



Debate

Oral Anticoagulation after Successful AF Ablation : Should We Quit or Keep?



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Disclosure

Relationships with commercial interests
: Nothing to disclose



OAC discontinuation after AFCA

: Can I win this debate?

Discontinuing OAC is **against** the guidelines.

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

The Task Force for the diagnosis and management of atrial fibrillation of the European Society of Cardiology (ESC)

Developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC

2014 AHA/ACC/HRS Guideline for the Management of Patients With Atrial Fibrillation

A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society



The guidelines recommend...

Even after **successful AF ablation or appendage closure**,

- Current guidelines recommend **life-long extension of OAC** in case of high thromboembolic risk and the decision **should not be based on the success of the ablation itself**.

Recommendations	Class ^a	Level ^b
Long-term OAC therapy is recommended in patients after AF surgery and appendage closure, based on the patient's thrombo-embolic risk assessed with the CHA ₂ DS ₂ -VASc score.	I	C

ESC 2020 AF Guidelines

Continuation of anticoagulation >2 months after AF catheter ablation, if the procedure is perceived as successful, should be based on consideration of the patient's thromboembolic risk profile, bleeding risk, and patient choice.

AHA 2014 AF Guidelines



Evidence Level of the Recommendations : Low (C)

- There are **no RCT data** regarding interruption of OAC over the **long term after AF ablation**

Recommendations	Class ^a	Level ^b
Long-term OAC therapy is recommended in patients after AF surgery and appendage closure, based on the patient's thrombo-embolic risk assessed with the CHA ₂ DS ₂ -VASc score.	I	C

- **ESC 2020 guideline**

The recommendations were **based only on the thoracic surgeon's guideline** (The Society of Thoracic Surgeons 2017 Clinical Practice Guidelines for the Surgical Treatment of Atrial Fibrillation) *saying that.....*

“Non-randomized studies with longer follow-up have shown better long-term freedom from stroke in patients with persistent sinus rhythm, but not in those with AF despite LAA exclusion.”

ESC 2020 AF Guidelines

- **AHA 2014 guideline**

deferred the judgement (Do or Do not?)

“Continuation of anticoagulation >2 months after AF catheter ablation should be based on consideration of the patient's thromboembolic risk profile, bleeding risk, and patient choice.”

And mentioned only

“Recurrence of AF after ablation is 3 to 7 times more likely to be asymptomatic compared with before ablation, and AF can recur late.”

AHA 2014 AF Guidelines



AF burden and risk of stroke (1)

- Traditional paradigm of **thrombotic risk equivalence** between paroxysmal and non-paroxysmal AF has been presented for 20 years,

460 people with intermittent AF : stroke **3.2%/yr**

1552 with sustained AF : **stroke 3.3%/yr**

Hart RG et al. J Am Coll Cardiol 2000

Limitations

- (1) Absence of long-term rhythm monitoring
- (2) Paroxysmal AF is not purely paroxysmal
- (3) Treatment was limited to aspirin.

- New evidences** from registries and NOAC pivotal trials **challenged** the traditional paradigm of risk equivalence

Takabayashi K et al. Stroke 2015.

Among those not treated with OAC from the Fushimi AF registry,

Paroxysmal AF : Stroke/SE **1.4%/yr**

Sustained AF : Stroke/SE **3.1%/yr**

ARISTOTLE trial : PAF showed 30% lower stroke risk than non-paroxysmal AF (HR 0.70, 95% CI 0.51-0.93)

Al-Khatib SM et al. Eur Heart J 2013.

ENGAGE-AF trial : PAF showed 21% lower stroke risk than persistent AF (HR 0.79, 95% CI 0.66-0.96)

Link MS et al. Circ Arrhythm Electrophysiol 2017.

ROCKET-AF trial : PAF showed 21% lower stroke risk than non-paroxysmal AF (HR 0.79, 95% CI 0.63-1.0)

Steinberg BA et al. Eur Heart J 2015.



