografia a distanza di tre mesi
- Lo sviluppo di incompetenza valvolare poplitea a distanza di 3-6 mesi
- L'alterazione marcata del test di flogosi (tra cui PCR) a distanza variabile dall'esordio di TVP
- Conduzione inadeguata di terapia dicumarolica (tempo speso al di sotto di un INR di almeno 2 in più del 50%)

Fattori predittivi di PTS

1

11. RECIDIVA A CARICO STESSO ARTO

- Potente
- Aumenta 4-6 volte rischio SPT

Amin EE, van Kuijk SMJ, Prandoni P et al. Thromb Haemost 2018

Clinical Prediction Model : SOX-PTS score

A clinical prediction model for the postthrombotic syndrome in a prospective cohort of patients with DVT

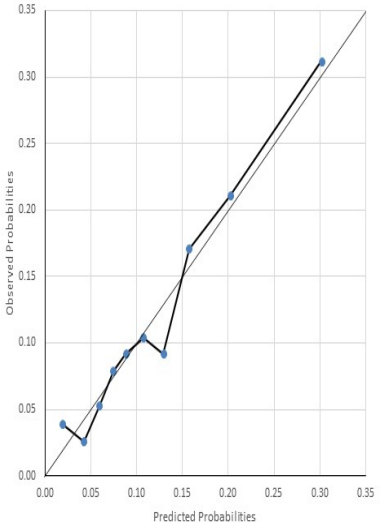
Essentials

High risk predictors were :

- iliac vein DVT* (OR 1,96)
- BMI > 35 Kg/m^2 ^ (OR 2,16)
- moderate-severe Villalta categoria° (OR 2,64)

Patients with a score ≥4 had an odds ratio of 5.9 (95% CI 2.1-16.6) for PTS.

*1 point, ^2 points, °1 or 2 points



Parameter Estimates for linear regression					
Variable	DF	Parameter Estimate	Standard Error	t Value	Pr > |t|
Intercept	1	0.01	0.01	0.83	0.43
B	1	0.94	0.06	15.05	<.0001

A.Rabinovich, J Thromb Haemost . 2018

IDEAL PTS SCORE

	Baseline risk assessment	Risk assessment after 6 months
Age > 56	2	1
Body mass index > 30	2	1
Varicose veins	4	3
Smoking	1	1
Residual thrombosis	-	1
Female gender	1	-
Provoked deep vein thrombosis	1	-
Iliofemoral deep vein thrombosis	1	-
History of deep vein thrombosis	1	-

