Supplementary Online Content

Kuramatsu JB, Gerner ST, Schellinger PD, et al. Anticoagulant reversal, blood pressure levels, and anticoagulant resumption in patients with anticoagulation-related intracerebral hemorrhage. JAMA. doi:10.1001/jama.2015.0846.

This supplementary material has been provided by the authors to give readers additional information about their work.

eMethods.

Variables of interest

Evaluated indications for oral anticoagulation consisted of: (i) atrial fibrillation (A-fib) including idiopathic atrial flutter, nonvalvular, and valvular A-fib, (ii) mechanical heart valves, (iii) prior diagnosis of pulmonary embolism, or (iv) deep vein thrombosis[1]. Examples of (v) other indications for OAC comprised: by-pass grafting, thrombus formation, structural cardiac disease, cerebral sinus thrombosis, arterial dissection, thrombophilia (i.e. Factor V-Leiden-mutation, etc.).

The investigated prior comorbidities consisted essentially of the $CHADS_2$ Score and HAS-BLED Score parameters. The $CHADS_2$ Score was scored as appropriate, 2 points given for prior history of cerebral ischemia, and one point each for other risk factor such as 75 years of age or older, congestive heart failure (based on objective evidence of cardiac dysfunction), hypertension[2] and, diabetes mellitus as defined[3,4]. Parameters of the HAS-BLED Score were defined and scored accordingly. Renal dysfunction was defined as serum creatinine ≥ 200 μmol/L, liver dysfunction bilirubin > 2 times upper limit with transaminase elevation 3 times upper normal limit, medication history in regard to antiplatelet agents, and alcohol abuse were evaluated[5]. Parameters such as coronary artery disease was defined and scored on the basis of a history of myocardial infarction or prior coronary artery by-pass crafting, and dyslipidemia such as hypercholesterolemia and increased triglycerides scored as commonly diagnosed[6].

We evaluated laboratory parameters at time of hospital admission and consecutively serial monitoring of coagulation parameters and blood counts within 72 hours were recorded from institutional laboratory databases. In referred patients initial laboratory values of transferring hospitals were strictly used for initial INR assessment. For INR-reversal analysis various time-points of serial INR monitoring were recorded at time of laboratory accessioning.

Evaluated in-hospital measures consisted of need for placement of external ventricular drains for occlusive hydrocephalus and its therapy with intraventricular lysis as previously defined[7,8]. Treatment of increased ICP or perihemorrhagic edema was summated as osmotherapy (consisting of various agents, Mannitol most frequently applied) and was scored if elevated intracranial pressures were present and medication was given. Moreover, the need for mechanical ventilation, mechanical ventilation on arrival, and duration of ventilation was noted. Infectious complications, i.e. pneumonia and sepsis were scored and recorded as appropriate[9,10].

Statistical analyses

Statistical analysis was performed using the SPSS 20.0 software package (www.spss.com) and R2.12.0 (www.r-project.org). Distribution of data was calculated by Kolmogorov-Smirnov and Shapiro-Wilk tests. Data are presented as mean±SD (compared using the Student-T-test) or as median and IQR (compared using the Mann-Whitney U-test), as appropriate. Frequency distribution of categorized variables was tested by Pearson`s-$\chi 2$ or Fisher`s-exact tests. Statistical tests were two-sided and the significance level was set at α=0.05 and consequently corrected for multiple comparisons by the Bonferroni method correcting for type 1 error accumulation before variables were entered into further analyses[11]. Generally, unadjusted and consequently adjusted analyses were calculated and presented to expose possible selection bias. All variables included into adjusted analyses of outcomes, i.e. (i) hematoma enlargement, (ii) OAC resumption and (iii) functional outcome, were formally tested and multivariable models calculated by log-binomial regression analyses[12]. Specific analyses for each outcome measure were carried out (see manuscript). For further analyses of hematoma enlargement we analyzed categorized frequency distributions of time-dependent INR thresholds (categorized by 0.10 intervals; INR range <1.20 to ≥1.50) and time intervals (presented as 120 min intervals, time range 0 to ≥360 min, starting at time of hospital admission until 1st INR-monitoring after reversal treatment confirmed corresponding INR thresholds) with hematoma enlargement. For analyses of systolic blood pressure we categorized blood pressure in 20 mm Hg intervals (range <120 to ≥180 mm Hg) assessed (at 4h intervals) from time of hospital admission until 24h. These categorized frequency distributions of systolic blood pressure levels were evaluated for associations with hematoma enlargement dichotomized into <160 mm Hg *versus* ≥160 mm Hg at each specific time point.

References

1. Go AS, Hylek EM, Chang Y, et al. Anticoagulation therapy for stroke prevention in atrial fibrillation: how well do randomized trials translate into clinical practice? *JAMA.* Nov 26 2003;290(20):2685-2692.
2. Reeves RA. The rational clinical examination. Does this patient have hypertension? How to measure blood pressure. *JAMA.* Apr 19 1995;273(15):1211-1218.
3. Report of the expert committee on the diagnosis and classification of diabetes mellitus. *Diabetes Care.* Jan 2003;26 Suppl 1:S5-20.
4. Gage BF, Waterman AD, Shannon W, Boechler M, Rich MW, Radford MJ. Validation of clinical classification schemes for predicting stroke: results from the National Registry of Atrial Fibrillation. *JAMA.* Jun 13 2001;285(22):2864-2870.
5. Pisters R, Lane DA, Nieuwlaat R, de Vos CB, Crijns HJ, Lip GY. A novel user-friendly score (HAS-BLED) to assess 1-year risk of major bleeding in patients with atrial fibrillation: the Euro Heart Survey. *Chest.* Nov 2010;138(5):1093-1100.
6. Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III). *JAMA.* May 16 2001;285(19):2486-2497.
7. van Gijn J, Hijdra A, Wijdicks EF, Vermeulen M, van Crevel H. Acute hydrocephalus after aneurysmal subarachnoid hemorrhage. *J Neurosurg.* Sep 1985;63(3):355-362.
8. Webb AJ, Ullman NL, Mann S, Muschelli J, Awad IA, Hanley DF. Resolution of intraventricular hemorrhage varies by ventricular region and dose of intraventricular thrombolytic: the Clot Lysis: Evaluating Accelerated Resolution of IVH (CLEAR IVH) program. *Stroke.* Jun 2012;43(6):1666-1668.
9. Hotchkiss RS, Karl IE. The pathophysiology and treatment of sepsis. *N Engl J Med.* Jan 9 2003;348(2):138-150.
10. A randomized trial of diagnostic techniques for ventilator-associated pneumonia. *N Engl J Med.* Dec 21 2006;355(25):2619-2630.
11. Streiner DL, Norman GR. Correction for multiple testing: is there a resolution? *Chest.* Jul 2011;140(1):16-18.
12. Robbins AS, Chao SY, Fonseca VP. What's the relative risk? A method to directly estimate risk ratios in cohort studies of common outcomes. *Ann Epidemiol.* Oct 2002;12(7):452-454.
13. Little RJ, D'Agostino R, Cohen ML, et al. The prevention and treatment of missing data in clinical trials. *N Engl J Med.* Oct 4 2012;367(14):1355-1360.

eFigure 1. Participating centers.

