L'Ospedale dei Fiorentini

Giornate Mediche di Santa Maria Nuova 2015

VII EDIZIONE

L'ECCELLENZA DELLE CURE IN OSPEDALE: *Santa Maria Nuova si confronta con la sua storia e con l'innovazione*

TAVOLA ROTONDA

La terapia con i Nuovi Anticoagulanti orali: la gestione "sul campo" di una classe di farmaci innovativi

LA GESTIONE DELLE COMPLICANZE EMORRAGICHE

LUCA MASOTTI

MEDICINA INTERNA SMN FIRENZE

Comparison of the efficacy and safety of new oral anticoagulants with warfarin in patients with atrial fibrillation: a meta-analysis of randomised trials

Christian T Ruff, Robert P Giugliano, Eugene Braunwald, Elaine B Hoffman, Naveen Deenadayalu, Michael D Ezekowitz, A John Camm, Jeffrey I Weitz, Basil S Lewis, Alexander Parkhomenko, Takeshi Yamashita, Elliott M Antman

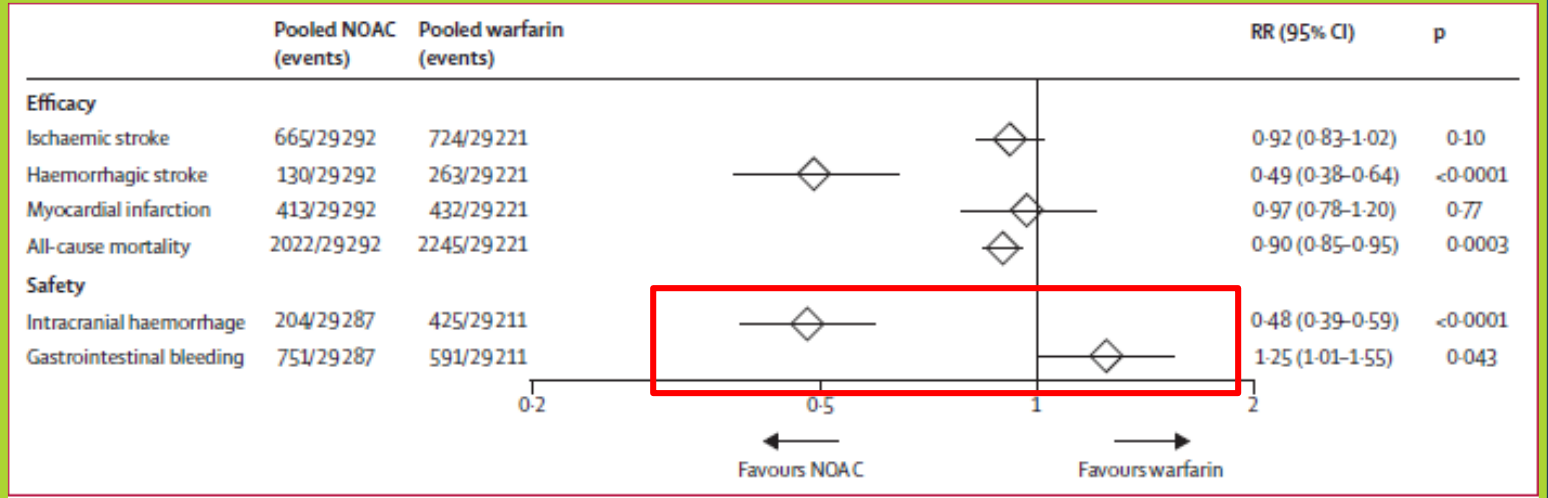


***Figure 2*: Secondary efficacy and safety outcomes**

Data are n/N, unless otherwise indicated. Heterogeneity: ischaemic stroke I^2=32%, p=0·22; haemorrhagic stroke I^2=34%, p=0·21; myocardial infarction I^2=48%, p=0·13; all-cause mortality I^2=0%, p=0·81; intracranial haemorrhage I^2=32%, p=0·22; gastrointestinal bleeding I^2=74%, p=0·009. NOAC=new oral anticoagulant. RR=risk ratio.

Cardiovascular, Bleeding, and Mortality Risks in Elderly Medicare Patients Treated With Dabigatran or Warfarin for Nonvalvular Atrial Fibrillation

David J. Graham, MD, MPH; Marsha E. Reichman, PhD; Michael Wernecke, BA; Rongmei Zhang, PhD; Mary Ross Southworth, PharmD; Mark Levenson, PhD; Ting-Chang Sheu, MPH; Katrina Mott, MHS; Margie R. Goulding, PhD; Monika Houstoun, PharmD, MPH; Thomas E. MaCurdy, PhD; Chris Worrall, BS; Jeffrey A. Kelman, MD, MMSc

Circulation. 2015;131:157-164.

