



ANTICOAGULANTES ORALES DE ACCIÓN DIRECTA en la práctica clínica



FJ Muñoz Hospital de Mollet

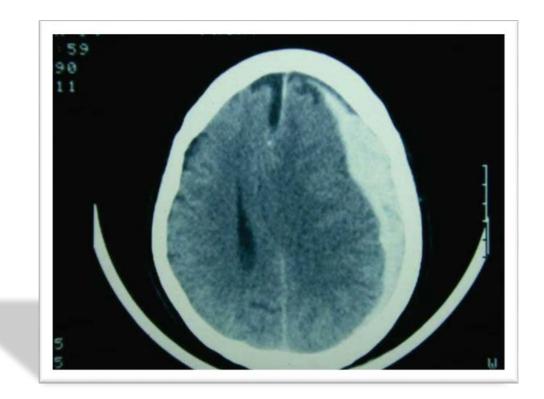
Caso clínico

- Varón de 67 años con antecedentes de HTA, Dislipemia, DM tipo2.
- Historia cardiológica: Cardiopatía isquémica con triple pontaje coronario en 1997. Actualmente en fase de cardiopatia dilatada con FE 23% y episodios de ICC con FE deprimida. Fibrilación auricular permanente.
- ► Enfermedad renal crónica estadío 3b con FGE de 40ml/min.
- ▶ 2015 sufrió una hemorragia intracraneal en forma de hematoma subdural tras TCE estando en tratamiento con acenocumarol, que requirió drenaje quirúrgico.
- ► CHA₂DS₂-VASc 4 y HAS-BLED 4.

Preguntas

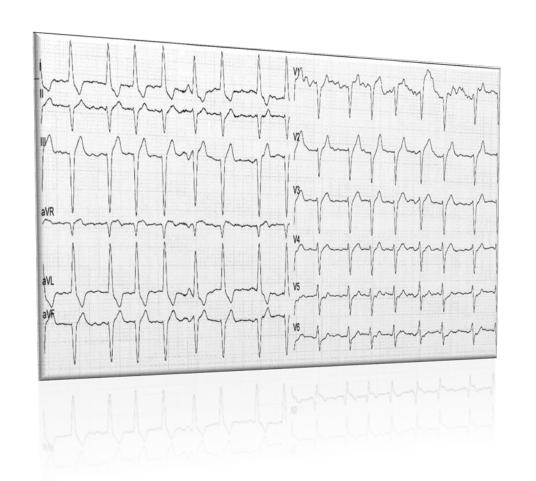
1. ¿Debemos administrar tratamiento anticoagulante a nuestro paciente?

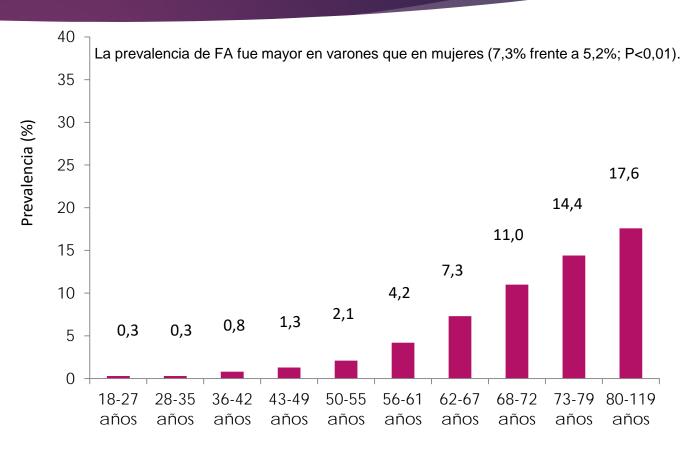
2. ¿Cuál sería la mejor opción terapéutica?



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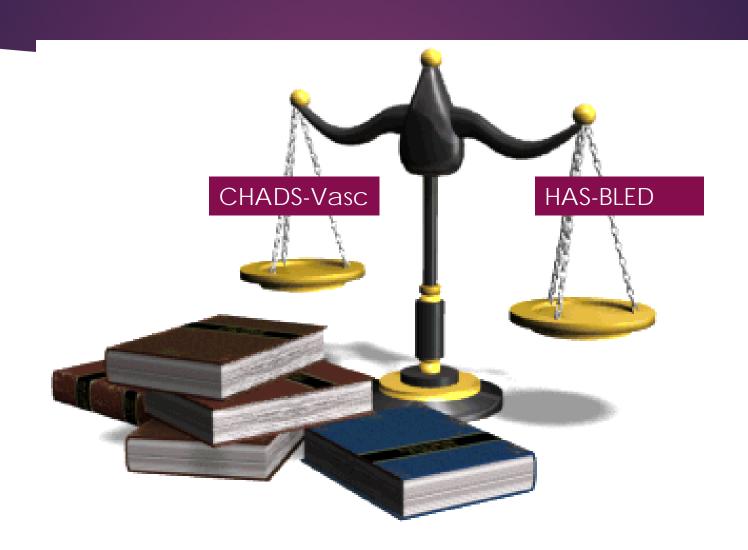
Prevalencia de FA en España de acuerdo con la edad. Estudio Val-FAAP





Barrios V. Rev Esp Cardiol 2012

¿Tenemos que anticoagular?



Escalas de riesgo

Table II Clinical risk factors for stroke, transient ischaemic attack, and systemic embolism in the CHA₂DS₂-VASc score

CHA2DS2-VASc risk factor	Points
Congestive heart failure Signs/symptoms of heart failure or objective evidence of reduced left ventricular ejection fraction	+1
Hypertension Resting blood pressure >140/90 mmHg on at least two occasions or current antihypertensive treatment	+1
Age 75 years or older	+2
Diabetes mellitus Fasting glucose >125 mg/dL (7 mmol/L) or treatment with oral hypoglycaemic agent and/or insulin	+1
Previous stroke, transient ischaemic attack, or thromboembolism	+2
Vascular disease Previous myocardial infarction, peripheral artery disease, or aortic plaque	+1
Age 65-74 years	+1
Sex category (female)	+1

 CHA_2DS_2 -VASc = Congestive Heart failure, hypertension, Age \geq 75 (doubled), Diabetes, Stroke (doubled), Vascular disease, Age 65–74, and Sex (female).

Table 10 Clinical characteristics comprising the HAS-BLED bleeding risk score

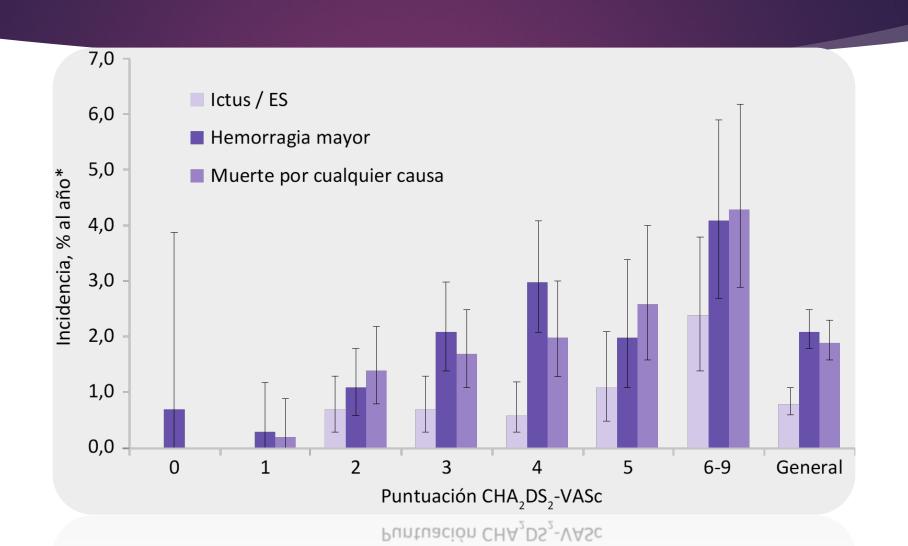
Letter	Clinical characteristic ^a	Points awarded
н	Hypertension	t
Α	Abnormal renal and liver function (I point each)	I or 2
S	Stroke	I.
В	Bleeding	Ĺ
L	Labile INRs	T.
Е	Elderly (e.g. age >65 years)	1
D	Drugs or alcohol (I point each)	I or 2
		Maximum 9 points

