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Prevalence and Distribution of Intracranial Vessel Occlusion on Angiography and Its Association with Functional Outcome in Patients with Atrial Fibrillation Presenting with Ischemic Stroke

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Objectives: To determine the prevalence and distribution of intracranial vessel occlusion identified on computed tomography (CT) or magnet resonance (MR) angiography and to explore its association with functional outcome in patients with atrial fibrillation (AF) and ischemic stroke.
Methods: Multicenter cohort study enrolling consecutive patients with AF with imaging-confirmed ischemic stroke who underwent CT- or MR-angiography on admission (2014–2022). Multivariable regression was used to explore the association between intracranial vessel occlusion and poor functional outcome (modified Rankin Scale score 3–6) at 90 days.
Results: The analysis included 10,164 patients (median age 81.5 years, 47.8% female, median National Institutes of Health Stroke Scale score on admission 6; 14.7% on a vitamin K antagonist [VKA], 27.5% on a direct oral anticoagulant [DOAC], 57.8% not receiving oral anticoagulation). Angiography showed intracranial vessel occlusion in 5,190 patients (51.1%), affecting the anterior cerebral circulation in 87.4%. Overall, 29.2% and 29.4% of patients received

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thrombolysis and mechanical thrombectomy, respectively. The proportion of patients with poor functional outcome at 90 days was 60.6% and 42.7% in those with and without vessel occlusion, respectively. In multivariable analyses, vessel occlusion was associated with poor functional outcome (adjusted odds ratio [aOR]: 1.95, 95% confidence interval [CI]: 1.71–2.22) with consistent results in subgroups according to oral anticoagulation use (VKA, aOR: 1.98, 95% CI: 1.40–2.80; DOAC, aOR: 2.35, 95% CI: 1.83–3.03; none, aOR: 1.76, 95% CI: 1.49–2.09).

Interpretation: Intracranial vessel occlusion is common in patients with AF with ischemic stroke, mainly affects the anterior circulation and is associated with poor functional outcome.

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Patients with atrial fibrillation (AF) carry an increased risk of ischemic stroke.[1] Thromboembolism, mainly originating from the left atrial appendage, may cause extensive territorial infarction due to proximal vessel occlusion.[2,3] Angiography by means of computed tomography (CT) or magnetic resonance imaging (MRI) can readily identify vessel occlusion and support decision making regarding acute revascularization treatment. However, despite major advances in the care of patients with acute stroke, large infarcts remain associated with poor functional outcome.[4–7]

Oral anticoagulation with a vitamin K antagonist (VKA) or a direct oral anticoagulant (DOAC) effectively reduces the risk of ischemic stroke in patients with AF.[8,9] Nonetheless, there are some patients who suffer an ischemic stroke while on oral anticoagulation.[10,11]

We aimed to determine the prevalence and distribution of embolic vessel occlusion detected on non-invasive angiography and to explore its association with functional outcome in patients with AF presenting with acute ischemic stroke while on or not on oral anticoagulation.

Methods

Patient Population

This analysis is based on data from the Swiss Stroke Registry (SSR). The SSR is a prospective, mandatory national registry including consecutive patients presenting with an acute cerebrovascular event at 25 certified stroke units and stroke centers across Switzerland.[12,13]

The study population included patients presenting with imaging-proven acute ischemic stroke and a diagnosis of AF (either known, or newly diagnosed during hospitalization for the qualifying stroke event) who underwent CT or MRI angiography following hospitalization (January 2014 to July 2022). Based on patient-reported use of oral anticoagulation before stroke onset, patients were categorized into 3 groups: (1) patients on a VKA, (2) patients on a DOAC, and (3) patients not treated with oral anticoagulation at the time of stroke. Patients who did not undergo angiography were excluded (Supplementary Fig S1). Further, patients with missing data on angiography and those with missing data on oral anticoagulation use at the time of the qualifying ischemic stroke were excluded.

