LA TERAPIA ANTICOAGULANTE ORALE NELLA FIBRILLAZIONE ATRIALE

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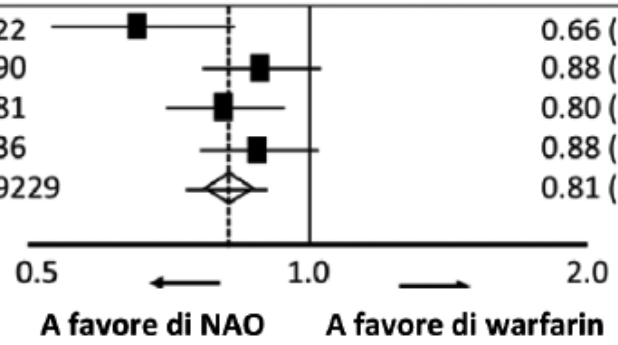
Risultati di efficacia e sicurezza dei NAO
A: ictus o eventi embolici sistemici; B: sanguinamenti maggiori

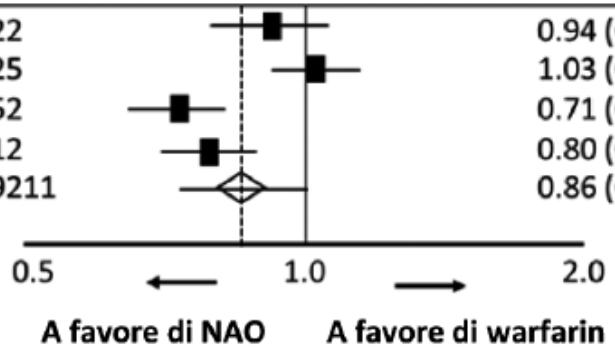
A

	NAO (eventi)	Warfarin (eventi)	RR (95% IC)	P
RE-LY	134/6076	199/6022	0.66 (0.53-0.82)	0.0001
ROCKET AF	269/7081	306/7090	0.88 (0.75-1.03)	0.12
ARISTOTLE	212/9120	265/9081	0.80 (0.67-0.95)	0.012
ENGAGE AF-TIMI 48	296/7035	337/7036	0.88 (0.75-1.02)	0.10
Combinati	911/29312	1107/29229	0.81 (0.73-0.91)	<0.0001



B

	NAO (eventi)	Warfarin (eventi)	RR (95% IC)	P
RE-LY	375/6076	397/6022	0.94 (0.82-1.07)	0.34
ROCKET AF	395/7111	386/7125	1.03 (0.90-1.18)	0.72
ARISTOTLE	327/9088	462/9052	0.71 (0.61-0.81)	<0.0001
ENGAGE AF-TIMI 48	444/7012	557/7012	0.80 (0.71-0.90)	0.0002
Combinati	1541/29287	1802/29211	0.86 (0.73-1.00)	0.06



***Lancet* 2014; 383: 955–62**

Effects of Non–Vitamin K Antagonist Oral Anticoagulants Versus Warfarin in Patients With Atrial Fibrillation and Valvular Heart Disease: A Systematic Review and Meta-Analysis

Kuo-Li Pan, MD; Daniel E. Singer, MD; Bruce Ovbiagele, MD, FRCP; Yi-Ling Wu, MS; Mohamed A. Ahmed, MD, MPH; Meng Lee, MD

Riduzione di:

- stroke ed embolia sistemica nei pz in FA con o senza VHD
- emorragie intracraniche nei pz in FA con o senza VHD
- mortalità globale nei pazienti senza VHD

J Am Heart Assoc. 2017;6:e005835. DOI: 10.1161/JAHA.117.

Effects of Non–Vitamin K Antagonist Oral Anticoagulants Versus Warfarin in Patients With Atrial Fibrillation and Valvular Heart Disease: A Systematic Review and Meta-Analysis

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Differenza non statisticamente significativa per:

- sanginamenti maggiori nei pazienti in FA con o senza VHD
- mortalità globale nei pazienti con VHD

J Am Heart Assoc. 2017;6:e005835. DOI: 10.1161/JAHA.117.

