RISK FACTORS FOR ISCHAEMIC STROKE RECURRENCE IN PATIENTS WITH A NON-CARDIOEMBOLIC ISCHAEMIC STROKE IN DENMARK: OBSERVATIONS FROM ASTRIS

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Introduction

- Between 2004 and 2018 in Denmark, ischaemic stroke (IS) accounted for 91% of all first-ever strokes[1].
- Despite advances in antithrombotic treatment, recurrence rates after an index IS remain high[2–4].
- Population-based epidemiological studies can provide insight into which patients with non-cardioembolic IS (NCIS) face an elevated risk of recurrent IS.
- The present analysis aimed to use real-world data to identify baseline risk factors associated with IS recurrence in patients with an NCIS in Denmark.

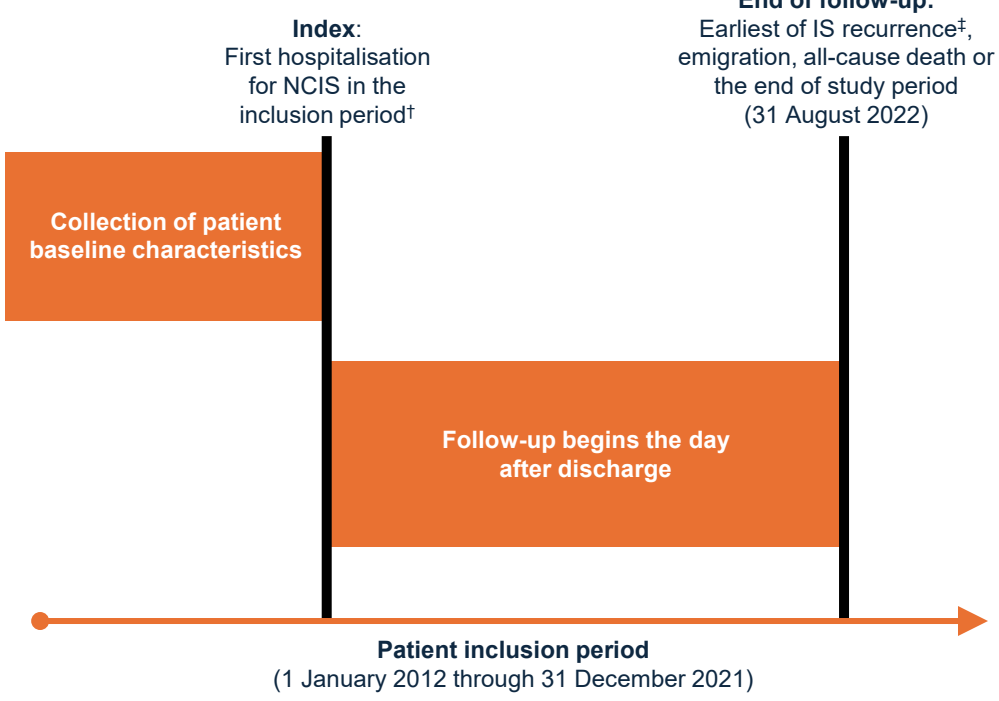
Methods

- ASTRIS Denmark is a retrospective cohort study that followed patients who had a first hospitalisation for NCIS (**Figure 1**).
  - The index date was 1 day after discharge of the index NCIS.
- Data were ascertained from the Danish Stroke Registry[5], Danish National Patient Registry[6] and the Danish Cause of Death Registry[7] between 2012 and 2022.
- Patients aged ≥18 years with a first admission for NCIS were included.
- Patients were excluded if they had:
  - A history of atrial fibrillation before index IS hospitalisation and ≤15 days post-discharge.
  - Oral anticoagulant use in 90 days before the index IS date and no record of deep vein thrombosis or pulmonary embolism up to 1 day before index IS hospitalisation.
- Patients were followed from the index date until the earliest of the following: first recurrent IS, emigration, all-cause death or end of study period (31 August 2022).

Statistical analysis

- IS incidence rates were calculated as cases during follow-up divided by the total person-years, with 95% confidence intervals (CIs) assuming a Poisson distribution.
- Baseline risk factors were identified using Cox proportional hazards regressions adjusted for age and sex with 95% CIs.
- Stroke severity, prospectively collected in the Danish Stroke Registry[5], was classified using the Scandinavian Stroke Scale: mild (43–58), moderate (26–42) and severe (0–25), corresponding closely with categories of the National Institutes of Health Stroke Scale (mild: 0−5; moderate: 6−14; severe: 15−31)[8].

Figure 1. Study design



†Index NCIS was identified through the Danish Stroke Registry[5]. ‡Recurrent IS was identified using the Danish Stroke Registry[5], Danish National Patient Registry[6] and the Danish Cause of Death Registry[7].

