SUPPLEMENTARY MATERIAL

Risk of cerebrovascular events in intracerebral hemorrhage survivors with atrial fibrillation: an analysis of the Danish Stroke Registry

Table S1. List of ICD-10, procedure, and ATC codes used to define the in- and exclusion criteria, comorbidities, medical therapies, and outcomes.

Table S2. Baseline patient characteristics of the subpopulation initiating/resuming oral anticoagulant therapy during follow-up.

Table S3. Absolute risk of cerebrovascular events and all-cause death 1 year after initiation/resumption of oral anticoagulant therapy in patients with intracerebral hemorrhage and atrial fibrillation.

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STROBE Statement

Table S1. List of ICD-10, procedure, and ATC codes used to define the in- and exclusion criteria, comorbidities, medical therapies, and outcomes.

		Data source		
	Variable definition	**ICD-10 code/ Procedure code**	**ATC drug code***	**Registry sources**
In- and exclusion criteria				
Atrial fibrillation	Yes/no	I48		Danish National Patient Registry
Thrombolysis	Yes/no			Danish Stroke Registry
Intracerebral hemorrhage	Yes/no	I61		Danish Stroke Registry
Previous intracerebral hemorrhage	Yes/no	I61; ICD-8:431		Danish National Patient Registry
Traumatic intracerebral hemorrhage	Yes/no	S063C; S064; S065; S066		Danish National Patient Registry
Brain imaging	Yes/no			Danish Stroke Registry
Previous venous thromboembolism	Yes/no	I801; I802; I803; I808; I809; I819; I636; I676; I822; I823; I828; I829; I26		Danish National Patient Registry
Recent acute myocardial	Yes/no	I21; I23; KFNG		Danish National Patient Registry

infarction or percutaneous coronary intervention				
Left atrial appendage occlusion device	Yes/no	KFFW98A		Danish National Patient Registry
Severe renal dysfunction requiring dialysis	Yes/no	BJFD		Danish National Patient Registry
Clinical characteristics and comorbidities				
Age	Number			Danish Civil Registration System
Sex	Female/male			Danish Civil Registration System
CHA_2DS_2-VASc score	Score 2-3, Score 4-6, Score >6			Danish National Patient Registry National Prescription Registry
Scandinavian Stroke Scale	Mild (>43), Moderate (26-43), Severe (<26) and as continuous variable			Danish Stroke Registry

Surgical evacuation of intracerebral hemorrhage	Yes/no			Danish Stroke Registry
Diabetes mellitus	Yes/no	Patient chart		Danish Stroke Registry
Hypertension	Yes/no	Patient chart		Danish Stroke Registry
Heart failure	Yes/no	Patient chart		Danish Stroke Registry
Chronic kidney disease	Yes/no	Patient chart		Danish Stroke Registry
Peripheral artery disease	Yes/no	Patient chart		Danish Stroke Registry
Previous myocardial infarction	Yes/no	Patient chart		Danish Stroke Registry
Chronic obstructive pulmonary disorder	Yes/no	Patient chart		Danish Stroke Registry
Previous ischemic stroke	Yes/no	I63; I64;		Danish National Patient Registry
Previous major extracranial bleeding	Yes/no	D62; J942; H113; H356; H431; N02; R04; R31; R58		Danish National Patient Registry
Smoking	Current, former, never, missing			Danish Stroke Registry

Alcohol	Recommended, above recommended, missing			Danish Stroke Registry
Civil status	Cohabitant, alone, other, missing			Danish Stroke Registry
Medications				
Statins	Yes/no			Danish Stroke Registry
Selective Serotonin Reuptake Inhibitor	Yes/no			Danish Stroke Registry
Antiplatelet therapy	Yes/no		B01AC06; B01AC04	National Prescription Registry
Oral anticoagulation therapy	Yes/no		B01AA03; B01AE07; B01AF01; B01AF02; B01AA04	National Prescription Registry
Outcomes				
Recurrent intracerebral hemorrhage	Yes/no			Danish Stroke Registry
All strokes (intracerebral	Yes/no			Danish Stroke Registry

hemorrhage or ischemic stroke)				
Cerebrovascular ischemic events (ischemic stroke, unspecified stroke, or transient ischemic attack)	Yes/no			Danish Stroke Registry
All-cause death	Yes/no			Danish Civil Registration System
* Prescription data from 180 days before diagnosis of intracerebral hemorrhage.				