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

Recommendations for stroke prevention in patients with atrial fibrillation

Recommendations	Class[a]	Level[b]
Oral anticoagulation therapy to prevent thromboembolism is recommended for all male AF patients with a CHA_2DS_2-VASc score of 2 or more.	I	A
Oral anticoagulation therapy to prevent thromboembolism is recommended in all female AF patients with a CHA_2DS_2-VASc score of 3 or more.	I	A
Oral anticoagulation therapy to prevent thromboembolism should be considered in male AF patients with a CHA_2DS_2-VASc score of 1, considering individual characteristics and patient preferences.	IIa	B
Oral anticoagulation therapy to prevent thromboembolism should be considered in female AF patients with a CHA_2DS_2-VASc score of 2, considering individual characteristics and patient preferences.	IIa	B
Vitamin K antagonist therapy (INR 2.0–3.0 or higher) is recommended for stroke prevention in AF patients with moderate-to-severe mitral stenosis or mechanical heart valves.	I	B
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.	I	A
When patients are treated with a vitamin K antagonist, time in therapeutic range (TTR) should be kept as high as possible and closely monitored.	I	A
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	A
Combinations of oral anticoagulants and platelet inhibitors increase bleeding risk and should be avoided in AF patients without another indication for platelet inhibition.	III (harm)	B
In male or female AF patients without additional stroke risk factors, anticoagulant or antiplatelet therapy is not recommended for stroke prevention.	III (harm)	B
Antiplatelet monotherapy is not recommended for stroke prevention in AF patients, regardless of stroke risk.	III (harm)	A
NOACs (apixaban, dabigatran, edoxaban, and rivaroxaban) are not recommended in patients with mechanical heart valves (Level of evidence B) or moderate-to-severe mitral stenosis (Level of evidence C).	III (harm)	B C

European Heart Journal (2016) **37**, 2893–2962
doi:10.1093/eurheartj/ehw210

The 2018 European Heart Rhythm Association Practical Guide on the use of non-vitamin K antagonist oral anticoagulants in patients with atrial fibrillation

Condition	Eligibility for NOAC therapy
Mechanical prosthetic valve	Contraindicated
Moderate to severe mitral stenosis (usually of rheumatic origin)	Contraindicated
Mild to moderate other native valvular disease (e.g., mild-moderate aortic stenosis or regurgitation, degenerative mitral regurgitation etc.)	Included in NOAC trials
Severe aortic stenosis	Limited data (excluded in RE-LY) Most will undergo intervention
Bioprosthetic valve (after > 3 months post operatively)	Not advised if for rheumatic mitral stenosis
	Acceptable if for degenerative mitral regurgitation or in the aortic position
Mitral valve repair (after > 3 months post operatively)	Some patients included in some NOAC trials
PTAV and TAVI	No prospective data yet May require combination with single or dual antiplatelet therapy
Hypertrophic cardiomyopathy	Few data, but patients may be eligible for NOACs

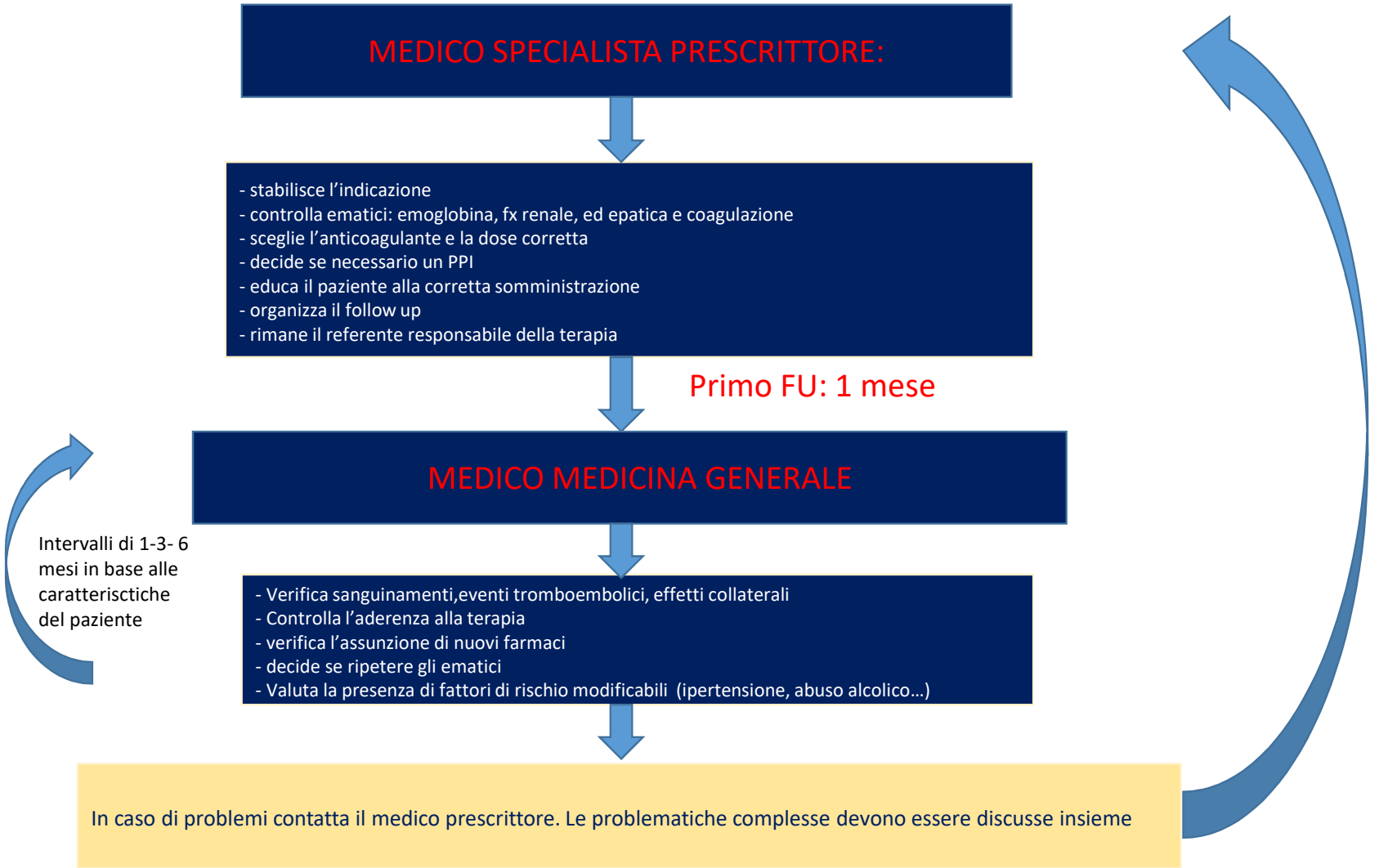
European Heart Journal (2018) **39**, 1330–1393
doi:10.1093/eurheartj/ehy136

