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ORIGINAL ARTICLE

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Transient ischemic attack and ischemic stroke patients with or without prior stroke

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Objectives: A history of stroke is common in patients with transient ischemic attack (TIA) and ischemic stroke (IS), but there are few reports characterizing this group of patients. We aimed to compare characteristics, risk factors, and secondary preventive treatment in patients with TIA or IS with vs without a history of stroke.

Methods: Hospital-based data on TIA and IS events, registered from July 2011 to June 2013, were obtained from the Swedish Stroke Register (Riksstroke). Previous stroke was not specified as hemorrhagic or ischemic.

Results: A history of stroke was present in 19.3% (2892/15012) of TIA and 24.6% (10853/44169) of IS patients. Patients with prior stroke were older, more often male, and more likely to have atrial fibrillation (AF) (TIA: 27.4% vs 16.4%; IS: 36.1% vs 28.0%), hypertension (TIA: 77.5% vs 56.4%; IS: 74.2% vs 59.0%), and diabetes mellitus (TIA: 22.2% vs 14.2%; IS: 26.3% vs 19.5%) compared with those without (all differences $P<.0001$).

At discharge, patients with prior stroke were more often treated with antihypertensive drugs than those without, whereas proportions treated with statins were similar in both groups. Patients with AF and prior stroke were less often treated with oral anticoagulant (OAC) medication than those without prior stroke.

Conclusions: Both in TIA and IS, vascular risk factors were more common in patients with a history of stroke compared with those without. In contrast to other secondary preventive medications, OAC treatment in the presence of AF was underutilized in patients with a history of stroke.

KEYWORDS
atrial fibrillation, cerebrovascular diseases, history of stroke, ischemic stroke, secondary prevention, transient ischemic attack

1 | INTRODUCTION

A history of stroke is not uncommon in patients with transient ischemic attack (TIA) and ischemic stroke (IS). In recent TIA cohorts, 12%-23% of patients had had a previous stroke,[1-7] whereas in patients with ischemic stroke (IS) this proportion ranged from 18 to 23%.[1,5,8,9]

Comparative data on patients with first-time or recurrent cerebrovascular events are scant. In a Danish community-based study on patients with both ischemic and hemorrhagic stroke, recurrent stroke was associated with male sex, a history of TIA, atrial fibrillation (AF),

and hypertension compared to first-time events.[9] In a Norwegian hospital-based study on patients with ischemic stroke only, an association of recurrent events to male sex, age, hypertension, AF, large-vessel disease, and leukoaraiosis on computed tomography was demonstrated.[10] We did not find any comparative report on patients with TIA with or without a history of stroke.

Based on data from a large national TIA and stroke register, we aimed to compare TIA and IS patients with versus without a prior stroke regarding patient characteristics, risk factors, and secondary preventive medical treatment at discharge.

2 | METHODS

2.1 | Study population

Data on TIA events, registered from July 1, 2011 to June 30, 2013, were obtained from the Swedish Stroke Register TIA module (Riksstroke-TIA, RS-TIA); 59 of 72 Swedish hospitals contributed with data to this register. TIA diagnosis was based on a time-based definition, that is an acute focal neurological deficit of presumed vascular origin with complete remission of symptoms <24 hours irrespective of neuroimaging findings. Magnetic resonance imaging was performed in less than 10% of all patients. A validation of the register was performed as reported previously.[11] Data on IS events, registered during the same period of time, were obtained from the Swedish Stroke Register (Riksstroke, RS) [12] to which all Swedish hospitals involved in acute stroke care contributed with data.

Patients 18 years or older with ICD-10 diagnoses of TIA (G45, excluding G45.4) and IS (I63) were included. For patients with more than one stroke during the course of 28 days, only the first event was included. All patients included in this study were treated as inpatients.

2.2 | Registered items

Both in RS-TIA and RS, data on demography, history, risk factors, and medical treatment at admission and discharge were registered.

