



2013

Norte

25 OUTUBRO — 6ª FEIRA

The background of the slide is a vibrant red, featuring a pattern of stylized red hearts of various sizes and shapes, along with numerous red blood cells, creating a medical and biological theme.

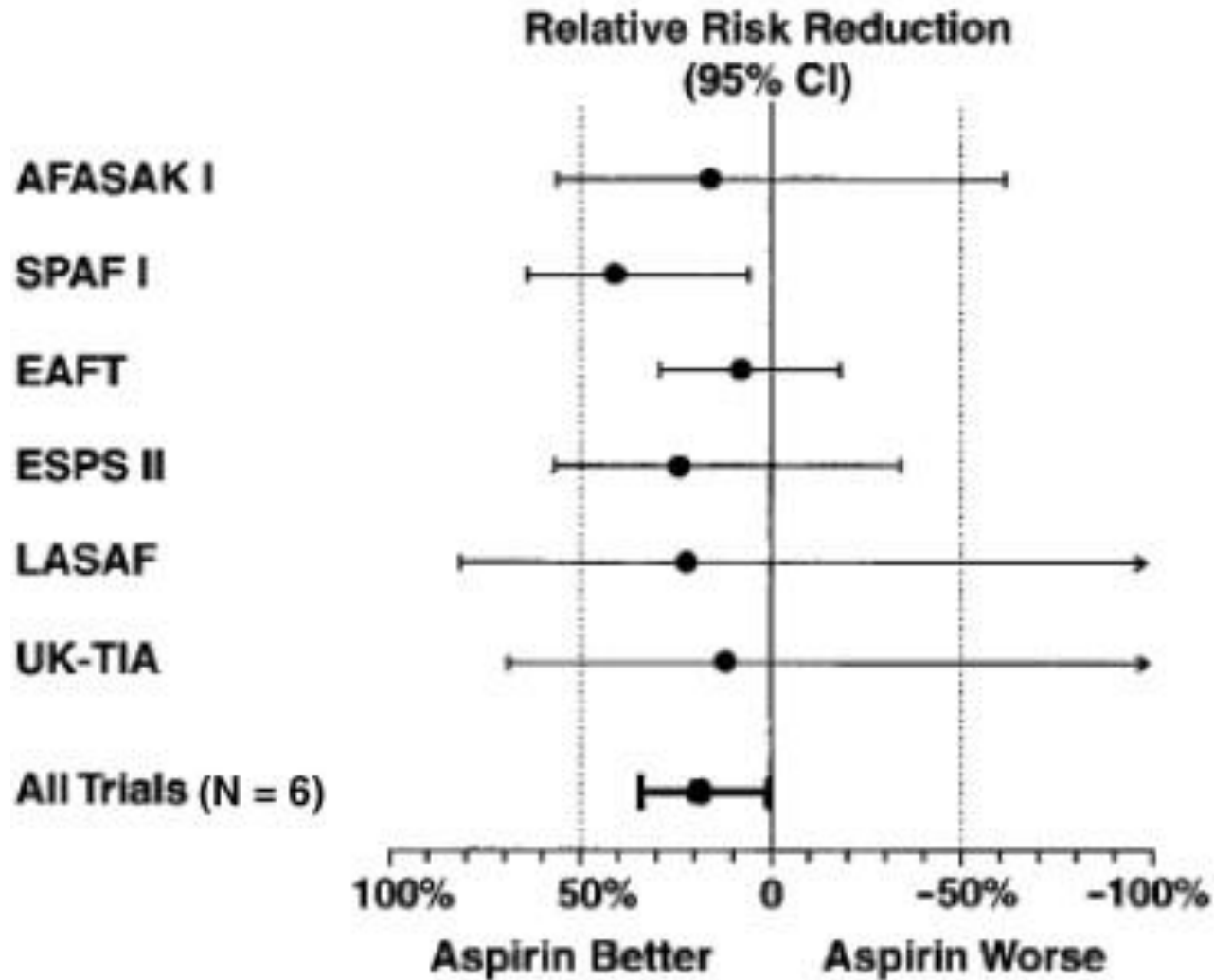
Anticoagulação oral Casos especiais

Arminda Veiga

Anticoagulação oral no doente com risco hemorrágico elevado

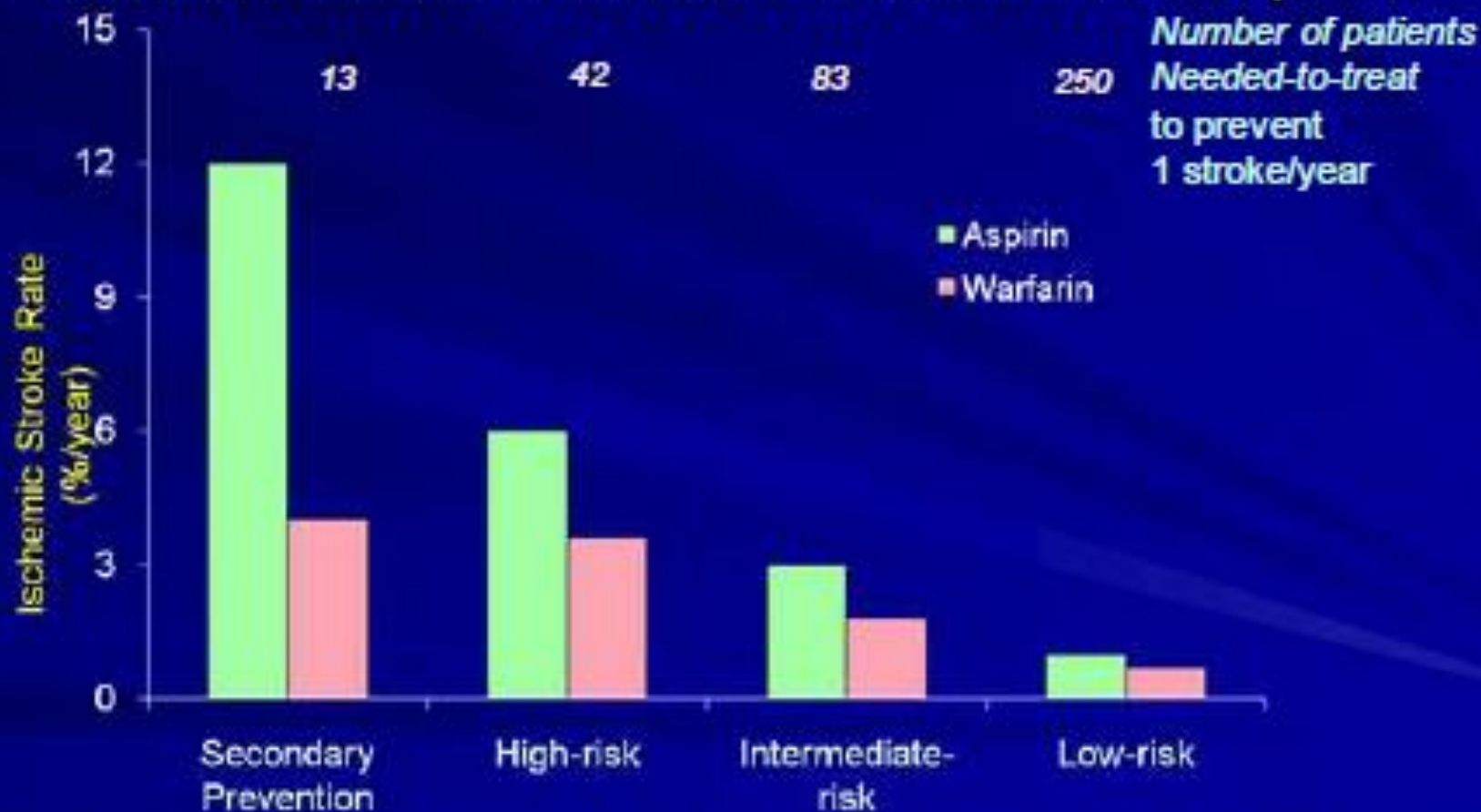


RCTs of Aspirin vs. Control



Warfarin Better Than Aspirin for All NVAF But Lowest Risk

Stroke Reduction with Warfarin Instead of Aspirin



Apixaban versus AAS

Medscape CRITICAL CARE ▾

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Dr. A Veiga



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Five Triggers in Multiple Sclerosis



New PET Probe for Myelin in MS



Three Major Advances in Multiple Sclerosis



Managing Opioid Overuse: A Case

Medscape Medical News from the:
International Stroke Conference (ISC) 2011

This coverage is not sanctioned by, nor a part of, the American Heart Association/American Stroke Association.

