Kreiskrankenhaus
osterholz

Schlaganfall unter oraler Antikoagulation

Was tun?

Fallbeispiel

Rev Port Cardiol. 2019;38(2):117–124

Revista Portuguesa de Cardiologia
Portuguese Journal of Cardiology
www.revportcardiol.org

ORIGINAL ARTICLE

Ischemic stroke in patients previously anticoagulated for non-valvular atrial fibrillation: Why does it happen?☆

Luís Fernandes[a], João Sargento-Freitas[b], James Milner[c], Alexandra Silva[b], Ana Novo[b], Tatiana Gonçalves[d], Ana Vera Marinho[c], Guilherme Mariano Pego[c], Luís Cunha[b], Natália António[a,b,*]

[a] *Faculdade de Medicina da Universidade de Coimbra, Coimbra, Portugal*
[b] *Serviço de Neurologia do Centro Hospitalar e Universitário de Coimbra, Coimbra, Portugal*
[c] *Serviço de Cardiologia A do Centro Hospitalar e Universitário de Coimbra, Coimbra, Portugal*
[d] *Serviço de Medicina Interna A do Centro Hospitalar e Universitário de Coimbra, Coimbra, Portugal*

Received 6 January 2018; accepted 3 June 2018
Available online 26 March 2019

Uni-Klinik Coimbra (Portugal) 2016-2017: 60 Pat. mit Schlaganfall unter OAK

- 18 Pat. unter VKA , 42 Pat. unter NOAK
- Gute Adhärenz: 63.3%. Adhärente Pat. sign. häufiger Analphabeten (26.3% vs. 4.5%)
- Patienten unter VKA sign. adhärenter als unter NOAK (83.3% vs. 54.8%).
- 91.7% der Pat. unter VKA hatten bei Aufnahme INR <2
- Unterdosierung bei NOAK 43%

Cerebrovascular Diseases Extra

Original Paper

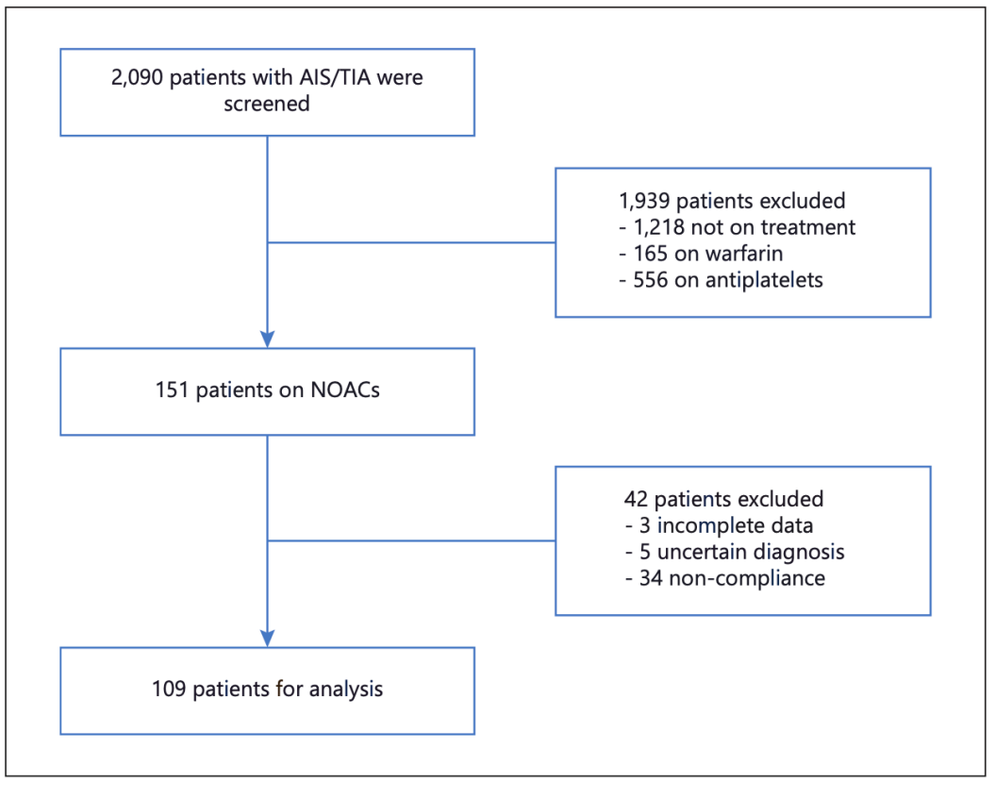
Cerebrovasc Dis Extra 2021;11:9–14
DOI: 10.1159/000513105

Received: August 28, 2020
Accepted: November 12, 2020
Published online: January 18, 2021

Residual Stroke Risk in Patients with Atrial Fibrillation Treated with Non-Vitamin K Oral Anticoagulants: An 8-Year Retrospective Cohort Study

Cheuk Ling Charing Szeto Kwok Fai Hui

United Christian Hospital, Hong Kong, China



Hong Kong 2012-2019

- 34 non-compliant: 5x zu langer Stopp peri-Op, 5x wg. Kosten, 5x wg. Vergesslichkeit, 3x wg. Intoleranz, 3x wg. Blutung, 13x „non-specified“
- 35/109 Bildgebung Hirnarterien: 19x sign. Stenose intra- oder extrakraniell
- 75/109 (68.8 %) reduzierte NOAK-Dosis, davon 49 (45 %) off-label
- 52.9 % lakunäre Läsionen (= eher nicht kardio-embolisch)

Ann Neurol May 2020

Ischemic Stroke despite Oral Anticoagulant Therapy in Patients with Atrial Fibrillation

