5 Convegno di Anticoagulazione.it
Bologna 6-7 febbraio 2020

Aggiornamenti sulla terapia delle trombosi dei seni venosi cerebrali

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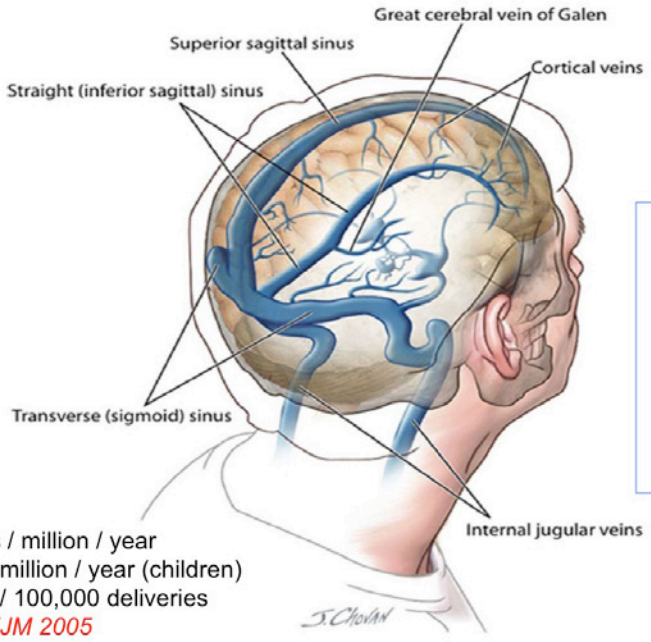
The anatomy and terminology of the cerebral and sinus veins.



Moll and Waldron, Circulation 2014

3-4 cases / million / year
7 cases / million / year (children)
12 cases / 100,000 deliveries
Stam, NEJM 2005

5 cases / million / year
Bousser & Ferro, Lancet 2007

Recurrent risk

19 studi; 1488 pazienti

Il 2.8% (range 0-11.7%) ha una recidiva di CVT diagnosticata obbiettivamente

Il 3.7% (range 0-8.6%) ha un altro evento tromboembolico venoso durante il follow up

Dentali F, Blood 2006
Dentali F, JTH 2012

2018

Journal of Thrombosis and Haemostasis, **16**: 1918–1931 DOI: 10.1111/jth.14210

REVIEW ARTICLE

Cerebral venous sinus thrombosis

M. CAPECCHI, M. ABBATTISTA and I. MARTINELLI
A. Bianchi Bonomi Hemophilia and Thrombosis Center, Fondazione IRCCS Ca' Granda - Ospedale Maggiore Policlinico, Milan, Italy

Summary of current guidelines for the anticoagulant treatment of cerebral vein thrombosis

Guidelines	Indications	Drug	Duration
Cerebral vein thrombosis			
EFNS, 2010[73] adult	• Anticoagulation for all CVT patients without contraindications • Concomitant ICH is not a contraindication	• Start with LMWH or UFH (LMWH is preferred in uncomplicated cases), followed by VKA (target INR 2.0–3.0)	• Anticoagulation given for 3 months if CVT secondary to a transient risk factor • Anticoagulation given for 6–12 months if idiopathic CVT or mild thrombophilia • Indefinite anticoagulation if recurrent CVT or VTE severe thrombophilia
AHA/ASA, 2011[55] Adult	• Start anticoagulation regardless of the presence of ICH	• Start with UFH or LMWH, followed by VKA (target INR 2.0–3.0)	• Anticoagulation given for 3–6 months if provoked CVT associated with a transient risk factor • Anticoagulation for 6–12 months if unprovoked CVT • Indefinite anticoagulation if recurrent CVT or VTE or severe thrombophilia
AHA/ASA, 2011[55] Neonates and children		• Neonates: start with LMWH or UFH and continue with LMWH for 6–12 weeks • Children (beyond the first 28 days of life): start with LMWH and continue with LMWH or VKA for 3–6 months	
EPNS/SFNP, 2012[74] Neonates and children	• Initiate anticoagulation during the acute phase if no contraindications	• Start with LMWH or UFH (UFH is preferred in precarious clinical situations) • After the acute phase, continue with VKA or LMWH (LMWH long-term might be easier in neonates and young children)	• Anticoagulation for 6–12 weeks in neonates • Anticoagulation for 3–6 months in children

Riva N, Vascular Med 2017

CVT:trattamento in fase acuta

ISCVT		CEVETIS	
UFH	64%	UFH	21.9%
LMWH	34.9%	LMWH	62.7%
Antiplatelets	5.9%	Antiplatelets	0%
Thrombolysis	2.1%	Thrombolysis	1.5%

Ferro J, Stroke 2004
Dentali F, JTH 2012

Trombolisi- Metanalisi

15 STUDI SELEZIONATI (156 Pazienti)

Mortalità	9.2% (95% CI 4.3 - 15.7%)
Emorragia Maggiore	9.8% (95% CI 5.3 - 15.6%)
Emorragia Intracranica	7.6% (95% CI 3.5 - 13.1%)