Medscape Medical News > Neurology

AVERROES Published: Apixaban Reduces Stroke Over Aspirin

Susan Jeffrey

February 10, 2011



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EDITORS' RECOMMENDATIONS

February 10, 2011 (Los Angeles, California) — Final results of the AVERROES trial confirm that apixaban (Pfizer/Bristol-Myers

Clopidogrel plus aspirin versus oral anticoagulation for atrial fibrillation in the Atrial fibrillation Clopidogrel Trial with Irbesartan for prevention of Vascular Events (ACTIVE W): a randomised controlled trial

The ACTIVE Writing Group on behalf of the ACTIVE Investigators*

Summary

Background Oral anticoagulation therapy reduces risk of vascular events in patients with atrial fibrillation. However, long-term monitoring is necessary and many patients cannot achieve optimum anticoagulation. We assessed whether clopidogrel plus aspirin was non-inferior to oral anticoagulation therapy for prevention of vascular events.

Methods Patients were enrolled if they had atrial fibrillation plus one or more risk factor for stroke, and were randomly allocated to receive oral anticoagulation therapy (target international normalised ratio of 2.0–3.0; n=3371) or clopidogrel (75 mg per day) plus aspirin (75–100 mg per day recommended; n=3335). Outcome events were adjudicated by a blinded committee. Primary outcome was first occurrence of stroke, non-CNS systemic embolus, myocardial infarction, or vascular death. Analyses were by intention-to-treat. This study is registered with ClinicalTrials.gov, number NCT00243178.

Results The study was stopped early because of clear evidence of superiority of oral anticoagulation therapy. There were 165 primary events in patients on oral anticoagulation therapy (annual risk 3.93%) and 234 in those on clopidogrel plus aspirin (annual risk 5.60%; relative risk 1.44 (1.18–1.76; p=0.0003). Patients on oral anticoagulation therapy who were already receiving this treatment at study entry had a trend towards a greater reduction in vascular events (relative risk 1.50, 95% CI 1.19–1.80) and a significantly (p=0.03 for interaction) lower risk of major bleeding with oral anticoagulation therapy (1.30; 0.94–1.79) than patients not on this treatment at study entry (1.27, 0.85–1.89 and 0.59, 0.32–1.08, respectively).

Conclusion Oral anticoagulation therapy is superior to clopidogrel plus aspirin for prevention of vascular events in patients with atrial fibrillation at high risk of stroke, especially in those already taking oral anticoagulation therapy.

Introduction

Atrial fibrillation is a common cardiac arrhythmia, especially in the elderly, and affects over 1% of the population. It increases the risk of stroke and other vascular events.^{1,2} Oral anticoagulation therapy such as warfarin reduces stroke by two-thirds compared with no treatment.^{3,4} Compared with aspirin, oral anticoagulation therapy reduces the risk of stroke by 45% and reduces cardiovascular events by 29%.⁵ However, it increases the risk of major bleeding by about 70% compared with aspirin. Oral anticoagulation therapy is currently the treatment of choice for patients at high risk of stroke.⁶

The response to oral anticoagulation therapy is affected by gut flora, variations in hepatic function, interactions with several drugs, and diet,⁷ requiring regular monitoring of the level of anticoagulation. Therefore, only about half of potentially eligible patients receive oral anticoagulation therapy.⁸ An effective, simple and safe alternative to this treatment could be of great clinical value.

Both aspirin and clopidogrel are antiplatelet agents that act through different mechanisms and are effective in preventing vascular events in patients at high risk.⁹

Aspirin reduces risk of stroke in patients with atrial fibrillation by 22%.¹⁰ The additive benefits of combining a thienopyridine with aspirin have been clearly shown in patients undergoing percutaneous coronary intervention, in those with acute coronary syndrome or acute myocardial infarction.^{10,11} Since aspirin has a documented protective effect in atrial fibrillation, it is reasonable to expect that the addition of clopidogrel to aspirin will provide incremental benefits so that this combination would be non-inferior to oral anticoagulation therapy alone in preventing vascular events. We aimed to assess whether clopidogrel plus aspirin was statistically non-inferior to oral anticoagulation therapy for prevention of vascular events in patients with atrial fibrillation at high risk of stroke and eligible for oral anticoagulation therapy.

Methods

Participants

Three separate inter-related trials comprise the ACTIVE programme. Patients eligible for and willing to take oral anticoagulation therapy were enrolled into ACTIVE W, in which clopidogrel plus aspirin was compared to oral

Lancet 2006; 367: 1903–12

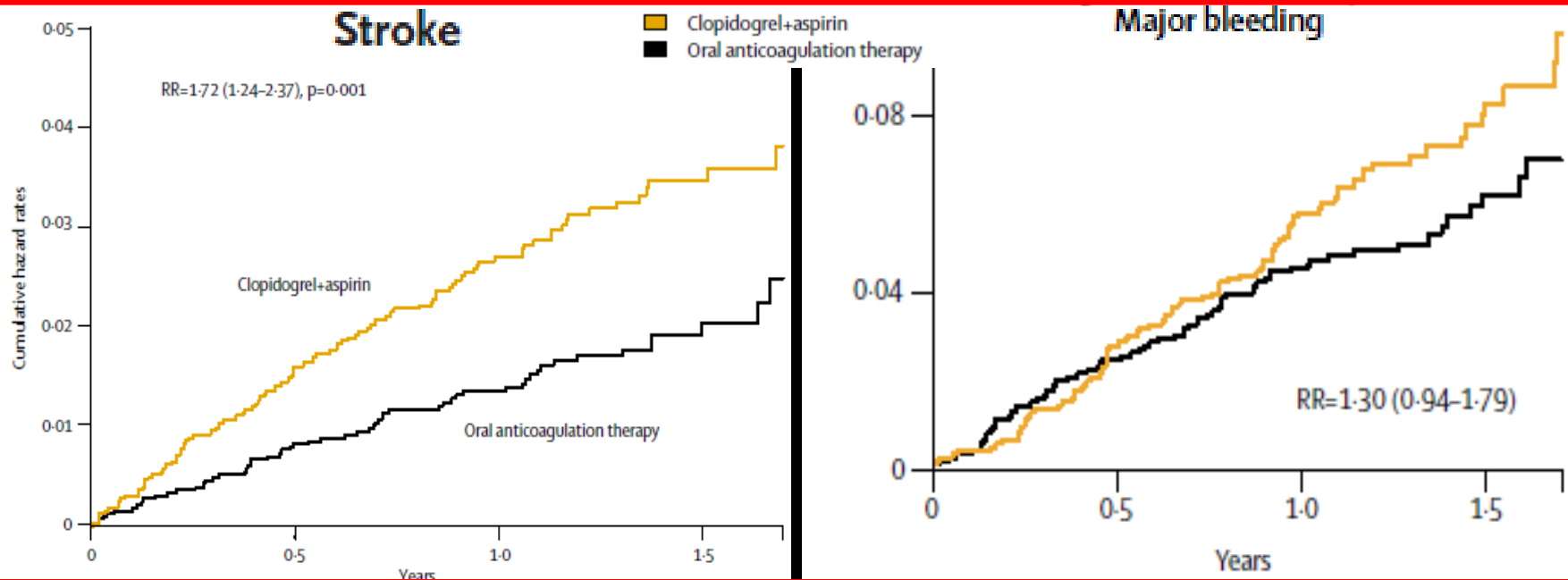
See Comment page 1877

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Clopidogrel plus aspirin versus oral anticoagulation for atrial fibrillation in the Atrial fibrillation Clopidogrel Trial with Irbesartan for prevention of Vascular Events (ACTIVE W): a randomised controlled trial

