



Physiopathology of lower extremity venous pain after deep vein thrombosis

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Disclosure

Speaker name: Fedor Lurie

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- ☐ I have the following potential conflicts of interest to report:
- ☐ Consulting
- ☐ Employment in industry
- ☐ Shareholder in a healthcare company
- ☐ Owner of a healthcare company
- ☐ Other(s)
- ☒ I do not have any potential conflict of interest

Antithrombotic Therapy for VTE Disease

CHEST Guideline and Expert Panel Report

Clive Kearon, MD, PhD; Elie A. Akl, MD, MPH, PhD; Joseph Ornelas, PhD; Allen Blaivas, DO, FCCP;
David Jimenez, MD, PhD, FCCP; Henri Bounameaux, MD; Menno Huisman, MD, PhD;
Christopher S. King, MD, FCCP; Timothy A. Morris, MD, FCCP; Namita Sood, MD, FCCP;
Scott M. Stevens, MD; Janine R. E. Vintch, MD, FCCP; Philip Wells, MD; Scott C. Woller, MD;
and COL Lisa Moores, MD, FCCP

Compression Stocking to Prevent PTS

***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.

Graduated compression stockings to treat acute leg pain associated with proximal DVT

A randomised controlled trial

Susan R. Kahn¹; Stan Shapiro^{1,2}; Thierry Ducruet¹; Philip S. Wells³; Marc A. Rodger^{3,4}; Michael J. Kovacs⁵; David Anderson^{6,7}; Vicky Tagalakos¹; David R. Morrison¹; Susan Solymoss⁸; Marie-José Miron⁹; Erik Yeo¹⁰; Reginald Smith¹¹; Sam Schulman^{12,13}; Jeannine Kassis¹⁴; Clive Kearon¹²; Isabelle Chagnon¹⁵; Turnly Wong¹⁶; Christine Demers¹⁷; Rajendar Hanmiah¹⁸; Scott Kaatz¹⁹; Rita Selby²⁰; Suman Rathbun²¹; Sylvie Desmarais²²; Lucie Opatrny²³; Thomas L. Ortel²⁴; Jean-Philippe Galanaud²⁵; Jeffrey S. Ginsberg¹²

What does this paper add?

- We performed a large, placebo controlled multicentre randomised trial of active versus placebo compression stockings in patients with proximal DVT.
- We found that active stockings did not reduce leg pain, compared with placebo stockings, at any of the time points measured (14 days, 30 days and 60 days after DVT).
- Results were similar for frequent stockings users and by categories of age, sex and extent of DVT.
- Thus, elastic compression stockings do not appear to reduce leg pain in patients with acute proximal DVT.

EFFECT OF ANTICOAGULANT TREATMENT ON PAIN IN DISTAL DEEP VEIN
THROMBOSIS: AN ANCILLARY ANALYSIS FROM THE CACTUS TRIAL

Marc RIGHINI, MD¹, Helia ROBERT-EBADI, MD¹, Frédéric GLAUSER, MD¹, Marc
BLONDON, MD¹, Pierre OUVRY, MD², Jean-Marc DIAMAND, MD³, Anne TISSOT,
MD⁴, Paul FRAPPE, MD⁵, Isabelle QUERE, MD⁶, Susan R. KAHN, MD⁷, Jean-
Philippe GALANAUD, MD^{6,8}, Grégoire LE GAL, MD, PhD⁹



