

## Strategy of anticoagulation before and after catheter ablation of atrial fibrillation

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# **Conflict of interest**

Bayer, Biosense Webster, Boehringer Ingelheim,  
Daiichi Sankyo, Dompè, Pfizer BMS



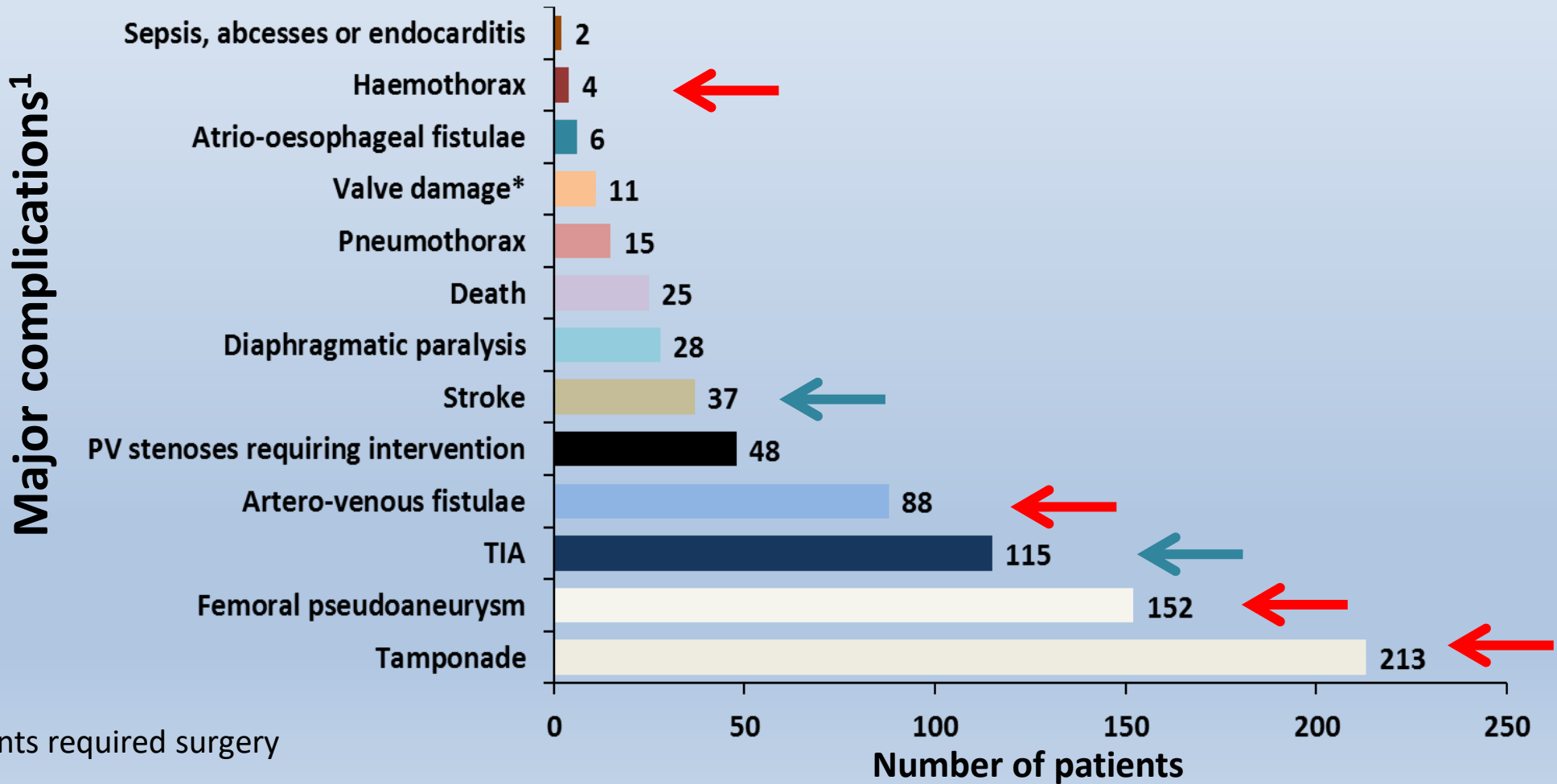


# Worldwide Report on the Ablation-Related Peri-procedural Complications

4.5% Major complications reported by 741 patients<sup>1</sup>

25 deaths, 37 strokes, 115 TIAs and 213 episodes of tamponade<sup>1</sup>

Tamponade, atrio-oesophageal fistulas, stroke and MI are the most common fatal complications<sup>2</sup>



\*7 patients required surgery

1. Cappato et al. Circ Arrhythm Electrophysiol 2010; 2. Cappato et al. J Am Coll Cardiol 2009

# Uninterrupted Warfarin versus LMWH Bridge

## Atrial Fibrillation Ablation in Patients With Therapeutic International Normalized Ratio

Comparison of Strategies of Anticoagulation Management in the Perioperative Period

**Table 2. Complications**

	Group 1 (n=105)	Group 2 (n=100)	Group 3 (n=150)	Exact <i>P</i>
Ischemic stroke, n	1	2	0	0.12
Pericardial effusion, n	1	2	1	0.69
Minor bleeding, n	23	19	8	<0.001
Major bleeding, n	9	0	0	<0.001

Group 1- LMWH 1 mg/kg BID, Group 2- LMWH 0.5 mg/kg BID, Group 3- on Warfarin

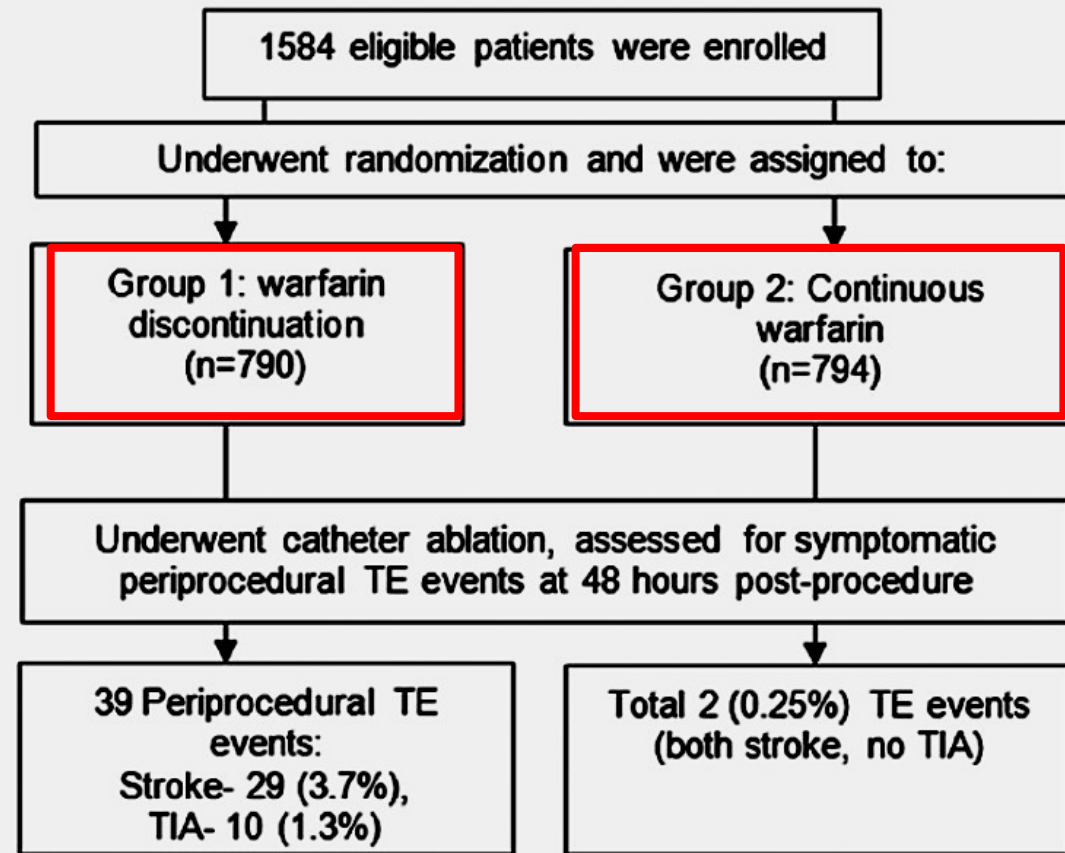


# Periprocedural Stroke and Bleeding Complications in Patients Undergoing Catheter Ablation of Atrial Fibrillation With Different Anticoagulation Management

## Results From the Role of Coumadin in Preventing Thromboembolism in Atrial Fibrillation (AF) Patients Undergoing Catheter Ablation (COMPARE) Randomized Trial

Luigi Di Biase, MD, PhD; J. David Burkhardt, MD; Pasquale Santangeli, MD;