Table S2. Baseline patient characteristics of the subpopulation initiating/resuming oral anticoagulant therapy during follow-up.

Characteristics, % (N)	**All**	**CHA_2DS_2-VASc score 2-3**	**CHA_2DS_2-VASc score 4-6**	**CHA_2DS_2-VASc score >6**
N (%)	526	159	243	124
Age, median (IQR)	78.0 (73.0-84.0)	75.0 (68.0-82.0)	78.0 (73.0-84.0)	82.0 (77.0-85.0)
≥65 years	93.7 (493)	88.7 (141)	94.7 (230)	98.4 (122)
≥75 years	67.7 (356)	50.3 (80)	70.0 (170)	85.5 (106)
Female sex	43.3 (228)	17.6 (28)	46.5 (113)	70.2 (87)
CHA_2DS_2-VASc score, median (IQR)	4.0 (3.0-5.0)	3.0 (2.0-3.0)	4.0 (4.0-5.0)	6.0 (6.0-7.0)
Scandinavian Stroke Scale score*, median (IQR)	47.0 (34.0-54.0)	49.0 (32.0-56.0)	46.5 (34.0-54.0)	46.0 (38.0-54.0)
Mild (58-44)	56.3 (296)	57.2 (91)	55.6 (135)	56.5 (70)
Moderate (26-43)	25.1 (132)	22.6 (36)	24.3 (59)	29.8 (37)
Severe (<26)	14.6 (77)	16.4 (26)	14.8 (36)	12.1 (15)

Missing	4.0 (21)	3.8 (6)	5.3 (13)	- (<5)
Surgical evacuation of intracerebral hemorrhage	2.3 (12)	- (<5)	2.1 (5)	- (<5)
Comorbidities				
Diabetes mellitus	18.8 (99)	5.7 (9)	18.1 (44)	37.1 (46)
Hypertension	80.0 (421)	65.4 (104)	82.3 (200)	94.4 (117)
Heart failure	30.2 (159)	17.0 (27)	30.5 (74)	46.8 (58)
Chronic kidney disease	8.2 (43)	6.9 (11)	7.8 (19)	10.5 (13)
Peripheral artery disease	18.4 (97)	10.1 (16)	14.4 (35)	37.1 (46)
Previous myocardial infarction	16.7 (88)	9.4 (15)	13.6 (33)	32.3 (40)
Chronic obstructive pulmonary disorder	16.0 (84)	13.2 (21)	16.0 (39)	19.4 (24)
Previous ischemic stroke	34.4 (181)	11.3 (18)	35.8 (87)	61.3 (76)
Previous major extracranial bleeding	17.7 (93)	18.9 (30)	18.1 (44)	15.3 (19)
Lifestyle				
Smoking				

Never	36.5 (192)	31.4 (50)	38.7 (94)	38.7 (48)
Former	32.7 (172)	35.8 (57)	29.6 (72)	34.7 (43)
Current	14.1 (74)	13.2 (21)	14.8 (36)	13.7 (17)
Missing	16.7 (88)	19.5 (31)	16.9 (41)	12.9 (16)
Alcohol intake†				
Recommended	76.2 (401)	68.6 (109)	78.6 (191)	81.5 (101)
Above recommended	9.7 (51)	14.5 (23)	8.2 (20)	6.5 (8)
Missing	14.1 (74)	17.0 (27)	13.2 (32)	12.1 (15)
Civil status				
Cohabitant	59.1 (311)	62.3 (99)	61.7 (150)	50.0 (62)
Alone	38.0 (200)	34.0 (54)	35.4 (86)	48.4 (60)
Other	1.0 (5)	- (<5)	- (<5)	- (<5)
Missing	1.9 (10)	- (<5)	- (<5)	- (<5)
Medication‡				
Statins	60.6 (319)	49.1 (78)	61.7 (150)	73.4 (91)
SSRI	11.4 (60)	8.2 (13)	12.3 (30)	13.7 (17)
Antithrombotic treatment				

