2023-06-24
13:30-14:30
20 min

Optimizing anticoagulation in procedures and benefits of Eliquis in AF patients

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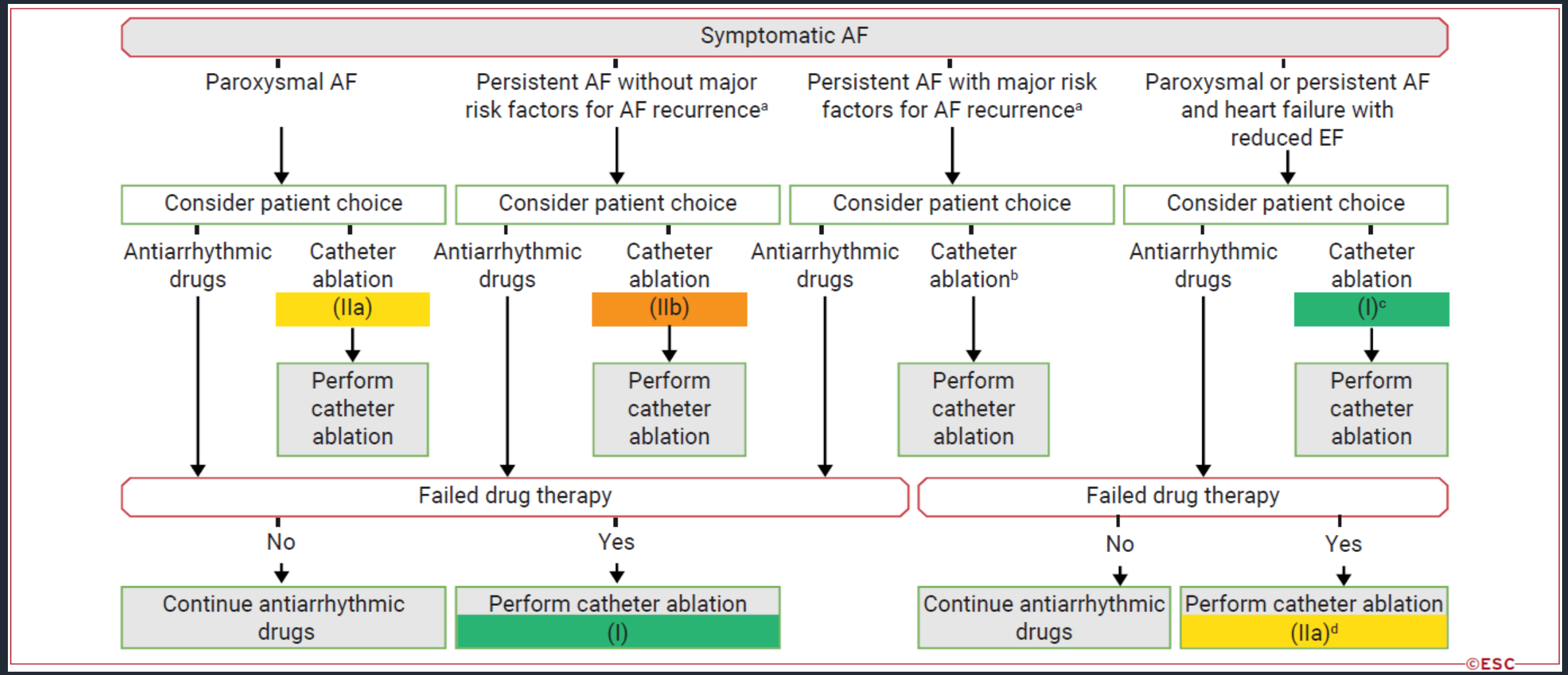
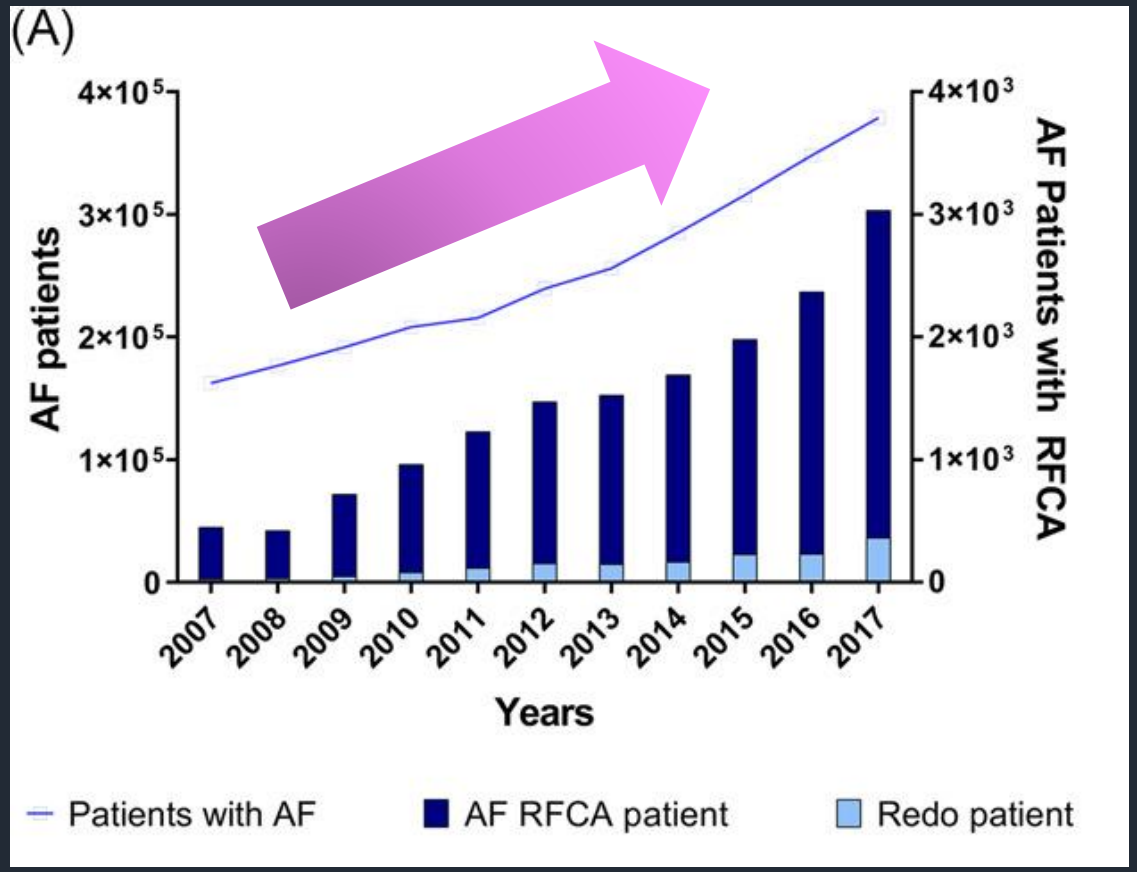
1. Catheter ablation
2. Cardioversion