2.3 | Definition of items

History of prior stroke is a register item, but not specified as hemorrhagic or ischemic. AF was registered as present or absent without specification whether it was diagnosed during the current hospital admission or previously known. AF was not further specified as permanent, persistent, or paroxysmal. For the presence of hypertension we used the recorded item of blood pressure lowering medication at arrival, which according to the Riksstroke secretariat was found to be the best proxy indicator for hypertension. This item has been used in several studies based on data from Riksstroke. Vitamin K antagonist and non-Vitamin K antagonist oral anticoagulants are referred to as oral anticoagulants (OAC).

2.4 | Descriptive and statistical analysis

SPSS 22.0 was used for all statistical analyzes. Categorical variables are summarized as proportions and quantitative variables as means. Age groups were reported in the intervals <45, 45-54, 55-64, 65-74, 75-84, and ≥85 years. Proportions were derived from the total of patients in whom the respective item was registered. Baseline data were tested by chi-square testing and Student's t test as appropriate.

2.5 | Ethics

The study was approved by the local ethics committee (Dnr 2013/719).

3 | RESULTS

During the 2-year study period, 15064 TIA patients were registered in RS-TIA and 44416 patients with IS in RS. A history of stroke was present in 19.3% (2892/15012) of patients with TIA and in 24.6% (10853/44169) of patients with IS. Missing data were <1% for the register item of a prior stroke. The proportion of patients with a previous stroke increased with age both in patients with TIA and IS; in patients with TIA, it ranged from 5.9% in those <45 years to 26.4% in patients ≥85 years, and in patients with IS from 9.7 to 28.2% for these age groups (Figure 1).

3.1 | Patient characteristics and risk factors

As shown in the Table 1, patients with a previous stroke, both in the TIA and IS group, were of older age and more likely to be male; they had higher proportions of AF, hypertension, and diabetes mellitus, and were less often smokers compared to patients with first-time events.

3.2 | Atrial fibrillation

In patients with TIA and a history of stroke, AF was present in 27.4% (785/2868), whereas this proportion was 16.4% (1983/12077) in TIA patients without prior stroke (P<.0001). The proportion of AF increased with age, and reached 41.4% (300/724) in TIA patients aged ≥85 years who had a history of stroke compared to 29.8% (604/2028, P<.0001) in those without prior stroke (Figure 2A).

Patients with IS and a prior history of stroke had AF in 36.1% (3896/10806) compared with 28.0% (9311/33225, P<.0001) in IS patients without a history of stroke. As in TIA, the proportion of AF increased with increasing age; in patients with IS aged ≥85 years, those with a history of stroke had AF in 51.2% (1698/3319), whereas this proportion was 44.8% (4676/8466) in those without a prior stroke (P<.0001) (Figure 2B).

3.3 | Antithrombotic medication at discharge

At discharge, the proportion of patients with TIA and AF that were treated with OAC was 64.1% (1769/2758); antiplatelet treatment as
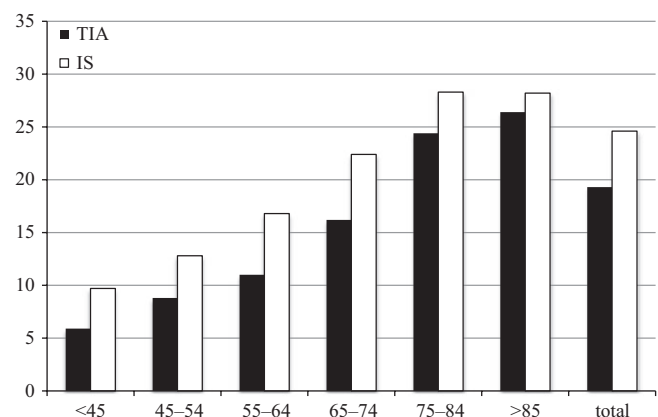

FIGURE 1 Proportion of a prior stroke (%) in patients admitted for transient ischemic attack (TIA) and ischemic stroke (IS)

TABLE 1 Characteristics and risk factors of patients admitted for TIA or IS with or without a previous stroke

