

Cerebral Venous Thrombosis Complications and Outcomes

Akademisk avhandling

Som för avläggande av medicine doktorsexamen vid Sahlgrenska akademien, Göteborgs universitet kommer att offentligens försvaras i Sahlgrenska Aula, Blå stråket 5, den 10 juni, klockan 09.00

av Erik Lindgren

Fakultetsopponent:
Professor Jan Stam

Department of Neurology, University of Amsterdam, Amsterdam, the Netherlands

Avhandlingen baseras på följande delarbeten:

- I. Erik Lindgren, Katarina Jood, Turgut Tatlisumak.
Vocational outcome in cerebral venous thrombosis: Long-term follow-up study. *Acta Neurol. Scand.* 2018;137(3):299-307.
- II. Erik Lindgren,* Suzanne M. Silvis,* Sini Hiltunen, Mirjam R. Heldner, Fabiola Serrano, Michele de Scisco, Johan Zelano, Susanna M. Zuurbier, Mayte Sánchez van Kammen, Maryam Mansour, Diana Aguiar de Sousa, Sara Penas, Saleem Al-Asady, Esme Ekizoglu, Petra Redfors, Awet Ahmed, Nilüfer Yesilot, Masoud Ghiasian, Miguel A. Barboza, Valencia Arnao, Paolo Aridon, Martin N.M. Punter, José M. Ferro, Timothy Kleinig, Antonio Arauz, Turgut Tatlisumak, Marcel Arnold, Jukka Putaala, Jonathan M. Coutinho,** and Katarina Jood.**
Acute seizures in cerebral venous thrombosis *Neurology.* 2020;95(12):e1706-e1715
- III. Mayte Sánchez van Kammen,* Erik Lindgren,* Suzanne M. Silvis, Sini Hiltunen, Mirjam R. Heldner, Fabiola Serrano, Johan Zelano, Susanna M. Zuurbier, Maryam Mansour, Diana Aguiar de Sousa, Patricia Canhão, Saleem Al-Asady, Esme Ekizoglu, Petra Redfors, Nilüfer Yesilot, Masoud Ghiasian, Miguel A. Barboza, Valentina Arnao, Paolo Aridon, Martin N.M. Punter, José M. Ferro, Antonio Arauz, Turgut Tatlisumak, Marcel Arnold, Jukka Putaala, Katarina Jood,** and Jonathan M. Coutinho.**
Late seizures in cerebral venous thrombosis *Neurology.* 2020;95(12):e1716-e1723
- IV. Erik Lindgren, Alexandros Rentzos, Sini Hiltunen, Fabiola Serrano, Mirjam R. Heldner, Susanna M. Zuurbier, Suzanne M. Silvis, Maryam Mansour, William Allingham, Martin N. M. Punter, Blake F. Giarola, Jeremy Wells, Mayte Sánchez van Kammen, Eike I. Piechowiak, Nicole Chiota-McCollum, Carlos Garcia-Esperon, Christophe Cognard, Timothy Kleinig, Masoud Ghiasian, Jonathan M. Coutinho, Marcel Arnold, Antonio Arauz, Jukka Putaala, Katarina Jood, Turgut Tatlisumak: the International CVT Consortium.
Dural arteriovenous fistulas in cerebral venous thrombosis: Data from the International Cerebral Venous Thrombosis Consortium. *Eur J Neurol.* 2022;29(3):761-770.
- V. Erik Lindgren,* Katarzyna Krzywicka,* Maria A. de Winter, Mayte Sánchez van Kammen, Mirjam R. Heldner, Sini Hiltunen, Diana Aguiar de Sousa, Maryam Mansour, Patricia Canhão, Esme Ekizoglu, Miguel Rodrigues, Elisa M. Silva, Carlos Garcia-Esperon, Valentina Arnao, Paolo Aridon, Naaem Simaan, Suzanne M. Silvis, Susanna M. Zuurbier, Mine Sezgin, Andrey Alasheev, Andrey Smolkin, Daniel Guisado-Alonso, Nilüfer Yesilot, Miguel A. Barboza, Masoud Ghiasian, Ronen R. Leker, José M. Ferro, Antonio Arauz, Marcel Arnold, Jukka Putaala, Turgut Tatlisumak, Jonathan M. Coutinho,** Katarina Jood.**
A scoring tool to predict mortality and dependency after cerebral venous thrombosis. *Manuscript.*

* Authors contributed equally as first authors. ** Authors contributed equally as senior authors.

Cerebral Venous Thrombosis Complications and Outcomes

Erik Lindgren

Sektionen för klinisk neurovetenskap, Institutionen för neurovetenskap och fysiologi,
Sahlgrenska akademien, Göteborgs universitet, Sverige.

Abstract

Cerebral venous thrombosis (CVT) is a relatively rare cause of stroke, which predominantly affects working-aged adults and particularly women. The clinical course is highly miscellaneous. Data from large cohorts are scarce and knowledge on CVT complications and outcomes are limited. The overarching aim of this thesis was to investigate prognostic factors affecting clinical outcome after CVT. We investigated adult patients consecutively diagnosed with CVT from a local registry, the Sahlgrenska CVT Registry (*study I*), and from a newly established large international cohort from, in total, 17 hospitals, the International CVT Consortium (*study II-V*).

Among 62 working-aged adults included from the Sahlgrenska CVT Registry, functional outcome was good as 87% were independent at long-term follow-up. However, 29% were unable to return to work and merely 19% were asymptomatic (*study I*). In study II-V, patients were included from the International CVT Consortium. Acute symptomatic seizure(s) occurred in 441/1,281 (34%) patients, predicted by variables related to parenchymal injury adjacent to the cerebral cortex (*study II*). Of 123/1,127 (11%) experiencing a first late seizure (>7 days after diagnosis), seizure recurrence rate was 70% (*study III*). A dural arteriovenous fistula was detected in 29/1,218 (2.4%) patients, most commonly concomitant or subsequently to the diagnosis of CVT (*study IV*). Acute symptomatic seizures, status epilepticus in the acute phase and dural arteriovenous fistulas were not associated with worse functional outcome (*study II and IV*). From risk factors affecting clinical outcome, we developed the combined SI₂NCAL₂C risk score to calculate individual risks of dependency or mortality at 6 months, mortality at 30-days and mortality at 1 year. The model showed promising performance in internal validations (*study V*).

This thesis indicates that although most patients recover well and achieve independency after CVT, residual symptoms are frequent and one-quarter of working-aged adults are unable to return to work. Seizures frequently complicate the acute phase and every tenth patient experiences late seizures after CVT. The high risk of late seizure recurrence supports the diagnosis of epilepsy at time of a first late seizure. Dural arteriovenous fistulas are infrequent and mostly appear simultaneously or after CVT. The SI₂NCAL₂C risk score can be used with information available in routine clinical practice, to predict dependency or mortality at 6 months, mortality at 30-days and mortality at 1 year, but warrant external validation prior to implementation in clinical practice.

Keywords: Cerebral venous thrombosis, complications, return to work, seizure, follow-up, dural arteriovenous fistula, outcome