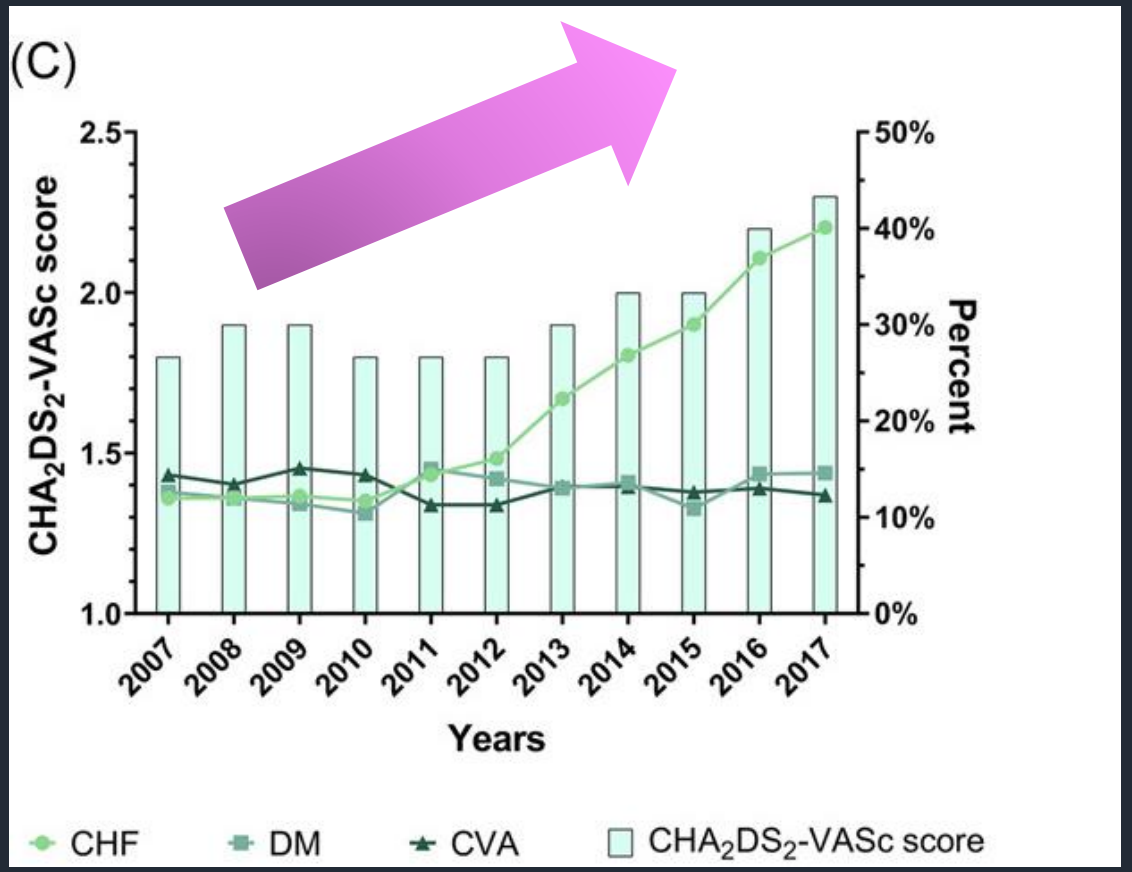
Indication for catheter ablation



[a]Significantly enlarged LA volume, advanced age, long AF duration, renal dysfunction, and other cardiovascular risk factors. [b]In rare individual circumstances, catheter ablation may be carefully considered as first-line therapy. [c]Recommended to reverse LV dysfunction when tachycardiomyopathy is highly probable.[d]To improve survival and reduce hospitalization.

Catheter ablation for AF patients





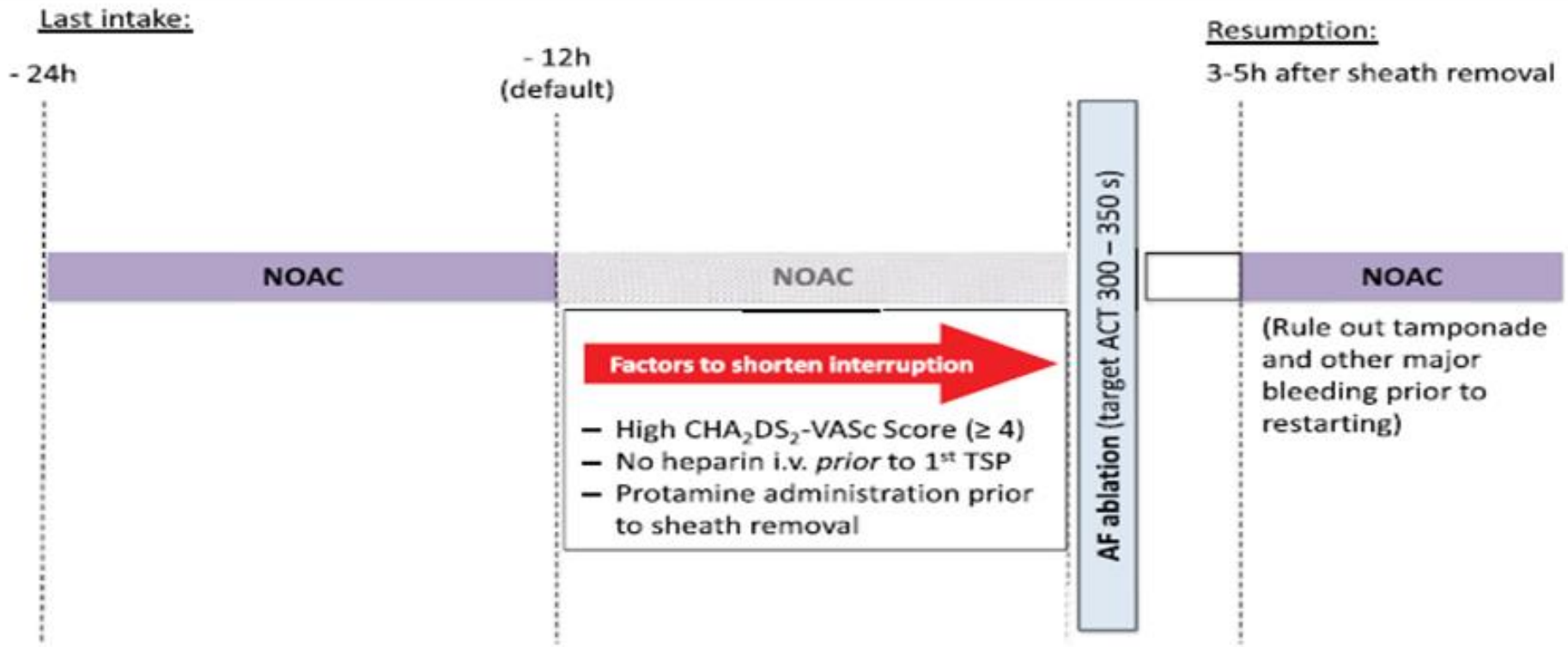
J Cardiovasc Electrophysiol. 2020;31:2616-2625.

Stroke risk management peri-catheter ablation

- Therapeutic OAC for at least 3 weeks before ablation
- Oral anticoagulants without interruption is recommended

Recommendations	Class[a]	Level[b]
In AF patients with stroke risk factors not taking OAC before ablation, it is recommended that pre-procedural management of stroke risk includes initiation of anticoagulation and:	I	C
• Preferably, therapeutic OAC for at least 3 weeks before ablation, or • Alternatively, the use of TOE to exclude LA thrombus before ablation.	IIa	C
For patients undergoing AF catheter ablation who have been therapeutically anticoagulated with warfarin, dabigatran, rivaroxaban, apixaban, or edoxaban, performance of the ablation procedure without OAC interruption is recommended.[878,879,881]	I	A

도자절제술(Catheter Ablation)



- 시술 3주 전부터 시술 8주 후까지 급여 인정[1]

Adapted from Steffel J et al, 2021

1. 보건복지부「요양급여의 적용기준 및 방법에 관한 세부사항(약제)」일부개정고시(2022-184호). 2022:1-22, 2. Steffel J et al. 2021 European Heart Rhythm Association Practical Guide on the Use of Non-Vitamin K Antagonist K Antagonist Oral Anticoagulants in Patients with Atrial Fibrillation. Europace. 2021 Oct 9;23(10):1612-1676.