Characteristic	Dabigatran, % (n=67 207)	Warfarin, % (n=67 207)	Standardized Mean Difference
Age group, y			
65–74	42	41	0.01
75–84	43	43	0.01
≥85	16	16	0.00
Female sex	51	52	0.01

Table 2. Outcome Event Counts, Incidence Rates, and Adjusted Hazard Ratios With 95% CIs Comparing Propensity Score–Matched New-User Cohorts of Dabigatran and Warfarin Treated for Nonvalvular Atrial Fibrillation, With Warfarin as the Reference Group

	No. of Events		Incidence Rate per 1000 Person-Years		Adjusted Hazard Ratio (95% CI)	*P* Value
	Dabigatran	Warfarin	Dabigatran	Warfarin		
Primary outcomes						
Ischemic stroke	205	270	11.3	13.9	0.80 (0.67–0.96)	0.02
Major hemorrhage	777	851	42.7	43.9	0.97 (0.88–1.07)	0.50
Gastrointestinal	623	513	34.2	26.5	1.28 (1.14–1.44)	<0.001
Intracranial	60	186	3.3	9.6	0.34 (0.26–0.46)	<0.001
Intracerebral	44	142	2.4	7.3	0.33 (0.24–0.47)	<0.001
Acute myocardial infarction	285	327	15.7	16.9	0.92 (0.78–1.08)	0.29
Secondary outcomes						
All hospitalized bleeds	1079	1139	59.3	58.8	1.00 (0.92–1.09)	0.97
Mortality*	603	744	32.6	37.8	0.86 (0.77–0.96)	0.006

*For 1064 deaths not preceded by a primary study outcome, the adjusted hazard ratio (95% confidence interval [CI]) was 0.89 (0.79–1.00; *P*=0.051), whereas for 283 deaths occurring within 30 days after a primary outcome, the adjusted hazard ratio (95% CI) was 0.77 (0.61–0.98; *P*=0.03).

XANTUS: a real-world, prospective, observational study of patients treated with rivaroxaban for stroke prevention in atrial fibrillation

A. John Camm[1]*, Pierre Amarenco[2], Sylvia Haas[3], Susanne Hess[4], Paulus Kirchhof[5,6], Silvia Kuhls[7], Martin van Eickels[4], and Alexander G.G. Turpie[8], on behalf of the XANTUS Investigators

European Heart Journal 2015

	Rivaroxaban (*N* = 6784)	
	Incidence proportion, *n* (%)	Incidence rate, events per 100 patient-years (95% CI)
Major bleeding	128 (1.9)	2.1 (1.8–2.5)
Fatal	12 (0.2)	0.2 (0.1–0.3)
Critical organ bleeding	43 (0.6)	0.7 (0.5–0.9)
Intracranial haemorrhage	26 (0.4)	0.4 (0.3–0.6)
Intraparenchymal	6 (0.1)	
Subarachnoid	5 (0.1)	
Intraventricular	6 (0.1)	
Subdural haematoma	6 (0.1)	
Epidural haematoma	1 (<0.05)	
Haemorrhagic transformation of ischaemic stroke	3 (<0.05)	
Missing	2 (<0.05)	
Mucosal bleeding[a]	60 (0.9)	1.0 (0.7–1.3)
Gastrointestinal	52 (0.8)	0.9 (0.6–1.1)
Haemoglobin decrease ≥2 g/dL[b]	52 (0.8)	0.9 (0.6–1.1)
Transfusion of ≥2 units of packed red blood cells or whole blood[b]	53 (0.8)	0.9 (0.6–1.1)

Table 3 Causes of treatment-emergent adjudicated death

Adjudicated causes of death	Number of patients (*N* = 118[a]), *n* (%)
Cardiovascular	49 (41.5)
Cardiac decompensation, heart failure	24 (20.3)
Sudden or unwitnessed death	14 (11.9)
MI	6 (5.1)
Non-haemorrhagic stroke	4 (3.4)
Dysrhythmia	1 (0.8)
Venous thromboembolism	0
Other vascular event	0
Cancer	23 (19.5)
Other	16 (13.6)
Bleeding	12 (10.2)
Extracranial haemorrhage	5 (4.2)
Intracranial bleeding	7 (5.9)
Infectious disease	10 (8.5)
Unexplained	9 (7.6)

Real-world Comparison of Bleeding Risks among Non-Valvular Atrial Fibrillation Patients on Apixaban, Dabigatran, Rivaroxaban:

Cohorts Comprising New Initiators and/or Switchers from Warfarin

P. Tepper, J. Mardekian, C. Masseria, H. Phatak, S. Kamble, Y. Abdulsattar, W. Petkun, **GYH. Lip**

ESC CONGRESS LONDON 2015

	Apixaban (N=8785)		
Inpatient bleeding	N	n/N (%)	Incidence %/year
Any	129	1.5	5.0
ICH	13	0.1	0.5
GI	80	0.9	3.1
Other	43	0.5	1.7

Gastrointestinal bleeding with the new oral anticoagulants – defining the issues and the management strategies

Jay Desai[1]; Jennifer M. Kolb[2]; Jeffrey I. Weitz[3]; James Aisenberg[2]

[1]Department of Medicine (Division of Gastroenterology), New York University, New York, New York, USA; [2]Department of Medicine (Division of Gastroenterology), Icahn School of Medicine at Mount Sinai, New York, New York, USA; [3]Departments of Medicine and Biochemistry and Biomedical Sciences, McMaster University and the Thrombosis and Atherosclerosis Research Institute, Hamilton, Ontario, Canada

Table 4: NOACs and GI bleeding: prevention strategies.

