10:10-11:10 **Simposio**

SCENARI CONTROVERSI SUI DOACs NEL PAZIENTE ANZIANO COMPLESSO

Moderatori: *Evaristo Ettorre (Roma), Giuseppe Rengo (Napoli)*

- Fibrillazione atriale ed ictus cerebrale emorragico: quando e con quali farmaci iniziare la terapia anticoagulante?
  Mario Bo (Torino)

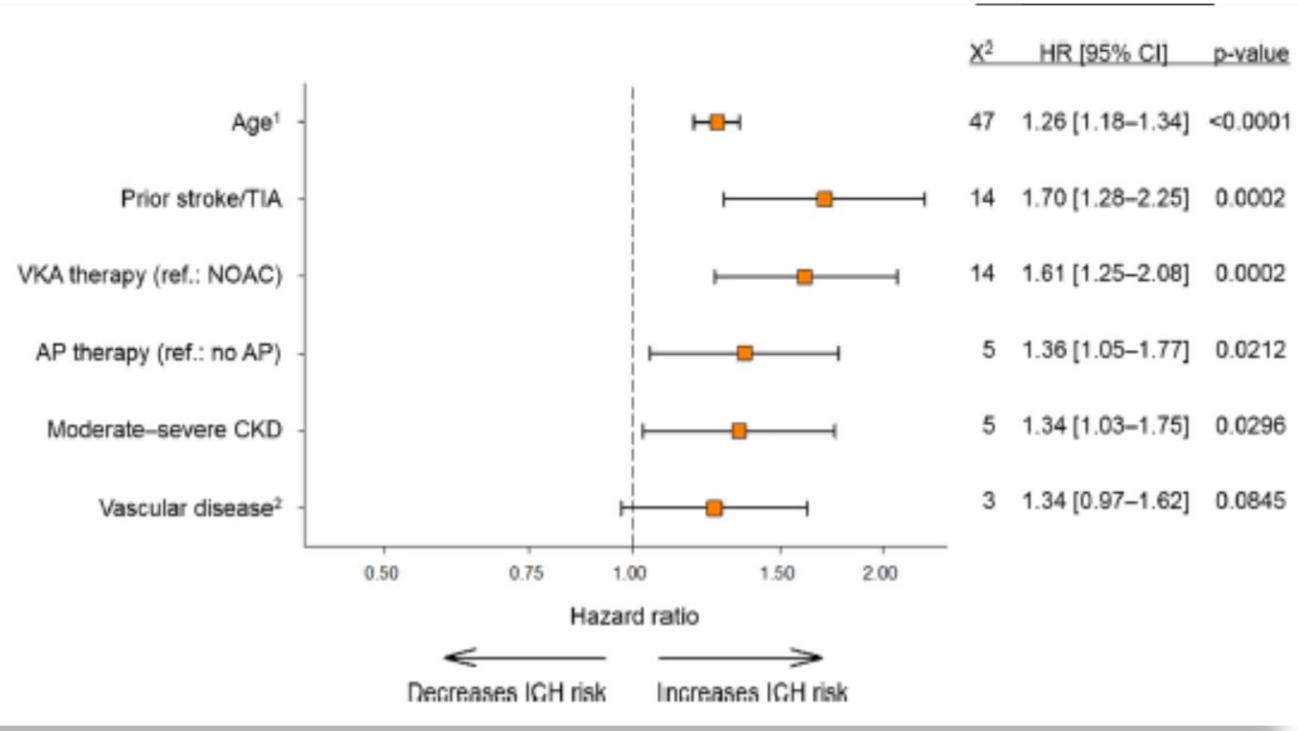
1. **Storia naturale dell'ICH e rischio di recidiva**
2. **Cosa ci dicono:**
   - gli studi osservazionali e le relative metanalisi
   - i (pochi) RCT sinora condotti e le relative metanalisi
3. **Cosa ci dicono le GLs e le raccomandazioni delle società scientifiche**
4. **Conclusioni**

ICH: FDR in pazienti con FA anticoagulati

Clin Cardiol. 2023;46:1398-1407.

Predictors of intracranial hemorrhage in patients with atrial fibrillation treated with oral anticoagulants: Insights from the GARFIELD-AF and ORBIT-AF registries

Among **53878 AF anticoagulated patients** (age median 72, male 56.5%) **284** (age median 77, male 52.5%) **had ICH** (0.31 per 100 person-years)



From The JAMA Network

Oral Anticoagulants and the Risk of Intracranial Hemorrhage

RESULTS Six studies (1 administering dabigatran etexilate mesylate, 2 administering rivaroxaban, and 3 administering apixaban) enrolling a total of 57 491 patients were included for analysis. The NOACs significantly reduced the risk of ICH against all comparators (odds ratio = 0.49; 95% CI, 0.36-0.65). Each of the 3 drugs reduced the risk of ICH, with Bayesian indirect comparison analysis not revealing a significant credible difference between the specific medications.

CONCLUSIONS AND RELEVANCE Novel oral anticoagulants are uniformly associated with an overall reduced risk of ICH when used for stroke prevention in atrial fibrillation. Any of the currently available NOACs can be considered first line for patients at high risk for ICH.

JAMA Neurol. 2013;70(12):1486-1490. doi:10.1001/jamaneurol.2013.4021.

ICH: storia naturale

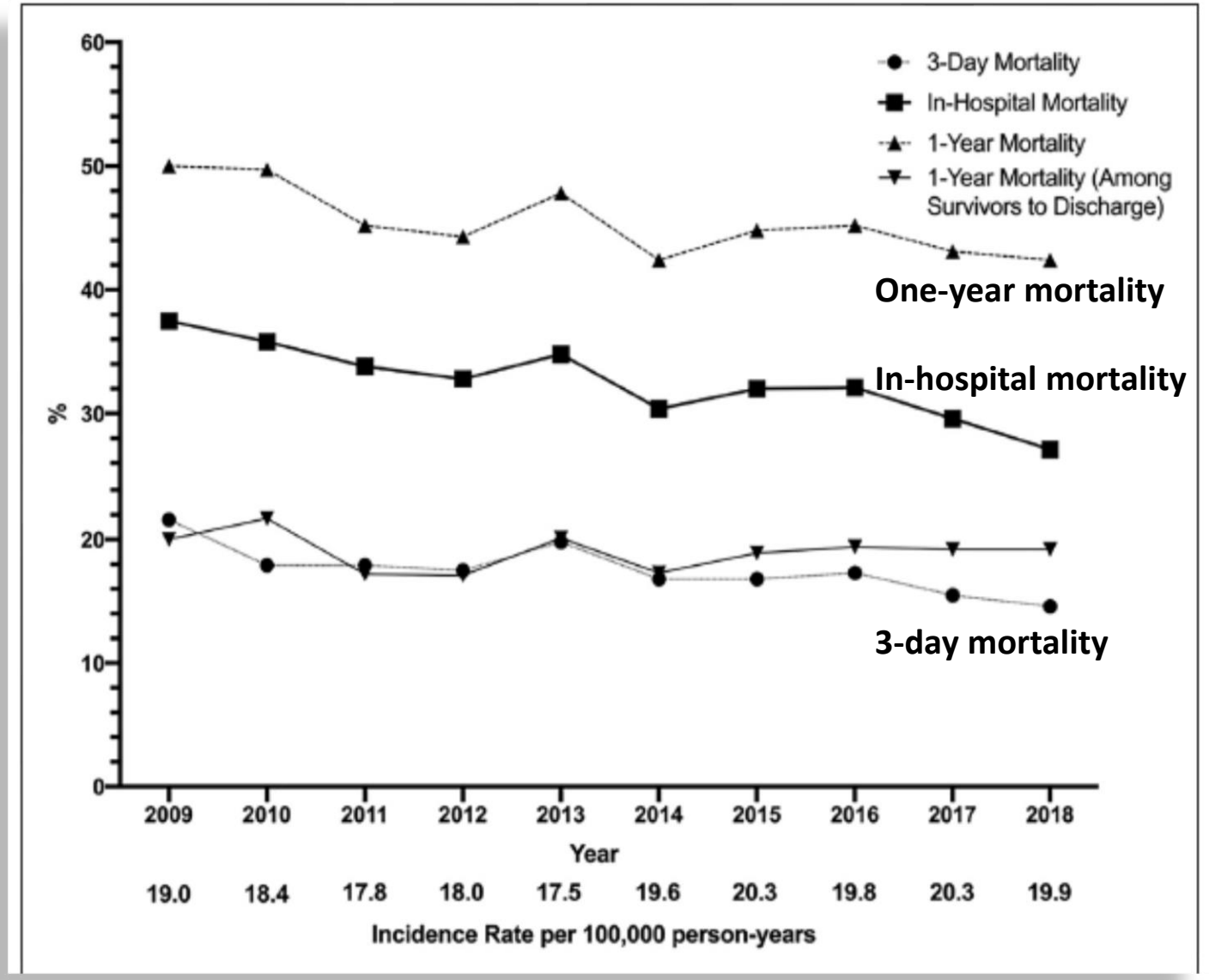
Intracerebral Hemorrhage Incidence, Mortality, and Association With Oral Anticoagulation Use

A Population Study

Stroke. 2021;52:1673–1681. DOI: 10.1161/STROKEAHA.120.032550

Retrospective cohort study of **20738 adults** (mean age **71.3** years, 52.6% male) with **ICH** in Ontario (april 2009-march 2020)

Primary outcome: **in-hospital and one-year mortality**



ICH: fattori prognostici di recidiva

Eur J Clin Invest. 2023;53:e13962.