Participating Tertiary Centers - Neurological Departments -		Number of Participants
1. Community hospital Altona	Hamburg	61
2. Community hospital St. Georg	Hamburg	38
3. University hospital Charité	Berlin	160
4. Community hospital Buch	Berlin	47
5. Community hospital	Minden	96
6. University hospital	Leipzig	47
7. Community hospital	Dortmund	58
8. University hospital	Jena	50
9. University hospital	Dresden	41
10. University hospital	Cologne	30
11. Community hospital	Bad Hersfeld	18
12. Community hospital	Fulda	85
13. Community hospital	Koblenz	19
14. Community hospital	Wiesbaden	73
15. University hospital	Würzburg	56
16. Community hospital	Ludwigshafen	22
17. University hospital	Erlangen	122
18. Community hospital	Nuremberg	125
19. Community hospital	Stuttgart	28
Overall		1176

Overview of all participating centers across Germany. Nationwide, 32 tertiary care referral centers (10 University hospitals and 22 University-affiliated community hospitals) were invited to participate and 19 centers (7 University hospitals and 12 University-affiliated large community hospitals) contributed data. The number of contributed participants is reflected by the proportional size of each circle. Germany's two largest cities (Berlin and Hamburg) were represented by two centers (ordered by number of participants). Invited tertiary care centers that did not participate in the study consisted of 3 University Hospitals and 10 University affiliated centers. Reasons for exclusion were: no response (n=4), no interest (n=3), no capacity to contribute data within requested time frame (n=6). In Germany there are ~60 existing tertiary care centers. Of these, we selected 32 centers for invitation according to current suggestions on clinical trial design in order to limit missing data[13]. Hence, selected centers have (i) participated in large cerebrovascular trials in recent years, (ii) Neurological Departments have dedicated teams of study nurses and fellows familiar in recruiting patients for stroke trials and (iii) the stroke and neurointensive care units are run by nationwide well-known stroke specialists. Overall, non-participating and non-invited centers were comparable to participating centers in terms of center setting and characteristics of treated patients according to German-wide stroke quality control database.

eTable 1. Characteristics of the entire cohort of OAC-ICH patients.

OAC-ICH	Overall (n=1,176)
Age† [yrs] (n=1176)	
mean (±SD)	74.1 (±9.2)
median (IQR)	75 (70-80)
Female sex* (n=1176)	486 (41.3%)
Prestroke mRS‡ (n=1142)	0 (0-2)
OAC indications (n=1176)	
Atrial fibrillation*	922 (78.4%)
Mechanical heart valve*	82 (7.0%)
Pulmonary embolism*	52 (4.4%)
Deep vein thrombosis*	46 (3.9%)
Other indications*	74 (6.3%)
Prior comorbidities	
Hypertension* (n=1176)	1002 (85.2%)
Diabetes mellitus* (n=1176)	330 (28.1%)
Dyslipidemia* (n=1176)	296 (25.2%)
Prior stroke* (n=1176)	326 (27.7%)
Coronary artery disease* (n=1176)	481 (40.9%)
Congestive heart failure* (n=1173)	150 (12.8%)
Abnormal kidney function* (n=1169)	288 (24.5%)
Abnormal liver function* (n=1171)	22 (1.9%)
Antiplatelet medication* (n=1170)	123 (10.5%)
$CHADS_2$ score‡ (n=922)	
mean (±SD)	2.4 (±1.2)
median (IQR)	2 (2-3)
High-Risk* (≥2)	713 (77.3%)
HAS-BLED score‡ (n=922)	
mean (±SD)	3.0 (±1.1)
median (IQR)	3 (2-4)
High-Risk* (≥3)	625 (67.8%)
Admission status	
Glasgow Coma Scale‡ (n=1176)	13 (8-15)
NIHSS‡ (n=1144)	13 (6-25)
ICH Score‡ (n=1176)	1 (0-3)
Initial imaging (n=1176)	
Deep ICH*	531 (45.1%)
Lobar ICH*	436 (37.1%)
Cerebellar ICH*	121 (10.3%)
Brainstem ICH*	50 (4.3%)
Primary IVH*	38 (3.2%)
ICH volume‡ [cm^3]	19.3 (6.9-52.8)
Intraventricular hemorrhage*	520 (44.2%)
Graeb Score‡ (n=520)	6 (3-9)
Initial coagulation parameters (n=1176)	
INR‡	2.77 (2.28-3.50)
PTT‡ [s]	42 (36-49)

In-hospital measures (n=1176)	
DNT/DNR orders after diagnosis*	172 (14.6%)
Mechanical ventilation*	456 (38.8%)
ICH-evacuation surgery*	160 (13.6%)
Pneumonia*	377 (32.1%)
Sepsis*	72 (6.1%)
Length of stay‡ [d]	10 (4-17)

Characteristics of the entire cohort of OAC-ICH patients including demographics, indications of OAC, prior comorbidities, initial imaging, and laboratory data as well as in-hospital measures. Scales, scores and abbreviations, with corresponding ranges: prestroke mRS: modified Rankin Scale prior to admission (range 0-5, no functional deficit to severe disability), CHADS2 score (range 0-6, low to high risk of thromboembolism), HAS-BLED score (range 0-9, low to high risk of bleeding complication under OAC), Glasgow Coma Scale (range 3-15, deep coma to alert), NIHSS: National Institutes of Health Stroke Scale (range 0-40 (42= maximum sum, in comatose ataxia is not scored), no deficit to severe neurological deficit), ICH Score: Intracerebral hemorrhage Score (range 0-6, low to high risk of mortality), Graeb Score: ventricular involvement (range 0-12, no intraventricular blood to tamponade of all ventricles); OAC: oral anticoagulation (coumadins), ICH: intracerebral hemorrhage, IVH: intraventricular hemorrhage, PCC: prothrombin-complex concentrates, FFP: fresh frozen plasma, INR: international normalized ratio, PTT: partial thromboplastin time, DNT/DNR: do not treat or resuscitate orders after initial diagnosis. Complete-case analysis for n=1,176; Left column: Number (n) given for patients with available data; * n (%); † mean (±SD); ‡ median (IQR; 25^{th} -75^{th} percentile).

eTable 2. Multivariable model for factors associated with hematoma enlargement.

Multivariable - parameters	Risk ratio (95% CI)	*P* Value *(<0.05)*
Onset to initial imaging [<130min], n=137/271 (50.6%) [≥130min], n=95/278 (34.2%)	**2.284 (1.445-2.949)**	**<0.001**
Diagnosis to treatment [≥80min], n=148/374 (39.6%) [<80min], n=123/371 (33.2%)	**1.559 (1.142-2.130)**	**0.005**
Deep ICH present, n=173/406 (42.6%) absent, n=134/447 (30.0%)	**1.389 (1.012-1.905)**	**0.04**
1st INR-monitoring after reversal reference increment 0.1	**2.294 (1.282-4.098)**	**0.005**
Systolic blood pressure at 4h reference increment 1 mmHg	**1.007 (1.002-1.014)**	**0.02**
NIHSS reference increment 1 point	1.017 (0.998-1.036)	0.07
Mechanical heart valve present, n=32/67 (47.8%) absent, n=275/786 (35.0%)	1.037 (0.496-1.961)	0.96
Coronary artery disease present, n=154/379 (40.6%) absent, n=153/474 (32.3%)	**1.531 (1.018-2.092)**	**0.007**

Multivariable log-binomial regression model analyzing parameters associated with hematoma enlargement. All variables showing significance (*P*-Value <0.05) in univariable analysis were included. Details of included variables: Time-scales were dichotomized by median-split (median of each variable calculated for all patients within analysis), deep ICH consisting of basal ganglia and thalamus ICH, '1st INR-monitoring after reversal' refers to first INR value obtained after initiation of reversal treatment, systolic blood pressure assessed at 4 hours of hospital admission, NIHSS: National Institutes of Health Stroke Scale (range 0-40 (42= maximum sum, in comatose ataxia is not scored), no deficit to severe neurological deficit), mechanical heart valve as indication for prior OAC treatment, coronary artery disease as prior comorbidity before admission for ICH; Potentially modifiable parameters consisting of: diagnosis to treatment, 1st INR-monitoring after reversal, systolic blood pressure at 4h; non-modifiable parameters: symptom onset to imaging, deep ICH location, NIHSS, mechanical heart valve, coronary artery disease; these parameters were used for further adjusted multivariable analysis of hematoma enlargement (Figure 3). For dichotomized variables "present" indicates No.[HE]/total No.[independent variable present] (%), "absent" indicates No.[HE]/total No.[independent variable absent] (%).
Model details (N=543): adjusted quasi-likelihood= 434.886; Wald-chi-square: onset to initial imaging: 5.6, diagnosis to treatment: 6.8, deep ICH: 3.3, 1st INR-monitoring after reversal: 7.4, systolic BP at 4h: 4.0, NIHSS: 2.3, mechanical heart valve: 1.2, CAD: 5.4. Significant parameters are expressed in bold.

eTable 3. Analysis of hematoma enlargement according to extent and timing of INR reversal.