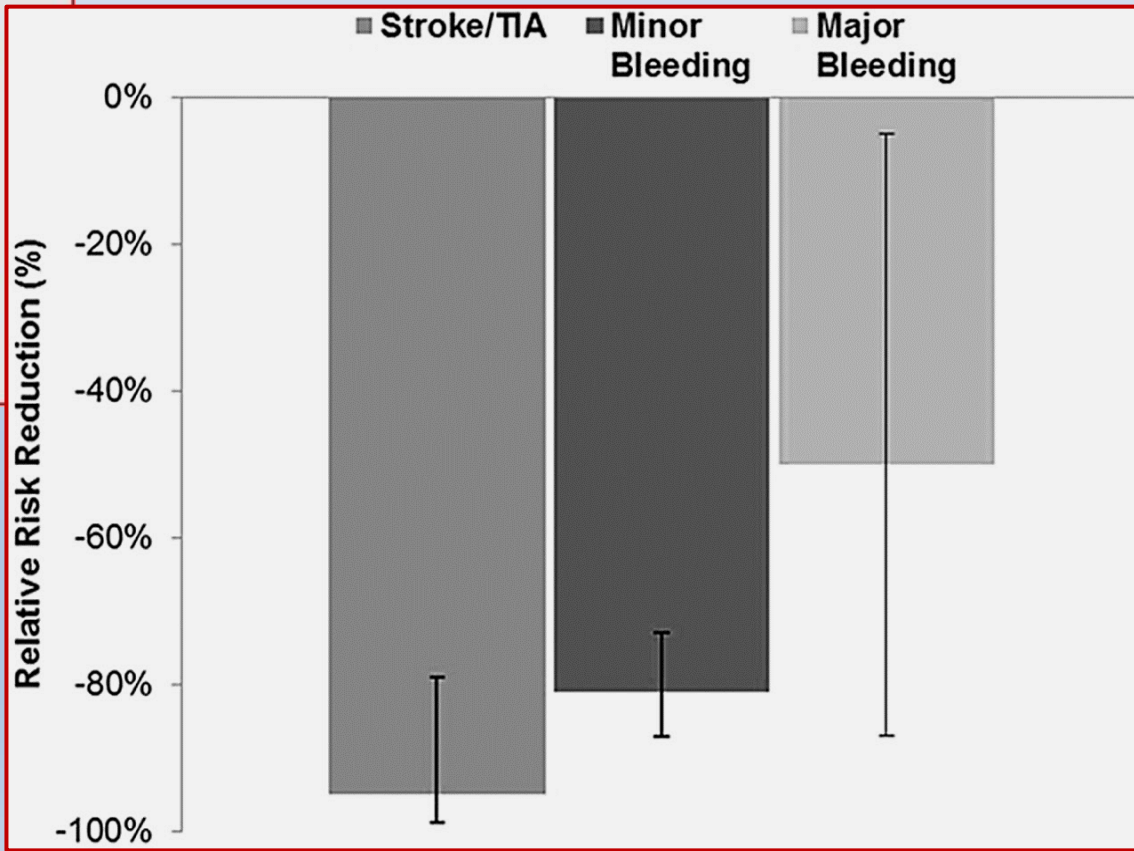
Prasant Mohanty, MPH, MBBS; Javier E. Sanchez, MD; Rodney Horton, MD; G. Joseph Gallinghouse, MD; Sakis Themistoclakis, MD; Antonio Rossillo, MD; Dhanunjaya Lakkireddy, MD; Madhu Reddy, MD; Steven Hao, MD; Richard Hongo, MD; Salwa Beheiry, RN, Jason Zagrodzky, MD; Bai Rong, MD; Sanghamitra Mohanty, MD; Claude S. Elayi, MD; Giovanni Forleo, MD; Gemma Pelargonio, MD; Maria Lucia Narducci, MD; Antonio Dello Russo, MD; Michela Casella, MD; Gaetano Fassini, MD; Claudio Tondo, MD; Robert A. Schweikert, MD; Andrea Natale, MD



**Table 2. Thromboembolic Events According to AF Type**

	Group 1 (Off Warfarin; n=790), n (%)	Group 2 (On Warfarin; n=794), n (%)	P Value
Stroke/TIA combined	39 (4.9)	2 (0.25)	<0.001
Paroxysmal	2 (0.87)	0 (0.0)	0.25
Persistent	4 (2.3)	0 (0.0)	0.06
LSP	33 (8.5)	2 (0.49)	<0.001
Stroke	29 (3.7)	2 (0.25)	<0.001
Paroxysmal	1 (0.44)	0 (0.0)	0.47
Persistent	2 (1.15)	0 (0.0)	0.25
LSP AF	26 (6.7)	2 (0.49)	<0.001
TIA	10 (1.27)	0 (0.0)	<0.001
Paroxysmal	1 (0.44)	0 (0.0)	1.00
Persistent	2 (1.15)	0 (0.0)	0.50
LSP	7 (1.81)	0 (0.0)	0.016

AF indicates atrial fibrillation; LSP, long-standing persistent; and TIA, transient ischemic attack.



## 2016 ESC Guidelines for the management of atrial fibrillation developed in collaboration with EACTS

### 11.3.4 Anticoagulation: before, during, and after ablation

Patients anticoagulated with VKAs **should continue therapy during ablation** (with an INR of 2–3).<sup>760</sup>



Anticoagulation with NOACs is an alternative to warfarin.<sup>478,761 – 765</sup>

**There is no safety signal from observational cohorts treated with uninterrupted NOAC therapy undergoing catheter ablation in experienced centres.**<sup>761,763,766,767</sup> **The first controlled trial comparing continuous NOAC and VKA therapy in AF ablation patients, enrolling around 200 patients, has recently been published.**<sup>768</sup>



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

## Recommendations for stroke risk management peri-catheter ablation

Recommendations	Class <sup>a</sup>	Level <sup>b</sup>
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:	<b>I</b>	<b>C</b>
<ul style="list-style-type: none"> <li>• Preferably, therapeutic OAC for at least 3 weeks before ablation, or</li> <li>• Alternatively, the use of TOE to exclude LA thrombus before ablation.</li> </ul>	<b>IIa</b>	<b>C</b>
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. <sup>878,879,881</sup>	<b>I</b>	<b>A</b>
After AF catheter ablation, it is recommended that:	<b>I</b>	<b>C</b>
<ul style="list-style-type: none"> <li>• Systemic anticoagulation with warfarin or a NOAC is continued for at least 2 months post ablation, and</li> <li>• Long-term continuation of systemic anticoagulation beyond 2 months post ablation is based on the patient's stroke risk profile and not on the apparent success or failure of the ablation procedure.</li> </ul>	<b>I</b>	<b>C</b>



# VENTURE AF: Complications During the Study Period

	Rivaroxaban	VKA	Total
Any adjudicated event	26	25	51
	n=123	n=121	N=244
Any bleeding event*	21	18	39
<b>Major bleeding event</b>	<b>0</b>	<b>1</b>	<b>1</b>
Vascular pseudoaneurysm	0	1	1
Non-major bleeding event	21	17	38
Most relevant:			
Arteriovenous fistula	0	1	1
Catheter/puncture site haemorrhage	1	1	2
Haematoma/vessel puncture site haematoma	8	10	18
Vascular pseudoaneurysm	3	1	4
	n=124	n=124	N=248
Any thromboembolic events (composite) <sup>#</sup>	0	2	2
Ischaemic stroke	0	1	1
Vascular death	0	1	1
	n=114	n=107	N=221
Any other procedure-attributable event <sup>†</sup>	5	5	10
Pericardial effusion without tamponade	0	1	1

\*safety population; <sup>#</sup>ITT population; <sup>†</sup>per-protocol population

Adapted from Cappato et al. Eur Heart J 2015;36:1805-11



## Uninterrupted Dabigatran versus Warfarin for Ablation in Atrial Fibrillation

Hugh Calkins, M.D., Stephan Willems, M.D., Edward P. Gerstenfeld, M.D., Atul Verma, M.D., Richard Schilling, M.D., Stefan H. Hohnloser, M.D., Ken Okumura, M.D., Ph.D., Harvey Serota, M.D., Matias Nordaby, M.D., Kelly Guiver, M.Sc., Branislav Biss, M.D., Marc A. Brouwer, M.D., Ph.D., and Massimo Grimaldi, M.D., Ph.D., for the RE-CIRCUIT Investigators\*