Secondary prevention after intracerebral haemorrhage

The rate **recurrence** was **6.1%** in the first year and **7.9%** at 5 years after **lobar-ICH** vs **2.6%** and **3.2%**, respectively, in **non-lobar ICH**…**CAA** is associated with a higher risk of recurrent events

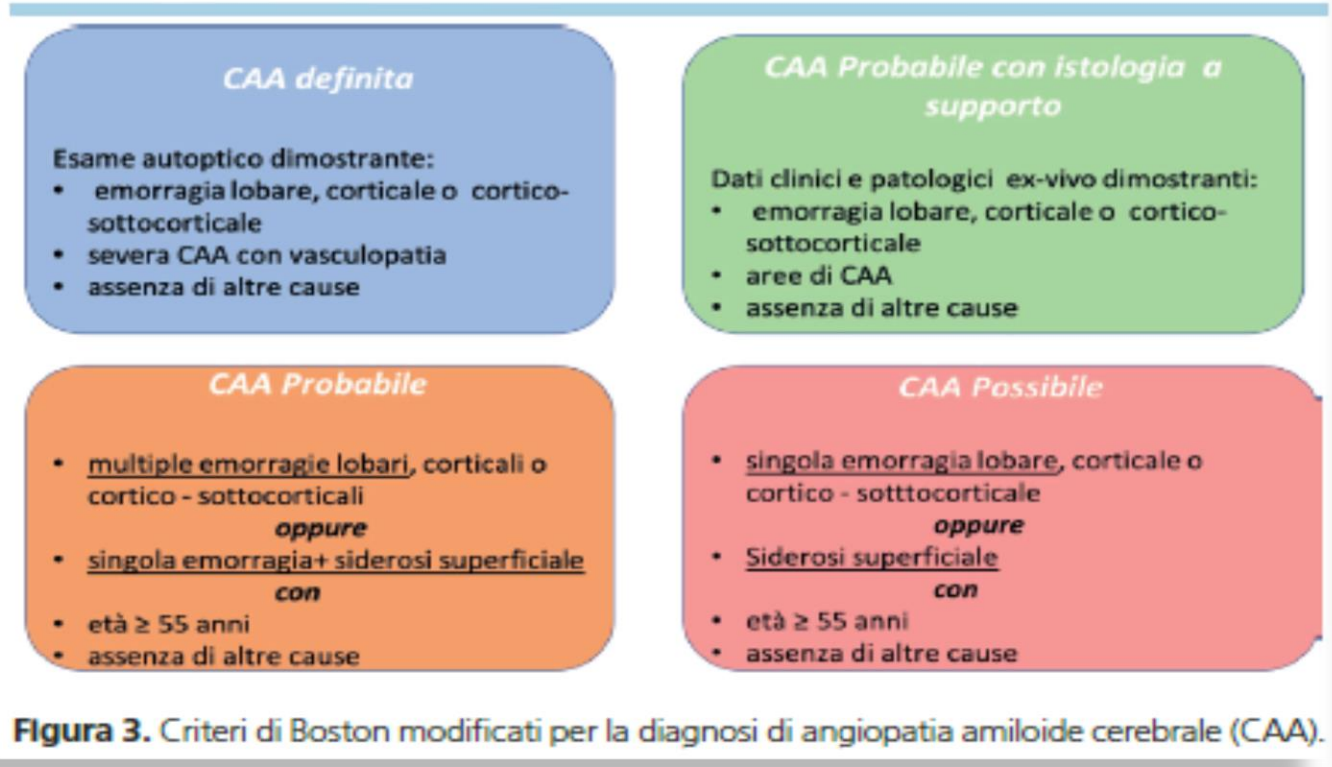


Figura 3. Criteri di Boston modificati per la diagnosi di angiopatia amiloide cerebrale (CAA).

Brain hemorrhage recurrence, small vessel disease type, and cerebral microbleeds

A meta-analysis

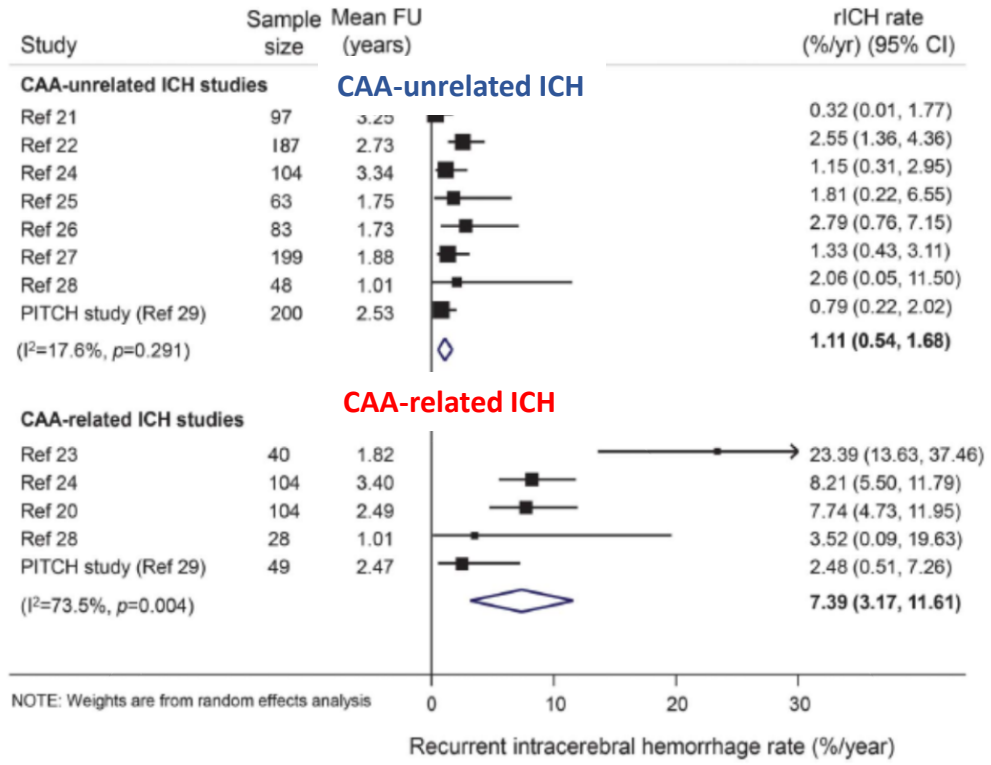
OPEN

Neurology® 2017;89:820-829

Pooled data from 10 studies including 1306 patients: 325 with **CAA-related** and 981 with **CAA-unrelated ICH**

Figure 2

Pooled risk of recurrent ICH

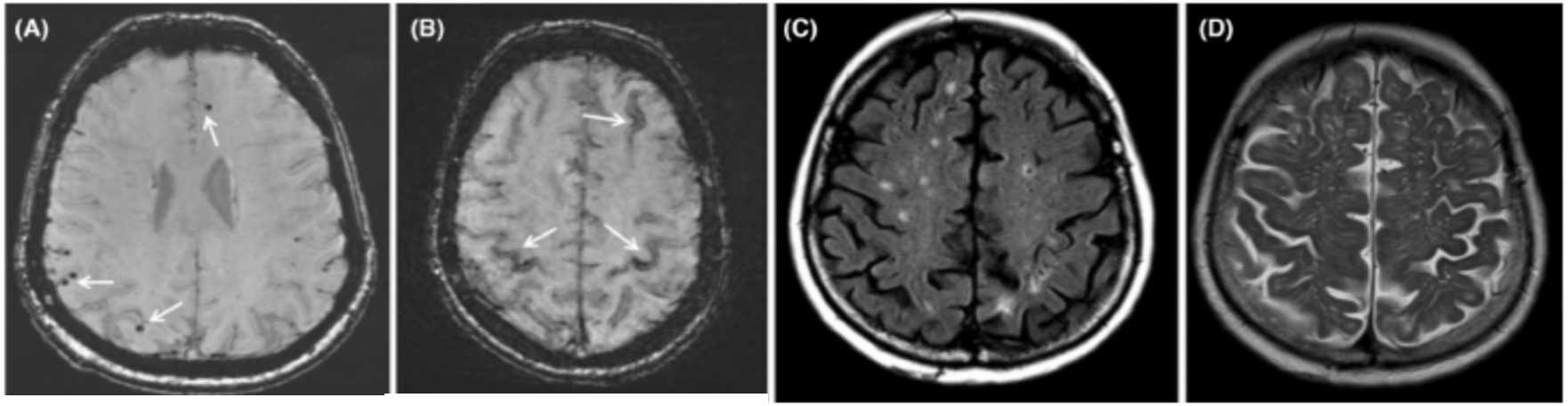


Weights are shown by the point estimate area. CAA = cerebral amyloid angiopathy; CI = confidence interval; rICH = recurrent ICH.

ICH: fattori prognostici di recidiva

Eur J Clin Invest. 2023;53:e13962.

MRI markers of ICH recurrence

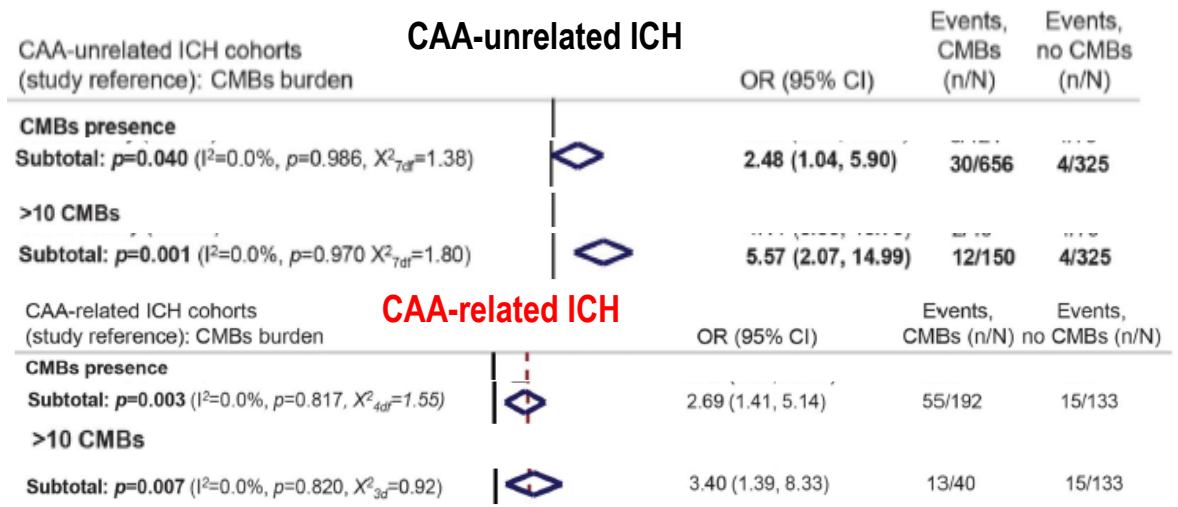


Multiple lobar microbleeds — **Multiple cortical superficial siderosis** — Suggestive of likely CAA

White matter hyperintinsities «spot-like» pattern

Enlarged perivascular spaces in the centrum semiovalis

Association of CMBs burden with risk of recurrent ICH



Brain hemorrhage recurrence, small vessel disease type, and cerebral microbleeds

A meta-analysis

OPEN

Neurology® 2017;89:820-829

Pooled data from 10 studies including 1306 patients: 325 with **CAA-related** and 981 with **CAA-unrelated ICH**

ICH: studi osservazionali OAT/DOACs/VKAs

Risk of Cerebrovascular Events in Intracerebral Hemorrhage Survivors With Atrial Fibrillation: A Nationwide Cohort Study *Stroke*. 2022;53:2559–2568.