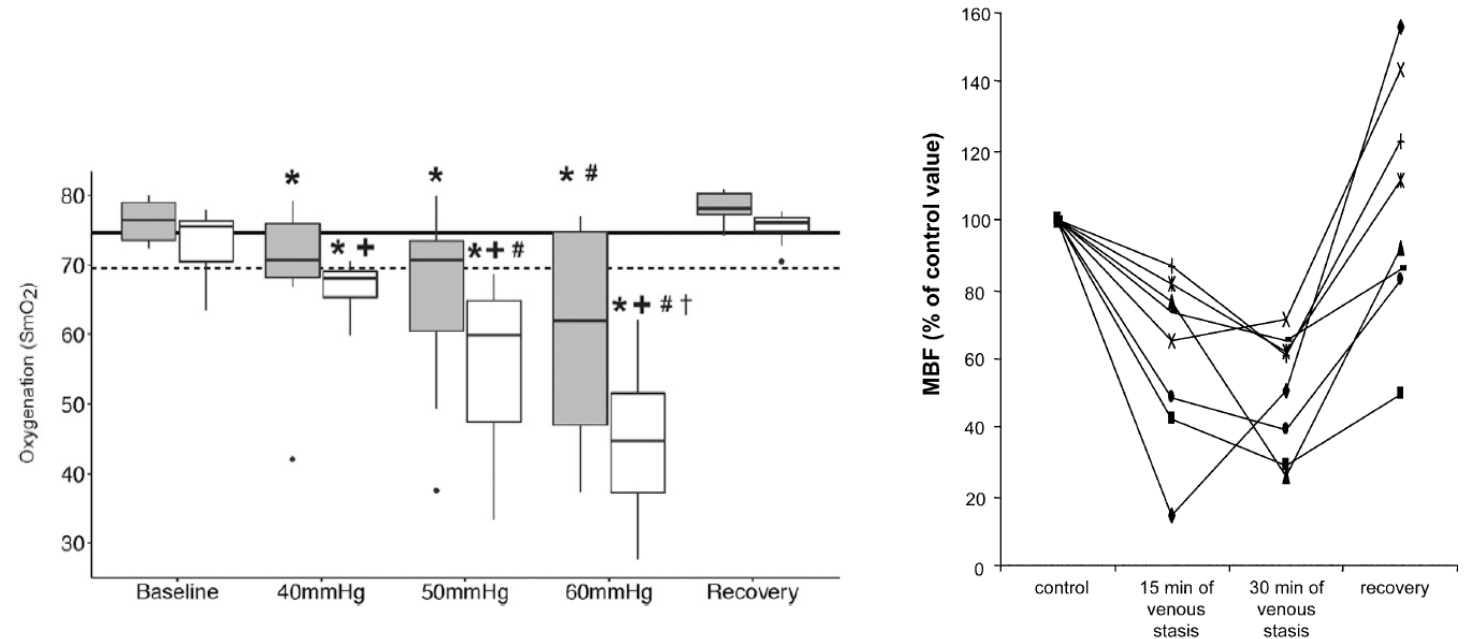
J Thromb Haemost. (2019)

“LMWH use does not improve pain control as compared with placebo in patients with acute distal DVT”

However, another reason put forward by advocates of anticoagulation, and in particular LMWH, is that LMWH might reduce pain thanks to their anti-inflammatory properties

Mechanisms of Pain in DVT and PTS

- Inflammation
- Obstruction – increased compartment pressure
- Hypoxia
- Central mechanisms





Predictive value of markers of inflammation in the postthrombotic syndrome: a systematic review

Inflammatory biomarkers and PTS

A. Rabinovich ^a, J.M. Cohen ^{a,b}, S.R. Kahn ^{a,b,c,*}

Association with PTS:

- CRP – **no**
- IL 6, 8, 10 – **no**
- ICAM-1, VCAM-1 – **no**
- TNF- α , MCP-1, P-selectin, MMP-9 - **no**