	Transient ischemic attack			Ischemic stroke		
	Prior stroke n=2892	No prior stroke n=12120	P	Prior stroke n=10853	No prior stroke n=33316	P
Female n (%)	1301/2892 (45.0)	5946/12120 (49.1)	<.0001	5013/10853 (46.2)	16279/33316 (48.9)	<.0001
Age mean (SD)	77.0 (10.4)	72.2 (12.5)	<.0001	78.1 (10.5)	74.9 (12.8)	<.0001
AF n (%)	785/2868 (27.4)	1983/12077 (16.4)	<.0001	3896/10806 (36.1)	9311/33225 (28.0)	<.0001
Hypertension[a] n (%)	2236/2884 (77.5)	6809/12073 (56.4)	<.0001	8023/10806 (74.2)	19590/33197 (59.0)	<.0001
Diabetes mellitus n (%)	639/2878 (22.2)	1717/12057 (14.2)	<.0001	2845/10835 (26.3)	6498/33283 (19.5)	<.0001
Smoking n (%)	274/2630 (10.4)	1382/11296 (12.2)	.010	1173/10074 (11.6)	4681/31036 (15.1)	<.0001

[a]in TIA patients defined by item blood pressure lowering medication at admission.
SD indicates standard deviation; AF, atrial fibrillation.

(A) Transient ischemic attack
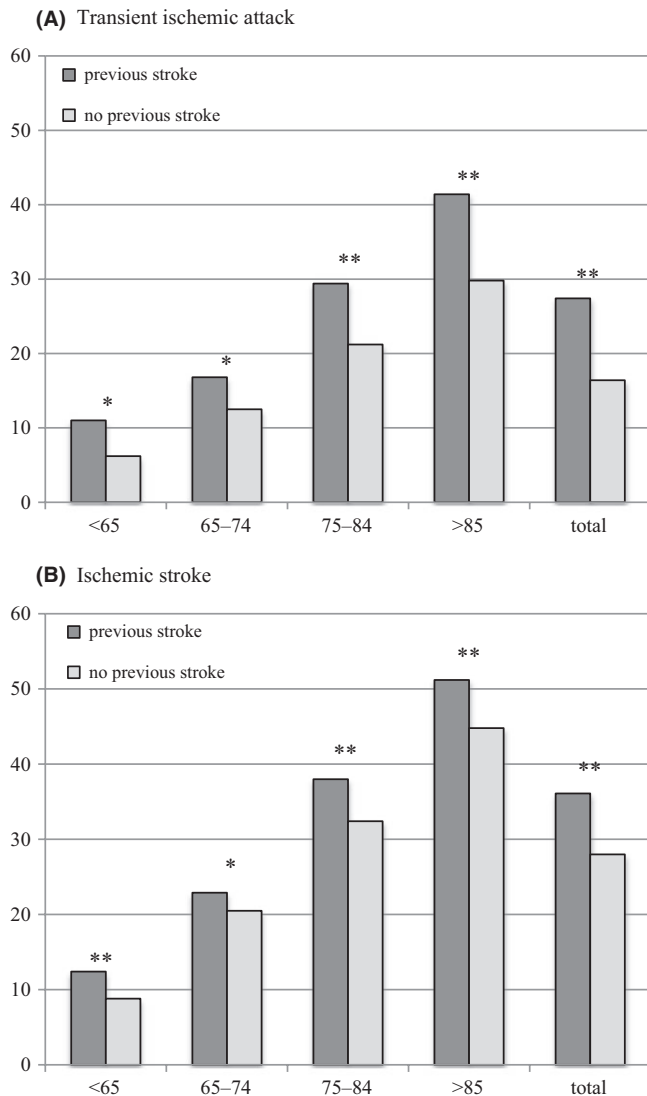

(B) Ischemic stroke

FIGURE 2 Proportion of atrial fibrillation (%) in patients with (A) transient ischemic attack and (B) ischemic stroke in relation to a history of stroke. **P<.0001; *P<.05

sole antithrombotic medication was prescribed in 31.3% (864/2758), and 4.5% (125/2758) were discharged on no antithrombotic medication. TIA patients with AF and a history of stroke were less often

treated with OAC than those without prior stroke (58.0%, 453/781 vs 66.5%, 1317/1979; P<.0001). Among patients with TIA and AF aged ≥85 years, OAC treatment at discharge was installed in 45.4% (409/900). In this age group, there was no significant difference of OAC treatment between patients with and without a history of stroke (43.6%, 130/298 vs 46.3%, 279/602; P=.440) (Figure 3A).