### Results: Secondary Endpoints

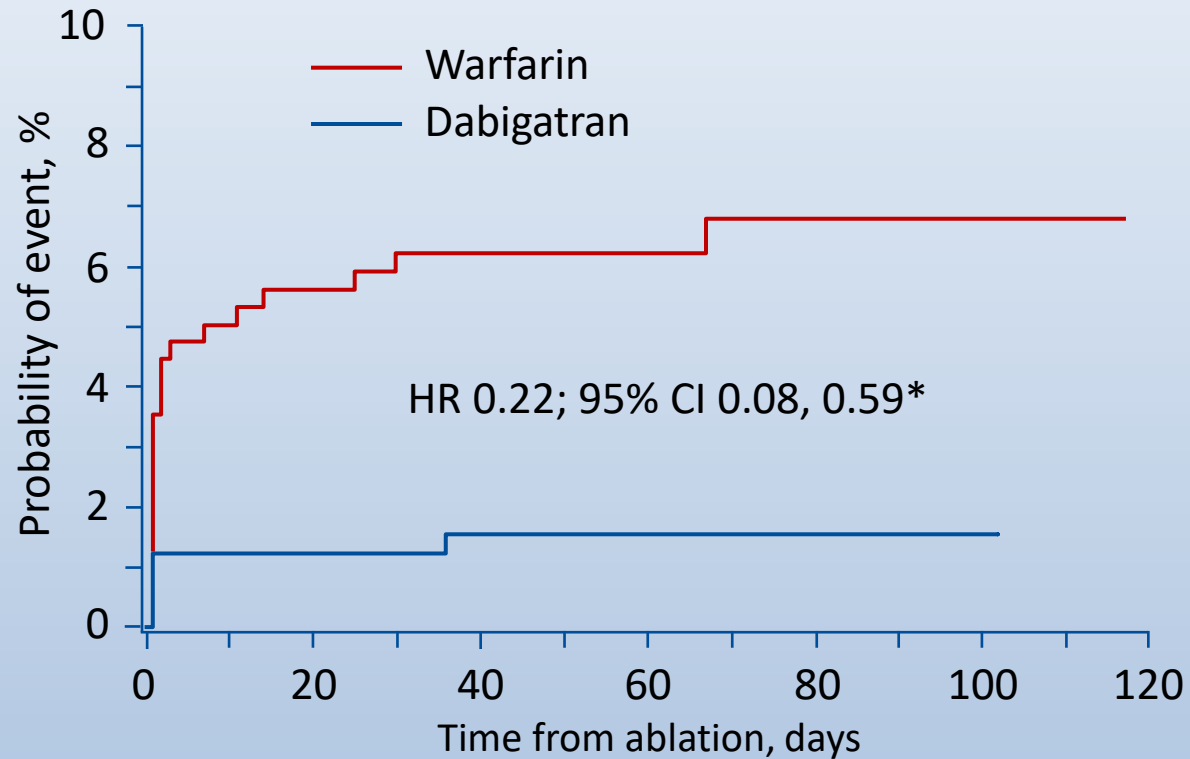
#### Low Rate of Thromboembolic Events

- Stroke: no events
- Systemic embolism: no events
- Transient ischemic attack: Dabigatran 0 vs warfarin 1

#### Minor Bleeding Events Similar Between Treatments

- Dabigatran 59 (18.6%) vs warfarin 54 (17.0%)

# Fewer Major Bleeding Events from the Time of Ablation

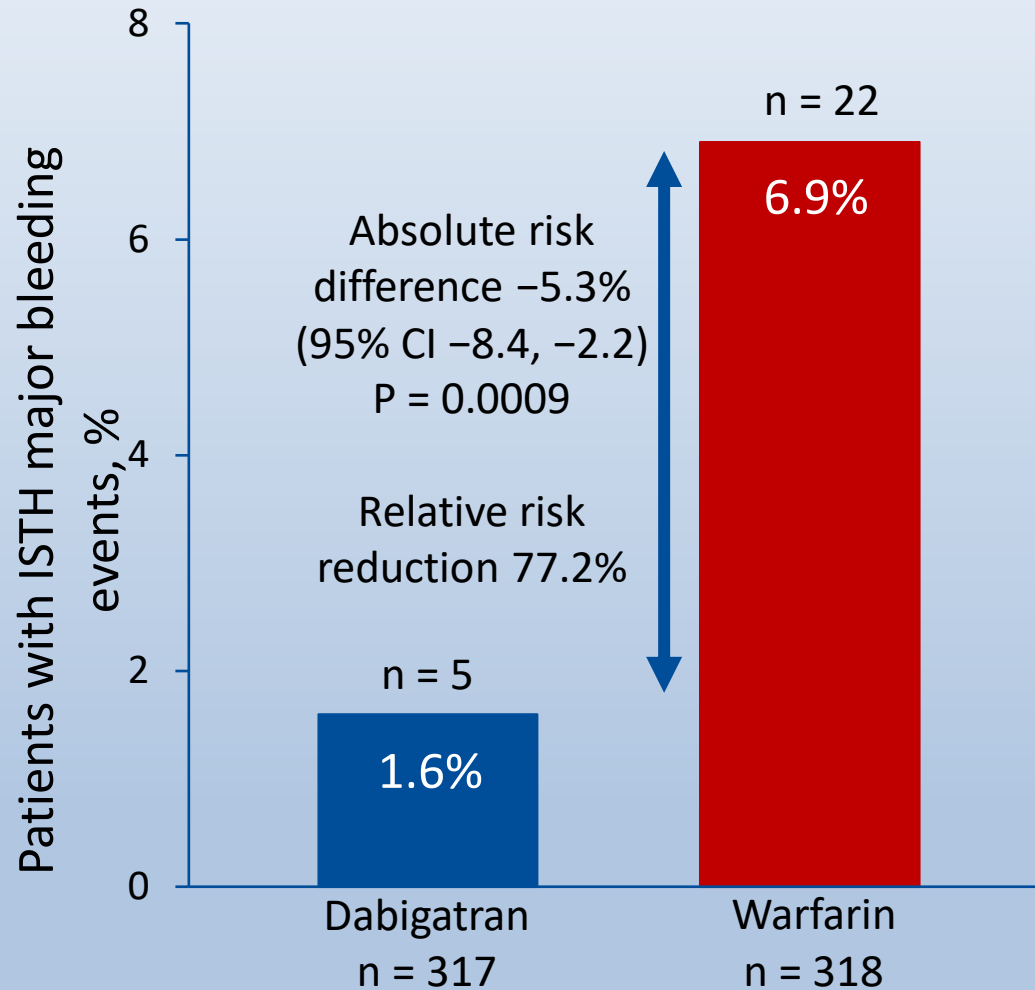


Patients at risk

Dabigatran	317	313	311	311	306	305	297	83	4	2	1	0	0
Warfarin	318	301	297	296	295	295	278	85	13	5	3	1	0

\*Cox proportional hazard model and Wald confidence limits.

