

Five-year readmission and mortality differ by ischemic stroke subtype

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ARTICLE INFO

Keywords:

Ischemic stroke
Transient ischemic attack
Readmission
Mortality
Ischemic stroke subtype

ABSTRACT

Background: Ischemic stroke subtype may influence the risk of readmission and mortality after ischemic stroke (IS) and transient ischemic attack (TIA) due to differences in comorbidity, risk factors, and stroke severity. We aimed to study the five-year incidence and risk of all-cause readmission, cause-specific readmission and mortality after IS or TIA by stroke subtype.

Methods: The medical records of 1453 patients admitted with IS or TIA to the stroke unit at Haukeland University Hospital, Norway, between 2007 and 2012 were reviewed for identification of unplanned readmissions within five years after discharge. Stroke etiology was classified as large-artery atherosclerosis (LAA), cardioembolism (CE), small vessel occlusion (SVO), stroke of other determined etiology (SOE), multiple etiologies (ME), or cryptogenic stroke (CS). Kaplan-Meier estimates and Cox regression analyses were used to determine incidences and risk of readmission and death.

Results: The five-year incidence of all-cause readmission was 72.6% (74% LAA, 81% CE, 65% SVO, 55% SOE, 71% ME, and 67% CS), with infections, cardiac disease, stroke-related events and fractures as the most frequent causes. Compared to patients with other subtypes, SVO subtype had a 21% lower risk of all-cause readmission and a 48% lower risk of death, whereas CE had a 25% higher risk of all cause readmission and a 34% higher risk of death. CE subtype also had a 75% higher risk of readmission due to cardiac disease, whereas CS subtype had a 44% lower risk of readmission with cardiac disease.

Conclusion: The five-year incidence of readmission and mortality varied among the stroke subtypes. The risk of readmission and death are especially high in patients with CE subtype, and lowest for patients with SVO subtype.

1. Introduction

Stroke patients are at increased risk of subsequent disease, and readmissions are common [1,2]. The risk of readmission is particularly high in the early phase after stroke, with 30-day estimates ranging from 6% to 21%, and one-year estimates from 31% to 55% [2–6]. Most studies on long-term outcome after stroke have focused on recurrent stroke, vascular events, and mortality [7]. However, nonvascular events such as infections and fractures are also frequent in the chronic phase of stroke [2,6,8,9], and < 15% of all stroke patients survive for more than five years without being readmitted [6,8].

Ischemic stroke and transient ischemic attack (TIA) are

heterogeneous disorders caused by various pathologies including large-artery atherosclerosis, cardioembolism, small vessel occlusion and other less common causes [10]. Risk factors, treatment and outcome highly depend on stroke subtype [11,12], which further may influence the risk and the causes of readmission. Previous studies on our population have demonstrated that large-artery atherosclerosis is associated with an increased risk of readmission within 30 and 90 days, whereas small vessel occlusion is associated with a decreased risk of readmission from day 91–365 after discharge [13,14]. However, most other studies investigating the risk of readmission after stroke have not differentiated between stroke subtypes which may be a useful approach when evaluating the risk of new diseases and unwanted readmissions.

Abbreviations: LAA, large-artery atherosclerosis; CE, cardioembolic; SVO, small vessel occlusion; SOE, stroke of other determined etiology; ME, multiple etiologies; CS, cryptogenic stroke; UTI, urinary tract infection; VTE, venous thromboembolism; GI, gastrointestinal

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<https://doi.org/10.1016/j.jns.2019.06.007>

Received 15 November 2018; Received in revised form 15 May 2019; Accepted 4 June 2019

Available online 05 June 2019

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The aim of this study was to investigate the five-year incidence of readmission after ischemic stroke or TIA. To elucidate the underlying causes of long-term hospital readmission, the risks of all-cause readmission and cause-specific readmission were examined for each stroke subtype.

2. Methods

2.1. Study design and data acquisition

All patients > 18 years of age with ischemic stroke or TIA admitted to the Stroke Unit at Haukeland University Hospital from July 2007 to October 2012, were prospectively registered in the Bergen NORSTROKE Registry. The study cohort included all patients living inside the hospital catchment area (\approx 275,000 residents). Patients with residence outside the hospital catchment area at the time of the index stroke admission were excluded to ensure complete follow-up. Patients who died during the index hospitalization or were discharged to palliative care were also excluded.