Data Collection

Local investigators and certified research staff collected predefined clinical variables using electronic case report forms for all patients enrolled in the SSR. Data were stored on a secured webserver based at the Clinical Trials Unit at the University Hospital Basel, Basel, Switzerland. All patients completed a research visit at the time of their index hospitalization and at 90 days following the qualifying stroke event. Further details on data collection and study definitions in the SSR have been reported previously.[12,13]

Outcomes

The primary outcome was occlusion (ie, a 100% stenosis) of at least 1 segment of the middle cerebral artery (MCA), the anterior cerebral artery (ACA), the posterior cerebral artery (PCA), or the vertebrobasilar artery attributable to the vascular territory of acute ischemia detected on angiography. Anterior circulation vessel occlusion was defined as the presence of occlusion of at least 1 segment of the MCA, the ACA, or both. The presence of vessel occlusion was determined by local investigators based on review of source imaging and/or radiological reports. In a subset of patients enrolled at the centers in Bern and Lausanne (both of which are thrombectomy-capable centers), vessel occlusion was additionally assessed by independent central review by a qualified neuroradiologist. Here, the exact location (ie, segment of the MCA, ACA, and other intracranial arteries) of the largest occluded vessel segment was determined for all patients enrolled at these centers. Proximal large vessel occlusion was defined as occlusion of the intracranial ICA, the M1 segment of the MCA, the basilar artery or vertebral artery, and distal medium vessel occlusion was defined as occlusion of either segment of the ACA, the M2-M4 segments of the MCA or either segment of the PCA.[14]

The modified Rankin Scale (mRS) was used to assess functional status at baseline and at 90 days following the qualifying ischemic stroke.[15] This scale ranges from 0 (no symptoms) to 6 (death), with higher values indicating worse outcomes. Poor functional outcome was defined as a mRS score of 3–6 at 90 days following stroke.

Statistical Analysis

Baseline characteristics as captured at the time of the qualifying ischemic stroke were summarized using median (interquartile range [IQR]) for continuous variables and counts (percentages) for categorical variables. The presence of right, left or bilateral vessel occlusion of at least 1 segment of the MCA, the ACA, the PCA, and the vertebrobasilar artery was descriptively analyzed.

Two of the enrolling centers (Bern and Lausanne) provided granular data on the exact intracranial segment(s) showing vessel occlusion on angiography. The distribution was descriptively analyzed, and the following order was specified to determine the largest occluded vessel segment: intracranial ICA > basilar artery > intracranial vertebral > M1 segment of the MCA > A1 segment of the ACA > P1 segment of the PCA > M2 segment of the MCA > A2/more distal segment of the ACA > P2/more distal segment of the PCA > M3 or more distal segment of the MCA. Isolated extracranial occlusions of the ICA or the vertebral artery were excluded from this analysis.

Functional outcome of patients with and without vessel occlusion on angiography was descriptively analyzed. Univariable and multivariable logistic regression models were built to explore the association of vessel occlusion with functional outcome at 90 days. Model 1 was adjusted for age, sex, prior stroke or transient ischemic attack, hypertension, diabetes, dyslipidemia, blood glucose and systolic blood pressure on admission, smoking status, oral anticoagulation use, antiplatelet use, and the pre-qualifying stroke mRS score. Model 2 was adjusted for all variables included in model 1 as well as acute revascularization treatment (thrombolysis and/or mechanical thrombectomy). Furthermore, post hoc sensitivity analyses that were additionally adjusted for National Institutes of Health Stroke Scale (NIHSS) score on admission, and inverse probability weighting analyses according to the type of revascularization treatment were conducted. Subgroup analyses were performed according to status of oral anticoagulation use at the time of the qualifying ischemic stroke. There was no imputation of missing data.

In addition, several post hoc analyses were conducted to compare the main findings to those in patients presenting with ischemic stroke during the same time period but who did not have AF.

All statistical analyses were conducted using SAS 9.4 (SAS Institute, Cary, NC, United States).

Ethics and Study Reporting

This analysis was approved by the institutional review board in Bern (project ID 2022-01465). According to Swiss legislation (law on highly specialized medicine; "Hochspezialisierte Medizin" HSM; Art. 39 Abs. 2^{bis} KVG) and ethics approval, all patients treated at one of the certified Swiss Stroke Units or Stroke Centers are enrolled in the SSR. Patients who refused data use for scientific purposes were excluded from this analysis.

