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# Acquired Epilepsy with a Focus on Stroke

## Treatment and Prognosis

Akademisk avhandling

Som för avläggande av medicine doktorsexamen vid Sahlgrenska akademin, Göteborgs universitet kommer att offentligen försvaras i Hjärtats aula, Vita stråket 12, Sahlgrenska Universitetssjukhuset, Göteborg, fredagen den 18 mars 2022, klockan 13:00.

av David Larsson

Fakultetsopponent:
Professor Ley Sander
UCL Queen Square Institute of Neurology, London, UK

**Avhandlingen baseras på följande delarbeten:**

I. Zelano J, Larsson D, Kumlien E, Åsberg S. Pre-stroke seizures: A nationwide register-based investigation. *Seizure* 2017; 49: 25-9.

II. Larsson D, Farahmand B, Åsberg S, Zelano J. Risk of stroke after new-onset seizures. *Seizure* 2020; 83: 76-82.

III. Larsson D, Åsberg S, Kumlien E, Zelano J. Retention rate of first antiepileptic drug in poststroke epilepsy: A nationwide study. *Seizure* 2019; 64: 29-33.

IV. Larsson D, Baftiu A, Johannessen Landmark C, von Euler M, Kumlien E, Åsberg S, Zelano J. Association between antiseizure drug monotherapy and mortality for patients with poststroke epilepsy. *JAMA Neurology* 2021; e-pub.

**SAHLGRENSKA AKADEMIN**
**INSTITUTIONEN FÖR NEUROVETENSKAP OCH FYSIOLOGI**

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# Acquired Epilepsy with a Focus on Stroke
## Treatment and Prognosis

**David Larsson**

Department of Clinical Neuroscience**,** Institute of Neuroscience and Physiology, Sahlgrenska Academy, University of Gothenburg, Sweden.

**Abstract**

The relationship between epilepsy and stroke is complicated. While stroke is a major cause of epilepsy after middle age, there is also evidence that the risk of stroke is increased in persons with epilepsy. The overall aim of this dissertation is to elaborate on the prognosis and treatment of epilepsy in older adults and its association to stroke. It is based on four studies which have been conducted using information from linked national registers, which offer unique opportunities to follow thousands of patients over a long period of time.

The results from Papers I-II indicate that a significant proportion of all new-onset seizures after middle age will herald a subsequent stroke. Using incidence data and population statistics, we estimated the 10-year risk of stroke to be between 5-20%, depending on age group. In relative terms, the risk appears to be almost two-fold (odds ratio [OR] 1.77; 95% confidence interval [95%CI] 1.65-1.89) compared with age-matched controls from the general population – and highest during the first year after seizure onset (OR 2.21; 95 % CI 1.79–2.72).

The studies described in Papers III-IV examined prognostic aspects of antiseizure medication (ASM) therapy in poststroke epilepsy. Paper III found the 5-year retention rate to be highest for lamotrigine (0.75, 95%CI 0.70–0.79) and levetiracetam (0.69, 95%CI 0.63–0.74), suggesting these drugs are well tolerated in this patient group. Paper IV used a similar methodology but investigated if mortality varied with different ASMs in monotherapy. Patients treated with lamotrigine had lower mortality (hazard ratio [HR] 0.72, 95%CI 0.60-0.86) than the reference group treated with carbamazepine, while patients treated with valproic acid had higher mortality (HR 1.40, 95%CI 1.23-1.59). Treatment with levetiracetam was associated with a reduced risk of cardiovascular death compared to carbamazepine (HR 0.77, 95%CI 0.60-0.99).

In conclusion, this thesis supports a tailored management approach in adults with new-onset seizures late in life, particularly in those with a history of stroke. Persons with late-onset seizures have high vascular risk, potentially warranting screening and treatment for vascular risk factors. Moreover, the association between ASM selection and mortality raises concerns about clinically relevant drug-drug or drug-disease interactions that may modify vascular risk. Overall, lamotrigine and levetiracetam seem sensible initial treatment options in this patient group.

**Keywords:** epilepsy, seizure, stroke, cerebrovascular disease, antiseizure medication, antiepileptic drug, prognosis.

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