Ischemic stroke was defined as a neurologic deficit lasting > 24 h or as clinical symptoms of transient ischemic attacks but with computed tomography or magnetic resonance imaging (MRI) evidence of acute infarction related to the initial symptoms [15]. TIA was defined as a transient episode of neurological dysfunction < 24 h with no objective evidence of acute brain infarction on imaging [16]. Electrocardiogram, duplex ultrasound of the carotid arteries, Holter monitoring, echocardiography and serology were obtained during hospital admission. Ischemic stroke etiology was classified by an experienced stroke neurologist (HN) according to the Trial of Org 10,172 in Acute Stroke Treatment (TOAST) criteria as large-artery atherosclerosis (LAA), cardioembolism (CE), small vessel occlusion (SVO), or stroke of other determined etiology (SOE). The TOAST category “stroke of undetermined etiology” was divided into multiple etiologies (ME) which included patients with two or more probable etiologies, and cryptogenic stroke, (CS) which included patients with no identified etiology [10]. The TOAST criteria were also applied for etiologic classification of TIAs, with findings of a ipsilateral significant (\geq 50%) atherosclerotic stenosis and no competing cause classified as LAA, findings of a cardioembolic source and no competing cause classified as CE, findings of lacunar clinic and no competing cause classified as SVO, findings of other specific etiology such as arterial dissection classified as SOE, in cases with no identified cause as CS, and in cases with two or more identified probable causes as ME. Stroke severity was determined by National Institutes of Health Stroke Scale (NIHSS) on admission and on day 7 or discharge if earlier. Short-term functional outcome was determined by modified Rankin Scale (mRS) on day 7 or discharge if earlier. Demographics, clinical characteristics, treatment, comorbidity, medical history and discharge destination were registered. Discharge date was defined as discharge from the stroke unit to either primary health care or an in-hospital transfer to another department/rehabilitation department. A variable representing the total number of traditional cardiovascular risk factors (hypertension, diabetes mellitus, smoking, angina pectoris, prior myocardial infarction and peripheral artery disease) was made and defined as the risk factor burden (0, 1, 2, and \geq 3 risk factors). Secondary prevention was based on the Norwegian guidelines for stroke treatment [17].

The study cohort were followed for five years after discharge by review of electronic medical records. The medical records are continuously updated with information on mortality and permanent addresses from the National Registry of Norway. Mortality and all unplanned readmissions to any department at the hospitals within the area of the Western Norway Regional Health Authorities were registered retrospectively. The Western Norway Regional Health Authorities includes ten hospitals serving approximately 1.1 million residents. Hospital readmission was defined as a new, unplanned admission to any hospital department lasting > 6 h. The main reason for readmission

was categorized as recurrent stroke, stroke-related event (neurological deterioration, hemorrhagic transformation of cerebral infarction, neurological complications after carotid endarterectomy, suspected stroke or TIA with no specific final diagnosis), seizure, cardiac disease, infection, fracture, gastrointestinal hemorrhage, venous thromboembolism, and other cause. Only the first readmission within each category was counted for each patient.

Written informed consent to participate in the registry was obtained from all patients. In cases where patients suffered severe strokes and were not able to give informed consent, this was obtained from their legally authorized representatives as required by the Regional Committee for Medical and Health Research Ethics in Western Norway. Research related to the NORSTROKE registry including extraction of information after discharge was approved by the Regional Committee for Medical and Health Research Ethics in Western Norway.

2.2. Statistics

Baseline characteristics were assessed by chi-squared test for categorical variables and *t*-test, rank-sum test, ANOVA or Kruskal-Wallis test for the continuous variables. The Bonferroni correction was applied for comparison within groups. Kaplan-Meier estimates and log-rank test were used to determine and compare the incidence of all-cause readmission, cause-specific readmission, and mortality for the stroke subtypes. Kaplan Meier failure curves were made to demonstrate readmission over time by stroke subtype (SOE excluded due to low number of subjects). Patients that died during follow-up or moved outside the region of the Western Norway Regional Health Authorities before each measured outcome event occurred were censored at the time of death or change of address in the respective analyses. To evaluate for possible bias, we compared the Kaplan-Meier incidence estimates of all-cause and cause-specific readmissions to age-adjusted cumulative incidence estimates from survival models that accounted death as a competing risk (Fine-Gray model) [18]. Cox regression was used to investigate the five-year risk of all-cause and cause-specific readmission for each stroke subtype, with SOE excluded from the analyses due to low number of subjects. Each stroke subtype was tested against any other stroke subtype. Covariates included in the regression models were age, sex, mRS score and risk factor burden, which are known risk factors for readmission after stroke that differ between the stroke subtypes [11,19,20]. Since the mRS score was measured on day 7, we also included pre-morbid care-status. Visual inspection of the proportional hazards-assumption showed no violation of proportionality in the models. Statistical analyses were performed using Stata 15.0 (Stata Corporation, College Station, TX, USA).

3. Results

Of the 1453 patients (89.7% IS and 10.3% TIA patients), 1007 patients (69.3%) were readmitted within five years. There was a total of 3021 readmissions, and the median time from discharge to the first readmission was 284 days (IQR 74, 736). Baseline characteristics of the study population stratified by readmission status after five years are shown in Table 1. Readmitted patients were older, had a poorer short-term functional (higher mRS score), more cardiovascular comorbidity, and had a higher risk factor burden.