Baseline model

0-2 points: 10%

3-4 points: 20%

≥ 5 points: 40%

After 6 months

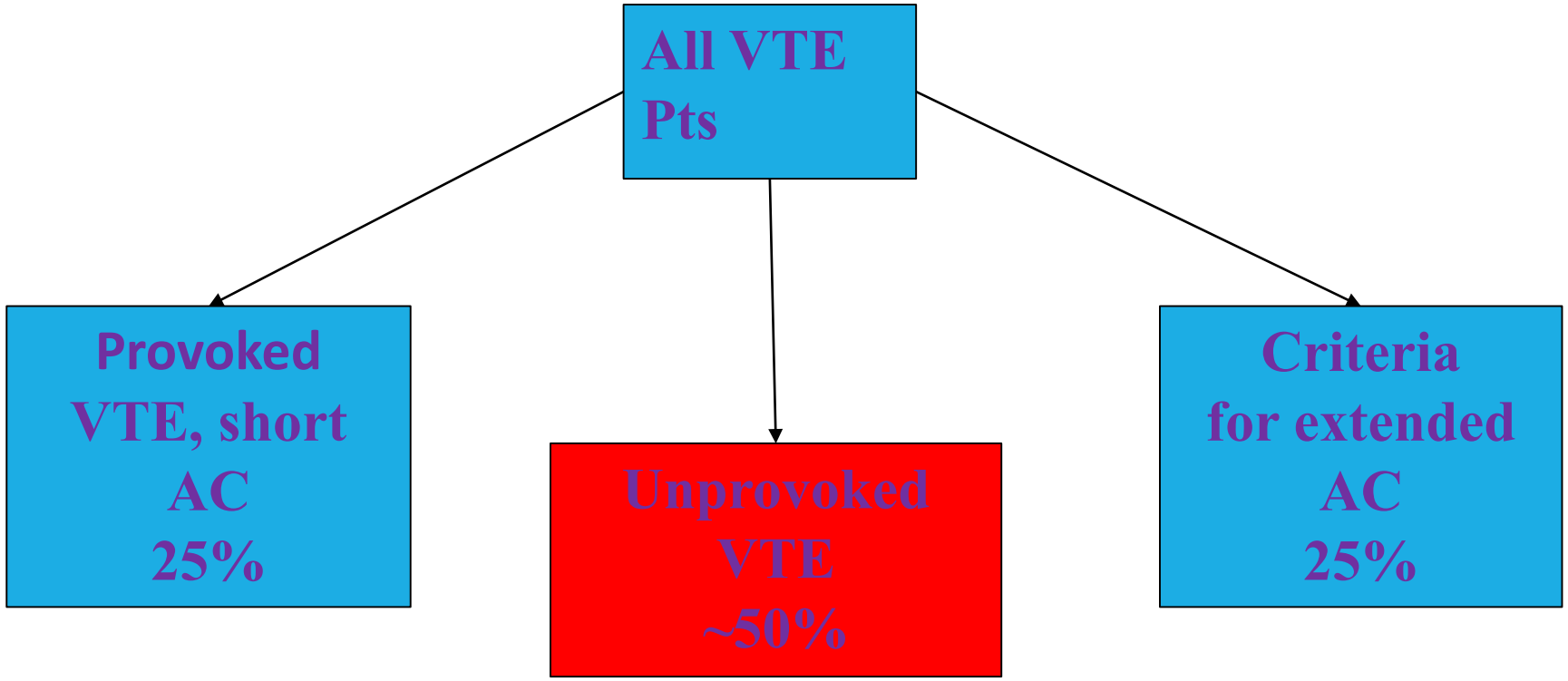
0-2 points: 25%

3-4 points: 45 %

≥ 5 points: 60%

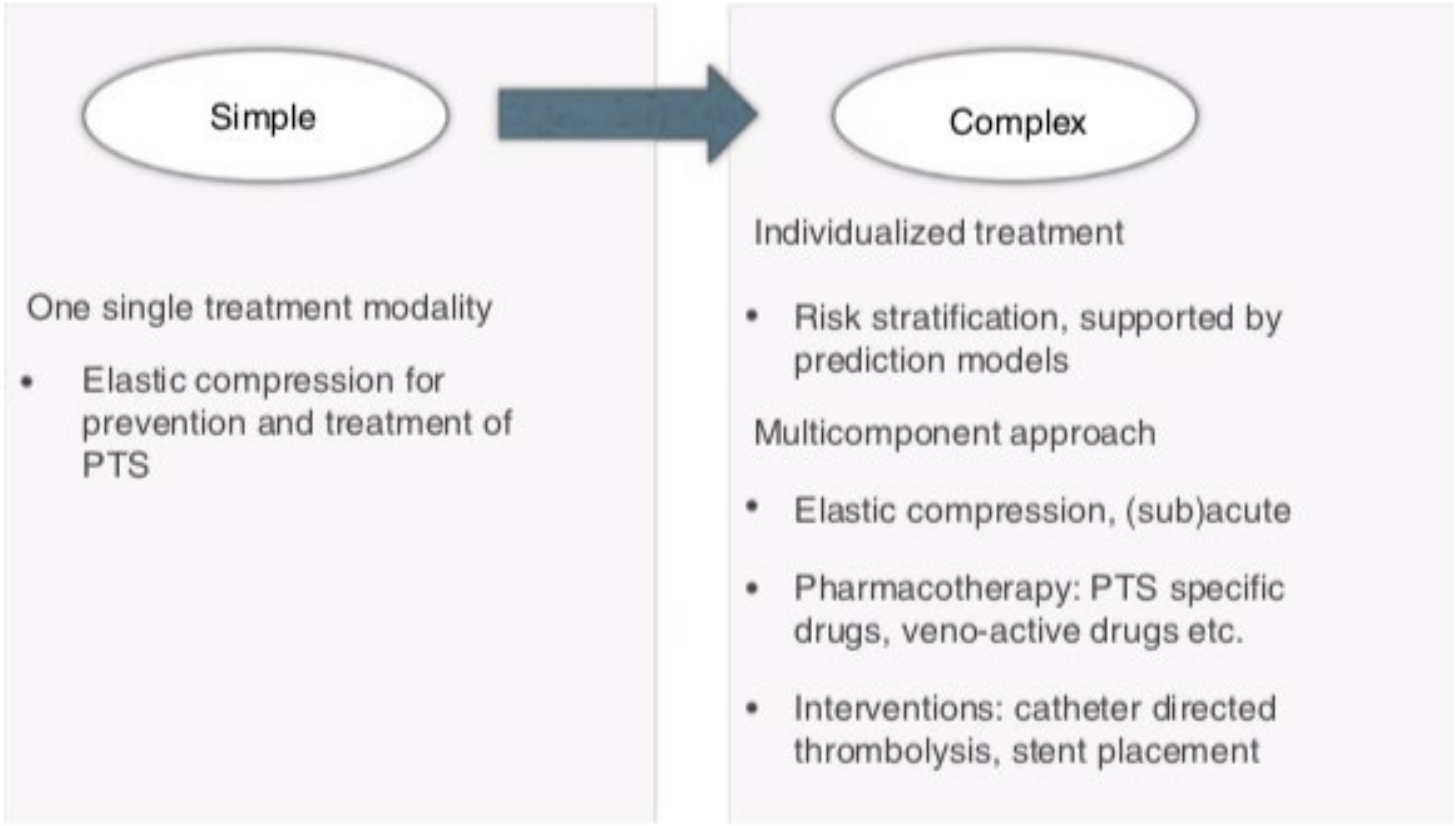
Amin EE Res Pract Thromb Haemo 2017

Example of distribution of VTE patients examined for deciding how long anticoagulation



PREVENZIONE SPT

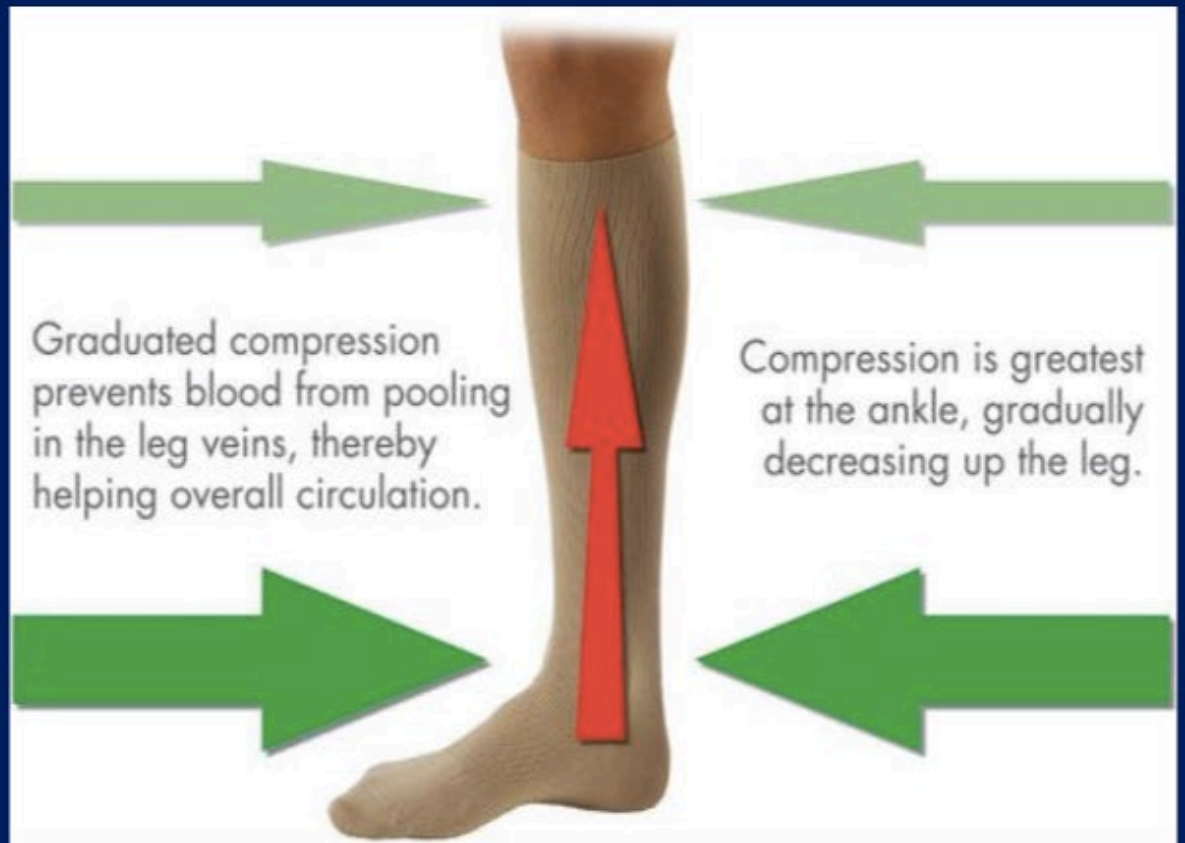
- Eliminazione Fattori di Rischio
- Esercizio Fisico
- Compressione
- Trattamento Farmacologico
- Trattamento invasivo ostruttivo /PTA, stent pacement/
- Trattamento Ulcere