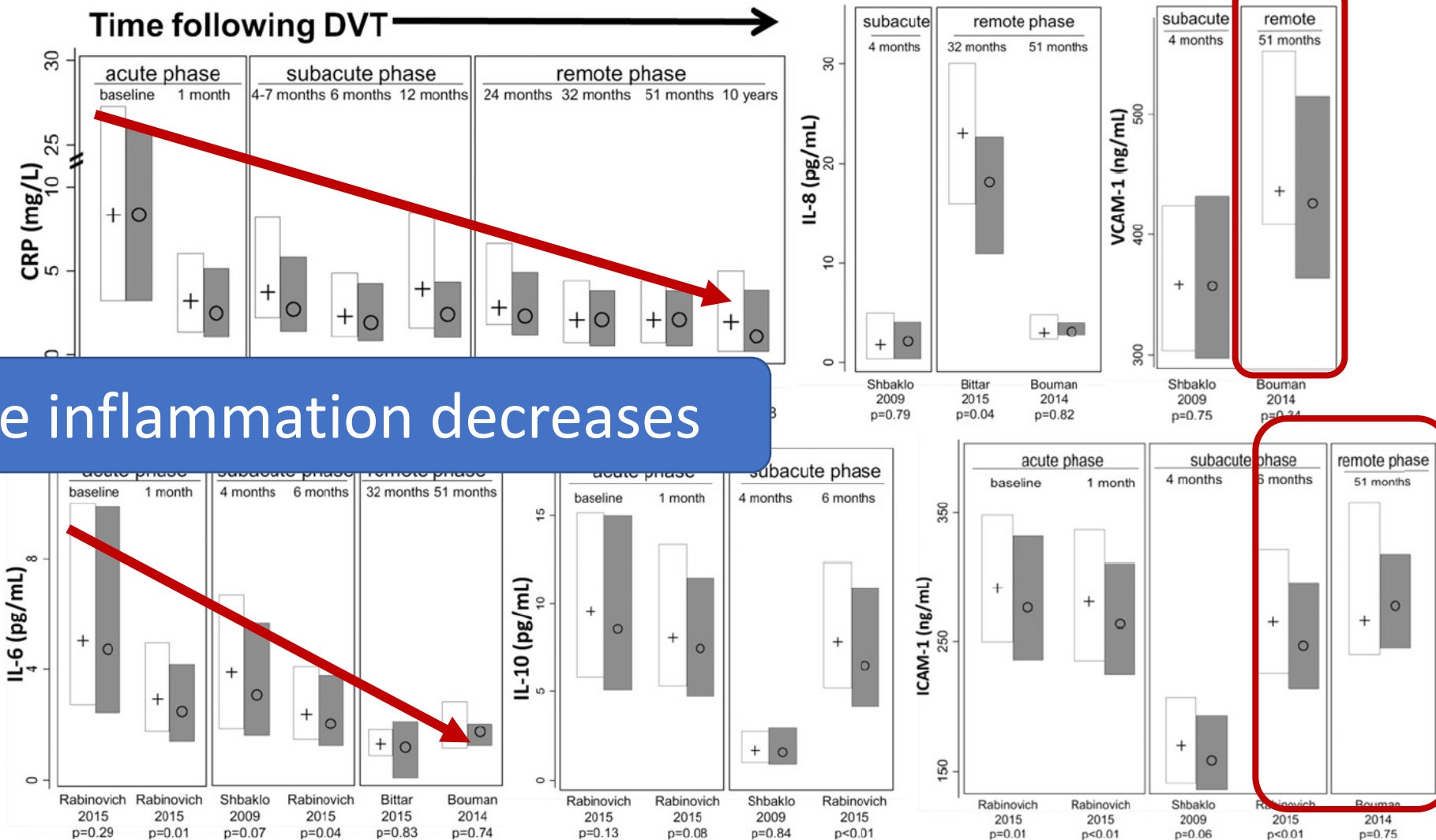
“In conclusion, available studies are conflicting and do not provide us with sufficient evidence to come to a firm conclusion on the importance of inflammation in the development of PTS”



Predictive value of markers of inflammation in the postthrombotic syndrome: a systematic review Inflammatory biomarkers and PTS