Table 2 demonstrates the baseline characteristics of the study population stratified by stroke subtype. Stroke patients with CE had the highest admission NIHSS score, whereas patients with SVO had the highest NIHSS score at discharge. The median mRS score was 2 for patients with LAA, CE, SVO and ME, but CE subtype had a significantly poorer short-term outcome than other subtypes when applying Bonferroni correction. Stroke patients with LAA had the highest risk factor burden, and the highest occurrence of peripheral artery disease, hypertension and smoking.

Kaplan-Meier incidence estimates of all-cause readmission, cause-

Table 1
Baseline characteristics of the study cohort.

Characteristics	Readmitted	Not readmitted	p
	N = 1007	N = 446	
Age (years), mean (SD)	74.9 (12.8)	69.2 (14.8)	< 0.001
Male sex, N (%)	540 (53.6)	242 (54.3)	0.823
Admission NIHSS score, median (IQR)	3 (1, 6)	2 (1, 5)	0.039
Discharge NIHSS score, median (IQR)	1 (0, 4)	1 (0, 3)	0.085
Discharge mRS score, median (IQR)	2 (1, 3)	1 (0, 3)	0.021
Stroke type, N (%)			0.714
Ischemic stroke	905 (89.9)	398 (89.2)	
TIA	102 (10.1)	48 (10.8)	
Stroke subtype, N (%)			0.002
Large artery atherosclerosis	138 (13.7)	55 (12.3)	
Cardioembolism	358 (35.6)	115 (25.8)	
Small vessel occlusion	99 (9.8)	60 (13.5)	
Other determined etiology	11 (2.0)	9 (1.1)	
Multiple etiologies	166 (16.5)	77 (17.3)	
Cryptogenic stroke	235 (23.3)	130 (29.2)	
Comorbidity, N (%)			
Prior stroke or TIA	233 (23.1)	66 (14.8)	< 0.001
Prior coronary artery disease	265 (26.3)	60 (13.5)	< 0.001
Prior peripheral artery disease	83 (8.2)	9 (4.3)	0.006
Atrial fibrillation	332 (33.0)	96 (21.5)	< 0.001
Hypertension	614 (61.0)	199 (44.6)	< 0.001
Diabetes mellitus	161 (16.0)	50 (11.2)	0.017
Prior/current smoking	583 (57.9)	249 (55.8)	0.463
Risk factor burden, N (%)			< 0.001
0	231 (22.9)	162 (36.3)	
1	381 (37.8)	177 (39.7)	
2	253 (25.1)	76 (17.0)	
≥ 3	142 (14.1)	31 (7.0)	
Prestroke care, N (%)			0.026
None	384 (38.5)	830 (83.7)	
Home nursing	44 (9.9)	141 (14.2)	
Permanently institutionalized	16 (3.6)	21 (2.1)	
Discharge destination, N (%)			< 0.001
Home	512 (51.0)	280 (62.8)	
Home nursing	141 (14.0)	23 (5.2)	
Rehabilitation department	72 (7.2)	40 (9.0)	
Nursing home	245 (24.4)	92 (20.6)	
Other department	35 (3.5)	11 (2.5)	
Employed before stroke, N (%)	162 (16.4)	151 (34.3)	< 0.001
Higher education level, N (%) ^a	99 (31.6)	64 (41.6)	0.034

SD indicates standard deviation; mRS, modified Rankin Scale; IQR, interquartile range; NIHSS, National Institutes of Health Stroke Scale; TIA, transient ischemic attack.

^a Missing data in 986 patients.

specific readmissions and mortality for the stroke subtypes are shown in Table 3. The cumulative incidence of all-cause hospital readmission was 9.9% at one month (95% CI 8.4–11.5), 39.9% at one year (95% CI 37.4–42.5) and 72.6% at five years (95% CI 70.2–74.9). The five-year incidence of all-cause readmission varied significantly among the stroke subtypes from 55% for SOE and 81% for CE subtype (Fig. 1). After adjusting for age, sex, mRS score, premorbid care-status, and risk factor burden, the risk of all-cause readmission was 25% higher for CE (HR = 1.25, 95% CI 1.09–1.43, $p = .001$) and 21% lower for SVO (HR = 0.79, 95% CI 0.64–0.98, $p = .033$) compared to other subtypes.

