L'aderenza al trattamento anticoagulante nel paziente con FA

Daniela Poli

Bologna 21-22 Gennaio 2016

Persistence

The length of time between initiation and discontinuation of a treatment.

Compliance

The extent to which medical recommendations are followed as defined, with patient's passive obedience to the physician's instructions.

'A complex behavioural process, strongly influenced by the environment in which the patients live, how healthcare providers practice, and how healthcare systems deliver care' American Heart Association, 1997

Adherence

Implies cooperation between patient and prescriber.

Review Article

Ensuring medication adherence with direct oral anticoagulant drugs Lessons from adherence with vitamin K antagonists (VKAs)

Alessandro Di Minno [a], Gaia Spadarella [b], Antonella Tufano [b], Domenico Prisco [c], Giovanni Di Minno [b,*]

Table 1
Factors that influence medication adherence in patient with chronic disorders [§].

Factors related to the	Factor Category
Patient	*Demographics* (age [young/old], educational level, socioeconomic status, information level about disease/ treatment, disability, race, ethnicity); *Patient-related medical conditions* (co-morbidities, poor baseline health, disability, low cognitive function, dementia, side effects of drugs, priorities, interventional fragility); *Attitudinal and behavioral factors* (substance abuse, social isolation, discomfort, depression, pessimism about future, lack of receptivity to details regarding illness).
Physician	Adherence to applying guideline recommendations; Indications for treatment (primary/secondary prevention); Mis-information about medication dosing; Office visits; interactions with patients (always meeting the same doctor).
Health system	Disability, race, ethnicity, cost of care, access to care, co-payment (low/high income status).

Thromb Res 2014

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Table 2
Rates of AF patients who permanently discontinued treatment during phase III trials with DOACs.[§]

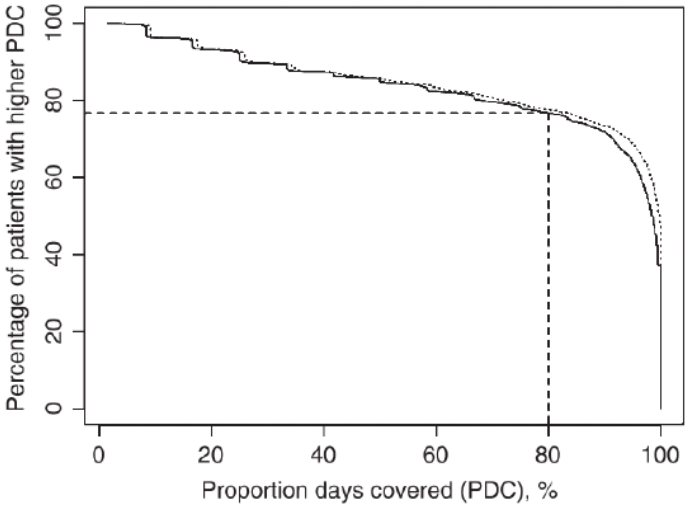
Study	Treatment Arm	% of patients who permanently discontinued the assigned treatment	RR (DOACs vs warfarin)	Study duration (years, median)	Study design
RE-LY *	Dabigatran 110 mg	20.7	1.247	2.0	PROBE: Prospective, randomized, open-label, blinded end-point evaluation
	Dabigatran 150 mg	21.2	1.277		
	Warfarin	16.6			
ROCKET AF **	Rivaroxaban	23.7	1.068	1.9	Double-blind, double-dummy, sham-INR
	Warfarin	22.2			
ARISTOTLE ***	Apixaban	25.3	0.923	1.8	Double-blind, double-dummy, sham-INR
	Warfarin	27.5			

Thromb Res 2014

ORIGINAL ARTICLE

Dabigatran adherence in atrial fibrillation patients during the first year after diagnosis: a nationwide cohort study