David J. Seiffge, MD,[1,2,3] Gian Marco De Marchis, MD,[2] Masatoshi Koga, MD, PhD,[4] Maurizio Paciaroni, MD,[5] Duncan Wilson, PhD,[1] Manuel Cappellari, MD,[6] Kosmas Macha, MD,[7] Georgios Tsivgoulis, MD,[8,9] Gareth Ambler, PhD,[10] Shoji Arihiro, MD,[4] Leo H. Bonati, MD,[2] Bruno Bonetti, MD,[6] Bernd Kallmünzer, MD,[7] Keith W. Muir, MD, PhD,[11] Paolo Bovi, MD,[6] Henrik Gensicke, MD,[2,12] Manabu Inoue, MD,[4] Stefan Schwab, MD,[7] Shadi Yaghi, MD,[13] Martin M. Brown, MD, PhD, FRCP,[1] Philippe Lyrer, MD,[2] Masahito Takagi, MD, PhD,[4] Monica Acciarrese, MD,[5] Hans Rolf Jager, MD, FRCP,[14] Alexandros A. Polymeris, MD,[2] Kazunori Toyoda, MD, PhD,[4] Michele Venti, MD,[5] Christopher Traenka, MD,[2] Hiroshi Yamagami, MD, PhD,[4] Andrea Alberti, MD,[5] Sohei Yoshimura, MD, PhD,[4] Valeria Caso, MD,[5] Stefan T. Engelter, MD,[2,12] and David J. Werring, MD, PhD, FRCP,[1] on behalf of the RAF, RAF-DOAC, CROMIS-2, SAMURAI, NOACISP, Erlangen, and Verona registry collaborators

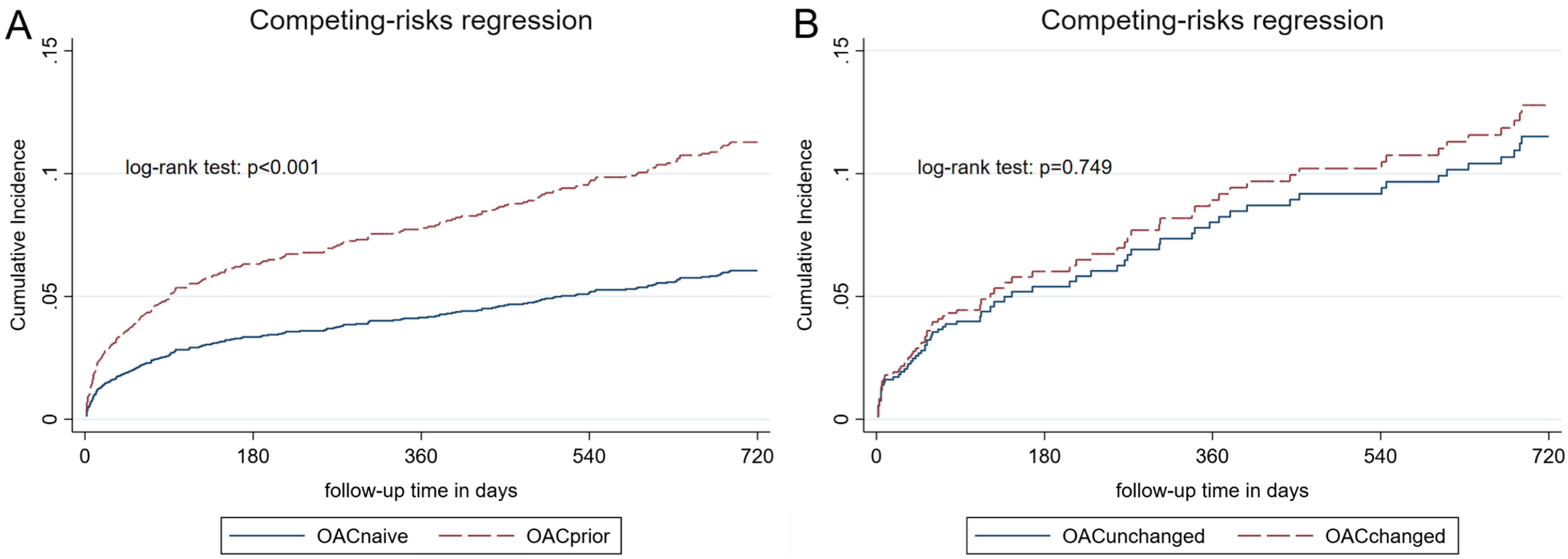


FIGURE 2: Cumulative incidence function curves for the main outcome of recurrent acute ischemic stroke. (A) Primary analysis of patients taking oral anticoagulation prior to the index event (OAC_{prior}, dashed line) compared to those not taking anticoagulants prior to the index event (OAC_{naive}, solid line). (B) Secondary analysis of patients that changed the type of anticoagulation ($OAC_{changed}$, dashed line) compared to those who continued the same type of anticoagulation ($OAC_{unchanged}$, solid line). [Color figure can be viewed at www.annalsofneurology.org]

Ann Neurol May 2020

TABLE 1. Baseline Characteristics of Patients with and without Oral Anticoagulation Therapy prior to Index Event and Patients Who Did and Did Not Change the Type of Anticoagulation