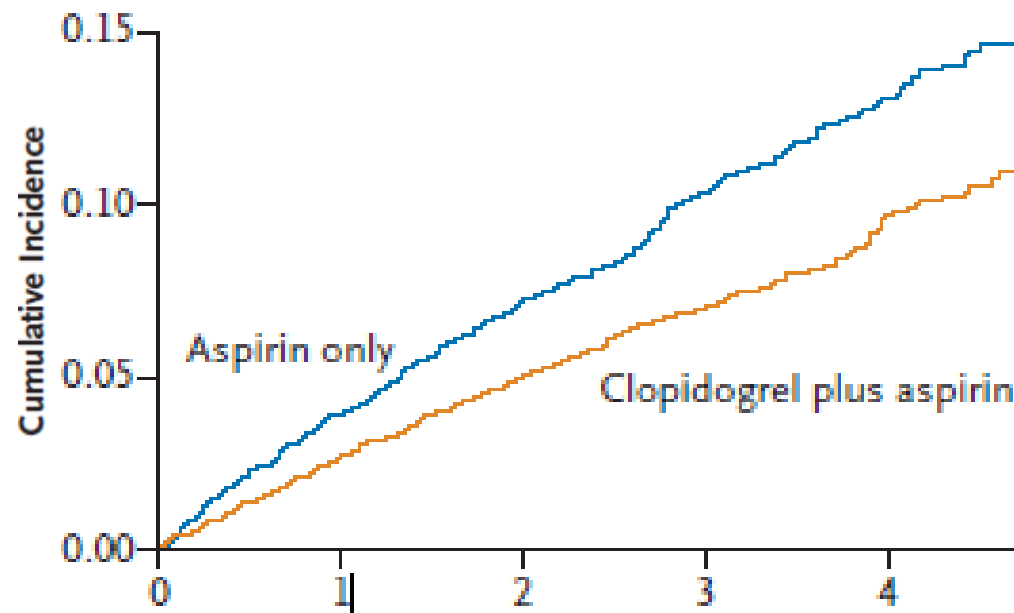
The ACTIVE Writing Group on behalf of the ACTIVE Investigators*



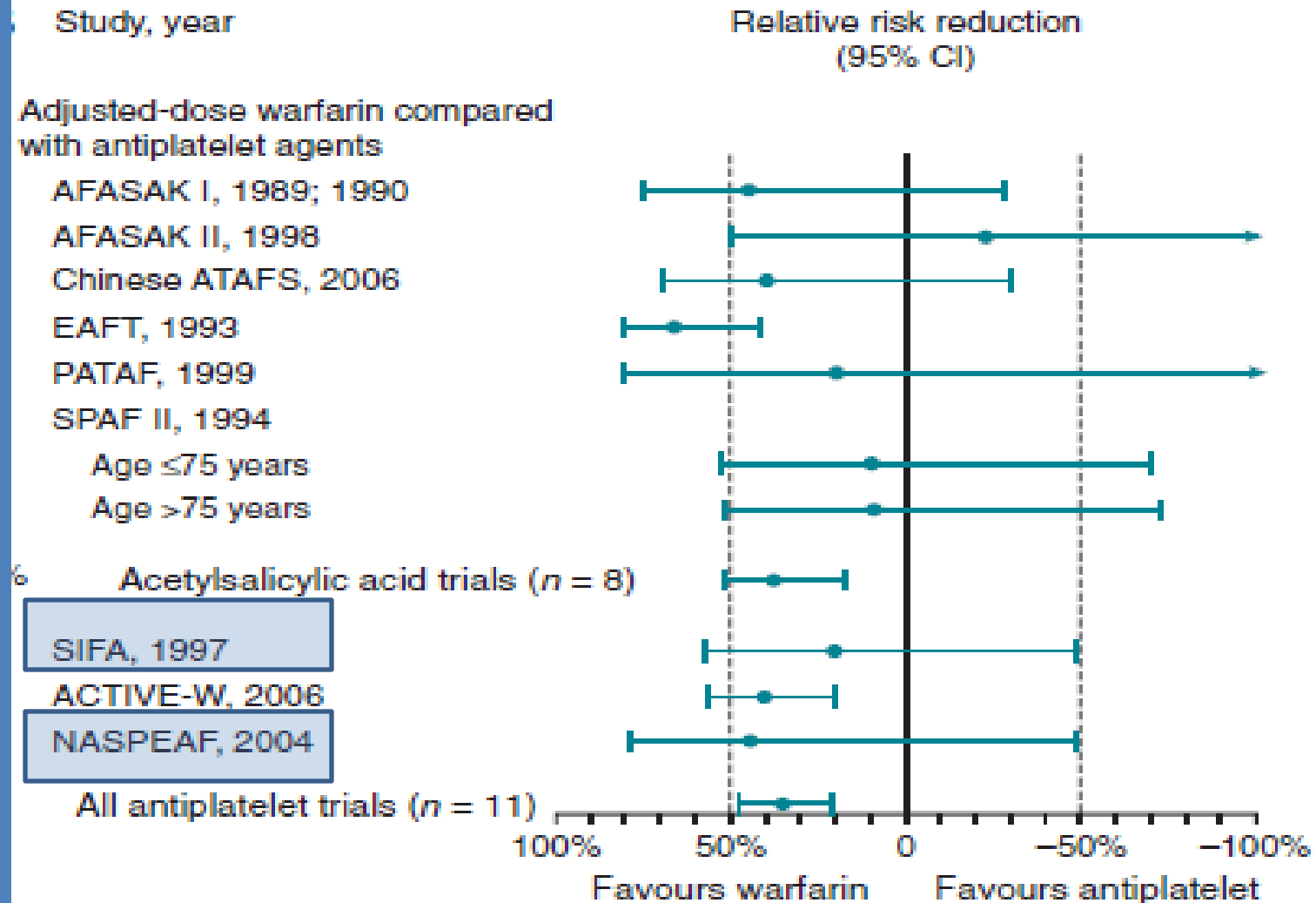
ORIGINAL ARTICLE

Effect of Clopidogrel Added to Aspirin in Patients with Atrial Fibrillation

The ACTIVE Investigators*



Antiagregantes plaquetares vs varfarina



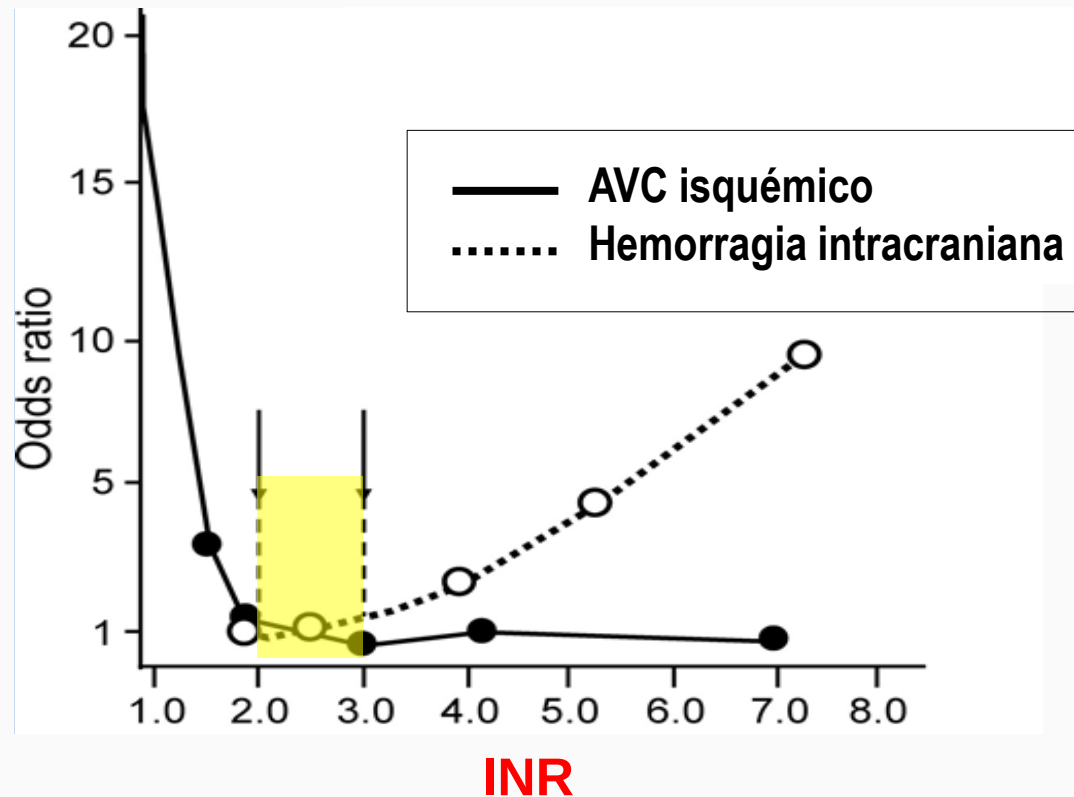
THE LANCET

Adjusted-dose warfarin versus low-intensity, fixed-dose warfarin plus aspirin for high-risk patients with atrial fibrillation: Stroke Prevention in Atrial Fibrillation III randomised clinical trial