	UNITA Anno 2016	UNITA Anno 2016 %V	UNITA Anno 2017	UNITA Anno 2017%V
ITALIA				
NAO	3.453.021	35,3%	5.199.803	47,5%

	UNITA Anno 2016	UNITA Anno 2016 %V	UNITA Anno 2017	UNITA Anno 2017%V
PIEMONTE				
NAO	323.721	36,7%	469.721	48,3%

	UNITA Anno 2016	UNITA Anno 2016 %V	UNITA Anno 2017	UNITA Anno 2017%V
ASL TO3				
NAO	49.840	38,1%	73.061	50,3%

COME ORGANIZZARE IL FOLLOW UP



GESTIONE SANGUINAMENTI

- Indagare circa l'ultima assunzione
- Stimare il tempo di eliminazione

Sanguinamenti minori

-ritardarel'assunzione/saltare una dose
-trattare la causa del sanguinamento
-in caso di recidive considerare NOAC alternativo

Sanguinamenti maggiori senza pericolo di vita

- Emostasi locale
-Trasfusione con sacche di EC o PTL
-Plasma fresco
-Ac. Tranexamico (1 gr ev. ripetibile ogni 6 ore)
-Desmopressina (infusione ev. 0,3 mcg/Kg)
-Mantenere la diuresi (ev. dialisi per Dabigatran)
-Considerare l'Idarucizumab per Dabigatran

Sanguinamenti maggiori con pericolo di vita

- Misure standard
- Idarucizumab 2,5 mg ev. x 2
. PCC (50 U/Kg + 25 U/kg se indicato)
- aPCC 50 U/Kg, max 200 U/Kg

INTERAZIONI FARMACOLOGICHE CUI DEVE FARE ATTENZIONE IL MMG

Table 8. Examples of In Vivo CYP3A and P-gp Inhibitors and Their Relative Potency

	P-gp Inhibitor	Non-P-gp Inhibitor
Strong CYP3A Inhibitor	Itraconazole, lopinavir/ritonavir, telaprevir, clarithromycin, ritonavir,* ketoconazole,* indinavir/ritonavir,*conivaptan	Voriconazole
Moderate CYP3A Inhibitor	Verapamil, erythromycin,* diltiazem, dronedarone	None identified
Weak CYP3A Inhibitor	Lapatinib, quinidine, ranolazine, amiodarone, felodipine, azithromycin*	Cimetidine

IL FOLLOW UP : PERCHE’

-Il rene e il fegato sono coinvolti nel metabolismo e nell’eliminazione dei NOACs

-interazioni farmacologiche (P-gp tutti i NOACs, CYP3A4 per apixaban e rivaroxaban)