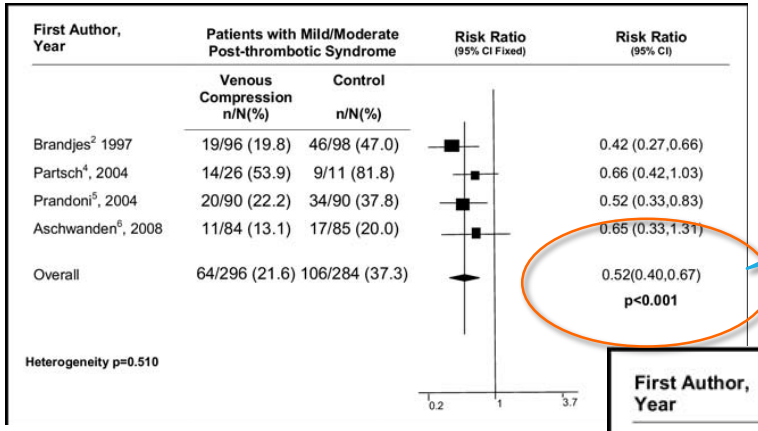
ten Cate-Hoek Res Pract Thromb Haemost. 2018;2:209–219.

Rationale for use of elastic compression stockings to prevent PTS

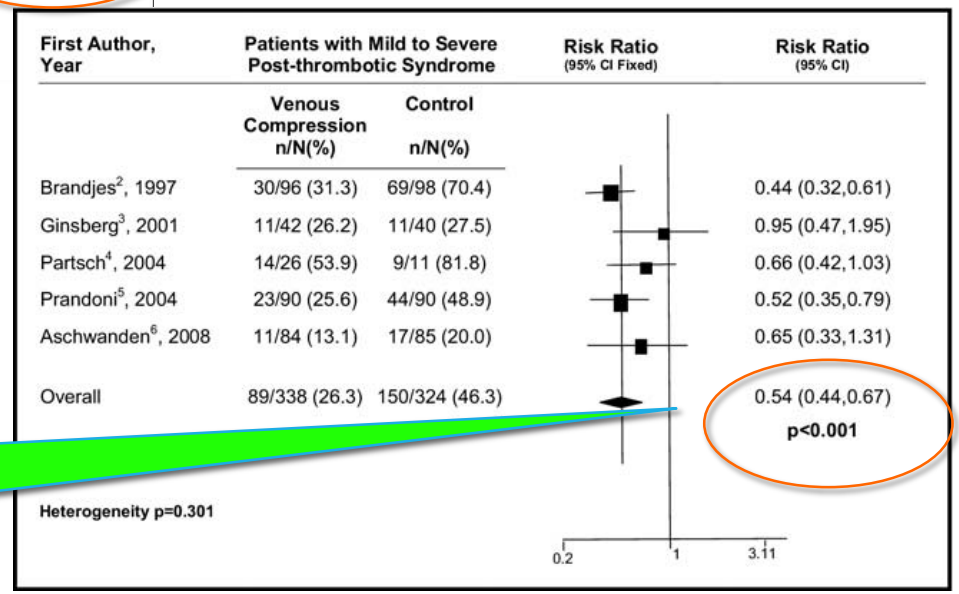
- assist calf muscle pump, reduce venous hypertension and reflux → reduce edema and improve tissue microcirculation



Prevenzione SPT
ELASTOCOMPRESSIONE (ECS)

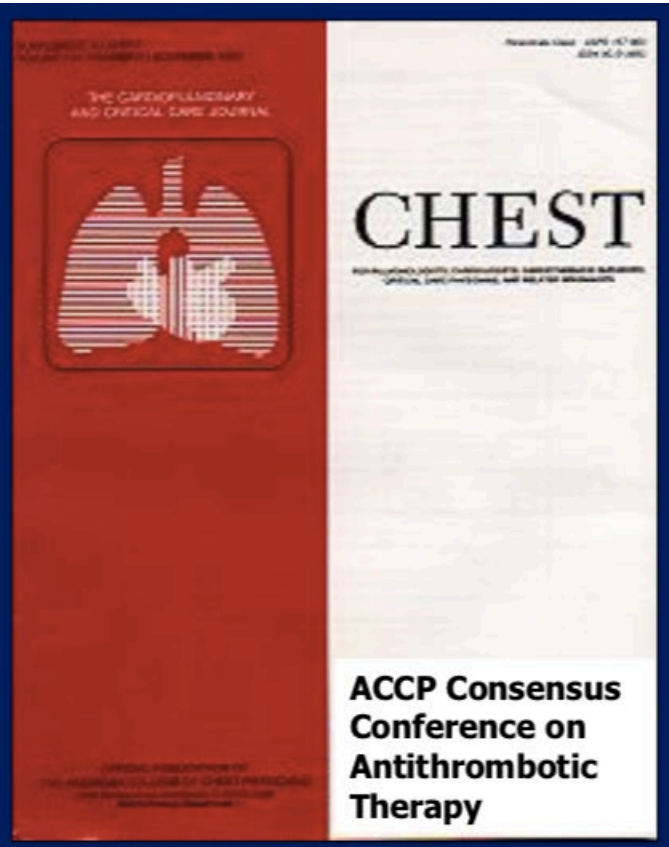


EFFICACIA
RR = 0.52
(0.40-0.67)



SICUREZZA
RR = 0.54 (0.44-
0.67)

Musani MH et al. Am J Med 2010



ACCP International Practice Guidelines Recommendation

"We recommend the use of an elastic compression stocking with a pressure of 30 to 40 mm Hg at the ankle during 2 years after an episode of DVT" (Grade 1A)

Chest 2004; Chest 2008

Chest 2012: downgraded to Grade 2B: "The evidence is of moderate quality because the assessment of PTS, which includes a large subjective component, was not blinded"

SOX

Lancet 2013

Articles

Compression stockings to prevent post-thrombotic syndrome: a randomised placebo-controlled trial

