Management of anticoagulation during elective interventional procedures

George Ntaios

Department of Medicine, University of Thessaly

ESO EUROPEAN STROKE ORGANISATION

HSO Hellenic Stroke Organization

Disclosures

- Scholarships: European Stroke Organization; Hellenic Society of Atherosclerosis.
- Honoraria: Medtronic; Quintiles; CHUV; Belgian Stroke Council; Boehringer-Ingelheim.
- Speaker fees: Sanofi; Boehringer-Ingelheim, Galenica
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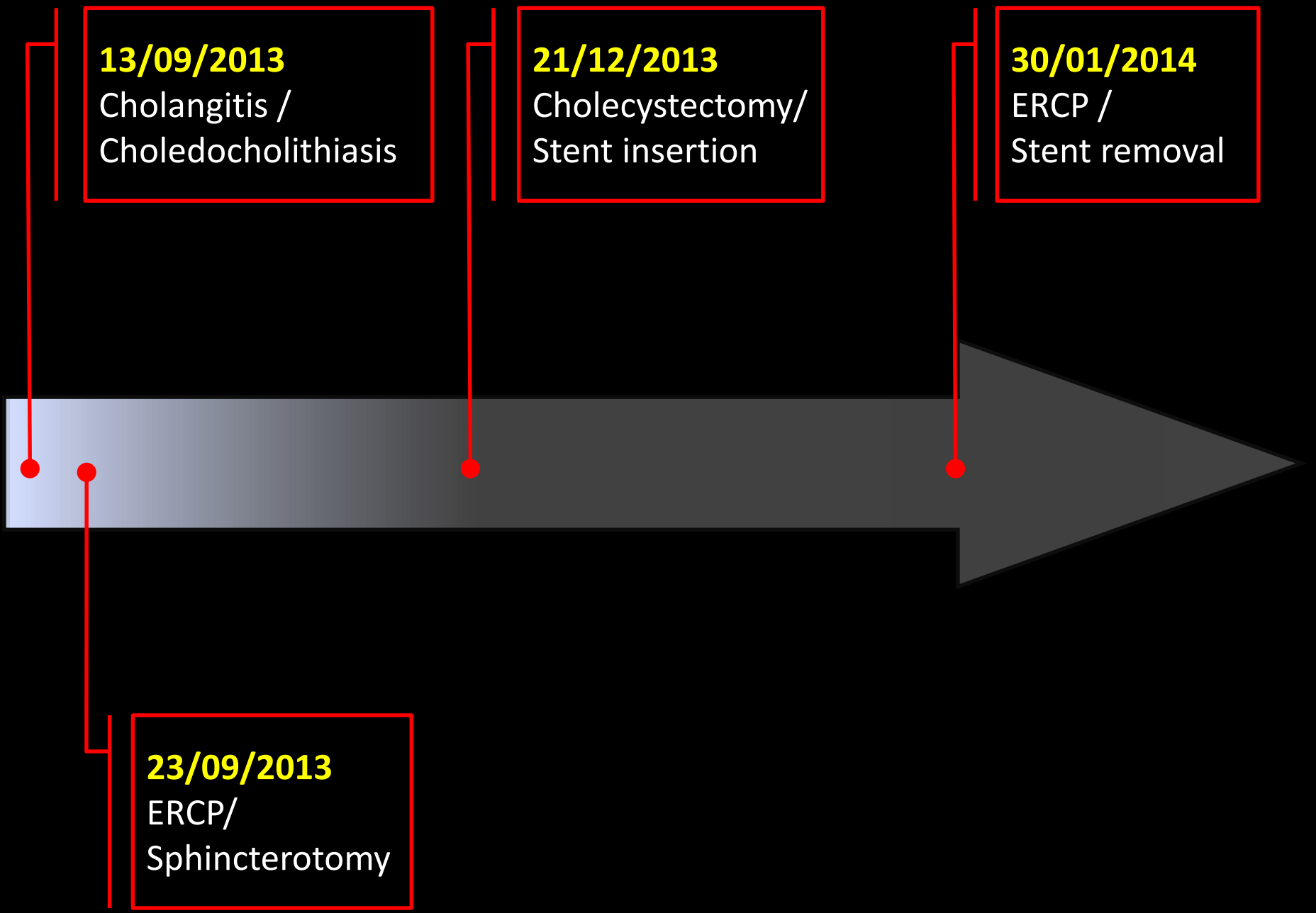
- Participation in trials:
  - ENOS / National coordinator (Greece).
  - PRECIOUS / National Coordinator (Greece).
  - BIOSIGNAL / Principal Investigator (Larissa).
  - EBBINGHAUS / Principal Investigator (Larissa).
  - FOURIER / Principal investigator (Larissa).
  - PREVISE / Principal investigator (Larissa).
  - GLORIA-AF / Sub-investigator (Larissa).