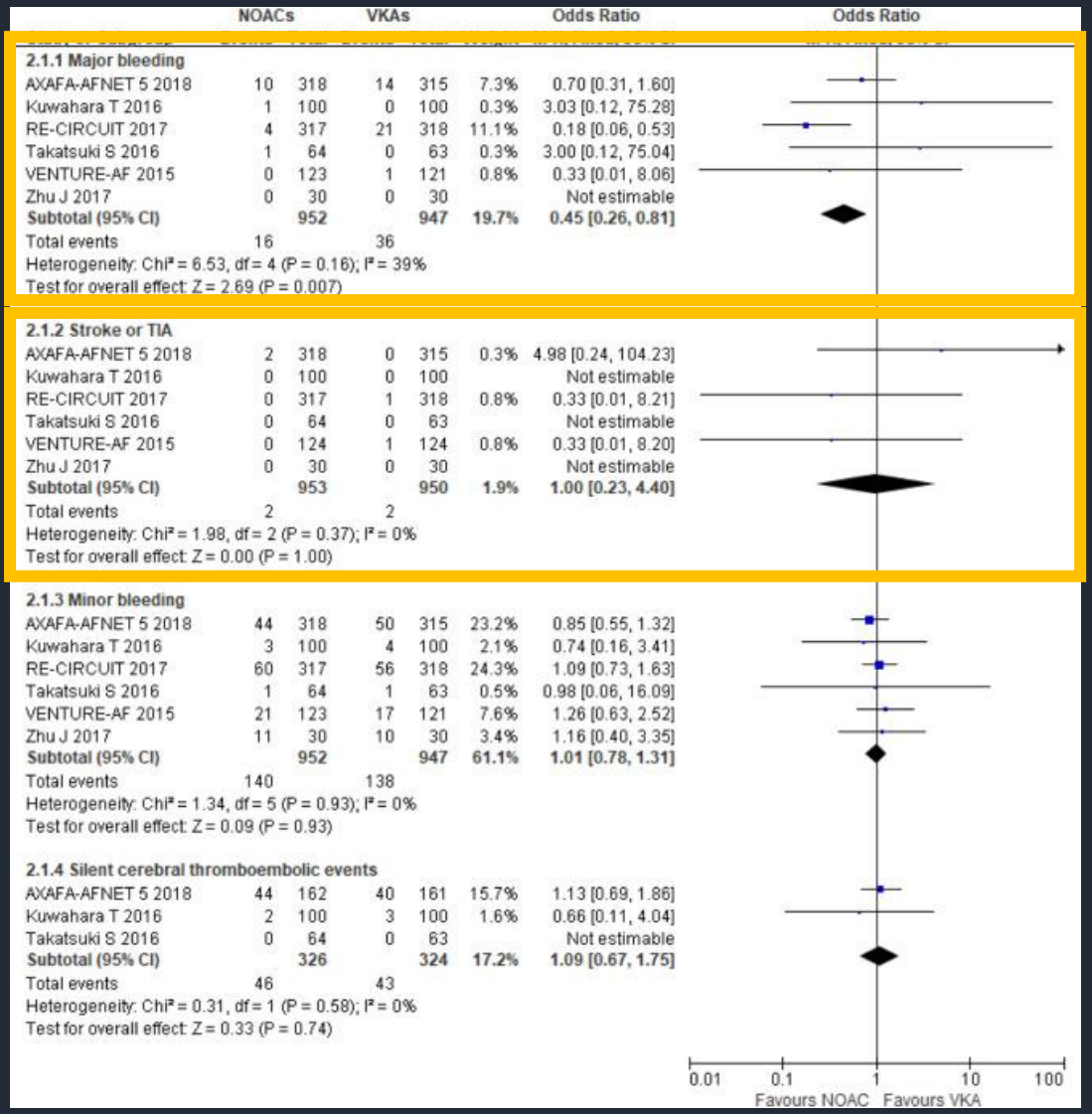
아픽사반의 급여확대: 2022년 8월 1일 약제 급여기준 고시개정

333 혈액응고저지제

구 분	세부인정기준 및 방법		사유
	현 행	개 정 (안)	
Apixaban 경구제 (품명: 엘리퀴스정 등)	허가사항 범위 내에서 아래와 같은 기준으로 투여 시 요양급여를 인정하며, 동 인정기준 이외에는 약값 전액을 환자가 부담토록 함. 아 래 가 (생략) 나 **비판막성 심방세동 환자에서 뇌졸중 및 전신 색전증의 위험 감소** • **비판막성 심방세동 환자 중 다음의 고위험군에 투여시 인정** - 다 음 - 1 뇌졸중, 일과성허혈발작, 혈전색전증의 과거력이 있거나 75세 이상 환자 또는 2 6가지 위험인자(심부전, 고혈압, 당뇨, 혈관성질환, 65-74세, 여성) 중 2가지 이상의 조건을 가지고 있는 환자 **<신 설>** 다 (생략)	허가사항 범위 내에서 아래와 같은 기준으로 투여 시 요양급여를 인정하며, 동 인정기준 이외에는 약값 전액을 환자가 부담토록 함. 아 래 가 (생략) 나 **비판막성 심방세동 환자에서 뇌졸중 및 전신 색전증의 위험 감소** • **비판막성 심방세동 환자 중 다음의 고위험군에 투여시 인정** - 다 음 - 1 뇌졸중, 일과성허혈발작, 혈전색전증의 과거력이 있거나 75세 이상 환자 또는 2 6가지 위험인자(심부전, 고혈압, 당뇨, 혈관성질환, 65-74세, 여성) 중 2가지 이상의 조건을 가지고 있는 환자 또는 3) 아래와 같은 시술 시행(또는 예정)이 진료기록부 상 확인된 경우 - 아 래 - **가) 전기적 심율동전환술(Electrical Cardioversion): 시술 3주전부터 시술 4주 후까지 투여 시** **나) 도자절제술(Catheter Ablation): 시술 3주 전부터 시술 8주후까지 투여 시** ※전기적 심율동전환술: 자588 제세동술 및 전기적 심조율전환 ※도자절제술: 자654가(2) 부정맥의 고주파절제술-심방세동 자654나(2) 삼차원 빈맥 지도화를 이용한 부정맥의 고주파절제술-심방세동 자654-1 부정맥의 냉각절제술-냉각풍선절제술 다 (생략)	국내외 허가사항, 교과서, 임상진료지침, 임상연구문헌, 관련 학회의견 등을 고려하여 비판막성 심방세동 환자의 전기적 심율동전환술 및 도자절제술시 NOAC 투여를 인정하며 투여기간을 명시함.

1.보건복지부「요양급여의 적용기준 및 방법에 관한 세부사항(약제)」일부개정고시(2022-184호). 2022:1-22

Meta-analysis: Uninterrupted NOACs



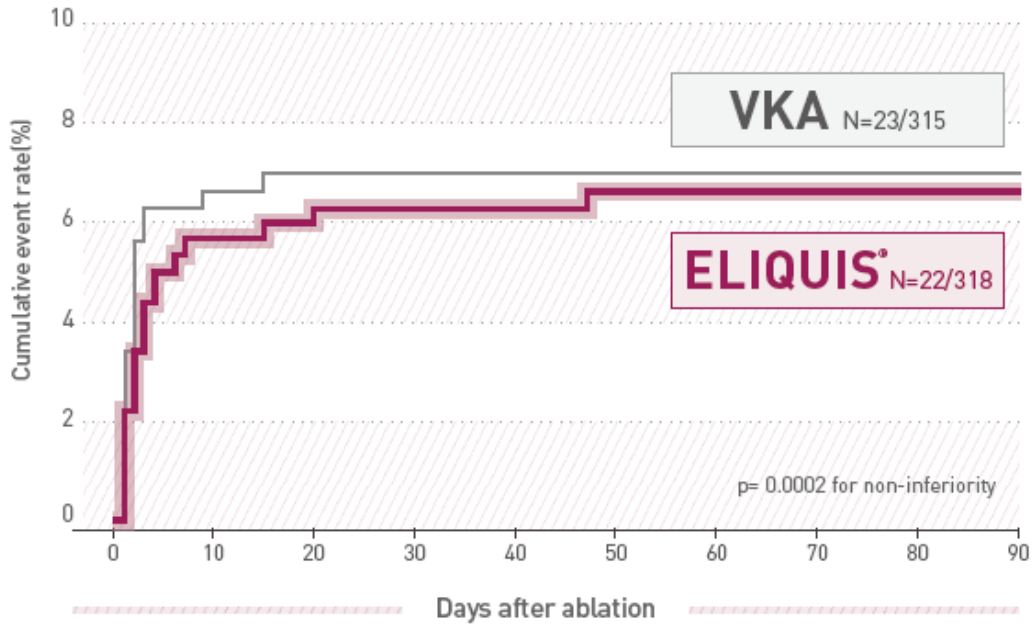
- The incidence of major bleeding was significantly lower in the NOAC group (1.68%) than the VKA group (3.80%) (OR = 0.45, 95% CI = 0.26–0.81, p = 0.007);
- The incidence of ischemic stroke or TIA was low and similar between NOAC (0.21%) and VKA groups (0.21%).

Zhao Y, et al. A meta-analysis of randomized controlled trials of uninterrupted periprocedural anticoagulation strategy in patients undergoing atrial fibrillation catheter ablation. Int J Cardiol. 2018;270:167-171.