# Patients on Uninterrupted Dabigatran had Significantly Fewer Major Bleeding Events Compared with Patients on Warfarin





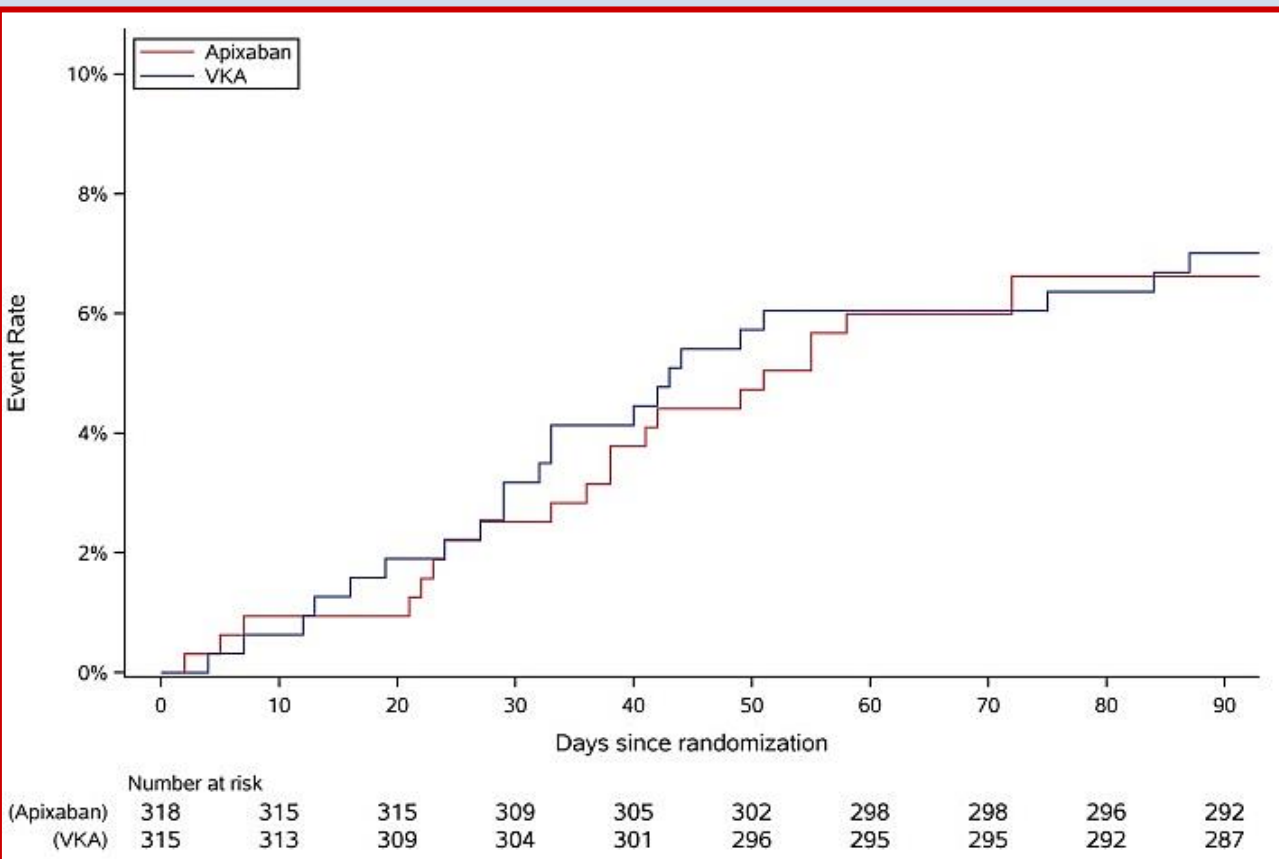


# Apixaban in patients at risk of stroke undergoing atrial fibrillation ablation

Paulus Kirchhof<sup>1,2,3,4\*</sup>, Karl Georg Haeusler<sup>4,5</sup>, Benjamin Blank<sup>4</sup>, Joseph De Bono<sup>1,3</sup>, David Callans<sup>6</sup>, Arif Elvan<sup>7</sup>, Thomas Fetsch<sup>8</sup>, Isabelle C. Van Gelder<sup>9</sup>, Philip Gentlesk<sup>10</sup>, Massimo Grimaldi<sup>11</sup>, Jim Hansen<sup>12</sup>, Gerhard Hindricks<sup>13</sup>, Hussein R. Al-Khalidi<sup>14</sup>, Tyler Massaro<sup>15</sup>, Lluís Mont<sup>16</sup>, Jens Cosedis Nielsen<sup>17</sup>, Georg Nölker<sup>18</sup>, Jonathan P. Piccini<sup>15,19</sup>, Tom De Potter<sup>20</sup>, Daniel Scherr<sup>21</sup>, Ulrich Schotten<sup>4,22</sup>, Sakis Themistoclakis<sup>23</sup>, Derick Todd<sup>24</sup>, Johan Vijgen<sup>25</sup>, and Luigi Di Biase<sup>26,27</sup>

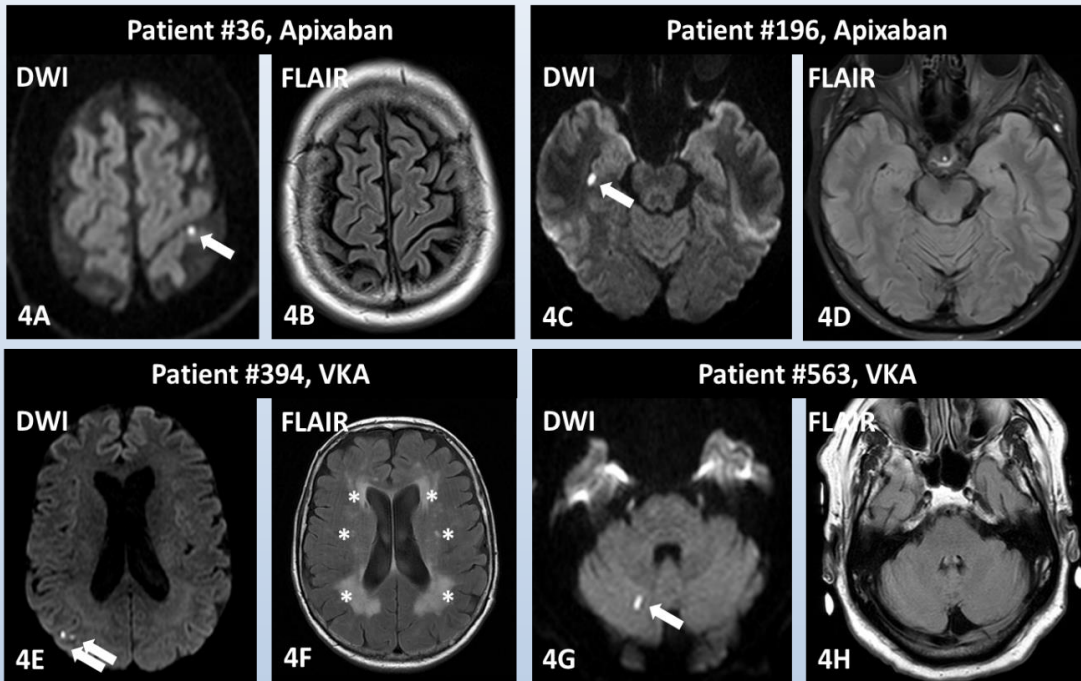
## Primary Outcome

Difference in primary outcome rate  $-0.38\%$   
90% confidence interval  $-4.0\%$ ,  $-3.3\%$   
non-inferiority  $p=0.0002$



	Apixaban	VKA
Composite of all-cause death, stroke or major bleeding	22/318 (6.9%), non-inferiority $p=0.0002$	23/315 (7.3%)
Death	1 (0.3%)	1 (0.3%)
Stroke or TIA	2 (0.6%)	0
Intracranial hemorrhage	0	1 (0.3%, fatal)
TIMI major bleeding	1 (0.3%)	3 (1%)
ISTH major bleeding	10 (3.1%)	14 (4.4%)
Tamponade	2 (0.6%)	5 (1.6%)

# AXAFA-AFNET 5 HD-DWI MRI Sub-study



	Apixaban (n=162)	VKA (n=161)	P-value
No lesion	118 (72.8%)	121 (75.2%)	0.635
1 lesion	27 (16.7%)	19 (11.8%)	0.211
2 lesion	7 (4.3%)	14 (8.7%)	0.111
>2 lesions	10 (6.2%)	7 (4.3%)	0.463

## Cognitive function [Montreal Cognitive Assessment (MoCA)]

Cognitive function at end of study (MoCA), median (q1, q3), n	28.0 (26.0, 29.0), n = 607	28.0 (26.0, 29.0), n = 305	28.0 (26.0, 29.0), n = 302
Abnormal MoCA at baseline (<26), n (%)	141 (23.2%)	75 (24.6%)	66 (21.9%)
Change in MoCA at end of study compared to baseline, median (q1, q3), n	1.0 (-1.0, 2.0), n = 597, P < 0.001*	0.0 (-1.0, 2.0), n = 301	1.0 (-1.0, 2.0), n = 296
Change in patients with abnormal MoCA at end of study compared to baseline, n (%)	141/607 (23.2%), -7.2%, P = 0.005*	75/305 (24.6%) -5.1%	66/302 (21.9%) -9.2%

# **Impairment of cognitive function linked to MRI-detected brain lesions in atrial fibrillation patients undergoing left atrial catheter ablation in the randomized AXAFA-AFNET 5 trial**