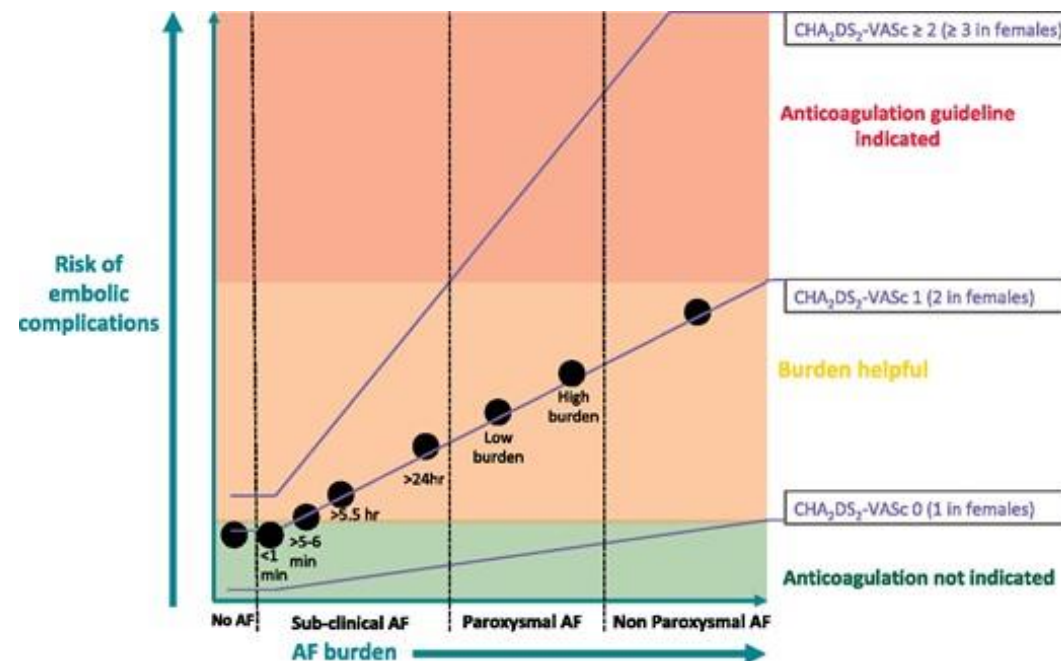
AF burden and risk of stroke (2)

- Paroxysmal atrial fibrillation: does burden make a difference?

- **The rate of thromboembolic events at follow-up increased with increasing AF duration** (continuous rhythm monitoring for 1 year)
: <5 min 1.2% of stroke risk / 5 min – 24hr 1.7% of stroke risk / >24hr 4.0% of stroke risk
- **Known PAF and conducted continuous cardiac monitoring for 14 days**
: tertile 1: AF burden 0.01–2.03%; tertile 2: 2.05–11.28%; tertile 3: 11.36–99.99%.
 - The tertile with **high AF burden** had **3.16-increased** stroke risk (95% CI 1.51–6.62) for after adjusting for CHA₂DS₂-VASc score.

Boriani G et al. Stroke 2011

Go AS et al. JAMA Cardiol 2018



Tiveret et al. Europace 2021



AF ablation reduces AF burden and maybe reduces stroke risk?

- AF ablation reduces AF burden in the CABANA and CASTLE-AF trials.

- AF ablation lowers stroke risk?

- Registry data? YES

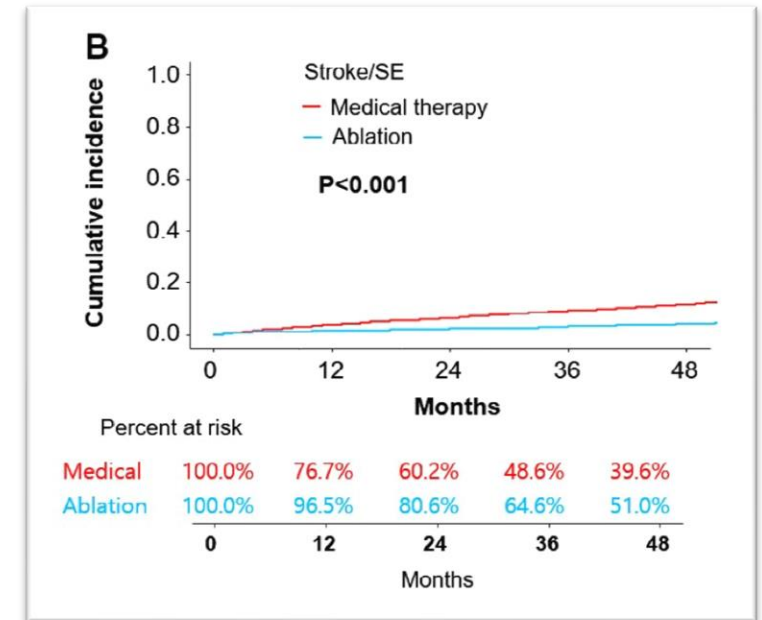
- RCT data? Not confirmed

- CABANA

- Disabling stroke rates over 4 years : 0.1% ablation vs. 0.7% Medical treatment (HR 0.42, P=0.19)