Study reporting follows the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.[16]

Results

Study Population

The analysis included 10,164 patients with AF presenting with ischemic stroke (Table 1). Of these, 1,496 (14.7%) were treated with a VKA and 2,793 (27.5%) with a DOAC prior to stroke onset. The remainder of patients (57.8%) were not treated with oral anticoagulation at the time of stroke. The median NIHSS score on admission was 6 (IQR 2–14). Overall, the median age of patients was 81.5 years, 47.8% were female and 26.1% of patients had already had a stroke or a transient ischemic attack (TIA) prior to the qualifying event. The majority of patients (84.5%) had a baseline mRS score of 0–2.

Imaging Results

All of the patients underwent CT (81.8%) or MR angiography (18.2%) on admission. Occlusion of at least 1 segment of a vessel supplying the ischemic territory was present in 5,190 patients (51.1%). In patients with vessel occlusion, the anterior circulation was affected in 87.4%. Segments of the MCA were most commonly affected (38.9% right, 43.1% left and 3.4% bilateral occlusion in patients with any vessel occlusion). A detailed overview of vessel occlusion of at least 1 segment of the ACA, the PCA and the vertebrobasilar artery and a breakdown according to the status of oral anticoagulation use at the time of the qualifying stroke are provided in Table 2.

Granular data on the exact location of the largest occluded vessel segment were available for a subset of patients enrolled at two thrombectomy-capable centers (Supplementary Table S1). Of 1,974 patients, 1,403 (71.1%) had occlusion of at least 1 vessel segment, including distal branches of the MCA, the ACA or the PCA. In patients with occlusion, the largest occluded segment was part of a vessel supplying the anterior cerebral circulation in 88.7%. A total of 746 patients (53.2%) had proximal large vessel occlusion, and 657 (46.8%) had distal medium vessel occlusion. The most frequently occluded largest segments were the M1 segment of the MCA (34.1%), the M2 segment of the MCA (29.6%) and the internal carotid artery (ICA) (14.5%) (Fig 1).

Acute Revascularization Treatment

Overall, 2,960 patients (29.2%) were treated with thrombolysis, and 2,990 (29.4%) received mechanical thrombectomy.

