Functional Impairment Patterns Following Recurrent Ischaemic Stroke in Patients With a History of Non-Cardioembolic Stroke: An Observational Study

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Introduction

- Ischaemic stroke (IS) is a major cause of morbidity and mortality worldwide[1,2] and the burden of disability after a stroke is expected to increase in the future.[3]
- Survivors are at risk of further strokes, with recurrence rates of around 10% at 1 year and 20% at 5 years.[4]
- Prevention of recurrence is a key priority for patients who have had a stroke;[5] however, there is limited information regarding the effects of recurrent IS following a non-cardioembolic IS (NCIS) on functional impairment.

Objectives

- This observational study in Danish patients with an index NCIS who subsequently had a recurrent IS aims to describe the impact of each stroke event on the patients' physical disability and functioning.

Methods

- Patients with a recurrent IS following an index NCIS were identified using IS diagnostic codes and medical records from the administrative system of Southern Denmark hospitals (January 2018–December 2023).
- IS was defined according to the World Health Organization criteria.[6]
  - Patients had to have undergone acute brain scan imaging at the time of stroke onset to determine stroke type.
- Information regarding patients' functional level and home arrangements before discharge following the index NCIS and recurrent IS was abstracted from medical records.
- Physical disability was evaluated retrospectively using the following information at the latest available date before discharge from the acute stroke unit:
  - Modified Rankin Scale (mRS) score.
  - Barthel's 10-item index score[7] (mean and median score, total score grouped into ≤40, 41–60, 61–85 and ≥85).
  - Ability to stand unaided by another person and ability to walk.
  - Key deficits at any time during the acute admission for stroke.

Statistical analysis

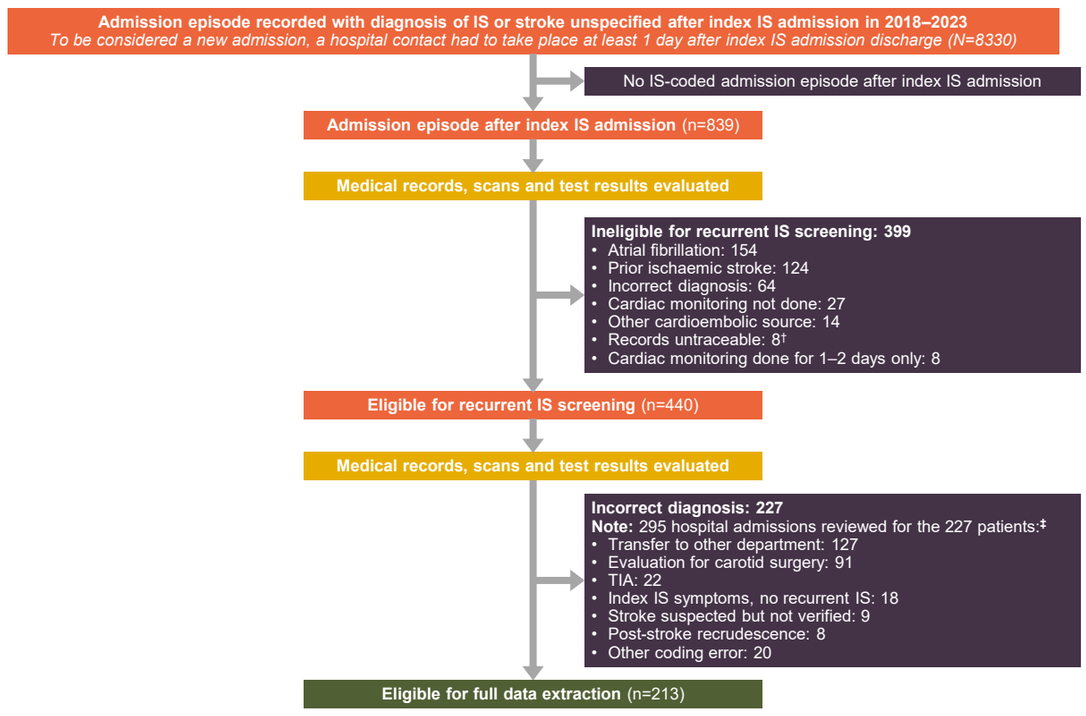
- Descriptive analyses using summary statistics were used for continuous and categorical data.
- Odds ratios (95% confidence intervals [CIs]) of a poor outcome at recurrent IS versus index NCIS were calculated using conditional logistical regression or multinomial logistic regression.

Results

Participants

- A total of 839 patients who had ≥2 IS coded-admissions were identified; of these, 213 were included in the analysis (**Figure 1**).