European Heart Journal (2010) **31**, 2369–2429 doi:10.1093/eurheartj/ehq278

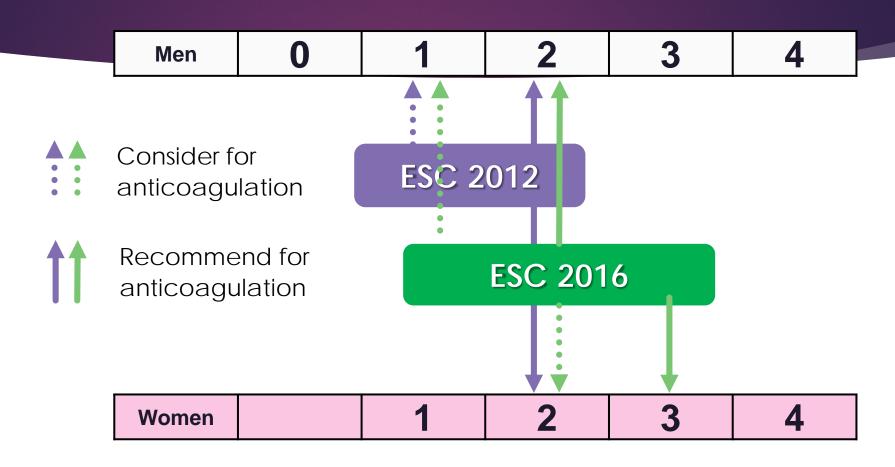




Incidencia de ictus / ES, hemorragia mayor y muerte por cualquier causa, según CHA₂DS₂-VASc (XANTUS)

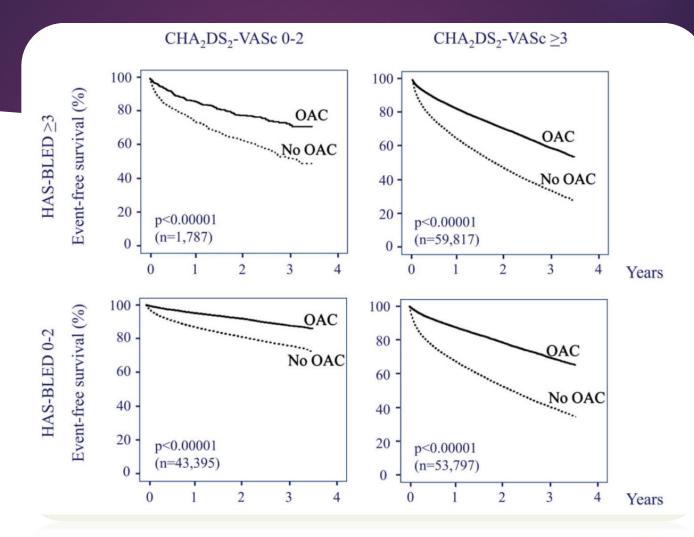


Indicación de anticoagulación



- 1. Camm AJ. Eur Heart J. 2012;33:2719-47.
- 2. Kirchhof P et al, Eur Heart J 2016; doi:10.1093/eurheartj/ehw210

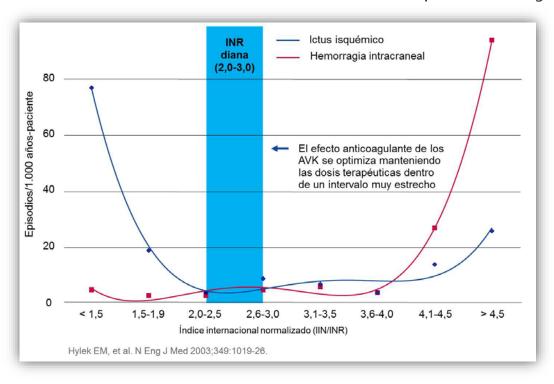
Beneficio clínico neto de la anticoagulación en FA

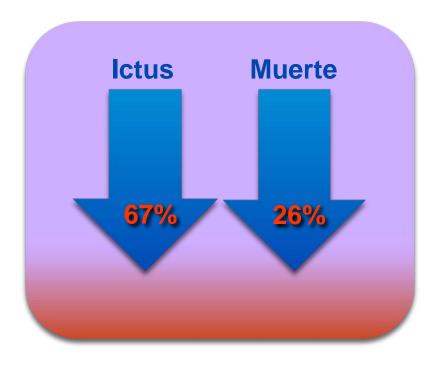


Supervivencia libre de eventos: muerte, ictus isquémico o hemorragia intracraneal

Tratamiento tradicional de la FA con AVK

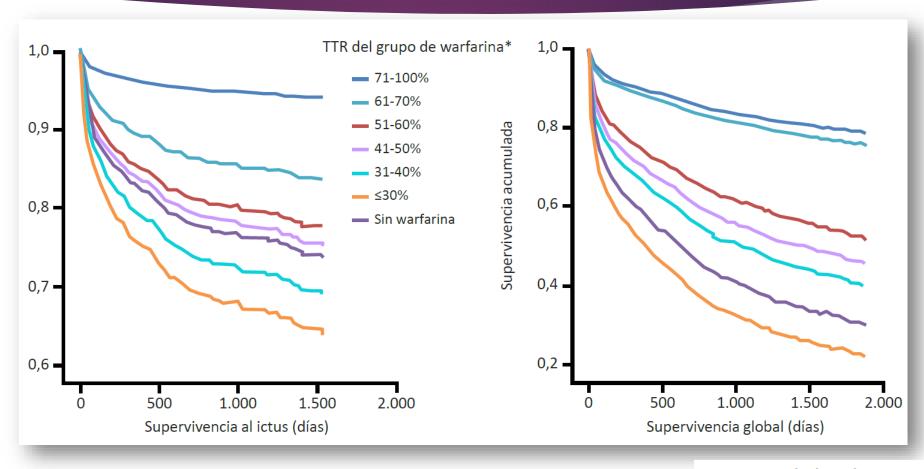
- 2/3 de los ictus por FA se pueden prevenir con un uso de AVK adecuado (INR 2-3)
- Un metaanálisis de 29 estudios en 28.044 pacientes demostró que una dosis ajustada de warfarina reduce el ictus isquémico y la mortalidad por todas la causas





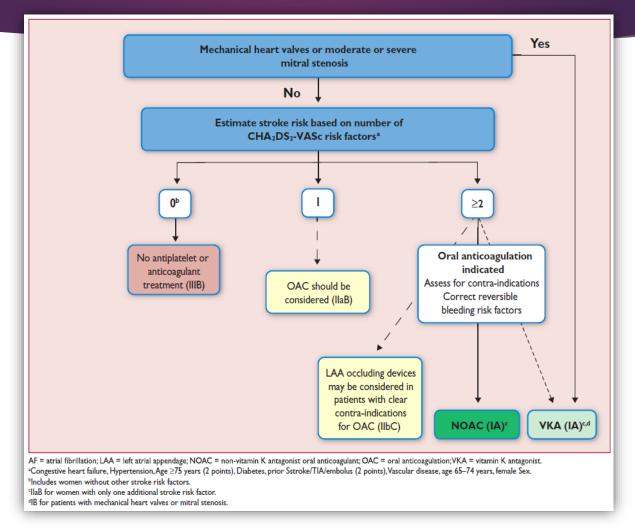
Hart RG. Ann Intern Med 2007

Riesgo de ictus y supervivencia según TRT





Initiation of Stroke Prevention Therapy in AF



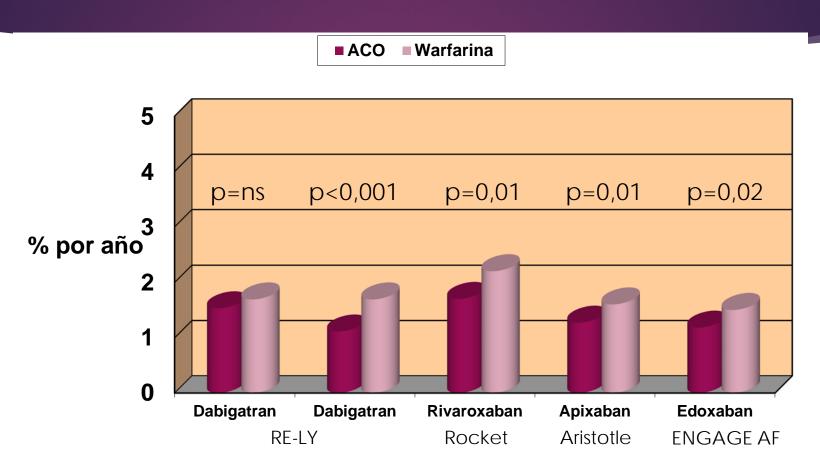


NOACs are the New Standard of Care for Stroke Prevention in Eligible Patients with AF*