Patients with TIA but without AF were discharged with antithrombotic medication in 96.6% of cases (11740/12150) with a minor difference between those with and without a history of stroke (95.9%, 1992/2077 vs 96.8%, 9748/10073; P=.05). The proportion of antithrombotic treatment in patients with TIA and no AF aged ≥85 years was 94.7% (1740/1842); in this age group, there was no significant difference between those with and without prior stroke.

In IS patients with AF, 50.5% (5478/10845) were discharged with OAC medication, 40.2% (4359/10845) with antiplatelet agents only, and 9.3% (1008/10845) without antithrombotic medication. As in TIA, IS patients with AF and a previous stroke were less often treated with OAC than those without previous stroke (45.2%, 1424/3149 vs 52.7%, 4067/7714; P<.0001). Patients with IS and AF aged ≥ 85 years were discharged with OAC treatment in 33.1% (1389/4197); there was no significant difference in patients with a history of stroke compared with those without (31.6%, 404/1277 vs 33.7%, 985/2920; P=.184) (Figure 3A).

Patients with IS and no AF were discharged with an antithrombotic drug in 94.3% of cases (26785/28393) with a subtle difference between patients with prior stroke and those without (93.6%, 5723/6114 vs 94.5%, 21062/22279; P=.005). Among patients with IS and no AF aged ≥85 years 91.9% (4957/5392) were treated with an antithrombotic drug; in this age group, there was no difference when comparing those with a history of stroke to those without.

3.4 | Blood pressure lowering and statin medication at discharge

As seen in Figure 3B, proportions of treatment with blood pressure lowering drugs at discharge increased by age and were higher in patients with a history of stroke compared to those without. This applied both to patients with TIA and IS. In patients with TIA and a history of stroke, 81.2% (2339/2882) were treated with blood pressure lowering medications compared to 66.4% (8034/12096; P<.0001)

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(A) Oral anticoagulants in AF