A. Rabinovich ^a, J.M. Cohen ^{a,b}, S.R. Kahn ^{a,b,c,*}

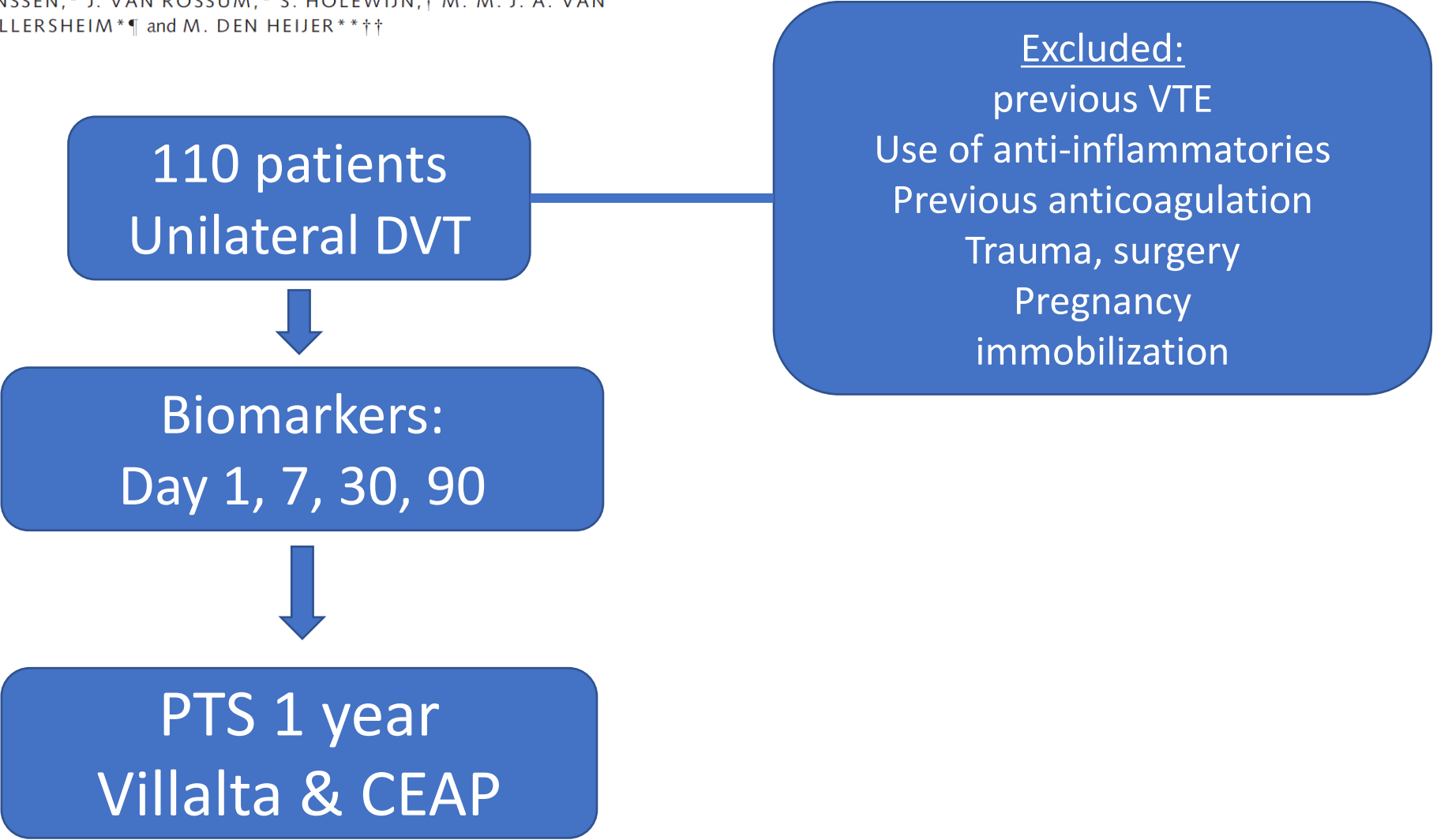
Inflammation caused by PTS



ORIGINAL ARTICLE

Inflammation in deep vein thrombosis and the development of post-thrombotic syndrome: a prospective study

E. M. ROUMEN-KLAPPE,* M. C. H. JANSSEN,* J. VAN ROSSUM,* S. HOLEWIJN,† M. M. J. A. VAN BOKHOVEN,‡ K. KAASJAGER,§ H. WOLLERSHEIM*¶ and M. DEN HEIJER**††