Time to Reversal (min)	**Achieved INR No. (HE-rate %) INR < 1.20**		**Hematoma enlargement**	
	Yes	**No**	**Risk ratio (95%CI)**	***P* Value**
0 - 119	**8/42 (19.0%)**	**299/811 (36.9%)**	**0.52 (0.28-0.97)**	**0.02**
120 - 239	**18/90 (20.0%)**	**289/763 (37.9%)**	**0.53 (0.35-0.81)**	**<0.001**
240 - 359	9/26 (34.6%)	298/827 (36.0%)	0.96 (0.56-1.64)	0.89
≥ 360	39/114 (34.2%)	268/739 (36.3%)	0.94 (0.72-1.24)	0.67
total	**74/272 (27.2%)**	**233/581 (40.1%)**	**0.68 (0.55-0.84)**	**<0.001**
	INR 1.20-1.29			
	Yes	**No**	**Risk ratio (95%CI)**	***P* Value**
0 - 119	**6/35 (17.1%)**	**301/818 (36.8%)**	**0.47 (0.22-0.97)**	**0.02**
120 - 239	**11/50 (22.0%)**	**296/803 (36.9%)**	**0.60 (0.35-1.00)**	**0.03**
240 - 359	7/21 (33.3%)	300/832 (36.1%)	0.92 (0.50-1.70)	0.79
≥ 360	18/54 (33.3%)	289/799 (36.2%	0.92 (0.63-1.36)	0.67
total	**42/160 (26.3%)**	**265/693 (38.2%)**	**0.69 (0.52-0.91)**	**0.004**
	INR 1.30-1.39			
	Yes	**No**	**Risk ratio (95%CI)**	***P* Value**
0 - 119	4/15 (26.7%)	303/838 (36.2%)	0.74 (0.32-1.72)	0.45
120 - 239	15/39 (38.5%)	292/814 (35.9%)	1.07 (0.71-1.61)	0.74
240 - 359	6/14 (42.9%)	301/839 (35.9%)	1.19 (0.65-2.20)	0.59
≥ 360	14/37 (37.8%)	293/816 (35.9%)	1.05 (0.69-1.61)	0.81
total	39/105 (37.1%)	268/748 (35.8%)	1.04 (0.79-1.35)	0.79
	INR 1.40-1.49			
	Yes	**No**	**Risk ratio (95%CI)**	***P* Value**
0 - 119	6/14 (42.9%)	301/839 (35.9%)	1.19 (0.65-2.20)	0.59
120 - 239	13/30 (43.3%)	294/823 (35.7%)	1.21 (0.80-1.85)	0.39
240 - 359	6/14 (42.9%)	301/839 (35.9%)	1.19 (0.65-2.20)	0.59
≥ 360	13/28 (46.4%)	294/825 (35.6%)	1.30 (0.87-1.96)	0.24
total	38/86 (44.2%)	269/767 (35.1%)	1.26 (0.98-1.63)	0.09
	INR ≥ 1.50			
	Yes	**No**	**Risk ratio (95%CI)**	***P* Value**
0 - 119	7/18 (38.9%)	300/835 (35.9%)	1.08 (0.60-1.95)	0.79
120 - 239	24/59 (40.7%)	283/794 (35.6%)	1.14 (0.83-1.57)	0.44
240 - 359	12/29 (41.4%)	295/824 (35.8%)	1.16 (0.74-1.80)	0.54
≥ 360	**71/124 (57.3%)**	**236/729 (32.4%)**	**1.77 (1.47-2.13)**	**<0.001**
total	**114/230 (49.6%)**	**193/623 (31.0%)**	**1.60 (1.34-1.90)**	**<0.001**

Data was categorized – "time of reversal" presented as 2h intervals (time range 0 to ≥360min) starting at time of hospital admission until 1st INR-monitoring after reversal treatment confirmed corresponding INR thresholds; – INR thresholds were categorized by 0.10 intervals (INR range <1.20 to ≥1.50). The frequency data was analyzed for its association with hematoma enlargement. Abbreviations: HE: hematoma enlargement, CI: confidence interval. Significant parameters are expressed in bold.

eTable 4. Analysis of hematoma enlargement according to systolic blood pressures at 4 hour intervals.

Systolic blood pressure	**Hematoma enlargement, No. (%)**	***Chi-square***
[mmHg]	**On admission**	***P* Value**
<120	12/36 (33.3%)	
120-139	16/53 (30.2%)	
140-159	58/168 (34.5%)	**0.04**
160-179	66/165 (40.0%)	
≥180	118/279 (42.3%)	
[mmHg]	**at 4 hours**	***P* Value**
<120	57/173 (32.9%)	
120-139	35/106 (33.0%)	
140-159	75/225 (33.3%)	**<0.001**
160-179	55/120 (45.8%)	
≥180	43/67 (64.2%)	
[mmHg]	**at 8 hours**	***P* Value**
<120	74/202 (36.6%)	
120-139	41/131 (31.3%)	
140-159	85/215 (39.5%)	0.20
160-179	44/101 (43.6%)	
≥180	13/33 (39.4%)	
[mmHg]	**at 12 hours**	***P* Value**
<120	36/123 (29.3%)	
120-139	90/236 (38.1%)	
140-159	71/197 (36.0%)	0.50
160-179	40/107 (37.5%)	
≥180	12/28 (42.9%)	
[mmHg]	**at 16 hours**	***P* Value**
<120	34/98 (34.7)	
120-139	84/226 (37.2%)	
140-159	77/233 (33.0%)	0.75
160-179	38/101 (37.6%)	
≥180	8/25 (32.0%)	

Systolic blood pressure was categorized as 20 mmHg intervals (range <120 to ≥180 mmHg) for its corresponding time points of assessment and (on admission until 16 hours thereafter), frequency data was analyzed for its association with hematoma enlargement dichotomized for < 160 mmHg *vs.* ≥ 160 mmHg at each specific time point (horizontal line between the 3rd and 4th blood pressure category with corresponding *P*-Value of dichotomized analysis). Note that blood pressure measurements were not available for all patients at exact time-points. Abbreviation: HE: hematoma enlargement. Significant parameters are expressed in bold.

eTable 5. Dichotomized analysis of OAC resumption-status for the entire cohort.