Recommendations	Class	Level
When oral anticoagulation is initiated in a patient with AF who is eligible for a NOAC (apixaban, dabigatran, edoxaban, or rivaroxaban), a NOAC is recommended in preference to a Vitamin K antagonist.	_	Α
AF patients already on treatment with a vitamin K antagonist may be considered for NOAC treatment if TTR is not well controlled despite good adherence, or if patient preference without contra-indications to NOAC (e.g. prosthetic valve).	IIb	Α
Antiplatelet monotherapy is not recommended for stroke prevention in AF patients, regardless of stroke risk.	III (harm)	Α

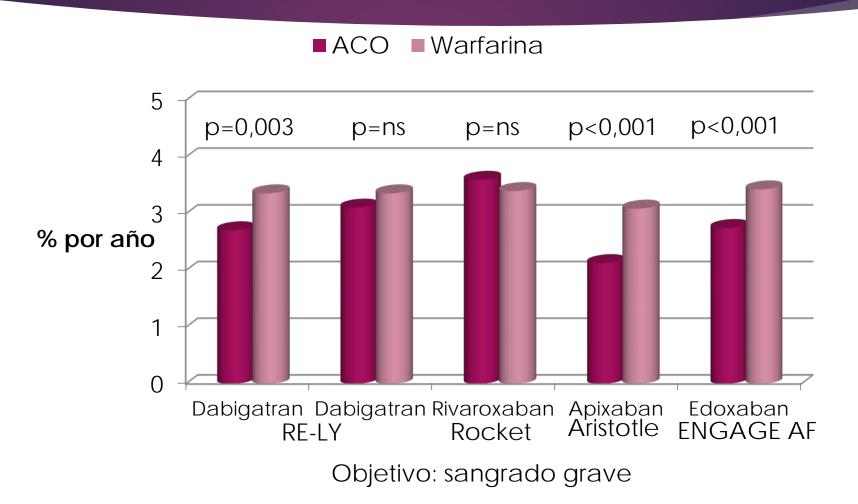
^{*}Those without mechanical heart valves or moderate or severe mitral stenosis

Fibrilación auricular Resultados de eficacia



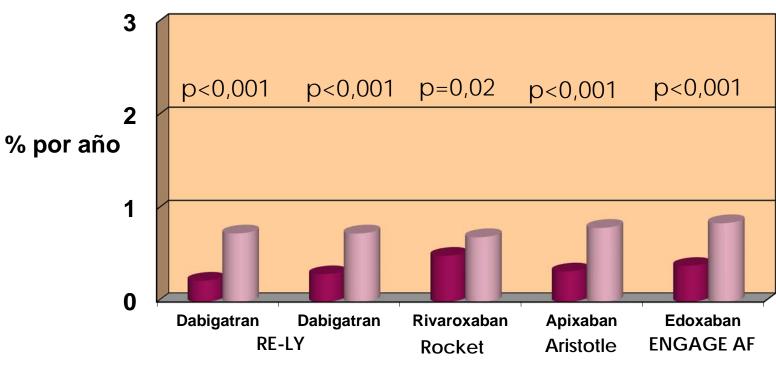
Objetivo primario: Ictus o embolismo sistémico

Resultados de seguridad



Fibrilación auricular Resultados de seguridad





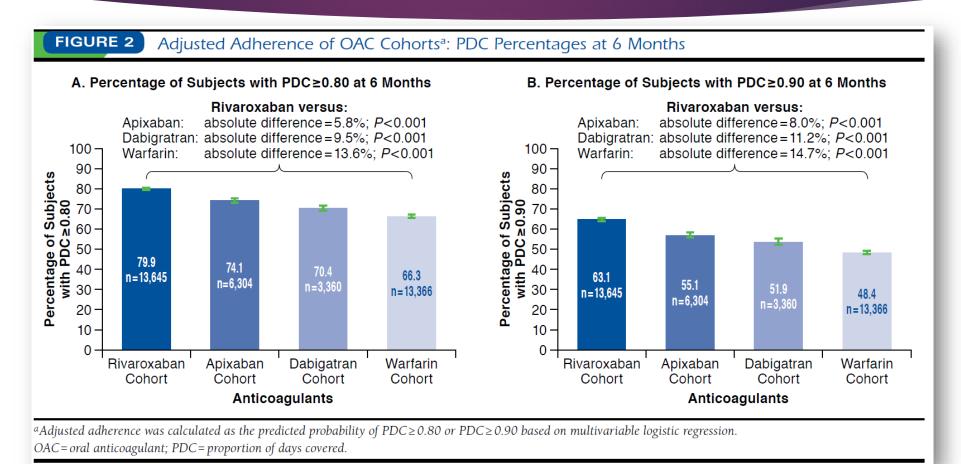
Objetivo: hemorragia intracraneal

Non-vitamin K antagonist oral anticoagulants compared withwarfarin at different levels of INR control in atrial fibrillation: A meta-analysis of randomized trials

