TERAPIA PUENTE PARA CIRUGÍA ELECTIVA EN PACIENTES ANTICOAGULADOS

IV CURSO EDUCATIVO 2015-TRUJILLO: ACTUALIZACIÓN EN HEMATOLOGÍA

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GENERALIDADES

- Manejo perioperatorio de pacientes que reciben Warfarina o antiplaquetarios y requieren una cirugía: Dilema
- Afecta a 250,000 pacientes en N.A.
- Escasez de estudios bien diseñados
- Objetivos de terapia anticoagulante puente:
  - Minimizar riesgo de tromboembolismo arterial en pacientes con válvula cardiáca mecánica o FA y minimizar TEV recurrente.

Douketics J. Perioperative management of antithrombotic therapy. Chest 2012;141;E326S-E350S.

ASPECTOS QUE CONSIDERAR

- Evaluación del paciente:
  - Riesgo para tromboembolismo
  - Riesgo para sangrado perioperatorio
- No hay esquemas de estratificación de riesgo validados
- Recomendaciones basadas en evidencia indirecta y experiencia cínica

Douketics J. Perioperative management of antithrombotic therapy. Chest 2012;141;E326S-E350S

Table 1—*[Introduction] Suggested Risk Stratification for Perioperative Thromboembolism*

Risk Stratum	Indication for VKA Therapy		
	Mechanical Heart Valve	Atrial Fibrillation	VTE
High[a]	• Any mitral valve prosthesis • Any caged-ball or tilting disc aortic valve prosthesis • Recent (within 6 mo) stroke or transient ischemic attack	• $CHADS_2$ score of 5 or 6 • Recent (within 3 mo) stroke or transient ischemic attack • Rheumatic valvular heart disease	• Recent (within 3 mo) VTE • Severe thrombophilia (eg, deficiency of protein C, protein S, or antithrombin; antiphospholipid antibodies; multiple abnormalities)
Moderate	• Bileaflet aortic valve prosthesis and one or more of the of following risk factors: atrial fibrillation, prior stroke or transient ischemic attack, hypertension, diabetes, congestive heart failure, age > 75 y	• $CHADS_2$ score of 3 or 4	• VTE within the past 3-12 mo • Nonsevere thrombophilia (eg, heterozygous factor V Leiden or prothrombin gene mutation) • Recurrent VTE • Active cancer (treated within 6 mo or palliative)
Low	• Bileaflet aortic valve prosthesis without atrial fibrillation and no other risk factors for stroke	• $CHADS_2$ score of 0 to 2 (assuming no prior stroke or transient ischemic attack)	• VTE > 12 mo previous and no other risk factors

$CHADS_2$ = congestive heart failure, hypertension, age ≥ 75 years, diabetes mellitus, and stroke or transient ischemic attack; VKA = vitamin K antagonist.

[a]High-risk patients may also include those with a prior stroke or transient ischemic attack occurring > 3 mo before the planned surgery and a $CHADS_2$ score < 5, those with prior thromboembolism during temporary interruption of VKAs, or those undergoing certain types of surgery associated with an increased risk for stroke or other thromboembolism (eg, cardiac valve replacement, carotid endarterectomy, major vascular surgery).

CIRUGÍAS/PROCEDIMIENTOS ASOCIADOS ALTO RIESGO SANGRADO

- Cirugía urológica
- Marcapaso
- Resección de polipos de colon
- Organos altamente vasculares
- Cirugía mayor con injuria tisular extensa
- Cirugía cardiáca, intracraneal o espinal

Douketics J. Chest 2012;141; E326s-E350s.

CHEST Supplement

ANTITHROMBOTIC THERAPY AND PREVENTION OF THROMBOSIS, 9TH ED: ACCP GUIDELINES

Perioperative Management of Antithrombotic Therapy

Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines

James D. Douketis, MD, FCCP; Alex C. Spyropoulos, MD, FCCP; Frederick A. Spencer, MD; Michael Mayr, MD; Amir K. Jaffer, MD, FHM; Mark H. Eckman, MD; Andrew S. Dunn, MD; and Regina Kunz, MD, MSc (Epi)

RECOMENDACIONES

Results: In patients requiring vitamin K antagonist (VKA) interruption before surgery, we recommend stopping VKAs 5 days before surgery instead of a shorter time before surgery (Grade 1B). In patients with a mechanical heart valve, atrial fibrillation, or VTE at high risk for thromboembolism, we suggest bridging anticoagulation instead of no bridging during VKA interruption (Grade 2C); in patients at low risk, we suggest no bridging instead of bridging (Grade 2C). In patients who require a dental procedure, we suggest continuing VKAs with an oral prohemostatic agent or stopping VKAs 2 to 3 days before the procedure instead of alternative strategies (Grade 2C).