Patients with 1y follow-up (n=719)	OAC resumption (n=172)	No OAC resumption (n=547)	*P* Value
Time to treatment‡ [days]	31 (18-65)	25 (13-46)	0.004^
Age† [y] (n=719)	70.6 (±9.9)	74.5 (±8.6)	**<0.001**
Female sex* (n=719)	53 (30.8%)	217 (39.7%)	0.04^
Prestroke mRS‡* (n=704)	0 (0-1)	0 (0-1)	0.18
OAC indications (n=719)			
Atrial fibrillation* (n=566)	110 (64.0%)	456 (83.4%)	**<0.001**
Mechanical heart valve* (n=50)	34 (19.8%)	16 (2.9%)	**<0.001**
Pulmonary embolism* (n=33)	8 (4.7%)	25 (4.6%)	0.86
Deep vein thrombosis* (n=31)	10 (5.8%)	21 (3.8%)	0.27
Other indications* (n=39)	10 (5.8%)	29 (5.3%)	0.79
Prior comorbidites			
Hypertension* (n=719)	149 (86.6%)	476 (87.0%)	0.89
Diabetes mellitus* (n=719)	48 (27.9%)	172 (31.4%)	0.38
Dyslipidemia* (n=719)	62 (36.0%)	169 (30.9%)	0.21
Prior stroke* (n=719)	43 (25.0%)	171 (31.3%)	0.12
Coronary artery disease* (n=719)	77 (44.8%)	239 (43.7%)	0.81
Congestive heart failure* (n=718)	18 (10.5%)	52 (9.5%)	0.71
Abnormal kidney function* (n=715)	42 (24.4%)	157 (28.7%)	0.27
Abnormal liver function* (n=717)	3 (1.7%)	11 (2.0%)	0.56
Antiplatelet medication* (n=716)	12 (7.0%)	48 (8.8%)	0.46
Admission status			
Glasgow Coma Scale‡ (n=719)	14 (13-15)	14 (13-15)	0.21
NIHSS‡ (n=707)	7 (3-14)	11 (5-18)	**0.001**
ICH Score‡ (n=719)	1 (0-1)	1 (0-2)	0.002^
Imaging (n=719)			
Deep ICH*	79 (45.9%)	247 (45.1%)	0.86
Lobar ICH*	65 (37.8%)	211 (38.6%)	0.86
Cerebellar ICH*	16 (9.3%)	65 (11.9%)	0.35
Brainstem ICH*	5 (2.9%)	11 (2.0%)	0.55
Primary IVH*	7 (4.1%)	13 (2.4%)	0.29
ICH volume‡ [cm^3]	11.5 (3.9-25.1)	13.5 (5.3-33.9)	0.08
Intraventricular hemorrhage*	49 (28.5%)	196 (35.8%)	0.08
Graeb Score‡ (n=245)	4 (3-7)	4 (2-7)	0.32
Hematoma enlargement* (n=672)	43/155 (27.7%)	175/517 (33.8%)	0.15
In-hospital measures (n=719)			
Ventilation*	46 (26.7%)	170 (31.1%)	0.28
Pneumonia*	51 (29.7%)	227 (41.5%)	0.005^
Sepsis*	7 (4.1%)	26 (4.8%)	0.71
External ventricular drain*	30 (17.4%)	108 (19.7%)	0.50
Length of stay‡ [d]	12 (8-19)	13 (9-20)	0.42

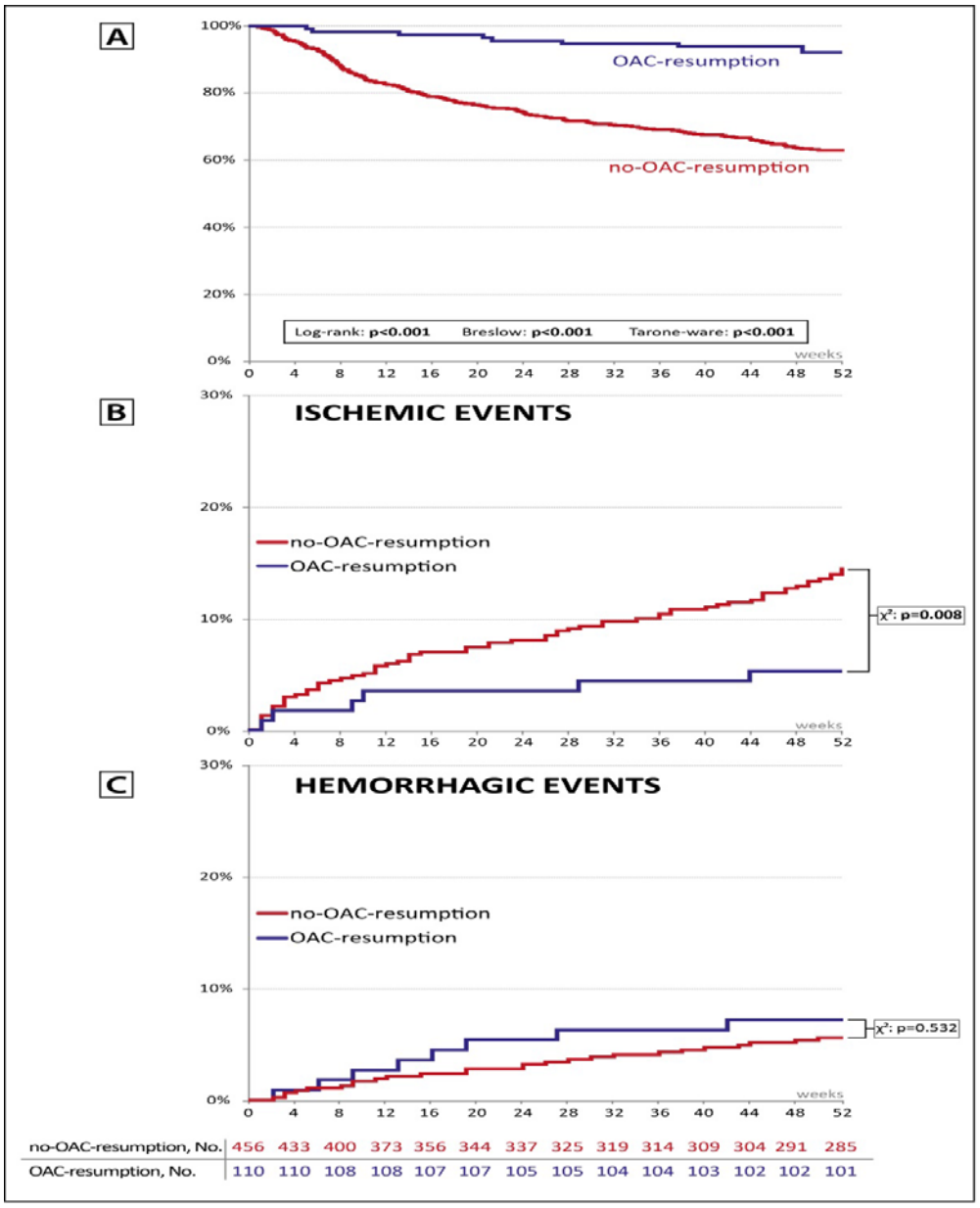
Dichotomized analysis of baseline characteristics, prior comorbidities, neurological admission status, imaging and treatment parameters according to OAC resumption status. Scales, scores and abbreviations, with corresponding ranges: prestroke mRS: modified Rankin Scale prior to admission (range 0-5, no functional deficit to severe disability), Glasgow Coma Scale (range 3-15, deep coma to alert), NIHSS: National Institutes of Health Stroke Scale (range 0-40 (42= maximum sum, in comatose ataxia is not scored), no deficit to severe neurological deficit), ICH Score: Intracerebral hemorrhage Score (range 0-6, low to high risk of mortality), Graeb Score: ventricular involvement (range 0-12, no intraventricular blood to tamponade of all ventricles); OAC: oral anticoagulation (coumadins), ICH: intracerebral haemorrhage, IVH: intraventricular hemorrhage. Complete case analysis for n=719; Left column: Number (n) of patients with available data; * n (%); † mean (±SD); ‡ median (IQR; 25^{th} -75^{th} percentile); ^ not sig. after Bonferroni correction (corrected significance level $P<0.00143$). Significant parameters are expressed in bold.

eTable 6. Dichotomized analysis of OAC resumption status for A-fib patients.