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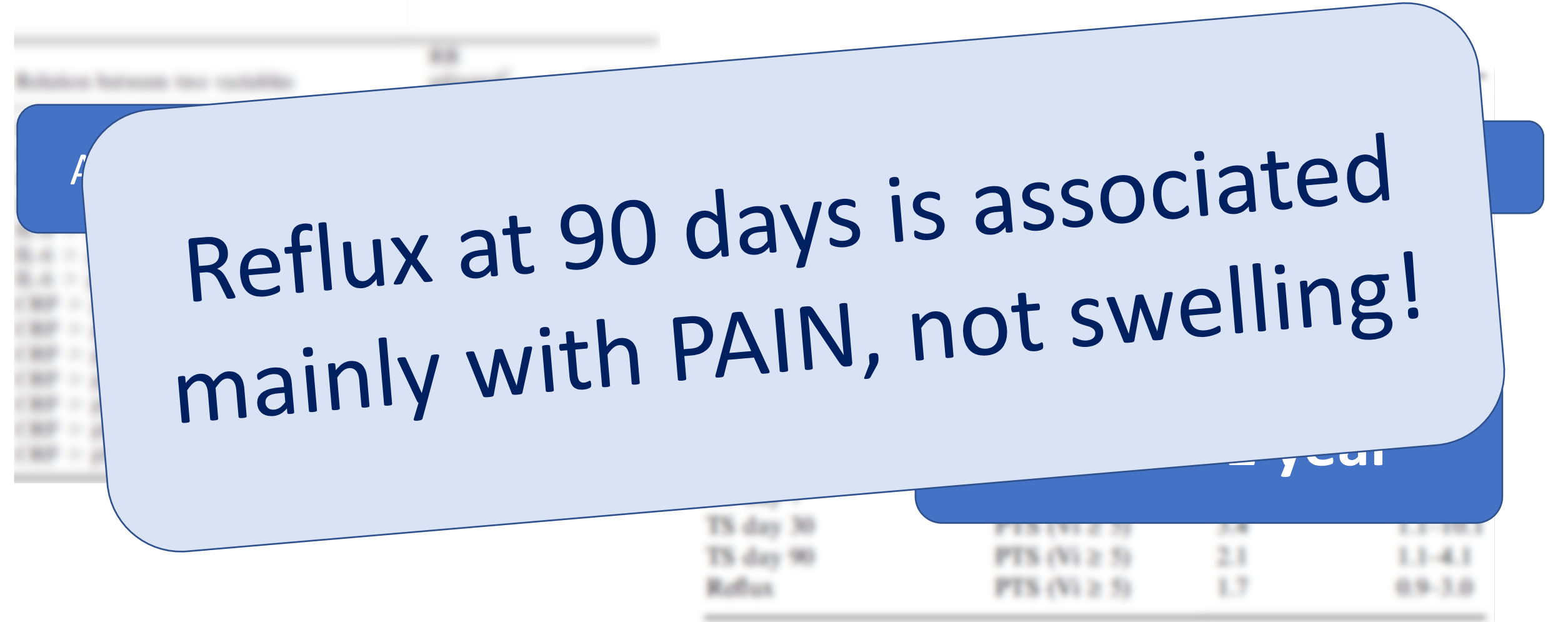
Relation between two variables		RR adjusted [†]	95% CI
IL-6 > p80	VOR day 7 > 0.8	1.3	1.0–1.7
IL-6 > p80	VOR day 30 > 0.8	1.5	1.1–2.2
IL-6 > p80	VOR day 90 > 0.8	2.4	1.5–3.9
IL-6 > p80	TS day 7	1.1	1.0–1.3
IL-6 > p80	TS day 30	1.2	1.0–1.5
IL-6 > p80	TS day 90	1.5	1.1–2.1
IL-6 > p80	reflux day 90	1.0	0.6–1.6
CRP > p80	VOR day 7 > 0.8	1.3	1.0–1.9
CRP > p80	VOR day 30 > 0.8	1.1	0.7–1.7
CRP > p80	VOR day 90 > 0.8	1.4	0.8–2.4
CRP > p80	TS day 7	1.0	0.8–1.2
CRP > p80	TS day 30	1.0	0.7–1.3
CRP > p80	TS day 90	1.0	0.7–1.4
CRP > p80	reflux day 90	1.1	0.7–1.8

Relation between two variables		RR adjusted [†]	95% CI
VOR day 7 > 0.8	PTS (CEAP ≥ 3)	2.1	0.9–5.1
VOR day 30 > 0.8	PTS (CEAP ≥ 3)	2.2	1.2–4.0
VOR day 90 > 0.8	PTS (CEAP ≥ 3)	2.1	1.2–3.7
TS day 7	PTS (CEAP ≥ 3)	2.5	0.5–12.9
TS day 30	PTS (CEAP ≥ 3)	2.0	0.8–5.4
TS day 90	PTS (CEAP ≥ 3)	2.0	1.1–3.7
Reflux	PTS (CEAP ≥ 3)	1.7	1.0–2.8
VOR day 7 > 0.8	PTS (Vi ≥ 5)	3.6	1.7–7.5
VOR day 30 > 0.8	PTS (Vi ≥ 5)	2.2	1.2–4.1
VOR day 90 > 0.8	PTS (Vi ≥ 5)	2.1	1.2–3.8
TS day 7	PTS (Vi ≥ 5)	6.0	0.9–41.1
TS day 30	PTS (Vi ≥ 5)	3.4	1.1–10.1
TS day 90	PTS (Vi ≥ 5)	2.1	1.1–4.1
Reflux	PTS (Vi ≥ 5)	1.7	0.9–3.0