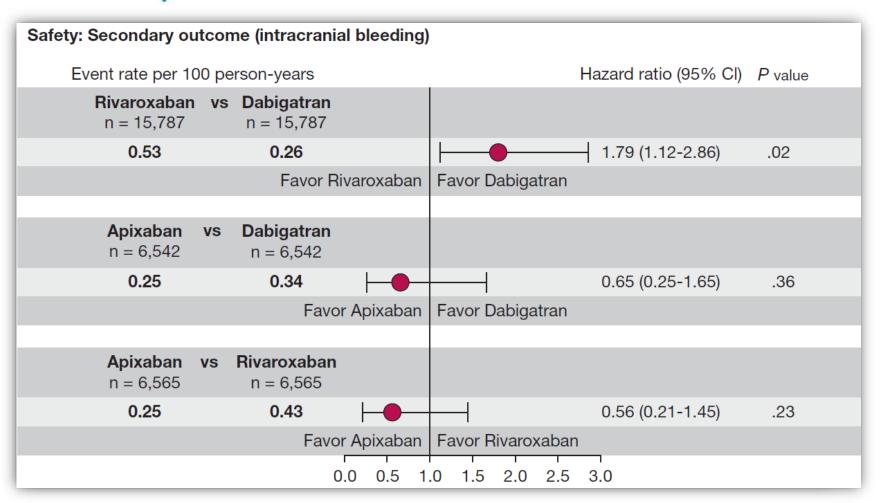
				Hazard Ratio	Hazard Ratio
Study or Subgroup	NOAC (n)	Warfarin(n)	Weight	IV, Random, 95% CI	IV, Random, 95% CI
4.5.1 TTR <60%					
ARISTOTLE Q1	2243	2251	6.0%	0.73 [0.53, 1.00]	
ENGAGE 30 Q1	1406	1406	4.6%	0.82 [0.56, 1.18]	+
ENGAGE 60 Q1	1413	1406	4.5%	0.80 [0.55, 1.16]	+
RELY 110 Q1	1497	1504	4.5%	1.00 [0.68, 1.45]	+
RELY 150 Q1	1509	1504	3.6%	0.57 [0.37, 0.88]	
ROCKET Q1	1735	1689	4.1%	0.70 [0.47, 1.04]	
ROCKET Q2 Subtotal (95% CI)	1746	1807	5.4% 32.8%	0.90 [0.64, 1.26]	<u> </u>
	0.00 51:3			0.79 [0.68, 0.90]	V
Heterogeneity: Tau ² =			= 0.57);	1' = 0%	
Test for overall effect:	Z = 3.39 (P	= 0.0007)			
4.5.2 TTR ≥60% to <	70%				
ARISTOTLE Q2	2287	2268	5.5%	0.94 [0.67, 1.31]	+
ARISTOTLE Q3	2301	2301	3.8%	0.64 [0.42, 0.97]	-
ENGAGE 30 Q2	2103	2196	6.2%	1.02 [0.75, 1.39]	+
ENGAGE 30 Q3	1906	2038	5.4%	1.22 [0.87, 1.72]	+-
ENGAGE 60 Q2	2104	2196	5.3%	0.73 [0.52, 1.02]	
ENGAGE 60 Q3	1908	2038	4.3%	0.74 [0.50, 1.09]	
RELY 110 Q2	1524	1514	4.7%	0.81 [0.56, 1.17]	-+
RELY 110 Q3	1474	1487	3.7%	0.89 [0.58, 1.36]	-
RELY 150 Q2	1526	1514	3.7%	0.50 [0.33, 0.77]	-
RELY 150 Q3	1484	1487	3.3%	0.69 [0.44, 1.09]	
ROCKET Q3	1734	1758	5.1%	0.88 [0.62, 1.25]	-
Subtotal (95% CI)			51.0%	0.82 [0.71, 0.95]	♦
Heterogeneity: Tau2 =	0.02; Chi2 =	15.80, df = 10	(P = 0.1)	1); $I^2 = 37\%$	
Test for overall effect:	Z = 2.74 (P	= 0.006)			
4.5.3 TTR ≥ 70%					
ARISTOTLE Q4	2289	2263	3.6%	0.88 [0.57, 1.35]	-
ENGAGE 30 Q4	1367	1364	3.1%	1.30 [0.81, 2.09]	
ENGAGE 60 Q4	1369	1364	2.8%	1.07 [0.65, 1.75]	+
RELY 110 Q4	1482	1509	3.3%	0.92 [0.59, 1.45]	+
RELY 150 Q4	1514	1509	3.4%	0.95 [0.61, 1.48]	+
Subtotal (95% CI)			16.3%	1.00 [0.82, 1.23]	*
Heterogeneity: Tau ² =			= 0.77);	$I^2 = 0\%$	
Test for overall effect:	Z = 0.04 (P	= 0.97)			
Total (95% CI)			100.0%	0.84 [0.77, 0.92]	•
Heterogeneity: Tau ² =	0.01; Chi ² =	26.25, df = 22	(P = 0.24)	$1); I^2 = 16\%$	0.01 0.1 1 10 100
Test for overall effect:	Z = 3.92 (P	< 0.0001)		5150	0.01 0.1 1 10 100 Favours NOAC Favours warfarin

Ictus o embolismo sistémico

Adherencia de los NACOS



Direct Comparison of Dabigatran, Rivaroxaban, and Apixaban for Effectiveness and Safety in Nonvalvular Atrial Fibrillation



Real-World Setting Comparison of Nonvitamin-K Antagonist Oral Anticoagulants Versus Vitamin-K Antagonists for Stroke Prevention in Atrial Fibrillation: A Systematic Review and Meta-Analysis

Dabigatran vs Warfarina

	HR	IC 95%	
Ictus isquémico	0,96	0,8-1,16	
Ictus isquémico y embolismo sistémico	1,17	0,92-1,5	
Cualquier ictus y embolismo sistémico	0,93	0,77-1,14	
Infarto de miocardio	0,96	0,77-1,21	

	HR	IC 95%
Hemorragia intracraneal	0,42	0,37-0,49
Hemorragia gastrointestinal	1,20	1,06-1,36
Hemorragia grave	0,83	0,65-1,05
Muerte	0,63	0,52-0,76

Real-World Setting Comparison of Nonvitamin-K Antagonist Oral Anticoagulants Versus Vitamin-K Antagonists for Stroke Prevention in Atrial Fibrillation: A Systematic Review and Meta-Analysis

Rivaroxaban vs Warfarina

	HR	IC 95%
Ictus isquémico	0,89	0,76-1,04
Ictus isquémico y embolismo sistémico	0,73	0,52-1,04
Cualquier ictus y embolismo sistémico	0,87	0,71-1,07
Infarto de miocardio	1,02	0,54-1,89

	HR	IC 95%
Hemorragia intracraneal	0,64	0,47-0,86
Hemorragia gastrointestinal	1,24	1,08-1,41
Hemorragia grave	1	0,92-1,08
Muerte	0,67	0,35-1,3

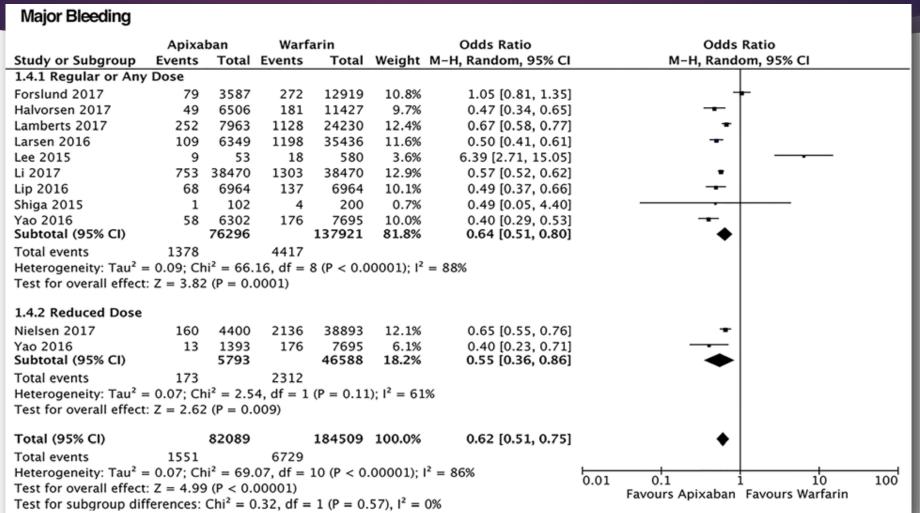
Real-World Setting Comparison of Nonvitamin-K Antagonist Oral Anticoagulants Versus Vitamin-K Antagonists for Stroke Prevention in Atrial Fibrillation: A Systematic Review and Meta-Analysis

Apixaban vs Warfarina

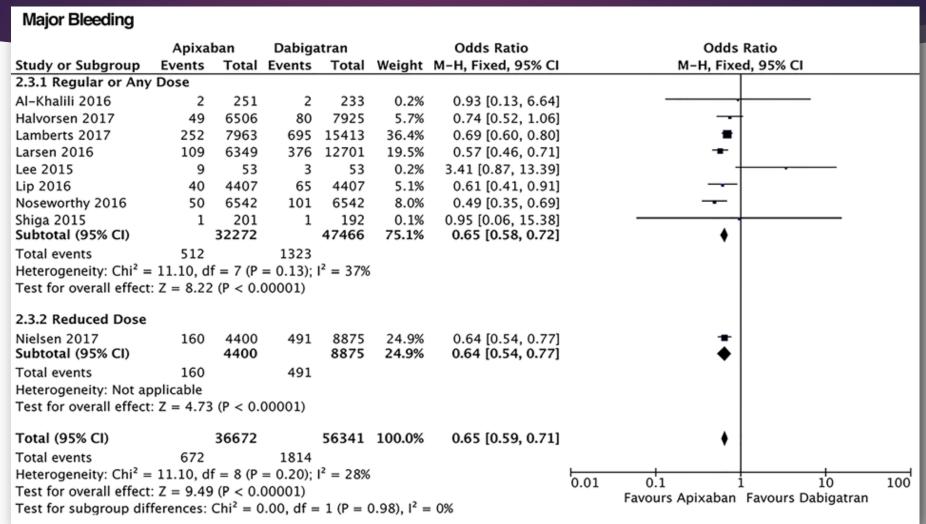
	HR	IC 95%
Ictus isquémico	0,95	0,75-1,19
Ictus isquémico y embolismo sistémico	1,07	0,87-1,31
Cualquier ictus y embolismo sistémico	0,67	0,46-0,98
Infarto de miocardio	ND	ND