Table 1. Characteristics of Patients with AF Presenting with Ischemic Stroke

Parameter	Total	VKA	DOAC	No Oral Anticoagulation
N	10,164	1,496	2,793	5,875
Age (years)	81.5 (74.6–86.8) [224]	83.0 (77.3–87.5) [78]	81.7 (75.9–86.6) [78]	81.0 (73.3–86.7) [119]
Female sex, n (%)	4,854 (47.8) [16]	703 (47.0)	1,290 (46.2) [3]	2,861 (48.8) [13]
Oral anticoagulation, n (%)				
VKA	1,496 (14.7)	1,496 (100.0)	0	0
DOAC	2,793 (27.5)	0	2,793 (100.0)	0
None	5,875 (57.8)	0	0	5,875 (100.0)
Antiplatelet use, n (%)	3,020 (29.7) [4]	155 (10.4)	296 (10.6) [4]	2,569 (43.7)
Prior stroke, n (%)	2,215 (21.9) [35]	415 (27.9) [8]	914 (32.8) [9]	886 (15.1) [18]
Prior TIA, n (%)	670 (6.6) [42]	133 (9.0) [11]	246 (8.8) [11]	291 (5.0) [20]
Prior stroke or TIA, n (%)	2,641 (26.1) [33]	500 (33.6) [8]	1,042 (37.4) [9]	1,099 (18.8) [16]
Functional status prior to qualifying event, n (%)				
mRS 0–2	7,957 (84.5) [753]	1,162 (82.0) [79]	2,182 (84.2) [201]	4,613 (85.4) [473]
mRS 3–5	1,454 (15.4)	255 (18.0)	410 (15.8)	789 (14.6)
Hypertension, n (%)	8,409 (82.8) [8]	1,316 (88.1) [3]	2,408 (86.3) [3]	4,685 (79.8) [2]
Diabetes, n (%)	2,253 (22.2) [14]	371 (24.9) [4]	706 (25.3) [3]	1,176 (20.0) [7]
Dyslipidemia, n (%)	6,288 (62.1) [38]	975 (65.6) [9]	1786 (64.2) [10]	3,527 (60.2) [19]
Smoking, n (%)	1,163 (11.6) [103]	129 (8.7) [13]	304 (10.9) [14]	730 (12.6) [76]
NIHSS (on admission)	6 (2–14) [85]	6 (3–15) [16]	5 (2–12) [24]	7 (3–15) [45]
Body mass index (kg/m^2)	25.3 (22.8–28.3) [2161]	25.5 (22.9–28.7) [309]	25.3 (22.8–28.3) [633]	25.2 (22.7–28.1) [1219]
Systolic blood pressure on admission (mmHg)	154 (137–173) [130]	152 (136–172) [23]	154 (136–172) [37]	155 (138–174) [70]
Diastolic blood pressure on admission (mmHg)	84 (73–96) [131]	84 (72–97) [23]	84 (72–96) [37]	84 (73–97) [71]
Glucose on admission (mmol/l)	6.6 (5.8–8.0) [1070]	6.7 (5.7–8.1) [199]	6.6 (5.7–8.0) [249]	6.6 (5.8–8.0) [622]
Acute revascularization treatment, n (%)				
Thrombolysis	2,960 (29.2) [17]	258 (17.3) [1]	240 (8.6) [7]	2,462 (42.0) [9]
Mechanical thrombectomy	2,990 (29.4) [11]	438 (29.3) [1]	710 (25.5) [4]	1842 (31.4) [6]

Continuous variables are presented as median (25th-75th) percentile. [n] denotes the number of patients with missing data.
Abbreviations: DOAC = direct oral anticoagulant; mRS = modified Rankin Scale; NIHSS = National Institutes of Health Stroke Scale; TIA = transient ischemic attack; VKA = vitamin K antagonist.

Thrombolysis was used more often in patients not receiving oral anticoagulation at the time of the qualifying stroke (42.0%) compared with patients treated with a VKA (17.3%) or a DOAC (8.6%), respectively. The proportion of patients receiving mechanical thrombectomy was highest in those not receiving oral anticoagulation (31.4%), and 29.3% and 25.5% in patients treated with a VKA or a DOAC, respectively.

Table 2. Vessel Occlusion Detectable on Imaging

Parameter	Total	VKA	DOAC	No Oral Anticoagulation
N	10,164	1,496	2,793	5,875
Occlusion in ischemic territory, n (%)	5,190 (51.1)	736 (49.2)	1,207 (43.2)	3,247 (55.3)
Anterior circulation, n (%)	4,456 (87.4) [91]	634 (87.8) [14]	1,045 (88.6) [27]	2,777 (86.9) [50}
MCA, n (%)				
None	740 (14.5) [91]	104 (14.4) [14]	155 (13.1) [27]	481 (15.0) [50]
Right	1986 (38.9)	280 (38.8)	449 (38.1)	1,257 (39.3)
Left	2,197 (43.1)	318 (44.0)	525 (44.5)	1,354 (42.4)
Bilateral	176 (3.5)	20 (2.8)	51 (4.3)	105 (3.3)
ACA, n (%)				
None	4,660 (91.5) [97]	664 (92.0) [14]	1,076 (91.2) [27]	2,920 (91.5) [56]
Right	195 (3.8)	33 (4.6)	48 (4.1)	114 (3.6)
Left	196 (3.8)	21 (2.9)	39 (3.3)	136 (4.3)
Bilateral	42 (0.8)	4 (0.5)	17 (1.4)	21 (0.7)
PCA, n (%)				
None	4,456 (87.5) [97]	638 (88.2) [13]	1,038 (88.0) [28]	2,780 (87.1) [56]
Right	290 (5.7)	37 (5.1)	65 (5.5)	188 (5.9)
Left	269 (5.3)	35 (4.8)	56 (4.7)	178 (5.6)
Bilateral	78 (1.5)	13 (1.8)	20 (1.7)	45 (1.4)
Vertebrobasilar, n (%)				
None	4,676 (91.8) [99]	661 (91.6) [14]	1,076 (91.3) [28]	2,939 (92.1) [57]
Right	108 (2.1)	14 (1.9)	32 (2.7)	62 (1.9)
Left	125 (2.5)	13 (1.8)	34 (2.9)	78 (2.4)
Bilateral	182 (3.6)	34 (4.7)	37 (3.1)	111 (3.5)
Stenosis (50–99%) in suspected ischemic territory, n (%)	1,282 (12.6)	198 (13.2)	412 (14.8)	672 (11.4)
No abnormality, n (%)	3,692 (36.3)	562 (37.6)	1,174 (42.0)	1956 (33.3)