To identify **cumulative incidence of recurrent ICH**, cerebrovascular **ischemic event and all-cause death** after one year, from the Danish Stroke Registry (2003-2018)

2277 patients with **incident ICH** and **prevalent AF** (3/2003-6/2018)	1885 **eligible** patients with **incident ICH** and **prevalent AF** (3/2003-6/2018)	608 **CHA_2DS_2-VASC 2-3** **78y**, F 30% SSS 40	866 **CHA_2DS_2-VASC 4-6** **80y**, F 49% SSS 42	416 **CHA_2DS_2-VASC >6** **83y**, F 71% SSS 43

		Events, n; Risk% (95%CI)	Events, n; Risk% (95%CI)	Events, n; Risk% (95%CI)
NOT initiating/resuming OAT (1359, 72.1%)	**Recurrent ICH**	7, 1.2 (0.5-2.3)	15, 1.8 (1.1-2.9)	6, 1.4 (0.8-3.0)
	CV ischemic event	14, 2.4 (1.4-3.9)	23, 2.8 (1.8-4.1)	10, 2.5 (1.3-4.4)
	All-cause death	147, 24.8 (21.5-28.5)	248, 29.3 (26.3-32.5)	166, 40.7 (36.1-45.6)
Initiating/resuming OAT (526, 27.9%)	**Recurrent ICH**	<5, 2.9 (1.0-6.9)	<5, 2.2 (0.7-5.3)	<5, 3.6 (1.2-8.4)
	CV ischemic event	<5, 2.9 (1.0-6.9)	6, 3.7 (1.4-7.8)	<5, 2.6 (0.7-7.0)
	All-cause death	17, 12.7 (8.0-19.9)	50, 28.6 (20.1-39.6)	22, 20 (13.6-29)

SSS= Scandinavian Stroke Scale score

ICH: studi osservazionali OAT/DOACs/VKAs

Danish nationwide registries 1997-2013 identified **patients with AF on OAT with incident ICH**. Outcome measures: **IS, SE, all-cause death, recurrent ICH, MB**.

Circulation. 2015;132:517-525.

Restarting Anticoagulant Treatment After Intracranial Hemorrhage in Patients With Atrial Fibrillation and the Impact on Recurrent Stroke, Mortality, and Bleeding
A Nationwide Cohort Study

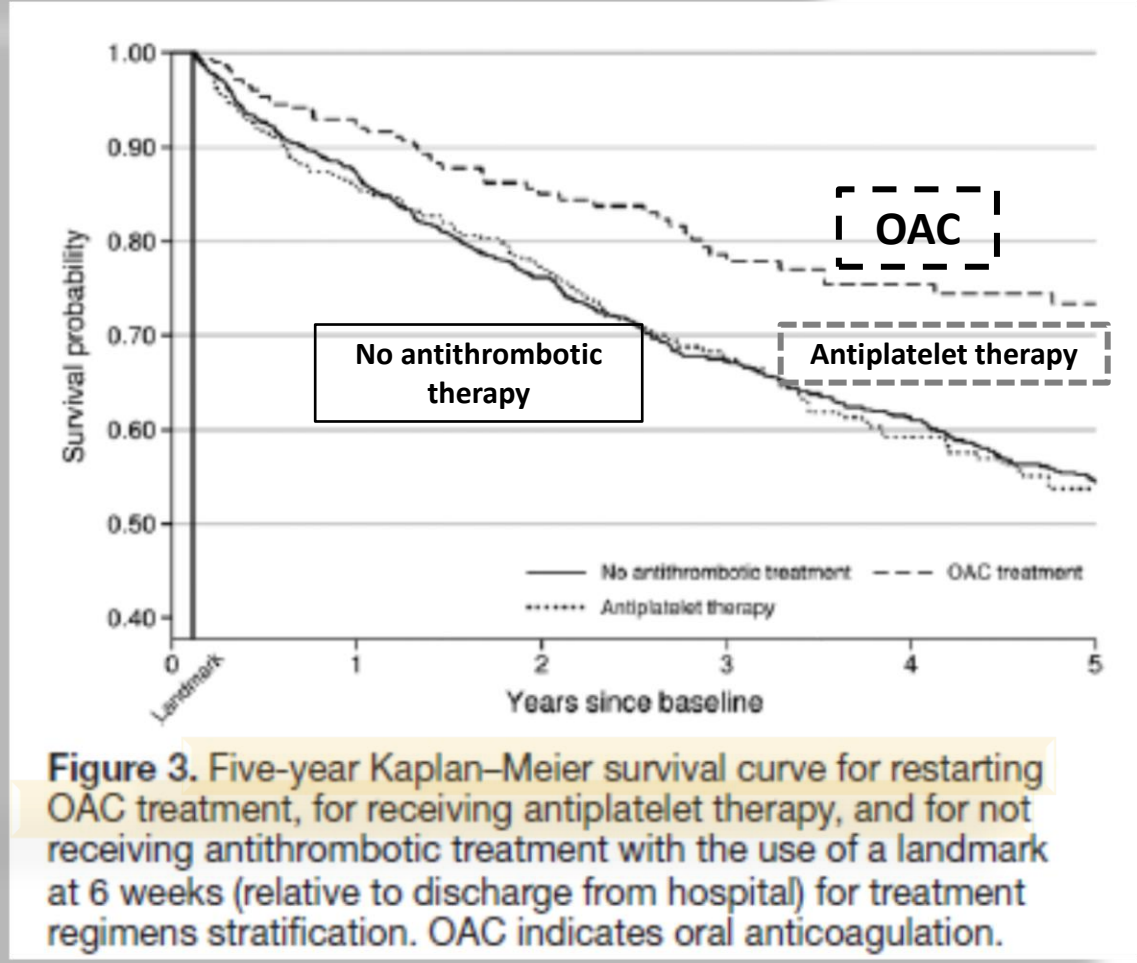
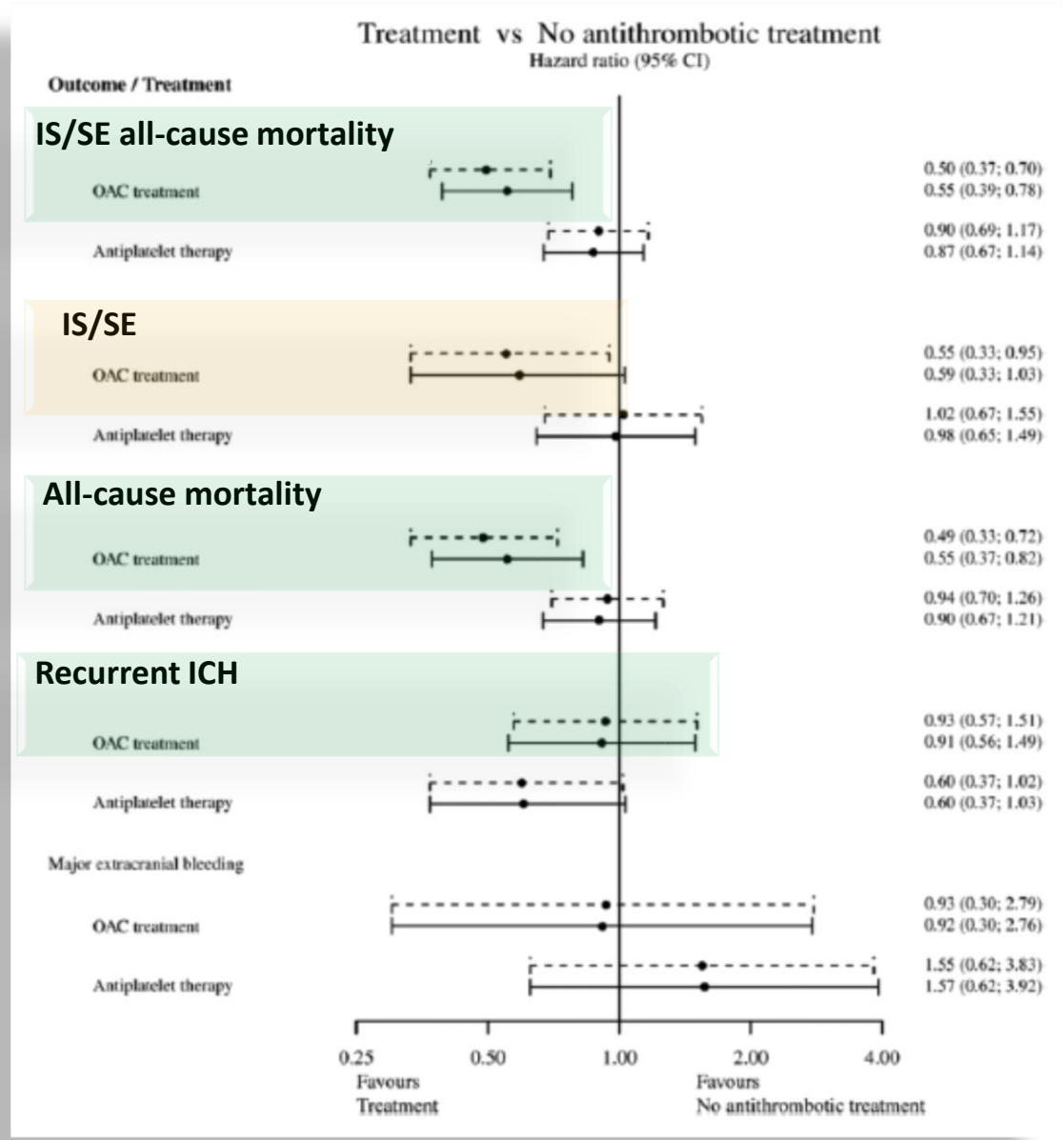


Figure 3. Five-year Kaplan–Meier survival curve for restarting OAC treatment, for receiving antiplatelet therapy, and for not receiving antithrombotic treatment with the use of a landmark at 6 weeks (relative to discharge from hospital) for treatment regimens stratification. OAC indicates oral anticoagulation.