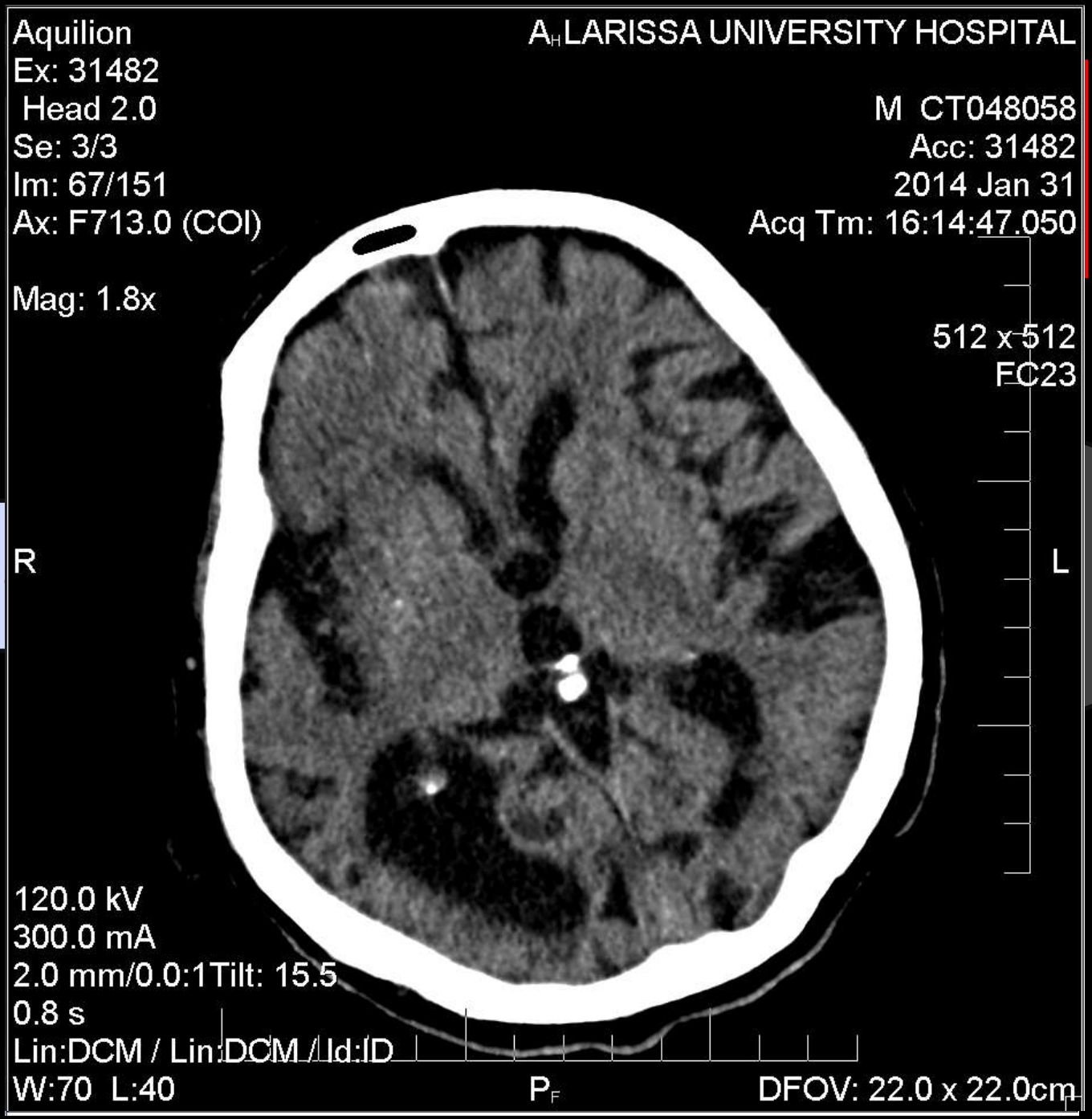
Clinical scenario

- ✓ ♂, 84yrs
- ✓ Arterial hypertension on amlodipine
- ✓ Atrial fibrillation on dabigatran
- ✓ Cardioembolic stroke (2011) – full recovery
- ✓ Deep venous thrombosis (right leg) 2009