The most common cause of readmission was infection (30%), followed by cardiac disease (20%), stroke-related event (15%), recurrent stroke (14%), and fracture (12%). The incidence of readmission due to infection, cardiac disease, and fractures varied significantly among the stroke subtypes (Fig. 2A–C). After adjusting for age, sex, mRS score, premorbid care-status, and risk factor burden, CE subtype had a 75% higher risk of readmission due to cardiac disease (HR = 1.75, 95% CI 1.35–2.25, $p < .001$), whereas the risk was 44% lower in patients with CS (HR = 0.66, 95% CI 0.47–0.91, $p = .011$). No stroke subtype was significantly associated with infection or fractures in the multivariate analyses (Supplementary Table 1).

There were no significant differences between the stroke subtypes in

readmission due to recurrent stroke (Fig. 3A), stroke-related events (Fig. 3B), seizures, venous thromboembolism or gastrointestinal hemorrhage between the stroke subtypes (Supplementary Table 1). Readmission due to ICH varied significantly among stroke subtypes, with the highest incidence in patients with SVO (4.0%).

After five years, 404 (40.1%) of the readmitted patients were dead compared to 88 (19.7%) of patients that had not been readmitted ($p < .001$). The five-year mortality varied significantly between the stroke subtypes, with the highest mortality observed in patients with CE (Fig. 2D). After adjusting for age, sex, mRS score, premorbid care-status, and risk factor burden, CE subtype had a 34% higher risk of death within 5 years (HR = 1.34, 95% CI 1.12–1.61, $p = .002$), and SVO had a 48% lower risk of death (HR = 0.52, 95% CI 0.36–0.74, $p < .001$).

The Kaplan-Meier incidence estimates of all-cause and cause-specific readmission were almost identical although marginally over-estimated for both the cohort as a whole and for each stroke subtype compared to estimates obtained from the survival model that accounted for the competing risk of death (Supplementary Table 2). Exclusion of SOE in all analyses did not alter the demonstrated differences in incidences of all-cause and cause-specific readmissions among the other stroke subtypes.

4. Discussion

Our study demonstrates that five-year readmission after ischemic stroke or TIA varies depending on the stroke subtype, with incidences ranging from 55% for patients with SOE to 81% for patients with CE. Similar to another Norwegian study, 69% of all patients were readmitted within five years [8]. This is lower than the 83% found in a study from the US [2], but the distribution of readmission causes were similar to other studies, with infections, cardiac disease, recurrent stroke, and stroke-related events as leading events [2,3,6,8].

Patients with CE subtype had a significantly increased risk of all-cause readmission compared to other subtypes, which previously has been demonstrated on stroke patients aged 45 to 64 [21]. We also found that SVO subtype had a decreased risk of readmission. The five-year risk of mortality was significantly higher in patients with CE and lower in patients with SVO, and the incidences of five-year readmission for the stroke subtypes followed the five-year mortality, as both were highest for CE, followed by LAA, ME, CS, SVO and SOE in descending order. Common risk factor between post-stroke readmission and death could be the cause of this pattern, but readmission may mediate the risk of death after stroke [22]. This implies that careful follow-up and adequate secondary prevention may be important to reduce both post-stroke readmissions and mortality.

CE subtype had the highest occurrence of readmissions due to cardiac disease, which likely relates to underlying cardiac pathology such as arrhythmias and heart failure. Interestingly, patients with CS had a significantly lower risk of readmission due to cardiac disease. Most CS are embolic, and could result from undetected cardiac conditions such as atrial fibrillation [23,24]. This finding could thus indicate that undetected cardiac disease was not a frequent cause of CS stroke in our study. The prevalence of conventional vascular risk factors was also relatively lower in CS patients compared to subtypes with higher incidence of readmission due to cardiac disease. However, CS patients may benefit from prolonged monitoring for atrial fibrillation and personalized secondary prevention to reduce the risk of recurrent stroke and other vascular disease [23].

The five-year incidence of recurrent stroke or TIA was 14%. A recent study found that 16.5% suffered a recurrent stroke or TIA within five years after minor stroke or TIA, whereas a meta-analysis found a pooled 5-year recurrence-risk of 26% [25,26]. Different five-year recurrence rates might be caused by a decreasing incidence of recurrent stroke [25], but also study design, study population, and use of secondary preventive treatment. We found no differences in the incidence or risk

Table 2
Baseline characteristics by stroke subtype.