Note: [n] denotes the number of patients with missing data.
Abbreviations: ACA = anterior cerebral artery; DOAC = direct oral anticoagulant; MCA = middle cerebral artery; PCA = posterior cerebral artery; VKA = vitamin K antagonist.

Functional Outcome

Data on functional outcome were available for 8,053 patients (79.2%). Overall, 4,193 patients (52.1%) had poor functional outcome (ie, a mRS score 3–6) at 90 days following stroke. The proportion of patients with poor functional outcome was 60.6% and 42.7% in patients with and without vessel occlusion on angiography, respectively (Fig 2). Mortality following stroke was more frequent in patients with compared to patients without vessel occlusion on angiography (32.1% vs. 15.1%).

In multivariable analyses adjusted for known prognostic factors and acute revascularization treatment, the presence of any vessel occlusion on angiography was associated with poor functional outcome (adjusted odds ratio [aOR]: 1.94, 95% confidence interval [CI]: 1.71–2.22). Similar results were obtained in subgroups according to

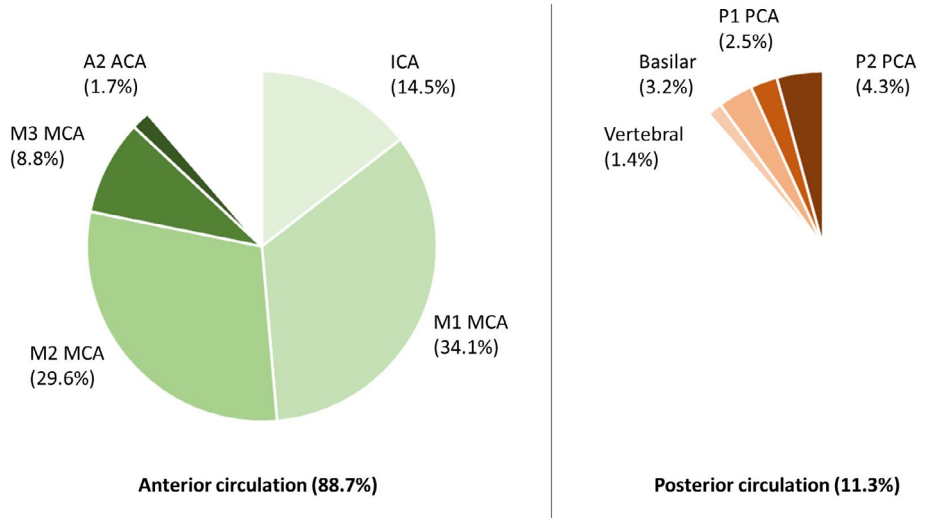

Figure 1: Largest occluded segment in patients with at least one intracranial vessel occlusion (N = 1,403). The largest occluded segment affected an intracranial vessel supplying the anterior circulation in 1,244 patients (88.7%). In 204 patients with intracranial ICA occlusion, the external segment also showed occlusion in 43 (21.1%). A total of 130 of 161 (80.7%) of isolated intracranial ICA occlusions (ie, without concomitant occlusion of the external segment) were L- or T-type occlusions. In 19 patients with intracranial vertebral artery occlusion, the external segment also showed occlusion in 7 (36.8%). There were no patients in whom the A1 segment of the ACA was the largest occluded vessel segment. Isolated extracranial occlusions of the ICA or the vertebral artery were excluded from this analysis. ACA = anterior cerebral artery; ICA = internal carotid artery; MCA = middle cerebral artery; PCA = posterior cerebral artery. [Color figure can be viewed at www.annalsofneurology.org]