OAC-ICH patients with A-fib (n=566)	OAC resumption (n=110)	No OAC resumption (n=456)	*P* Value
Time to treatment‡ [days]	32 (20-69)	33 (14-55)	0.24
Age† [y] (n=566)	72.9 (±7.7)	75.5 (±7.8)	0.002^
Female sex* (n=566)	36 (32.7%)	182 (39.9%)	0.16
Pre-mRS‡ (n=554)	0 (0-1)	0 (0-1)	0.37
Prior comorbidities			
Hypertension* (n=566)	95 (86.4%)	383 (84.0%)	0.54
Diabetes mellitus* (n=566)	38 (34.5%)	144 (31.6%)	0.55
Dyslipidemia* (n=566)	39 (35.5%)	141 (30.9%)	0.36
Prior stroke* (n=566)	29 (26.4%)	138 (30.3%)	0.42
Coronary artery disease* (n=566)	54 (49.1%)	203 (44.5%)	0.39
Congestive heart failure* (n=565)	11 (10.0%)	46 (10.1%)	0.89
Abnormal kidney function* (n=563)	23 (20.9%)	123 (27.0%)	0.19
Abnormal liver function* (n=565)	1 (0.9%)	5 (1.1%)	0.87
Antiplatelet medication* (n=563)	9 (8.2%)	40 (8.8%)	0.84
$CHADS_2$ score‡ (n=566)			
median (IQR)	2 (1-3)	2 (2-3)	0.09
High-Risk* (≥2)	81 (73.6%)	364 (79.8%)	0.16
HAS-BLED score‡ (n=566)			
median (IQR)	3 (2-4)	3 (2-4)	0.23
High-Risk* (≥3)	69 (62.7%)	310 (68.0%)	0.29
Admission status			
Glasgow Coma Scale‡ (n=566)	14 (13-15)	14 (13-15)	0.06
NIHSS‡ (n=554)	7 (3-13)	10 (4-17)	0.002^
ICH Score‡ (n=566)	1 (0-1)	1 (0-2)	**0.001**
Imaging (n=566)			
Deep ICH*	52 (47.3%)	201 (44.1%)	0.54
Lobar ICH*	38 (34.5%)	179 (39.3%)	0.36
Cerebellar ICH*	11 (10.0%)	54 (11.8%)	0.58
Brainstem ICH*	4 (3.6%)	12 (2.6%)	0.75
Primary IVH*	5 (4.5%)	10 (2.2%)	0.18
ICH volume‡ [cm^3]	11.0 (3.9-22.0)	11.9 (4.8-31.8)	0.10
Intraventricular hemorrhage*	30 (27.3%)	156 (34.2%)	0.16
Graeb Score‡ (n=186)	4 (2-8)	4 (2-7)	0.47
Hematoma enlargement* (n=519)	22/103 (21.4%)	128/416 (30.8%)	0.06
In-hospital measures (n=566)			
Ventilation*	25 (22.7%)	137 (30.0%)	0.13
Pneumonia*	32 (29.1%)	186 (40.8%)	0.02^
Sepsis*	3 (2.7%)	20 (4.4%)	0.59
External ventricular drain*	15 (13.6%)	82 (18.0%)	0.28
Length of stay* [d]	12 (8-16)	13 (9-19)	0.11
mRS at discharge (0-3)	55 (50.0%)	123 (27.0%)	**<0.001**

Dichotomized analysis according to OAC resumption status of baseline characteristics, prior comorbidities, neurological admission status, imaging and treatment parameters for patients with A-fib only. Scales, scores and abbreviations, with corresponding ranges: prestroke mRS: modified Rankin Scale prior to admission (range 0-5, no functional deficit to severe disability), CHADS2 score (range 0-6, low to high risk of thromboembolism), HAS-BLED score (range 0-9, low to high risk of bleeding complication under OAC), Glasgow Coma Scale (range 3-15, deep coma to alert), NIHSS: National Institutes of Health Stroke Scale (range 0-40 (42= maximum sum, in comatose ataxia is not scored), no deficit to severe neurological deficit), ICH-Score: Intracerebral hemorrhage Score (range 0-6, low to high risk of mortality), Graeb Score: ventricular involvement (range 0-12, no intraventricular blood to tamponade of all ventricles); OAC: oral anticoagulation (coumadins), ICH: intracerebral haemorrhage, IVH: intraventricular hemorrhage. Complete case analysis for n=566; Left column: Number (n) of patients with available data; † mean (±SD); ‡ median (IQR; 25^{th} -75^{th} percentile); ^ not sig. after Bonferroni correction (corrected significance level $P<0.00143$). Significant parameters are expressed in bold.

eFigure 2. Unmatched survival and event rates in A-fib patients – analyzing OAC resumption-status.



Unmatched Kaplan-Meier survival curves, ischemic, and hemorrhagic event rates in A-fib patients with and without OAC resumption. (A) Kaplan-Meier survival rates of patients with A-fib with and without OAC resumption from index-ICH until 1-year follow-up, analyzed by log-rank, Breslow and Tarone-Ware testing, with corresponding *P* Values. (B) Incidence rates of new ischemic events over the 1-year follow-up period in patients with and without OAC resumption. (C) Incidence rates of hemorrhagic events over the 1-year follow-up period in patients with and without OAC resumption. Numbers for patients at risk apply to part A-C. One year after OAC-ICH 8.2% (n=9/110) of resumed patients versus 37.5% (n=171/456) of patients without OAC resumption had died (*P* <0.001). The crude incidence of bleeding events was not significantly different among A-fib patients with and without OAC resumption (OAC resumed: 7.3% (n=8/110) *versus* 5.7% (n=26/456) non resumed patients; *P* =0.532), the incidence of new ischemic events was significantly increased in patients without OAC resumption (5.4% (n=6/110) versus 14.9% (n=68/456); *P* =0.008).

eTable 7. Analyses of confounders within OAC resumption analysis for A-fib patients – before and after propensity score matching.

OAC-ICH patients with atrial fibrillation (n=566)	OAC resumption (n=110)	No OAC resumption (n=456)	*P* Value	std. mean diff.
Before propensity matching				
Age† [y]	72.9 (±7.7)	75.5 (±7.8)	0.002	**0.35**
Prestroke mRS‡	0 (0-1)	0 (0-1)	0.37	**0.09**
$CHADS_2$ score‡				
median (IQR)	2 (1-3)	2 (2-3)	0.09	**0.18**
Admission status‡				
NIHSS‡	7 (3-13)	10 (4-17)	0.002	**0.33**
Imaging				
ICH volume‡ [cm^3]	11.0 (3.9-22.0)	11.9 (4.8-31.8)	0.10	**0.30**
Intraventricular hemorrhage*	30 (27.3%)	156 (34.2%)	0.16	**0.17**
Hematoma enlargement*	22/103 (21.4%)	128/416 (30.8%)	0.06	**0.19**
Hospital discharge				
mRS‡	3 (2-4)	4 (3-5)	<0.001	**0.55**
OAC-ICH patients with atrial fibrillation (n=261)	**OAC resumption (n=108)**	**No OAC resumption (n=153)**	***P* Value**	**std. mean diff.**
After propensity matching				
Age† [y]	73.1 (±7.6)	74.2 (±8.8)	0.29	**0.07**
Prestroke mRS‡	0 (0-1)	0 (0-1)	0.57	**0.06**
$CHADS_2$ score‡				
median (IQR)	2 (1-3)	2 (2-3)	0.57	**0.04**
On admission status‡				
NIHSS‡	7 (3-13)	7 (3-14)	0.97	**0.05**
Imaging				
ICH volume‡ [cm^3]	10.5 (3.5-20.2)	9.9 (3.6-20.7)	0.98	**0.05**
Intraventricular hemorrhage*	29 (26.9%)	47 (30.7%)	0.50	**0.03**
Hematoma enlargement*	22 (20.4%)	31 (20.3%)	0.88	**0.04**
Hospital discharge				
mRS‡	4 (3-4)	4 (3-4)	0.29	**0.01**