Characteristics	LAA	CE	SVO	SOE	ME	CS	P
	N = 193	N = 473	N = 159	N = 20	N = 243	N = 365	
Age (years), mean (SD)	74.3 (9.9)	75.5 (14.3)	69.2 (13.4)	45.2 (15.0)	73.9 (12.7)	72.3 (13.3)	< 0.001
Male sex, N (%)	123 (63.7)	236 (49.9)	95 (59.8)	13 (65.0)	129 (53.1)	186 (51.0)	0.010
Diagnose							
Ischemic stroke	159 (82.4)	447 (94.5)	159 (100.0)	20 (100.0)	217 (89.3)	301 (82.5)	< 0.001
TIA	34 (17.6)	26 (5.5)	0 (0.0)	0 (0.0)	26 (10.7)	64 (17.5)	
Acute treatment							
Intravenous thrombolysis	39 (20.2)	74 (15.6)	8 (5.0)	3 (15.0)	39 (16.1)	50 (13.7)	0.004
Mechanical thrombectomy	2 (1.0)	11 (2.33)	0 (0.0)	0 (0.0)	2 (0.8)	2 (0.6)	0.106
Admission NIHSS score, median (IQR)	2 (0, 6)	3 (1, 8)	2 (1, 4)	1 (0, 3)	2 (1, 5)	2 (1, 5)	< 0.001
Discharge NIHSS score, median (IQR)	1 (0, 4)	1 (0, 5)	2 (1, 3)	0 (0, 3)	1 (0, 3)	1 (0, 3)	0.026
Discharge mRS score median (IQR)	2 (0, 3)	2 (1, 4)	2 (1, 3)	1 (0, 2)	2 (1, 3)	1 (0, 3)	< 0.001
Comorbidity, N (%)							
Prior stroke or TIA	47 (24.4)	86 (18.2)	25 (15.7)	2 (10.0)	48 (19.8)	91 (24.9)	0.045
Coronary artery disease	55 (28.5)	120 (25.4)	22 (13.9)	1 (5.0)	61 (25.1)	66 (18.1)	0.001
Peripheral artery disease	38 (19.7)	25 (5.3)	6 (3.8)	0 (0.0)	24 (9.9)	9 (2.5)	< 0.001
Atrial fibrillation	9 (4.7)	343 (72.5)	1 (0.6)	0 (0.0)	75 (30.9)	0 (0.0)	< 0.001
Hypertension	124 (64.3)	288 (60.9)	81 (50.9)	3 (15.0)	137 (56.4)	180 (49.3)	< 0.001
Diabetes mellitus	30 (15.5)	63 (13.3)	25 (15.7)	2 (10.0)	41 (16.9)	50 (13.7)	0.775
Prior/current smoking	138 (71.5)	229 (48.4)	96 (60.4)	11 (55.0)	147 (60.5)	211 (57.8)	< 0.001
Risk factor burden, N (%)							< 0.001
0	27 (14.0)	129 (27.3)	41 (25.8)	10 (50.0)	60 (24.7)	126 (34.5)	
1	70 (36.3)	183 (38.7)	72 (45.3)	10 (50.0)	94 (38.7)	129 (35.3)	
2	51 (26.4)	113 (23.9)	32 (20.1)	0 (0.0)	55 (22.6)	78 (21.4)	
≥ 3	45 (23.3)	48 (10.2)	14 (8.8)	0 (0.0)	34 (14.0)	32 (8.8)	
Prestroke care							0.443
None	165 (87.3)	382 (81.6)	135 (85.4)	19 (95.0)	204 (84.7)	309 (85.8)	
Home nursing	21 (11.1)	74 (15.8)	18 (11.4)	1 (5.0)	32 (13.3)	39 (10.8)	
Permanently institutionalized	3 (1.6)	12 (2.6)	5 (3.2)	0 (0.0)	5 (2.1)	12 (3.3)	

LAA, large-artery atherosclerosis; CE, cardioembolism; SVO, small vessel occlusion; ME, multiple etiologies; CS, cryptogenic stroke; SD, standard deviation; TIA, transient ischemic attack; mRS, modified Rankin Scale; IQR, interquartile range; NIHSS, National Institutes of Health Stroke Scale.

Table 3
Incidence estimates of death, all-cause and cause-specific readmission within 5 years after IS or TIA.