Figure 1. Flowchart of patients who met the eligibility criteria for full data extraction.



†Includes <5 untraceable records for recurrent IS. ‡Numbers refer to contacts and not patients.
IS, ischaemic stroke; TIA, transient ischaemic attack.

- At baseline, for the 213 patients identified, mean age was 69.3 years and 62.4% were male (**Table 1**).
  - Patients frequently had hypertension (74.2%), diabetes (21.6%), a history of ischaemic heart disease (18.8%) and hyperlipidaemia (14.1%).
  - Common medications patients were taking at the time of index NCIS included antihypertensives (58.7%), statins (32.4%) and antiplatelets (28.6%).

Table 1. Baseline characteristics of patients with non-cardioembolic index ischaemic stroke in 2018–2022.

Characteristic No. (%) unless otherwise stated		Index NCIS (n=213)
Sex	Men	133 (62.4)
	Women	80 (37.6)
Age, years, mean (SD)		69.3 (11.5)
Age, years, groups	<65 years	65 (30.5)
	65–75 years	81 (38.0)
	>75 years	67 (31.5)
Smoker (current)		74 (34.7)
High alcohol consumption†,‡		17 (7.9)
Comorbidities prior to index stroke	Hypertension§,‖	158 (74.2)
	Diabetes§,‖	46 (21.6)
	Ischaemic heart disease§	40 (18.8)
	Cancer§	34 (16.0)
	Hyperlipidaemia§,‖	30 (14.1)
	Disorders indicative of high alcohol use	22 (10.3)
	Peripheral artery disease§	19 (8.9)
	Chronic obstructive pulmonary disorder	12 (5.6)
	History of TIA§	10 (4.7)
	Chronic kidney failure§	10 (4.7)
	Dementia§	<5 (<2.3)
eGFR, mL/min/1.73m² (latest in 12-month period up to admission for index stroke)¶,#	≥60 (normal)	169 (79.3)
	30–59	37 (17.4)
	<30	7 (3.3)
Medication use, prior to index stroke	Antihypertensives	125 (58.7)
	Statins	69 (32.4)
	Antiplatelet	61 (28.6)
	Anticoagulant	<5 (<2.3)
Stroke onset to first hospital evaluation††	≤4.5 hours	90 (42.2)
	>4.5 to ≤24 hours	50 (23.4)
	>24 hours	73 (34.4)
GCS score, mean (SD)		14.8 (0.9)
Stroke severity on admission	NIHSS score, mean (SD)	4.1 (3.8)
	NIHSS score, median (IQR)	3.0 (2.0; 5.0)
	NIHSS score, groups	
	Mild (0–5)	171 (80.3)
	Moderate or severe (6–31)	42 (19.7)
Acute treatment	Thrombolysis	72 (33.8)
	Thrombectomy	5–10 (2.3–4.6)
	Neither of above	137 (64.3)
Admitted to stroke unit		>207 (>97.2)
Admitted to intensive care unit		9 (4.2)
Inpatient rehabilitation		30 (14.1)
Duration of admission‡‡, days	Acute unit, mean (SD)	4.6 (3.2)
	Acute unit, median (IQR)	4.0 (3.0; 6.0)
	Inpatient rehabilitation, days, mean (SD)§§	23.3 (14.4)
	Inpatient rehabilitation, days, median (IQR)§§	21 (12; 31)