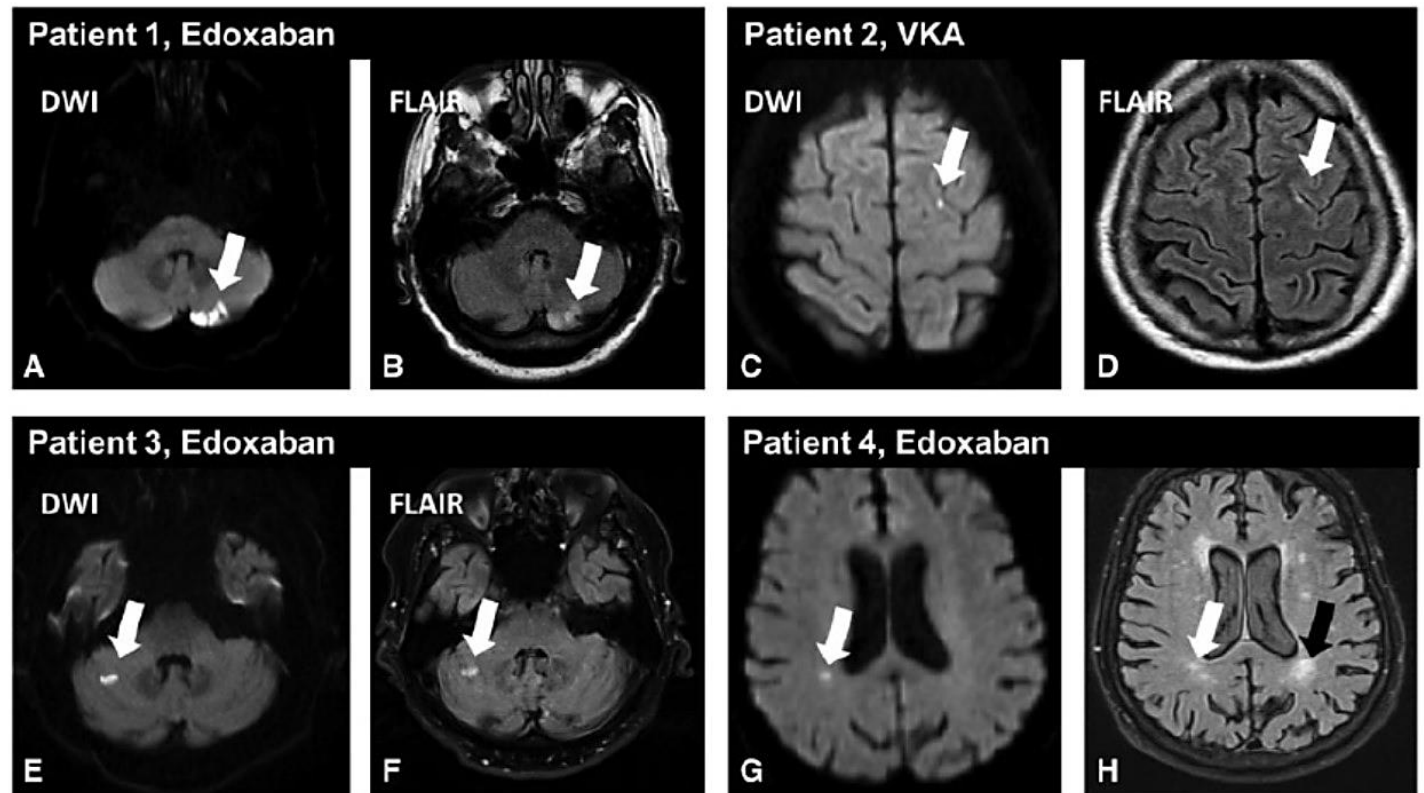
Karl Georg Haeusler, MD<sup>1,2</sup>, Felizitas A. Eichner, PhD<sup>3</sup>, Peter U. Heuschmann, MD<sup>3,4</sup>, Jochen B. Fiebach, MD<sup>5</sup>, Tobias Engelhorn, MD<sup>6</sup>, Benjamin Blank, PhD<sup>1</sup>, David Callans, MD<sup>7</sup>, Arif Elvan, MD<sup>8</sup>, Massimo Grimaldi, MD<sup>9</sup>, Jim Hansen, MD<sup>10</sup>, Gerhard Hindricks, MD<sup>11</sup>, Hussein R. Al-Khalidi, MD<sup>12</sup>, Lluís Mont, MD<sup>13-15</sup>, Jens Cosedis Nielsen, MD<sup>16</sup>, Jonathan P. Piccini, MD<sup>17, 18</sup>, Ulrich Schotten, MD, PhD<sup>1,19</sup>, Sakis Themistoclakis, MD<sup>20</sup>, Johan Vijgen, MD<sup>21</sup>, Luigi Di Biase, MD<sup>22;23</sup>, Paulus Kirchhof, MD<sup>1,24-26</sup>

**While hrDWI-detected acute brain lesions were not associated with cognitive function at 3-months after ablation, we observed an association between chronic white matter damage and lower MoCA scores before and after ablation**



# Uninterrupted edoxaban vs. vitamin K antagonists for ablation of atrial fibrillation: the ELIMINATE-AF trial

Stefan H. Hohnloser<sup>1\*</sup>, John Camm<sup>2</sup>, Riccardo Cappato<sup>3</sup>, Hans-Christoph Diener<sup>4</sup>, Hein Heidbüchel<sup>5</sup>, Lluís Mont<sup>6</sup>, Carlos A. Morillo<sup>7</sup>, Khalid Abozguia<sup>8</sup>, Massimo Grimaldi<sup>9</sup>, Heiko Rauer<sup>10</sup>, Paul-Egbert Reimitz<sup>10</sup>, Rüdiger Smolnik<sup>10</sup>, Christoph Mönninghoff<sup>11</sup>, and Josef Kautzner<sup>12</sup>