AXAFA-AFNET 5

PATIENTS WITH PRIMARY ENDPOINT

Composite of all-cause death, stroke, or major bleeding



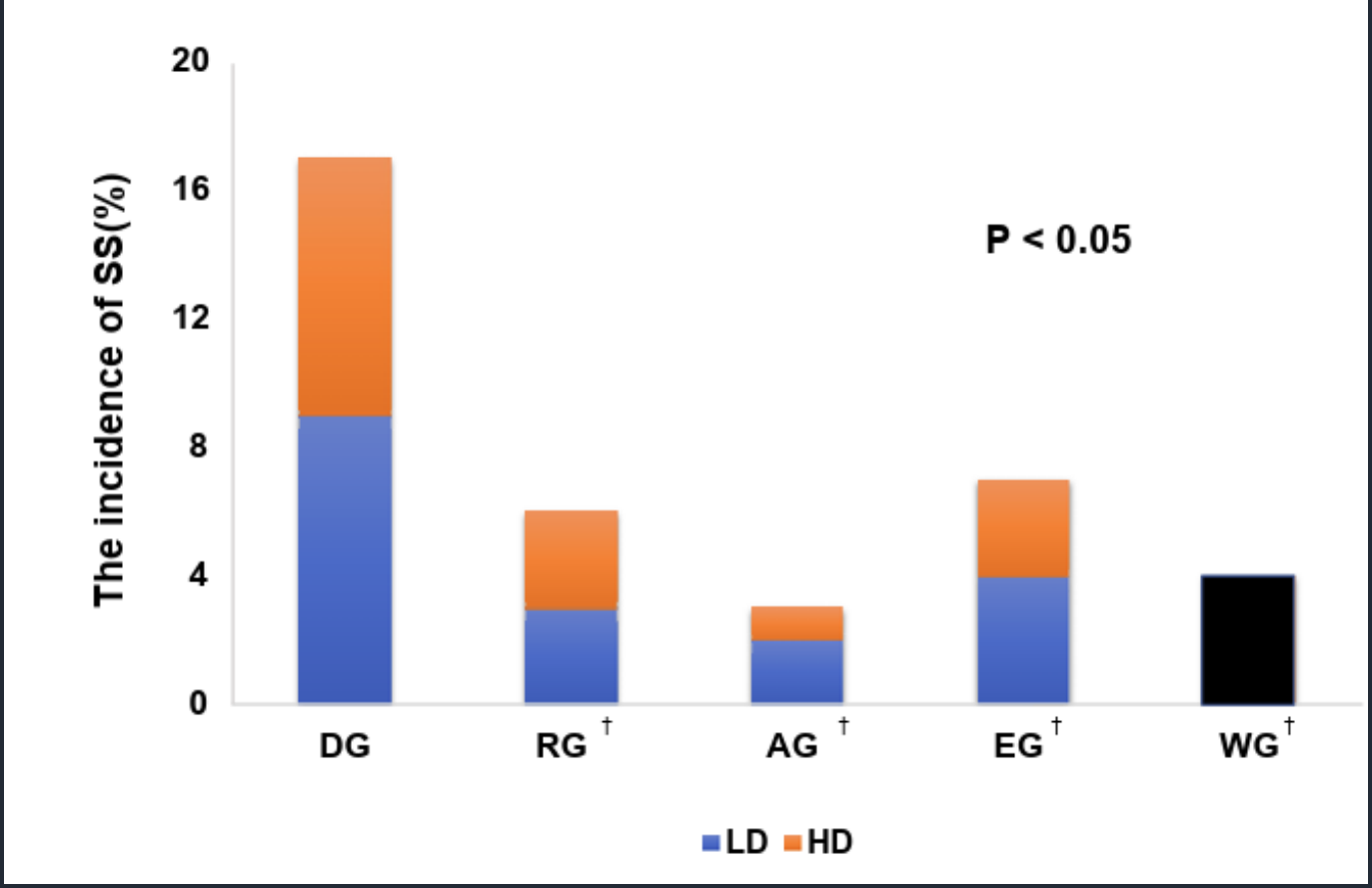
Adapted from: Kirchhof P et al. 2018.[1]

RESULTS OF ENDPOINTS IN DETAIL

	ELIQUIS® n=318	VKA n=315
» 사망	1 (0.3%)	1 (0.3%)
» 뇌졸중 혹은 일과성허혈성 발작	2 (0.6%)	0 (0.0%)
» 주요 출혈 (BARC 2-5)	20 (6.2%)	25 (7.9%)
» 주요 출혈 (ISTH)	10 (3.1%)	14 (4.4%)

Adapted from: Kirchhof P et al. 2018.[1]

Incidence of Silent stroke (SS) detected via MRI-DW after the procedure



- The incidence of SS detected via MRI-DW after the proced ure in DG was significantly higher than in the other groups

  (DG 17%, RG 6%, AG 3%, EG 7%, WG 4%; P <.05)

Comparison of the incidence of periprocedural silent stroke (SS) among anticoagulant groups.
†P <.05 vs dabigatran group(DG).HD=high dose; LD = low dose

Adapted from Nagao T et al.2020

Incidence of Silent stroke (SS) detected via MRI-DW after the procedure

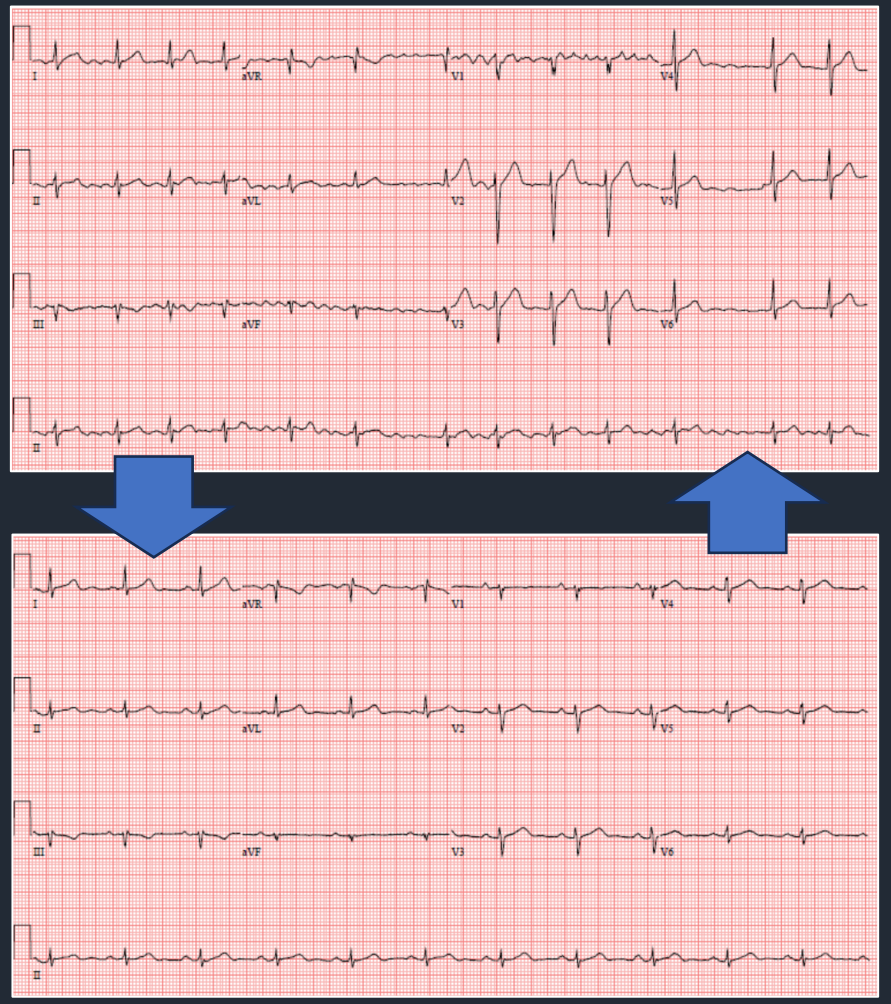
Table 2 Procedural values

	DG (n = 64)	RG (n = 62)	AG (n = 60)	EG (n = 59)	WG (n = 30)	*P* value
AF at the start of session	31 (49)	30 (48)	26 (43)	37 (62)	15 (50)	.56
ACT before heparin bolus (s)	170 ± 42	143 ± 33	132 ± 23	148 ± 38	147 ± 45	<.001
First ACT after heparin bolus (s)	309 ± 52	294 ± 57	280 ± 52	308 ± 78	317 ± 40	.18
First ACT <300 s after heparin bolus	34 (53)	33 (53)	37 (62)	29 (49)	14 (48)	.29
First ACT <350 s after heparin bolus	51 (80)	53 (85)	52 (87)	44 (75)	27 (90)	.41
Maximum ACT (s)	336 ± 76	338 ± 72	336 ± 77	358 ± 59	362 ± 99	.40
Minimum ACT (s)	240 ± 33	238 ± 39	229 ± 32	243 ± 35	252 ± 30	.81
Mean ACT (s)	290 ± 40	289 ± 33	290 ± 33	302 ± 37	305 ± 53	.28
Time required to reach target ACT (min)	24 ± 15	28 ± 17	35 ± 17	30 ± 19	23 ± 11	<.05
UFH (U/kg)	129 ± 38	146 ± 59	162 ± 62	131 ± 25	105 ± 46	<.001
Procedure time (min)	191 ± 43	194 ± 47	186 ± 42	185 ± 41	171 ± 35	.23
AM session	44 (68)	35 (57)	38 (63)	35 (59)	16 (53)	.22
Cardioversion	24 (38)	19 (31)	16 (26)	25 (42)	8 (27)	.57
Additional procedure	20 (31)	22 (35)	20 (33)	21 (36)	10 (32)	.51
Total delivered energy (kJ)	55 ± 17	52 ± 23	52 ± 15	54 ± 22	44 ± 20	.41
Application time (min)	30 ± 12	28 ± 11	29 ± 7	28 ± 12	24 ± 11	.36