status of oral anticoagulation use at the time of the qualifying stroke (VKA, aOR: 1.98, 95% CI: 1.40–2.80; DOAC, aOR: 2.35, 95% CI: 1.83–3.03; no oral anticoagulation, aOR: 1.76, 95% CI: 1.49–2.09) (Table 3). Post hoc sensitivity analysis that were additionally adjusted for NIHSS score on admission as well as inverse probability weighting analyses according to the type of revascularization treatment yielded consistent results (Supplementary Table S2).

Findings in Patients without AF

A post hoc analysis showed that the prevalence of vessel occlusion in 30,680 patients without AF who presented with ischemic stroke during the same time period was 32.2% (Supplementary Table S3). In such patients with occlusion, the anterior circulation was affected in 76.1%. A total of 29.7% and 15.4% of patients without AF were treated with thrombolysis and mechanical thrombectomy, respectively. The proportion of patients with poor functional outcome was 42.7% and 22.1% in patients with and without vessel occlusion, respectively. Consistent with the main findings in patients with AF, vessel occlusion was similarly associated with poor functional outcome in patients without AF after adjustment for known prognostic factors and acute revascularization treatment (aOR: 2.04, 95% CI: 1.88–2.22) (Supplementary Table S4).

Discussion

We explored the clinical significance of imaging detected intracranial vessel occlusion affecting the cerebral circulation in patients with AF presenting with ischemic stroke. Approximately half of the patients had total occlusion of at least 1 vessel segment in the vascular territory of brain ischemia on CT or MR angiography. Vessel occlusion predominantly affected the anterior circulation, and the majority of occlusions were located in the M1 or M2 segments of the MCA, followed by the intracranial ICA. Adjusting for known prognostic factors and potential confounders including revascularization therapies, any detectable vessel occlusion was associated with poor functional outcome at 90 days. This finding was independent of oral anticoagulation use at the time of the qualifying stroke event. A post hoc analysis showed that intracranial vessel occlusion was ~1.6-fold more common in patients presenting with ischemic stroke with versus without AF.

Our study addresses an important gap in knowledge as there is a paucity of data on the prevalence of vessel occlusion in patients with AF presenting with ischemic stroke. Using the Bamford classification, historical data show that among patients with AF suffering an ischemic stroke, 9% presented with posterior circulation and 13% with lacunar (ie, non-large vessel occlusion) stroke syndrome.[17,18] However, this classification relies on the pattern of neurological deficits and clinical syndrome but does not include brain imaging and/or angiography.

The diameters of the main segments of vessels supplying the anterior circulation typically range from ~3 mm (intracranial ICA) to ~1.5 mm (distal M2).[19–22] Occlusion of these vessels due to large thromboembolism