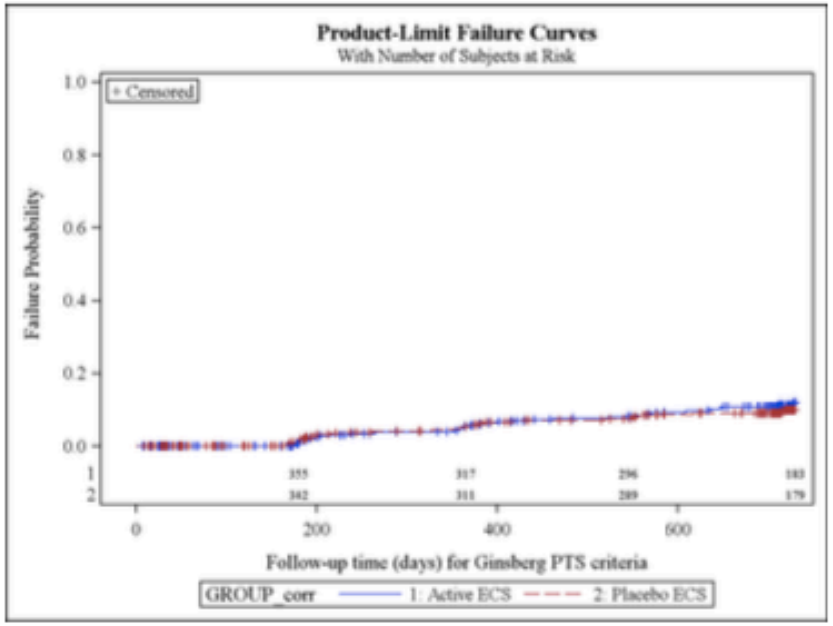
Susan R Kahn, Stan Shapiro, Philip S Wells, Marc A Rodger, Michael J Kovacs, David R Anderson, Vicky Tagalakis, Adrielle H Houweling, Thierry Ducruet, Christina Holcroft, Mira Johri, Susan Solymoss, Marie-José Miron, Erik Yeo, Reginald Smith, Sam Schulman, Jeannine Kassis, Clive Kearon, Isabelle Chagnon, Turnly Wong, Christine Demers, Rajendar Hanmiah, Scott Kaatz, Rita Selby, Suman Rathbun, Sylvie Desmarais, Lucie Opatrny, Thomas L Ortel, Jeffrey S Ginsberg, for the SOX trial investigators

Study Intervention

- Patients with a first proximal DVT were randomized to Active ECS (A-ECS) or Placebo ECS (P-ECS)
- A-ECS: knee-length graduated ECS, 30-40 mm Hg pressure at ankle
- P-ECS: manufactured to look identical to A-ECS, lacked therapeutic compression (~5 mm Hg at ankle)
- Study stockings:
  - Cotton & lycra, available in 16 sizes
  - Applied within 2 weeks of DVT diagnosis and replaced every 6 months at planned study follow-up visits, or earlier if stocking tore or leg size changed
  - Patients instructed to wear stocking on affected leg daily (from waking to retiring) for two years

Results: Primary Outcome (intent to treat analysis)

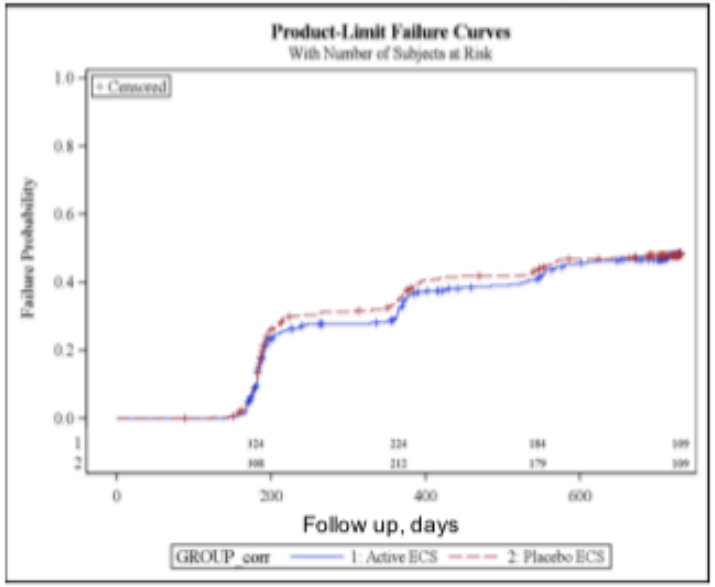
	Active ECS (n=409)	Placebo ECS (n=394)	Hazard Ratio (95% CI)
PTS (Ginsberg measure)	44 Cumulative Incidence* 14.2%	37 Cumulative incidence* 12.7%	1.13 (0.73, 1.76) p=0.58



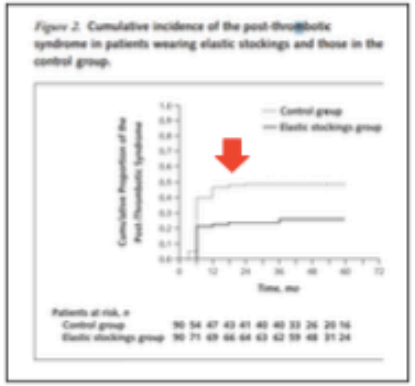
* by 750 days

Results: Secondary Outcomes

	Active ECS (n=409)	Placebo ECS (n=394)	Hazard Ratio (95% CI)
PTS (Villalta measure) Villalta score of 5 or higher at or after the 6 month visit	**176 Cumulative incidence* 52.6%**	**168 Cumulative incidence* 52.3%**	**1.0 (0.81-1.24) p=0.96**