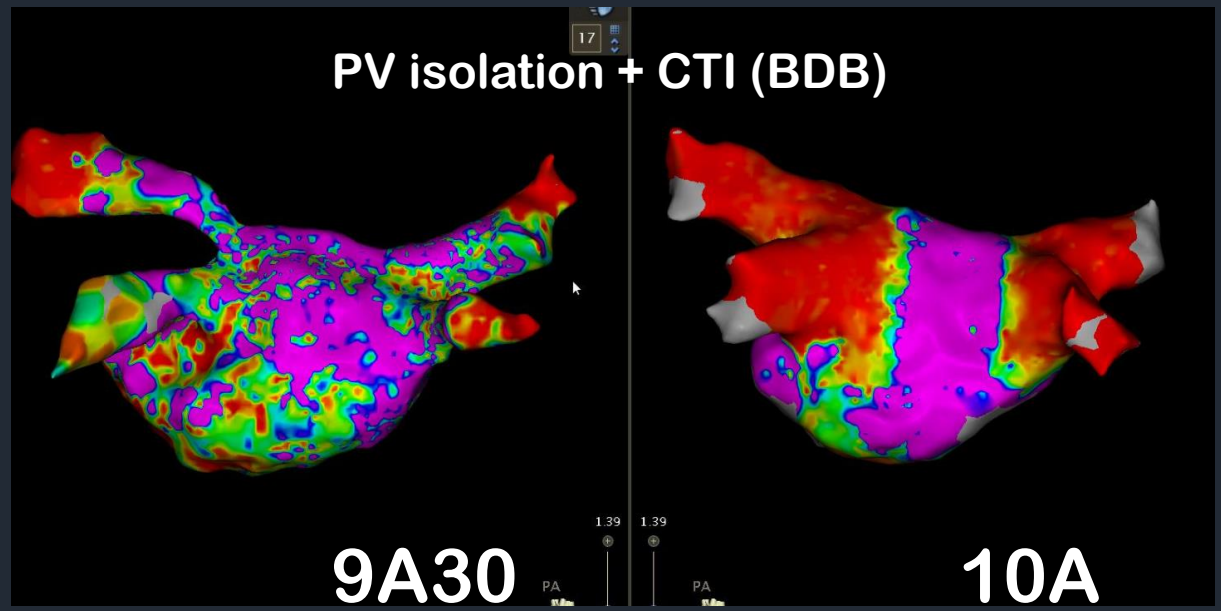
Adapted from Nagao T et al.2020

CASE. Uninterrupted apixaban

- Male / 49 YO
- Paroxysmal atrial fibrillation
- Palpitation → Atrial fibrillation
  - Refractory to Flecainide
  - Refractory to Dronedarone
  - Planned RF catheter ablation
- On once daily NOAC
- → Changed to Eliquis 5mg bid



CASE. Uninterrupted apixaban



Eliquis

Eliquis

9A

9A30

10A

10A30

30min

30min

Baseline ACT 192 sec

Bolus heparin
(7000U)

ACT 289 sec

Bolus heparin
(3000U)

ACT 325 sec

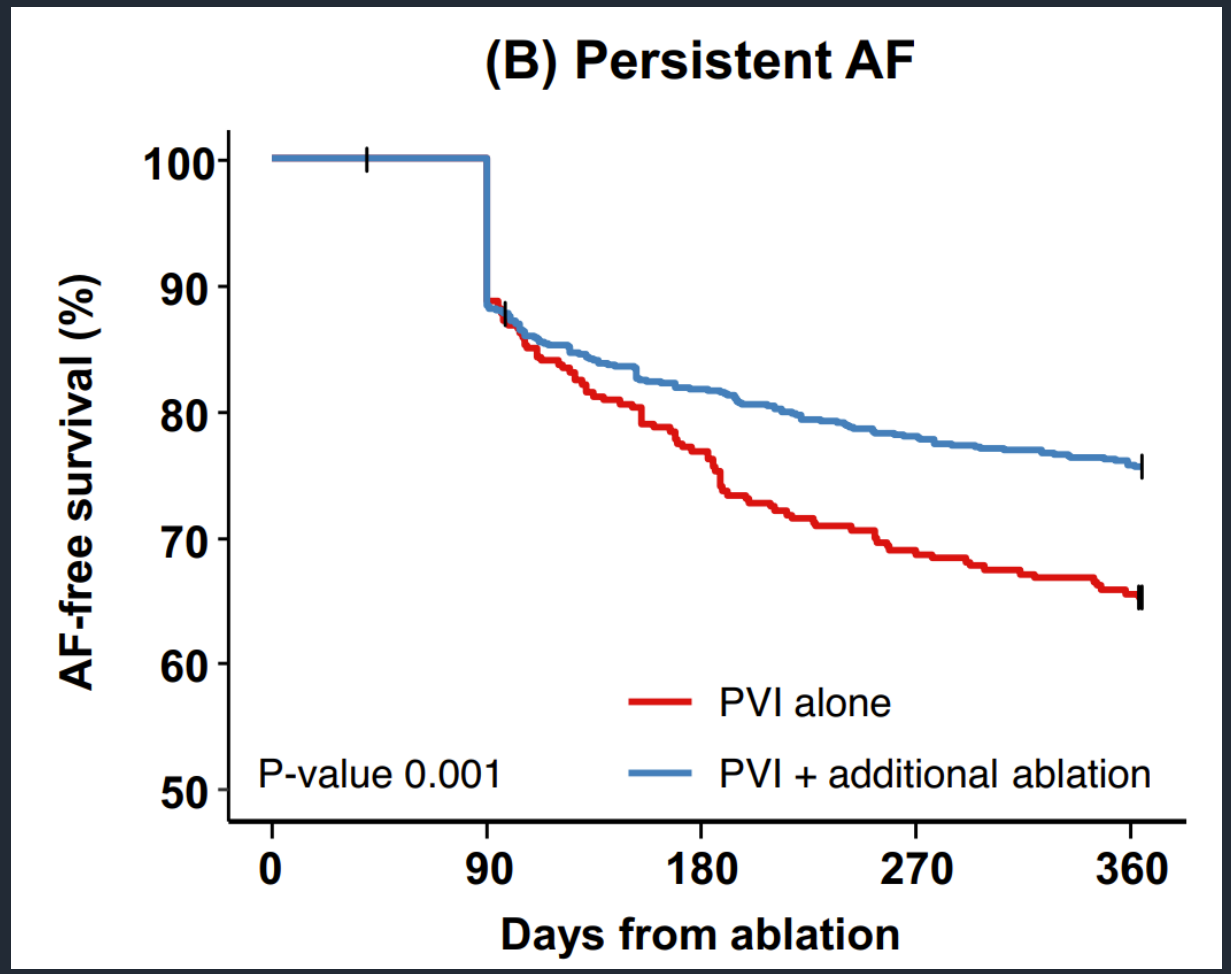
Increasing number of persistent AF cases

RESEARCH Open Access

Catheter ablation of atrial fibrillation in Korea: results from the Korean Heart Rhythm Society Ablation Registry for Atrial Fibrillation (KARA)