	HR	IC 95%
Hemorragia intracraneal	0,45	0,31-0,63
Hemorragia gastrointestinal	0,63	0,42-0,95
Hemorragia grave	0,55	0,48-0,63
Muerte	0,65	0,56-0,75

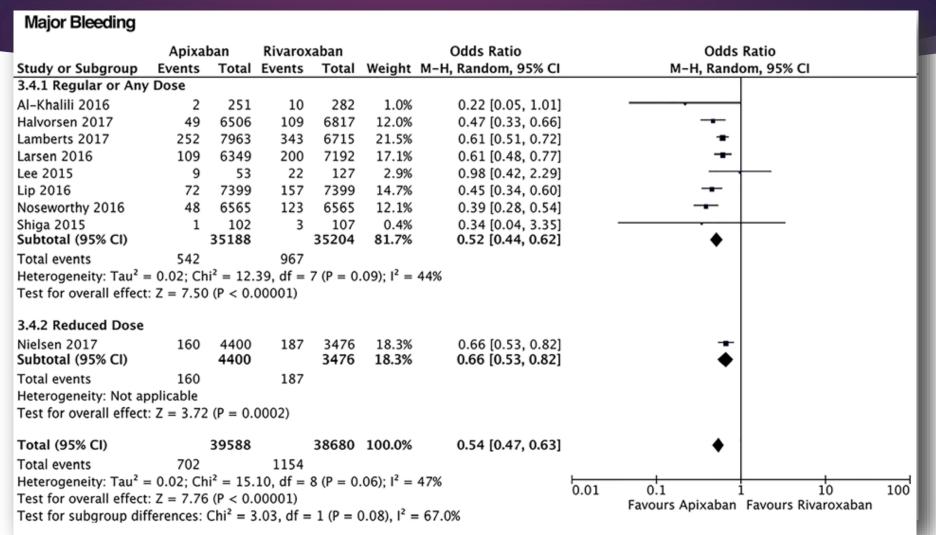
Real-World Use of Apixaban for Stroke Prevention in Atrial Fibrillation: A Systematic Review and Meta-Analysis



Real-World Use of Apixaban for Stroke Prevention in Atrial Fibrillation: A Systematic Review and Meta-Analysis



Real-World Use of Apixaban for Stroke Prevention in Atrial Fibrillation: A Systematic Review and Meta-Analysis



Direct Oral Anticoagulants Versus Vitamin K Antagonists in Real-life Patients With Atrial Fibrillation. A Systematic Review and Meta-analysis

Ictus isquémico

Rivaroxaban redujo significativamente el riesgo de ictus isquémico en comparación con warfarina (HR 0.83, 95% Cl 0.73–0.94). Este hallazgo resultó ser muy consistente entre estudios.

> Rivaroxaban RRR 17 %

			DO40	Modernia		UD	LID
Study or Subgroup	log[HR]	SE	Total	Warfarin Total		HR IV, Random, 95%CI	HR IV, Random, 95%Cl
Apixaban	log[rird]	- OL	Total	rotar	wogn	TV, Trandom, 307001	14, 141100111, 307001
	0.100	0.42	4002	4002	C 00/	4 42 [0 40 2 64]	
Coleman et al. ²² Forslund et al. ²⁴	0.122 -0.186	0.42	4083 3587	4083 12919	6.8% 15.8%	1.13 [0.49-2.61] 0.83 [0.57-1.21]	-
Larsen et al. ³⁶	0.104	0.19	6349	35436	21.5%	1.11 [0.94-1.31]	 -
Li et al. ³⁷	-0.400	0.07	38470	38470	22.0%	0.67 [0.58-0.77]	-
Nielsen et al. ³⁹	0.173	0.11	4400	38893	20.0%	1.19 [0.95-1.49]	├ •-
Yao et al. ⁴⁵	-0.183	0.22	15390	51390	13.8%	0.83 [0.53-1.49]	
Subtotal (95%CI)	-0.103	0.22		181191		0.93 [0.71-1.20]	
Heterogeneity: Tau ² =	0.07: chi-sai	are = 2					
Test for ove rall effect:	,		,		.,, .		
	(.	,					
Dabigatran							
Bengtson et al.17	0.182	0.12	13937	63460	9.1%	1.20 [0.95-1.52]	├• ─
Bengtson et al.17	-0.430	0.11	18891	37707	9.2%	0.65 [0.52-0.81]	
Chan et al.19	-0.342	0.15	5921	5251	8.3%	0.71 [0.53-0.95]	
Forslund et al.24	-0.174	0.17	3322	12919	7.7%	0.84 [0.60-1.18]	-+
Graham et al.26	-0.223	0.09	67207	67207	9.8%	0.80 [0.67-0.96]	
Larsen et al. rdcd35	0.548	0.18	412	1918	7.4%	1.73 [1.21-2.47]	I —
Larsen et al. stnd35	0.582	0.21	547	1918	6.6%	1.79 [1.18-2.72]	
Larsen et al.36	0.215	0.14	12701	35436	8.5%	1.24 [0.94-1.64]	 •
Nielsen et al.39	-0.083	0.07	8875	38893	10.1%	0.92 [0.79-1.07]	*
Seeger et al.42	-0.597	0.20	15529	15529	6.9%	0.55 [0.37-0.82]	<u> </u>
Villines et al.44	-0.174	0.15	12793	12793	8.1%	0.84 [0.62-1.14]	
Yao et al.45	0.058	0.15		28614	8.3%	1.06 [0.79-1.42]	
Subtotal (95%CI)				321645		0.95 [0.80-1.13]	Y
Heterogeneity: Tau ² =			3.92, df	= 11 (P <	.00001);	r = 80%	
Test for overall effect:	Z = 0.56 (P	= .5/)					
Rivaroxaban							
Chan et al. ¹⁹	-0.562	0.20	3916	5251	8.5%	0.57 [0.38-0.85]	_ - _
Coleman et al. ²²	-0.342	0.21	11411	11411	8.2%	0.71 [0.47-1.07]	
Forslund et al. ²⁴	-0.356	0.21	2370	12919	8.0%	0.70 [0.46-1.07]	
Laliberté et al. 33	-0.212	0.18	3654	14616	11.0%	0.81 [0.57-1.15]	
Larsen et al. ³⁶	-0.150	0.09	7192	35436	32.4%	0.86 [0.72-1.03]	-
Nielsen et al. 39	-0.072	0.14	3476	38893	17.3%	0.93 [0.71-1.22]	
Yao et al. ⁴⁵	0.010	0.15	32350	32350	14.7%	1.01 [0.75-1.36]	<u> </u>
Subtotal (95%CI)			64369	150876	100.0%	0.83 [0.73-0.94]	◇
Heterogeneity: Tau ² =	0.00; chi-squ	uare = 6	.99, df =	6 (P = .32	2); f = 14	%	
Test for overall effect:	Z = 2.97 (P =	(2003 =					
	-	-					
All DOAC							_
Forslund et al.24	-0.210	0.12	9272	12919		0.81 [0.64-1.03]	-
Gieling et al.25	0.198	0.30	1306		26.4%	1.22 [0.67-2.22]	
Subtotal (95%CI)			10578		100.0%	0.90 [0.63-1.29]	
Heterogeneity: Tau ² =			.55, df =	1 (P = .2)	1); $I^2 = 36$	3%	
Test for overall effect:	Z = 0.57 (P = 0.57)	= .57)					
						0.2	0.5 1 2 5
Test for subgroup diffe	erences: chi-	square =	= 1.90, df	= 3 (P =	.59), f =	0% Favors D	OAC Favors Warfarin

Direct Oral Anticoagulants Versus Vitamin K Antagonists in Real-life Patients With Atrial Fibrillation. A Systematic Review and Meta-analysis

Ictus isquémico/ES

Rivaroxaban redujo significativamente el riesgo de eventos isquémicos (ictus/ES) en comparación con warfarina (HR 0.80, 95% Cl 0.69–0.93), un hallazgo consistente entre estudios.