ICH: studi osservazionali OAT/DOACs/VKAs

Restarting anticoagulant therapy after intracranial hemorrhage in patients with atrial fibrillation: A nationwide retrospective cohort study

Korean national health insurance claims data between 2002 and 2017 including **4964 participants** (878 using OAT, 2070 using antiplatelet agents, while the remaining were non anti-thrombotic users)

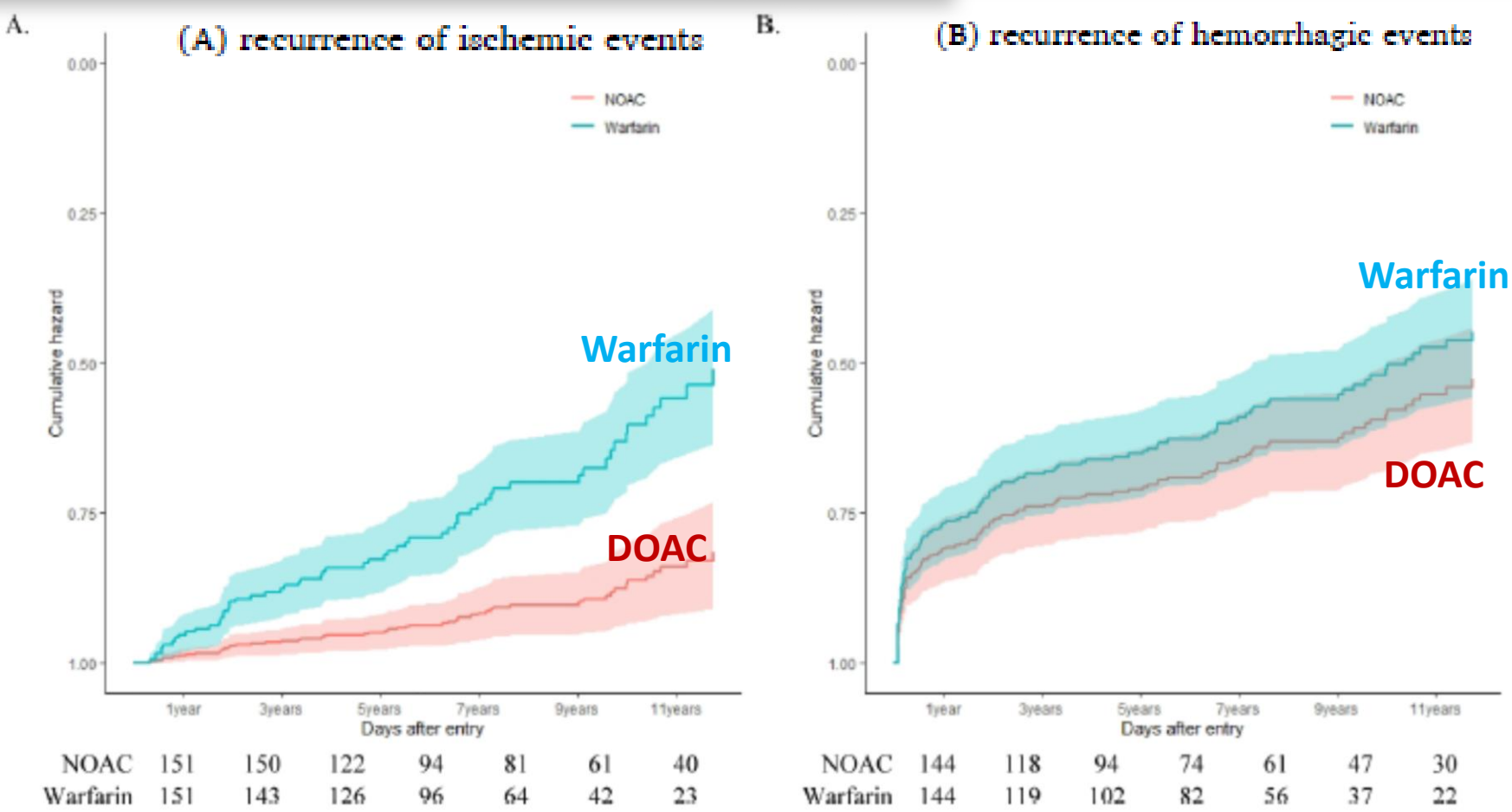


Fig. 3. Cox proportional hazards plots for (A) recurrence of ischemic events and (B) recurrence of hemorrhagic events, related to class of anticoagulant.

IJC Heart & Vasculature 40 (2022) 101037

ICH: studi osservazionali OAT/DOACs/VKAs

International Journal of Cardiology
https://doi.org/10.1016/j.ijcard.2023.131369

ISCHEMIC STROKE AND MAJOR BLEEDING WHILE ON DIRECT ORAL ANTICOAGULANTS IN NAÏVE PATIENTS WITH ATRIAL FIBRILLATION: IMPACT OF RESUMPTION OR DISCONTINUATION OF ANTICOAGULANT TREATMENT. A population-based study.

N. Gennaro [a], E. Ferroni [a], M. Zorzi [a], G. Denas [b], V. Pengo [b,c,*]

Crude and adjusted HRs of cumulative events (blanking period = 120 days).

	Crude HR (95% CI)	Adjusted HR (95% CI)
Entire cohort (n = 1.029)	0.38 (0.30–0.48)	0.45 (0.35–0.57)
IS (n = 237)	0.15 (0.07–0.28)	0.19 (0.10–0.40)
ICH (n = 185)	0.36 (0.21–0.62)	0.36 (0.20–0.65)
MB (n = 607)	0.42 (0.31–0.57)	0.51 (0.24–0.68)

Index event: Intracerebral Haemorrhage

64% resuming OAT

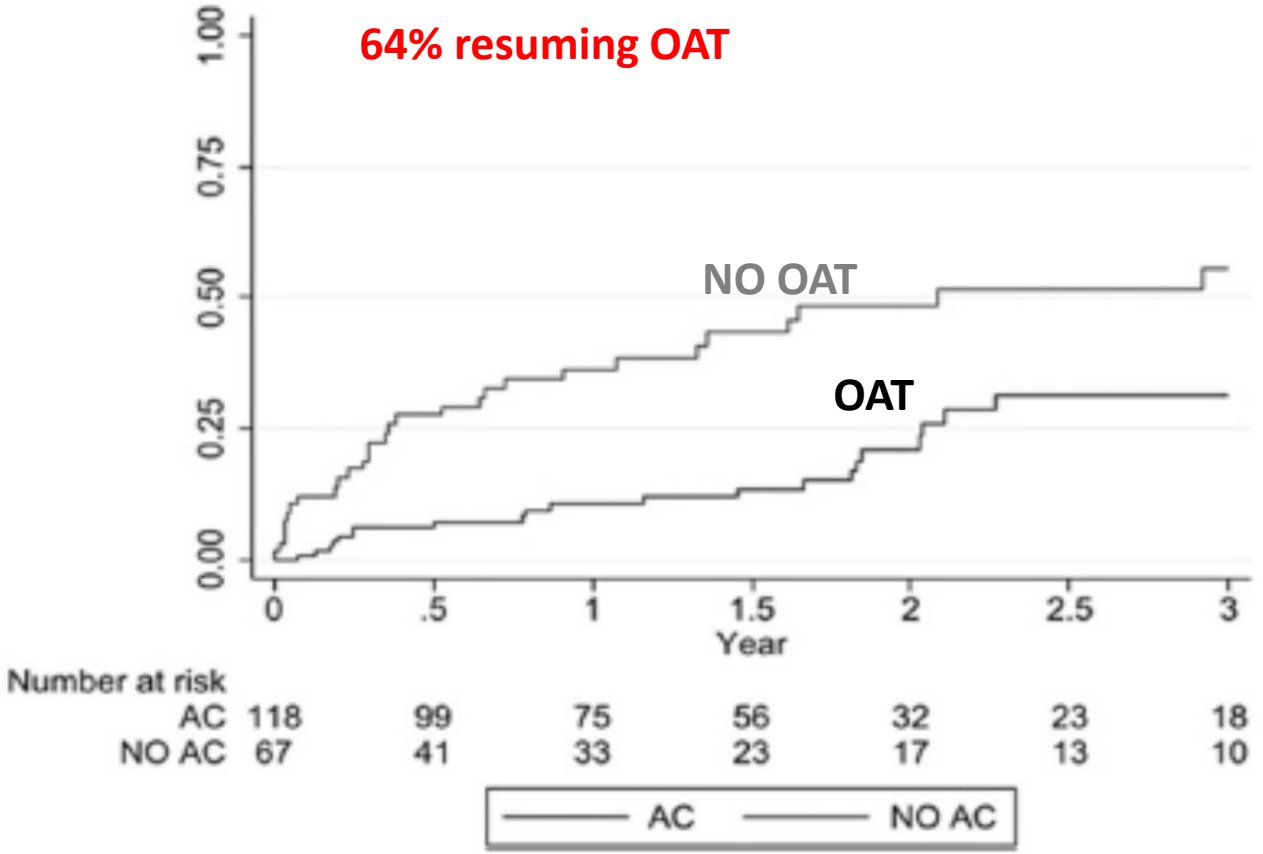


Fig. 4. Kaplan-Meier curves of cumulative events (IS. ICH. MB and death) in patients after an intracerebral haemorrhage while on DOACs according on whether (blue line) or not (red line) anticoagulant therapy is resumed. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

ICH: meta-analysis & sist rev OAT/DOACs/VKAs

ANN NEUROL 2017;82:755–765

Oral Anticoagulation and Functional Outcome after Intracerebral Hemorrhage

Meta-analysis including **1012 OAT-related ICH survivors** (**633 non-lobar**, **379 lobar**) from (1) the RETRACE study (2) a US cohort based single center ICH study and (3) the Ethnic/Racial Variaitions of ICH study . Primary outcome **OAT association with one-year mortality, favorable functional outcome, and stroke incidence**

TABLE 4. Oral Anticoagulation Resumption and Long-Term Outcomes following Intracerebral Hemorrhage

	All ICH			Nonlobar ICH			Lobar ICH		
Outcome[a]	HR	95% CI	*p*	HR	95% CI	*p*	HR	95% CI	*p*
Mortality	0.32	0.15–0.66	0.002[b]	0.30	0.10–0.91	0.035[b]	0.33	0.12–0.87	0.026[b]
Favorable outcome, mRS = 0–3	3.99	1.76–9.05	0.001[b]	4.10	1.24–13.57	0.022[b]	3.89	1.26–11.98	0.019[b]
All-cause stroke	0.50	0.32–0.79	0.003[b]	0.49	0.26–0.93	0.031[b]	0.51	0.26–0.99	0.047[b]
Recurrent ICH	1.10	0.96–1.26	0.20	1.10	0.94–1.28	0.23	1.21	0.86–1.70	0.27
Ischemic stroke	0.46	0.28–0.75	0.002[b]	0.44	0.22–0.90	0.025[b]	0.48	0.25–0.94	0.032[b]

[a]All analyses were adjusted by means of propensity score matching using the following parameters: Glasgow Coma Scale at presentation, ICH volume, presence of intraventricular hemorrhage, discharge mRS, CHA_2DS_2-VASc score, and HAS-BLED score.
[b]Statistically significant.
CI = confidence interval; HR = hazard ratio; ICH = intracerebral hemorrhage; mRS = modified Rankin Scale.