13/09/2013
Cholangitis /
Choledocholithiasis
21/12/2013
Cholecystectomy/
Stent insertion
30/01/2014
ERCP /
Stent removal
23/09/2013
ERCP/
Sphincterotomy

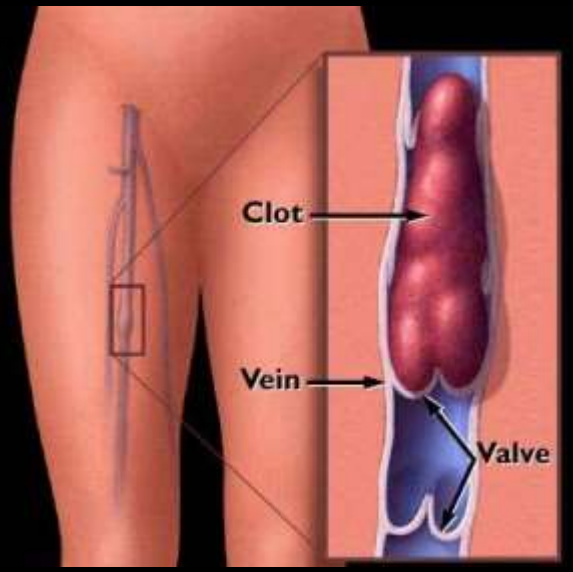
Question

1. Continue with dabigatran, no need to interrupt it.
2. Stop dabigatran 5 days before the intervention and start it again 1 day after the intervention.
3. Stop dabigatran 1 day before the intervention and start it again 1 day after the intervention.
4. Stop dabigatran 5 days before the intervention and continue with low-dose LMWH; switch back to dabigatran 1 day after the intervention.
5. Stop dabigatran 5 days before the intervention and continue with high-dose LMWH; switch back to dabigatran 1 day after the intervention.
6. Stop dabigatran 5 days before the intervention and continue with acenocoumarol; switch back to dabigatran 1 day after the intervention
7. I don’t know, ask Valeria Caso.



30/01/2014
ERCP /
Stent removal

31/01/2014
Left hemiplegia
Drowsiness


Clot
Vein
Valve

Interventions in anticoagulated patients: not rare

Periprocedural Bleeding and Thromboembolic Events With Dabigatran Compared With Warfarin

Results From the Randomized Evaluation of Long-Term Anticoagulation Therapy (RE-LY) Randomized Trial

Jeff S. Healey, MD, MSc; John Eikelboom, MD; James Douketis, MD; Lars Wallentin, MD, PhD; Jonas Oldgren, MD, PhD; Sean Yang, MSc; Ellison Themeles, BA; Hein Heidbuchel, MD; Alvaro Avezum, MD; Paul Reilly, PhD; Stuart J. Connolly, MD; Salim Yusuf, MD, DPhil; Michael Ezekowitz, MB, ChB, DPhil; on behalf of the RE-LY Investigators

Background—Dabigatran reduces ischemic stroke in comparison with warfarin; however, given the lack of antidote, there is concern that it might increase bleeding when surgery or invasive procedures are required.