1. Confirm that NOAC indication is appropriate and that there are no absolute contra-indications to NOAC administration.
2. Confirm that NOAC dosage is appropriate (e.g. dose dabigatran as indicated by creatinine clearance).
3. Screen all patients for presence of on-going GI bleeding by history (history of recent melena or rectal bleeding) and physical exam (digital rectal exam). Consider screening with laboratory testing (faecal occult blood testing, haemoglobin evaluation and evaluation of iron stores). If GI bleeding is suggested, consider GI investigation prior to initiating NOAC treatment.
4. Assess for history of previous GI bleeding and consider diagnostic interventions (e.g. endoscopy) or therapeutic interventions (e.g. concomitant administration of a PPI) where indicated.
5. Assess for co-administration of drugs such as anti-platelet agents or NSAIDs which increase the risk NOAC related GI bleeding.
6. If patient is concurrently taking anti-platelet medication, weigh the risks, benefits, and alternatives continuing NOAC plus anti-platelet agent.
7. If patient is taking chronic NSAIDs, consider alternative therapies and/or co-administration of a gastroprotective agent such as a PPI.
8. Consider non-medication risk factors such as alcohol intake, and encourage risk factor modification
9. Assess creatinine clearance and institute renal protective measures as indicated (especially in patients receiving dabigatran).
10. Counsel the patient regarding the potential for increased risk of GI bleeding in the setting of dehydration, concomitant illness, or concomitant medication use, and the recommended measures in these settings (e.g. seeking prompt medical attention, maintaining hydration, performing laboratory assessments of renal function).

clinical bleeding. Orally-administered antithrombotic drugs may abet the tendency of the GI tract to bleed via at least four mechanisms: 1) systemic anticoagulant effect; 2) topical anticoagulant effect; 3) topical direct caustic action; 4) topical biological action of the drug unrelated to coagulation (e.g. inhibition of mucosal healing). These mechanisms may occur in combination: for example, aspirin may promote gastroduodenal ulcer bleeding via topical injury and systemic anti-platelet effects.

Management dei sanguinamenti in corso di trattamento con farmaci anticoagulanti: obiettivi

- Neutralizzare l'attività anticoagulante
  - Reverse e monitorizzazione dell'effetto anticoagulante
- Far cessare il sanguinamento e trattare le complicanze, talora gravi, secondarie all'emorragia
  - Gestione e monitorizzazione clinica

Definizione di emorragie maggiori/a rischio di vita in corso di terapia antitrombotica. Criteri ISTH

- Emorragia intracranica ed altro sanguinamento in organi critici (midollo spinale, peritoneo, retroperitoneo, tratto gastro-enterico, torace, articolazioni, occhio, sindrome compartimentale)
- Emorragie che determinano un calo di 2 g/dl di Hb o che richiedono almeno 2 sacche di GR per trattarle
- Emorragie che richiedono l'intervento chirurgico o manovre invasive per arrestarle
- Emorragie fatali

Schulman S et al. JTH 205

Definizione di emorragie minori in corso di terapia antitrombotica. Criteri ISTH

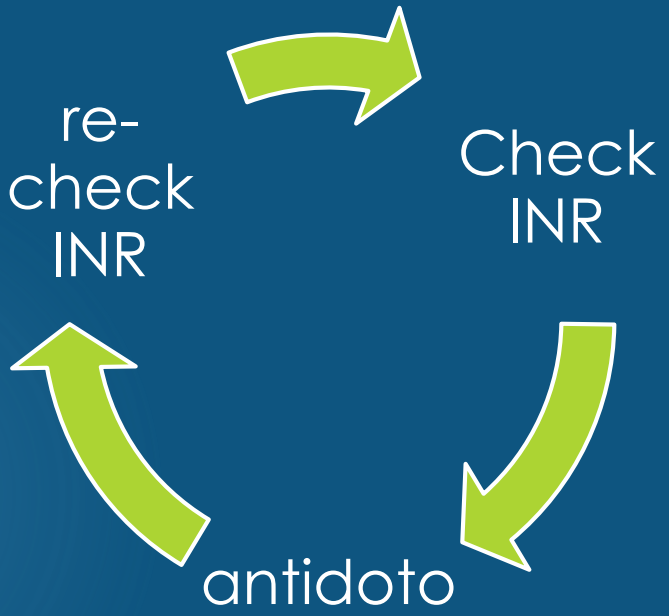
- Ecchimosi e petecchie
- Ematomi sottocutanei e muscolari
- Epistassi
- Emorragia congiuntivale e palpebrale
- Gengivorragie
- Emoftoe
- Otorragia
- Ematuria
- Meno-metrorragie

Schulman S et al. JTH 205

Reverse
Antidoti specifici

- Vitamina K per i VKA
- Solfato di protamina per la UFH

Reverse dei AVK



Flow-chart reverse AVK

Se il valore dell'INR non è ancora disponibile

CCP a 3 fattori 20 UI/Kg infusione in 10 min

Appena disponibile il risultato INR:

CCP a 3 fattori completare dose:

INR < 2.0 nessuna dose aggiuntiva

INR 2.0-3.0 aggiungere 10 UI/Kg

INR 3.0-4.0 aggiungere 20 UI/kg

INR > 4.0 aggiungere 30 UI/Kg

Se valore di INR disponibile

CCP a 3 fattori infusione in 10 min

INR 1.5-2.0	**20 UI/Kg**
INR 2.0-3.0	**30 UI/ Kg**
INR 3.0-4.0	**40 UI/ Kg**
INR > 4.0	**50 UI/ Kg**

Considerare CCP a 4 fattori se INR > 4.0

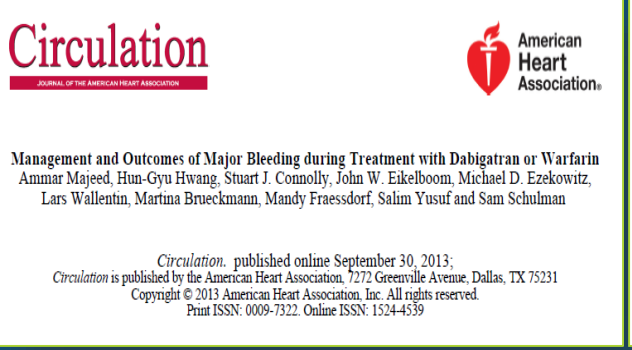
+

Vitamina K1 5-10 mg in soluzione fisiologica 250 cc alla velocità di 1mg/min

In alternativa al CCP (se non disponibile) PFC 15-30 ml/Kg o FVIIra 90 microg/Kg

Controllo INR al termine infusione

Se INR ≥ 1.5 ripetere infusione di CCP come sopra



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American Heart Association.