ICH: meta-analysis & sist rev OAT/DOACs/VKAs

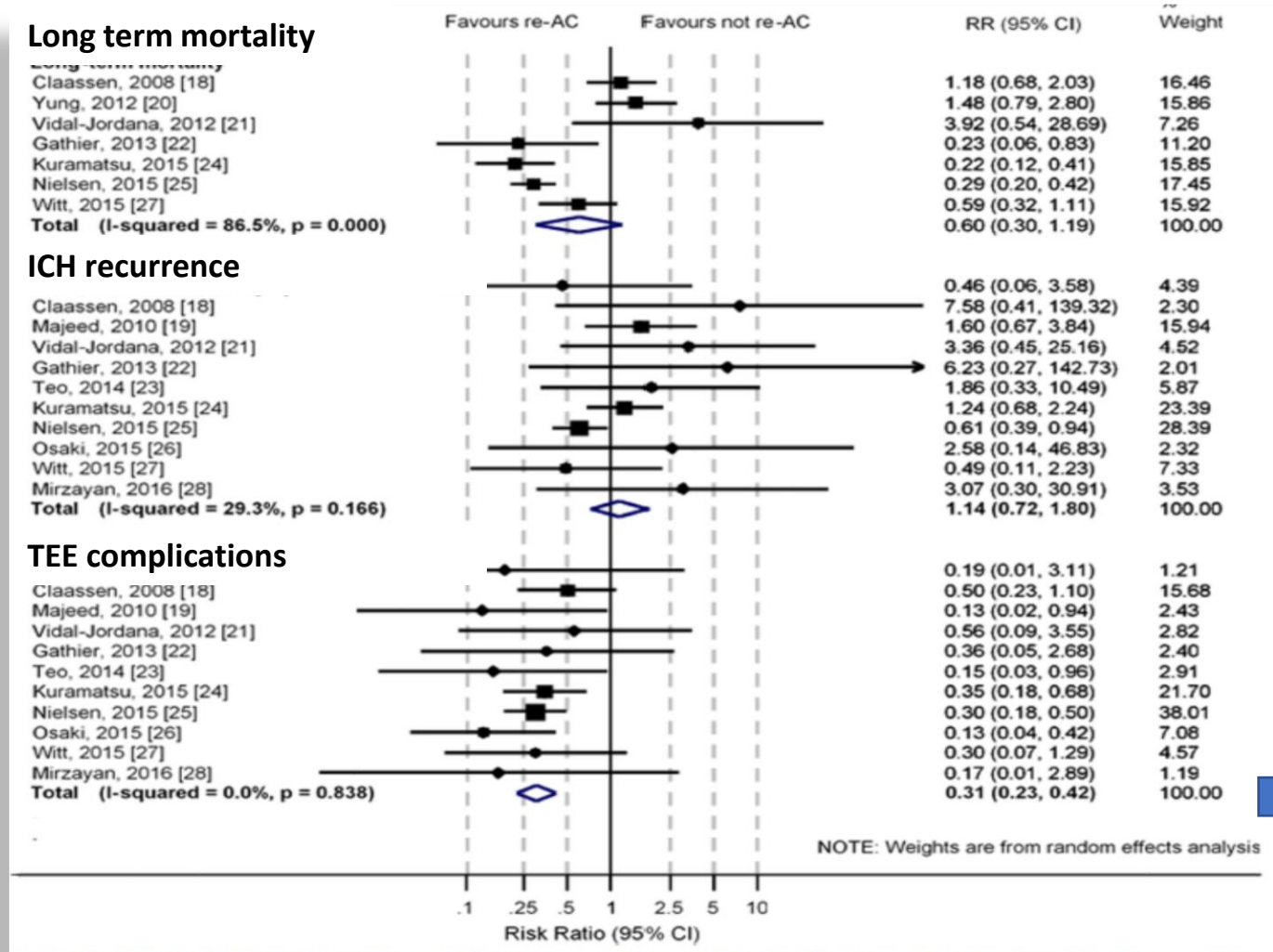


Figure 2 Meta-analysis of primary outcomes. ICH, intracranial haemorrhage; re-AC, resumption of anticoagulant therapy; RR, relative risk; TEE, thromboembolic events.

To cite: Zhou Z, Yu J, Carcel C, *et al*. Resuming anticoagulants after anticoagulation-associated intracranial haemorrhage: systematic review and meta-analysis. *BMJ Open* 2018;**8**:e019672. doi:10.1136/bmjopen-2017-019672

Resuming anticoagulants after anticoagulation-associated intracranial haemorrhage: systematic review and meta-analysis

Strengths and limitations of this study

- A greater number of potentially eligible articles were screened and included for pooling.
- We paid careful attention to include participants who received anticoagulant therapy at the time of intracranial haemorrhage occurrence and survived the acute phase or hospitalisation.
- There are many confounders (anticoagulation indication, age, clinical severity, haematoma location, etc) related to resumption of anticoagulation in existing observational studies.
- The confounders cannot be adjusted in this study-level meta-analysis which limits the formation of management recommendations or improve clinical practice.

ICH: meta-analysis & sist rev OAT/DOACs/VKAs

Efficacy and safety of anticoagulation in atrial fibrillation patients with intracranial hemorrhage: A systematic review and meta-analysis

frontiers | Frontiers in Pharmacology

TYPE Review
PUBLISHED 09 March 2023
DOI 10.3389/fphar.2023.1122564

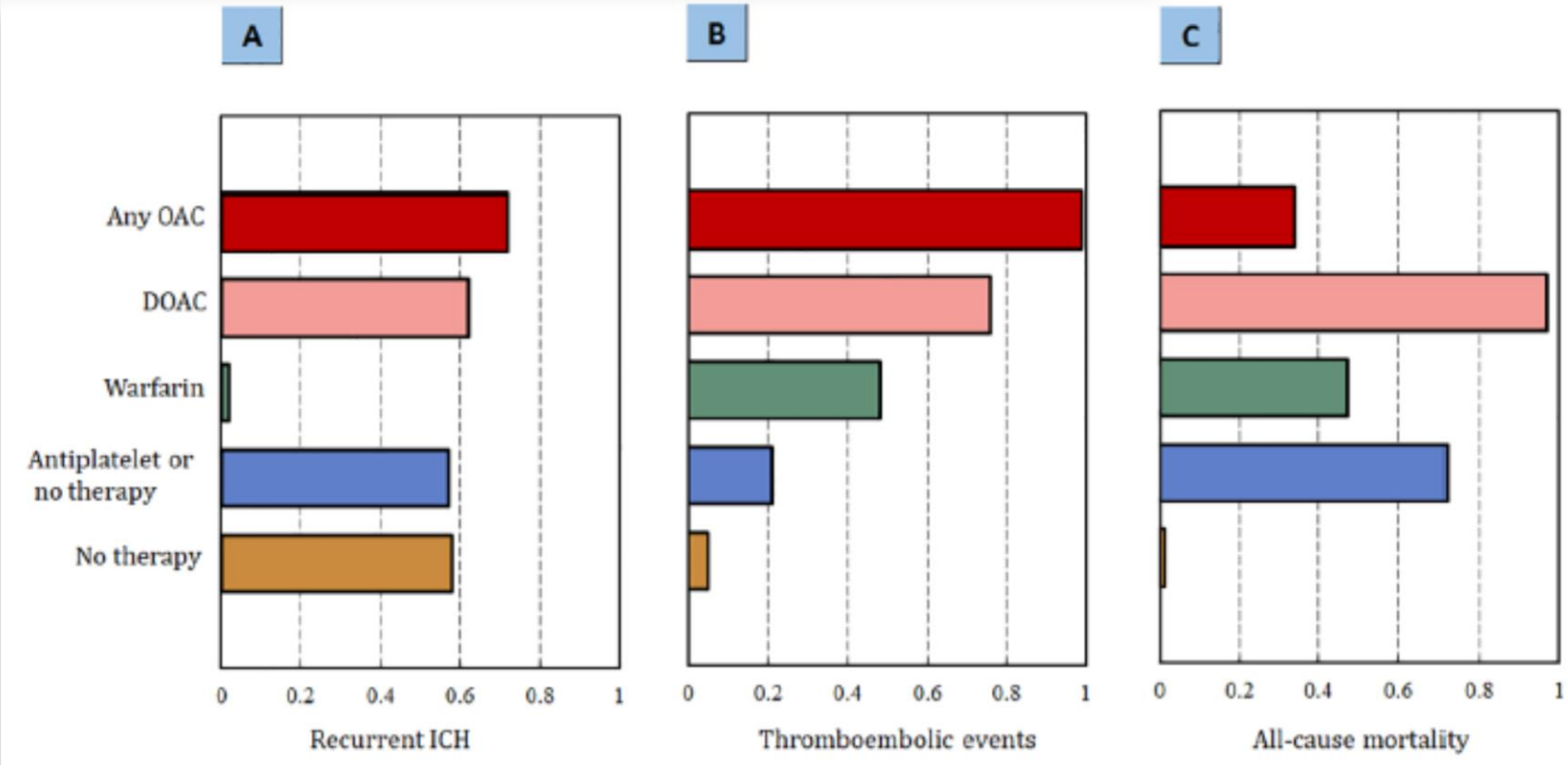
TABLE 3 Results of Comparison effectiveness and safety of DOACs *versus* warfarin.