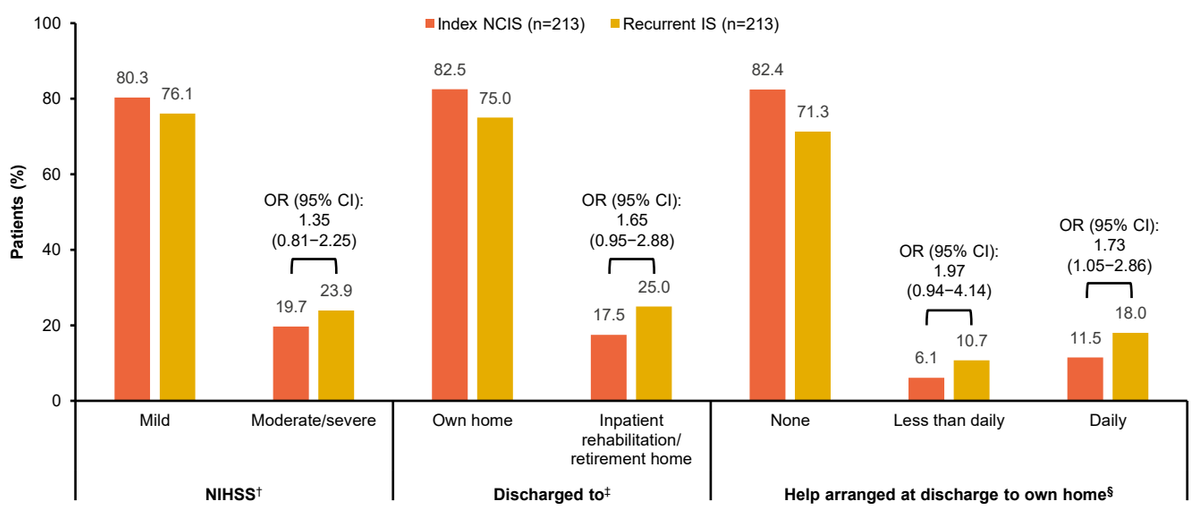
Some cells are only reported as less than or larger than a certain number. This is done to safeguard anonymity and in accordance with regulations by the Danish Health Data Authority.
†High alcohol use classified according to prevailing limits recommended by the Danish Health Authority.
‡Numbers (%) calculated using multiple imputations due to 59 missing values.
§Classification based on information from the Danish National Patient Registry.
‖Classification based on information from the Danish National Prescription Registry.
¶Based on information from the Clinical Laboratory Information Register.
#Numbers (%) calculated using multiple imputations due to 14 missing values.
††Numbers (%) calculated using multiple imputations due to 13 missing values.
‡‡For patients transferred between hospitals or departments for the same stroke episode, duration of stay counted from date of first contact until discharge from last department.
§§Based on 30 patients with inpatient rehabilitation after an index ischaemic stroke.
eGFR, estimated glomerular filtration rate; GCS, Glasgow Coma Scale; IQR, interquartile range; NCIS, non-cardioembolic ischaemic stroke; NIHSS, National Institutes of Health Stroke Scale; SD, standard deviation; TIA, transient ischaemic attack.

- The distributions of stroke subtypes of index NCIS versus recurrent IS were similar:
  - Small vessel occlusion 28.2% versus 24.9%.
  - Large artery atherosclerosis 18.8% versus 20.2%.
  - Undetermined aetiology 49.8% versus 45.5%.
- Ten (4.7%) recurrent IS events were classified as cardioembolic.

Severity of stroke and functional impairment

- Following a recurrent IS, more patients had a moderate/severe National Institutes of Health Stroke Scale (NIHSS) rating at admission (24% vs 20%), fewer were discharged home (75% vs 83%), and more required help at home (29% vs 18%) compared with the index NCIS (**Figure 2**).

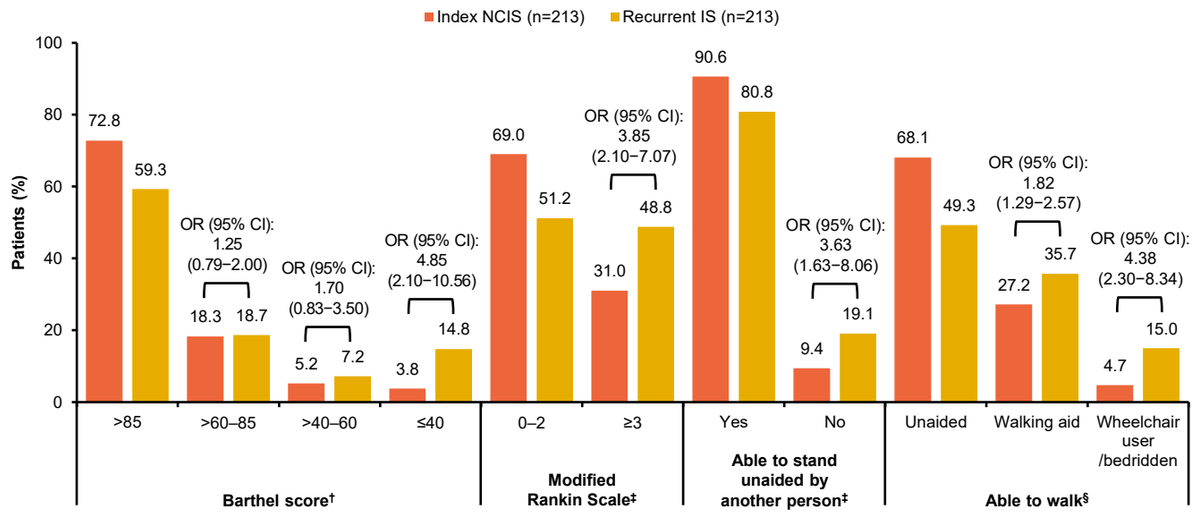
Figure 2. Stroke severity on admission and information recorded before discharge regarding home arrangements following a NCIS and a subsequent recurrent IS.