Douketics J. Chest 2012;141; E326s-E350s.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Perioperative Bridging Anticoagulation in Patients with Atrial Fibrillation

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NEJM.org 22 june,2015

ESTUDIO BRIDGE

- ¿ En pacientes con fibrilación auricular, es necesaria la terapia puente con heparina durante la suspensión de la warfarina, antes y después de una operación o procedimiento?
- Diseño: estudio controlado-placebo, doble ciego y aleatorizado.

NEJM.org 22 june,2015

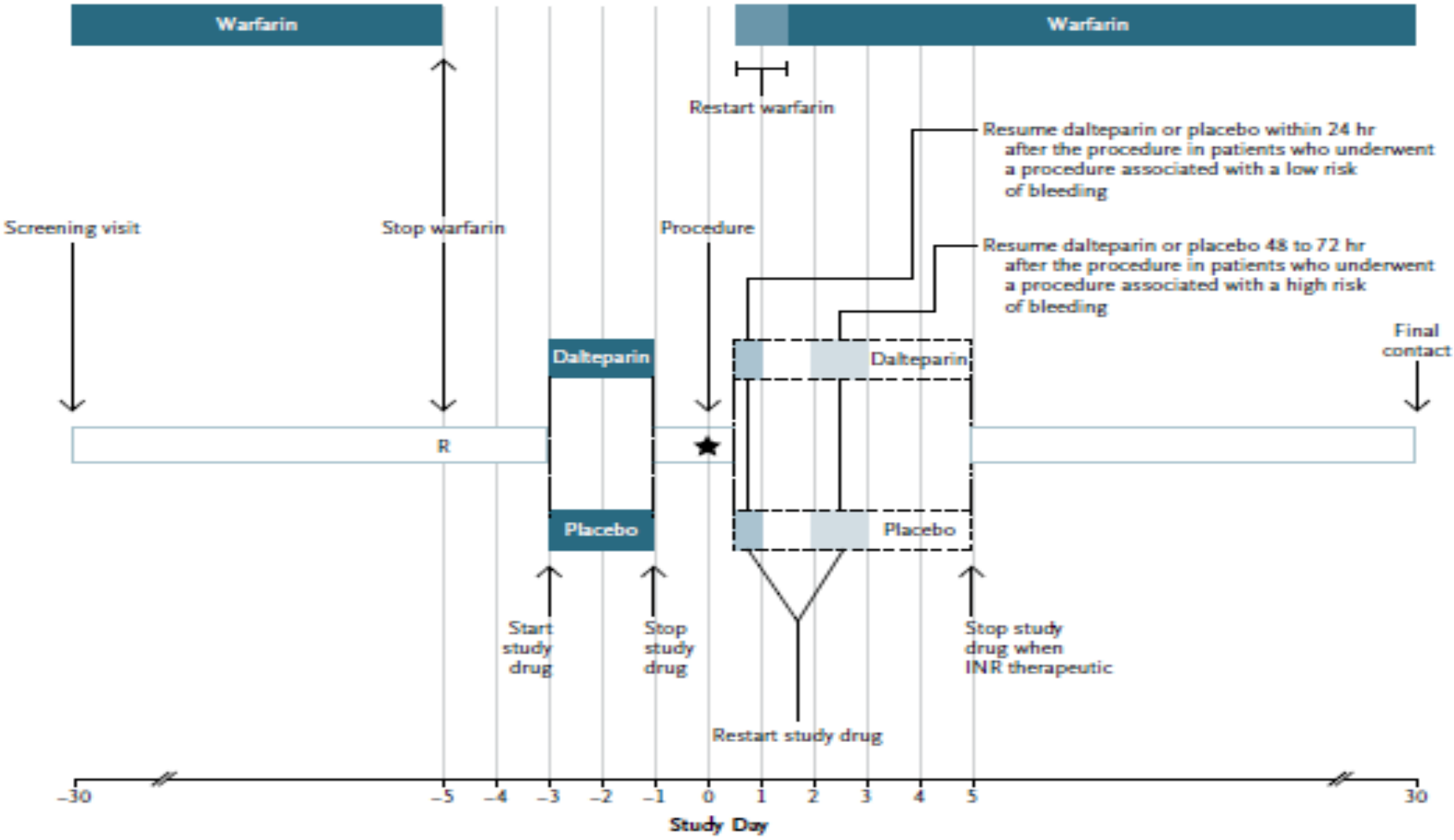

Figure 1. BRIDGE Study Design.