ORIGINAL ARTICLE

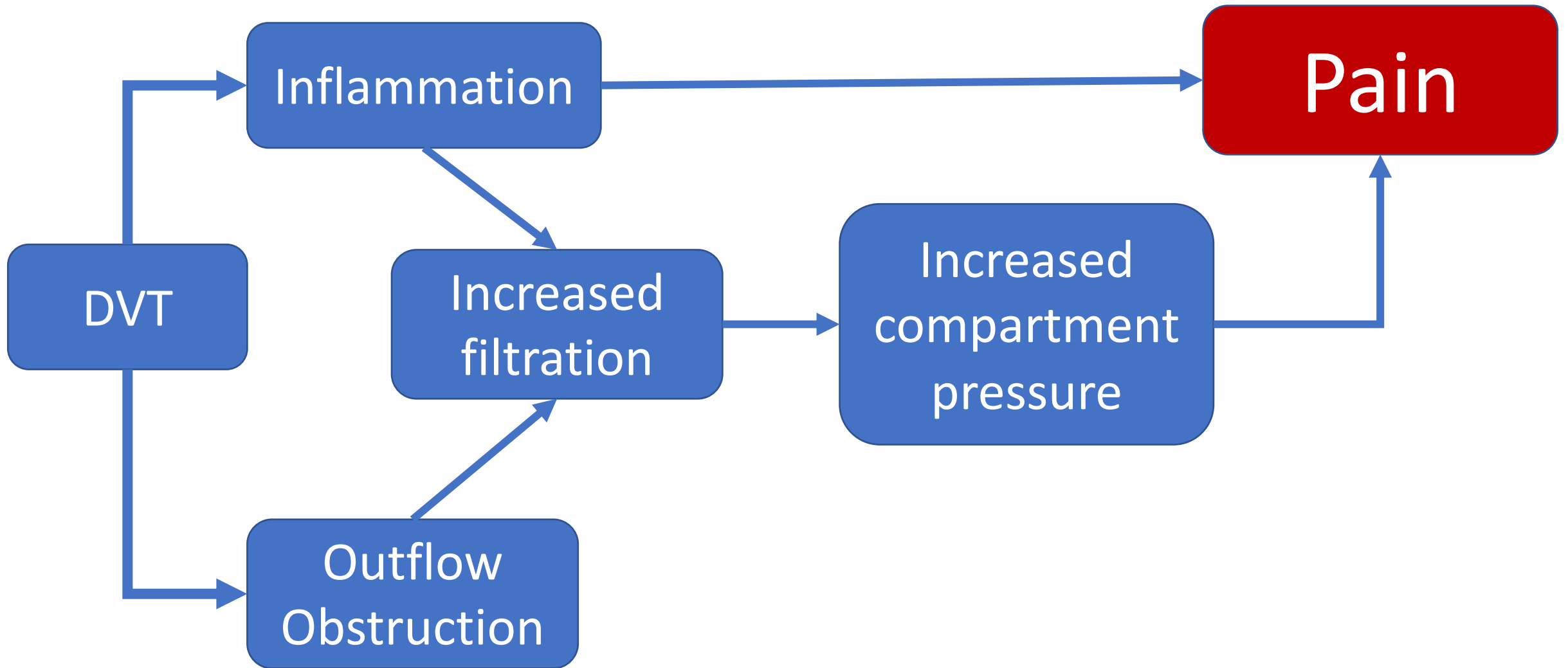
Inflammation in deep vein thrombosis and the development of post-thrombotic syndrome: a prospective study

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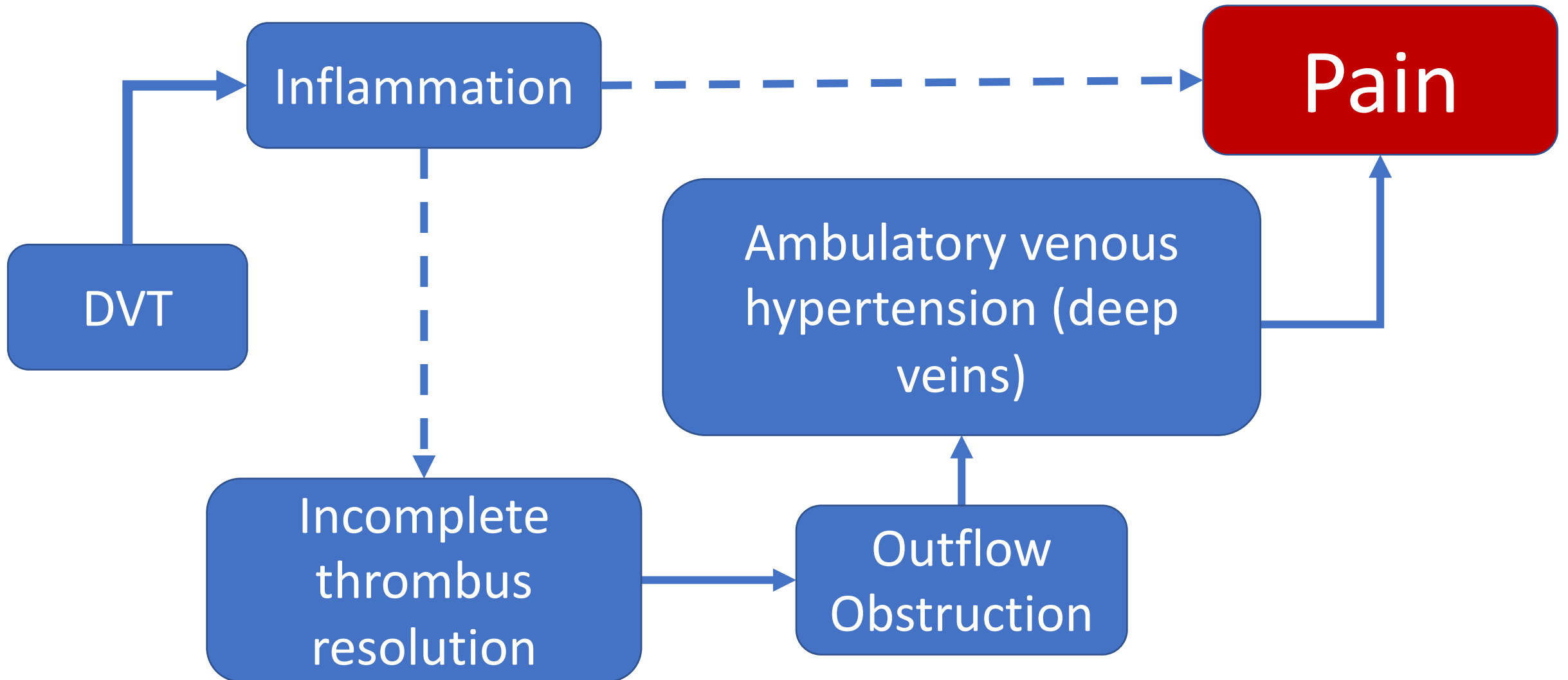