- CASTLE-AF

- Stroke rates over 3 years : 2.8% ablation vs. 6.0% Medical treatment (HR 0.46, P=0.15)



Packer DL et al. CABANA. JAMA 2019.

Marrouche et al. CASTLE-AF. N Engl J Med. 2018.

Bunch TJ et al. Heart Rhythm. 2013.

Yang PS, Joung B et al. J Am Heart Assoc. 2020.



Non-randomized data regarding stopping OAC after AFCA (1)

OAC discontinuation after AFCA is **not rare** in clinical practice.

Data from **ORBIT-AF registry** from **United States**

23.1% of patients with with a **CHA₂DS₂-VASc score of ≥ 2 for men and ≥ 3 for women discontinued OACs after 7 (median) months since AFCA.**

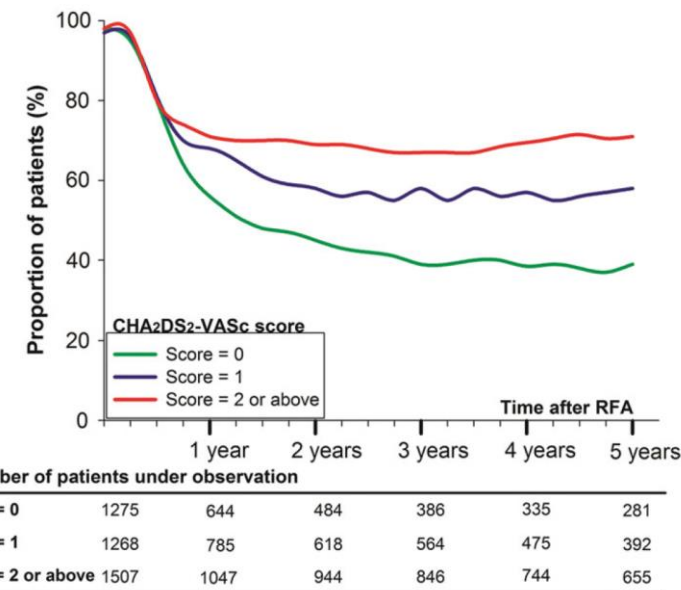
Freeman et al. Circ Arrhythm Electrophysiol. 2019.



Non-randomized data regarding stopping OAC after AFCA (2)

Data from the Danish administrative registries

- About 30% of high-risk patients (CHA₂DS₂-VASc score of ≥2) discontinued OAC therapy at the first year after AFCA
- In high-risk patients (median FU : 3.4 years) OAC continuation was **not associated** with a **decreased stroke risk** but **associated** with a **2 to 3-fold elevated major bleeding risk**.



	Overall		On-OAC		Off-OAC		Univariate comparison	Multivariable comparison
	N	IR (95% CI)	N	IR (95% CI)	N	IR (95% CI)	HR (95% CI)	HR (95% CI) ^a
Thromboembolism	71	0.60 (0.48–0.76)	36	0.56 (0.40–0.78)	35	0.64 (0.46–0.89)	1.13 (0.71–1.78)	1.42 (0.86–2.35)
CHA ₂ DS ₂ -VASc = 0	21	0.51 (0.33–0.77)	8	0.50 (0.25–1.00)	13	0.51 (0.30–0.88)	1.01 (0.42–2.42)	1.09 (0.42–3.36)
CHA ₂ DS ₂ -VASc = 1	13	0.37 (0.22–0.62)	3	0.14 (0.05–0.44)	10	0.59 (0.32–1.10)	3.51 (0.98–12.5)	3.84 (1.01–14.6)
CHA ₂ DS ₂ -VASc ≥ 2	37	0.95 (0.68–1.30)	25	0.93 (0.63–1.38)	12	0.97 (0.55–1.71)	1.05 (0.53–2.07)	1.16 (0.56–2.38)
							HR (95% CI)	HR (95% CI) ^b
Serious bleeding	87	0.73 (0.60–0.90)	63	0.99 (0.77–1.27)	24	0.44 (0.29–0.65)	2.06 (1.26–3.36)	2.05 (1.25–3.35)
HAS-BLED ≤ 1	46	0.58 (0.43–0.77)	28	0.73 (0.51–1.07)	18	0.43 (0.27–0.69)	1.62 (0.87–3.04)	1.84 (0.99–3.42)
HAS-BLED = 2	27	0.98 (0.67–1.43)	23	1.31 (0.87–1.98)	4	0.40 (0.15–1.06)	2.77 (0.93–8.23)	2.77 (0.93–8.28)
HAS-BLED ≥ 3	14	1.21 (0.72–2.05)	12	1.45 (0.82–2.56)	2	0.60 (0.15–2.42)	2.50 (0.54–11.6)	3.05 (0.63–14.7)