Dentali F, TH 2010

European Stroke Organization guideline for the diagnosis and treatment of cerebral venous thrombosis – Endorsed by the European Academy of Neurology

EUROPEAN STROKE JOURNAL
European Stroke Journal
0(0) 1–27
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2017

José M Ferro[1,2], Marie-Germaine Bousser[3], Patrícia Canhão[1,2], Jonathan M Coutinho[4], Isabelle Crassard[3], Francesco Dentali[5], Matteo di Minno[6,7], Alberto Maino[8], Ida Martinelli[8], Florian Masuhr[9], Diana Aguiar de Sousa[1,2] and Jan Stam[4]; for the European Stroke Organization

Recommendation: we recommend treating adult patients with acute cerebral venous thrombosis with heparin in therapeutic dosage. This recommendation also applies to patients with an intracerebral hemorrhage at baseline. No recommendation can be given on the treatment of children with CVT.

Quality of evidence: moderate

Strength of recommendation: strong

Recommendation: we suggest treating patients with acute cerebral venous thrombosis with low-molecular weight heparin instead of unfractionated heparin. This recommendation does not apply to patients with a contraindication for LMWH (e.g. renal insufficiency) or situations where fast reversal of the anticoagulant effect is required (e.g. patients who have to undergo neurosurgical intervention).

Quality of evidence: low

Strength of recommendation: weak

European Stroke Organization guideline for the diagnosis and treatment of cerebral venous thrombosis – Endorsed by the European Academy of Neurology

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José M Ferro[1,2], Marie-Germaine Bousser[3], Patrícia Canhão[1,2], Jonathan M Coutinho[4], Isabelle Crassard[3], Francesco Dentali[5], Matteo di Minno[6,7], Alberto Maino[8], Ida Martinelli[8], Florian Masuhr[9], Diana Aguiar de Sousa[1,2] and Jan Stam[4]; for the European Stroke Organization

Recommendation: we cannot provide a recommendation on thrombolysis for cerebral venous thrombosis.

Quality of evidence: very low

Strength of recommendation: uncertain

Recommendation. We suggest using oral anticoagulants (vitamin K antagonists) for a variable period (3-12 months) after CVT to prevent recurrent CVT and other venous thromboembolic events

Quality of evidence: very low

Strength of recommendation: weak

DOAC in cerebral vein thrombosis

Study	Design	Patient number	Treatment	Outcomes
RE-SPECT CVT	RCT	TBA	Dabigatran	TBA October 20th
Rao et al, 2017	Case report	3	Apixaban	Resolution
Hon et al, 2012	Case report	15	Dabigatran	Resolution in 12
Geisbusch, 2014	Case report	7	Rivaroxaban	Minor bleeding in 1 patient
Mendonca, 2015	Case report	15	Dabigatran	Resolution in 12
Mutgi, 2015	Case report	2	Rivaroxaban	Good resolution

Awaiting results of the RE-SPECT CVT RCT comparing Dabigatran vs warfarin

Novel Factor Xa Inhibitor for the Treatment of Cerebral Venous and Sinus Thrombosis

First Experience in 7 Patients

Christina Geisbüsch, MD; Daniel Richter, MD; Christian Herweh, MD; Peter A. Ringleb, MD; Simon Nagel, MD

Background and Purpose—Thrombosis of cerebral veins and sinus (cerebral venous thrombosis) is a rare stroke pathogenesis. Pharmaceutical treatment is restricted to heparin and oral anticoagulation with vitamin K antagonists (VKAs).

Methods—Between January 2012 and December 2013, we recorded data from our patients with cerebral venous thrombosis. The modified Rankin scale was used to assess clinical severity; excellent outcome was defined as modified Rankin scale 0 to 1. Recanalization was assessed on follow-up MR angiography. Patients were then divided into 2 treatment groups: phenprocoumon (VKA) and a novel factor Xa inhibitor. Clinical and radiological baseline data, outcome, recanalization status, and complications were retrospectively compared.

Results—Sixteen patients were included, and 7 were treated with rivaroxaban. Overall outcome was excellent in 93.8%, and all patients showed at least partial recanalization. No statistical significant differences were found between the groups, except the use of heparin before start of oral anticoagulation (P=0.03). One patient in the VKA and 2 patients in the factor Xa inhibitor group had minor bleeding (P=0.55) within the median (range) follow-up of 8 months (5–26).

Conclusions—Factor Xa inhibitor showed a similar clinical benefit as VKA in the treatment of cerebral venous thrombosis. Further systematic prospective evaluation is warranted. (***Stroke*. 2014;45:2469-2471.)**

Key Words: cerebral veins ■ rivaroxaban ■ thrombosis

Research

Oral direct thrombin inhibitor as an alternative in the management of cerebral venous thrombosis: a series of 15 patients

Marcelo D. Mendonça[1,2]*, Raquel Barbosa[1], Vera Cruz-e-Silva[3], Sofia Calado[1,2], and Miguel Viana-Baptista[1,2]

Int Jour Stroke, 2015

Results **Eighteen patients were admitted for cerebral vein thrombosis. Dabigatran was started in 11 patients, and warfarin was started in 7. Four patients on warfarin were switched to dabigatran because of adverse effects at 0·5, 1, 3·5, and 4 months. A total of 15 patients were treated with dabigatran with median follow-up time of 19 months. Excellent outcome was observed in 87% of patients and recanalization in 80%.**