> Rivaroxaban RRR 20 %

				C Warfa		HR	HR
Study or Subgroup	log[HR]	SE	Total	Total	Weight	IV, Random, 95%C	I IV, Random, 95%CI
Apixaban							
Larsen et al.36	0.076	0.08	7192	35436	26.6%	1.08 [0.91-1.28]	*
Li et al.37	-0.400	0.06			27.6%	0.67 [0.59-0.76]	•
Nielsen et al.39	0.173	0.11	4400	38893	25.2%	1.19 [0.95-1.49]	-
Yao et al. ⁴⁵ Subtotal (95%CI)	-0.400	0.19			20.6%	0.67 [0.46-0.98]	
, ,	= 0.00; ob					0.88 [0.64-1.21]	Y
Heterogeneity: Tau ² Test for overall effe				, ui – 3	(P < .000	01); 1 = 90%	
rest for overall effe	U. Z - U.73	(r	40)				
Dabigatran							
Bouillon et al.18	0.095	0.23	4370	10705	11.5%	1.10 [0.70-1.73]	-
Chan et al.19	-0.446	0.13	5921	5251	20.1%	0.64 [0.49-0.84]	-
Larsen et al.36	0.157	0.14	12701	35436	19.7%	1.17 [0.89-1.54]	-
Nielsen et al.39	-0.116	0.07	8875	38893	27.9%	0.89 [0.77-1.03]	•
Yao et al.45	-0.020	0.13	28614	28614	20.8%	0.98 [0.76-1.26]	†
Subtotal (95%CI)			60481	118899	100.0%	0.92 [0.76-1.11]	•
Heterogeneity: Tau ²				, df = 4	(P = .03);	f = 64%	
Test for overall effe	ct: Z = 0.87	(P =	38)				
Rivaroxaban							
Bouillon et al. 18	-0.2871	0.34	2335	10705	4.7%	0.75 [0.39-1.44]	
Chan et al.19	-0.673	0.19	3916	5251	12.0%	0.51 [0.35-0.74]	-
Laliberté et al.33	-0.261	0.17	3654	14616	14.2%	0.77 [0.55-1.08]	
Larsen et al.36	-0.186	0.09	7192	35436	28.4%	0.83 [0.69-1.00]	•
Nielsen et al.39	-0.116	0.13	3476	38893	20.4%	0.89 [0.69-1.15]	•
Yao et al.45	-0.072	0.13	32350	32350	20.3%	0.93 [0.72-1.20]	<u>+</u>
Subtotal (95%CI)						0.80 [0.69-0.93]	0
Heterogeneity: Tau ²				df = 5 (F	P = .18);	$I^2 = 35\%$	
Test for overall effe	ct: Z = 2.92	(P = .	003)				
All DOAC							_
Arihiro et al. 15	-0.821	0.78	475	662	100.0%	0.44 [0.09-2.04]	
Subtotal (95%CI)			475		100.0%	0.44 [0.09-2.04]	
Heterogeneity: Not a	applicable						
Test for overall effe		(P = .	29)				
			-				
						0.05	0.2 1 5 20
Test for subgroup di	ifferences:	chi-sq	uare = 2.0)2, df = 3	3 (P = .57		
		- 4			,		

Direct Oral Anticoagulants Versus Vitamin K Antagonists in Real-life Patients With Atrial Fibrillation. A Systematic Review and Meta-analysis

Hemorragia grave

Se observó una reducción del riesgo de Hemorragia Grave tanto con apixaban como con dabigatran en comparación con warfarina (HR 0.66, 95% CI 0.55–0.80; HR 0.81, 95% CI 0.69 to –0.95, respectivamente), sin embargo la heterogeneidad estadística fue muy elevada entre los estudios.

Apixaban RRR 34%

Dabigatran RRR 19%

Rivaroxaban no mostró una reducción del riesgo de Hemorragia Grave en comparación con warfarina (HR 1.02, 95% CI 0.95–1.10).

				Warfarin		HR	HR
Study or Subgroup	log[HR]	SE	Total	Total	Weight	IV, Random, 95%CI	IV, Random, 95%CI
Apixaban							
Forslund et al.24	0.048	0.12	3587	12919	12.9%	1.05 [0.82-1.34]	†
Halvorsen et al.28	-0.579	0.17	6506	11427	10.8%	0.56 [0.40-0.78]	
Hohnloser et al.31	-0.385	0.15	3633	16179	12.0%	0.68 [0.51-0.91]	
Larsen et al.36	-0.494	0.11	6349	35436	13.5%	0.61 [0.49-0.76]	*
Li et al.37	-0.510	0.05	38470	38470	15.8%	0.60 [0.54-0.67]	*
Lip et al.38	-0.634	0.16	7438	15461	11.5%	0.53 [0.39-0.72]	-
Nielsen et al.39	0.039	0.16	4400	38893	11.3%	1.04 [0.76-1.42]	+
Yao et al.45	-0.798	0.14	15390	51390	12.1%	0.45 [0.34-0.60]	
Subtotal (95%CI)			85773	220175	100.0%	0.66 [0.55-0.80]	♦
Heterogeneity: Tau ² = 0.0	06; chi-squa	are = 34	.52, df = 7	(P < .00	01); $f = 8$	30%	
Test for overall effect: Z =	= 4.34 (P <	.0001)					
Dabigatran							
Forslund et al.24	-0.040	0.11	3322	12919	7.1%	0.96 [0.77-1.20]	+
Graham et al.26	-0.030	0.05	67207	67207	7.9%	0.97 [0.88-1.07]	†
Halvorsen et al.28	-0.400	0.13	7925	11427	6.8%	0.67 [0.52-0.86]	~
Hemandez et al. ²⁹	0.457	0.07	1302	8102	7.6%	1.58 [1.36-1.84]	+
Hohnloser et al.31	-0.274	0.15	3138	16179	6.5%	0.76 [0.57-1.01]	T
Larsen et al. rdcd34	0.157	0.14	2038	8504	6.6%	1.17 [0.89-1.54]	 • -
Larsen et al. stnd34	-0.150	0.15	2214	8504	6.4%	0.86 [0.64-1.16]	- *
Larsen et al.36	-0.544	0.11	12701	35436	7.2%	0.58 [0.47-0.72]	-
Lip et al.38	-0.371	0.16	4661	15461	6.2%	0.69 [0.50-0.95]	
Nielsen et al.39	-0.139	0.07	8875	38893	7.6%	0.87 [0.75-1.01]	*
Nishtala et al.40	-0.798	0.09	2153	4835	7.3%	0.45 [0.37-0.55]	+
Seeger et al.42	-0.223	0.08	15529	15529	7.6%	0.80 [0.68-0.94]	*
Villineset al.44	-0.139	0.08	12793	12793	7.6%	0.87 [0.74-1.02]	₹
Yao et al.45	-0.235	0.08	28614	28614	7.5%	0.79 [0.67-0.93]	<u>†</u>
Subtotal (95%CI)			172472	284403	100.0%	0.83 [0.70-0.97]	9
Heterogeneity: Tau ² = 0.0	08; chi-squa	are = 13	7.96, df =	13(P < .	00001); <i>f</i>	= 91%	
Test for overall effect: Z	= 2.31 (P =	.02)					
Rivaroxaban							
Forslund et al. ²⁴	0.048	0.12	2370	12919	9.0%	1.05 [0.83-1.33]	†
Halvorsen et al. ²⁸	-0.150	0.12	6817	11427	9.1%	0.86 [0.68-1.09]	*
Hohnloser et al.31	-0.062	0.15	12063	16179	5.2%	0.94 [0.69-1.28]	+
Laliberté et al.33	0.076	0.21	3654	14616	2.8%	1.08 [0.71-1.64]	
Larsen et al.36	0.058	0.07	7192	35436	21.4%	1.06 [0.91-1.23]	†
Lip et al.38	-0.020	0.08	17801	15461	18.1%	0.98 [0.83-1.16]	†
Nielsen et al.39	0.157	0.11	3476	38893	10.4%	1.17 [0.94-1.46]	 -
Yao et al.45	0.039	0.07	32350	32350	23.9%	1.04 [0.90-1.20]	†
Subtotal (95%CI)			85723	177281	100.0%	1.02 [0.95-1.10]	Ŷ
Heterogeneity: Tau ² = 0.00; chi-square = 4.46, df = 7 (P = .73); f = 0%							
Test for overall effect: Z =	= 0.67 (P =	.50)					
All DOAC							
Arihiro et al. ¹⁵	-0.462	0.61	475	662	16.3%	0.63 [0.19-2.09]	
Forslund et al. ²⁴	0.009	0.07	9272	12919	47.1%	1.01 [0.87-1.17]	# _
Gieling et al. ²⁵	0.732	0.24	1306	13643	36.6%	2.08 [1.28-3.38]	<u>_</u>
Subtotal (95%CI)			11053	27224	100.0%	1.22 [0.67-2.20]	
Heterogeneity: Tau ² = 0.1	19; chi-squa	are = 8.	52, df = 2 (P = .01);	f = 77%		
Test for overall effect: Z = 0.65 (P = .51)							
							, [
						0.05	0.2 1 5 20
Test for subgroup differen	nces: chi-s	quare =	22.42, df	= 3 (P < .	0001), I ²		
					,,,		