TS day 30	PTS (N=25)	2.8	1.1-6.1
TS day 90	PTS (N=25)	2.1	1.1-4.1
Reflux	PTS (N=25)	1.7	0.9-3.0

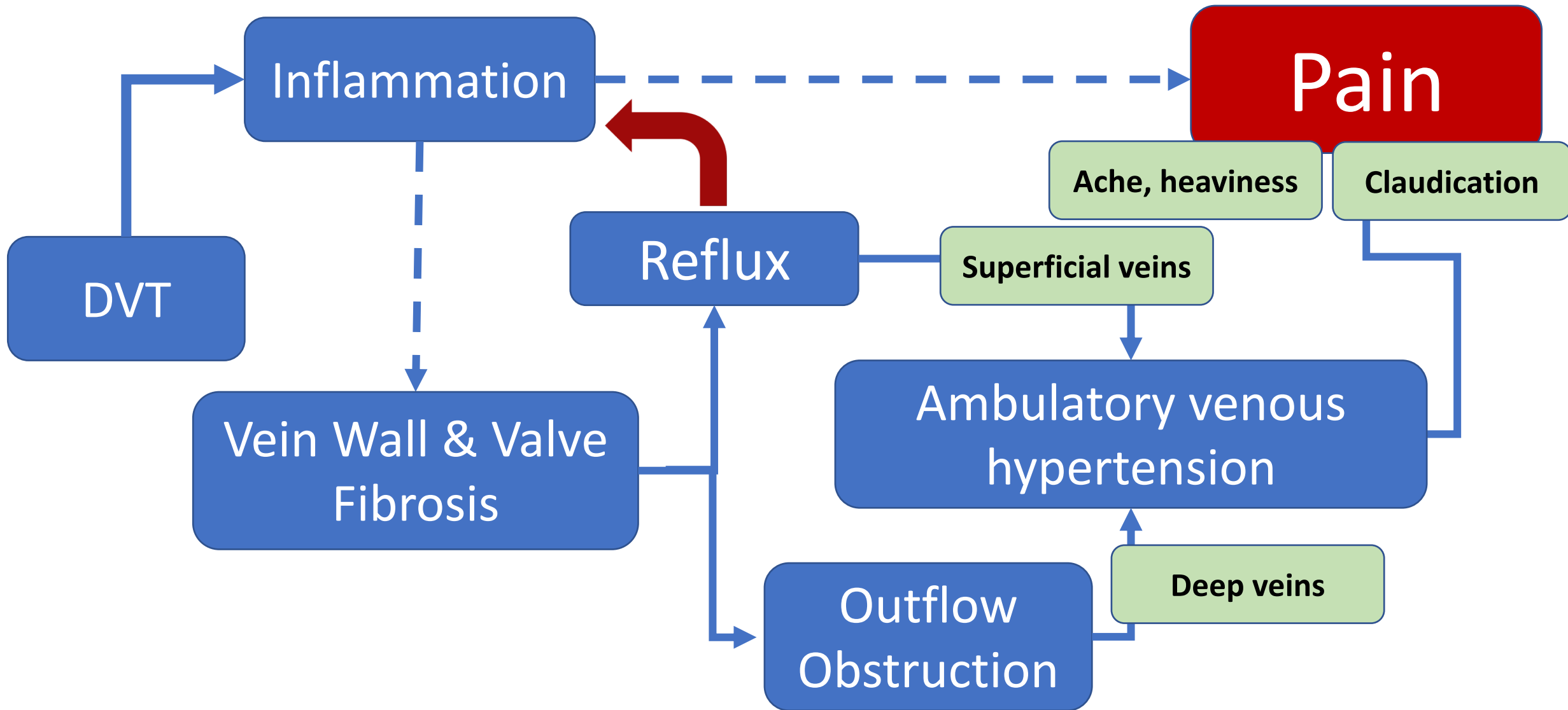
ACUTE PHASE



SUB-ACUTE PHASE



CHRONIC PHASE



Uninterrupted acute pain causes chronic pain

fMRI, evoked potentials

Recording and imaging includes information from the periphery to spinal cord tracts

fMRI, evoked potentials, QST

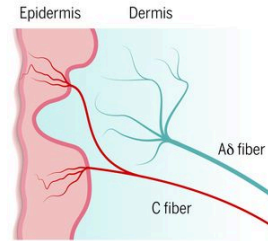
Recording and imaging includes information from the whole neuraxis

Brainstem reflexes

Blink reflex, masseter inhibitory reflex, jaw jerk