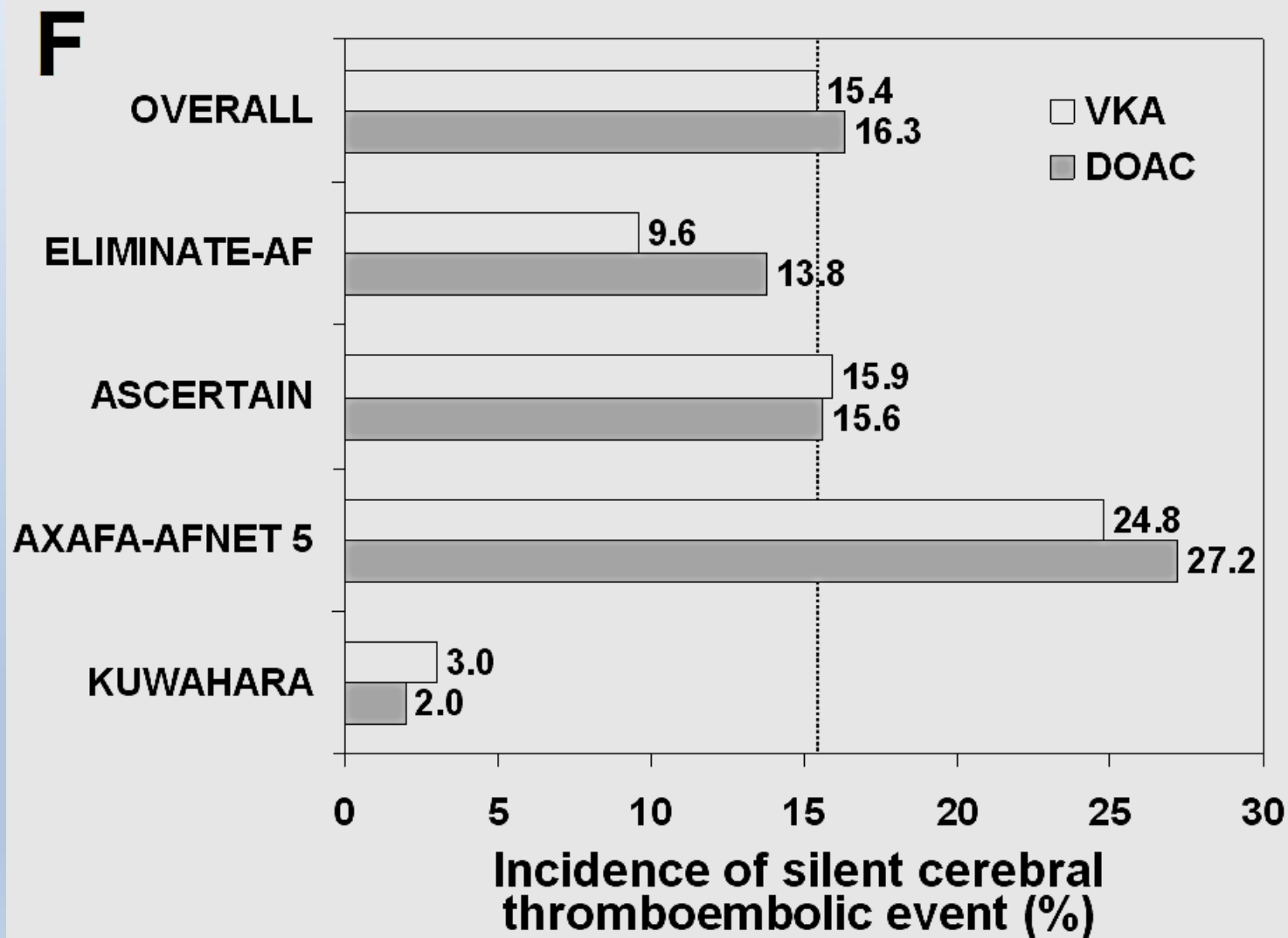


381 citations retrieved from  
Pubmed and Scopus

14 studies considered for a more  
detailed evaluation

8 articles excluded according  
to explicit criteria

6 studies finally included in the  
meta-analysis

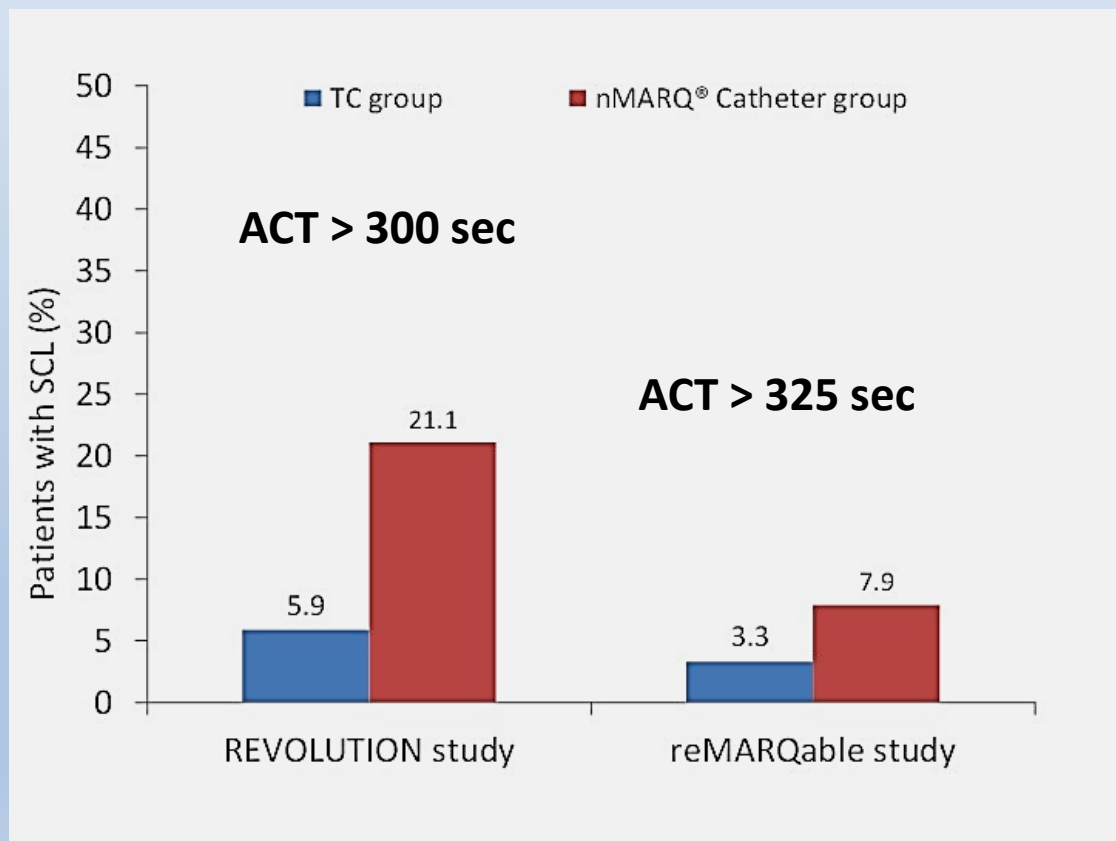
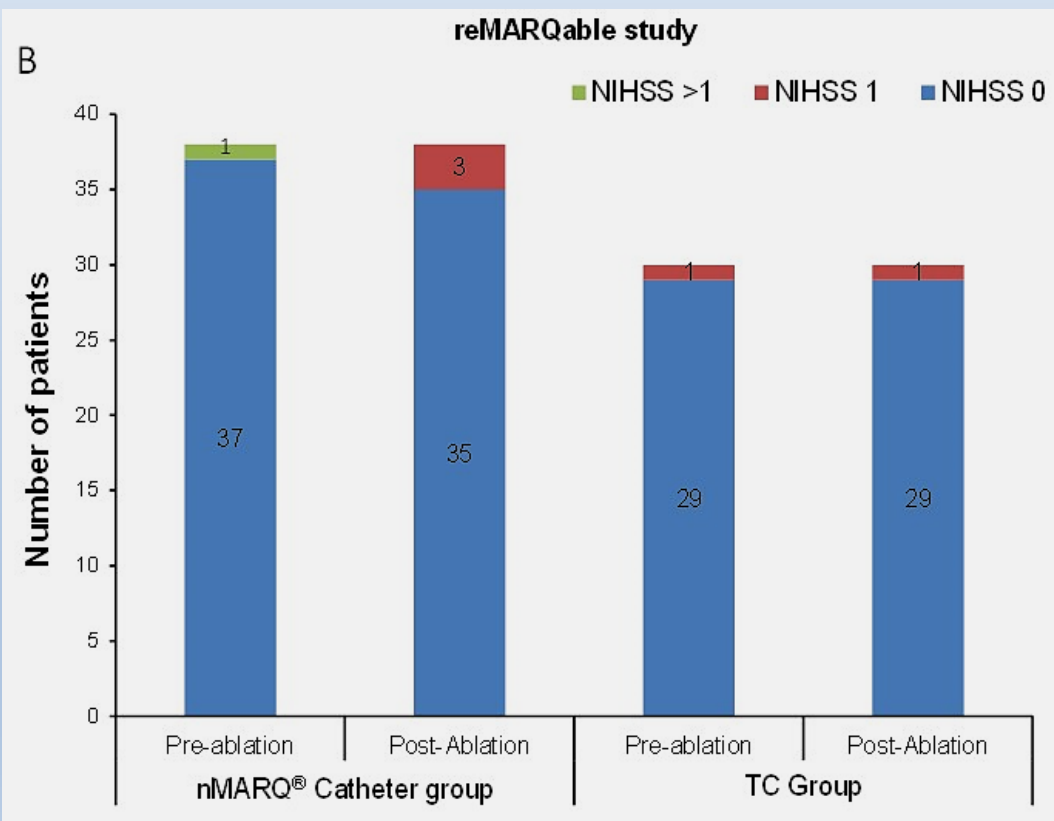


**Supplementary Table 4.** Subcortical and deep white matter hyperintensities according to the Fazekas scale (MRI sub-study)

	<b>Total (N=173)</b>	<b>Edoxaban (N=118)</b>	<b>VKA (N=55)</b>
Deep white matter: % (n)			
0	68.2 (118)	67.8 (80)	69.1 (38)
1	21.4 (37)	21.2 (25)	21.8 (12)
2	8.1 (14)	8.5 (10)	7.3 (4)
3	2.3 (4)	2.5 (3)	1.8 (1)
Subcortical white matter: % (n)			
0	56.6 (98)	55.9 (66)	58.2 (32)
1	34.7 (60)	33.9 (40)	36.4 (20)
2	6.9 (12)	7.6 (9)	5.5 (3)
3	1.7 (3)	2.5 (3)	0 (0)
		Acute: 13,8	9,6

# Importance of anticoagulation and postablation silent cerebral lesions: Subanalyses of REVOLUTION and reMARQable studies

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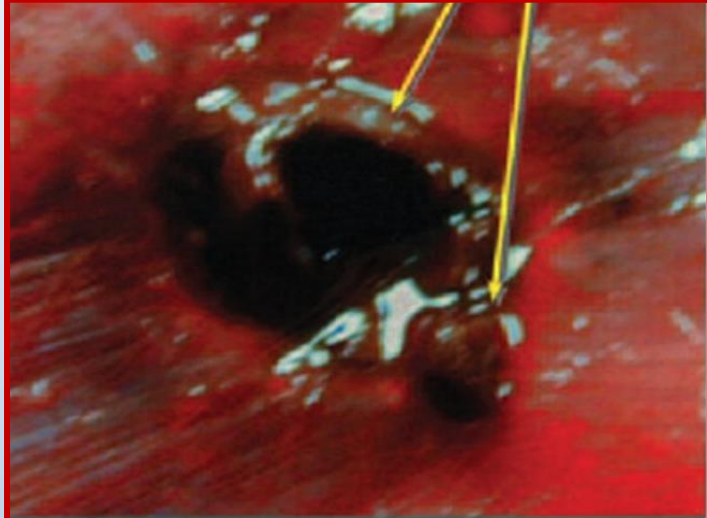




Anticoagulant management					
		REVOLUTION		reMARQable	
		nMARQ <sup>®</sup> Catheter group	TC group	nMARQ <sup>®</sup> Catheter group	TC group
		Mean±SD (Min, Max)		Mean±SD (Min, Max)	
Pre-ablation INR	All patients	2.042±0.413	2.315±0.310	2.507±0.3872	2.364±0.3666
ACT during ablation	All patients	410.2±123.6 (325, 737)	333.8±87.1 (251, 621)	383.1±58.7 (249, 598)	384.6±42.9 (323, 487)
	Patients with no SCL	431.7±133.0 (331, 737)	336.8±89.1 (251, 621)	384.0±60.4 (249, 598)	385.3±43.4 (323, 487)
	Patients with SCL	335.2±13.9 (325, 355)	286.0±N/A (286, 286)	372.9±40.8 (326, 400)	362.8±N/A (363, 363)