Management and Outcomes of Major Bleeding during Treatment with Dabigatran or Warfarin

Ammar Majeed, Hun-Gyu Hwang, Stuart J. Connolly, John W. Eikelboom, Michael D. Ezekowitz, Lars Wallentin, Martina Brueckmann, Mandy Fraessdorf, Salim Yusuf and Sam Schulman

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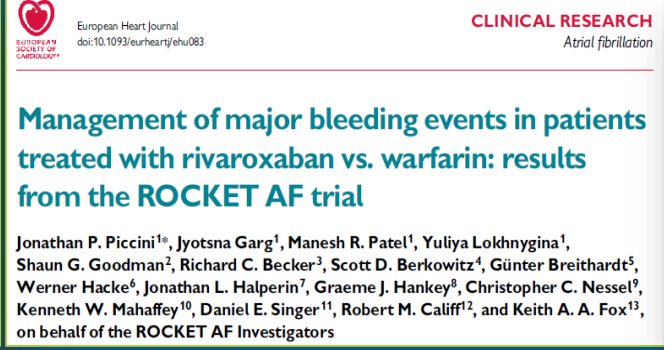
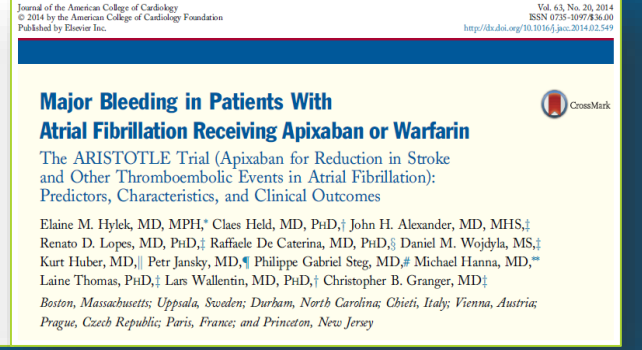


European Heart Journal
doi:10.1093/eurheartj/ehu083

CLINICAL RESEARCH
Atrial fibrillation

Management of major bleeding events in patients treated with rivaroxaban vs. warfarin: results from the ROCKET AF trial

Jonathan P. Piccini[1]*, Jyotsna Garg[1], Manesh R. Patel[1], Yuliya Lokhnygina[1], Shaun G. Goodman[2], Richard C. Becker[3], Scott D. Berkowitz[4], Günter Breithardt[5], Werner Hacke[6], Jonathan L. Halperin[7], Graeme J. Hankey[8], Christopher C. Nessel[9], Kenneth W. Mahaffey[10], Daniel E. Singer[11], Robert M. Califf[12], and Keith A. A. Fox[13], on behalf of the ROCKET AF Investigators



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Major Bleeding in Patients With Atrial Fibrillation Receiving Apixaban or Warfarin

The ARISTOTLE Trial (Apixaban for Reduction in Stroke and Other Thromboembolic Events in Atrial Fibrillation): Predictors, Characteristics, and Clinical Outcomes

Elaine M. Hylek, MD, MPH,* Claes Held, MD, PhD,† John H. Alexander, MD, MHS,‡ Renato D. Lopes, MD, PhD,‡ Raffaele De Caterina, MD, PhD,§ Daniel M. Wojdyla, MS,‡ Kurt Huber, MD,‖ Petr Jansky, MD,¶ Philippe Gabriel Steg, MD,# Michael Hanna, MD,** Laine Thomas, PhD,‡ Lars Wallentin, MD, PhD,† Christopher B. Granger, MD‡

Boston, Massachusetts; Uppsala, Sweden; Durham, North Carolina; Chieti, Italy; Vienna, Austria; Prague, Czech Republic; Paris, France; and Princeton, New Jersey

- Emorragie meno gravi in termini di mortalità
- Emorragie che impattano meno come durata di degenza