A. GORST-RASMUSSEN,*† F. SKJØTH,*† T. B. LARSEN,*† L. H. RASMUSSEN,† G. Y. H. LIP†‡ and D. A. LANE†‡



JTH, 2015

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	PDC, percent (PDC_{grace}*)	PDC ratio (95% CI)
Sex		
Male	81.6 (82.8)	1.00 (reference)
Female	86.5 (87.5)	1.06 (1.03-1.08)
Age (years)		
≤54	64.1 (65.3)	0.82 (0.75-0.89)
55-64	78.3 (79.4)	1.00 (reference)
65-74	86.9 (88.0)	1.11 (1.07-1.15)
≥75	86.6 (87.7)	1.11 (1.06-1.15)
Original dose		
110 mg	86.2 (87.3)	1.00 (reference)
150 mg	82.4 (83.4)	0.96 (0.93-0.98)
CHA_2DS_2-VASc score		
0	58.1 (59.4)	0.75 (0.68-0.82)
1	77.7 (78.9)	1.00 (reference)
≥2	87.2 (88.3)	1.12 (1.08-1.17)
History of bleeding		
No	83.7 (84.8)	1.00 (reference)
Yes	85.3 (86.3)	1.02 (0.98-1.06)
History of stroke/SE/TIA		
No	82.5 (83.6)	1.00 (reference)
Yes	89.9 (90.9)	1.09 (1.06-1.12)
Cardiovascular prescriptions†, past year		
≤3	77.4 (78.6)	1.00 (reference)
>3	86.8 (87.8)	1.12 (1.09-1.15)
Hospitalization, past year		
No	82.1 (83.3)	1.00 (reference)
Yes	84.3 (85.3)	1.03 (0.99-1.06)

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-More than 75% of patients adhered to dabigatran >80% of the time

-Patients at high risk (CHA2DS2-VASc score≥2) were significantly more adherent than low risk patients

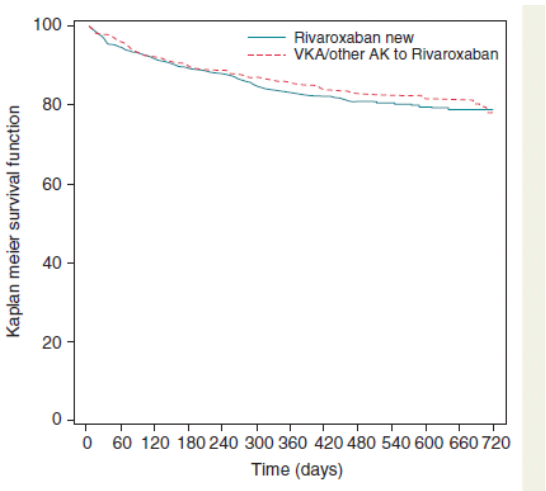
-Patients with prior bleeding were less adherent

-Regular contact with the healthcare system and patients understanding may improve adherence.

JTH, 2015

Drug persistence with rivaroxaban therapy in atrial fibrillation patients—results from the Dresden non-interventional oral anticoagulation registry

Jan Beyer-Westendorf[1]*, Kati Förster[1], Franziska Ebertz[1], Vera Gelbricht[1], Thomas Schreier[1], Maria Göbelt[1], Franziska Michalski[1], Heike Endig[1], Kurtulus Sahin[2], Luise Tittl[1], and Norbert Weiss[1]



EUROPACE, 2015

Discontinuation rate 15% in the first year

Drug persistence with rivaroxaban therapy in atrial fibrillation patients—results from the Dresden non-interventional oral anticoagulation registry

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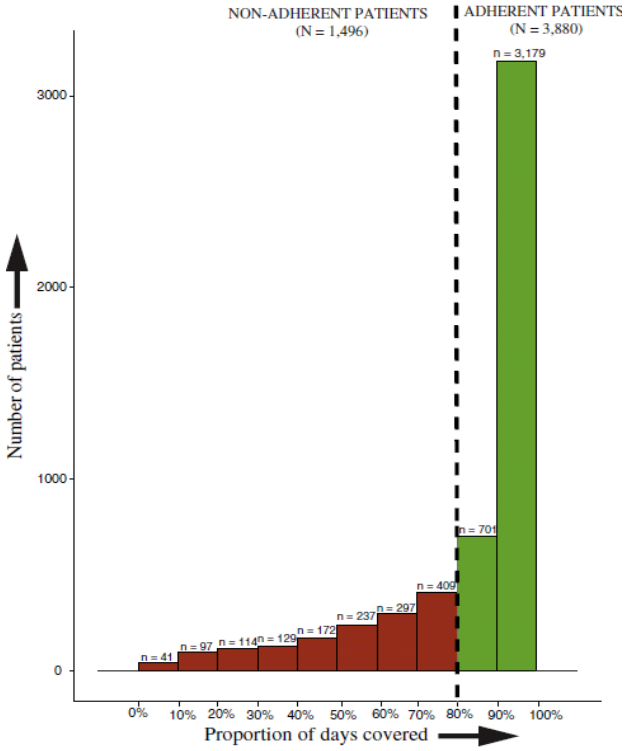
Table 4 Cox proportional hazard model of potential risk factors for rivaroxaban discontinuation