Karasoy et al. Eur Heart J. 2015.

Does the **bleeding risk** outweigh the **uncertain benefit** of stroke prevention?

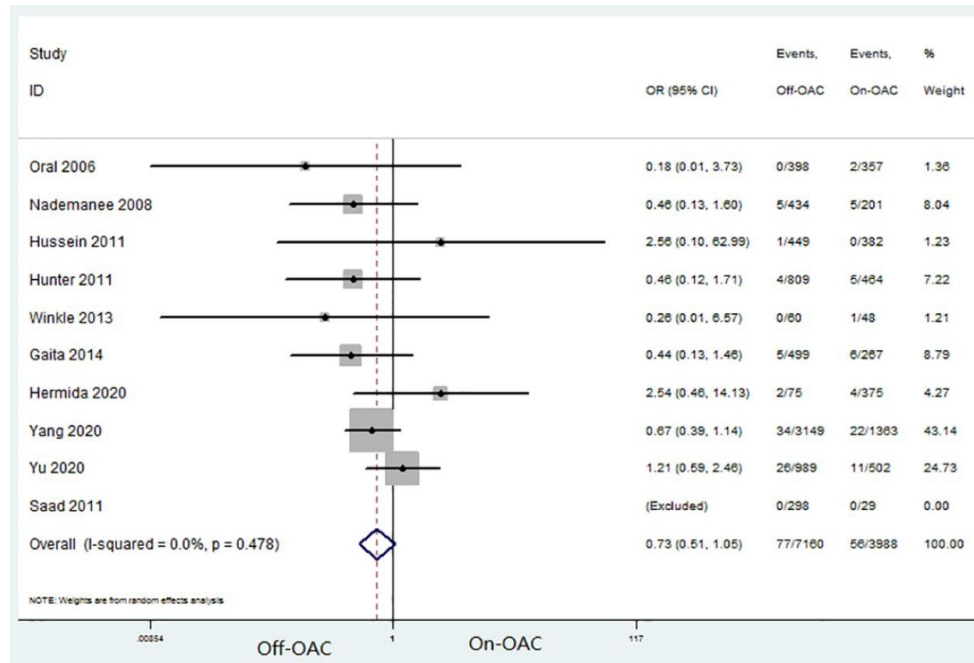


Non-randomized data regarding stopping OAC after AFCA (3)