* by 750 days

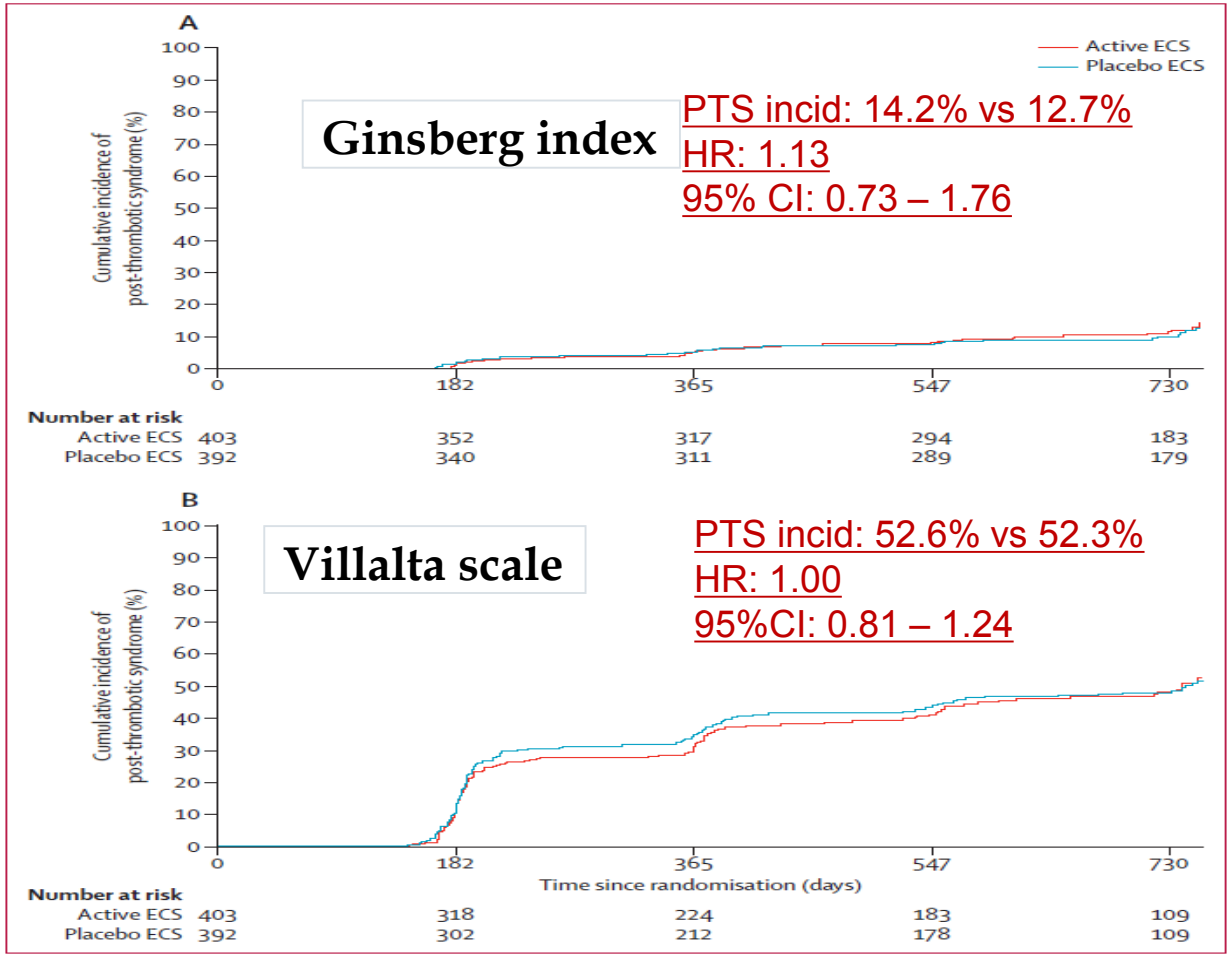


Prandoni P et al, 2004

Conclusions

- In a large multicenter randomized placebo-controlled trial, active ECS did not prevent PTS after a first proximal DVT, and did not influence the severity of PTS, rate of recurrent VTE, or QOL.
- Benefits of ECS to prevent PTS reported in two previous smaller, single-centre studies could be due, at least in part, to their open-label design.
- **Our results do not support consensus guideline recommendations to routinely use ECS for 2 years after proximal DVT to prevent PTS**

PREVENZIONE SPT
Studio SOX (ECS)



800 pazienti:
a 2 anni non sono emerse differenze significative fra il gruppo con compressione attiva e quello placebo.

Lo studio presenta *bias* metodologici importanti:

ECS attiva (20mm Hg)
vs
ECS placebo (5mm Hg)

Follow-up telefonico

Aderenza alla terapia
54,5% frequent users
(almeno 3gg./settimana !!!)

Kahn SR et al. Lancet 2013

Prevenzione della SPT
RACCOMANDAZIONI (ECS)

AHA Consensus Statement Circulation 2014

The effectiveness of ECS to prevent PTS is uncertain, but ECS may be reasonable to consider after diagnosis of proximal DVT to reduce swelling

(Class IIb; Level of Evidence A).

ACCP Guidelines 2016

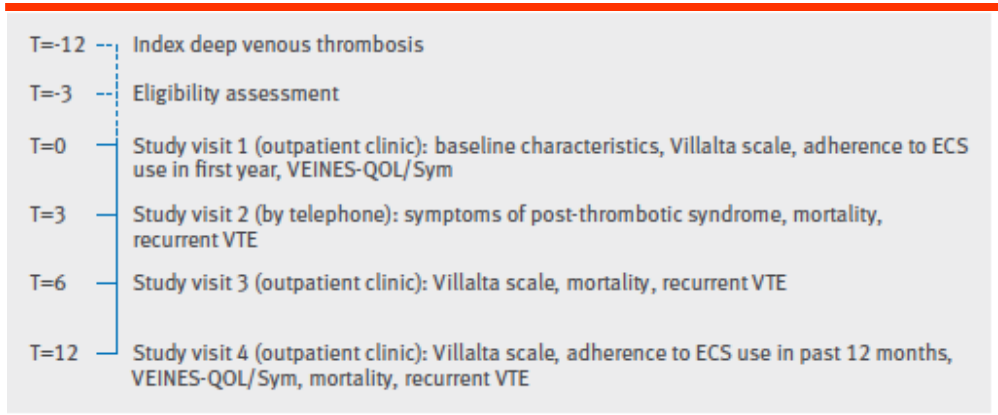
Compression Stocking to Prevent Post-Thrombotic Syndrome

18. **In patients with acute DVT of the leg, we suggest not using compression stockings routinely to prevent PTS** (Grade 2B).

Remarks: This recommendation focuses on prevention of the chronic complication of PTS and not on the treatment of symptoms. For patients with acute or chronic symptoms, a trial of graduated compression stockings is often justified.

Prevenzione della SPT

Studio OCTAVIA (ECS)



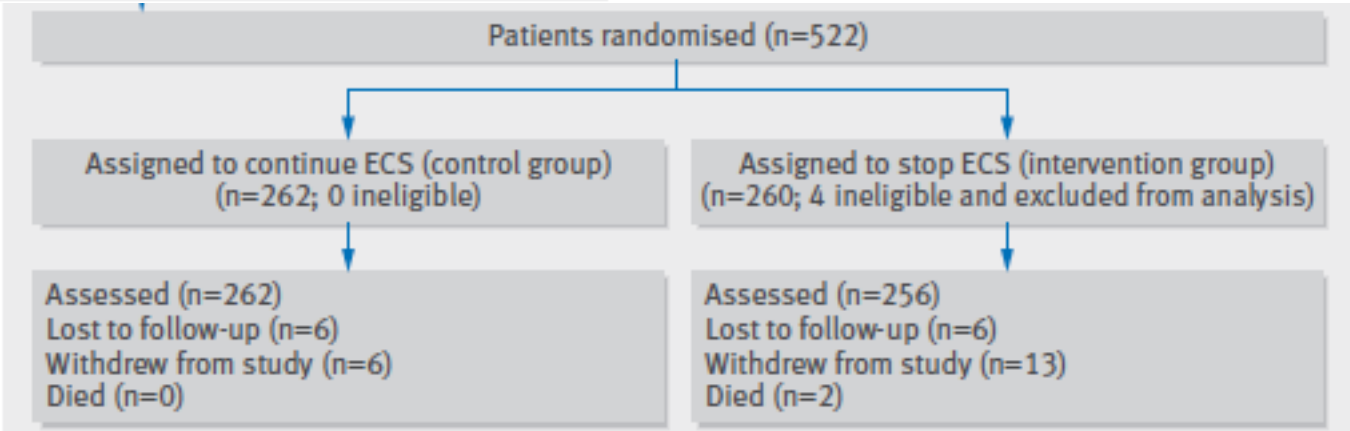


Table 1 | Baseline characteristics. Values are numbers (percentages) unless stated otherwise

Characteristics	Stop-ECS (n=256)	Continue-ECS (n=262)
Frequent users of ECS at baseline (≥6 days/week)	232 (91)	249 (95)
Mean (SD) baseline Villalta score	1.9 (1.3)	1.8 (1.3)