-intolleranza/allergia al farmaco

-sanguinamenti/eventi ischemici

DOPO UN ANNO RINNOVO PIANO TERAPEUTICO: FUNZIONE RENALE RECENTE

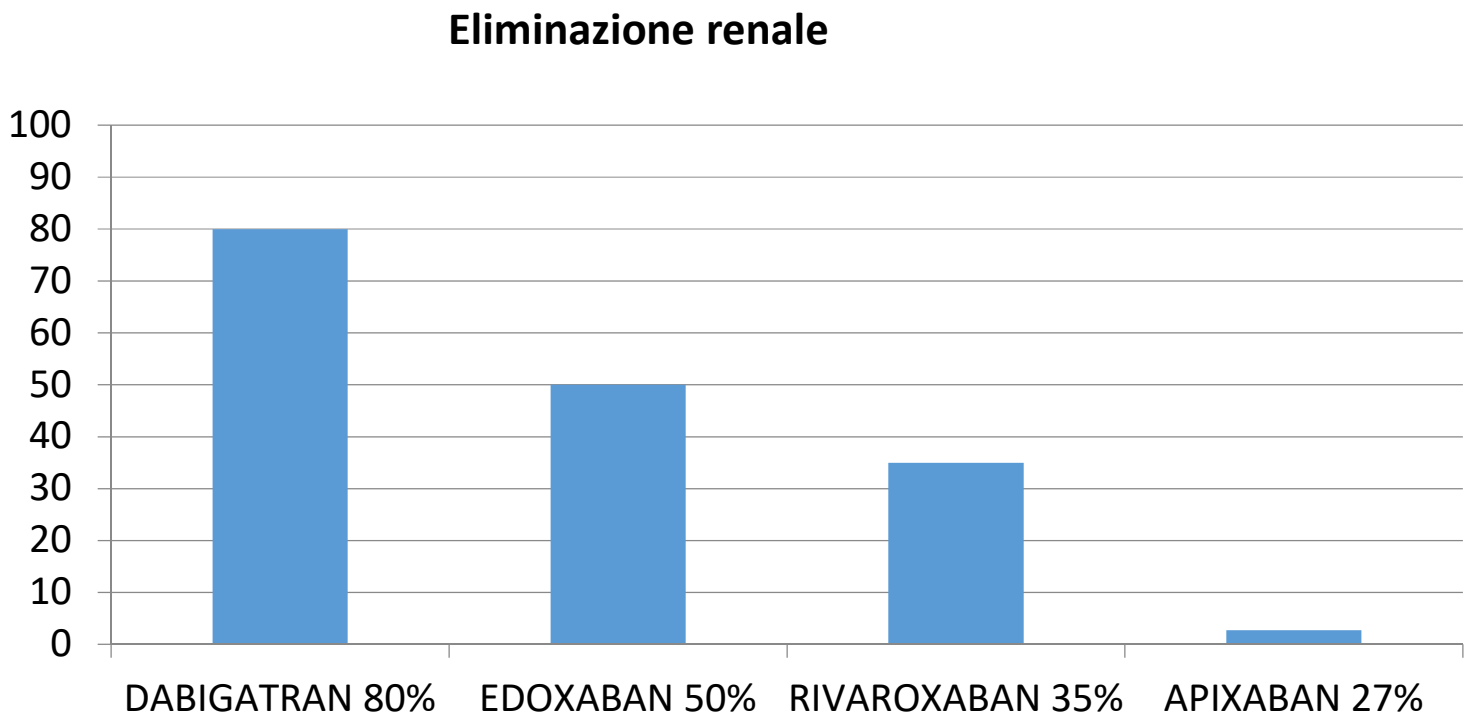
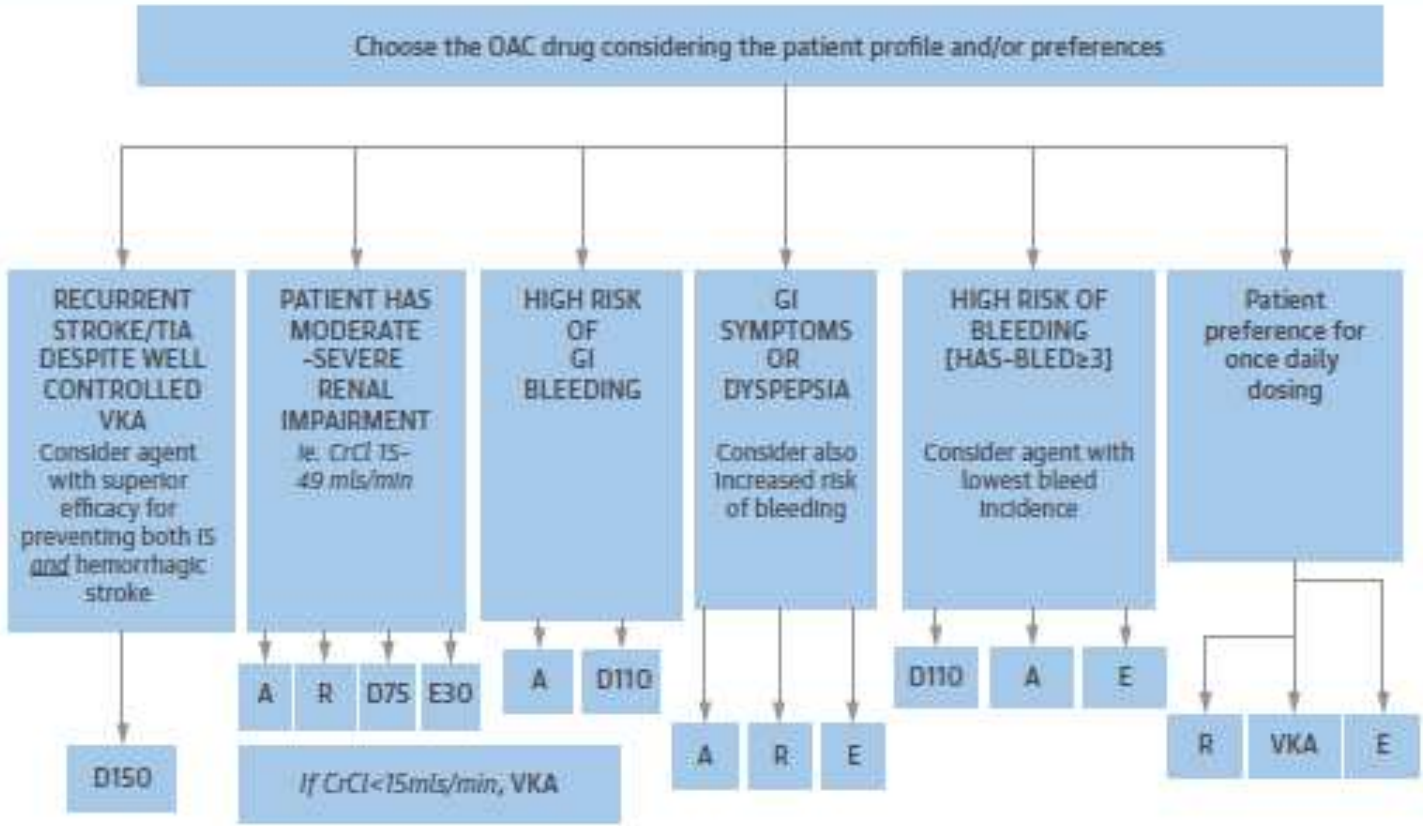