Gestione dei sanguinamenti negli studi di fase III

European Heart Journal
doi:10.1093/eurheartj/ehu083

CLINICAL RESEARCH
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bleed

Characteristic	Rivaroxaban (*n* = 431)	Warfarin (*n* = 409)
Within 1 day post-bleed		
Vitamin K	32 (7.4%)	54 (13.2%)
Protamine	0 (0.0%)	0 (0.0%)
Desmopressin	0 (0.0%)	0 (0.0%)
Epsilon-aminocaproic acid	2 (0.5%)	3 (0.7%)
Tranexamic acid	2 (0.5%)	11 (2.7%)
Prothrombin complex concentrates	4 (0.9%)	9 (2.2%)
Recombinant factor VIIa	0 (0.0%)	1 (0.2%)
Factor VIII concentrate	1 (0.2%)	1 (0.2%)
Factor IX concentrate	0 (0.0%)	3 (0.7%)
Within 2 days post-bleed		
Vitamin K	34 (7.9%)	60 (14.7%)
Protamine	0 (0.0%)	0 (0.0%)
Desmopressin	0 (0.0%)	0 (0.0%)
Epsilon-aminocaproic acid	2 (0.5%)	3 (0.7%)
Tranexamic acid	3 (0.7%)	14 (3.4%)
Prothrombin complex concentrates	4 (0.9%)	9 (2.2%)
Recombinant factor VIIa	0 (0.0%)	1 (0.2%)
Factor VIII concentrate	1 (0.2%)	1 (0.2%)
Factor IX concentrate	0 (0.0%)	3 (0.7%)
Aspirin discontinued	31 (7.2%)	38 (9.3%)
Within 3–5 days post-bleed		
Vitamin K	6 (1.4%)	18 (4.4%)
Protamine	0 (0.0%)	0 (0.0%)
Desmopressin	0 (0.0%)	1 (0.2%)
Epsilon-aminocaproic acid	0 (0.0%)	0 (0.0%)
Tranexamic acid	3 (0.7%)	8 (2.0%)
Prothrombin complex concentrates	0 (0.0%)	0 (0.0%)
Recombinant factor VIIa	0 (0.0%)	0 (0.0%)
Factor VIII concentrate	0 (0.0%)	0 (0.0%)
Factor IX concentrate	0 (0.0%)	0 (0.0%)
Aspirin discontinued	38 (8.8%)	41 (10.0%)

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Management and Outcomes of Major Bleeding during Treatment with Dabigatran or Warfarin

Ammar Majeed, Hun-Gyu Hwang, Stuart J. Connolly, John W. Eikelboom, Michael D. Ezekowitz, Lars Wallentin, Martina Brueckmann, Mandy Fraessdorf, Salim Yusuf and Sam Schulman

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Table 3. Hemostatic treatment for all major bleeding events in the RE-LY trial, GEE method*

	D 110 mg	D 150 mg	Dabigatran	Warfarin	P-value D 110 vs D 150	P-value D vs Warfarin	P-value D110 vs Warfarin	P-value D 150 vs Warfarin
Fresh frozen plasma, %	18	22	20	30	0.12	<0.001	<0.001	0.01
Cryoprecipitate, %	0.7	1.0	0.9	1.4	0.65	0.36	0.30	0.55
Platelets, %	3.2	3.7	3.5	5.0	0.69	0.17	0.17	0.31
Vitamin K, %	9.1	11	10.2	26	0.34	<0.001	<0.001	<0.001
Prothrombin complex concentrate, %	0.7	0.4	0.6	1.0	0.52	0.36	0.64	0.25
Recombinant factor VIIa, %	0.2	1.4	0.9	0.6	0.05	0.96	0.39	0.21
Coagulation factor replacement, %	0.2	0.6	0.4	1.0	0.39	0.21	0.13	0.47

*The generalized estimating equation for estimation of the parameters of a [illegible] linear model with a possible unknown correlation between outcomes. Includes events on treatment and up to 3 days after last dose.

Review Article

Management of the Bleeding Patient Receiving New Oral Anticoagulants: A Role for Prothrombin Complex Concentrates

Hindawi Publishing Corporation
BioMed Research International
Volume 2014, Article ID 583794, 7 pages

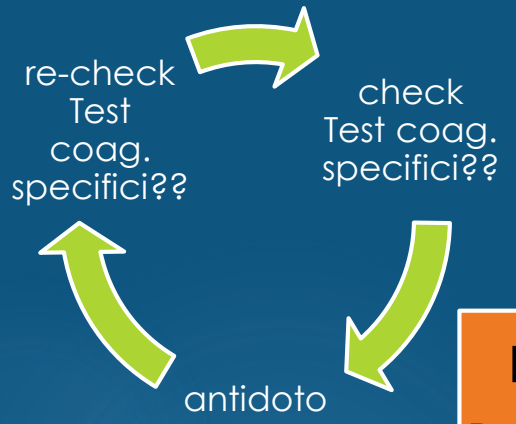
Lisa M. Baumann Kreuziger,[1] Joseph C. Keenan,[1] Colleen T. Morton,[2] and David J. Dries[2]

TABLE 3: Summary of animal and human data for reversal of dabigatran, rivaroxaban, and apixaban using factor concentrates.

	Dabigatran		Rivaroxaban		Apixaban	
	Animal	Human	Animal	Human	Animal	Human
3-factor PCC		Case report +/−				
4-factor PCC	Rats +/− Rabbits + Mice − Mice ICH +	In vitro + In vivo − Case report −	Rats + Rabbits +/−	In vitro +/− In vivo +		In vitro +
aPCC	Rats +/− Mice −	In vitro +	Rat + Primate +	In vitro +		In vitro +
rfVIIa	Rats +/− Mice +/− Mice ICH −	In vitro + Case report +/−	Rat + Rabbits +/− Primate +/−	In vitro +/−		In vitro +

+: effective; −: ineffective; +/−: mixed results between studies or between coagulation testing and bleeding outcomes; PCC: prothrombin complex concentrate; aPCC: activated prothrombin complex concentrate; rfVIIa: recombinant factor VIIa.