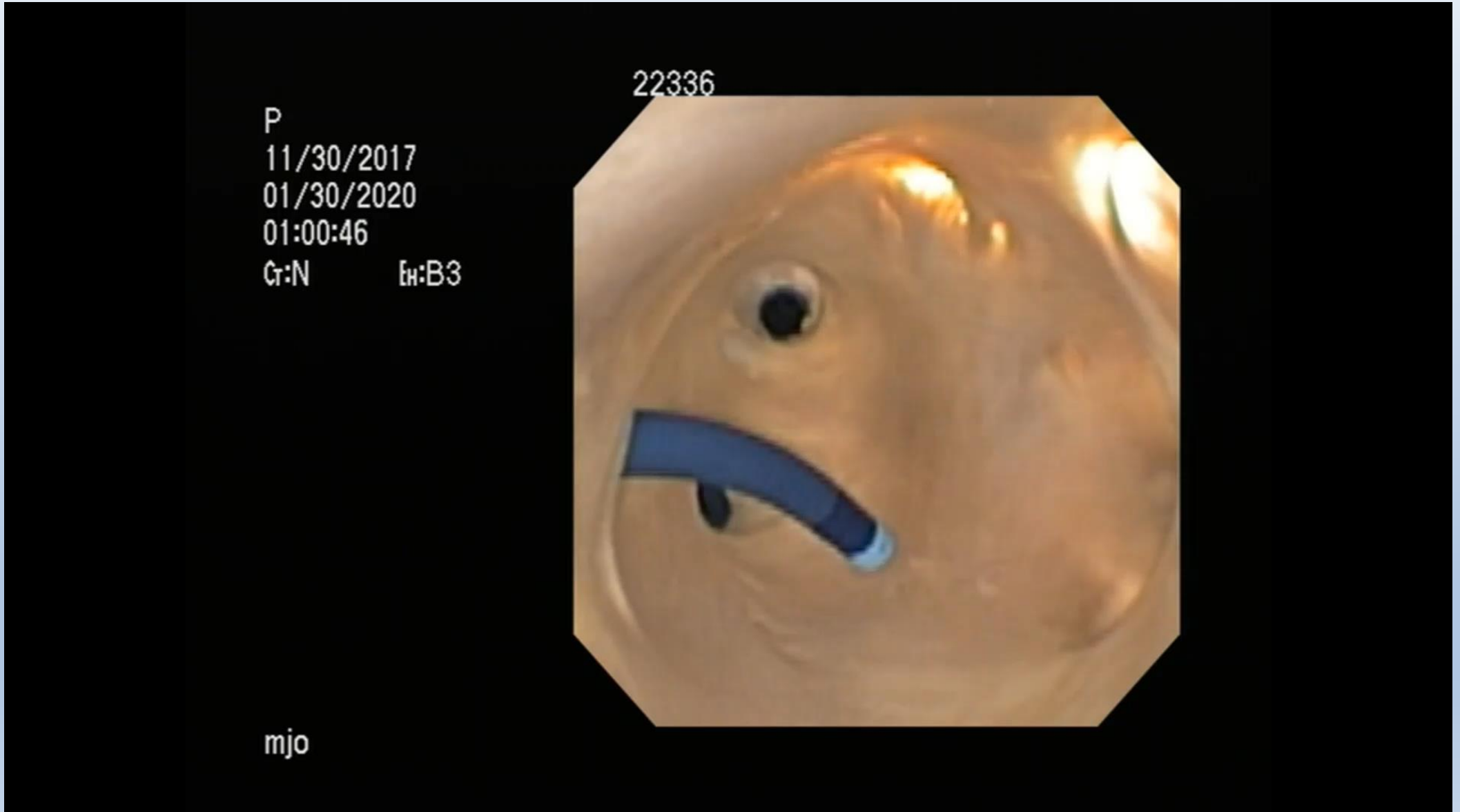
ACT=activated clotting time; INR=international normalized ratio; N/A=not applicable; SCL=silent cerebral lesion; SD=standard deviation; TC=THERMOCOOL<sup>®</sup> Catheter.

# Procedural and periprocedural embolic sources in AF ablation



# Bubble Formation

## Ballon catheter insertion in long sheath









**ESC**

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**CLINICAL RESEARCH**

*Atrial fibrillation*

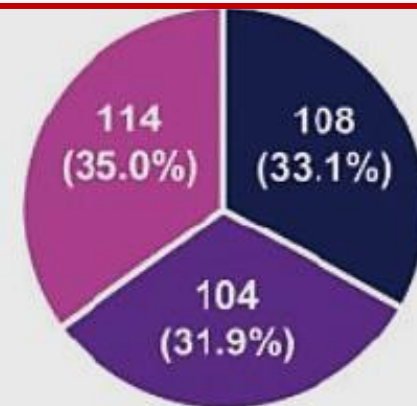
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# **When is it appropriate to stop non-vitamin K antagonist oral anticoagulants before catheter ablation of atrial fibrillation?**

## **A multicentre prospective randomized study**

**Hee Tae Yu<sup>1</sup>, Jaemin Shim<sup>2</sup>, Junbeom Park<sup>3</sup>, Tae-Hoon Kim<sup>1</sup>, Jae-Sun Uhm<sup>1</sup>, Jong-Youn Kim<sup>1</sup>, Boyoung Joung<sup>1</sup>, Moon-Hyoung Lee<sup>1</sup>, Young-Hoon Kim<sup>2</sup>, and Hui-Nam Pak<sup>1\*</sup>**

Randomized  
(N=326)



Uninterrupted  
(N=106)

Single dose skipped  
(N=110)

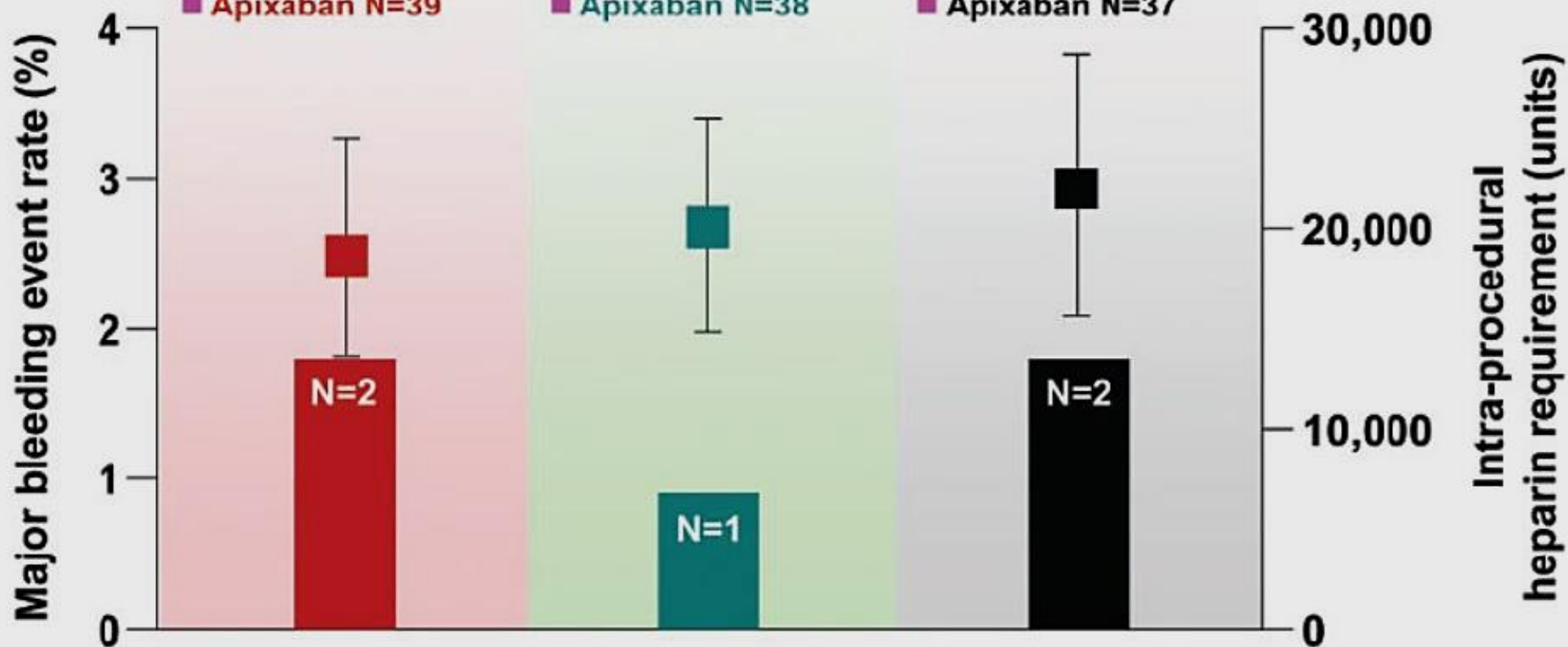
24 hour skipped  
(N=110)