FIGURE 1 Selecting the Optimal Oral Anticoagulant for Stroke Prevention in Atrial Fibrillation: Some Suggestions for Initial Treatment Options



A = apixaban; CrCl = creatinine clearance; D = dabigatran (D75, 75 mg bid does in United States only; D110 = 110 mg bid dose, not in the United States); E = edoxaban; E30 = edoxaban 30 mg; GI = gastrointestinal; IS = ischemic stroke; OAC = oral anticoagulation; R = rivaroxaban; TIA = transient ischemic attack; VKA = vitamin K antagonist.

SINTESI e CONCLUSIONI

I NAO SONO UNA REALTA' ORMAI CONSOLIDATA. MIGLIORANO GLI OUTCOME , MA ANCHE LA QUALITA' DI VITA E QUINDI L'ADERENZA TERAPEUTICA

SE IL PAZIENTE E' ELEGGIBILE SONO DA PREFERIRE NELLA FANV - CLASSE I (TRANNE IRC GRAVE)

NON ESISTE IL NAO IDEALE O PERFETTO. LA SCELTA DEL NAO GIUSTO PER QUEL PAZIENTE E' FUNZIONALE AL PROFILO DI RISCHIO (TROMBOTICO E/O EMORRAGICO) E CARATTERISTICHE CLINICHE (IRC, CAD , DAPT etc)

LA COLLABORAZIONE COL MMG E' FONDAMENTALE NEL MONITORARE L'ADERENZA TERAPEUTICA E LE POSSIBILI COMPLICANZE