Possibilità di monitoraggio di laboratorio dei DOACs in ASF



Urgenza ed elezione

Dabigatran
Profilo cod 348

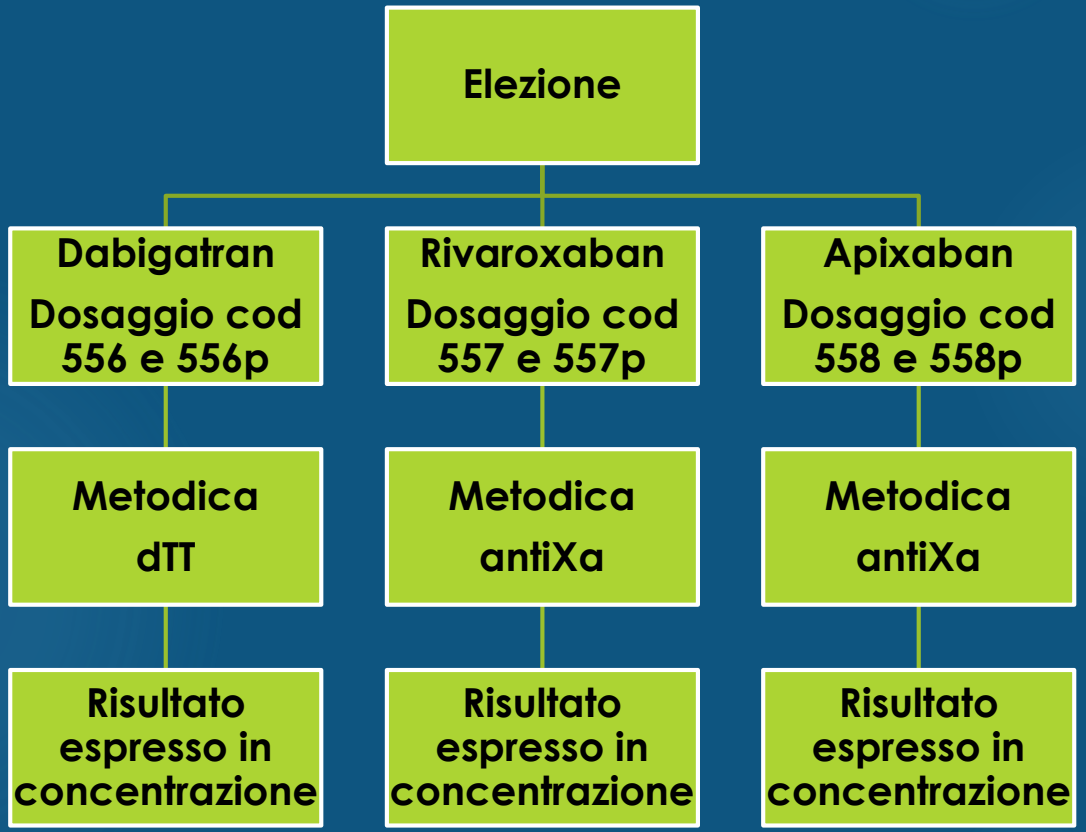
Rivaroxaban
Profilo cod 347

aPTT ratio

TT ratio

PT ratio

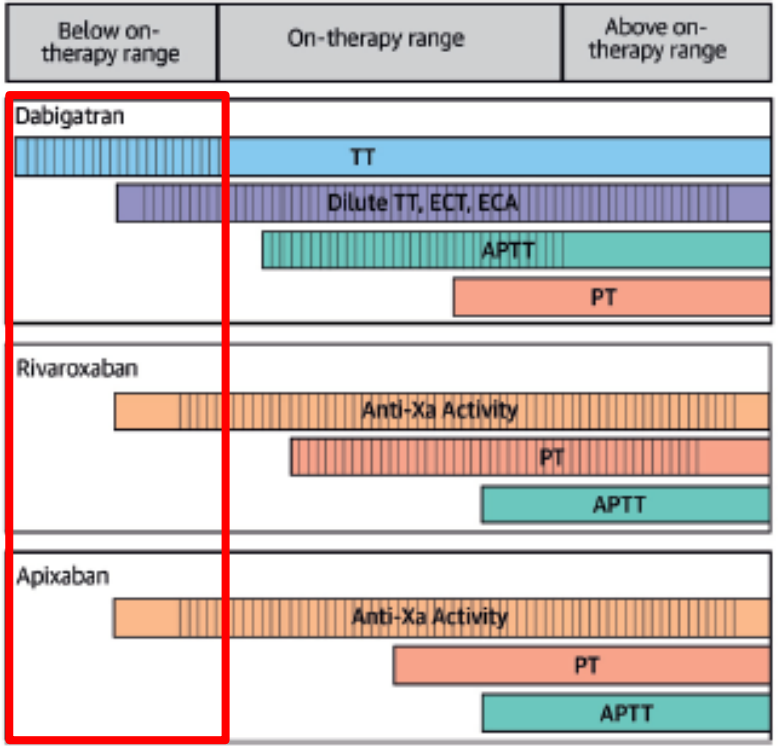
Possibilità di misurazione della concentrazione dei DOACs in ASF



Laboratory Measurement of the Anticoagulant Activity of the Non–Vitamin K Oral Anticoagulants

Adam Cuker, MD, MS,* Deborah M. Siegal, MD, MSc,† Mark A. Crowther, MD, MSc,† David A. Garcia, MD‡

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY



CENTRAL ILLUSTRATION Sensitivity and Linearity of Coagulation Assays to Below, Within, and Above Typical On-Therapy Concentrations of Dabigatran, Rivaroxaban, and Apixaban

Flow-chart reverse in corso di emorragia maggiore NAO correlata: possibile approccio in ASL 10

Supportive measures :

- mechanical compression
- endoscopic hemostasis if gastro-intestinal bleed
- surgical hemostasis
- fluid replacement (colloids if needed)
- RBC substitution if needed
- fresh frozen plasma (as plasma expander)
- platelet substitution (if platelet count ≤60x10^9/L)

Carbone attiv

Acido tranexa

CCP a 3 o 4 f

In caso d

FVIIra 90 microg/Kg

o

FEIBA 30-50 U/Kg

Ultrafiltrazione in casi selezionati

aban

l'assunzione

xtracraniche)