■ previous stroke
□ no previous stroke

(B) Blood pressure lowering medication

■ previous stroke
□ no previous stroke

(C) Statin treatment

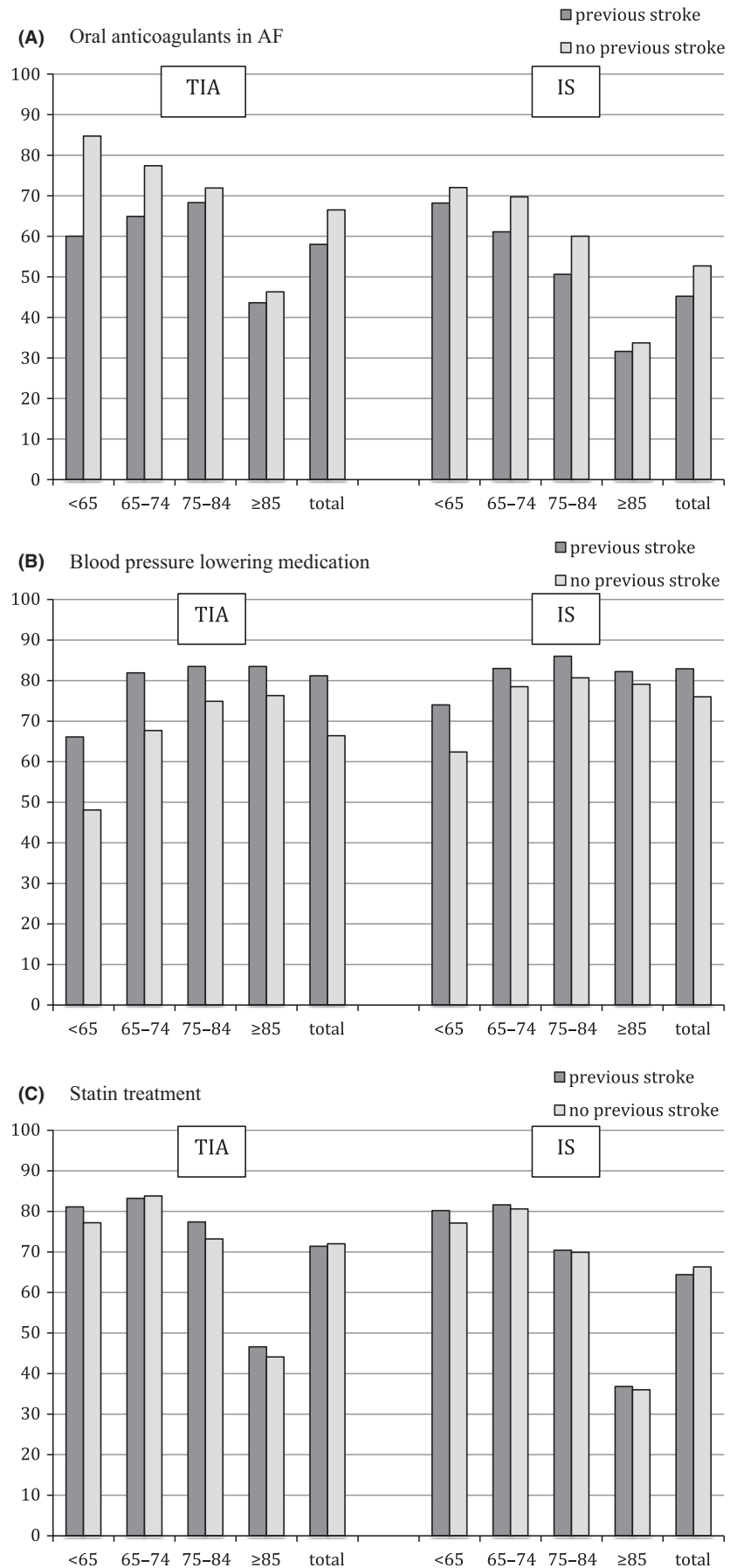■ previous stroke
□ no previous stroke

FIGURE 3 Proportions of treatment (%) at discharge: (A) oral anticoagulants in patients with AF, (B) blood pressure lowering medication, and (C) statin treatment in relation to a history of stroke, separately for patients with transient ischemic attack (TIA) and ischemic stroke (IS)

in patients without a prior stroke. In patients with IS, corresponding proportions were 82.9% (7928/9569) vs 76.0% (23018/30306; $P<.0001$).

Proportions of statin treatment at discharge were 71.4% (2060/2884) in patients with TIA and a history of stroke compared to 72.0% (8712/12 106) in patients with TIA and no prior stroke ($P=.586$). In patients with IS and a history of stroke, 64.4% (6182/9570) were treated with statins compared to 66.3% (20 100/30 304; $P=.008$) in those without a prior stroke.

Whereas statin treatment was found in roughly 80% of TIA and IS patients up to an age of 74 years, proportions of treatment decreased stepwise in older age groups. In those aged ≥85 years, 44.8% (1234/2756) of patients with TIA and 36.2% (3505/9686) of patients with IS were treated with statins with no significant difference between patients with and without a history of stroke (Figure 3C).

4 | DISCUSSION

Based on data from a large national TIA and ischemic stroke register, our study shows that as many as one in five patients with TIA and one in four patients with IS have a history of stroke. Vascular risk factors were more common in patients with a history of stroke, which applied not only to patients with IS but also to those with TIA. The proportion of AF increased steeply by age, and in patients aged ≥85 years with a history of stroke more than 40% of patients with TIA and more than half of patients with IS had AF.

However, patients discharged after a TIA or an IS who had AF and a history stroke, that is patients with at least two cerebrovascular events, were less likely to be treated with OAC than patients without a prior stroke. This treatment pattern was contrasted by proportions of antiplatelet (in patients without AF) and statin medication (irrespective of the presence of AF) being on similar levels in patients with and without a history of stroke. Blood pressure lowering treatment was more common in those with a history of stroke.