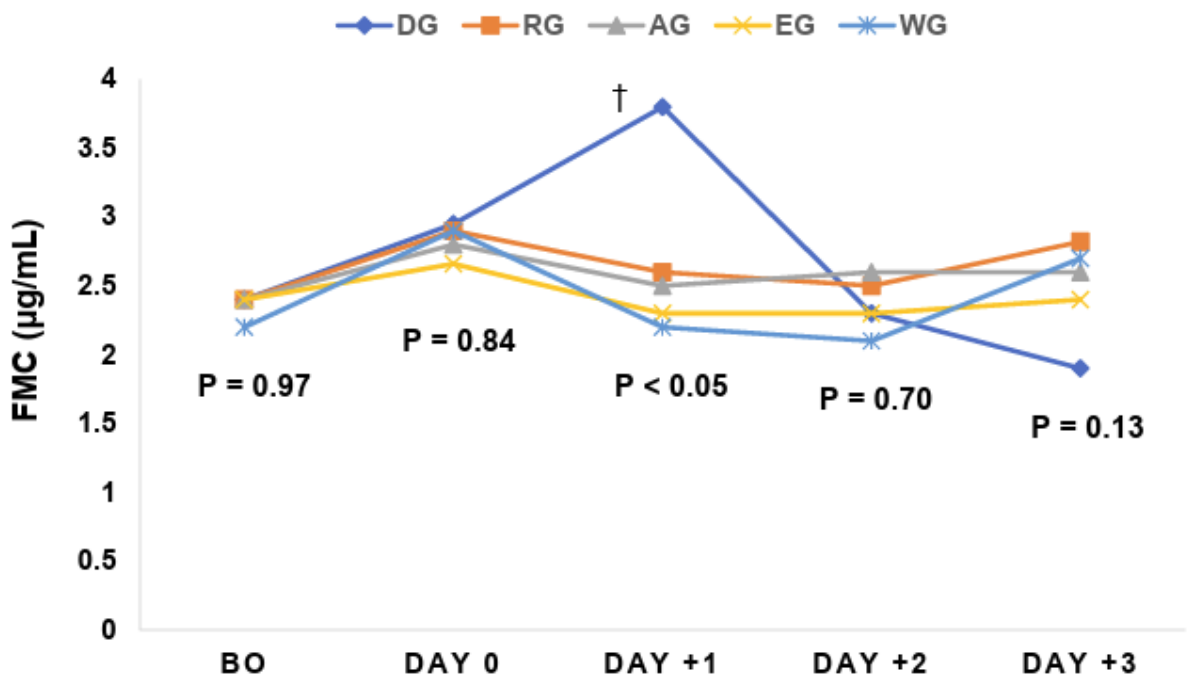
Table 1 Baseline demographic characteristics of the study population

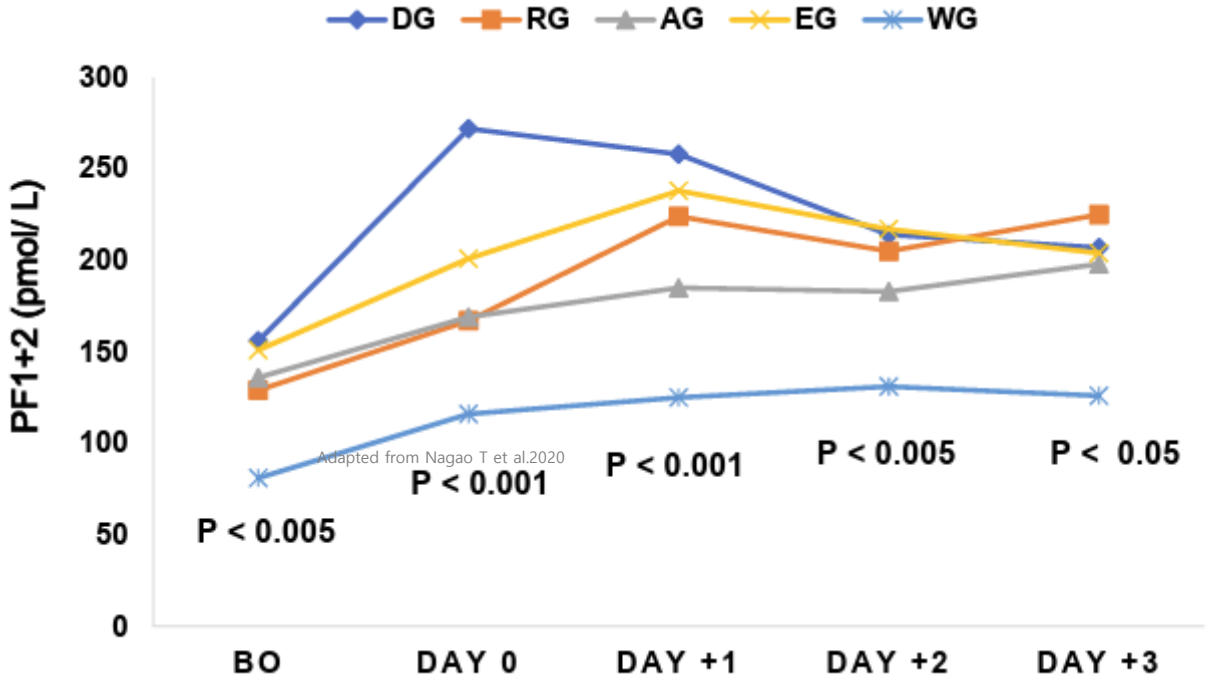
Variables	Total ($N = 2402$)
Age	60.2 ± 9.6
Male	1767 (73.6%)
Height (cm)	166.9 ± 8.6
Weight (kg)	71.7 ± 12.0
Paroxysmal AF	1097 (45.7%)
Persistent AF	1035 (43.1%)
Hypertension	1218 (50.7%)
Diabetes mellitus	434 (18.1%)
Heart failure	259 (10.8%)
Ischemic stroke/TIA/SE	219 (9.1%)
Ischemic heart disease	178 (7.4%)



Euijae Lee et al. Int J Arrhythm (2021) 22:20

Trends in coagulation markers during the periprocedural period





FMC and PF112 levels during the periprocedural period of AF ablation were higher in Dabigatran group than in the other groups.

Trends for coagulation markers, including mean fibrin monomer complex (FMC) and prothrombin fragment 112 (PF112), among the anticoagulant groups. †P <.05 vs before operation (BO). AG =apixaban group; DG=dabigatran group; EG =edoxaban group; RG = rivaroxaban group; WG=warfarin group.

Nagao T, et al. Prospective comparison of periprocedural coagulation markers among uninterrupted anticoagulants for atrial fibrillation ablation. Heart Rhythm. 2020;17:391-397

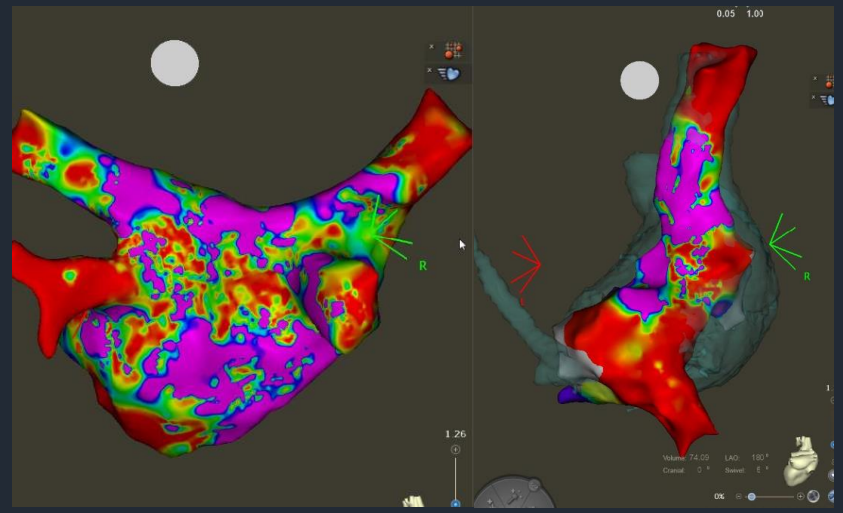
Case. Persistent AF

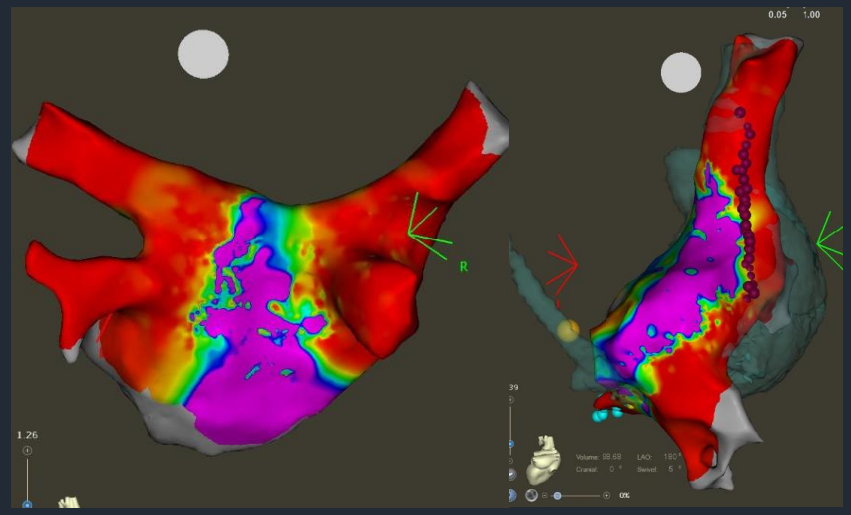
- Male / 78 YO
- Persistent atrial fibrillation since 1YA
- Hypertension
- H/O stroke (3YA)