	Primary Analysis			Secondary Analysis		
	OAC_{prior}, n = 1,195	OAC_{naive}, n = 4,119	*p*	$OAC_{changed}$, n = 307	$OAC_{unchanged}$, n = 585	*p*
Age[a]	79 (73–84)	77 (70–84)	<0.001	79 (74–84)	79 (72–83)	0.046
Female (%)	555/1,195 (46.4)	2,004/4,119 (48.7)	0.178	155/307 (50.6)	249/585 (42.6)	0.023
Prior treatment with VKA (%)	865/1,195 (72.4)	0	N/A	291/306 (95.1)	519/584 (88.8)	0.002
Ischemic stroke as index event (%)	1,144/1,195 (95.7)	3,992/4,119 (96.9)	0.045	229/307 (74.6)	519/585 (88.7)	0.002
History of ischemic stroke (other than index event) (%)	458/1,192 (38.4)	788/4,111 (19.2)	<0.001	119/306 (38.9)	222/583 (38.1)	0.828
History of ICH (%)	17/780 (2.2)	34/2,769 (1.2)	0.060	5/275 (1.8)	9/414 (2.2)	1.000
Hypertension (%)	1,026/1,195 (85.9)	2,958/4,089 (72.3)	<0.001	259/306 (84.6)	499/584 (85.4)	0.766
Hypercholesterinemia (%)	438/1,026 (42.7)	1,262/3,387 (37.3)	0.002	145/306 (47.4)	240/584 (41.1)	0.075
Smoking (%)	188/1,150 (16.3)	694/4,021 (17.3)	0.505	33/286 (11.5)	80/568 (14.1)	0.336
Diabetes mellitus (%)	442/1,194 (37.0)	890/4,109 (21.7)	<0.001	109/305 (35.7)	226/584 (38.7)	0.423
Normal renal function, CrCl > 50ml/min (%)	638/894 (71.4)	2,638/3,321 (79.4)	<0.001	207/273 (75.8)	105/305 (74.4)	0.719
Modest kidney failure, CrCl = 30–50ml/min (%)	185/894 (20.7)	554/3,321 (16.7)		66/273 (24.2)	105/410 (25.6)	
Severe kidney failure, CrCl < 30ml/min (%)	71/894 (7.9)	129/3,321 (3.9)		0	0	
Intravenous thrombolysis (%)	156/1,193 (13.1)	929/4,095 (22.7)	<0.001	51/304 (16.8)	60/584 (10.3)	0.007
Intraarterial treatment (%)	48/1,057(4.5)	141/3,897 (3.6)	0.174	15/278 (5.4)	18/483 (3.7)	0.274
NIHSS on admission[a]	5 (2–11)	6 (2–12)	<0.001	4 (2–10)	5 (2–11	0.222
CHA_2DS_2-Vasc[a]	5 (4–6)	5 (4–6)	0.103	6 (4–6)	5 (4–6)	0.014
HAS-BLED[a]	3 (3–4)	3 (3–4)	0.626	3 (2–4)	3 (3–4)	0.097

year of ischemic stroke.[28] Nevertheless, the actual observed rate of recurrent ischemic strokes was twice as high in patients who had their index stroke despite taking anticoagulants (annualized rate = 8.9%, 95% CI = 7.3–10.8%) compared to those who were not on anticoagulation therapy at the time of index stroke (annualized rate = 3.9%, 95% CI = 3.3–4.4%). This raises the key questions of why patients with OAC_{prior} are at increased risk and what the optimal prevention strategy might be to reduce this risk.

Our data show that despite similar median CHA_2DS_2-VASc scores, several cerebrovascular risk factors (hypertension, diabetes, hypercholesterinemia, kidney failure) were more frequent in patients with prior anticoagulation. Furthermore, 38% of patients on prior

coagulation therapy.[2] Further research needs to focus on mechanisms, competing risk factors, and etiology of (recurrent) stroke in patients taking anticoagulants. This could include taking into account competing causes as in the ASCO[34] or ASCOD[35] (A = atherosclerosis, S = small-vessel disease, C = cardiac pathology, O = other causes, D = dissection) causality score systems.

Open Access Full Text Article

ORIGINAL RESEARCH

Real-world effectiveness and safety of oral anticoagulation strategies in atrial fibrillation: a cohort study based on a German claims dataset

This article was published in the following Dove Press journal:
Pragmatic and Observational Research

Sabrina Mueller[1]
Antje Groth[1]
Stefan G Spitzer[2,3]
Anja Schramm[4]
Andreas Pfaff[5]
Ulf Maywald[6]

[1]Institute for Pharmacoeconomics and Medication Logistics, University of Wismar, Wismar, Germany; [2]Praxisklinik Herz und Gefäße Dresden, Academic Educational Practice Clinic, TU Dresden, Dresden, Germany; [3]Institute of Medical Technology, Brandenburg University of Technology Cottbus–Senftenberg, Senftenberg, Germany; [4]AOK Bayern, Regensburg, Germany; [5]AOK Baden-Württemberg, Stuttgart, Germany; [6]AOK PLUS, Dresden, Germany

Objective: To compare the real-world effectiveness and safety of non-vitamin-K-antagonist oral anticoagulant (NOAC) treatment in atrial fibrillation (AF) patients with a vitamin-K-antagonist (VKA)-based treatment.

Methods: This was a retrospective analysis of an anonymized claims dataset from 3 German health insurance funds covering the period from January 01, 2010 to June 30, 2014, with a minimum observation time of 12 months. All continuously insured patients with at least 2 outpatient AF diagnoses and/or 1 inpatient respective diagnosis who received at least 1 outpatient prescription of a NOAC or VKA were included.

Outcomes and measures: Death, ischemic strokes (IS), non-specified strokes, transient ischemic attacks (TIAs), myocardial infarctions (MIs), arterial embolism (AE), hemorrhagic strokes, severe bleedings, and composite outcomes. Main comparisons were done based on propensity score-matched (PSM) cohorts. Results were reported as incidence rate ratios and hazard ratios (HRs).

Results: We assigned 37,439 AF patients to each PSM cohort (NOAC cohort: mean age 78.2 years, mean CHA_2DS_2VASc score 2.96, mean follow-up 348.5 days; VKA cohort: mean age 78.2 years, mean CHA_2DS_2VASc 2.95, mean follow-up 365.5 days). NOAC exposure was associated with significantly higher incidence rate ratios; 95% CI/HRs; 95% CI for the following outcomes: death (1.22; 1.17–1.28/1.22; 1.17–1.28), IS (1.90; 1.69–2.15/1.92; 1.69–2.19), non-specified strokes (2.04; 1.16–3.70/1.93; 1.13–3.32), TIAs (1.52; 1.29–1.79/1.44; 1.21–1.70), MIs (1.26; 1.10–1.15/1.31; 1.13–1.52), AE (1.75; 1.32–2.32/1.81; 1.36–2.34) and severe bleeding (1.92; 1.71–2.15/1.95; 1.74–2.20). Multivariable Cox regression analyses and additional sensitivity analysis, including analysis of PSM-matched NOAC/VKA treatment-naive patients, only confirmed the above results. The study was documented under clinicaltrials.gov (NCT02657616).