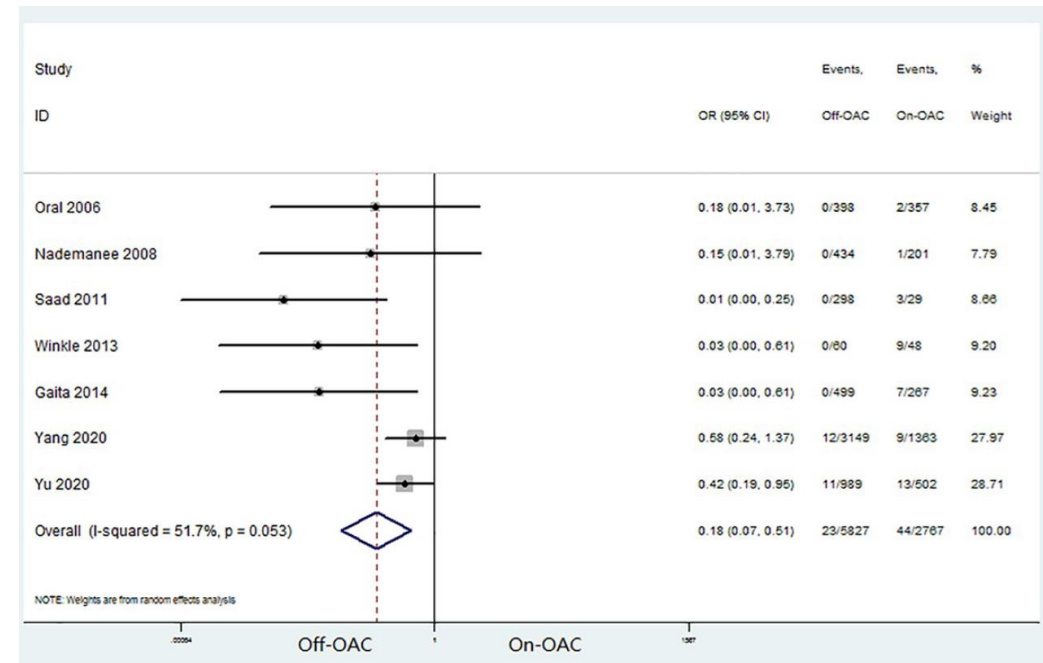
Meta-analysis of prospective studies

- OAC discontinuation was **not associated** with an **increased stroke risk** but **associated** with **82% decreased major bleeding risk**.

Thromboembolism



Major bleeding



Non-randomized data regarding the issue (4)

- Korean unpublished data

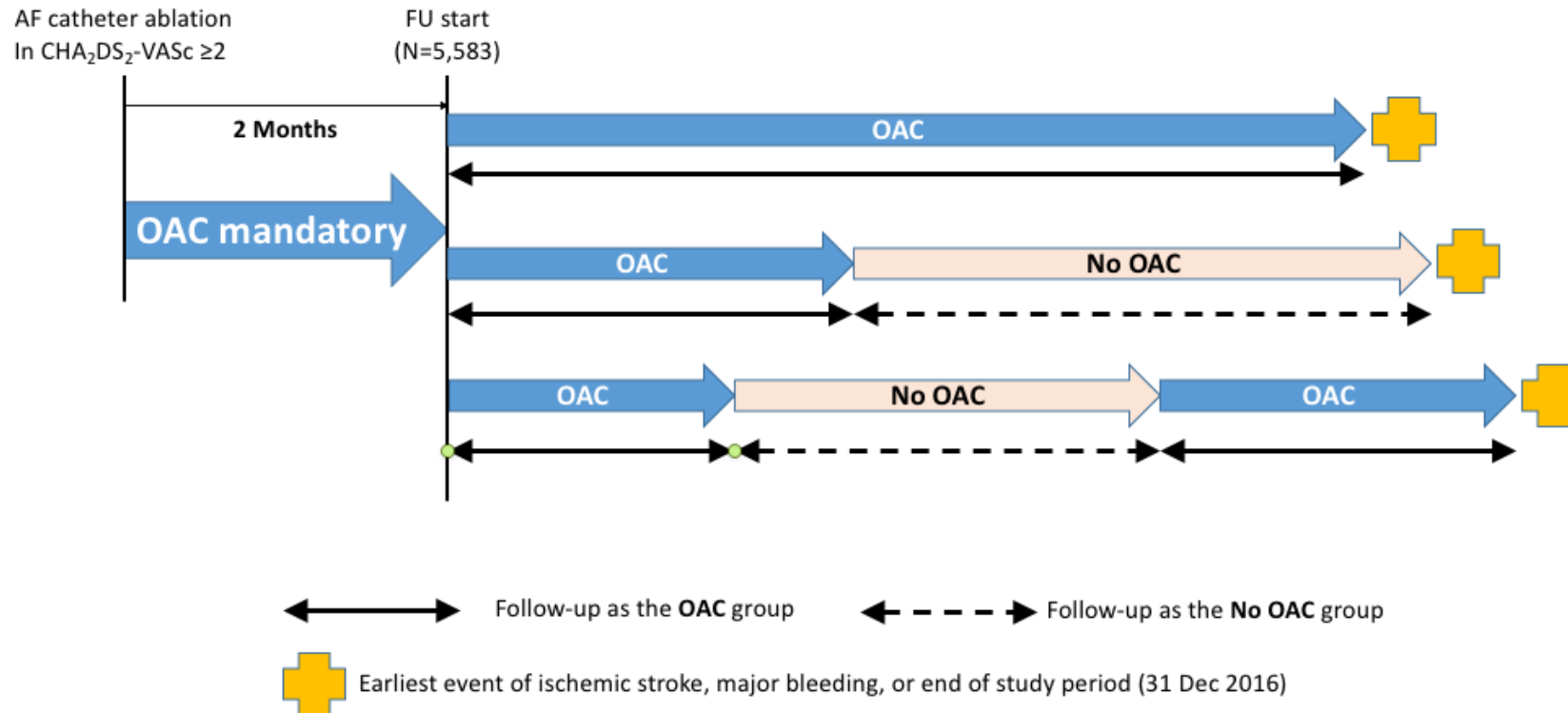
- **Study hypothesis**
: Discontinuation of OAC at 2 months after ablation in patients with no AF recurrence would.... 1) **Not increase the risk of stroke** / 2) **Decrease the risk of bleeding**
- **Population-based retrospective cohort study**
- **Data source**
: National Health Insurance Service (NHIS) of Korea
- **Participants**
: 5,583 AF adults undergoing catheter ablation in Korea between 2005 and 2015
 - With **CHA₂DS₂-VASc score ≥2**
 - Receiving at least **mandatory eight weeks of anticoagulation after ablation** in accordance with guidelines
- **Primary outcome: Net adverse clinical event**
→ First occurrence of ischemic stroke or major bleeding