- Enlarged RV with moderate functional TR
- Biatrial enlargement (LA size 46mm)

- → Refractory to antiarrhythmics

Longer procedure time





Eliquis

Eliquis

30min

30min

30min

30min

No baseline ACT

Bolus heparin
(6500U)

ACT 301 sec

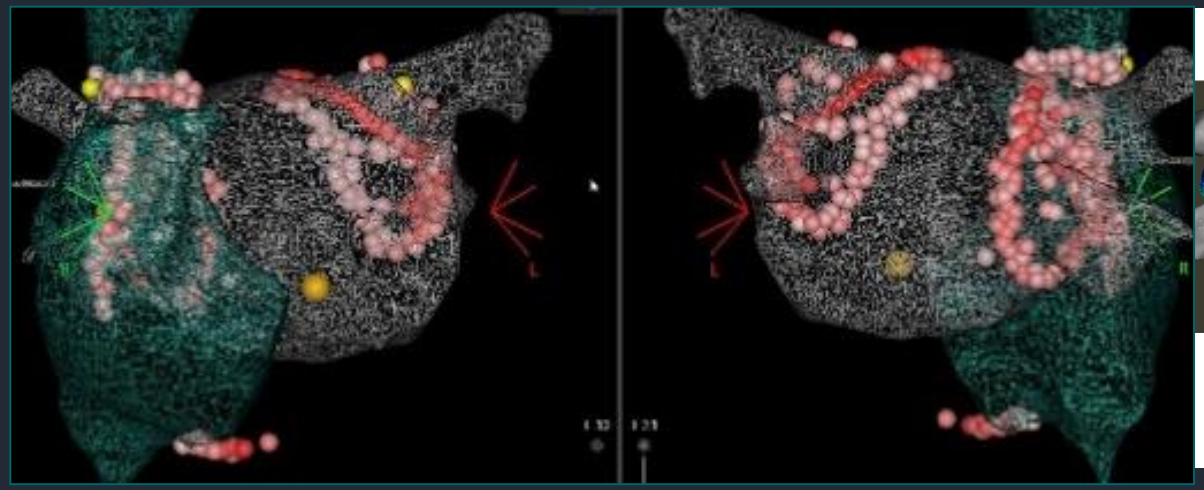
Bolus heparin

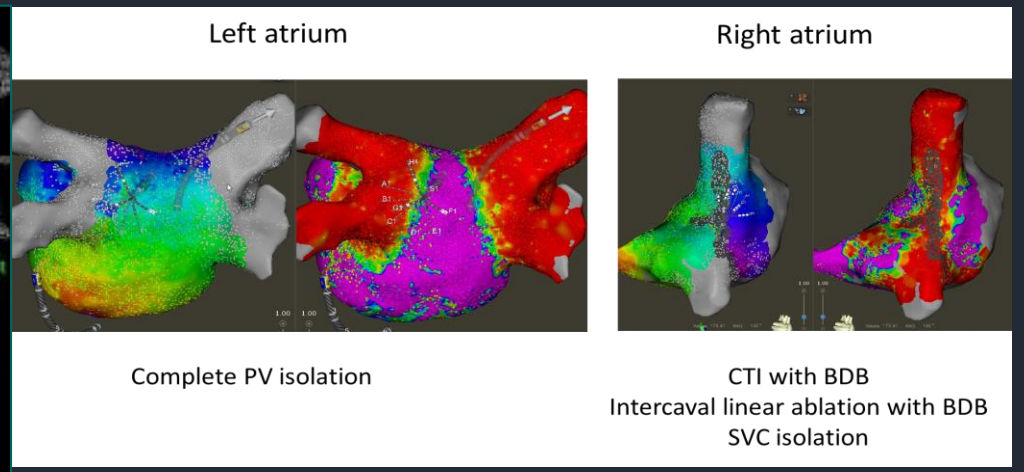
ACT 325 sec

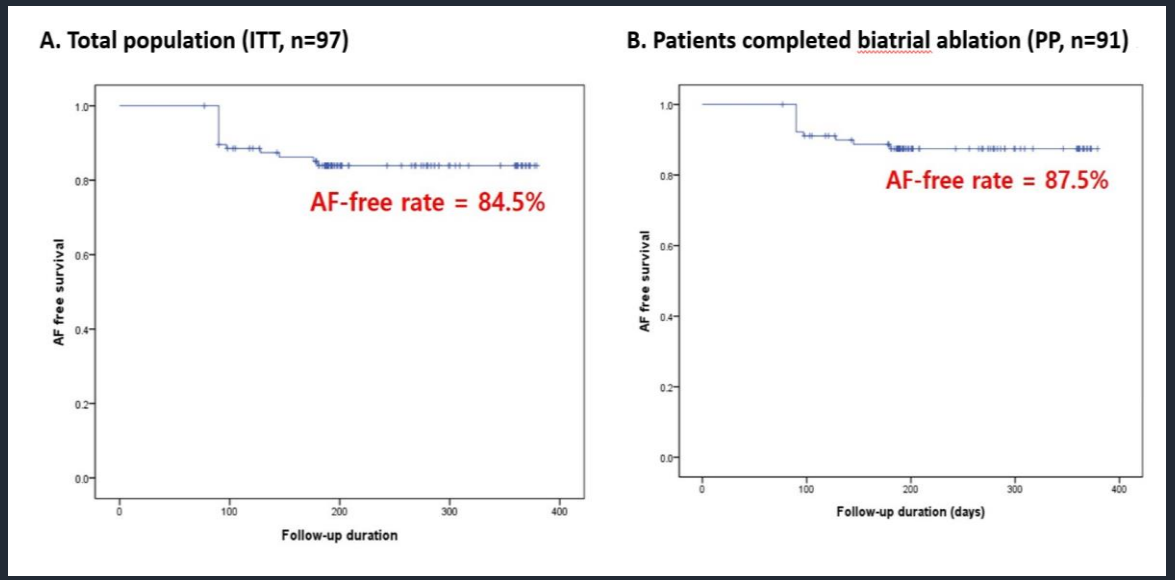
Bolus heparin

ACT 303 sec

Need for studies on catheter ablation lesion set for long-standing persistent atrial fibrillation







This interim analysis of the prospective registry showed that biatrial catheter ablation is a safe and effective treatment option for persistent AF, which presents 84.5% of AF-free survival at average 8-month follow-up (87.5 % in per-protocol analysis).

MJ Cha, Jun Kim et al. KHRS 2023, e-poster

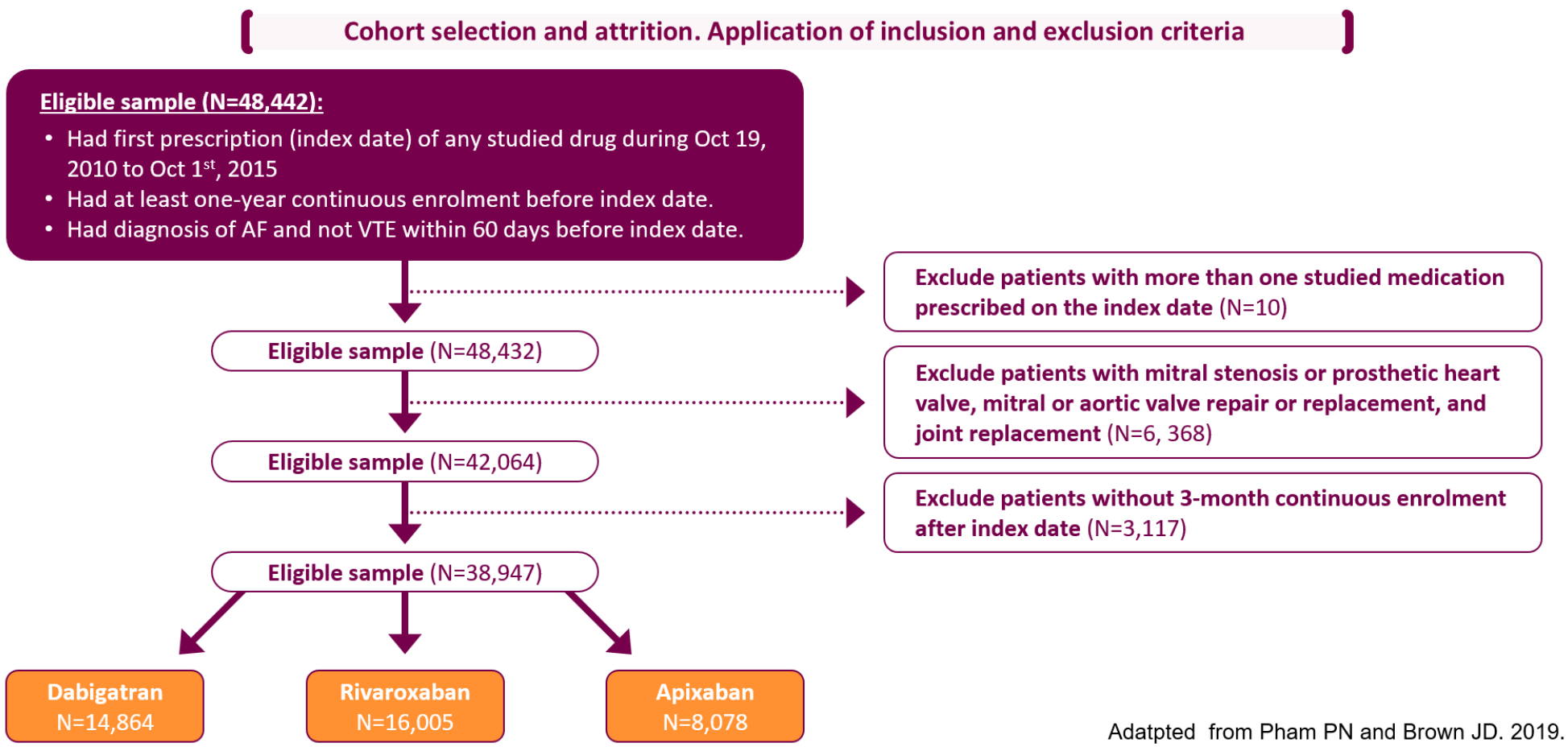
Recommendations for stroke risk management peri-cardioversion