Methods and Results—The current analysis was undertaken to compare the periprocedural bleeding risk of patients in the Randomized Evaluation of Long-Term Anticoagulation Therapy (RE-LY) trial treated with dabigatran and warfarin. Bleeding rates were evaluated from 7 days before until 30 days after invasive procedures, considering only the first procedure for each patient. A total of 4591 patients underwent at least 1 invasive procedure: 24.7% of patients received dabigatran 110 mg, 25.4% received dabigatran 150 mg, and 25.9% received warfarin, $P=0.34$. Procedures included: pacemaker/defibrillator insertion (10.3%), dental procedures (10.0%), diagnostic procedures (10.0%), cataract removal (9.3%), colonoscopy (8.6%), and joint replacement (6.2%). Among patients assigned to either dabigatran dose, the last dose of study drug was given 49 (35–85) hours before the procedure on comparison with 114 (87–144) hours in patients receiving warfarin, $P<0.001$. There was no significant difference in the rates of periprocedural major bleeding between patients receiving dabigatran 110 mg (3.8%) or dabigatran 150 mg (5.1%) or warfarin (4.6%); dabigatran 110 mg versus warfarin: relative risk, 0.83; 95% CI, 0.59 to 1.17; $P=0.28$; dabigatran 150 mg versus warfarin: relative risk, 1.09; 95% CI, 0.80 to 1.49; $P=0.58$. Among patients having urgent surgery, major bleeding occurred in 17.8% with dabigatran 110 mg, 17.7% with dabigatran 150 mg, and 21.6% with warfarin: dabigatran 110 mg; relative risk, 0.82; 95% CI, 0.48 to 1.41; $P=0.47$; dabigatran 150 mg: relative risk, 0.82; 95% CI, 0.50 to 1.35; $P=0.44$.

Conclusions—Dabigatran and warfarin were associated with similar rates of periprocedural bleeding, including patients having urgent surgery. Dabigatran facilitated a shorter interruption of oral anticoagulation.

Clinical Trial Registration—URL: http://www.clinicaltrials.gov. Unique identifier: NCT00262600.

(*Circulation*. 2012;126:343-348.)

Interventions in anticoagulated patients: types

Type of surgery	Dabigatran 110 mg BID (N=1487)	Dabigatran 150 mg BID (N=1546)	Warfarin (N=1558)
Pacemaker or ICD	11.6	9.5	9.8
Dental procedure	9.5	9.2	11.4
Other diagnostic procedure*	9.7	10.1	10.1
Cataract removal	8.3	10.1	9.6
Colonoscopy	9.6	8.9	7.4
Total hip or knee replacement	5.9	6.1	6.7
Coronary angiography	7.0	5.3	6.4
Cystoscopic procedure	5.2	4.7	5.0
Inguinal hernia repair	3.0	2.4	3.3
Laparoscopic cholecystectomy	2.2	2.7	2.6
CABG or valve	2.0	1.6	2.4
Colectomy (partial or total)	1.3	2.8	1.7
Peripheral angioplasty	1.4	1.4	0.8
Prostate biopsy	0.7	0.9	0.7
Carotid endarterectomy	0.4	0.7	0.7
Limb amputation	0.5	0.7	0.4

Healey. Circulation. 2012;126:343-348

Interventions in anticoagulated patients: not rare

Outcomes of Temporary Interruption of Rivaroxaban Compared With Warfarin in Patients With Nonvalvular Atrial Fibrillation

Results From the Rivaroxaban Once Daily, Oral, Direct Factor Xa Inhibition Compared With Vitamin K Antagonism for Prevention of Stroke and Embolism Trial in Atrial Fibrillation (ROCKET AF)