■ Dabigatran N=35  
■ Rivaroxaban N=32  
■ Apixaban N=39

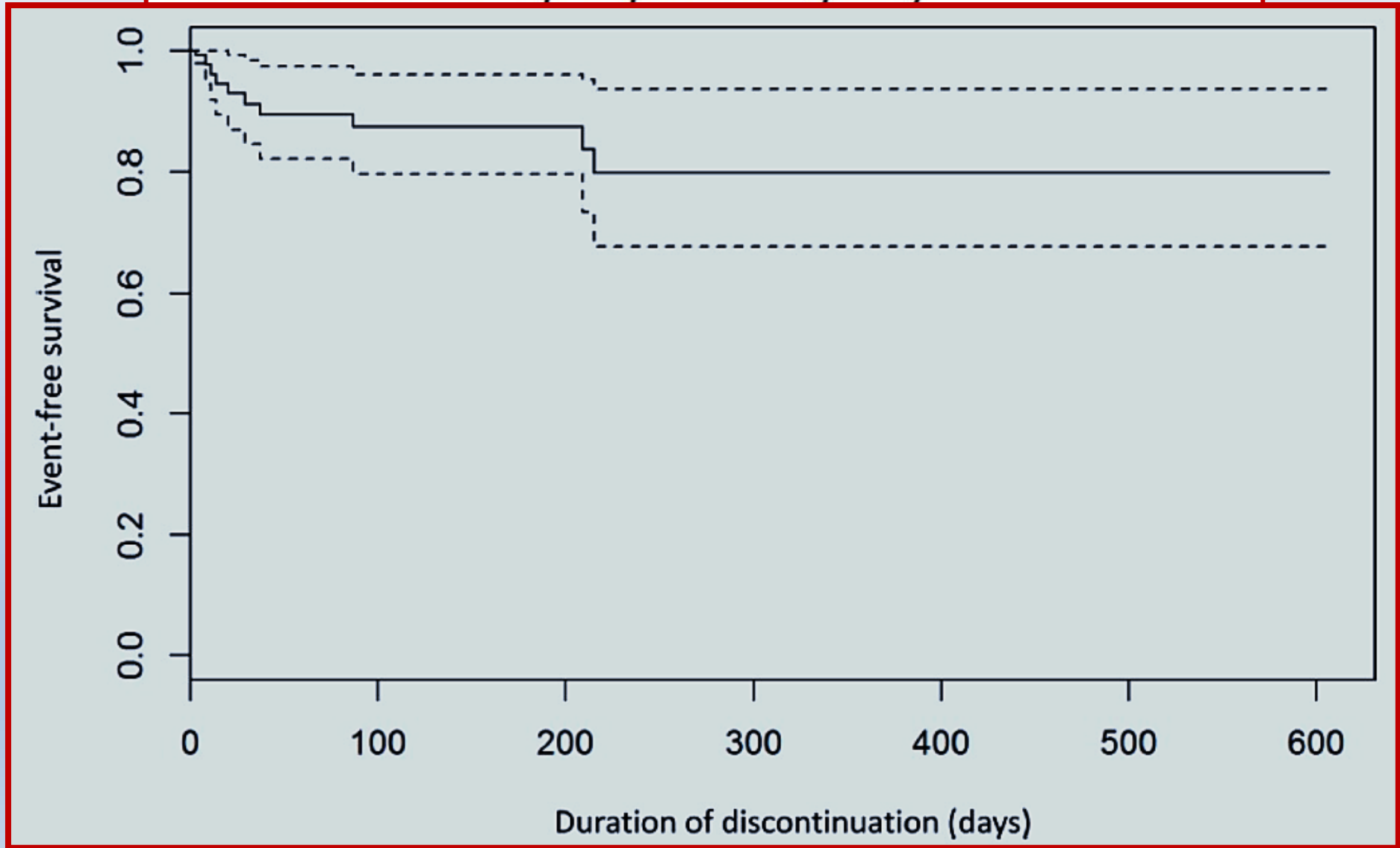
■ Dabigatran N=36  
■ Rivaroxaban N=36  
■ Apixaban N=38

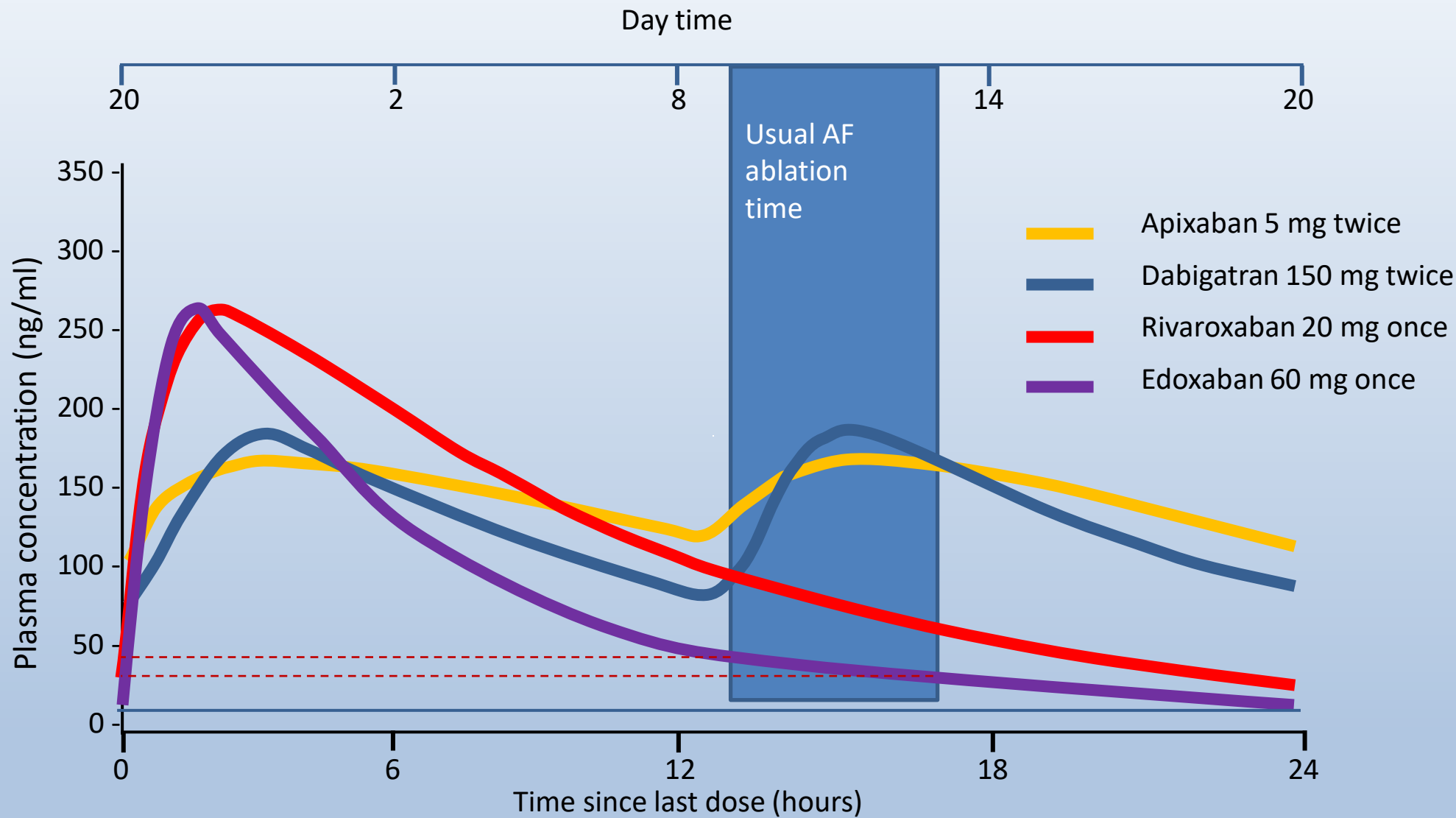
■ Dabigatran N=37  
■ Rivaroxaban N=36  
■ Apixaban N=37

■ Dabigatran  
■ Rivaroxaban  
■ Apixaban



# Risk of Thromboembolic Events in Patients with Non-Valvular Atrial Fibrillation After Dabigatran or Rivaroxaban Discontinuation – Data from the Ljubljana Registry





Modified from Gong et al, Can J Cardiol 2013;29:S24-33; Parasrampur et al. Clin Pharmacokinetic 2016;36:127-36



## Idarucizumab – Andexanet alfa



# Comparison of combined event rates in all randomized ablation trials comparing continuous NOAC therapy with continuous VKA therapy