Comparison of parameters possibly showing confounding by indication for OAC resumption analysis, presented are standardized mean differences before and after the matching procedure. Variables used for calculation of the propensity score in patients with A-fib only, were showing a statistical association with OAC resumption status (*P* <0.2), prestroke mRS included for direct effects on discharge mRS value. Scales, scores and abbreviations, with corresponding ranges: pre- and at hospital discharge mRS: modified Rankin Scale prior (range 0-6, no functional deficit to death), $CHADS_2$ Score (range 0-6, low to high risk of thromboembolism), NIHSS: National Institutes of Health Stroke Scale (range 0-40 (42= maximum sum, yet in comatose ataxia is not scored), no deficit to severe neurological deficit), ICH: intracerebral hemorrhage. Given in bold are standardized mean differences before and after matching of all variables used for calculation. * n (%); † mean (±SD); ‡ median (IQR; 25^{th} -75^{th} percentile);

eTable 8. Propensity-matched analysis of event and incidence rates in A-fib patients – new ischemic stroke *versus* recurrent ICH.

Patients with atrial fibrillation	**No. of Patients**	**No. of events (%)**	***P* Value**	**Incidence rate per 100 patient years (95%CI)**	***P* Value**
New cerebral Infarction	261	20 (7.7%)		8.7 (3.8-12.6)	
According to treatment					
OAC resumption	108	4 (3.7%)	**0.04**	3.9 (1.9-5.8)	**0.02**
No OAC resumption	153	16 (10.5%)		12.7 (6.5-19.1)	
Recurrent ICH	261	9 (3.4%)		3.9 (1.4-6.5)	
According to treatment					
OAC resumption	108	4 (3.7%)	0.55	3.9 (1.9-5.8)	0.92
No OAC resumption	153	5 (3.3%)		3.9 (2.2-5.7)	

Analysis included all OAC-ICH patients with A-fib after propensity matching. Given are: total number of patients for analysis, raw number of events and incidence rates (per 100 patient-years) calculated for time on each specific treatment (OAC *versus* no-OAC as defined) during 1 year of follow-up. Significant parameters are expressed in bold.

eTable 9. Propensity-matched Cox regression analyses of long-term mortality in A-fib patients.

Patients with atrial fibrillation (n=261)	No. of patients	No. of events (%)	Hazard ratio (95%CI)	*P* Value	Adjusted Hazard ratio 95%CI)	*P* Value
Overall	261	56 (21.5%)				
OAC resumption	108	9 (8.3%)	0.233 (0.114-0.476)	**<0.001**	0.258 (0.125-0.534)	**<0.001**
No OAC resumption	153	47 (30.7%)	1 (reference)		1 (reference)	

Cox regression analysis included all OAC-ICH patients with A-fib after propensity matching. Hazard ratio model was adjusted for events (new ischemic, recurrent hemorrhagic) during 1 year of follow-up and by propensity score (age, ICH volume, IVH, hematoma growth, NIHSS, $CHADS_2$ score as well as pre- and discharge-mRS). Assumption of proportionality was tested by locally weighted scatterplot smoothing of partial Schoenfeld residuals and PH testing. All covariates met the assumption. Significant parameters are expressed in bold.

eTable 10. Multivariable model of functional improvement (mRS ≤3) for poor grade survivors (mRS =4-5).

Multivariable - parameters	Risk ratio (95% CI)	*P* Value *(<0.05)*
Age reference increment 1 year	**0.968 (0.945-0.993)**	**0.011**
NIHSS reference increment 1 point	**0.956 (0.922-0.992)**	**0.016**
ICH volume [≥16.1cm³], n=40/227 (17.6%) [<16.1cm³], n=78/284 (27.5%)	**0.576 (0.334-0.994)**	**0.035**
Lobar ICH present, n=49/184 (26.6%) absent, n=69/327 (21.1%)	1.543 (0.916-2.599)	0.103
Hematoma enlargement present, n=36/159 (22.6%) absent, n=67/279 (24.0%)	0.810 (0.496-1.324)	0.401
Intraventricular hemorrhage present, n=39/215 (18.1%) absent, n=79/296 (26.7%)	0.728 (0.433-1.225)	0.232
Hemoglobin level on admission reference increment 10 g/L	**1.197 (1.070-1.338)**	**0.002**
New ischemic stroke present, n=3/53 (5.7%) absent, n=115/458 (25.1)	**0.113 (0.016-0.792)**	**0.028**

Multivariable log-binomial regression model analyzing parameters associated with functional improvement (mRS≤3) of poor-grade survivors (mRS 4-5) during 1 year follow-up. All variables showing a significant *P* Value < 0.05 in univariate analysis were included. Details of included variables: NIHSS: National Institutes of Health Stroke Scale (range 0-40 (42= maximum sum, in comatose ataxia is not scored), no deficit to severe neurological deficit), ICH volume included by median split (≥16.1ml), Lobar ICH location, hematoma enlargement > 33% relative volume increase, hemoglobin level on hospital admission, new ischemic stroke during 1 year follow-up; for dichotomized variables "present" indicates No.[mRS 0-3]/total No.[independent variable present] (%), "absent" indicates No.[mRS 0-3]/ total No.[independent variable absent] (%). Model details (N=351): adjusted quasi-likelihood: 340.238; Wald-chi-square: age: 6.5, NIHSS: 5.8, ICH-volume: 4.0, Lobar-ICH: 3.2, Hematoma enlargement: 1.5, IVH: 1.7, new ischemic stroke: 4.8, Significant parameters are expressed in bold.

eTable 11. Analysis of long-term outcome – favorable *versus* unfavorable functional outcome.

OAC-ICH	1 Year Follow-up (n=1,083)		*P* Value
	mRS 0-3 (n=298)	mRS 4-6 (n=785)	
Age† [y] (n=1083)	72.7 (±9.1)	74.7 (±9.1)	**<0.001**
Female sex* (n=1083)	111 (37.2%)	336 (42.8%)	0.10
Prestroke mRS‡ (n=1062)	0 (0-1)	1 (0-2)	**<0.001**
Prior comorbidities			
Hypertension* (n=1083)	253 (84.9%)	671 (85.5%)	0.81
Diabetes mellitus* (n=1083)	83 (27.9%)	229 (29.2%)	0.67
Dyslipidemia* (n=1083)	108 (36.2%)	176 (22.4%)	**<0.001**
Prior stroke* (n=1083)	71 (23.8%)	233 (29.7%)	0.06
Coronary artery disease* (n=1083)	125 (41.9%)	341 (43.4%)	0.65
Congestive heart failure* (n=1080)	33 (11.1%)	91 (11.6%)	0.81
Abnormal kidney function* (n=1077)	73 (24.5%)	208 (26.5%)	0.50
Abnormal liver function* (n=1076)	3 (1.0%)	18 (2.3%)	0.17
Antiplatelet medication* (n=1081)	26 (8.7%)	79 (10.1%)	0.51
OAC indications (n=1083)			
Atrial fibrillation*	233 (78.2%)	613 (78.1%)	0.98
Mechanical heart valve*	24 (8.1%)	53 (6.8%)	0.46
Pulmonary embolism*	13 (4.4%)	36 (4.6%)	0.89
Deep vein thrombosis*	13 (4.4%)	27 (3.4%)	0.47
Other indications*	15 (5.0%)	56 (7.1%)	0.21
$CHADS_2$ score‡ (n=846)			
median (IQR)	2 (1-3)	2 (2-3)	0.06
High-Risk* (≥2)	171 (73.4%)	489 (79.8%)	0.04^
HAS-BLED score‡ (n=846)			
median (IQR)	3 (2-3)	3 (2-4)	0.02
High-Risk* (≥3)	141 (60.5%)	438 (71.5%)	0.002^
Admission status (n=1083)			
Glasgow Coma Scale‡	15 (14-15)	12 (5-14)	**<0.001**
NIHSS‡	5 (3-11)	19 (11-28)	**<0.001**
ICH Score‡	1 (0-1)	2 (1-3)	**<0.001**
Initial imaging (n=1083)			
Deep ICH*	117 (39.3%)	380 (48.4%)	0.007^
Lobar ICH*	135 (45.3%)	271 (34.5%)	**0.001**
Cerebellar ICH*	31 (10.4%)	71 (9.0%)	0.49
Brainstem ICH*	6 (2.0%)	40 (5.1%)	0.02^
Primary IVH*	9 (3.0%)	23 (2.9%)	0.92
ICH volume‡ [cm^3]	9.3 (3.1-21.1)	30.4 (11.3-77.3)	**<0.001**
Intraventricular hemorrhage*	63 (21.1%)	430 (54.8%)	**<0.001**
Graeb Score‡ (n=493)	4 (2-6)	6 (3-9)	**<0.001**
Hematoma enlargement* (n=838)	42/249 (16.9%)	262/589 (44.5%)	**<0.001**
Initial coagulation parameters (n=1083)			
INR‡	2.60 (2.20-3.30)	2.87 (2.30-3.70)	**<0.001**
PTT‡ [s]	40 (36-49)	43 (36-50)	0.17