Conclusion and relevance: A VKA therapy seems to be more effective and safer than a NOAC therapy in a real-world cohort of German AF patients.

74.878 (von 483.149) Pat. 2010-2014

(AOK PLUS, AOK Bayern, AOK Baden-Württemberg)

Study outcomes

All observed patients were followed with regard to the following events:

a. all-cause death;

and acute hospitalizations with the following events as main hospital admission diagnosis (ICD-10 codes):

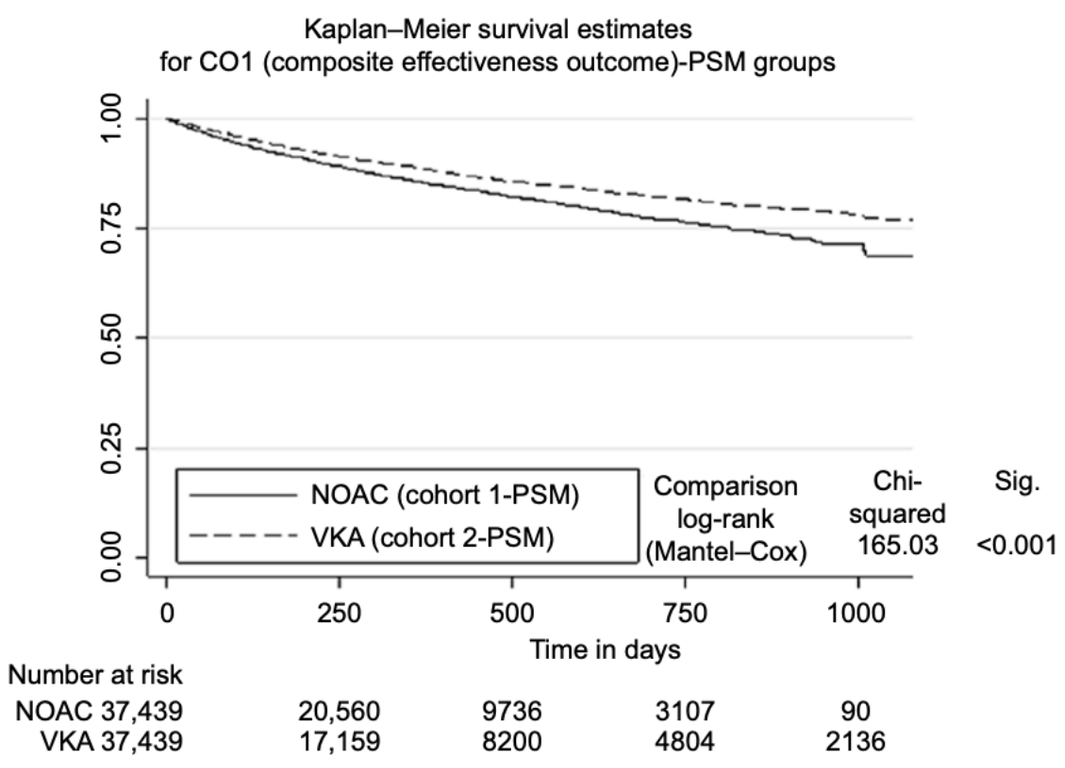
b. ischemic stroke (IS; I63.x)
c. non-specified stroke (I64.x)
d. transient ischemic attack (TIA; G45.x)
e. myocardial infarction (MI; I21.x/I22.x)
f. arterial embolism (AE; H34.x/I26.x/K55.0)
g. hemorrhagic stroke (I60.x/I61.x/I62.x)
h. severe bleeding (ICD-10 codes: K92.2, K62.5, K55.22, R04.x, K25.0, K25.2, K25.4, K25.6, K26.0, K26.2, K26.4, K26.6, K27.0, K27.2, K27.4, K27.6, K28.0, K28.2, K28.4 or K28.6).