Gives information on brainstem excitatory and inhibitory circuits

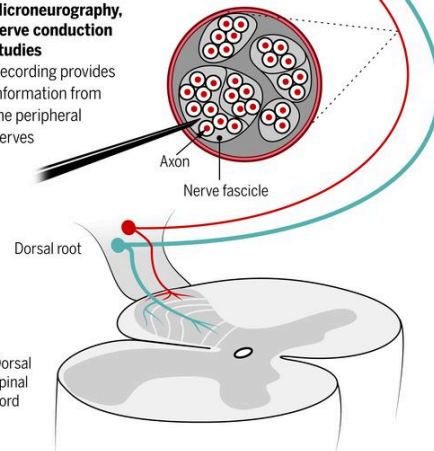
Skin biopsy

Analysis gives information on local processes in skin

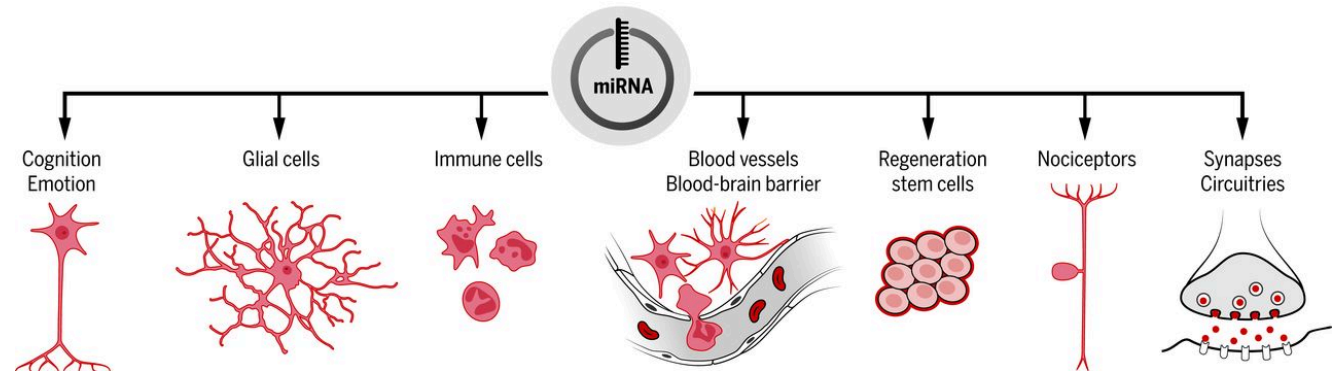


Microneurography, nerve conduction studies

Recording provides information from the peripheral nerves



Claudia Sommer Science 2016;354:588-592



Mechanisms of Pain in DVT and PTS

- Inflammation, Obstruction, Reflux
- Different veins - Different mechanisms
- Different time of action
- Acute pain causes chronic pain

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