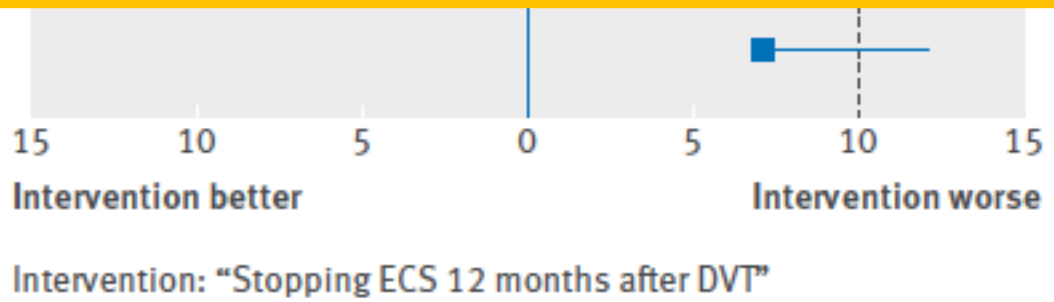
Mol GC et al., BMJ 2016

Prevenzione della SPT
Studio OCTAVIA (ECS)

Table 2 | Primary and secondary endpoints by treatment group

	Stop-ECS group (n=256)	Continue-ECS group (n=262)	Adjusted hazard ratio
Primary endpoint			
PTS incidence, % (95% CI)	19.9 (16 to 24)	13.0 (9.9 to 17)	1.6 (1.02 to 2.5)*
Absolute No (%) of mild PTS (Villalta scale 5-9)	43 (84)	31 (91)	–
Absolute No (%) of moderate PTS (Villalta scale 10-14)	8 (16)	2 (6)	–
Absolute No (%) of severe PTS (Villalta scale >14)	0	1 (3)	–

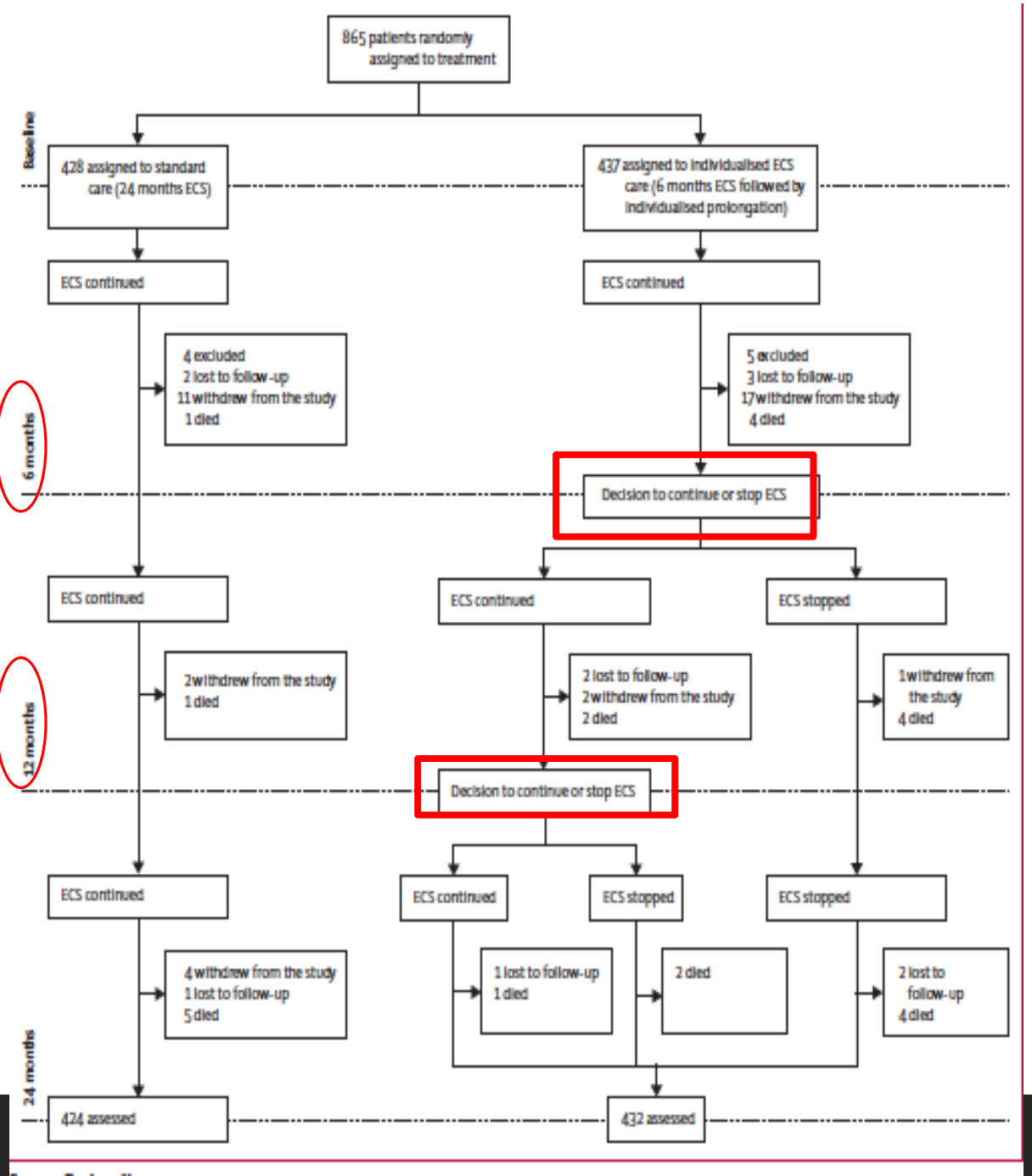
lo studio OCTAVIA, ha evidenziato un'incidenza di SPT significativamente inferiore nel gruppo che ha continuato la prevenzione con ECS per ulteriori 12 mesi (13,0%) rispetto al gruppo STOP ECS dopo i primi 12mesi (19,9%)



Intervention: "Stopping ECS 12 months after DVT"