O ensaio foi prematuramente interrompido ao fim de 1.1 anos

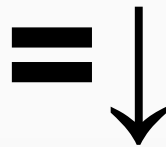
	AVC isquémico + Embolismo sistémico	Evento primário ou Morte vascular	
Varfine (INR: 1.2-1.5) + AAS	7.9% ao ano	11.8% ao ano	P<0.0001
Varfarina (INR: 2-0-3.0)	1.9% ao ano	6.4% ao ano	P=0.002

Varfarina - Intervalo terapêutico estreito

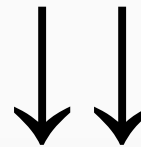


Novos anticoagulantes orais

AVC isquêmico



AVC hemorrágico



Novos anticoagulantes orais

NOAC/Trial	Redução tromboembolismo	AVC hemorrágico	Hemorragia Major
DABIGATRANO RE-LY	 34%	 74%	Similar
RIVAROXABANO ROCKET	Similar	 40%	Similar
APIXABANO ARISTOTLE	 20%	 50%	 30%

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Heartwire

Portola Antidote to Factor Xa Inhibitors Advances in Dosing, Safety Studies

Steve Stiles

October 17, 2013

4 comments



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EDITORS' RECOMMENDATIONS**Antidote for Factor Xa Inhibitors
Goes to Phase 2 Study****Another Novel Oral Anticoagulant as
Safe as Warfarin in AF****Safe as Warfarin in AF****Atrial Fibrillation News &
Perspectives****Topic Alert**Receive an email from Medscape
whenever new articles on this topic are
available.[Add Arrhythmias to My Topic Alert](#)

SOUTH SAN FRANCISCO, CA — A [possible antidote](#) (PRT4445, Portola Pharmaceuticals) to the anticoagulant effects of the new oral factor Xa inhibitors reversed the effects of one such agent, **apixaban** (Eliquis, Bristol-Myers Squibb/Pfizer), by >90% within two minutes of an initial IV bolus and maintained that level throughout a two-hour infusion^[1].

Antidotes to the new generation of oral factor Xa inhibitors. of

Antidotes to the new generation of oral factor Xa inhibitors, of which none are yet available, would be valued for managing otherwise uncontrolled bleeding. The search for one is among the most closely watched areas of cardiology research.

The new findings were from a comparison of six persons given the agent (tentatively named andexanet alfa pending possible approval) and three controls who received placebo, Portola announced in a press release. They were part of a phase 2 study that randomized 54 volunteers, with double blinding, to

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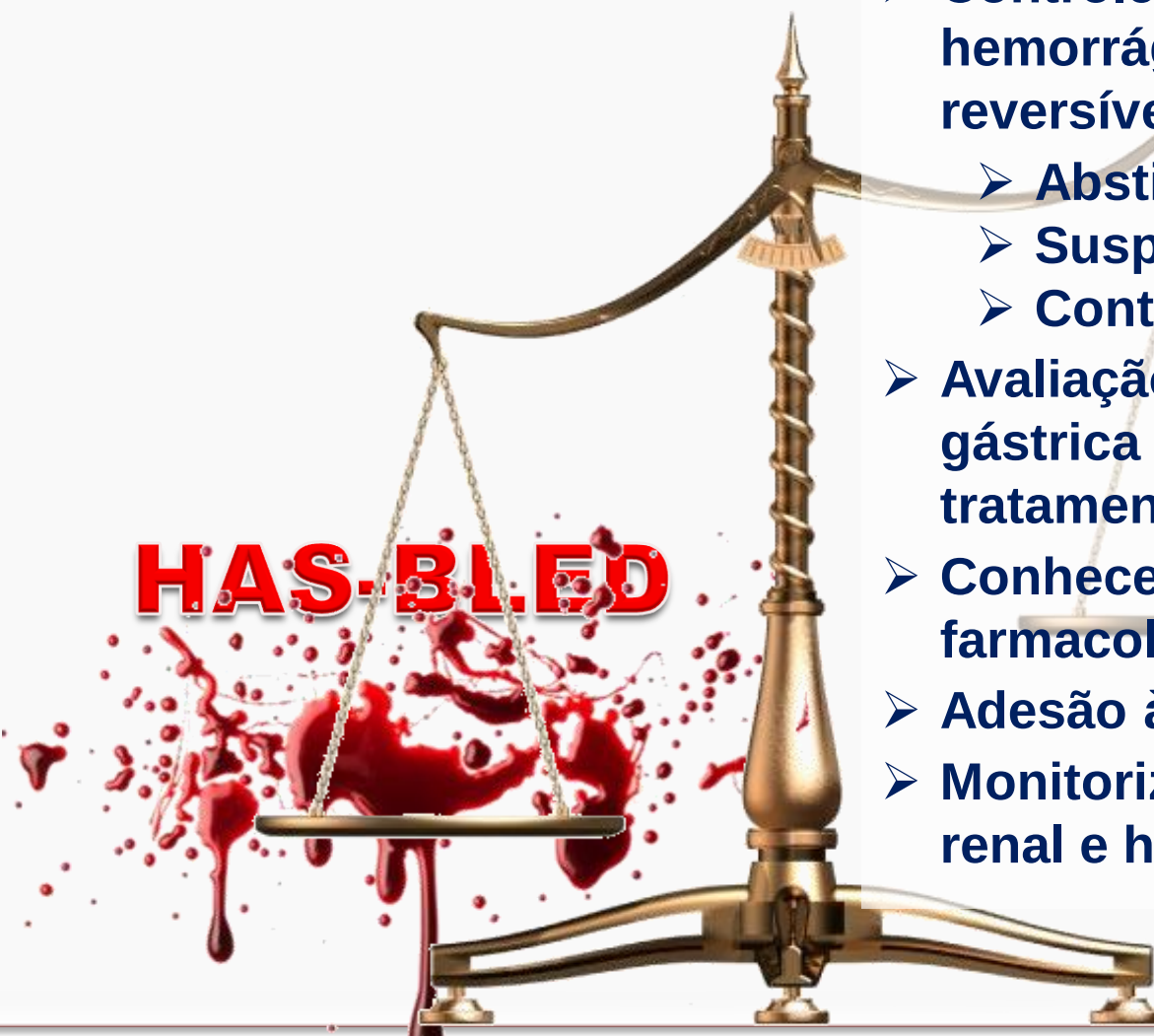
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MOST POPULAR ARTICLES**MOST POPULAR ARTICLES**

According to CARDIOLOGISTS

1. 'Normal' Angiogram Rates for Suspected CAD Differ Widely Among Hospitals
2. Should Ischemia Be the Main Target in Selecting a Percutaneous Coronary Intervention Strategy?

Avaliação e minimização do risco hemorrágico em doentes com indicação para anticoagulação



HAS-BLED

- Controle de factores de risco hemorrágico potencialmente reversíveis
  - Abstinência alcoólica
  - Suspensão dos AINE
  - Controlo da PA
- Avaliação de patologia gástrica e eventual tratamento
- Conhecer as interferências farmacológicas potenciais
- Adesão à terapêutica
- Monitorização da função renal e hepática.

Hemorragia em doente anticoagulado com AVK

Avalie a repercussão hemodinâmica e faça INR.

Minor

- Suspenda AVK até INR NL e hemostase adequada
- VitK se INR >4

Moderada a grave

- **Medidas de suporte**
- **Compressão mecânica**
- **Administração de fluídos**
- **Transfusão sanguínea**
- **VitK**
- **Factor VIIa recombinado**
- **Complexo protrombínico**

Grave

Hemorragia em doente anticoagulado com NOAC

Avalie a repercussão hemodinâmica, faça testes de coagulação (APTT para dabigatran, PT ou actividade anti-Xa para os inibidores do factor Xa), função renal, etc.