	Incidence rates (%)							P
	Total	LAA	CE	SVO	SOE	ME	CS	
	N = 1453	N = 193	N = 473	N = 159	N = 20	N = 243	N = 365	
Death	34.5	36.3	42.8	20.1	10.0	35.8	26.9	< 0.001*
All-cause readmission	72.6	73.7	81.3	65.0	55.0	70.8	66.8	< 0.001*
Recurrent stroke	13.8	13.9	13.9	12.8	20.3	17.0	11.9	0.755
IS	11.3	11.0	12.0	9.4	20.3	14.4	9.3	0.452
ICH	1.3	0.5	1.6	4.0	0.0	0.6	0.6	0.033*
TIA	2.0	3.1	1.1	0.0	0.0	3.2	2.7	0.145
Stroke-related event	14.9	16.4	16.0	12.9	15.0	15.4	13.6	0.846
Seizure	4.3	4.1	6.1	1.4	5.0	3.5	3.9	0.184
Cardiac disease	20.8	19.4	29.1	15.9	10.0	21.3	14.5	< 0.001*
MI	6.9	8.6	6.8	5.5	5.3	8.6	6.0	0.657
Arrhythmia	7.0	6.1	11.9	6.3	0.0	6.1	3.2	< 0.001*
Heart failure	5.2	1.9	9.6	1.5	5.0	7.0	2.2	< 0.001*
Other	5.9	6.5	8.4	3.5	0.0	4.7	5.1	0.147
Infection	29.7	35.4	33.6	23.4	10.3	32.6	24.4	0.002*
Pneumonia	15.0	17.7	19.7	9.6	5.0	16.9	10.2	0.003*
UTI	9.1	10.8	8.2	8.7	0.0	12.8	7.5	0.186
Sepsis	4.4	8.5	4.2	2.9	0.0	4.8	3.3	0.060*
Other	8.8	8.0	11.3	7.1	5.6	8.9	7.3	0.486
Fracture	12.3	6.5	16.6	8.8	0.0	13.8	11.6	0.007*
Hip fracture	6.6	2.1	8.9	5.5	0.0	6.8	7.0	0.061
Other	6.6	4.5	9.4	4.7	0.0	8.1	5.1	0.115
VTE	1.6	1.9	1.3	1.4	5.3	1.4	1.6	0.852
GI hemorrhage	4.4	5.0	4.3	4.9	0.0	3.2	4.9	0.829
Other diagnosis	46.5	51.3	52.7	39.8	25.6	45.2	41.6	0.003*

IS, ischemic stroke; TIA, transient ischemic attack; LAA, large artery atherosclerosis; CE, cardioembolism; SVO, small vessel occlusion; SOE, stroke of other determined etiology; ME, multiple etiologies; CS, cryptogenic stroke; ICH, intracerebral hemorrhage; UTI, urinary tract infection; MI, myocardial infarction; VTE, venous thromboembolism; GI, gastrointestinal.

* $P < .05$ after exclusion of SOE

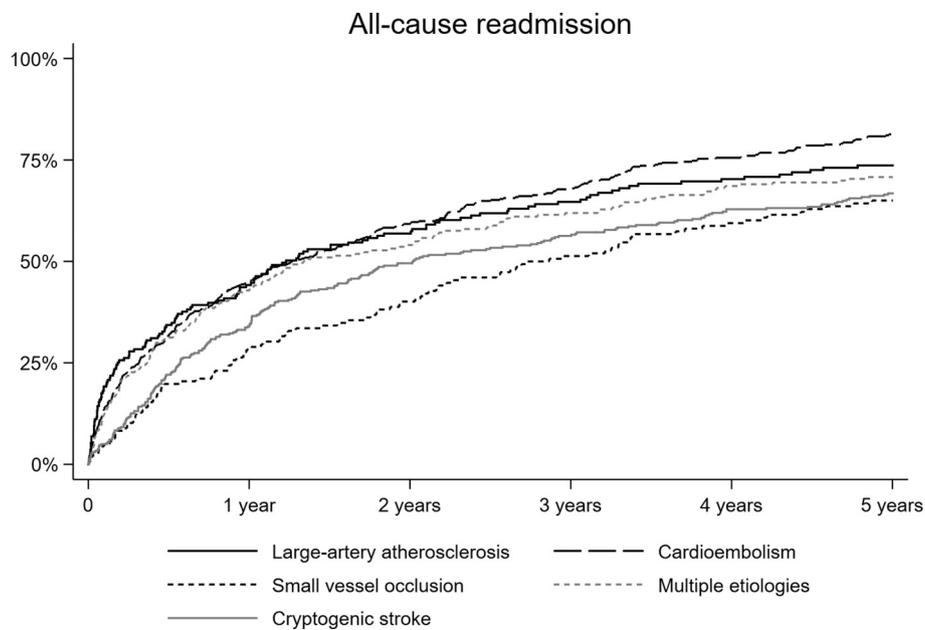


Fig. 1. Kaplan Meier failure curves showing incidence estimates of all-cause readmission within 5 years after ischemic stroke or TIA distributed by stroke subtype.