Screening visits occurred between 30 days and 5 days before the planned procedure, and randomization (R) occurred 5 days before the procedure. Warfarin treatment was discontinued 5 days before the procedure, and administration of the study drug was initiated 3 days before the procedure. It was recommended that the international normalized ratio (INR) be measured 1 day before the procedure; if the INR was greater than 1.8, oral vitamin K (1.0 to 2.5 mg) was recommended; if the INR was 1.5 to 1.8, oral vitamin K was optional. If the procedure or surgery was delayed up to 3 days, administration of the study drug was continued until 24 hours before the procedure. Warfarin treatment was restarted on the evening of or the day after the procedure, and the study drug was restarted 12 to 24 hours after a minor (or low-bleeding-risk) procedure and 48 to 72 hours after a major (or high-bleeding-risk) procedure. Administration of the study drug was continued after the procedure until the INR was 2.0 or higher on one occasion. The final patient follow-up occurred 30 days after the procedure. LMWH denotes low-molecular-weight heparin.

CRITERIOS DE INCLUSIÓN

Inclusion/Exclusion Criteria

Inclusion criteria
All of the following 5 criteria must be satisfied for trial eligibility:

1) Adult male or female, age 18 years or older
2) Receiving warfarin therapy (for at least 3 months), administered to achieve a target international normalized ratio range of 2.0 to 3.0
3) Require temporary interruption of warfarin for pre-specified elective procedure or surgery
4) Have *at least one* of the following conditions:
    a. Chronic (permanent or paroxysmal) nonvalvular atrial fibrillation* or atrial flutter, confirmed by at least one prior electrocardiography recording or pacemaker/ACD interrogation
    b. Chronic (permanent or paroxysmal) valvular atrial fibrillation* or atrial flutter with evidence of mitral valvular heart disease, confirmed by same criteria as nonvalvular atrial fibrillation* or atrial flutter
5) Have *at least one* of the following major stroke risk factors:
    a. Age >75 years
    b. Hypertension
    c. Diabetes mellitus
    d. Congestive heart failure or left ventricular dysfunction
    e. Previous ischemic stroke, systemic embolism, or transient ischemic attack

CRITERIOS DE EXCLUSIÓN

Exclusion criteria

One or more of the following criteria precludes trial eligibility:

1) Any mechanical prosthetic heart valve
2) Stroke (ischemic or hemorrhagic), systemic embolism, or transient ischemic attack within past 12 weeks
3) Venous thromboembolism (deep vein thrombosis and/or pulmonary embolism) within past 12 weeks
4) Major bleeding within past 6 weeks
5) Severe renal insufficiency (calculated creatinine clearance <30 mL/min)
6) Thrombocytopenia (platelet count $<100 \times 10^9$/L)
7) Life expectancy <1 month
8) Condition that impairs compliance with trial protocol (e.g., cognitive impairment, uncontrolled psychiatric condition, geographic inaccessibility)
9) Pregnancy
10) Allergy to heparin or history of heparin-induced thrombocytopenia
11) Having one of the following surgeries/procedures during warfarin interruption
    a. Cardiac surgery (*e.g.*, coronary artery bypass, heart valve replacement)
    b. Neurosurgery that is intracranial or intraspinal (*e.g.*, tumor resection, aneurysm repair)
    c. High-risk non-surgical procedures (*e.g.*, brain biopsy)

TIPO DE CIRUGÍA/ PROCEDIMIENTO

Minor or low-bleeding-risk surgery/procedure

- gastrointestinal endoscopy (with or without biopsy)
- cardiac catheterization (with or without percutaneous coronary intervention)
- dental surgery or other dental procedure
- dermatologic surgery or other dermatologic procedure
- cataract removal or other ophthalmologic procedure
- any other surgery or procedure lasting <1 hour

Major or high-bleeding-risk surgery/procedure

- intra-abdominal surgery (e.g., bowel or visceral organ resection)
- intra-thoracic surgery (e.g., lung resection)
- major orthopedic surgery (e.g., hip or knee replacement)
- peripheral arterial revascularization (e.g., abdominal aortic aneurysm repair, vascular bypass)
- urologic surgery (e.g., prostatectomy, bladder tumor resection)
- permanent pacemaker or internal defibrillator insertion
- major procedure (e.g., colonic polyp resection, biopsy of kidney or prostate)
- any other surgery or procedure lasting ≥1 hour

*Patients who satisfied the trial eligibility criteria were classified according to this suggested classification, although the final designation as minor/low bleeding risk or major/high bleeding risk was left to the discretion of the site investigator.