Minor

Não faça a próxima toma ou suspenda o tratamento

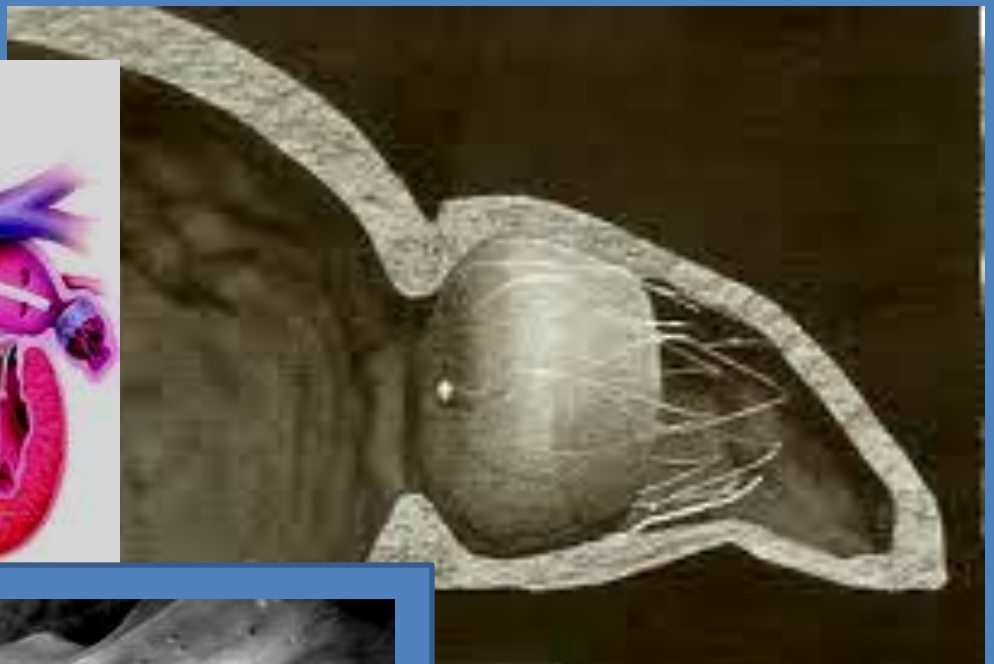
Moderada a grave

Medidas de suporte
Compressão mecânica
Administração de fluídos
Transfusão sanguínea
Carvão activado se toma recente do ACO

Grave

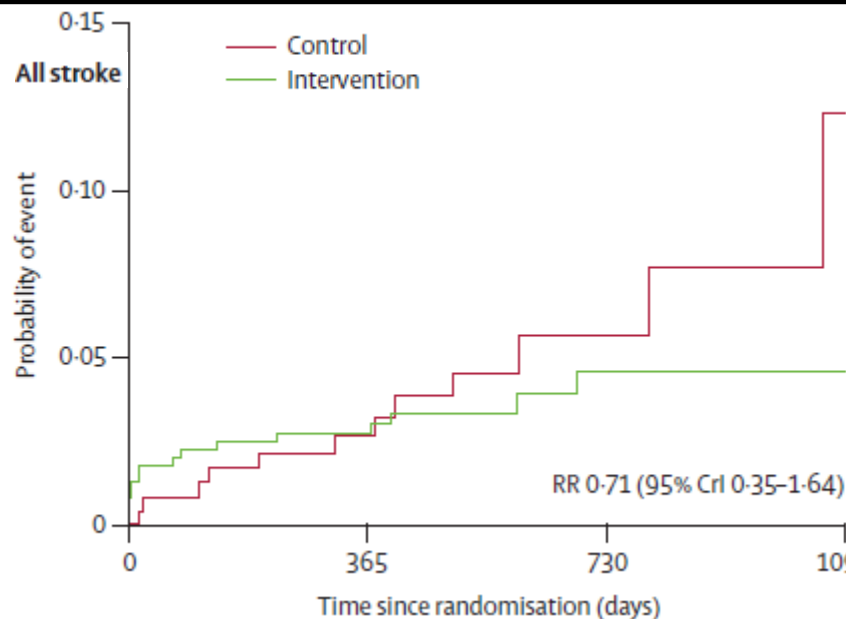
Factor VIIa recombinado
Complexo protrombínico
Hemodiálise (dabigatran)

Encerramento do apêndice auricular esquerdo com dispositivo próprio (WATCHMAN)



➤ Percutaneous closure of the left atrial appendage versus warfarin therapy for prevention of stroke in patients with atrial fibrillation: a randomised non-inferiority trial

David R Holmes, Vivek Y Reddy, Zoltan G Turi, Shephal K Doshi, Horst Sievert, Maurice Buchbinder, Christopher M Mullin, Peter Sick, for the PROTECT AF Investigators*



PROTECT AF

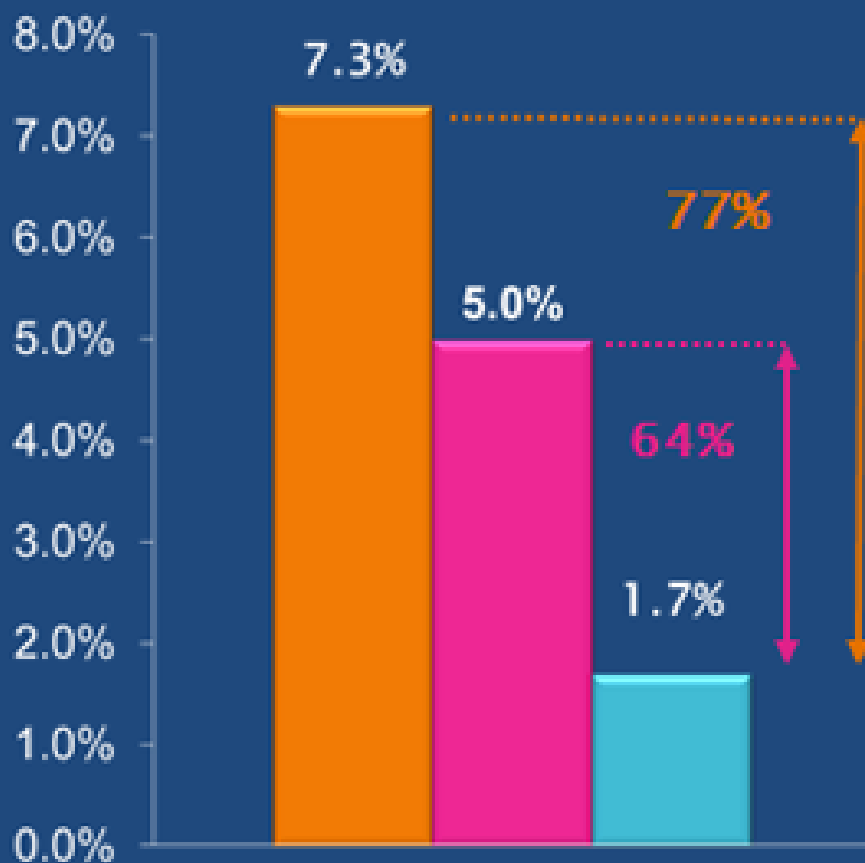
Thus, our strategy for closing the LAA was non-inferior to warfarin therapy in terms of the primary efficacy endpoint of all stroke, cardiovascular death, and systemic embolism. Although there is a higher initial safety event rate for device implantation, adverse events were without long-term sequelae for most patients. Closure of the LAA might provide an alternative strategy to chronic warfarin therapy for stroke prophylaxis in patients with non-valvular atrial fibrillation.



[Home](#) > [Clinical Trial Data](#) > ASAP Study

ASAP Registry

ASA Plavix Feasibility Study with WATCHMAN™ Left Atrial Appendage Closure Technology



Expected, based on
CHADS₂ Score

Expected, if
Clopidogrel was used
throughout follow-up

Observed rate in
ASAP



Anticoagulação oral na Cardiopatia isquêmica

A photograph of a doctor in a white coat, seen from the side, holding a clipboard and pen. He is smiling and talking to an elderly couple. The man, on the left, has white hair, wears glasses, and a blue button-down shirt. The woman, in the middle, has short, curly blonde hair and wears a green top. They are both smiling and looking at the doctor. The background is a bright, out-of-focus indoor setting with light blue and white vertical stripes.