IS, ischaemic stroke; NCIS, non-cardioembolic ischaemic stroke.

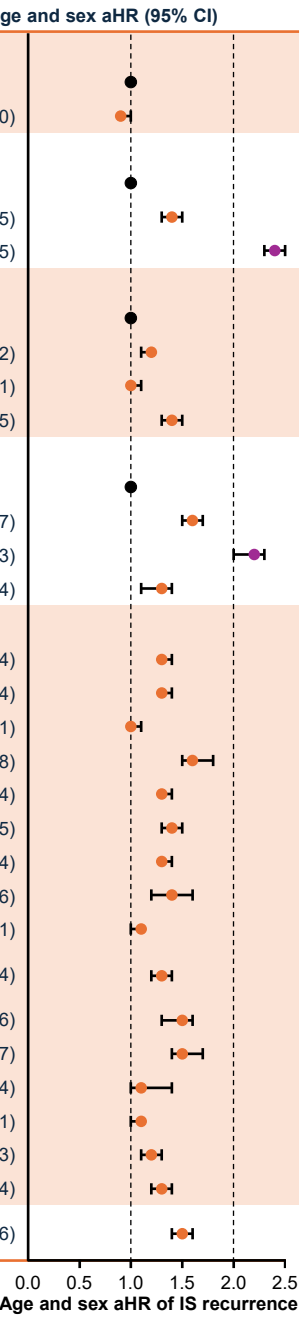
Results

Patient characteristics and incidence of recurrent IS

- Among the 59,590 patients included in the study (56% male), 8348 patients experienced a recurrent IS.
- The mean follow-up was 3.9 years.
- Most patients with an index NCIS had mild severity (n=45,877, 77.0%) and most recurrent IS events occurred in patients with a mild index NCIS (n=5710, 68.4%; **Table 1**).
- Older age was strongly (adjusted hazard ratio [aHR] ≥2) associated with an increased risk of IS recurrence (aged >75 compared with <65, aHR 2.4 [95% CI 2.3–2.5]).
- Higher stroke severity at index NCIS was strongly (aHR ≥2) associated with an increased risk of IS recurrence (severe index NCIS compared with mild index NCIS, aHR 2.2 [95% CI 2.0–2.3]).

Table 1. Patient characteristics and incidence of recurrent IS since index NCIS

	Patients, n (%)†	Events, n (%)	IR per 100 P-Ys‡	Age and sex aHR (95% CI)
Sex				
Male	33,483 (56.2)	4615 (55.3)	3.4	1 (ref)
Female	26,107 (43.8)	3733 (44.7)	3.6	0.9 (0.9–1.0)
Age at index NCIS, years				
<65	20,030 (33.6)	2046 (24.5)	2.1	1 (ref)
65–75	17,502 (29.4)	2313 (27.7)	3.1	1.4 (1.3–1.5)
>75	22,058 (37.0)	3989 (47.8)	5.7	2.4 (2.3–2.5)
Smoker status				
Never smoker	19,013 (31.9)	2627 (31.5)	3.3	1 (ref)
Current	18,032 (30.3)	2463 (29.5)	3.2	1.2 (1.1–1.2)
Past smoker	16,068 (27.0)	2207 (26.4)	3.5	1.0 (1.0–1.1)
Missing smoker status	6477 (10.9)	1051 (12.6)	5.0	1.4 (1.3–1.5)
Severity of index NCIS§				
Mild	45,877 (77.0)	5710 (68.4)	3.0	1 (ref)
Moderate	8821 (14.8)	1621 (19.4)	5.5	1.6 (1.5–1.7)
Severe	3548 (6.0)	813 (9.7)	7.0	2.2 (2.0–2.3)
Missing	1344 (2.3)	204 (2.4)	3.6	1.3 (1.1–1.4)
Comorbidity prior to index NCIS‖				
Hypertension	39,537 (66.4)	6142 (73.6)	4.0	1.3 (1.3–1.4)
Diabetes	9646 (16.2)	1605 (19.2)	4.6	1.3 (1.3–1.4)
Hyperlipidaemia	16,826 (28.2)	2493 (29.9)	3.4	1.0 (1.0–1.1)
Peripheral artery disease	3255 (5.5)	670 (8.0)	6.5	1.6 (1.5–1.8)
Ischaemic heart disease	9239 (15.5)	1655 (19.8)	5.0	1.3 (1.3–1.4)
Congestive heart failure	2597 (4.4)	457 (5.5)	5.6	1.4 (1.3–1.5)
Prior transient ischaemic attack	4808 (8.1)	906 (10.9)	4.9	1.3 (1.3–1.4)
Prior intracranial haemorrhage	1294 (2.2)	229 (2.7)	5.2	1.4 (1.2–1.6)
Major bleeding event	12,615 (21.2)	1909 (22.9)	3.7	1.1 (1.0–1.1)
Deep vein thrombosis or pulmonary embolism	3333 (5.6)	557 (6.7)	5.0	1.3 (1.2–1.4)
Dementia	1873 (3.1)	351 (4.2)	7.4	1.5 (1.3–1.6)
Chronic kidney disease	1600 (2.7)	293 (3.5)	6.6	1.5 (1.4–1.7)
Hepatic failure	932 (1.6)	125 (1.5)	3.9	1.1 (1.0–1.4)
Cancer	8998 (15.1)	1286 (15.4)	4.5	1.1 (1.0–1.1)
COPD	4603 (7.7)	690 (8.3)	4.5	1.2 (1.1–1.3)
Alcohol misuse	6079 (10.2)	867 (10.4)	3.6	1.3 (1.2–1.4)
Antiplatelet use prior to index NCIS	16,126 (27.1)	2808 (33.6)	5.3	1.5 (1.4–1.6)