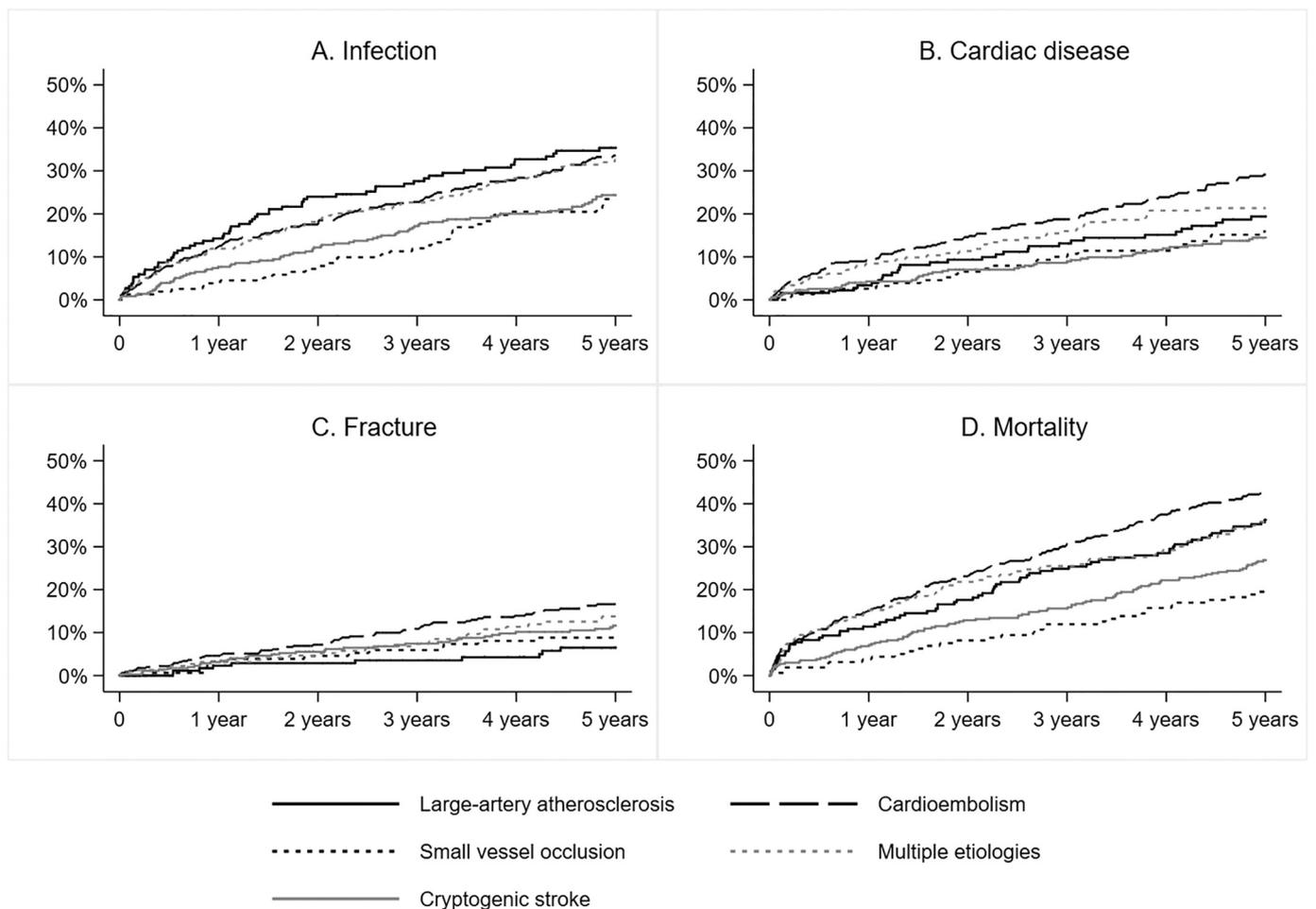


Fig. 2. Kaplan Meier failure curves showing incidence estimates of outcome events within five years after ischemic stroke or TIA distributed by stroke subtype for readmission due to infection (A), readmission due to cardiac disease (B), readmission due to fractures (C), and mortality (D).