eTable 11. continued.

OAC-ICH patients	1 Year Follow-up (n=1,083)		*P* Value
	mRS 0-3 (n=298)	mRS 4-6 (n=785)	
In-hospital measures (n=1083)			
Intubated on arrival*	8 (2.7%)	155 (19.7%)	**<0.001**
Mechanical ventilation*	38 (12.8%)	400 (51.0%)	**<0.001**
Pneumonia*	57 (19.1%)	343 (43.7%)	**<0.001**
Sepsis*	2 (0.7%)	82 (10.4%)	**<0.001**
Length of stay‡ [d]	11 (8-15)	8 (2-16)	**<0.001**
ICH-evacuation surgery*	30 (10.1%)	116 (14.8%)	0.04^
External ventricular drain*	27 (9.1%)	155 (19.7%)	**<0.001**
Intraventricular lysis* (n=182)	10/27 (37.0%)	24/155 (15.5%)	0.008^
Osmotherapy*	20 (6.7%)	119 (15.2%)	**<0.001**
Thrombosis prophylaxis*	237 (79.5%)	455 (58.0%)	**<0.001**

Dichotomized analysis of favorable (mRS 0-3) *versus* unfavorable (mRS 4-6) functional outcome comparing baseline characteristics, prior comorbidities, neurological admission status, imaging and treatment parameters for all patients with 1-year follow-up. Scales, scores and abbreviations, with corresponding ranges: pre-mRS: modified Rankin Scale prior to admission (range 0-5, no functional deficit to severe disability), CHADS2 Score (range 0-6, low to high risk of thromboembolism), HAS-BLED (range 0-9, low to high risk of bleeding complication under OAC), Glasgow Coma Scale (range 3-15, deep coma to alert), NIHSS: National Institutes of Health Stroke Scale (range 0-40 (42= maximum sum, yet in comatose ataxia is not scored), no deficit to severe neurological deficit), ICH Score: Intracerebral hemorrhage Score (range 0-6, low to high risk of mortality), Graeb Score: ventricular involvement (range 0-12, no intraventricular blood to tamponade of all ventricles); OAC: oral anticoagulation (coumadins), ICH: intracerebral haemorrhage, IVH: intraventricular hemorrhage. Complete-case analysis for n=1083, Left column: Number (n) of patients with available data, † mean (±SD); ‡ median (IQR; 25^{th} -75^{th} percentile); ^ not sig. after Bonferroni correction (corrected significance level p<0.00111). Significant parameters are expressed in bold.

eTable 12. Multivariable model of unfavorable long-term outcome for the entire cohort.

Multivariable - parameters	Risk ratio (95% CI)	*P* Value *(<0.05)*
Age reference increment 1 year	**1.019 (1.003-1.036)**	**0.018**
NIHSS reference increment 1 point	**1.057 (1.034-1.079)**	**<0.001**
ICH volume [≥16.1cm³], n=483/564 (85.6%) [<16.1cm³], n=302/519 (58.2%)	**1.388 (1.020-1.889)**	**0.037**
Hematoma enlargement present, n=262/304 (86.2%) absent, n=327/534 (61.2%)	**1.569 (1.186-2.075)**	**0.002**
Intraventricular hemorrhage present, n=430/493 (87.2%) absent, n=355/590 (60.2%)	**1.608 (1.193-2.167)**	**0.002**
New ischemic stroke present, n=45/63 (71.4%) absent, n=384/656 (58.5%)	**1.554 (1.101-2.419)**	**0.024**
Recurrent ICH present, n=27/30 (90.0%) absent, n=394/689 (57.2%)	**2.884 (1.203-8.636)**	**0.028**
OAC resumption present, n=54/172 (31.4%) absent, n=367/547 (67.1%)	**0.330 (0.205-0.531)**	**<0.001**

Multivariable log-binomial regression model analyzing factors associated with unfavorable functional long-term outcome (mRS 4-6) at 1 year. Details of included variables: NIHSS: National Institutes of Health Stroke Scale (range 0-40 (42= maximum sum, in comatose ataxia is not scored), no deficit to severe neurological deficit), ICH volume included by median split (≥16.1ml), hematoma enlargement > 33% relative volume increase, new ischemic stroke during 1 year follow-up, recurrent ICH during 1 year follow-up, OAC resumption after index ICH; for dichotomized variables "present" indicates No.[mRS 4-6]/total No.[independent variable present] (%), "absent" indicates No.[mRS 4-6]/total No.[independent variable absent] (%). Model details (N=515): adjusted quasi-likelihood= 490.832; Wald-chi-square: age=5.6, NIHSS=25.4, ICH-volume=5.4, hematoma enlargement=10.0, Intraventricular hemorrhage=9.7, new ischemic stroke=5.1, recurrent ICH=4.9, OAC resumption=20.9; Significant parameters are expressed in bold.

eTable 13. Multivariable model of unfavorable long-term outcome for propensity-matched A-fib patients.

Multivariable – parameters	Risk ratio (95% CI)	*P* Value *(<0.05)*
Age reference increment 1 year	1.005 (0.990-1.021)	0.520
NIHSS reference increment 1 point	**1.047 (1.027-1.067)**	**<0.001**
ICH volume [≥10.3cm³], n=63/131 (48.1%) [<10.3cm³], n=48/130 (36.9%)	1.305 (0.994-1.715)	0.055
Intraventricular hemorrhage present, n=45/76 (59.2%) absent, n=66/185 (35.7%)	1.223 (0.893-1.673)	0.209
New ischemic stroke present, n=13/20 (65.0%) absent, n=98/241 (40.7%)	**1.432 (1.055-1.943)**	**0.021**
Recurrent ICH present, n=8/9 (88.9%) absent, n=103/252 (40.9%)	**2.581 (1.708-3.900)**	**<0.001**
OAC resumption present, n=30/108 (27.8%) absent, n=91/153 (59.5%)	**0.552 (0.394-0.775)**	**0.001**

Multivariable log-binomial regression model of the propensity-matched cohort analyzed for factors associated with unfavorable functional long-term outcome (mRS 4-6) at 1 year. Details of included variables: NIHSS: National Institutes of Health Stroke Scale (range 0-40 (42= maximum sum, in comatose ataxia is not scored), no deficit to severe neurological deficit), ICH volume included by median split (≥10.3ml), new ischemic stroke during 1 year follow-up, recurrent ICH during 1 year follow-up, OAC resumption after index ICH; for dichotomized variables "present" indicates No.[mRS 4-6]/total No.[independent variable present] (%), "absent" indicates No.[mRS 4-6]/total No.[independent variable absent] (%). Model details (N=242): adjusted quasi-likelihood= 159.346; Wald-chi-square: age=1.4, NIHSS=22.9, ICH-volume=3.7, IVH=1.6, new ischemic stroke: 5.3, recurrent ICH: 20.2, OAC-resumption: 11.8; Significant parameters are expressed in bold.

eTable 14. Comparison of surviving patients included versus those excluded for resumption and long-term outcome analyses.