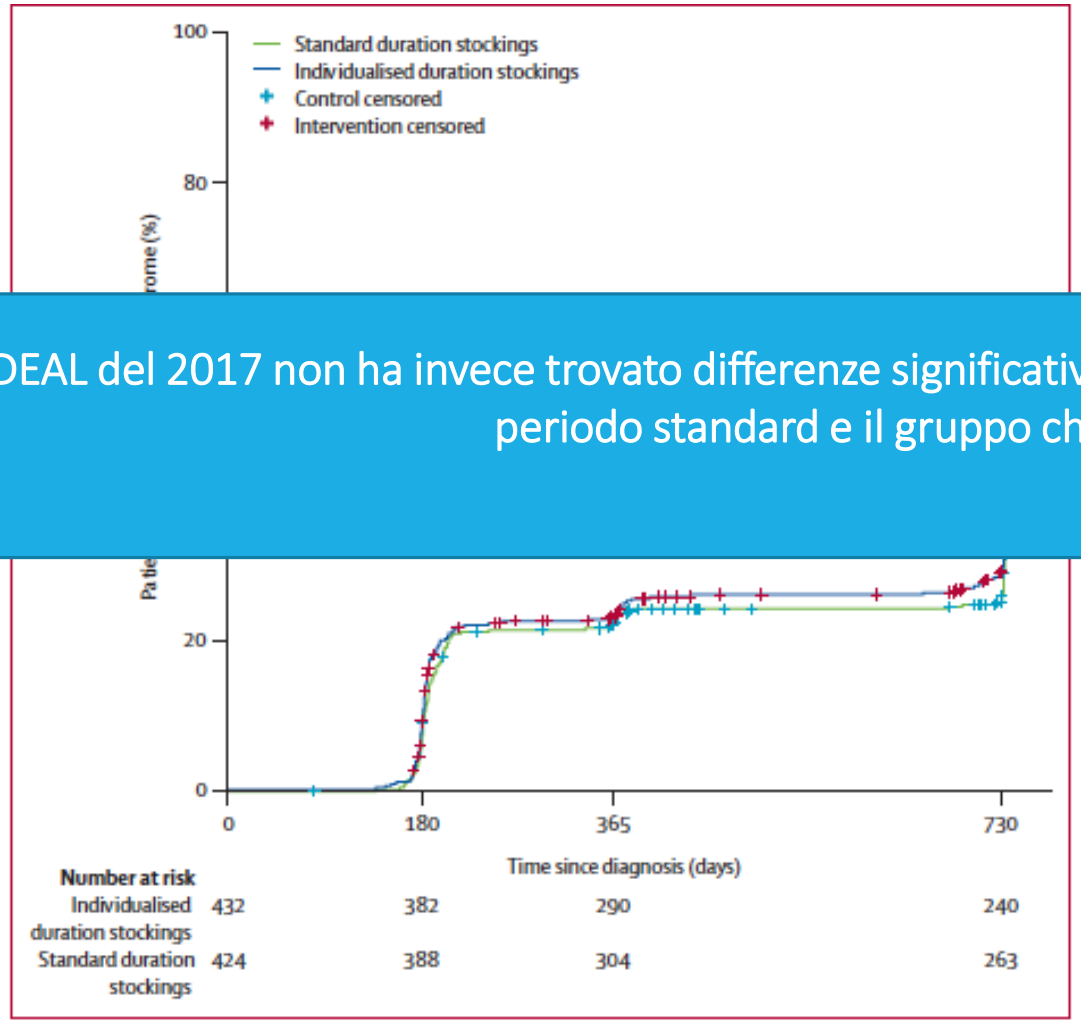
Mol GC et al., BMJ 2016

Prevenzione della SPT
Studio IDEAL (ECS)



ten Cate- Hoek AJ et al.,the Lancet Haemat 2017

Prevenzione della SPT
Studio IDEAL (ECS)



SPT (%)

28% vs 29%

OR = 1.06 (0.78 -1.44)

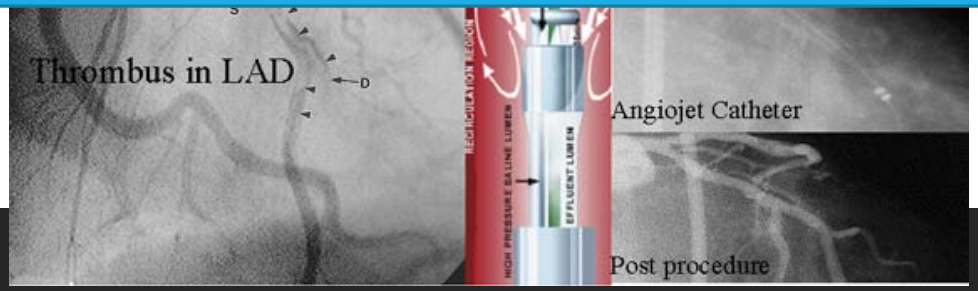
Lo studio IDEAL del 2017 non ha invece trovato differenze significative a 2 anni fra il gruppo che ha portato la calza per un periodo standard e il gruppo che ha proseguito

*I pazienti dovevano indossare o non indossare le calze per almeno l'80% del periodo di monitoraggio, in linea con il gruppo di assegnazione

Ten Cate- Hoek AJ et al.,the Lancet Haemat 2017

Prevenzione della SPT:
trombolisi per il trattamento inziale della TVP?

TROMBOLISI CATETERE GUIDATA E FARMACOMECCANICA
infusione di fibrinolitico direttamente in loco permette di somministrare una dose ridotta di trombolitico con conseguente riduzione del rischio emorragico



CaVenT

Trial multicentrico, randomizzato controllato che ha confrontato

Fibrinolisi locoregionale versus la terapia anticoagulante convenzionale.

Pazienti con trombosi femoro-iliaca

CAVENT Study,Lancet 2012

	CDT (n=90)		Standard therapy (n=99)		*p*
	n	% (95%CI)	n	% (95%CI)	
Ilio-femoral					
24 months		(31.5-51.4)		(45.7-65.0)	

Maggior tasso di ricanalizzazione nei pazienti CDT
Riduzione appena significativa di incidenza PTS a 24 mesi
Incremento delle emorragie maggiori 3%

CaVenT: Efficacy endpoint

CAVENT Study,Lancet 2012

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Pharmacomechanical Catheter-Directed Thrombolysis for Deep-Vein Thrombosis

S. Vedantham, S.Z. Goldhaber, J.A. Julian, S.R. Kahn, M.R. Jaff, D.J. Cohen, E. Magnuson, M.K. Razavi, A.J. Comerota, H.L. Gornik, T.P. Murphy, L. Lewis, J.R. Duncan, P. Nieters, M.C. Derfler, M. Filion, C.-S. Gu, S. Kee, J. Schneider, N. Saad, M. Blinder, S. Moll, D. Sacks, J. Lin, J. Rundback, M. Garcia, R. Razdan, E. VanderWoude, V. Marques, and C. Kearon, for the ATTRACT Trial Investigators*

Among patients with acute proximal deep-vein thrombosis, the addition of pharmacomechanical catheter-directed thrombolysis to anticoagulation did not result in a lower risk of the post-thrombotic syndrome but did result in a higher risk of major bleeding.