†An index stroke event was defined as NCIS if the patient had no history of atrial fibrillation any time before the index hospitalisation and up to 15 days after discharge, and had not received oral anticoagulant therapy within 90 days before hospitalisation for IS unless they had a record of either deep vein thrombosis/pulmonary embolism or hip/knee surgery. ‡Calculated from day 30 after discharge from the index date until the end of follow-up. §SSS scores: mild, 43–58; moderate, 26–42; severe, 0–25. ‖Classified based on registry information from 1995 and up to the day of admission for the index NCIS.

aHR, adjusted hazard ratio; CI, confidence interval; COPD, chronic obstructive pulmonary disease; IR, incidence rate; IS, ischaemic stroke; NCIS, non-cardioembolic ischaemic stroke; P-Y, patient-years; ref, reference; SSS, Scandinavian Stroke Scale.

Severity of index NCIS and recurrent IS

- A larger proportion of recurrent IS events were classified as moderate (19.6%) or severe (9.6%) compared with index strokes (13.8% and 3.6%, respectively; **Table 2**).

Table 2. Severity of NCIS and recurrent IS according to the Scandinavian Stroke Scale score assessed on admission

	Severity of recurrent IS				
Severity of index NCIS, n (%)	**Mild (score 43–58)**	**Moderate (score 26–42)**	**Severe (score 0–25)**	**Missing**	**Total**
Mild (score 43–58)	3244 (72.8)	748 (16.8)	342 (7.7)	124 (2.8)	4458 (80.5)
Moderate (score 26–42)	363 (47.3)	248 (32.3)	130 (17.0)	26 (3.4)	767 (13.8)
Severe (score 0–25)	78 (39.4)	60 (30.3)	50 (25.3)	10 (5.1)	198 (3.6)
Missing	70 (59.8)	28 (23.9)	10 (8.6)	9 (7.7)	117 (2.1)
Total	3755 (67.8)	1084 (19.6)	532 (9.6)	169 (3.1)	5540 (100)

Green boxes indicate cases where recurrent IS severity matched the index NCIS. Yellow boxes represent higher recurrent IS severity vs the index NCIS, and blue boxes represent lower recurrent IS severity vs the index NCIS.

IS, ischaemic stroke; NCIS, non-cardioembolic ischaemic stroke.

Conclusions

- Most recurrent IS events occurred in patients with a mild index NCIS.
- Older age and higher stroke severity at the index NCIS were significant predictors of IS recurrence.
  - All other patient characteristics showed weak to moderate associations with IS recurrence.
  - Future studies may consider assessing the combination of several comorbidities.
- Recurrent IS events were more frequently moderate or severe than index NCIS, a finding that highlights the need for better secondary prevention strategies for patients who have suffered an NCIS.
- A complementary study in England, ASTRIS UK, showed similar results regarding IS recurrence rates.

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Conflicts of interest / Disclosures

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References

1. Ebbesen MQB et al. *Stroke*. 2024;55(4):972–982.
2. Khanevski AN et al. *Acta Neurol Scand*. 2019;140(1):3–8.
3. Mohan KM et al. *Stroke*. 2011;42(5):1489–1494.
4. Kolmos M et al. *J Stroke Cerebrovasc Dis*. 2021;30(8):105935.
5. Johnsen SP et al. *Clin Epidemiol*. 2016;8:697–702.
6. Schmidt M et al. *Clin Epidemiol*. 2015;7:449–490.
7. Helweg-Larsen K. *Scand J Public Health*. 2011;39(7 Suppl):26–29.
8. Govan L et al. *Stroke*. 2009;40(10):3396–3399.

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