Surviving Patients (n=812)	**included (n=719)**	**excluded (n=93)**	***P* Value**
Age† [y]	73.6 (±9.1)	72.4 (±9.2)	0.24
Female sex*	270 (37.6%)	37 (39.8%)	0.68
Prestroke mRS‡*	0 (0-1)	0 (0-1)	0.47
OAC indication			
Atrial fibrillation*	566 (78.7%)	73 (78.5%)	0.99
Mechanical heart valve*	50 (7.0%)	5 (5.4%)	0.57
Pulmonary embolism*	33 (4.6%)	3 (3.2%)	0.61
Deep vein thrombosis*	31(4.3%)	6 (6.5%)	0.42
Other indications*	39 (5.4%)	6 (6.5%)	0.68
Prior comorbidites			
Hypertension*	625 (86.9%)	78 (83.9%)	0.42
Diabetes mellitus*	220 (30.6%)	23 (24.7%)	0.25
Dyslipidemia*	231 (32.1%)	22 (23.7%)	0.10
Prior stroke*	214 (29.8%)	22 (23.7%)	0.22
Coronary artery disease*	316 (43.9%)	41 (44.1%)	0.99
Congestive heart failure*	70 (9.7%)	5 (5.4%)	0.17
Abnormal kidney function*	199 (27.7%)	17 (18.3%)	0.05
Abnormal liver function*	14 (1.9%)	2 (2.2%)	0.99
Antiplatelet medication*	60 (8.3%)	10 (10.8%)	0.43
Admission status			
Glasgow Coma Scale‡	14 (12-15)	14 (13-15)	0.06
NIHSS‡	9 (4-17)	7 (2-12)	0.002^
ICH Score‡	1 (0-2)	1 (0-1)	0.08
Imaging			
Deep ICH*	327 (45.5%)	39 (41.9%)	0.52
Lobar ICH*	277 (38.5%)	33 (35.5%)	0.57
Cerebellar ICH*	81 (11.3%)	11 (11.8%)	0.86
Brainstem ICH*	16 (2.2%)	4 (4.3%)	0.27
Primary IVH*	18 (2.5%)	6 (6.4%)	0.05^
ICH volume‡ [cm^3]	12.8 (4.9-31.7)	10.8 (5.2-19.4)	0.15
Intraventricular hemorrhage*	245 (34.1%)	28 (30.1%)	0.45
Graeb Score‡ (n=273)	4 (2-7)	3 (1-5)	0.04^
Hematoma enlargement*	218/672 (32.4%)	17/52 (32.7%)	0.98
In-hospital measures (n=719)			
Ventilation*	216 (30.0%)	24 (25.8%)	0.40
Pneumonia*	278 (38.7%)	26 (28.0%)	0.04^
Sepsis*	33 (4.6%)	5 (5.4%)	0.79
External ventricular drain*	138 (19.2%)	16 (17.2%)	0.65
Length of stay‡ [d]	13 (9-20)	13 (8-20)	0.54

Dichotomized comparison of baseline characteristics, prior comorbidities, neurological admission status, imaging and treatment parameters for patients included versus those excluded of resumption and long-term outcome analyses. Scales, scores and abbreviations, with corresponding ranges: pre-mRS: modified Rankin Scale prior to admission (range 0-5, no functional deficit to severe disability), Glasgow Coma Scale (range 3-15, deep coma to alert), NIHSS: National Institutes of Health Stroke Scale (range 0-40 (42= maximum sum, in comatose ataxia is not scored), no deficit to severe neurological deficit), ICH-Score: Intracerebral hemorrhage Score (range 0-6, low to high risk of mortality), Graeb Score: ventricular involvement (range 0-12, no intraventricular blood to tamponade of all ventricles); OAC: oral anticoagulation (coumadins), ICH: intracerebral hemorrhage. Complete-case analysis for n=719; Left column: Number (n) of patients with available data; * n (%); † mean (±SD); ‡ median (IQR; 25^{th} -75^{th} percentile); ^ not sig. after Bonferroni correction (corrected significance level *P* <0.00143). Significant parameters are expressed in bold.

eTable 15. Comparison of investigated outcomes between complete-case versus multiple imputation analysis.

	Complete-case Analysis	Multiple imputation Analysis
OAC resumption overall A-fib	 n=172/719 (23.9%) n=110/566 (19.4%)	 n=188/812 (23.2%) n=122/628 (19.4%)
Ischemic events entire cohort OAC resumption No OAC resumption	 n=9/172 (5.2%) n=82/547 (15.0%)	 n=15/188 (8.0%) n=110/624 (17.6%)
Hemorrhagic events entire cohort OAC resumption No OAC resumption	 n=14/172 (8.1%) n=36/547 (6.6%)	 n=23/188 (12.2%) n=76/624 (12.2%)
Ischemic events A-fib cohort OAC resumption No OAC resumption	 n=6/110 (5.5%) n=68/456 (14.9%)	 n=7/122 (5.7%) n=78/506 (15.4%)
Hemorrhagic events A-fib cohort OAC resumption No OAC resumption	 n= 8/110 (7.3%) n= 26/456 (5.7%)	 n=13/122 (10.7%) n=56/506 (11.1%)
Ischemic stroke A-fib cohort OAC resumption No OAC resumption	 n=5/110 (4.5%) n=51/456 (11.2%)	 n=9/122 (7.4%) n=85/506 (16.8%)
Hemorrhagic stroke A-fib cohort OAC resumption No OAC resumption	 n=4/110 (3.6%) n=18/456 (3.9%)	 n=11/122 (9.0%) n=50/506 (9.9%)
Mortality at 1 year Unfavorable outcome at 1 year	n=608/1083 (56.1%) n=786/1083 (72.6%)	n=623/1176 (53.0%) n=835/1176 (71.0%)

We here present, the comparison of multiple imputation [MI] versus complete-case analysis of variables of interest regarding both OAC resumption and long-term outcome analysis. We calculated MI including all parameters available for outcome analyses: baseline characteristics (age, sex, comorbidities, OAC-indication, $CHADS_2$ Score, HAS-BLED Score, prestroke mRS), neurological status (GCS, NIHSS), imaging (ICH location, initial ICH volume, IVH, hematoma enlargement), in-hospital measures (ventilation, pneumonia, sepsis, LOS, EVD, mRS at discharge), follow-up measures (time of survival, mRS at 3 months and 1 year, mortality at 3 months and 1 year, ischemic and hemorrhagic complications, ischemic and hemorrhagic stroke, duration until each complication, OAC resumption, duration until treatment initiation). MI would increase both incidences of ischemic and hemorrhagic complications, yet without changing statistical significance. Specifically, MI for the entire cohort would introduce 83 new events, 34 ischemic- and 49 hemorrhagic events, though rate of clinical end points such as mortality and functional outcome would paradoxically decrease at 3 months and 1 year of follow-up. Therefore, it appears that MI rather introduces possible bias, especially when these rates are compared to existing data.