Hemorragia Intracraneal

Tanto apixaban como dabigatran y rivaroxaban redujeron significativamente el riesgo de HIC en comparación con warfarina (HR 0.56, 95% CI 0.42–0.73; HR 0.42, 95% CI 0.37– 0.48; HR 0.66, 95% CI 0.49–0.88; respectivamente).

Apixaban RRR 44% Dabigatran RRR 58%

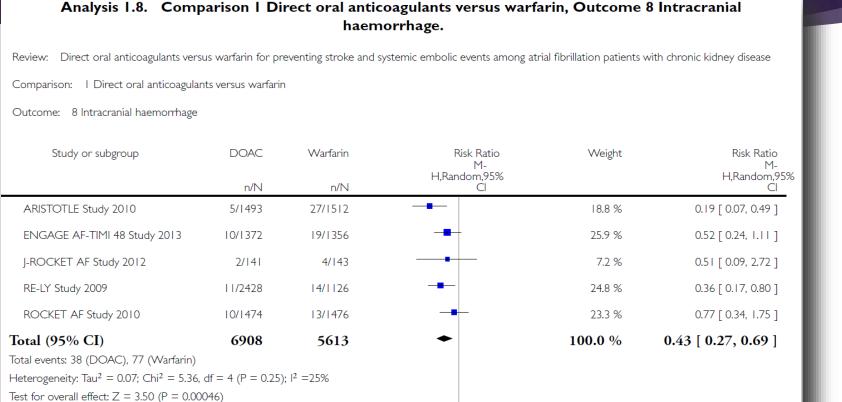
Rivaroxaban RRR 34 %

Ohudu an Out-	In all time	0.5		Warfarin		HR	HR
Study or Subgroup	log[HR]	SE	ı otal	i otal	vveight	iv, Random, 95%	CI IV, Random, 95%CI
Apixaban							
Coleman et al. ²²	-0.967				8.9%	0.38 [0.17-0.85]	_
Forslund et al. ²⁴	-0.287				16.4%	0.75 [0.45-1.25]	
Halvorsen et al.28					19.1%		-1
Larsen et al.36	-0.328				15.4%		
Li et al. ³⁷					29.0%	0.64 [0.50-0.82]	_
Yao et al. ⁴⁵	-1.427	0.35			11.1%		
Subtotal (95%CI)	05 1.1				100.0%		*
Heterogeneity: Tau ² = 0.				f = 5 (P)	= .09); <i>r</i>	= 47%	
Test for overall effect: Z :	= 4.16 (P	< .000	n)				
Dabigatran							
Avgil et al. < 75 ¹⁶	0.624	0.22	6270	14262	7 40/	0 52 [0 24 0 92]	- -
Avgil et al. > 75 ¹⁶	-0.634 -0.510				7.1% 15.6%	0.53 [0.34-0.83]	- 1
Bengtson et al. 17	-0.867					0.60 [0.47-0.77]	<u></u>
Bengtson et al. 17	-0.867			37707	4.3% 4.1%	0.42 [0.23-0.77]	
Chan et al. 19	-0.994				6.9%	0.44 [0.28-0.68]	- -
Forslund et al. ²⁴	-0.653			12919	6.1%	0.52 [0.32-0.85]	
Graham et al. 26					14.1%	0.34 [0.26-0.44]	•
Halvorsen et al. ²⁸	-0.776			11427	7.5%	0.46 [0.30-0.71]	-
Hernandez et al. ²⁹	-1.140					0.32 [0.20-0.51]	-
Larsen et al. rdcd ³⁴	-0.371				4.7%		
Larsen et al. stnd ³⁴	-0.693					0.50 [0.23-1.09]	
Larsen et al. 36					6.5%		
Nishtala et al. ⁴⁰	-1.560			4835			
Villines et al. ⁴⁴				12793			
Yao et al. 45	-1.021				7.0%	0.36 [0.23-0.56]	
Subtotal (95%CI)					100.0%	0.45 [0.39-0.51]	Λ Ι
Heterogeneity: Tau ² = 0.0	01: chi-so						
Test for overall effect: Z =					(,	, , .	
	(,				
Rivaroxaban							
Chan et al. 20	-1.204	0.35	3916	5251	10.0%	0.30 [0.15-0.60]	- -
Coleman et al.22	-0.634	0.21	11411	11411	15.5%	0.53 [0.35-0.80]	*
Forslund et al. ²⁴	-0.116	0.23	2370	12919	14.8%	0.89 [0.57-1.39]	+
Halvorsen et al.28	-0.072	0.17	6817	11427	17.5%	0.93 [0.67-1.29]	†
Laliberté et al.33	0.157	0.29	3654	14616	12.2%	1.17 [0.66-2.07]	
Larsen et al.36	-0.579	0.25	7192	35436	13.6%	0.56 [0.34-0.92]	~
Yao et al. 45	-0.673	0.19	32350	32350	16.4%	0.51 [0.35-0.74]	*
Subtotal (95%CI)					100.0%	0.66 [0.49-0.88]	♥
Heterogeneity: Tau ² = 0.	10; chi-sa	uare :	= 17.92,	df = 6 (H	o= .006)	; <i>f</i> = 67%	
Test for overall effect: Z =	2.77 (P	006)				
All DOAC							
All DOAC							
Arihiro et al. 15	-1.897	1.38	475				_
Forslund et al. ²⁴	-0.371	0.15			64.1%		
Gieling et al.25	0.350	0.47		13643		1.42 [0.56-3.60]	
Subtotal (95%CI)	4011			27224		0.79 [0.40-1.54]	Y
Heterogeneity: Tau ² = 0.			= 3.41, 0	$\pi = 2 (P)$	= 0.18);	Γ = 41%	
Test for overall effect: Z =	0.70 (P	= .48)					
						-	
						0.005	0.1 1 10 200
Test for subgroup differen	ces: chi-s	quare	= 8.54,	df = 3 (I	?= .04),	f = 64.9% Favor	rs DOAC Favors Warfarin

NACO: Farmacocinética

	Dabigatran	Rivaroxaban	Apixaban	Edoxaban
Administración	Oral	Oral	Oral	Oral
Biodisponibilidad	6,5%	>80%	>50%	60%
Tmax (h)	1,25-3	2-4	1-3	1-2
Vida media (h)	12-14	9-13	8-15	9-10
Metabolismo hepático	No	CYP3A4	CYP3A4	CYP3A4
Eliminación renal	85%	66% (1/3 activa)	25%	33%
Interferencia con alimentos	No	No	No	No