To the best of our knowledge, this is the first report comparing TIA patients with and without a history of stroke, and we were able to show that proportions of AF, hypertension, and diabetes are significantly higher in the presence of previous stroke. Our results regarding mean age and sex distribution in stroke patients with and without prior stroke are in line with previous reports.[9,10,13] Our data confirm that AF, hypertension, and diabetes mellitus are more common in patients with recurrent than in those with first-time stroke.[9,10]

The proportion of AF in patients with recurrent stroke was higher in this study with 36% compared to 24%-29% in previous reports.[9,10,13] In unselected IS patients, AF has been reported to be present in about 25% of cases, and reaching about 30% in patients aged 80-89 years and about 45% in those ≥90 years.[14] In comparison, our patients aged ≥85 years with a history of stroke had AF in more than 40% of cases when admitted due to a TIA, and in more than 50% when admitted with IS. As our data did not include results on monitoring for AF after discharge, the reported proportions of AF in patients with TIA and IS may be considered a conservative estimate. These results emphasize

the prominent role of AF not only in IS but also in TIA and even more so in patients with recurrent cerebrovascular events.

Levels of OAC treatment at discharge in patients with AF were overall moderate and lower in patients with a history of stroke compared to those without, both when discharged after a TIA or an IS. According to the CHA_2DS_2-VASc score,[15] a previous stroke indicates a substantially increased risk of a new stroke and should warrant treatment with OAC. A history of a hemorrhagic stroke might have prevented the prescription of OAC drugs in some patients with AF. According to guidelines, however, OAC might still be considered even in case of a prior hemorrhagic stroke, especially when indication is strong [16] which a new TIA or IS associated with AF should be considered to be. Moreover, about 85% of previous stroke can be expected to have been ischemic,[17,18] so treatment levels clearly appear insufficient.

In IS, lower treatment rates in patients with AF and a prior stroke compared to patients with first-time stroke have been reported[19]; overall, treatment rates in this Swedish study were low and further decreased with increasing stroke risk according to CHA_2DS_2-VASc score. We here report similar findings for patients with TIA and previous stroke. Immediate initiation of OAC treatment is recommended in patients with TIA.[20] There is no apparent reason why TIA patients with a prior stroke should be treated to a lesser extent. However, we did not have access to data on contraindications such as previous bleeding, renal or liver failure, cognitive impairment, dementia, or other reasons such as patients' own choice.

Antihypertensive treatment appears adequate in all age groups and is likely to reflect proportions of prevalent hypertension with regard to age.[13,18,21] Hypertension has been reported to be more common in patients with recurrent stroke than in those with first-time events,[9,10] and therefore, higher proportions of treatment in patients with a history of stroke can be expected.

Statin medication varied in relation to age but was similar in those with and without a prior stroke. Proportions of statin treatment decreased in patients older than 75 years and dropped substantially in those aged ≥85 years. Statin treatment is recommended in TIA and IS associated with large-vessel disease [22] and has been shown to be beneficial also in the elderly.[23] This age-related decrease appears to reflect an undertreatment of the elderly as the prevalence of large-vessel disease increases with age.[24] We did not assess causes for the recurrence of cerebrovascular events such as etiology, adherence to treatment recommendations, compliance, or levels of INR at admission.

The strength of this study is that data were obtained from the comprehensive Swedish Stroke Register (Riksstroke) with consistent data registration and high numbers of included patients. It is the first time that such a study is performed for both TIA and IS events in the same cohort and in a national perspective. There are limitations to our study. We were not able to distinguish if the registered prior stroke was ischemic or hemorrhagic in nature. Neither did we have access to information on patients' adherence to prescribed secondary preventive medication after their prior stroke. AF was registered as a dichotomous variable (present or absent) without information whether it was a previously known condition or newly diagnosed or if it was a permanent, persistent, or

paroxysmal arrhythmia. These details might have had an impact on OAC treatment decisions. However, according to guidelines,[25–27] treatment would have been recommended irrespective of these details.

5 | CONCLUSIONS

Not only in IS but also in TIA, vascular risk factors were more common in patients with a history of stroke compared to those without. Proportions of AF increased markedly in the presence of prior stroke in both TIA and IS patients. In contrast to other secondary preventive medications, levels of OAC treatment in patients with AF were low and even less common in patients with a history of stroke and high risk of recurrence.

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CONFLICT OF INTEREST

None.

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