Non-randomized data regarding stopping OAC after AFCA (4)

- Korean unpublished data

- Time-varying analysis to avoid immortal time bias



Non-randomized data regarding stopping OAC after AFCA (4)

- Korean unpublished data

Net adverse clinical event (Ischemic stroke + Major bleeding)

Outcome	OAC stopped			OAC continued			Absolute rate difference per 100 person-years* (95% CI)	Weighted HR (95% CI)	P value
	Number of events	Person-years	Event rate, %/yr	Number of events	Person-years	Event rate, %/yr			
Net adverse clinical event	181	13,661	1.37	128	6,148	2.00	-0.63 (-1.23 to -0.03)	0.85 (0.66–1.10)	0.220
Ischemic stroke	89	13,661	0.67	57	6,148	0.88	-0.21 (-0.61 to 0.20)	0.96 (0.67–1.39)	0.841
Major bleeding	99	13,661	0.75	74	6,148	1.17	-0.42 (-0.88 to 0.04)	0.76 (0.53–1.08)	0.124

No difference in net adverse event, stroke, or bleeding, generally

Non-randomized data regarding stopping OAC after AFCA (4)

- Korean unpublished data

Results – Stratified analysis according to AF recurrence

: New AAD prescription after 3M blanking period, Cardioversion, or redo AFCA

Outcome	OAC stopped			OAC continued			Absolute rate difference per 100 person-years* (95% CI)	Weighted HR (95% CI)	P value
	Number of events	Person -years	Event rate*	Number of events	Person -years	Event rate*			
AF recurrence									
Net adverse clinical event	72	5,511	1.31	42	3,238	1.30	0.01 (-0.49 to 0.50)	1.30 (0.81–2.08)	0.281
Ischemic stroke	37	5,511	0.70	20	3,238	0.61	0.09 (-0.42 to 0.59)	1.29 (0.68–2.45)	0.432
Major bleeding	38	5,511	0.72	24	3,238	0.73	-0.01 (-0.55 to 0.53)	1.13 (0.59–2.15)	0.710
No AF recurrence									
Net adverse clinical event	109	8,150	1.38	86	2,910	2.81	-1.43 (-2.44 to -0.42)	0.65 (0.47–0.90)	0.010
Ischemic stroke	52	8,150	0.66	37	2,910	1.19	-0.53 (-1.19 to 0.13)	0.76 (0.47–1.24)	0.274
Major bleeding	61	8,150	0.77	50	2,910	1.66	-0.89 (-1.66 to -0.12)	0.58 (0.37–0.89)	0.013

- No difference of clinical outcome in patients with AF recurrence**
- Positive net clinical benefit of OAC discontinuation in patients without recurrence, driven by decrease of bleeding**