Direct oral anticoagulants versus warfarin for preventing stroke and systemic embolic events among atrial fibrillation patients with chronic kidney disease (Review)



0.02 0.1 Less with DOAC

Test for subgroup differences: Not applicable

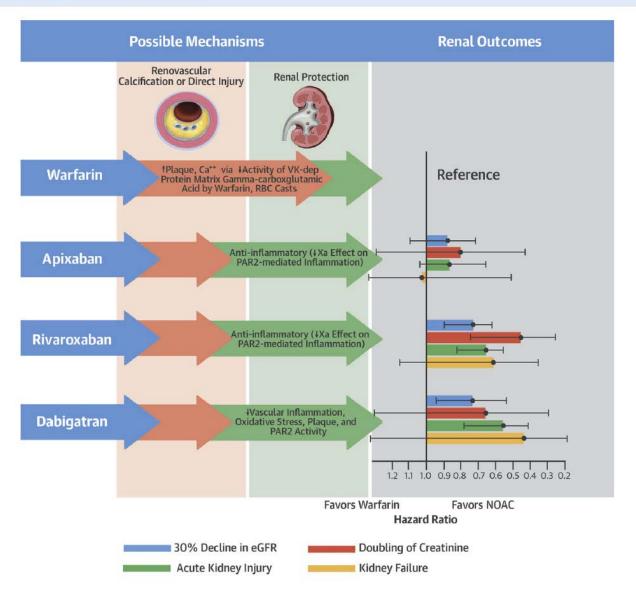
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Less with warfarin

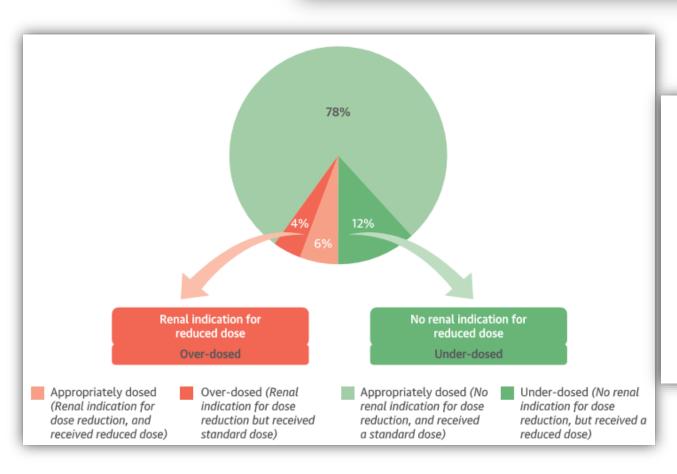
Renal Outcomes in Anticoagulated Patients With Atrial Fibrillation

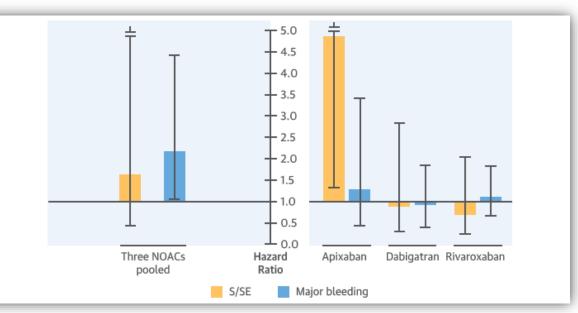
The cumulative risk at the end of 2 years for each outcome was 24.4%, 4.0%, 14.8%, and 1.7% for >30% decline in eGFR, doubling of serum creatinine, AKI, and kidney failure, respectively.

CENTRAL ILLUSTRATION Renal Outcomes Associated With the Various Oral Anticoagulant Agents: Possible Mechanisms and Outcomes

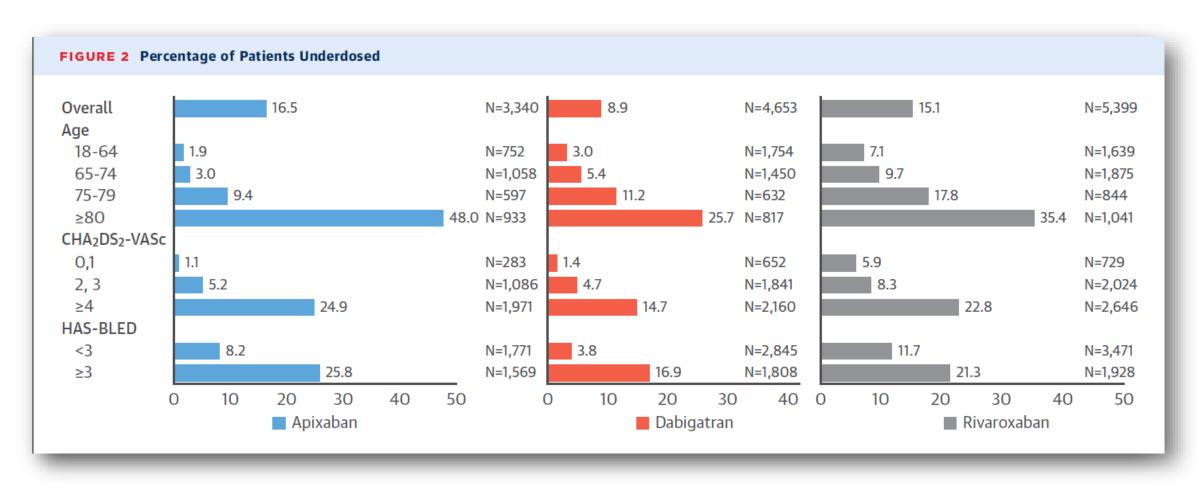


Non-Vitamin K Antagonist Oral Anticoagulant Dosing in Patients With Atrial Fibrillation and Renal Dysfunction





Non-Vitamin K Antagonist Oral Anticoagulant Dosing in Patients With Atrial Fibrillation and Renal Dysfunction



CENTRAL ILLUSTRATION Proposed Algorithm for Oral Anticoagulant Choices in Patients With Atrial Fibrillation and Chronic Kidney Disease



Patient with atrial fibrillation and chronic kidney disease

Determine stroke risk (CHA₂DS₂-VASc Score) Consider oral anticoagulation if score is ≥ 1 in males $/ \geq 2$ in females

Determine bleeding risk (HAS-BLED Score)

Estimate creatinine clearance (CrCl) to determine appropriate oral anticoagulant (OAC)						
OAC options:	CrCl < 15 ml/min or ESRD on RRT	CrCl 15-29 ml/min	CrCl 30-49 ml/min	CrCl ≥ 50 ml/min		
Vitamin K antagonist	When time in therapeutic range >70%					
Apixaban	5 mg, b.i.d.*	2.5 mg, b.i.d.	5 mg, b.i.d.†	5 mg, b.i.d.†		
Dabigatran	×	75 mg, b.i.d. [‡]	150 or 110 mg, b.i.d. [§]	150 mg, b.i.d.		
Edoxaban	×	30 mg, o.d.	30 mg, o.d.	60 mg, o.d. ¹		
Rivaroxaban	*	15 mg, o.d.	15 mg, o.d.	20 mg, o.d.		

Address bleeding risk factors, frequent follow up, and closely monitor renal function in NOAC users

Conclusiones

- Actualmente los NACOS son el tratamiento anticoagulante de elección en pacientes con fibrilación auricular no valvular.
- Todos los estudios en la práctica clínica habitual siguen demostrando que son tan o más eficaces que los anti-vitamina K e igual o más seguros.
- Entre ellos el perfil de eficacia parece similar.
- Todos reducen de forma significativa la hemorragia intracraneal, aunque Apixaban parece mostrar un mejor perfil de seguridad respecto a las hemorragias graves.
- Se debe utilizar siempre la dosis adecuada de cualquier NACO de acuerdo con la función renal del paciente para evitar los efectos de la infra o sobredosificación.