Recommendations	Class[a]	Level[b]
In patients with AF undergoing cardioversion, NOACs are recommended with at least similar efficacy and safety to warfarin.[868–873]	I	A
For cardioversion of AF/AFL, effective anticoagulation is recommended for a minimum of 3 weeks before cardioversion.[866–870]	I	B
TOE is recommended to exclude cardiac thrombus as an alternative to 3-week pre-procedural anticoagulation when early cardioversion is planned.[866,868–870,875]	I	B

Recommendations for stroke risk management peri-cardioversion

It is recommended that the importance of adherence and persistence to NOAC treatment both before and after cardioversion is strongly emphasized to patients.	I	C
In patients with AF duration of >24 h undergoing cardioversion, therapeutic anticoagulation should be continued for at least 4 weeks, even after successful cardioversion to sinus rhythm (beyond 4 weeks, the decision about long-term OAC treatment is determined by the presence of stroke risk factors).[860,861]	IIa	B

Adherence to NOACs in NVAF is important to maintain effectiveness over the course of treatment



Adatpted from Pham PN and Brown JD. 2019.

Apixaban users had the highest overall adherence despite BID vs. OD for rivaroxaban

Adjusted Odds Ratio for high adherence to index OAC and to any OAC during 3, 6, 9 and 12 months of follow up

	3 months		6months		9 months		12 months	
	Adj OR	95% CI	Adj OR	95% CI	Adj OR	95% CI	Adj OR	95% CI
PDC ≥ 0.80 to index OAC								
R vs. D	1.34	1.27-1.40*	1.32	1.25-1.39*	1.37	1.30-1.44*	1.40	1.32-1.48*
A vs. D	1.41	1.33-1.50*	1.52	1.42-1.62*	1.67	1.56-1.79*	1.73	1.60-1.88*
A vs. R	1.06	0.99-1.12	1.15	1.08-1.23*	1.22	1.14-1.31*	1.24	1.14-1.34*
PDC ≥ 0.80 to any OAC								
R vs. D	1.26	1.20-1.33*	1.23	1.17-1.29*	1.29	1.23-1.36*	1.32	1.25-1.40*
A vs. D	1.28	1.20-1.36*	1.40	1.31-1.49*	1.55	1.44-1.66*	1.62	1.50-1.76*
A vs. R	1.01	0.95-1.08	1.13	1.06-1.21*	1.20	1.12-1.29*	1.23	1.13-1.34*

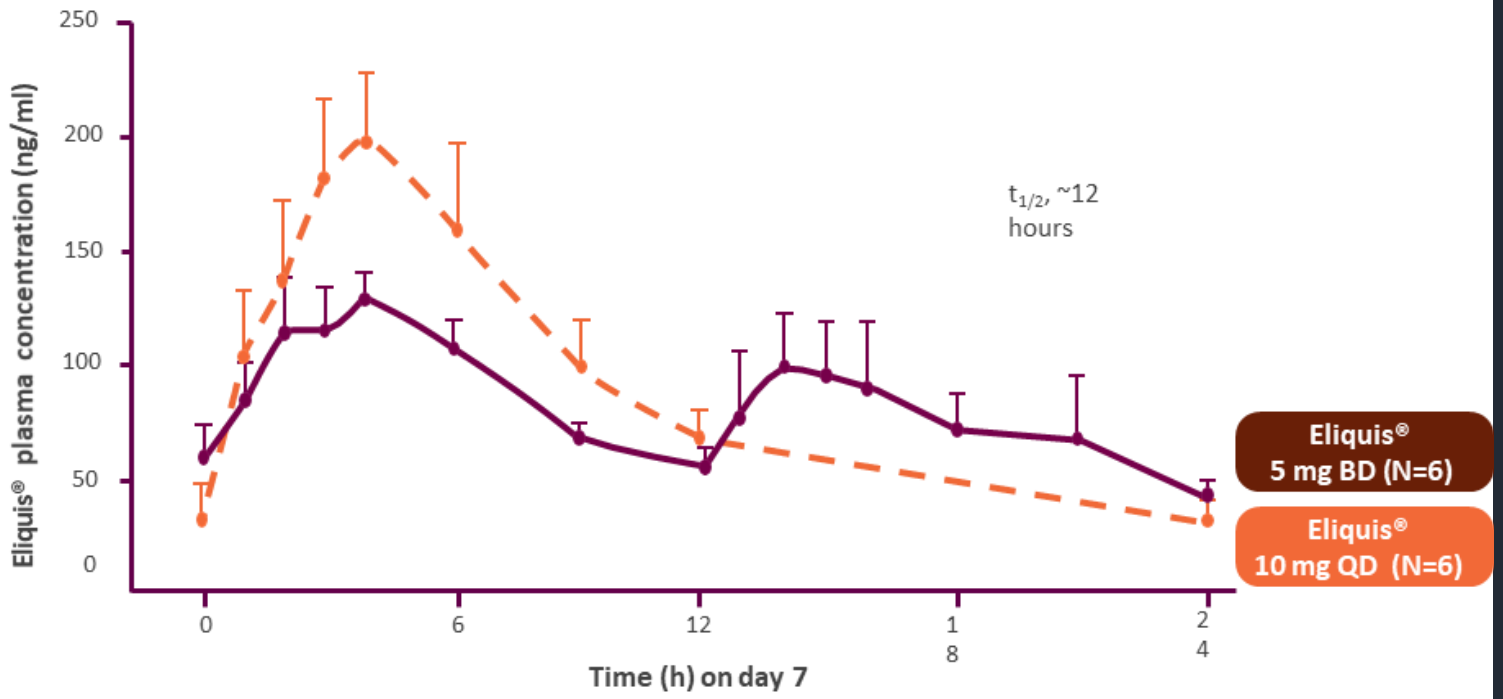
* **Denotes statistical significance at p <0.05**

Adatpted from Pham PN and Brown JD. 2019.

Twice-daily dosing was specially chosen as the optimal dosing regimen for Eliquis®

Data from a PK / PD study in healthy patients (N=36)[1*]

Mean plasma concentration following multiple oral Eliquis® doses.
(double-blind, randomized, multiple ascending dose study in 48 healthy subjects over 24 hours)



Adapted from Frost et al.[1]
Eliquis® 10 mg QD is not an approved dose of Eliquis®.[2]

Take Home message

- In patients with AF undergoing catheter ablation or cardioversion, NOACs are preferable to Warfarin.
- Eliquis demonstrates a good safety profile and is highly effective in stroke risk prevention.
- Given the bleeding risks associated with catheter ablation, the low bleeding risk of Eliquis, as substantiated by extensive data, is a crucial consideration.
- Eliquis, shown for good adherence, ensures stable drug concentrations pre- and post-procedure due to its BID administration.
- As procedures become increasingly complex, Eliquis, backed by extensive data, is a safe and effective therapeutic option to consider for AF patients.