Non-randomized data regarding stopping OAC after AFCA (4)

- Korean unpublished data

Results – Annual Stroke and Bleeding Rate

	OAC stopped				OAC continued			
	N of Pts	N of events	Person-years	Event rate, %/year	N of Pts	N of events	Person-years	Event rate, %/year
Stroke								
CHA₂DS₂-VASc								
2	1814	20	6082	0.33	2054	11	1804	0.61
3	1171	23	3594	0.64	1466	8	1578	0.51
4	684	21	2068	1.02	958	9	1259	0.71
5	435	17	1237	1.37	633	16	906	1.77
≥6	294	8	680	1.18	472	13	601	2.16
Major bleeding								
HAS-BLED								
0 – 1	1349	19	3888	0.49	1174	9	1242	0.72
2	2052	39	5173	0.75	1630	20	2234	0.90
3	1465	25	3293	0.76	1098	21	1794	1.17
4	599	13	1106	1.18	410	19	746	2.55
≥5	118	3	202	1.49	86	5	132	3.79

Even after OAC discontinuation, Lower stroke rates than general AF patients not ablated
High bleeding rate in OAC continued patients

Non-randomized data regarding stopping OAC after AFCA (5)

- Summary

- Observational studies suggest...

As long as there was no evidence of AF recurrence,

discontinuing OAC after AFCA was associated with a **positive net clinical outcome** (35% risk reduction), mainly driven by...

no difference in stroke risk and **decreased risk for major bleeding** (42 ~ 82% risk reduction).

- Limitations....

1) OAC discontinued patients tend to have less burden or 0% burden of AF (lower AF burden after AFCA) than OAC continued patients (higher AF burden after AFCA) in routine clinical practice.

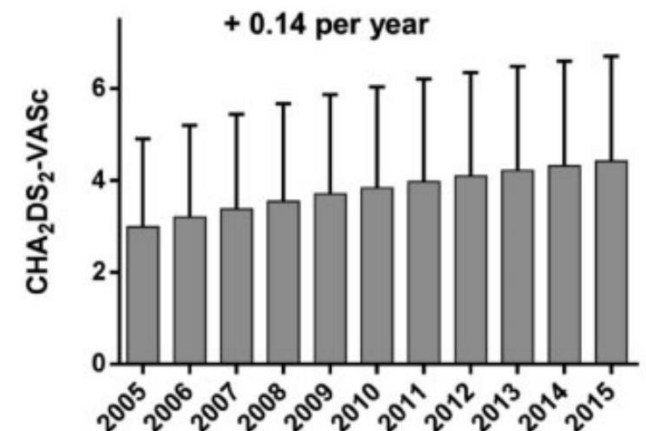
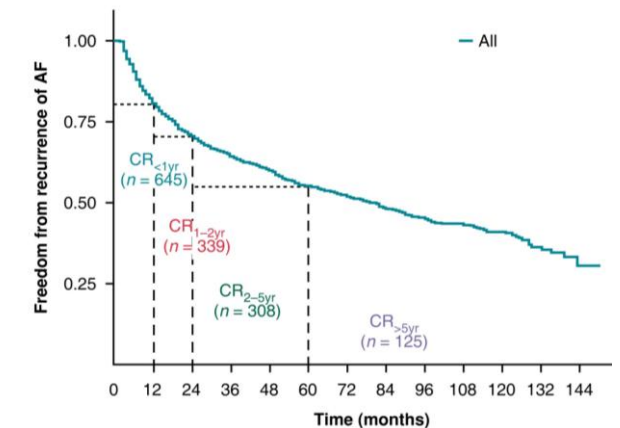
→ The results of the data were probably **biased**.

2) How about patients with **long-term late recurrence of AF**?

→ Is it really OK to keep stopping OAC even after 5 to 10 years?

- Thrombotic risk (CHA₂DS₂-VASC score) **keeps dynamically increasing** as time goes by (Patients get older and have more comorbidities!!!)