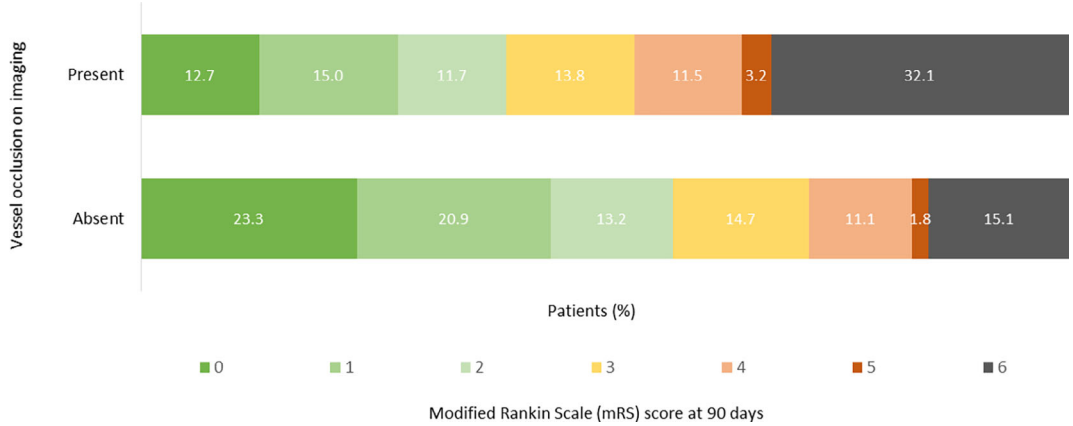

Figure 2: Functional outcome at 90 days according to the presence or absence of intracranial vessel occlusion on angiography in patients with atrial fibrillation presenting with ischemic stroke (N = 10,164). Intracranial vessel occlusion was present in 5,190 patients (51.1%). [Color figure can be viewed at www.annalsofneurology.org]

Table 3. Association of Vessel Occlusion with Functional Outcome

	Association of Vessel Occlusion Detectable on Imaging with mRS 3–6 at 90 days, OR (95% CI)			
Parameter	**Total**	**VKA**	**DOAC**	**No Oral Anticoagulation**
Univariable[a]	2.07 (1.89–2.26)	2.77 (2.18–3.52)	2.32 (1.96–2.76)	1.85 (1.65–2.09)
Multivariable				
Model 1[b]	2.21 (1.98–2.47)	2.89 (2.15–3.87)	2.77 (2.24–3.41)	1.86 (1.61–2.15)
Model 2[c]	1.95 (1.71–2.22)	1.98 (1.40–2.80)	2.35 (1.83–3.03)	1.76 (1.49–2.09)

Note: Model 1 was adjusted for age, sex, prior stroke or transient ischemic attack, hypertension, diabetes, dyslipidemia, blood glucose and systolic blood pressure on admission, smoking status, oral anticoagulation use, antiplatelet use, and pre-qualifying stroke mRS score. In the subgroups according to the use of antithrombotic therapy, oral anticoagulation use was omitted from the analysis.
Model 2 was adjusted for all variables included in Model 1 + acute revascularization treatment (thrombolysis, mechanical thrombectomy).
Abbreviations: CI = confidence interval; DOAC = direct oral anticoagulant; VKA = vitamin K antagonist; OR = odds ratio.
[a]Number of observations read 10,164, number of observations used 8,053.
[b]Number of observations read 10,164, number of observations used 6,732.
[c]Number of observations read 10,164, number of observations used 6,721.

causes severe ischemia and may lead to large cerebral infarcts resulting in significant disability or death.[23] In contrast, small emboli not resulting in vessel occlusion detectable on imaging may typically lead to minor, non-disabling strokes. Our findings suggest that patients diagnosed with AF presenting with ischemic stroke often suffer from occlusion of a significant artery supplying the brain, predominantly in the anterior circulation.

In high-resource settings, patients with disabling acute ischemic stroke presenting with an occlusion of the ICA or M1/M2 segments of the MCA are preferably treated with mechanical thrombectomy, a therapy that significantly reduces morbidity.[5] A 24/7 availability of mechanical thrombectomy is provided by 10 certified stroke centers across Switzerland, with at least 1 center within a radius of <1 hour for the majority of ~8 million inhabitants.[24] In our study, despite ~29% of patients receiving mechanical thrombectomy, vessel occlusion was independently associated with poor functional outcome at 90 days following stroke. This finding highlights the detrimental effects of vessel occlusion despite best medical treatment and suggests that there may be great potential in tailored prevention strategies.