**Terapêutica antitrombótica
na
Doença Coronária Estável**

The New England Journal of Medicine

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VOLUME 347

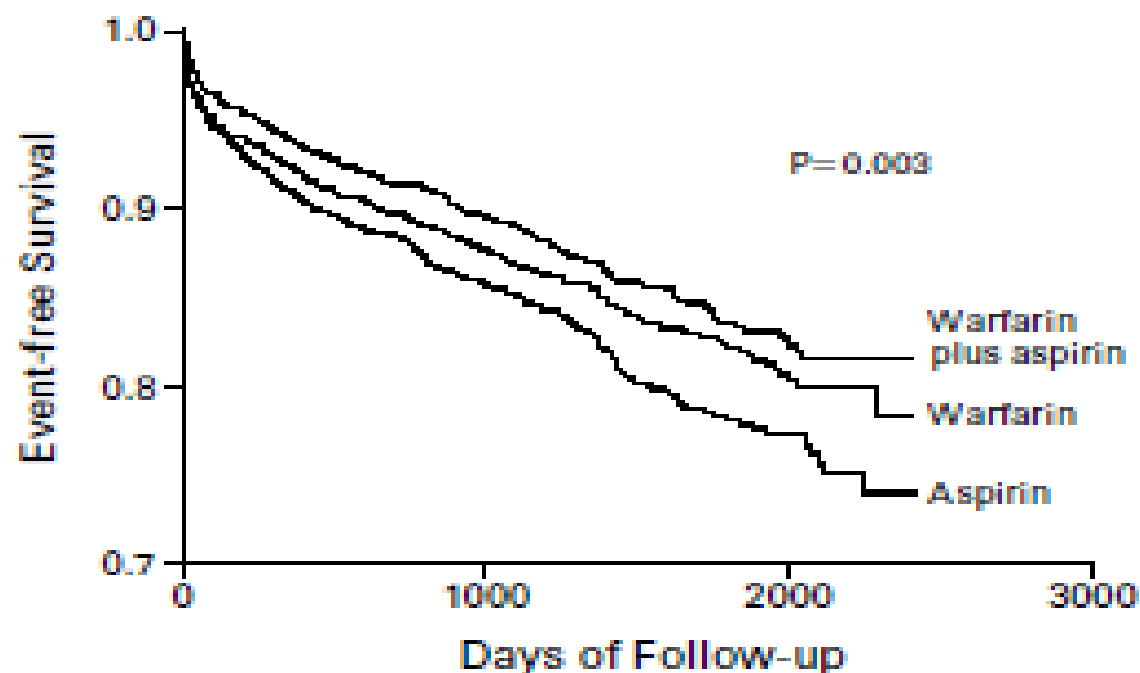
SEPTEMBER 26, 2002

NUMBER 13



WARFARIN, ASPIRIN, OR BOTH AFTER MYOCARDIAL INFARCTION

METTE HURLEN, M.D., MICHAEL ABDELNOOR, M.P.H., PH.D., PÁL SMITH, M.D., PH.D., JAN ERIKSSON, M.D., PH.D.,
AND HARALD ARNESEN, M.D., PH.D.*



Novos anticoagulantes orais

NOAC/Trial	Redução tromboembolismo	AVC hemorrágico	Hemorragia Major
DABIGATRANO RE-LY	 34%	 74%	Similar
RIVAROXABANO ROCKET	Similar	 40%	Similar
APIXABANO ARISTOTLE	 20%	 50%	 30%

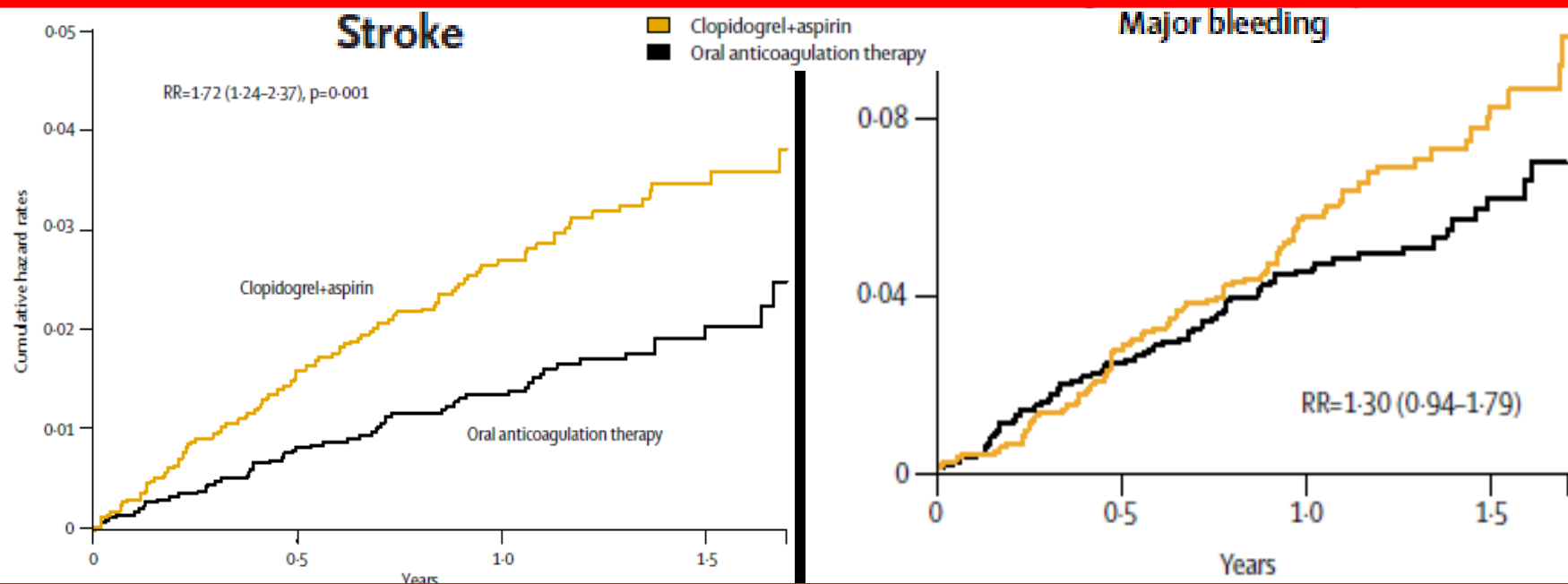
European Heart Rhythm Association Practical Guide on the use of new oral anticoagulants in patients with non-valvular atrial fibrillation

Table 13 Recommendations concerning new onset AF in patients with a remote (>1 year) ACS

1. As VKAs alone are superior to aspirin post-ACS, anticoagulation without additional antiplatelet agents is considered sufficient for most AF patients with stable CAD
2. As the advantages of NOACs over VKAs are likely to be preserved in stable CAD patients with AF, NOACs may be safe and effective alternatives to VKAs
3. In general, no preference is given to either one of the NOACs although a small increase was noted with dabigatran (but without impacting overall clinical benefit)
4. If dabigatran is chosen, a lower dose (110 mg bid) plus low-dose aspirin might be a sensible option (or clopidogrel in case of allergy to aspirin) especially in patients with high atherothrombotic risk and low bleeding risk

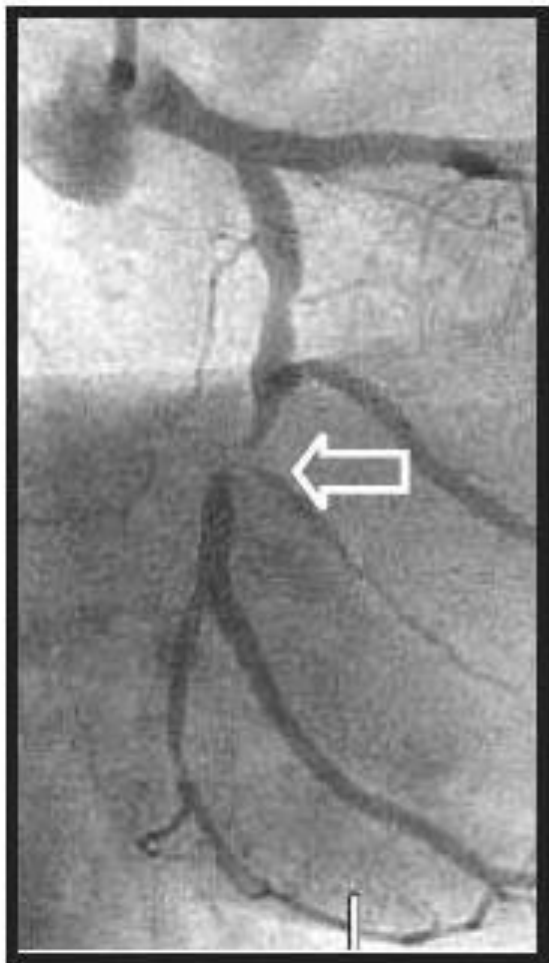
Clopidogrel plus aspirin versus oral anticoagulation for atrial fibrillation in the Atrial fibrillation Clopidogrel Trial with Irbesartan for prevention of Vascular Events (ACTIVE W): a randomised controlled trial