AF Recurrence after de novo procedures

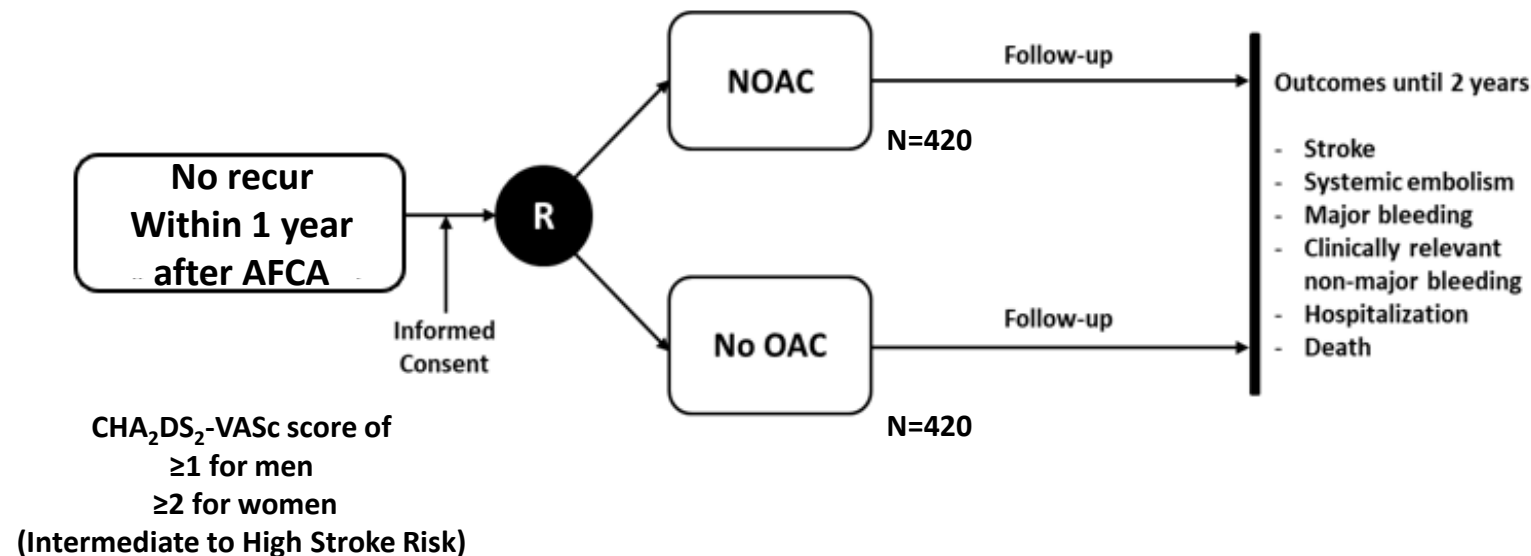


Awaiting RCT evidence...

- The **OCEAN trial** (Optimal Anti-Coagulation for Enhanced-Risk Patients Post-Catheter Ablation for Atrial Fibrillation) is nearing its completion

Verma A, Ha ACT, Kirchhof P, et al. Am Heart J 2018

- The **ALONE trial** (Anticoagulation ONE year after ablation of atrial fibrillation in patients with Atrial Fibrillation) from **South Korea** completed the enrollment.



Summary

Available data that support the strategy of **stopping OAC after ablation** in a patient who **no longer has AF**

- The risk of stroke is linked to the type of AF and also to the burden of atrial fibrillation (**dose-dependent relationship**)
 - Patients with a low AF burden have a lower stroke risk than those with a high burden
- Patients who undergo AFCA have a **lower risk of stroke** than matched controls who do not undergo ablation and furthermore that their risk of stroke is **similar to that in patients without AF**.
- Patients who stop anticoagulation therapy after ablation have a **low risk of stroke and bleeding**.
- It might be feasible to use a **“pill in the pocket”** approach to anticoagulation in patients with a low AF burden
- More active surveillance of AF burden in daily-life is now feasible (wearable ECG patch, Smartwatches, and ILR)



Conclusion

On the premise of that....

1. **No clinical recurrence** during long-term and regular **follow-up by EP specialist** (who understands the progressive nature of AF),
2. **No detected sustained AF** in active surveillance of **AF burden in daily-life** using continuous monitoring or at-least intermittent monitoring
3. The patient is **informed about the advantages and disadvantages of a strategy of anticoagulation** as compared with no anticoagulation,

Individualizing OAC treatment after ablation, instead of blindly taking OAC, might be a safer (lowering bleeding risk), tailored therapy for patients with AF