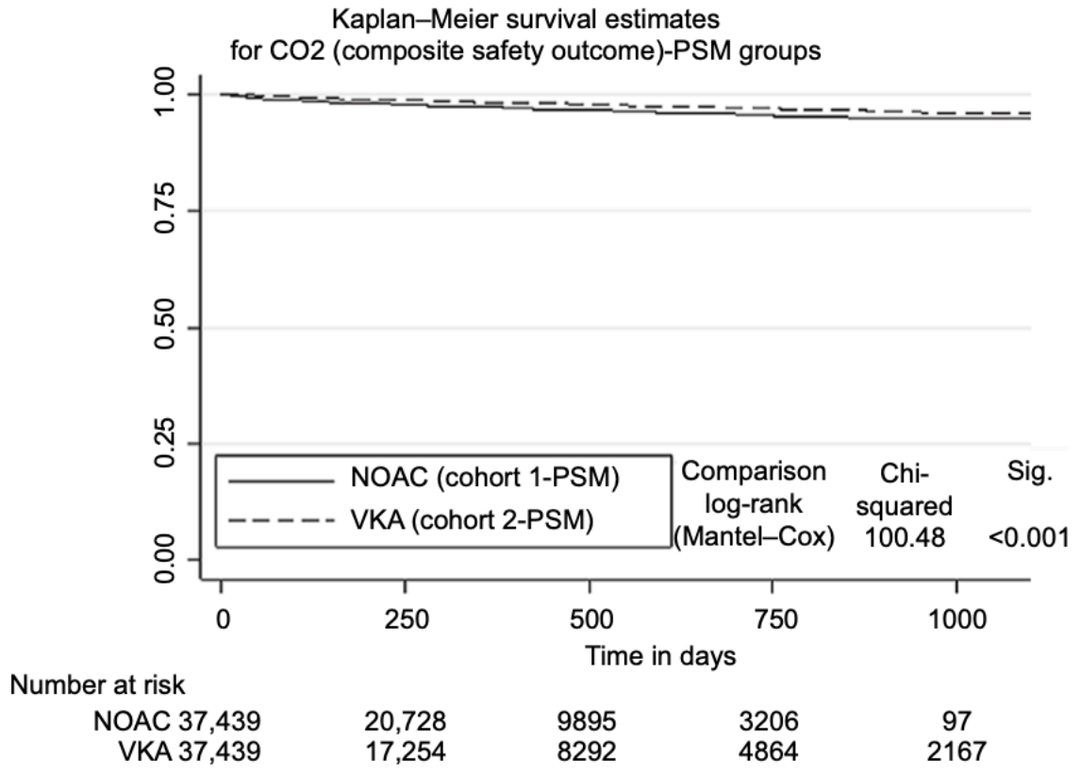
CO1

CO2

CO3

Above outcomes were aggregated to 3 composite outcomes (CO): effectiveness CO1 covering outcomes a–f; safety CO2 covering outcomes g and h; and a general CO3 covering all outcomes a–h.





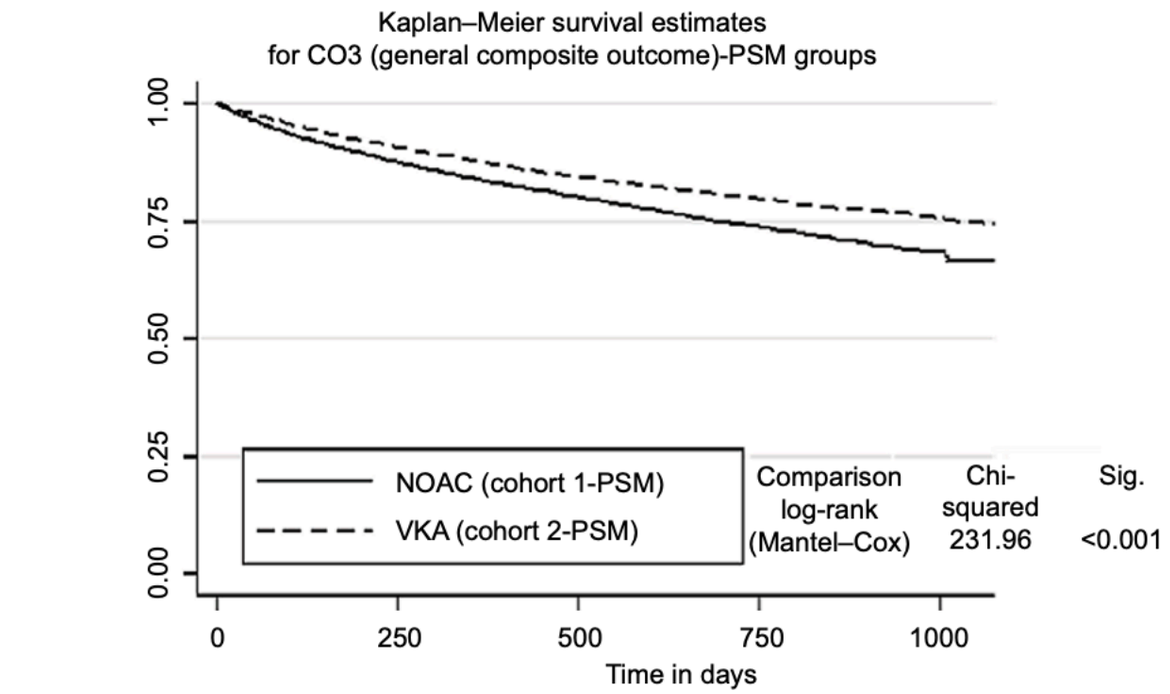


Figure 2 Kaplan–Meier curves (time to event: CO1, CO2, CO3) for PSM-matched Cohorts 1 and 2.
Abbreviations: CO1: effectiveness composite outcome 1; CO2: safety composite outcome 2; CO3: general composite outcome 3; NOAC, non-vitamin K antagonist oral anticoagulants; PSM, propensity score matching; VKA, vitamin-K-antagonist.

Paschke *et al. BMC Medicine* (2020) 18:254
https://doi.org/10.1186/s12916-020-01695-7