The ACTIVE Writing Group on behalf of the ACTIVE Investigators*

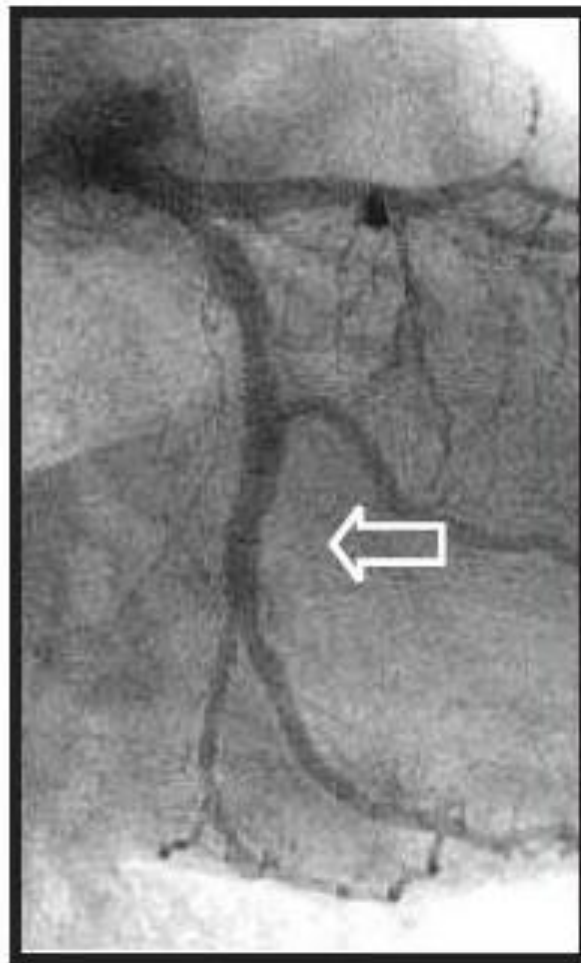


**Terapêutica antitrombótica
após
Angioplastia Coronária**

Angiografia coronária pré e pós angioplastia da Cx

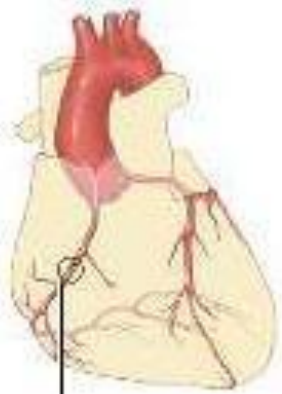


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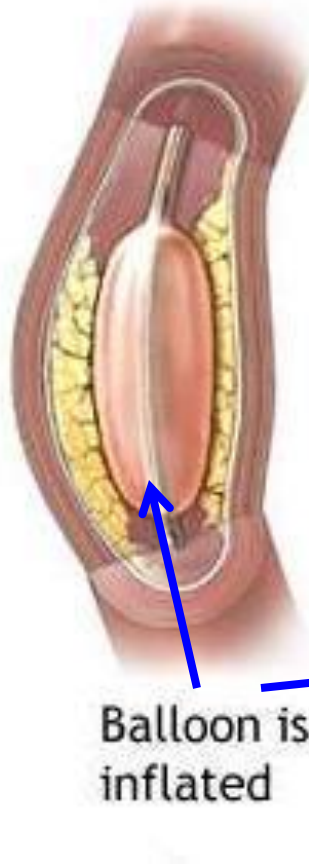


PÓS

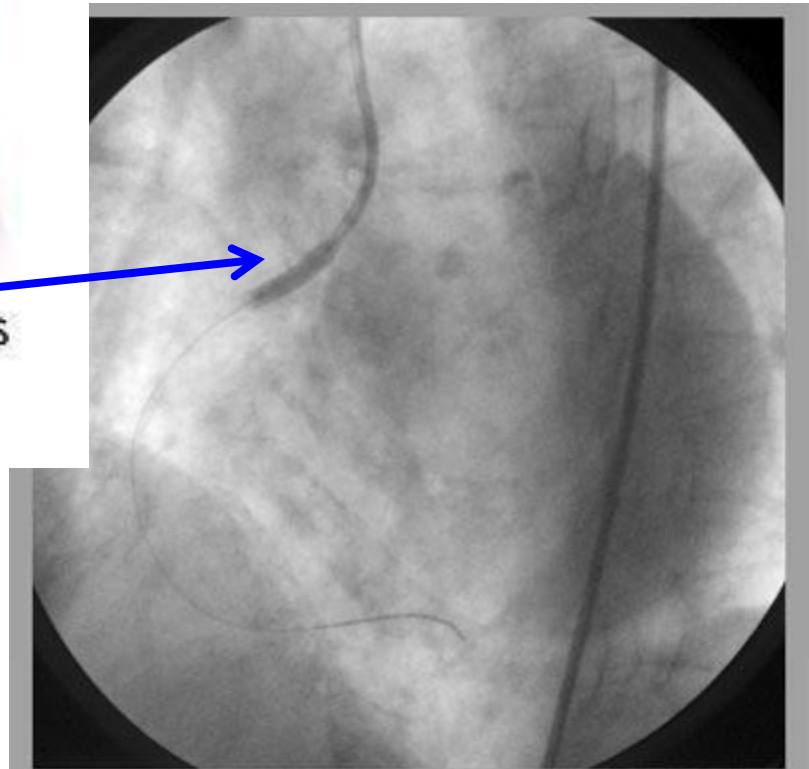
ANGIOPLASTIA DE LESÃO CORONÁRIA



Balloon is
inserted in
coronary
artery



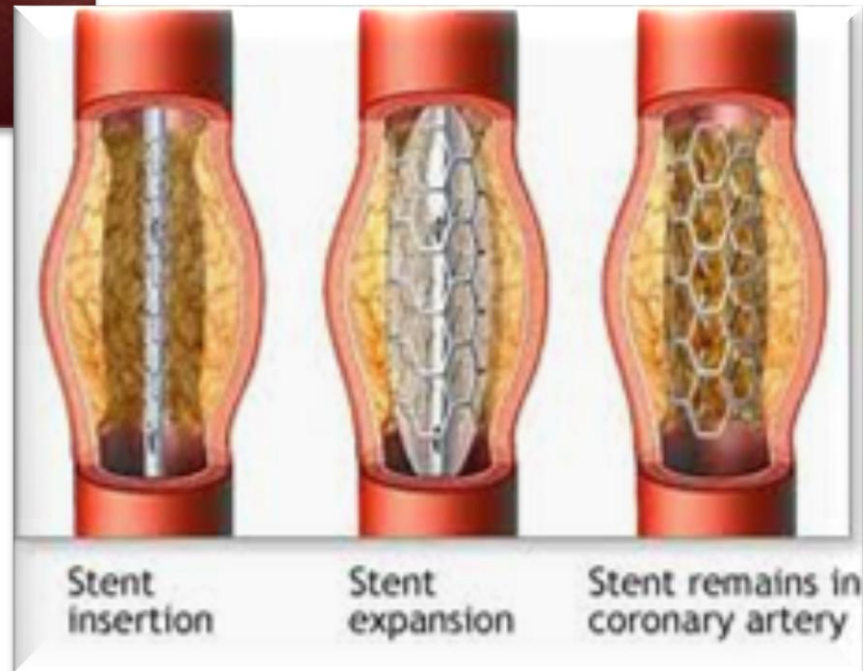
Balloon is
inflated



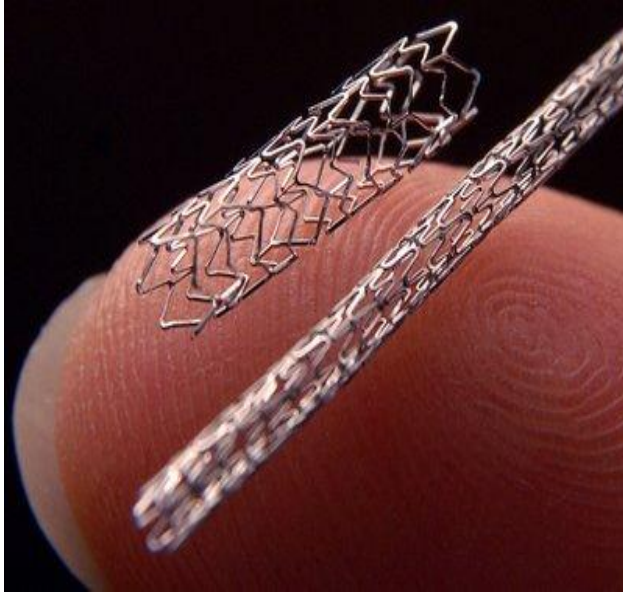


STENTS CORONÁRIOS

Reduzem a reestenose pós angioplastia



STENTS CORONÁRIOS



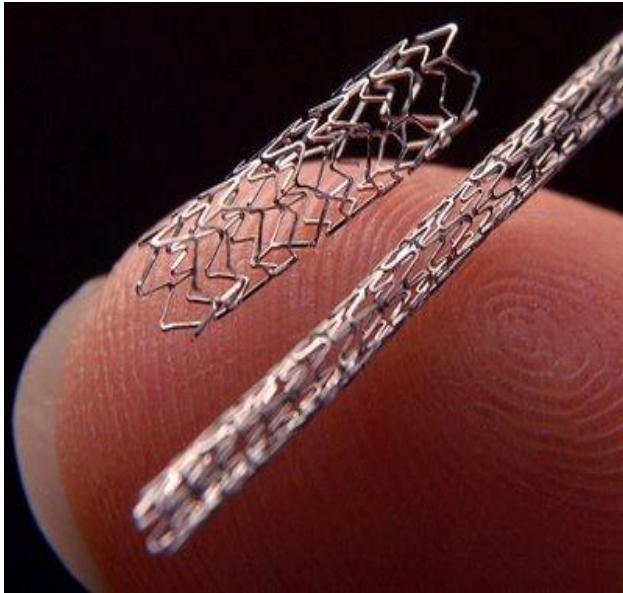
Podem ser:

- **Metálicos**
- **Revestidos** por fármaco que inibe a proliferação intimal.