UI/Kg,

volte

In caso di mancata risposta clinica

FVIIra 90 microg/Kg

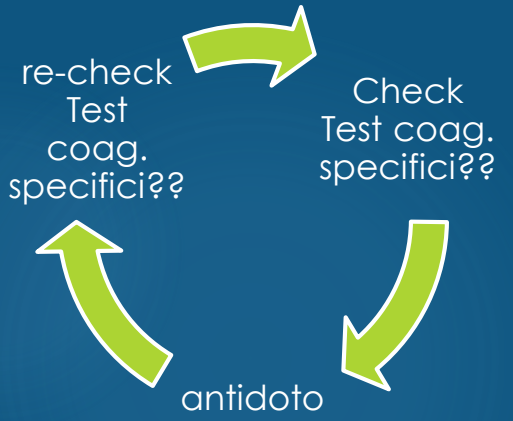
o

FEIBA 30-50 U/Kg

Reversing the new oral anticoagulants with prothrombin complex concentrates (PCCs): what is the evidence?

Gerhard Dickneite[1]; Maureane Hoffman[2]
[1]CSL Behring, Preclinical R&D, Marburg, Germany; [2]Department of Pa

Thromb Haemost 2014; 111: 189–198



Conclusions

- PCCs (including activated PCCs) show promise for reversing the anticoagulant effects of the new oral anticoagulants.
- Conventional laboratory assays do not correlate well with bleeding or reversal of anticoagulation in this setting; thrombin generation assays appear to have the best predictive value. However, it should be noted that there are significant differences in the methods for conducting such assays, which can complicate comparisons between studies.
- Both activated (e.g. FEIBA®) and non-activated PCCs correct most parameters of thrombin generation assays (initial rate, peak and ETP) *in vitro*. However, non-activated PCCs seem to lack the ability to correct the lag time before onset of thrombin generation while FEIBA® partially corrects the lag time.
- It is possible to "overshoot" and enhance parameters of thrombin generation to supranormal levels. This effect is more prominent with FEIBA® than non-activated PCCs. Thus, while FEIBA® might be more haemostatically effective than non-activated PCC, it may also pose a greater risk of thrombosis.
- The dosing and effectiveness of a strategy for reversal of the new oral anticoagulants probably depends on the level of the anticoagulant present.
- No studies have yet examined the effectiveness of any reversal strategy in bleeding human patients.

Possibili metodi per lo studio dell'emostasi nel suo complesso: ipotesi di studio o possibilità concrete?

- Tromboelastografia
  - TEG
  - ROTEM
- Test di generazione di trombina??
- Analisi delle curve dell'aPTT??

Reverse dei NAO: il prossimo futuro….

- Antidoti specifici (in corso studi di fase III con buoni dati preliminari)
  - Anticorpi monoclonali
    - Idarucizumab per dabigatran
  - Proteine competitive
    - AndeXanet per gli antiXa
    - Ciraparantag (Aripazine, PER977) per dabigatran, antiXa, LMWH e fondaparinux

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Table 1. Clinical Characteristics of the Patients.*

Characteristic	Group A (N=51)	Group B (N=39)	Total (N=90)
Age — yr			
Median	77.0	76.0	76.5
Range	48–93	56–93	48–93
Male sex — no. (%)	32 (63)	18 (46)	50 (56)
Race or ethnic group — no. (%)†			
Asian	5 (10)	1 (3)	6 (7)
Hawaiian or Pacific Islander	3 (6)	3 (8)	6 (7)
White	43 (84)	35 (90)	78 (87)
Weight — kg			
Median	70.5	73.0	71.9
Range	42.4–127.5	49.5–116.0	42.4–127.5
Creatinine clearance‡			
Value — ml/min			
Mean	59±33	65±36	62±35
Median	54	60	58
Range	16–187	11–171	11–187
Distribution — no. (%)			
<30 ml/min	5 (10)	7 (18)	12 (13)
30 to <50 ml/min	14 (27)	6 (15)	20 (22)
50 to <80 ml/min	16 (31)	11 (28)	27 (30)
≥80 ml/min	6 (12)	9 (23)	15 (17)
Missing data	10 (20)	6 (15)	16 (18)
Dose of dabigatran — no. (%)			
150 mg twice daily	14 (27)	15 (38)	29 (32)
110 mg twice daily	34 (67)	24 (62)	58 (64)
75 mg twice daily	1 (2)	0	1 (1)
Other	2 (4)	0	2 (2)
Indication for dabigatran — no. (%)			
Atrial fibrillation	47 (92)	39 (100)	86 (96)
Venous thromboembolism	1 (2)	0	1 (1)
Other	3 (6)	0	3 (3)
Time since last intake of dabigatran			
Median — hr	15.2	16.6	15.4
Distribution — no. (%)			
<12 hr	17 (33)	15 (38)	32 (36)
12 to <24 hr	21 (41)	10 (26)	31 (34)
24 to <48 hr	12 (24)	10 (26)	22 (24)
≥48 hr	1 (2)	4 (10)	5 (6)
Elevated dilute thrombin time at baseline — no. (%)	40 (78)	28 (72)	68 (76)
Elevated ecarin clotting time at baseline — no. (%)	47 (92)	34 (87)	81 (90)
Type of bleeding — no. (%)§			
Intracranial	18 (35)	—	18 (20)
Trauma-related	9 (18)	—	9 (10)
Gastrointestinal	20 (39)	—	20 (22)
Other	11 (22)	—	11 (12)