Baseline variable	HR (95% CI)	No discontinuation vs. discontinuation (%)	*P*-value
VKA pretreatment (yes vs. no)	0.85 (0.65–1.12)	No: 18.9% Yes: 18.0%	0.25
BMI (normal vs. underweight)	0.74 (0.55–0.99)	Normal: 21.8% Underweight: 20.0%	0.04
Heart failure (yes vs. no)	1.41 (1.08–1.85)	No: 16.1% Yes: 22.5%	0.01
Arterial hypertension (yes vs. no)	0.73 (0.52–1.01)	No: 22.4% Yes: 17.7%	0.06
Diabetes (yes vs. no)	1.35 (1.03–1.77)	No: 16.4% Yes: 21.7%	0.03
Prior TIA, stroke or systemic embolism (yes vs. no)	1.34 (0.95–1.87)	No: 17.7% Yes: 23.3%	0.09
Renal dysfunction (yes vs. no)	1.32 (0.92–1.90)	No: 17.7% Yes: 24.5%	0.13

BMI, body mass index; CI, confidence interval; TIA, transient ischaemic attack; VKA, vitamin K antagonist

EUROPACE, 2015

Adherence to dabigatran therapy and longitudinal patient outcomes: Insights from the Veterans Health Administration



28% of patients poor adherent

Shore S et al. Am Heart J, 2014

Adherence to dabigatran therapy and longitudinal patient outcomes: Insights from the Veterans Health Administration

Conclusions

…The advantages of dabigatran relative to warfarin in terms of laboratory monitoring and reduced interactions must be weighed against the implications of non-adherence on patient outcomes.

Shore S et al. Am Heart J, 2014

Cognitive Impairment Is Not a Predictor of Failure to Adhere to Anticoagulation of Stroke Patients with Atrial Fibrillation

Solveig Horstmann[a] Timolaos Rizos[a] Michaela Saribas[a] Evdokia Efthymiou[a]
Geraldine Rauch[b] Roland Veltkamp[a, c]

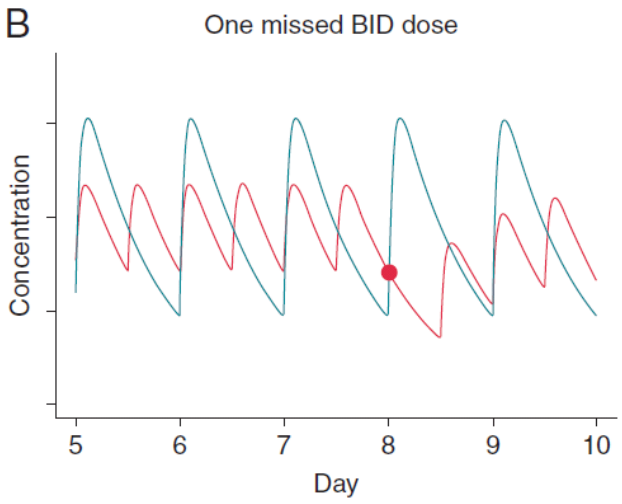
Conclusions

In stroke and TIA patients with AF, the multifactorial medical and functional constellation rather than cognitive impairment specifically can be an obstacle for long-term OAC.

Cerebrovascular Disease , 2015

Non-vitamin K antagonist oral anticoagulants: considerations on once- vs. twice-daily regimens and their potential impact on medication adherence

Bernard Vrijens[1,2] and Hein Heidbuchel[3]*



EUROPACE, 2014

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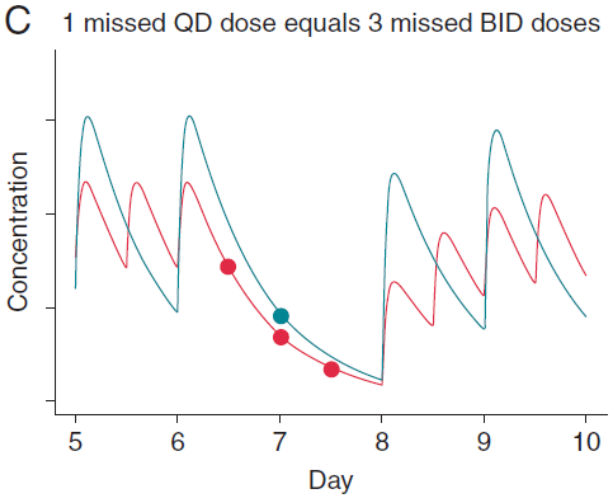