BMC Medicine

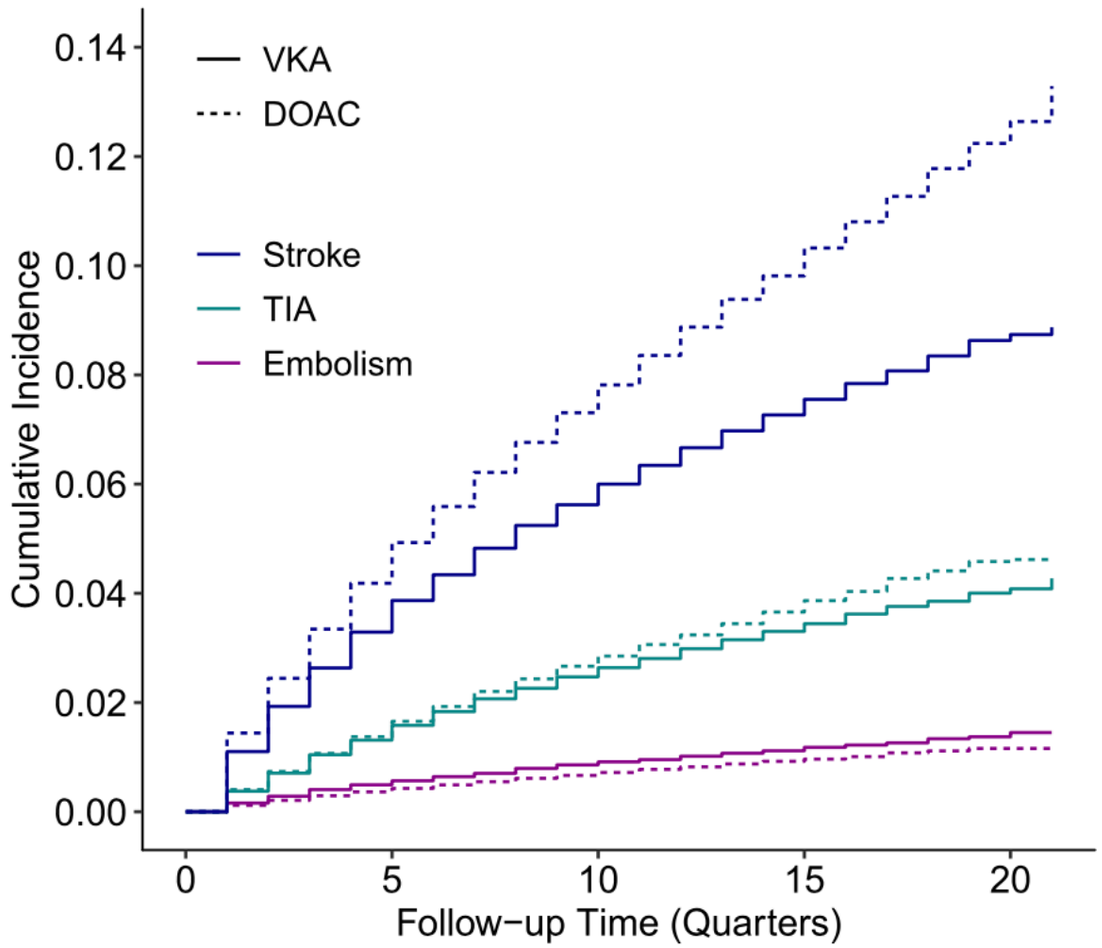
RESEARCH ARTICLE Open Access

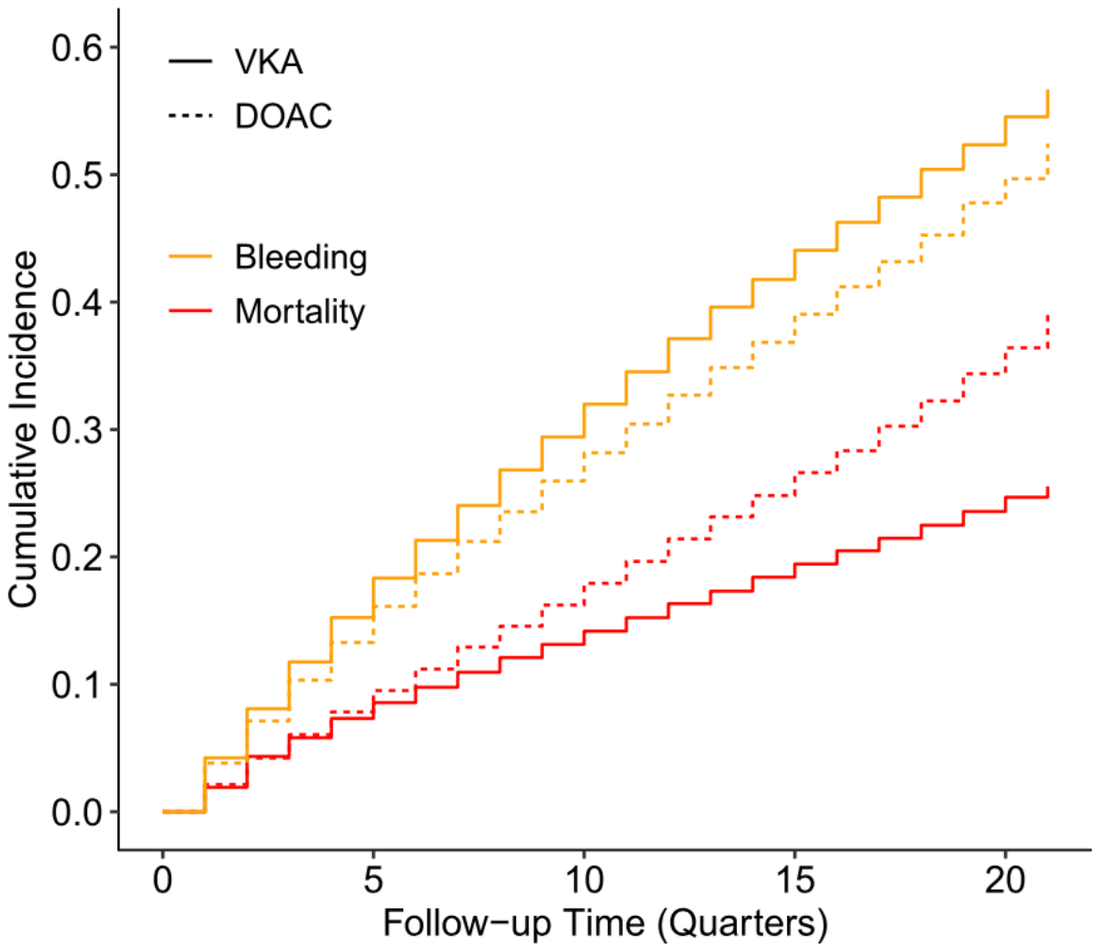
Comparing stroke prevention therapy of direct oral anticoagulants and vitamin K antagonists in patients with atrial fibrillation: a nationwide retrospective observational study