NEJM 2017

Prevenzione SPT

TERAPIA RIPERFUSIVA PRECOCE

Study	n	Type/time	PTS -2 years (%)		RR	p
			Cath-Thr	Placebo		
CaVenT (2011)	209		41.1	55.6	-	0.047
Attract (2017)	692	Any	47	48	0.96 (0.82-1.11)	0.56
Cavent (2011)	209	24 m	12	6		
Attract (2017)	692	1st 10 d	4%	2%	2.64(1.04-6.68)	0.03
		24 m	14%	11%	1.26 (o.85-1.89)	0.25
			Recurrent VTE %			
			Cath-Thr	Placebo		
Attract (2017)	692	24 m	12	8	1.47 (0.94-2.29)	0.09

ATTRACT NEJM 2017

Among patients with acute proximal deep-vein thrombosis, the addition of pharmacomechanical catheter-directed thrombolysis to anticoagulation did not result in a lower risk of the post-thrombotic syndrome but did result in a higher risk of major bleeding.

STUDIO CAVENT (2011) risultato leggermente significativo su piccoli

2017)

a

di

Enden et al, Lancet 2011, Vedantham S et al, NEJM 2017

In patients with acute iliofemoral deep vein thrombosis, PCDT did not influence the occurrence of PTS or recurrent venous thromboembolism.

However, PCDT significantly reduced early leg symptoms and, over 24 months, reduced PTS severity scores, reduced the proportion of patients who developed moderate-or-severe PTS

Endovascular Thrombus Removal for Acute Iliofemoral Deep Vein Thrombosis

Analysis From a Stratified Multicenter Randomized Trial

AJ Comerota, Circulation. 2019;139:1162–1173. DOI: 10.1161

PTS 2019

PTS is a chronic complication of DVT that imposes significantly morbidity, reduces quality of life, and is costly

After DVT 20-50% of patients will develop PTS, and up to 5% will develop severe PTS

Principal risk factors: anatomically extensive DVT , recurrent ipsilateral DVT, obesity , and older age

Rabinovich A, Kahn S Blood 2018

PTS 2019

PREVENTION

By preventing the initial DVT and DVT recurrence, primary and secondary prophylaxis of DVT will reduce the occurrence of PTS

The effectiveness of elastic compression stockings (ECS) for PTS prevention is controversial

Catheter- directed thrombolysis is not effective to prevent PTS overall, but my prevent more severe forms of PTS, and should be reserved for selected patients with extensive thrombosis, recent symptoms onset, and low bleeding risk

Rabinovich A, Kahn S Blood 2018

Research Needs

PTS prevention
Studies to improve understanding of the pathophysiology of PTS and to suggest future therapeutic targets for PTS prevention
Validation of clinical prediction rules to predict risk of PTS
Studies of the relative effect of DOACs compared to VKAs on the risk of PTS
Studies exploring the role of statins and targeted anti-inflammatory medications as an adjunct to anticoagulation for PTS prevention
Studies of the effectiveness of ECS to prevent PTS in high risk subgroups
RCTs of CDT , PCDT and surgical thrombectomy in high risk patients with long-term follow up and analysis of cost effectiveness and benefit to harm ratio for PTS prevention
Management of established PTS
RCTs evaluating the long-term benefit of venoactive drugs for PTS management
RCTs to assess the long term effectiveness and safety of endovascular and surgical techniques to treat established PTS


Grazie per l’attenzione

Post-thrombotic Syndrome: definition

Because there is **no gold standard objective test** to establish its presence, PTS is diagnosed primarily on the basis of the presence of **typical symptoms and clinical signs** in a limb that was affected by DVT

ISTH committee 2009

Definition of PTS of the leg for the use in clinical investigation: A recommendation for standardization

Vantaggi

- Comprensiva di segni e sintomi
- Valutazione del grado di severità delle manifestazioni cliniche
- Valutazione della progressione e della risposta al trattamento

Limiti

- Aspecificità di alcuni sintomi e segni
- Richiede pratica e addestramento
- Non è inclusa la claudicatio venosa, la circonferenza dell'arto, l'impotenza funzionale

Journal Thromb Haemost, 2009

Residual vein thrombosis as a predictive factor of the PTS

Vein abnormalities	Incidence of PTS RR (95% CI)	*p*
Only residual vein thrombosis	1.92 (1.39 – 2.64)	0.0001
Only popliteal valve insufficiency	1.11 (0.66 – 1.89)	0.69
Residual vein thrombosis + valve insufficiency	1.83 (1.26 – 2.66)	0.003

Vedovetto et al, Thromb Haemost. 2013

- 391/692 pazienti di ATTRACT coinvolgimento femorale/iliaco PTS (Villalta score) 49% CDT e 51% terapia anticoagulante convenzionale (RR=0.95; 95% CI: 0.78 – 1.15; p =0.59)

- PTS moderata o severa 18% CDT e 28% terapia anticoagulante convenzionale (RR=0.65; 95% CI: 0.45 - 0.94; p =0.021

- PTS severe (score di Villalta > 14 od ulcera cutanea), 8.7% CDT e 15% terapia anticoagulante convenzionale (RR=0.57; 95% CI: 0.32 - 1.01; p=0.048)

- Complicanze emorragiche maggiori 1.5% CDT e 0.5% terapia anticoagulante convenzionale p =0.36)

- Recidive tromboemboliche in 13.3% CDT e 9.2% terapia anticoagulante convenzionale; p =0.21)

CDT non determina in questi così come nell'intera coorte dello studio ATTRACT una riduzione della PTS, però si accompagna ad una riduzione del 35% delle complicanze moderate o severe e del 40% delle complicanze più severe, quelle che deteriorano pesantemente la qualità di vita dei pazienti.

Da considerarla almeno nel sottogruppo TVP vena femorale e/o la vena iliaca ??

NO

Attract 2: torna in corsa la trombolisi farmacomeccanica

- Risultati subanalisi non differiscono sostanzialmente da ATTRACT NEJM né per quanto riguarda lo sviluppo della PTS totale né PTS Severa
- PTS severa: frequenza 5% e complica sia poplitee-femorarali che iliaco femorali
- A prescindere dalla localizzazione la PTS severa nei pazienti assegnati alla terapia AC convenzionale è 5-10%
- La CTD riduce rischio di forma severe di circa 40%
- Rischio emorragico minore per queste iliaco-femorali rispetto all'ATTRACT dipende alla minor numerosità
- Centri di esperienza aumentato rischio EP, necessità Filtro, e probabilità stenting

Score per identificare pazienti con TVP a più alto rischio di SPT (SOX PTS)

JTH 2018; 16: 262-270

Development of a clinical prediction model for the postthrombotic syndrome in a prospective cohort of patients with proximal deep vein thrombosis

A. RABINOVICH,* T. DUCRUET† and S. R. KAHN‡ FOR THE SOX TRIAL INVESTIGATORS[1]

Essentials

- We developed a prediction model for postthrombotic syndrome (PTS) after deep vein thrombosis (DVT).
- High risk predictors were iliac vein DVT, BMI>35 and moderate-severe Villalta category.
- Patients with a score ≥4 had an odds ratio of 5.9 (95% CI 2.1-16.6) for PTS.
- SOX-PTS score may select DVT patients for close monitoring or aggressive strategies to treat DVT.

The Bio-Sox Study: results