Conclusions **We report the largest series of cerebral vein thrombosis patients treated with dabigatran. Clinical outcome was excellent in most patients and not different from other studies. Dabigatran could possibly be considered an alternative to warfarin; nevertheless, further prospective assessment with randomized controlled studies is warranted.**

Contents lists available at ScienceDirect

Thrombosis Research

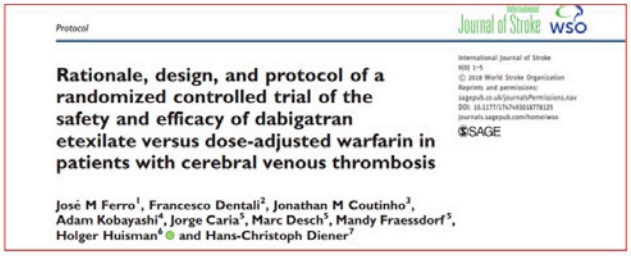
journal homepage: www.elsevier.com/locate/thromres

Covut et al. 2019

Letter to the Editors-in-Chief

Apixaban and rivaroxaban in patients with cerebral venous thrombosis

Monocentrico, retrospettivo
5 paz trattati con apixaban; 4 con rivaroxaban



Protocol

Journal of Stroke WSO

Rationale, design, and protocol of a randomized controlled trial of the safety and efficacy of dabigatran etexilate versus dose-adjusted warfarin in patients with cerebral venous thrombosis

José M Ferro[1], Francesco Dentali[2], Jonathan M Coutinho[3], Adam Kobayashi[4], Jorge Caria[5], Marc Desch[5], Mandy Fraessdorf[5], Holger Huisman[6] and Hans-Christoph Diener[7]

International Journal of Stroke
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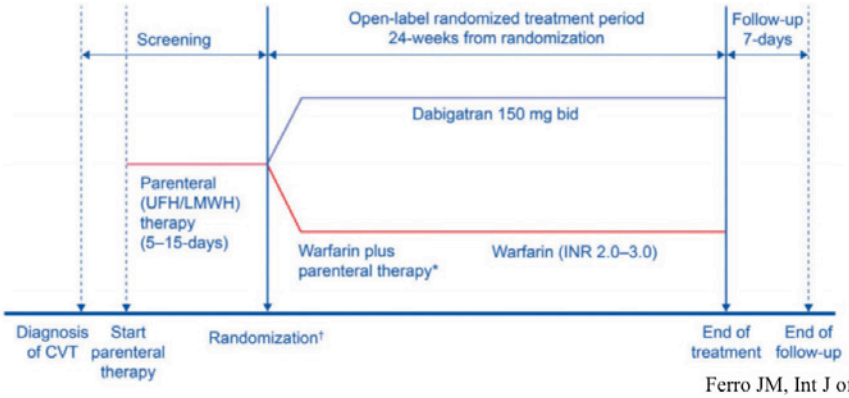
SAGE

RESPECT-CVT
NCT02913326

Primary endpoint	Secondary endpoints
• Number of patients with composite of VTE (recurring CVT; deep venous thrombosis of any limb, pulmonary embolism, splanchnic vein thrombosis) or major bleeding (ISTH criteria)[9]	• Efficacy – Number of patients with VTE • Safety – Number of patients with major bleeding (ISTH criteria)[9] and clinically relevant non-major bleeding events – Number of patients with composite of new ICH or worsening of the hemorrhagic component of a previous lesion[12] – Number of patients with any bleeding[5]



Ferro JM, Int J of Stroke 2018

Safety and Efficacy of Dabigatran Etexilate vs Dose-Adjusted Warfarin in Patients With Cerebral Venous Thrombosis: A Randomized Clinical Trial

(Ferro et al., JAMA Neurol 2019)

- 5-15 gg eparina parenterale
- Esclusi se: infezione cerebrale, trauma maggiore
- Terapia: dabigatran 150 mg x 2; oppure warfarin (60 paz per gruppo)
- Durata: 24 settimane
- Risultati: ITT = nessuna recidiva; MB: 1 (1,7%) in dab. 2 (3,3%) in warf.
  Uguale ricanalizzazione (≈ 60%)

Therapeutic interventions for CVT

Without active bleeding

Antithrombotic drug of choice	LMWH (UFH), VKA recommended for most pts. (DOAC)
Suggested dosing	LMWH: 200 aXa/kg/day; UFH: 2.5-fold PTT VKA: INR 2–3; DOAC: approved VTE treatment dosages
Suggested duration	At least 3 months for all pts. Discontinuation in pts. With transient risk factors. Long-term in pts. with permanent major risk factors including severe thrombophilia
Search for underlying conditions	Thrombophilia, estrogen exposure, PNH, JAK-2 mutation, myeloproliferative neoplasm. Steroid use/abuse
Role of thrombolysis	Selected patients with severe symptoms (coma) or deterioration during anticoagulant therapy

Ageno W, JTT 2016