RESULTADOS

Table 3. Study Outcomes.

Outcome	No Bridging (N=918)	Bridging (N=895)	P Value
	number of patients (percent)		
Primary			
Arterial thromboembolism	4 (0.4)	3 (0.3)	0.01*, 0.73†
Stroke	2 (0.2)	3 (0.3)	
Transient ischemic attack	2 (0.2)	0	
Systemic embolism	0	0	
Major bleeding	12 (1.3)	29 (3.2)	0.005†
Secondary			
Death	5 (0.5)	4 (0.4)	0.88†
Myocardial infarction	7 (0.8)	14 (1.6)	0.10†
Deep-vein thrombosis	0	1 (0.1)	0.25†
Pulmonary embolism	0	1 (0.1)	0.25†
Minor bleeding	110 (12.0)	187 (20.9)	<0.001†

* P value for noninferiority.
† P value for superiority.

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- ¿ Cómo es el manejo de los pacientes que usan los nuevos anticoagulantes orales y requieren una cirugía o procedimiento electivo?

How I treat

How I treat anticoagulated patients undergoing an elective procedure or surgery

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Blood 2012,120(15):2954-62.

Table 4. Preoperative interruption of new oral anticoagulants: a suggested management approach

Drug (dose)*	Patient renal function	Low bleeding risk surgery† (2 or 3 drug half-lives between last dose and surgery)	High bleeding risk surgery‡ (4 or 5 drug half-lives between last dose and surgery)
Dabigatran (150 mg twice daily)			
$t_{1/2}$ = 14-17 h	Normal or mild impairment (CrCl > 50 mL/min)	Last dose: 2 days before surgery (skip 2 doses)	Last dose: 3 days before surgery (skip 4 doses)
$t_{1/2}$ = 16-18 h	Moderate impairment (CrCl 30-50 mL/min)	Last dose: 3 days before surgery (skip 4 doses)	Last dose: 4-5 days before surgery (skip 6-8 doses)
Rivaroxaban (20 mg once daily)			
$t_{1/2}$ = 8-9 h	Normal or mild impairment (CrCl > 50 mL/min)	Last dose: 2 days before surgery (skip 1 dose)	Last dose: 3 days before surgery (skip 2 doses)
$t_{1/2}$ = 9 h	moderate impairment (CrCl 30-50 mL/min)	Last dose: 2 days before surgery (skip 1 dose)	Last dose: 3 days before surgery (skip 2 doses)
$t_{1/2}$ = 9-10 h	Severe impairment§ (CrCl 15-29.9 mL/min)	Last dose: 3 days before surgery (skip 2 doses)	Last dose: 4 days before surgery (skip 3 doses)
Apixaban (5 mg twice daily)			
$t_{1/2}$ = 7-8 h	Normal or mild impairment (CrCl > 50 mL/min)	Last dose: 2 days before surgery (skip 2 doses)	Last dose: 3 days before surgery (skip 4 doses)
$t_{1/2}$ = 17-18 h	Moderate impairment (CrCl 30-50 mL/min)	Last dose: 3 days before surgery (skip 4 doses)	Last dose: 4 days before surgery (skip 6 doses)

Table 5. Postoperative resumption of new oral anticoagulants: a suggested management approach

Drug	Low bleeding risk surgery	High bleeding risk surgery
Dabigatran	Resume on day after surgery (24 h postoperative), 150 mg twice daily	Resume 2-3 days after surgery (48-72 h postoperative), 150 mg twice daily*
Rivaroxaban	Resume on day after surgery (24 h postoperative), 20 mg once daily	Resume 2-3 days after surgery (48-72 h postoperative), 20 mg once daily†
Apixaban	Resume on day after surgery (24 h postoperative), 5 mg twice daily	Resume 2-3 days after surgery (48-72 h postoperative), 5 mg twice daily†

*For patients at high risk for thromboembolism, consider administering a reduced dose of dabigatran (eg, 110-150 mg once daily) on the evening after surgery and on the following day (first postoperative day) after surgery.

†Consider a reduced dose (ie, rivaroxaban 10 mg once a day or apixaban 2.5 mg twice a day) in patients at high risk for thromboembolism.


Muchas gracias