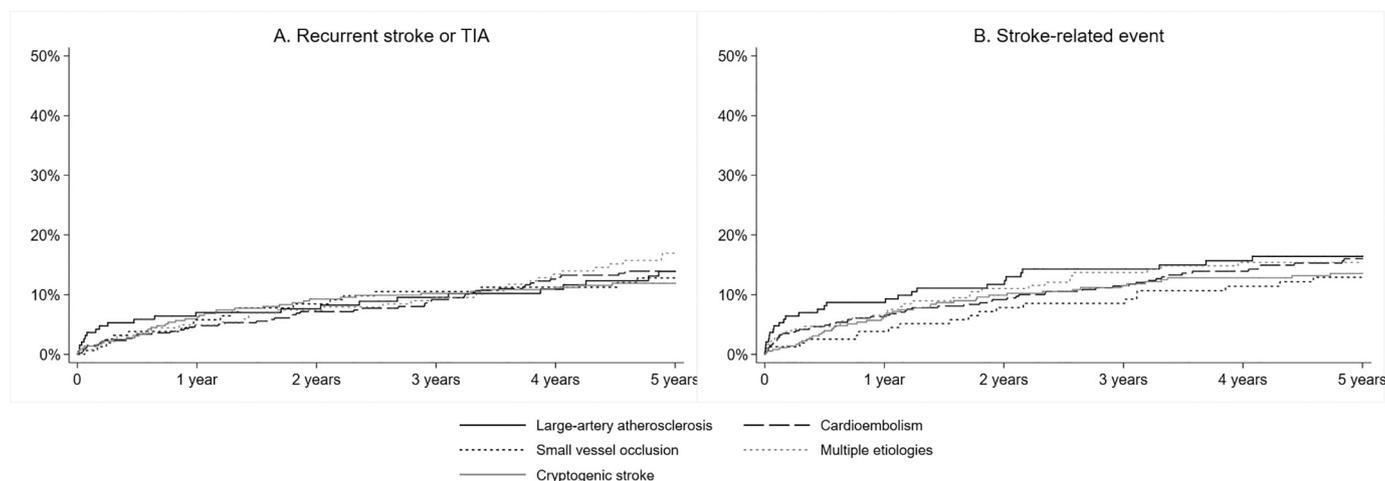


Fig. 3. Kaplan Meier failure curves showing incidence estimates by stroke subtype of readmission due to recurrent stroke or TIA (A) and stroke-related event (B) within five years after ischemic or TIA.

of recurrent stroke between the stroke subtypes. LAA subtype have an increased risk of early stroke recurrence, but the long-term risk seems to be equal for all stroke subtypes [12,27]. SVO subtype had a four-fold higher incidence of intracerebral hemorrhage. This might be due to the high occurrence of hypertension and the underlying pathology in small brain vessels that also can lead to hemorrhagic strokes [11,28].

Infection was the most common cause of readmission in our study. Severe strokes and increased disability are associated with infections [29]. The median NIHSS score and mRS score was unusually low in our study, a trend which resonates in the Norwegian stroke registry covering 86% of all Norwegian stroke patients [30]. This could be due to a high awareness of stroke symptoms as a result of population-based campaigns and a low threshold for hospital readmission. Readmission with infection varied significantly between the subtypes, with higher incidences for LAA and CE. Functional disability, cardiovascular risk factors, age and sex are known predictors of post-stroke infection [29,31], but we found no differences between the stroke subtypes in the risk of readmission with infection after controlling for these factors. We therefore believe that the demonstrated differences in the incidence of post-stroke infection in our study is likely caused by other factors than the subtype itself.

There were significant variations in the incidence of fractures among the stroke subtypes in our study, with the highest incidence observed in patients with CE subtype, and the lowest in LAA subtype. However, no subtype was associated with fractures in the multivariate models. The varying incidence of fractures among the stroke subtypes might be influenced by differences in factors associated with post-stroke falls and fractures, such as age, sex, stroke severity, functional outcome, medications and underlying diseases like atrial fibrillation and osteoporosis [32,33]. Identification of patients at high risk of falls and fractures is important, as both events could be prevented. Prevention of falls and fractures require multifactorial risk assessment and simultaneous management with exercise to improve mobility and prevent increased bone resorption.

Stroke patients are more often readmitted than matched cohorts without stroke [2], and prevention of new diseases and readmissions is important for reducing the burden of stroke. Secondary prevention in stroke patients mainly aims at reducing recurrent strokes and cardiovascular disease, but our study demonstrates that non-vascular diseases are prevalent in stroke patients. Our study also contributes with information which may be helpful for health care providers in determining the risk of new diseases after stroke with information that is easy accessible in a clinical setting.

A limitation to our study is the lack of information on medications and follow-up received after discharge. Some readmissions may not

have been accounted for if patients were readmitted to hospitals outside the area of the Western Norwegian Regional Health authorities. Also, we did not have enough information to generate a general comorbidity index, which might have influenced our results. Stroke of undetermined etiology represented a high proportion of our cohort, despite extensive evaluations, and the study was observational, thus, we cannot conclude that there is a direct causative relationship between stroke subtype and readmissions. The single-hospital design limits the generalizability of our study. The median NIHSS score both in our study and in Norwegian stroke patients is low, and all our stroke patients were treated in a stroke unit, which further limits the generalizability of our study to countries with lower percentages of patients cared in stroke units [30]. The strength of our study is the relatively large study population investigated according to a predefined protocol, and the review of their medical charts for identification of readmissions.

5. Conclusions

Within five years, a majority of our patients who survived stroke hospitalization were readmitted, with infections, stroke-related events, recurrent strokes, cardiac diseases, and fractures as the most frequent causes. Both the incidences of all-cause readmission, cause-specific readmission and mortality depended on stroke subtype. Although our findings need confirmation by other studies, they emphasize the need for tailored treatment and handling of stroke patients according to their underlying diseases to prevent new vascular events as well as the development of nonvascular diseases.

Declarations of interest

The authors declare that there is no conflict of interest.

Informed consent

Written informed consent was obtained from all patients or their legal guardian.

Sources of funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Ethical approval

Ethics approval was obtained from the Western Regional Ethics

Committee.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jns.2019.06.007>.

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