Sendo material protésico **são trombogênicos, sobretudo os revestidos**, em que o revestimento endotelial do stent aposto é retardado pelo fármaco

Os stents revestidos obrigam a dupla antiagregação mais prolongada (3 a 6 meses) contra 1 mês dos metálicos.

STENTS CORONÁRIOS



A escolha do stent a usar deve ter em conta:

1. O risco hemorrágico do doente (HAS-BLED)

HAS-BLED ≥ 3 → stent metálico
HAS-BLED ≤ 2 → stent revestido

2. O tipo de lesão coronária

*Doentes **diabéticos** com **vasos pequenos** e **lesões longas e complexas** tem mais tendência para reestenose pelo que são os que mais **beneficiam** com os **stents revestidos**.*

Terapêutica antitrombótica após Angioplastia coronária electiva

Risco hemorrágico	Tipo de stent	Regime de Anticoagulação
Baixo-moderado (HAS-BLED=0-2)	Metálico	1M: Terapêutica tripla Depois: Só Varfarina (INR 2.0-3.0) ou NOAC
	Revestido	3-6 meses: Terapêutica tripla Até 12M: Terapêutica dupla Depois: Só Varfarina (INR 2.0-3.0) ou NOAC
Elevado (HAS-BLED ≥ 3)	Metálico	1M: Terapêutica tripla Depois: Só Varfarina (INR 2.0-3.0) ou NOAC

Terapêutica antitrombótica após Angioplastia coronária no EAM

Risco hemorrágico	Tipo de stent	Regime de Anticoagulação
Baixo-moderado (HAS-BLED=0-2)	Revestido	6 meses: Terapêutica tripla Até 12M: : Terapêutica dupla Depois: Só Varfarina (INR 2.0-3.0) ou NOAC
Elevado (HAS-BLED ≥ 3)	Metálico	1M: Terapêutica tripla Até 12M: Terapêutica dupla Depois: Só Varfarina (INR 2.0-3.0) ou NOAC

Terapêutica antitrombótica no peri-operatório



Cirurgias de alto risco hemorrágico

Interromper anticoagulação oral

Cirurgia urológica

Cirurgia abdominal (hemicolecomia, esplenectomia etc)

Cirurgia vascular

Cirurgia oncológica

Cirurgia ortopédica

Cirurgias/Procedimentos de baixo risco hemorrágico

Não Interromper anticoagulação oral

Tratamentos estomatológicos (extração dentária, tratamento de raízes)

Cirurgia de cataratas

Cirurgias dermatológicas minor

Endoscopia/colonoscopia sem biópsia

Devem fazer “*bridging*” com HBPM

Doentes com elevado risco tromboembólico

Prótese mecânica mitral

FA com CHA_2DS_2 VASc=5-6

AVC ou AIT < 3-6 meses + FA ou prótese valvular mecânica

Trombofilia major

TEV <3 Meses

Devem fazer “*bridging*” com HBPM

Doentes com risco tromboembólico moderado

Prótese mecânica aórtica e FA

FA com CHA₂DS₂ VASc = 3-4

Não necessitam “*bridging*” com HBPM

Doentes com baixo risco tromboembólico

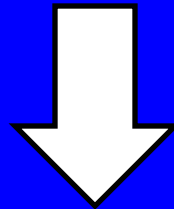
Prótese mecânica aórtica sem FA

FA com CHA₂DS₂ VASc= 0-2



Doente com elevado risco tromboembólico sob AVK

Suspender varfarina 5 dias antes da cirurgia



***“Bridging”* com HBPM (1mg/Kg/d) 12/12h
Entre o 4º dia e 24 h antes da cirurgia**

Doente com elevado risco tromboembólico sob AVK

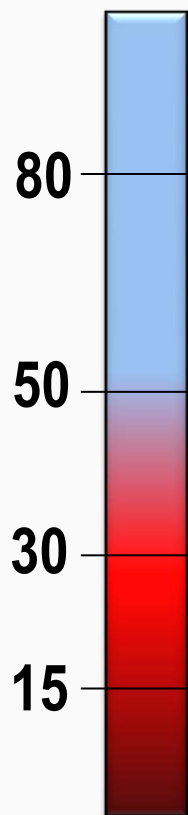
Reinicia varfarina 12-24h após a cirurgia

**Cirurgia de Bx risco hemorrágico: Inicia HBPM
(1mg/Kg/d) 24h depois da cirurgia**

**Cirurgia de Alto risco hemorrágico: Inicia HBPM
(1mg/Kg/d) 48-72h depois da cirurgia**

Timing de interrupção pre-operatória dos NOAC

Cl. Creat.
mL/min.



Dabigatran

Rivaroxaban

Apixaban

CARH: $\geq 48h$ antes
CRHN: $\geq 24h$ antes

Cirg Alto risco hemor.
 $\geq 48h$ antes

Cirg Alto risco hemor.
 $\geq 48h$ antes

CARH: $\geq 36h$ antes
CRHN: $\geq 72 h$ antes

Cirg risco hemor. NL
 $\geq 24h$ antes

Cirg risco hemor. NL
 $\geq 24h$ antes

CARH: $\geq 96h$ antes
CRHN: $\geq 48h$ antes

CARH: $\geq 48h$ antes

CRHN: $\geq 36 h$ antes

CARH: $\geq 48h$ antes
CRHN: $\geq 36h$ antes

Eliminação renal

80%

35%

27%

Timing de reinício pos-operatório dos NOAC

Dabigatran

Rivaroxaban

Apixaban

Cirurgia de alto risco hemorrágico

Doente de alto risco hemorrágico

≥ 48-72h depois

Cirurgia de baixo risco hemorrágico

Doente de baixo risco hemorrágico

24 h depois

Terapêutica antitrombótica na gravidez



Indicações para anticoagulação na grávida



1. **Próteses mecânicas**
2. **Estenose mitral com fibrilhação auricular persistente ou paroxística documentada**
3. **Estenose mitral em ritmo sinusal mas com trombo na AE**
4. **Estenose mitral em ritmo sinusal mas com história prévia de embolismo sistémico**
5. **5. FA não valvular em mulher com score CHA2DS2 VASc ≥ 2 (Ex: Grávida com FA paroxística, miocardiopatia dilatada com Fej diminuída e antecedentes de embolismo sistémico)**

Indicações para anticoagulação na grávida



- 1. Grávidas previamente sob anticoagulação oral por Hx prévia de TEV de repetição**
- 2. Grávidas previamente sob anticoagulação oral por S. antifosfolípido com hx prévia de TEV**
- 3. Grávidas previamente anticoaguladas por Trombofilia e TEV de repetição**
- 4. Grávidas com Trombose venosa profunda durante a actual gravidez**



Varfarina

A incidência de embriopatia é dose dependente

- Dose < 5mg risco <3%
- Dose > 5mg risco >8%

Até à 6ª semana o risco é de morte *in* útero (gravidez anembrionica)

Entre a 6ª e a 12ª semana o risco é de malformações do SNC, anomalias nos ossos longos e da face.

Varfarina

No **último trimestre** associa-se a maior risco de hemorragia retroplacentária e de parto prematuro.

É eliminada no leite materno em quantidades ínfimas pelo que não contraindica a amamentação.



Protocolo para terapêutica antitrombótica na gravidez



1º Trimestre

HBPM em dose adaptada ao peso (1mg/Kg 12/12h)

Atenção! a dose deve ser ajustada à medida que o peso da grávida aumenta.

2º e 3º trimestres (até 36ªS)

Varfarina . INR terapêutico (2.5-3.0)

36ª semana em diante

HBPM até 24h antes do parto ou HNF até 4-6h antes do parto