OR was calculated using conditional logistic regression for 'discharged to own home' and using multinomial regression with clustering for 'help arranged at time of discharge to own home'. Missing values were imputed.
†Grouped: number (%) calculated using multiple imputations due to missing values among <5 patients with recurrent IS. Imputed numbers were rounded.
‡Does not include 13 patients who died during admission for recurrent IS; of these 13, seven were discharged to their own home from the acute unit after their index NCIS.
§Only includes patients discharged from acute unit to own home.
CI, confidence interval; IS, ischaemic stroke; NCIS, non-cardioembolic ischaemic stroke; NIHSS, National Institutes of Health Stroke Scale; OR, odds ratio.

- Before discharge, more patients with a recurrent IS had indicators of reduced functioning compared with the index NCIS: a larger percentage had Barthel scores ≤40 (15% vs 4%), mRS scores ≥3 (49% vs 31%), were unable to stand unaided by another person (19% vs 9%), needed a walking aid (36% vs 27%) or were a wheelchair user or remained in bed (15% vs 5%; **Figure 3**).

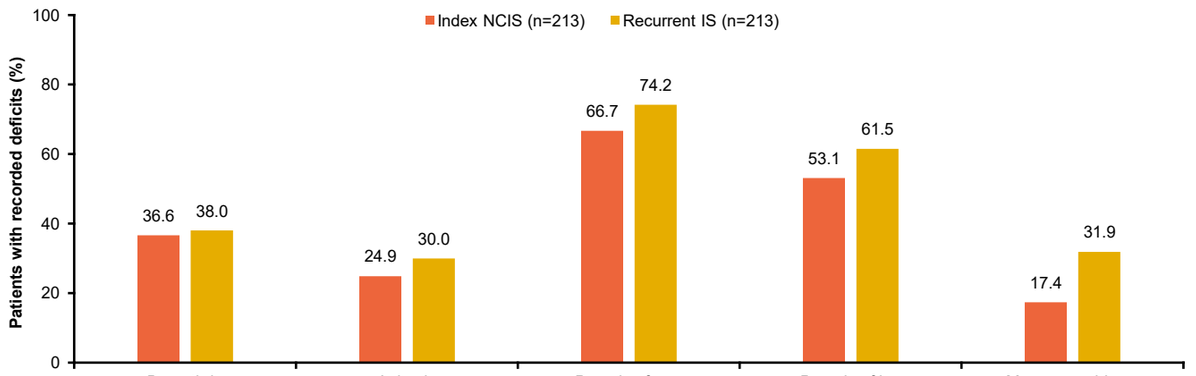
Figure 3. Functional levels following a NCIS and a subsequent recurrent IS.



OR was calculated using conditional logistic regression for 'modified Rankin Scale' and 'able to stand unaided by another person' and using multinomial regression with clustering for 'Barthel score' and 'able to walk'. Missing values were imputed.
†Number (%) calculated using multiple imputations due to missing values in <5 patients with recurrent IS.
‡Number (%) calculated using multiple imputations due to missing values in <5 among index NCIS and 13 among recurrent IS. Imputed numbers were rounded.
§Number (%) calculated using multiple imputations due to missing values among 13 patients with recurrent IS. Imputed numbers were rounded.
CI, confidence interval; IS, ischaemic stroke; NCIS, non-cardioembolic ischaemic stroke; OR, odds ratio.

- A larger percentage of patients were recorded in medical records as having dysarthria, aphasia, paresis of arm or leg, or memory problems during admissions for recurrent IS than index NCIS (**Figure 4**).

Figure 4. Deficits recorded in medical record by physician, nurse or therapists (physio/speech/ergo) at any time during admission to acute unit.



Note. We did not have information on whether the deficit was caused by the stroke or whether it was already present prior to stroke/recurrent stroke occurrence. Also, we did not have information on whether the deficit was still present on discharge.
IS, ischaemic stroke; NCIS, non-cardioembolic ischaemic stroke.

Conclusions

- This observational study is the first to directly assess functional scores/disability between index NCIS and recurrent IS within the same individuals.
- Our results indicate that patients who experience a recurrent IS following a first-ever NCIS have more severe strokes and greater functional decline after their second than their first stroke.
  - Recurrent IS increases likelihood of need for inpatient rehabilitation and for daily care if discharged to home.
- These findings emphasise the need for effective secondary stroke prevention strategies for patients with NCIS.

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