Lena M. Paschke[1*], Kerstin Klimke[1], Attila Altiner[2], Dominik von Stillfried[1] and Maike Schulz[1]

837.430 Pat. (1.27 Mio Pat.-Jahre) 2010-2017

(Zentralinstitut f. d. Kassenärztliche Versorgung)





Stroke	VKA	347240	135927	58981	24143	3628
	DOAC	347240	202742	89971	29007	2491
TIA	VKA	347247	137947	60331	24741	3772
	DOAC	347247	209005	94731	31073	2762
Embolism	VKA	347297	139148	61340	25244	3866
	DOAC	347297	211066	96596	31961	2874

Bleeding		346343	120890	46703	17188	2366
		346343	185028	74705	22103	1740
Mortality		347351	140385	61896	25634	3930
		347351	212466	97572	32322	2899

Fig. 2 Cumulative incidence. VKA, vitamin K antagonist; DOAC, direct oral anticoagulant; TIA, transient ischemic attack; table indicates number of patients at risk. For number of censored patients, see Table S19 and S20

Table 2 Number of patient populations

		Number of patients before matching					
		VKA	**DOAC**	**Dabigatran**	**Rivaroxaban**	**Apixaban**	**Edoxaban**
Study population	Stroke	405,437	430,940	53,057	228,609	131,751	14,276
	Embolism	404,823	431,816	52,796	228,522	132,872	14,556
	TIA	405,012	431,574	52,839	228,593	132,547	14,442
	Bleeding	408,402	427,477	53,233	229,934	127,613	13,266
	Mortality	404,695	431,978	52,763	228,499	133,059	14,586
		Number of patients after matching					
		VKA	**DOAC**	**Dabigatran***	**Rivaroxaban***	**Apixaban***	**Edoxaban***
Study population	Stroke	347,240	347,240	53,057	228,600	131,748	14,276
	Embolism	347,297	347,297	52,796	228,513	132,869	14,556
	TIA	347,247	347,247	52,839	228,584	132,544	14,442
	Bleeding	346,343	346,343	53,233	229,926	127,610	13,266
	Mortality	347,351	347,351	52,763	228,490	133,056	14,586

VKA vitamin K antagonist, *DOAC* direct oral anticoagulant, *TIA* transient ischemic attack
*Number of VKA patients equals number of DOAC patients

Table 3 Results of joint DOAC vs. VKA

Events	Incidence rate per 1000 PY		Adjusted HR (95% CI)	*p* value
	VKA	DOAC		
Stroke	26.69	33.45	1.32 (1.29–1.35)	< .001
TIA	11.16	11.71	1.10 (1.06–1.14)	< .001
Embolism (systemic)	4.01	2.99	0.78 (0.73–0.83)	< .001
Bleeding	136.57	117.7	0.89 (0.88–0.90)	< .001
Mortality (all cause)	61.36	73.5	–	–

VKA vitamin K antagonist, *DOAC* direct oral anticoagulant, *TIA* transient ischemic attack, *PY* person years, *HR* hazard ratio, *CI* confidence interval

Table 4 Results of separate DOAC vs. VKA

Events	Incidence rate per 1000 PY		Adjusted HR (95% CI)	*p* value
	VKA	Dabigatran		
Stroke	26.77	45.94	1.93 (1.82–2.03)	< .001
TIA	11.64	14.13	1.33 (1.22–1.45)	< .001
Embolism (systemic)	3.69	3.07	0.93 (0.79–1.10)	.42
Bleeding	134.82	107.77	0.85 (0.83–0.88)	< .001
Mortality (all cause)	52.34	63.49	–	–
	VKA	Rivaroxaban		
Stroke	25.88	27.77	1.13 (1.10–1.17)	< .001
TIA	10.69	10.83	1.06 (1.01–1.11)	.02
Embolism (systemic)	3.79	2.99	0.83 (0.77–0.90)	< .001
Bleeding	135.19	133.23	1.03 (1.01–1.04)	< .001
Mortality (all cause)	57.79	75.02	–	–
	VKA	Apixaban		
Stroke	27.58	38.81	1.52 (1.46–1.58)	< .001
TIA	11.58	12.33	1.15 (1.08–1.22)	< .001
Embolism (systemic)	3.77	2.75	0.75 (0.67–0.85)	< .001
Bleeding	137.8	93.36	0.71 (0.70–0.73)	< .001
Mortality (all cause)	64.26	74.45	–	–
	VKA	Edoxaban		
Stroke	26.24	15.53	0.88 (0.74–1.05)	.16
TIA	11.18	5.18	0.71 (0.53–0.95)	.02
Embolism (systemic)	3.94	1.31	0.29 (0.17–0.51)	< .001
Bleeding	133.92	69.82	0.74 (0.68–0.81)	< .001
Mortality (all cause)	53.58	30.62	–	–