Our findings have important implications. Stroke due to large emboli is highly prevalent in patients with AF presenting with ischemic stroke. Vessel occlusion predominantly affects the anterior circulation and is associated with poor functional outcome, irrespective of anticoagulation use at the time of stroke or contemporary revascularization therapy. Therefore, novel strategies beyond oral anticoagulation are needed to reduce the burden of large embolic stroke in this population.[25] The

Left Atrial Appendage Occlusion Study (LAAOS) III showed that surgical occlusion of the left atrial appendage in patients with AF undergoing cardiac surgery for another indication reduced stroke in addition to usual care which included guideline-recommended use of oral anticoagulation.[2] Analogous, percutaneous closure of the left atrial appendage has the potential to reduce stroke, but this remains unproven.[26] An ongoing academic trial assesses whether additional left atrial appendage occlusion on top of direct oral anticoagulation therapy in patients with atrial fibrillation who had an ischemic stroke despite anticoagulation therapy is beneficial (ELAPSE: Early Closure of Left Atrial Appendage for Patients With Atrial Fibrillation and Ischemic Stroke Despite Anticoagulation Therapy, NCT05976685). Moreover, permanent bilateral filters placed in the common carotid artery may provide mechanical protection of the anterior cerebral circulation.[27] A currently planned trial will assess whether these filters may reduce the risk of large vessel occlusion ischemic stroke on top of oral anticoagulation therapy (INTERCEPT: Carotid Implants for PreveNtion of STrokE ReCurrEnce From Large Vessel Occlusion in Atrial Fibrillation Patients Treated With Oral Anticoagulation, NCT05723926). This approach is particularly promising to protect the anterior circulation from large emboli, which seems a valuable target based on our findings. Randomized trials are needed to determine the efficacy and safety of such strategies used in conjunction with oral anticoagulation use.[25]

Strengths and Limitations

Here, we reported data from a large, national, multicenter cohort study including >10,000 patients with AF presenting with ischemic stroke. Data collection was done using pre-specified case report forms and followed definitions unrelated to this analysis. CT- and MR-angiography on admission is standard of care for all patients presenting with suspected ischemic stroke in Switzerland, allowing for a comprehensive analysis of the prevalence and distribution of vessel occlusion.

Our study has several limitations. First, this was a retrospective analysis using prospectively collected data. Second, there was no central core lab assessing the prevalence of vessel occlusion in the main study population, and no information on inter- and intra-observer reproducibility of the imaging findings. Third, the analysis included both patients with known AF as well as AF diagnosed during hospitalization for the qualifying ischemic stroke. Fourth, the dataset used for this analysis did not contain information on the quality of anticoagulation control (eg, time in therapeutic range in patients on a VKA or on-label dosing of DOACs). Fifth, data on functional outcome were not available for all patients included in the analysis. In addition, domains such as quality of life or specific cognitive functions are not represented in the mRS. Finally, detailed information on the exact location of the largest occluded vessel segment was only available for a subset of patients enrolled at 2 major thrombectomy-capable stroke centers.

Conclusions

In patients with AF presenting with ischemic stroke, vessel occlusion detectable on angiography is common and mainly affects the anterior circulation. Vessel occlusion is associated with poor functional outcome despite contemporary revascularization therapy, and independent of the use of oral anticoagulation at the time of stroke. Novel treatment strategies are needed to reduce the burden of stroke due to large thromboembolism in patients with AF.

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Author Contributions

A.B., A.S.h., S.C., and D.S. contributed to the conception and design of the study.

A.B., T.R.M., A.Sal., M.B., D.Str., J.K., T.K., M.K., S.T.E., E.C., E.D., N.P., C.C., G.K., S.R., S.W., M.B., L.B., U.F., M.R., P.M., and D.S. contributed to the acquisition and analysis of data.

A.B, A.S.h., S.C., and D.S. contributed to drafting the text or preparing the figures.

Potential Conflicts of Interest

A.B. reports lecture fees from Bristol-Myers Squibb (manufacturer of apixaban). M.K. reports honoraria from Bristol-Myers Squibb/Pfizer, manufacturer of apixaban. A.S.h. reports research support and advisory/speaker bureau honoraria from Daiichi Sankyo, manufacturer of edoxaban, Bristol Myers Squibb, manufacturer of apixaban, Bayer AG, manufacturer of rivaroxaban. D.S. reports personal fees from Bayer, manufacturer of rivaroxaban. All other authors report that they have nothing to declare.

Data Availability

The data supporting these analyses may be made available to qualified investigators upon reasonable request to the SSR Steering Committee.

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