Outcomes	Number of studies/patients	I^2 (%)	Meta-analysis results	
			aHR (95% CI)	*p*-value
Ischemic Stroke/SE	3/8,188	0	0.84 (0.70–1.00)	0.049
Major bleeding	2/2,484	84.2	0.54 (0.26–1.10)	0.088
Recurrent ICH	3/8,188	0	0.63 (0.49–0.82)	0.001
All-cause mortality	3/8,188	82	0.65 (0.48–0.88)	0.005

ICH: meta-analysis & sist rev OAT/DOACs/VKAs

Journal of Thrombosis and Thrombolysis (2023) 56:1–11

Anticoagulation medication in nontraumatic intracranial hemorrhage survivors with atrial fibrillation



In the current network meta-analysis, both DOAC and warfarin were associated with lower risks of thromboembolic events for patients with AF who experienced ICH, whereas patients who were prescribed warfarin had a higher risk of recurrent ICH compared to those who were prescribed DOAC. DOAC was associated with lower rates of thromboembolic events, repeat ICH or all-cause mortality compared with warfarin. Our study suggests DOAC is a reasonable alternative to anti-platelet therapy and warfarin.

Fig. 5 Summary of the SUCRA scores of each agent in each outcome. (**A**) Recurrent ICH. (**B**) Thromboembolic events. (**C**) All-cause mortality. ICH: intracranial hemorrhage. SUCRA: surface under the cumulative ranking curve

ICH: RCT OAT vs no-OAT

SoSTART Collaboration*

Effects of oral anticoagulation for atrial fibrillation after spontaneous intracranial haemorrhage in the UK: a randomised, open-label, assessor-masked, pilot-phase, non-inferiority trial

Lancet Neurol 2021; 20: 842–53

SoSTART Collaboration*

	Start oral anticoagulation (n=101)	Avoid oral anticoagulation (n=102)
Median age, years	79 (74–85)	79 (74–84)
Sex		
Male	62 (61%)	65 (64%)
Female	39 (39%)	37 (36%)
Intended type of oral anticoagulation (if allocated to start)*		
Direct oral anticoagulant	97 (96%)	101 (99%)
Other	4 (4%)	1 (1%)

	Start oral anticoagulation (n=101)	Avoid oral anticoagulation (n=102)	Unadjusted HR (95% CI), p value	Adjusted* HR (95% CI), p value
Primary outcome				
Recurrent symptomatic spontaneous intracranial haemorrhage	8 (8%)	4 (4%)	2·31 (0·69–7·68), p=0·173	2·42 (0·72–8·09), p=0·152
Composite secondary outcomes				
Any symptomatic major vascular event	12 (12%)	24 (24%)	0·51 (0·26–1·03), p=0·061	0·51 (0·26–1·03), p=0·060
Any stroke	11 (11%)	22 (22%)	0·53 (0·25–1·09), p=0·082	0·53 (0·25–1·09), p=0·084
Any stroke or vascular death	12 (12%)	23 (23%)	0·55 (0·27–1·10), p=0·092	0·55 (0·27–1·10), p=0·090

HR=hazard ratio. *Cox proportional hazards models were adjusted for two of the six minimisation variables: time since intracranial haemorrhage symptom onset (<10 weeks [reference] vs ≥10 weeks) and type of qualifying intracranial haemorrhage (lobar intracerebral haemorrhage vs non-lobar intracerebral haemorrhage and lobar intracerebral haemorrhage vs other); model non-convergence due to the low number of events prevented the inclusion of any more minimisation variables.

Table 2: **Risks of the first occurrence of primary and composite secondary outcome events during follow-up**

ICH: RCT OAT vs no-OAT

Apixaban versus no anticoagulation after anticoagulation-associated intracerebral haemorrhage in patients with atrial fibrillation in the Netherlands (APACHE-AF): a randomised, open-label, phase 2 trial

Lancet Neurol 2021; 20: 907–16

	Apixaban group (n=50)	Avoid anticoagulation group (n=51)
Sex		
Men	27 (54%)	28 (55%)
Women	23 (46%)	23 (45%)
Age		
Median, years	77 (74–83)	79 (72–83)
≥75 years	36 (72%)	30 (59%)

	Apixaban group (n=50)	Avoid anticoagulation group (n=51)	Unadjusted analysis		Adjusted analysis	
			HR (95% CI)	p value	Adjusted HR (95% CI)	p value
Primary outcome						
Non-fatal stroke or vascular death	13 (26%)	12 (24%)	1·07 (0·49–2·34)	0·87	1·05 (0·48–2·31)	0·90
Secondary outcomes*						
Intracerebral haemorrhage	4 (8%)	1 (2%)	4·12 (0·46–36·94)	0·21	4·08 (0·45–36·91)	0·21
All major haemorrhagic events	6 (12%)	3 (6%)	2·14 (0·53–8·57)	0·29	2·11 (0·52–8·51)	0·29
Ischaemic stroke	6 (12%)	6 (12%)	0·97 (0·31–3·00)	0·96	0·96 (0·31–2·97)	0·94
All major occlusive events	6 (12%)	11 (22%)	0·46 (0·17–1·25)	0·13	0·46 (0·17–1·25)	0·13
All major vascular events according to the protocol†	14 (28%)‡	16 (31%)§	0·81 (0·39–1·66)	0·56	0·80 (0·39–1·64)	0·54
All major vascular events (myocardial infarction, stroke, or vascular death)¶	13 (26%)	13 (25%)	0·94 (0·43–2·02)	0·87	0·93 (0·43–2·00)	0·85

ICH: meta-analysis RCT OAT vs no-OAT

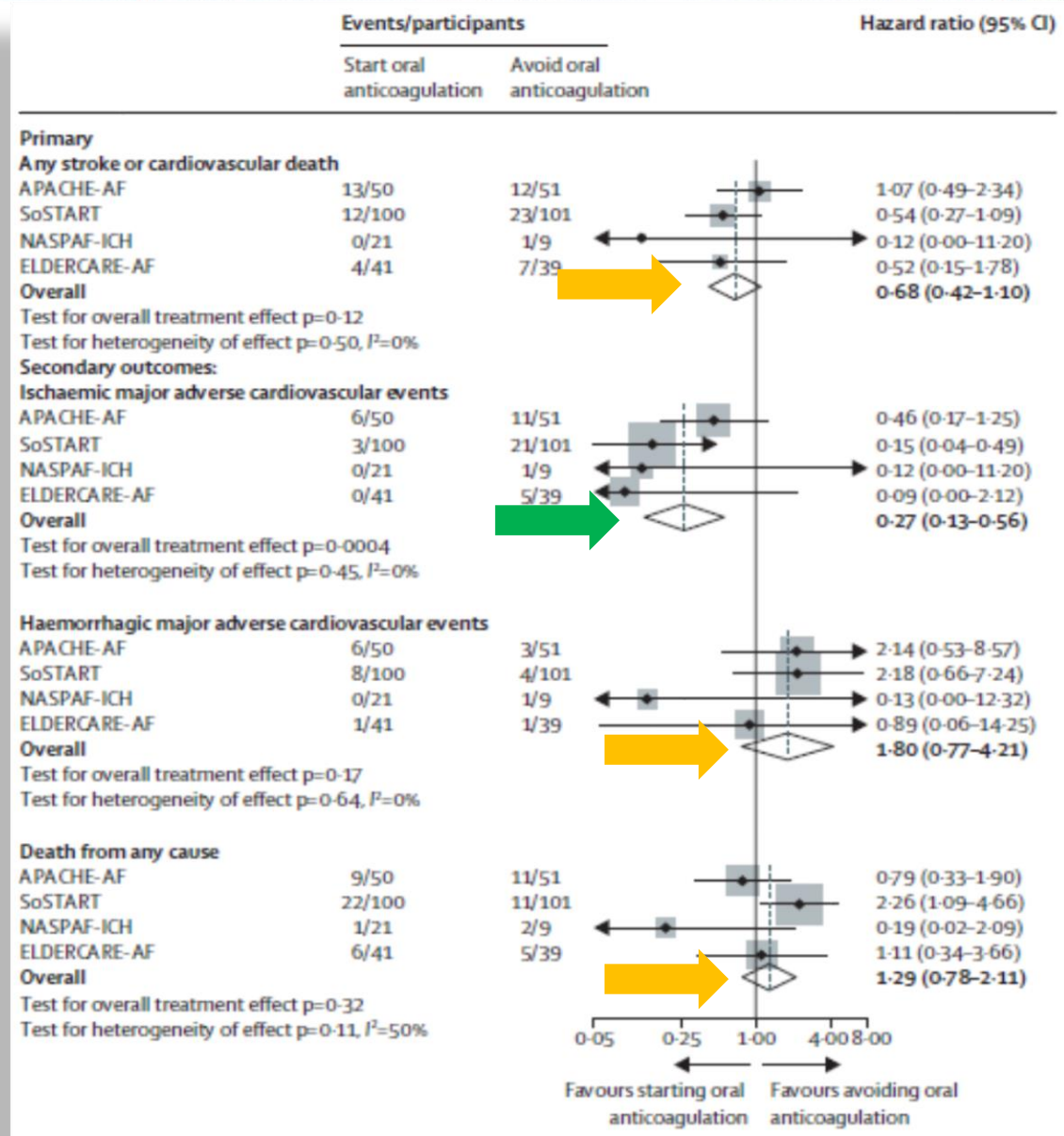
Effects of oral anticoagulation in people with atrial fibrillation after spontaneous intracranial haemorrhage (COCROACH): prospective, individual participant data meta-analysis of randomised trials

Lancet Neurol 2023; 22: 1140–49

412 participants (**51% 75-85 years, 22% >85 years**) from SoSTART, APACHE-AF, NASPAF-ICH and ELDERCARE-AF

Implications of all the available evidence

Although oral anticoagulation reduces the risk of ischaemic major adverse cardiovascular events, uncertainties remain for survivors of intracranial haemorrhage with atrial fibrillation with respect to the hazards and net effects of oral anticoagulation overall and in subgroups, whether assessed by ischaemic and haemorrhagic outcomes, or by functional outcome. Completion of the five ongoing trials, which might add about 2000 participants to this meta-analysis in the next 5 years, could resolve these uncertainties.