None	9.3 (49)	9.4 (15)	11.5 (28)	4.8 (6)
Antiplatelet therapy alone	9.5 (50)	5.0 (8)	7.8 (19)	18.5 (23)
Oral anticoagulant therapy alone	63.3 (333)	67.9 (108)	62.1 (151)	59.7 (74)
Antiplatelet and oral anticoagulant therapy	17.9 (94)	17.6 (28)	18.5 (45)	16.9 (21)

Numbers are % (*N*) unless otherwise noted. SD: Standard deviation. ICH: Intracerebral hemorrhage. IQR: Interquartile range. SSRI: Selective Serotonin Reuptake Inhibitor.

*Severity of the index ICH was graded by the Scandinavian Stroke Scale, which (among others) includes assessment of the patient's level of consciousness, eye movements, coordination ability, and ability to speak.(35) The total of the score is a maximum of 58 and lower scores indicate more severe intracerebral hemorrhage events; categories of severity were defined as: 58-44 'mild'; 43-26 'moderate'; and <26 'severe'.

†Recommended alcohol intake per week: ≤7 for women and ≤14 for men.

‡Patients with a claimed prescription of the medication within 180 days before the incident intracerebral hemorrhage.

If the patient number is below five (<5), the exact number is not allowed to be presented due to individual data protection.

Table S3. Absolute risk of cerebrovascular events and all-cause death 1 year after initiation/resumption of oral anticoagulant therapy in patients with intracerebral hemorrhage and atrial fibrillation.

Absolute risk after 1 year after initiation/resumption of oral anticoagulant therapy	*Recurrent intracerebral hemorrhage*		*Cerebrovascular ischemic event**		*All-cause death*	
OAC initiation during follow-up	Events, n	Risk % (95% CI)	Events, n	Risk % (95% CI)	Events, n	Risk % (95% CI)
All (N=526)	12	2.4 (1.3 to 4.1)	15	3.1 (1.8 to 4.9)	100	20.0 (16.7 to 23.8)
CHA_2DS_2-VASc score 2-3 (N=602)	<5	2.7 (0.9 to 6.2)	6	4.2 (1.7 to 8.2)	20	13.3 (8.8 to 19.9)
CHA_2DS_2-VASc score 4-6 (N=866)	<5	1.8 (0.6 to 4.2)	6	2.7 (1.1 to 5.4)	55	23.9 (18.8 to 29.9)
CHA_2DS_2-VASc score >6 (N=416)	<5	3.6 (1.2 to 8.4)	<5	2.5 (0.7 to 6.6)	25	20.9 (14.6 to 29.4)

*Composite of ischemic stroke, unspecified stroke, or transient ischemic attack.

†Composite of intracerebral hemorrhage, ischemic stroke, unspecified stroke, or transient ischemic attack.

The exact number is masked because of individual level data protection if the event count is less than five (<5),

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STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	Page
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6 and 7
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	Fig 1
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	N/A
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	7 Suppl. Table 1
Bias	9	Describe any efforts to address potential sources of bias	8 and 9
Study size	10	Explain how the study size was arrived at	Fig 1
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8 and 9
		(*b*) Describe any methods used to examine subgroups and interactions	9
		(*c*) Explain how missing data were addressed	N/A

		(*d*) If applicable, explain how loss to follow-up was addressed	9
		(*e*) Describe any sensitivity analyses	9
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	10
		(b) Give reasons for non-participation at each stage	Fig 1
		(c) Consider use of a flow diagram	Fig 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 1
		(b) Indicate number of participants with missing data for each variable of interest	N/A
		(c) Summarise follow-up time (eg, average and total amount)	10
Outcome data	15*	Report numbers of outcome events or summary measures over time	10 and 11 Table 2
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Table 2 10 and 11
		(*b*) Report category boundaries when continuous variables were categorized	N/A
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	11
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	11 Table 3
Discussion			
Key results	18	Summarise key results with reference to study objectives	13
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	15 and 16
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	13 and 14
Generalisability	21	Discuss the generalisability (external validity) of the study results	14 and 15

Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	1

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.