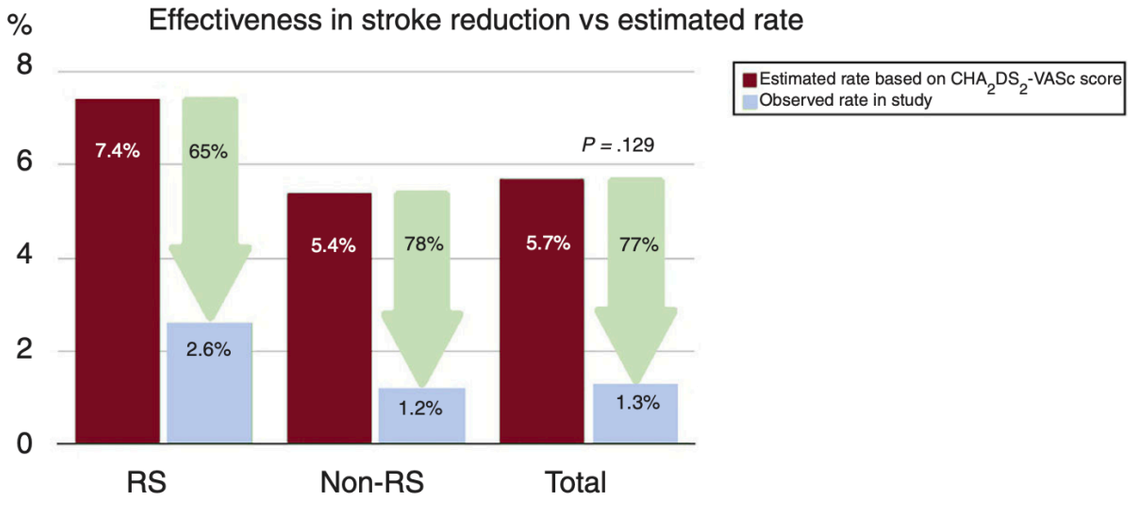
VKA vitamin K antagonist, *DOAC* direct oral anticoagulant, *TIA* transient ischemic attack, *PY* person years, *HR* hazard ratio, *CI* confidence interval

Rev Esp Cardiol. 2020;73(1):28–34

Original article

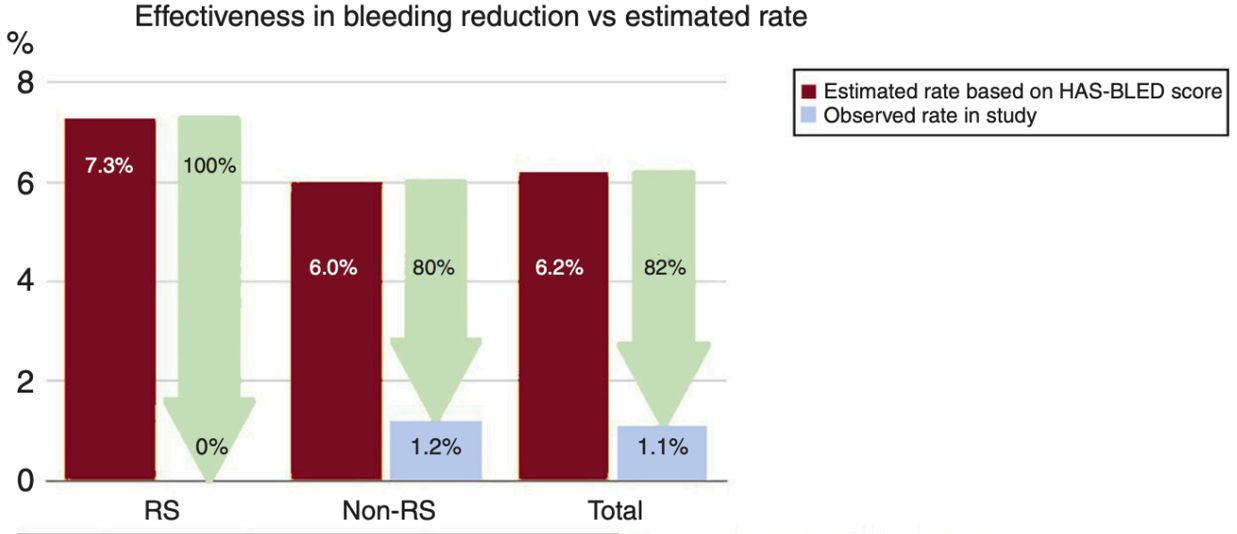
Left atrial appendage occlusion for stroke despite oral anticoagulation (resistant stroke). Results from the Amplatzer Cardiac Plug registry

Ignacio Cruz-González,[a,*] Rocío González-Ferreiro,[a] Xavier Freixa,[b] Sameer Gafoor,[c] Samera Shakir,[d] Heyder Omran,[e] Sergio Berti,[f] Gennaro Santoro,[g] Joelle Kefer,[h] Ulf Landmesser,[i] Jens Erik Nielsen-Kudsk,[j] Prapa Kanagaratnam,[k] Fabian Nietlispach,[d,i] Steffen Gloekler,[d] Adel Aminian,[l] Paolo Danna,[m] Marco Rezzaghi,[f] Friederike Stock,[e] Miroslava Stolcova,[g] Luis Paiva,[n] Marco Costa,[n] Xavier Millán,[o] Reda Ibrahim,[p] Tobias Tichelbäcker,[q] Wolfgang Schillinger,[q] Jai-Wun Park,[r] Horst Sievert,[c] Bernhard Meier,[d] and Apostolos Tzikas[s]



	Patients	Total patients-year	CHA2DS2-VASc score
RS	111	149	5.5%
Non-RS	890	1200	4.3%
Total	1001	1349	4.5%

	Estimated annual stroke rate per CHA2DS2-VASc	Observed annual stroke rate
RS	7.4%	2.6% (4)
Non-RS	5.4%	1.2% (14)
Total	5.7%	1.3% (18)



	Patients	Total patients-year	HAS-BLED score
RS	111	149	3.9%
Non-RS	890	1200	3.1%
Total	1001	1349	3.1%

	Estimated annual bleeding rate per HAS-BLED	Observed annual stroke rate
RS	7.3%	0% (0)
Non-RS	6.0%	1.2% (15)
Total	6.2%	1.1% (15)

- Vormedikation (OAK) penibel recherchieren
  - ggf. Plausibilität mit HA/HÄ abgleichen
- Art des Schlaganfalls
  - lakunär: +Clopidogrel od. ASS?
  - embolisch: LAA-Okkluder?
- DOAK: Dosisreduktionskriterien vergleichen
  - Wechsel zu VKA?
- VKA: Höherer INR-Zielwert?
  - INR-Selbstkontrolle?
  - Wechsel zu DOAK?
    - z.B. Op-Pausen, TTR<70%