ICH: RCT OAT vs no-OAT

Published Online
October 12, 2023
https://doi.org/10.1016/
S0140-6736(23)02025-1

Anticoagulation in patients with cerebral amyloid angiopathy

*Ashkan Shoamanesh, on behalf of the ENRICH-AF Steering Committee
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Department of Medicine, Population Health Research Institute, McMaster University, Hamilton, Canada

Although **observational data have suggested net benefit from anticoagulation** in ICH survivors with AF, including those with lobar and cerebral amyloid angiopathy-related ICH (CAA-related ICH), the propensity for confounding by indication and immortal time bias limit their interpretation…..

Three large RCTs comparing anticoagulation vs no anticoagulation in survivors of ICH with AF are ongoing…Following a safety review of the first 699 patients in the **ENRICH-AF** study (Edoxaban 60/30 vs no OAT) the data safety monitoring recommended that **participants with lobar ICH and convexity subarachnoid haemorrhage (SH) stop receiving the drug as soon as possible** and that no further patients with these ICH subtypes be enrolled….based on observations of **unacceptably high risk of recurrent ICH and convexity SH in the edoxaban arm**….**Caution is warranted regarding the use of anticoagulation in survivors of lobar ICH and convexity SH** with AF outside of ongoing RCTs until more data become available….

ICH: GL & Recommendations

European Heart Journal (2020) **42**, 373–498

Consider factors favouring withholding (×) vs. (re-)starting a NOAC, including:

- × No reversible/treatable cause of bleeding
- × Multiple cerebral microbleeds
- × Severe intracranial bleed
- × Older age
- × Bleeding during interruption of anticoagulation
- × Uncontrolled hypertension
- × Bleed on adequately or under-dosed NOAC
- × Chronic alcohol abuse
- × Need for dual antiplatelet therapy after PCI

Net assessment in favour of (re-)starting anticoagulation according to a multidisciplinary decision

No → **Consider no anticoagulation vs. LAA occlusion[a]**

Yes → **Consider (re-)initiation of (N)OAC after 4-8 weeks[b] after multi-disciplinary team assessment[a]**

2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS)

Risk factors for ICH

Modifiable

- (Uncontrolled) hypertension
- Low LDL/triglycerides
- Excessive alcohol consumption
- Current smoking
- Concomitant antiplatelet drugs
- Anticoagulant therapy
- Sympathomimetic drugs (cocaine, heroin, amphetamine, ephedrine, etc.)

Non-modifiable

- Older age
- Male sex
- Asian ethnicity
- Chronic kidney disease
- Cerebral disease:
  - Cerebral amyloid angiopathy
  - Small vessel disease

(Re)institution of OAC:
Decision-making post ICH in patients with AF

Consider risk factors for recurrent ICH

↓

Address modifiable bleeding risk factors

↓

Weight the risks and benefits of OAC (re)institution
in consultation with neurologist/stroke specialist

OAC use (with/without cerebral diseaes):
(observational data, RCTs are ongoing)

- Significant decrease in stroke and mortality
- Comparable risk for recurrent ICH vs. OAC non-use

OAC
Class IIa, LoE C
2–4 weeks after ICH

Irreversible cause of ICH, non-modifiable risk factors, etc.
LAA occlusion
Class IIb, LoE B

No stroke prevention therapy

RCTs are ongoing

Additional considerations:

- No reversible/treatable cause of ICH
- ICH during OAC interruption
- ICH on adequate or underdosed OAC
- The need for concomitant antiplatelet therapy (e.g., ACS/PCI)

CMB on cerebral imaging:

- The risk of ICH increases with the presence and increasing CMB burden, but
- Regardless of CMB presence, burden and distribution, the obsolute risk of ischaemic stroke is consistently substantially higher than that of ICH in post-stroke/ TIA patients

≥10 CMBs:
64 IS vs. 27 ICH events/1000 person-years
>20 CMBs:
73 IS vs. 39 ICH events/1000 person-years

ICH: GL & Recommendations

AHA/ASA GUIDELINE *Stroke.* 2022;53:e282–e361.

2022 Guideline for the Management of Patients With Spontaneous Intracerebral Hemorrhage: A Guideline From the American Heart Association/American Stroke Association

9.1. Secondary Prevention

9.1.1. Prognostication of Future ICH Risk

Recommendations for Prognostication of Future ICH Risk
Referenced studies that support recommendations are summarized in Data Supplement 74.

COR	LOE	Recommendation
2a	B-NR	1. In patients with spontaneous ICH in whom the risk for recurrent ICH may facilitate prognostication or management decisions, it is reasonable to incorporate the following risk factors for ICH recurrence into decision-making: (a) lobar location of the initial ICH; (b) older age; (c) presence, number, and lobar location of microbleeds on MRI; (d) presence of disseminated cortical superficial siderosis on MRI; (e) poorly controlled hypertension; (f) Asian or Black race; and (g) presence of apolipoprotein E ε2 or ε4 alleles.[562–571]

9.1.3. Management of Antithrombotic Agents

Recommendations for Management of Antithrombotic Agents
Referenced studies that support recommendations are summarized in Data Supplements 77 through 79.

COR	LOE	Recommendations
2a	C-LD	1. In patients with spontaneous ICH and conditions placing them at high risk of thromboembolic events, for example, a mechanical valve or LVAD, early resumption of anticoagulation to prevent thromboembolic complications is reasonable.[586,587]
2b	B-R	2. In patients with spontaneous ICH with an indication for antiplatelet therapy, resumption of antiplatelet therapy may be reasonable for the prevention of thromboembolic events based on consideration of benefit and risk.[588,589]
2b	B-NR	3. In patients with nonvalvular atrial fibrillation (AF) and spontaneous ICH, the resumption of anticoagulation to prevent thromboembolic events and reduce all-cause mortality may be considered based on weighing benefit and risk.[590–595]
2b	C-LD	4. In patients with AF and spontaneous ICH in whom the decision is made to restart anticoagulation, initiation of anticoagulation ≈7 to 8 weeks after ICH may be considered after weighing specific patient characteristics to optimize the balance of risks and benefits.[596,597]
2b	C-LD	5. In patients with AF and spontaneous ICH deemed ineligible for anticoagulation, left atrial appendage closure may be considered to reduce the risk of thromboembolic events.[598–602]

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Cochrane Library
Cochrane Database of Systematic Reviews
Cochrane Database of Systematic Reviews 2017, Issue 5. Art. No.: CD012144.
DOI: 10.1002/14651858.CD012144.pub2.

Antithrombotic treatment after stroke due to intracerebral haemorrhage (Review)

Perry LA, Berge E, Bowditch J, Forfang E, Rønning OM, Hankey GJ, Villanueva E, Al-Shahi Salman

AUTHORS' CONCLUSIONS

Implications for practice

The available evidence from two RCTs of short-term parenteral anticoagulation after ICH neither support nor discourage the use of short-term antithrombotic treatment after ICH.

There are no published RCTs on long-term antithrombotic treatment after ICH, but seven RCTs are ongoing at the time of this review.

At the present time, clinicians will have to use other sources of information to support clinical judgements.

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Management of oral anticoagulant therapy after intracranial hemorrhage in patients with atrial fibrillation

Front. Cardiovasc. Med. 10:1061618.
doi: 10.3389/fcvm.2023.1061618

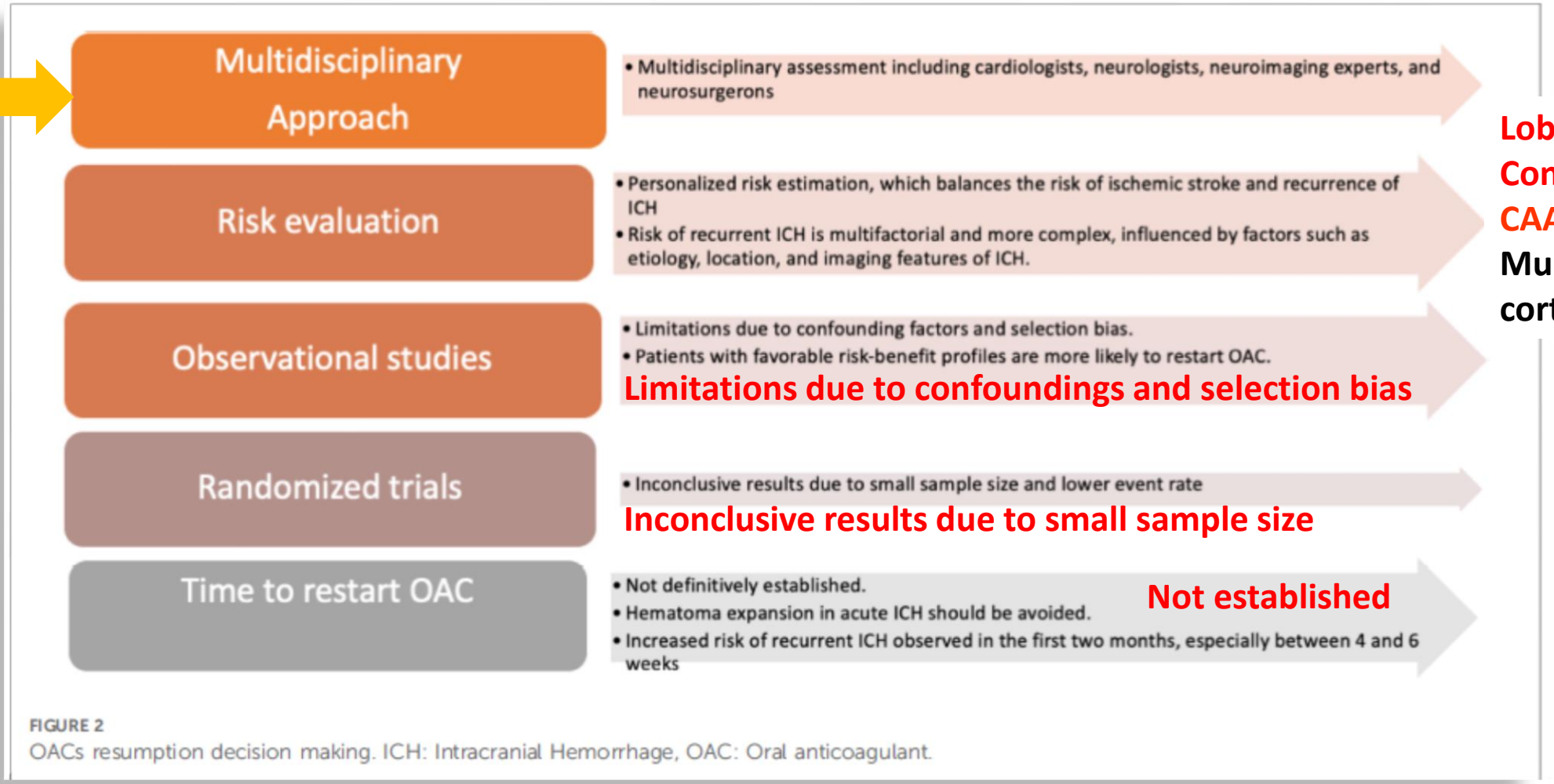

FIGURE 2
OACs resumption decision making. ICH: Intracranial Hemorrhage, OAC: Oral anticoagulant.