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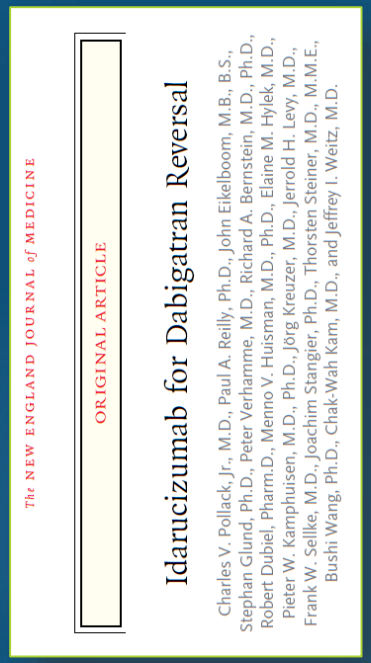
Costo e costo/beneficio ??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- 18 decessi su 90 pazienti (20%)
  - 9 nei 51 pazienti con emorragia grave (17,6%)
  - 9 nei 39 pazienti sottoposti a chirurgia d'urgenza (23%)
- 5 sanguinamenti fatali
  - 3 nei pazienti con emorragia grave (5,8%)
  - 2 nei pazienti sottoposti a chirurgia d'urgenza (5,1%)
- 3 casi su 18 ICH (16,6%) hanno presentato progressione della ICH o ri-sanguinamento
- 5 eventi trombotici (5,5%)

Emorragie minori

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

arco Alings[3], Matthias Antz[4], Jonas Oldgren[7], Peter Sinnaeve[2],

EH

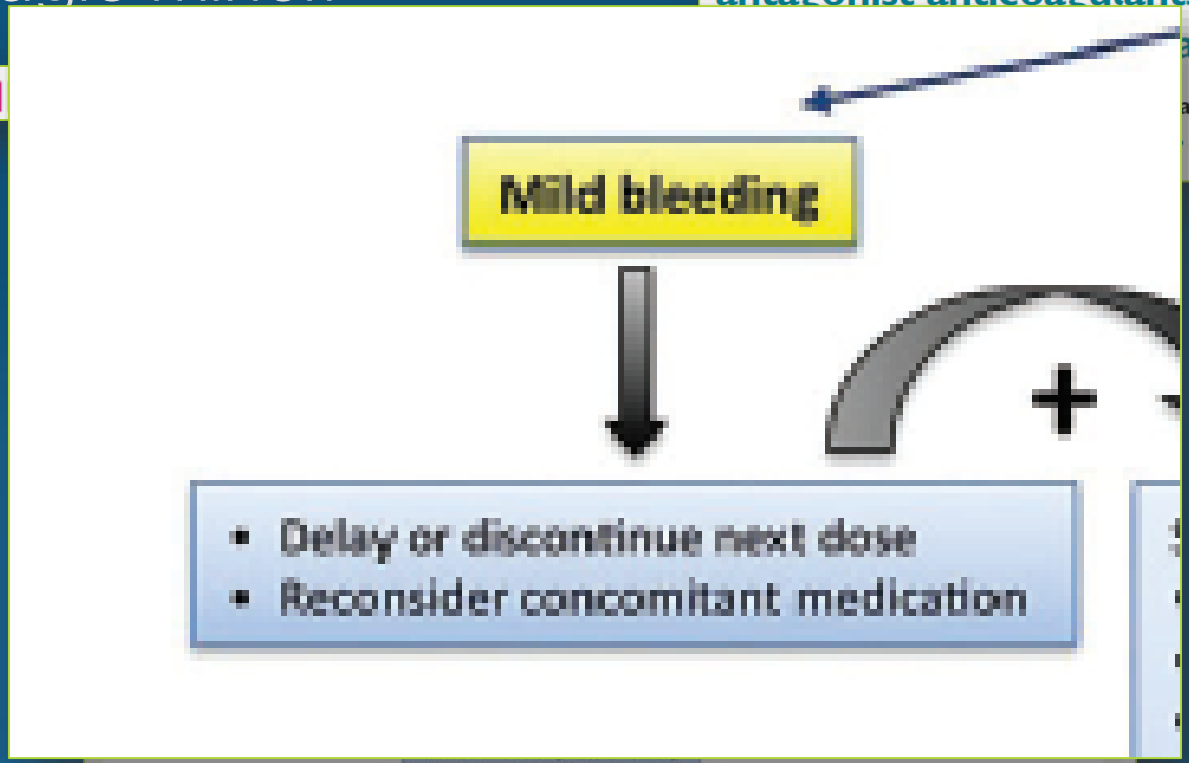

Figure 5 Management of bleeding in patients taking NOACs. Possible therapeutic measures in case of minor or severe bleeding in patients on NOAC therapy. Based on van Ryn *et al.*[39]

Take home messages

- Il reverse urgente rappresenta il cornerstone del management pratico dei sanguinamenti maggiori/a rischio di vita in corso di terapie anticoagulanti in combinazione con misure generali
- La gestione del reverse urgente dei NAO è ancora controversa perché non sono ancora disponibili antidoti specifici (**di prossima commercializzazione**) ed i fattori pro-emostatici non specifici hanno prodotto risultati non univoci negli studi sperimentali e ci sono pochi dati di vita reale
- L'uso di misure di supporto generale sembra essere efficace nella maggior parte dei casi di sanguinamento da NAO, specie per le emorragie extracraniche
- Tra i punti di maggior controversia vi è come monitorare il reverse. Per molti casi, il solo monitoraggio clinico potrebbe essere il target