EUROPACE, 2014

Updated European Heart Rhythm Association Practical Guide on the use of non-vitamin K antagonist anticoagulants in patients with non-valvular atrial fibrillation

Table 3 Checklist during follow-up contacts of AF patients on anticoagulation[a]

	Interval	Comments
1. Adherence	Each visit	Instruct patient to bring NOAC card and remaining medication: make note and assess average adherence Re-educate on importance of strict intake schedule Inform about adherence aids (special boxes, smartphone applications, etc.)
2. Thromboembolism	Each visit	Systemic circulation (TIA, stroke, and peripheral) Pulmonary circulation
3. Bleeding	Each visit	'Nuisance' bleeding: preventive measures possible? (PPI, haemorrhoidectomy, etc.). Motivate patient to diligently continue anticoagulation Bleeding with impact on quality of life or with risk: prevention possible? Need for revision of anticoagulation indication or dose?
4. Other side effects	Each visit	Carefully assess relation with NOAC: decide for continuation (and motivate), temporary cessation (with bridging), or change of anticoagulant drug
5. Co-medications	Each visit	Prescription drugs; over-the-counter drugs, especially aspirin and NSAID (see 'Drug–drug interactions and pharmacokinetics of non-vitamin K antagonist anticoagulants' section) Careful interval history: also temporary use can be risky!
6. Blood sampling	Yearly 6-monthly x-monthly On indication	Haemoglobin, renal and liver function ≥75–80 years (especially if on dabigatran or edoxaban), or frail[b] If renal function ≤60 mL/min: recheck interval = CrCl/10 If intercurrent condition that may impact renal or hepatic function

Hedbuchel H et al. Europace, 2015

Updated European Heart Rhythm Association Practical Guide on the use of non-vitamin K antagonist anticoagulants in patients with non-valvular atrial fibrillation

5. Ensuring adherence to prescribed oral anticoagulant intake

Hedbuchel H et al. Europace, 2015

1. **Patient education** on the relevance of strict adherence is of utmost importance. Many simultaneous approaches should be employed in this regard: leaflets and instructions at initiation of therapy; a patient anticoagulation card; group sessions; re-education at every prescription renewal. Several organizations also offer online patient support websites, including EHRA (http://www.afibmatters.org/), the AF Association in the UK (http://www.atrialfibrillation.org.uk/), Anticoagulation Europe (http://www.anticoagulationeurope.org/)
2. **Family members** should be involved in this education, so that they can understand the importance of adherence, and help the patient in this regard. professionals providing care. Each of those actors has responsibility to reinforce adherence.

Nurse-coordinated AF centres may be helpful in coordinating patient follow-up and checking on adherence.

Updated European Heart Rhythm Association Practical Guide on the use of non-vitamin K antagonist anticoagulants in patients with non-valvular atrial fibrillation

Hedbuchel H et al. Europace, 2015

5. Ensuring adherence to prescribed oral anticoagulant intake

3. **Many technological aids** are being explored to enhance adherence: the format of the blisters; medication boxes (conventional or with electronic verification of intake); smartphone applications with reminders and/or SMS messages to alert the patient about the next intake some even requiring confirmation that the dose has been taken. Again, the longterm effects of such tools are unknown and one tool may not suit all patients. The prescribing physician, however, should consider individualization of these aids.
4. **An OD dosing regimen was related to greater adherence vs. BID** regimens in cardiovascular patients, and in AF patients (for diabetes and hypertension drugs).

Updated European Heart Rhythm Association Practical Guide on the use of non-vitamin K antagonist anticoagulants in patients with non-valvular atrial fibrillation

Hedbuchel H et al. Europace, 2015

5. Ensuring adherence to prescribed oral anticoagulant intake

5. Some patients may explicitly **prefer INR monitoring** to no monitoring or NOAC over VKA therapy. Patient education needs to discuss these preferences before starting/converting to NOAC therapy and management decisions have to take these preferences into account to optimize health outcomes.