Lobar ICH
Convexity SH
CAA-related ICH
Multiple lobar MBs and cortical siderosis

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		Specialty		
		Stroke Neurology (n = 94)	Thrombosis (n = 74)	Neurosurgery (n = 60)
LOBAR ICH	Within 7 days	0.0%	3.20%	9.3%
	1–2 weeks	1.1%	9.70%	18.5%
	3–4 weeks	20.5%	17.70%	33.3%
	1–3 months	20.5%	27.40%	31.5%
	4–6 months	8.0%	8.10%	0.0%
	7–12 months	2.3%	1.60%	0.0%
	Never	47.7%	32.30%	7.4%
LARGE HEMATOMA	Within 7 days	0.0%	4.30%	8.6%
	1–2 weeks	2.2%	8.60%	15.5%
	3–4 weeks	15.6%	18.60%	31.0%
	1–3 months	33.3%	22.90%	37.9%
	4–6 months	13.3%	7.10%	1.7%
	7–12 months	5.6%	2.90%	0.0%
	Never	30.0%	35.70%	5.2%
PREVIOUS ICH	Within 7 days	1.2%	3.40%	6.1%
	1–2 weeks	1.2%	5.10%	2.0%
	3–4 weeks	9.3%	10.20%	24.5%
	1–3 months	7.0%	5.10%	16.3%
	4–6 months	7.0%	3.40%	4.1%
	7–12 months	0.0%	0.00%	0.0%
	Never	74.4%	72.90%	46.9%

Oral anticoagulant re-initiation following intracerebral hemorrhage in non-valvular atrial fibrillation: Global survey of the practices of neurologists, neurosurgeons and thrombosis experts

PLoS ONE 13(1): e0191137.

Overall response from survey participants on timing of OAC re-initiation across 11 clinical scenarios.

ICH: GL & Recommendations

Oral anticoagulant re-initiation following intracerebral hemorrhage in non-valvular atrial fibrillation: Global survey of the practices of neurologists, neurosurgeons and thrombosis experts

PLoS ONE 13(1): e0191137.

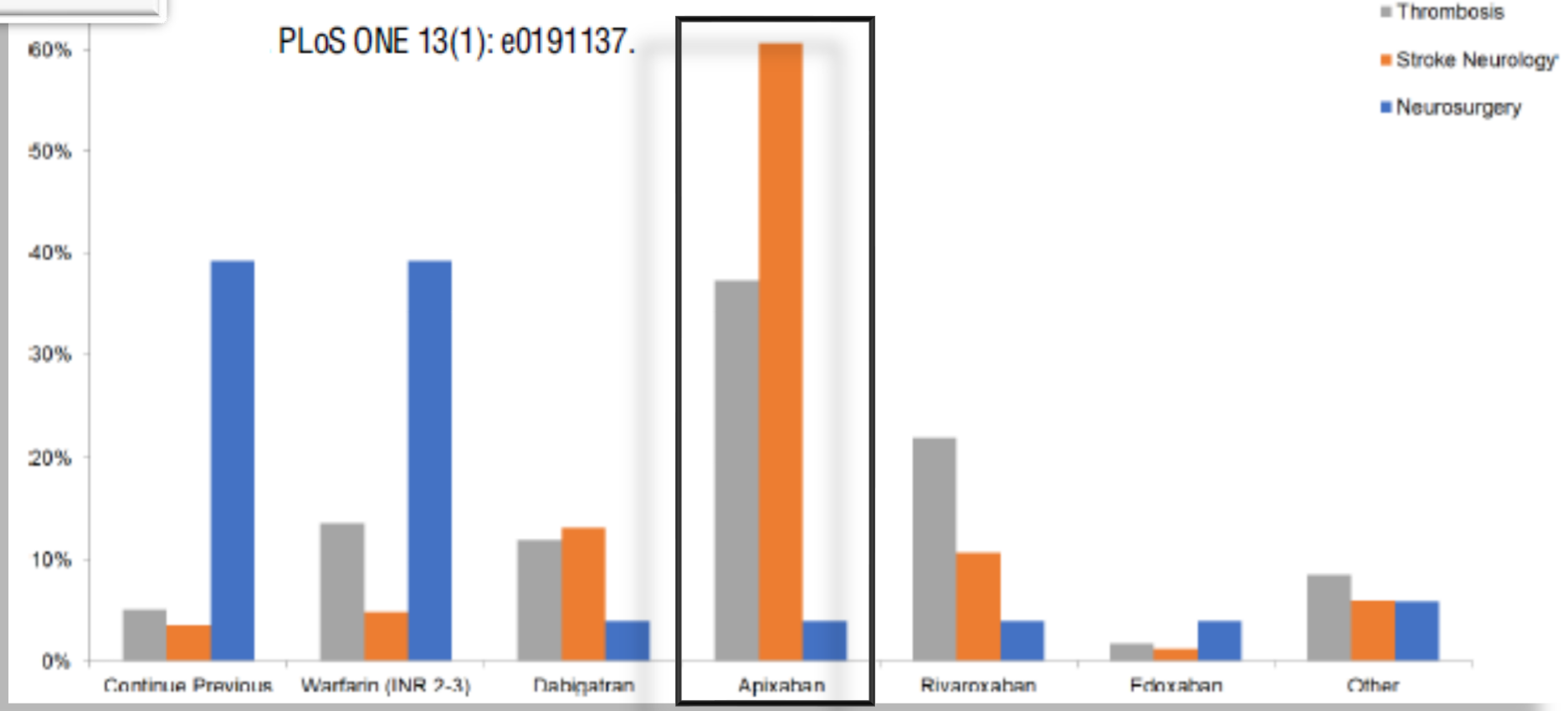

Fig 2. Choice of anticoagulant for re-initiation across thrombosis experts, stroke neurologists and neurosurgeons.

Oral anticoagulant therapy for older patients with atrial fibrillation: a review of current evidence

European Journal of Internal Medicine 41 (2017) 18–27

Mario Bo [a], Enrica Grisoglio [a], Enrico Brunetti [a,*], Yolanda Falcone [a], Niccolò Marchionni [b]

Efficacy and safety outcomes in patients >=75 years

	RE-LY		ROCKET-AF	ARISTOTLE	ENGAGE-AF	
Patients>75 years, n (%)	7528/18113 (40.1%)		6229/14624 (43.7%)	5678/18201 (31.2%)	8474/21105 (40.2%)	
	Dabi 150	Dabi 110	Rivaroxaban	Apixaban	Edoxaban HD	Edoxaban LD
STROKE/SE	0.67 (0.49-0.90)	0.88 (0.66-1.17)	0.80 (0.63-1.02)	0.71 (0.53-0.95)	0.83 (0.67-1.04)	1.12 (0.91-1.40)
MAJOR BLEEDING	1.18 (0.98-1.42)	1.01 (0.83-1.23)	1.11 (0.92-1.34)	0.64 (0.52-0.79)	0.83 (0.70-0.99)	0.47 (0.38-0.58)
IC BLEEDING	0.42 (0.25-0.70)	0.37 (0.21-0.64)	0.80 (0.50-1.28)	0.34 (0.20-0.57)	0.40 (0.26-0.62)	0.31 (0.19-0.49)

American Geriatrics Society 2023 updated AGS Beers Criteria® for potentially inappropriate medication use in older adults

Recommendations

Avoid rivaroxaban for long-term treatment of AF or VTE in favor of safer anticoagulant alternatives

Use caution in selecting dabigatran over other DOACs (e.g. apixaban) for long term treatment of AF or VTE

J Am Geriatr Soc. 2023;1–30.

- Fibrillazione atriale ed ictus cerebrale emorragico: quando e con quali farmaci iniziare la terapia anticoagulante?
  Mario Bo (Torino) **Take-home messages**

I risultati estremamente favorevoli in termini di outcome clinici nei pazienti **iniziati o re-iniziati all'OAT dopo ICH** originano da **studi osservazionali** e, come tali, intrinsecamente **gravati da bias di selezione e plurimi fattori confondenti**. Inoltre, verosimilmente, non riflettono la complessità e la vulnerabilità dei pazienti afferenti alle unità di Geriatria. Di contro, i **pochi RCT** finora condotti su casistiche esigue, hanno prodotto **risultati inconclusivi**.

Al momento non vi sono raccomandazioni attendibili per il trattamento dei **pazienti con FA e ICH**, la cui gestione dovrebbe quindi prioritariamente basarsi **soprattutto nei più anziani** su di una **stima accurata 1) del rischio di recidiva di ICH** (*lobar ICH, convexity SH, CAA-related ICH e cortical microbleeds burden*), **2) del rischio cardioembolico** (*protesi meccanica, bioprotesi mitralica, CHA_2DS_2-VASC>5*), **dell'esito «funzionale» dell'ICH** e della **spettanza di vita globale** del paziente nonché, laddove possibile, delle sue desiderata.

Se il bilancio è decisamente a favore della necessità di TAO, i **DOACs sono l'opzione di prima scelta**, fatte salve condizioni per le quali non sono approvati *(protesi meccaniche e valvulopatie reumatiche*). Sebbene non vi siano studi specifici di confronto **LAAO vs DOACs** in questi pazienti, a mio modesto avviso, la **LAAO rappresenta l'opzione potenzialmente più «vantaggiosa»** in pazienti candidabili alla procedura.