6. In NOAC patients in whom **low adherence** is suspected despite proper education and additional tools, **conversion to VKAs** (preferably with long half-life like phenprocoumon) could be considered.

AEGEAN objectives

Primary Objective:

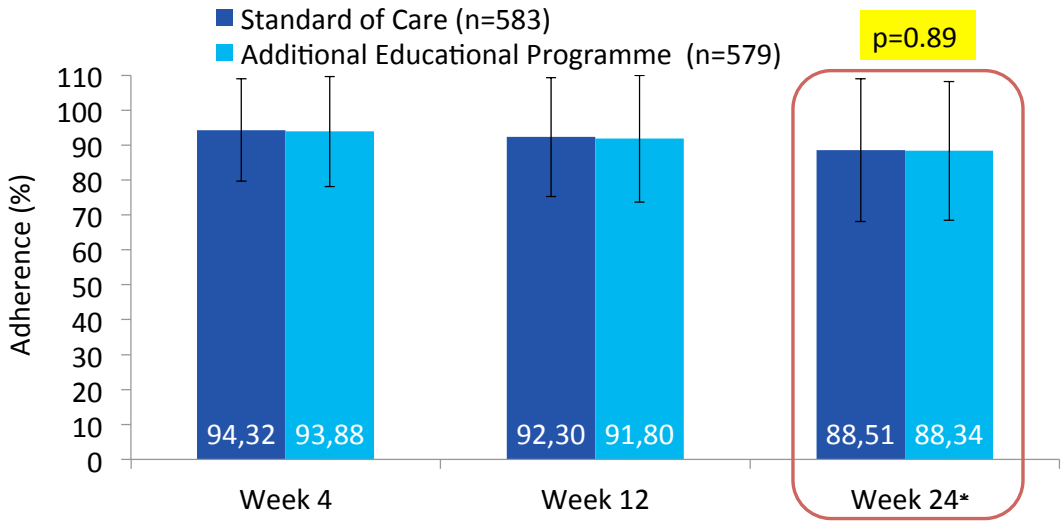
- To assess the impact of an educational program on implementation phase adherence in patients taking apixaban for SPAF. Assessed at 24 weeks after initiation using an EMD, Helping Hand®

Secondary Objectives:

- To assess the impact of an educational program on persistence at 24 weeks in patients taking apixaban
- To identify predictive risk factors linked to non-adherence in patients treated with apixaban
- To evaluate impact of an educational program on efficacy/safety profile of apixaban

EMD, electronic monitoring device; SPAF, stroke prevention in atrial fibrillation

Adherence (primary endpoint)



* Primary Endpoint (24 weeks)

Patient Preference and Adherence

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REVIEW

Interventional tools to improve medication adherence: review of literature

Poor adherence is associated with high health care costs, lower quality of life, and poor health outcomes.

Medication adherence remains a challenge for health care professional and scientists, as their efforts to improve and explain patients' adherence appear to be ineffective.

A lot of interventions to improve adherence to medical plans have been described in literature, despite some isolated success, most interventions failed in their aims.

Costa E et al.2015

Interventions for improving modifiable risk factor control in the secondary prevention of stroke (Review)

Lager KE, Mistri AK, Khunti K, Haunton VJ, Sett AK, Wilson AD

THE COCHRANE COLLABORATION®

Main results

This review included 26 studies involving 8021 participants. There were no significant effects of organisational interventions medication adherence or recurrent cardiovascular events. Educational and behavioural interventions were not generally associated with clear differences in any of the review outcomes, with only two exceptions.

Authors' conclusions

Pooled results indicated that educational interventions were not associated with clear differences in any of the review outcomes. The estimated effects of organisational interventions were compatible with improvements and no differences in several modifiable risk factors. We identified a large number of ongoing studies, suggesting that research in this area is increasing.

The Cochrane Collaboration , 2014

G.AM; F anni 66

indicazione alla TAO: TEV recidivante
Valvuloplastica mitralica
Pregresso stroke

11/2011 inizia warfarin INR 2.0-3.0
passa a Sintrom per elevato fabbisogno
maggio 2013 torna a warfarin
fino al giugno 2013: tempo in range 34%
tempo sotto range 37%
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12 volte/18 mesi INR> 4.0

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