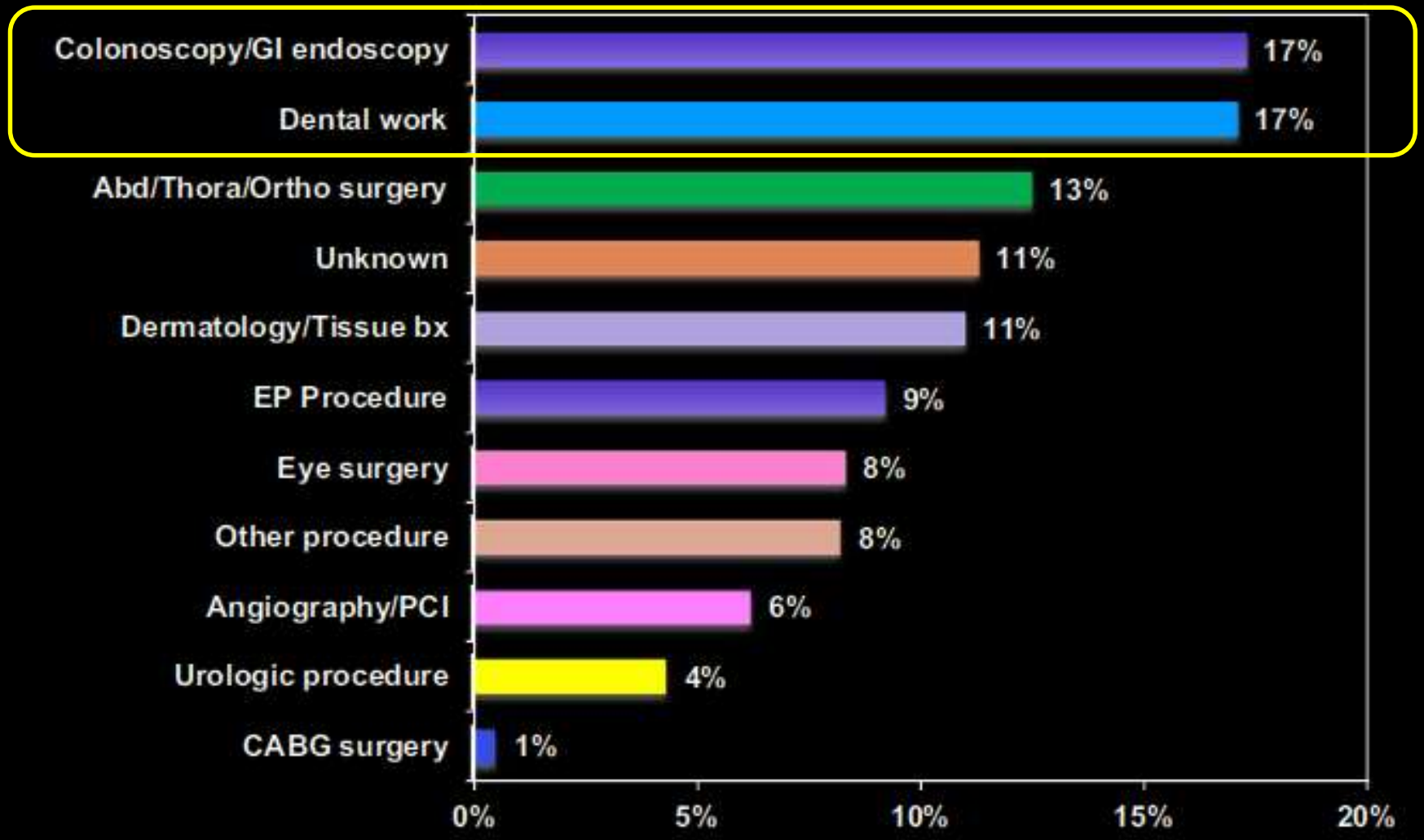
Matthew W. Sherwood, MD; James D. Douketis, MD; Manesh R. Patel, MD; Jonathan P. Piccini, MD, MHS; Anne S. Hellkamp, MS; Yuliya Lokhnygina, PhD; Alex C. Spyropoulos, MD; Graeme J. Hankey, MD; Daniel E. Singer, MD; Christopher C. Nessel, MD; Kenneth W. Mahaffey, MD; Keith A. A. Fox, MB, ChB; Robert M. Califf, MD; Richard C. Becker, MD; on behalf of the ROCKET AF Investigators

Background—During long-term anticoagulation in atrial fibrillation, temporary interruptions (TIs) of therapy are common, but the relationship between patient outcomes and TIs has not been well studied. We sought to determine reasons for TI, the characteristics of patients undergoing TI, and the relationship between anticoagulant and outcomes among patients with TI.

Methods and Results—In the Rivaroxaban Once Daily, Oral, Direct Factor Xa Inhibition Compared With Vitamin K Antagonism for Prevention of Stroke and Embolism Trial in Atrial Fibrillation (ROCKET AF), a randomized, double-blind, double-dummy study of rivaroxaban and warfarin in nonvalvular atrial fibrillation, baseline characteristics, management, and outcomes, including stroke, non–central nervous system systemic embolism, death, myocardial infarction, and bleeding, were reported in participants who experienced TI (3–30 days) for any reason. The at-risk period for outcomes associated with TI was from TI start to 30 days after resumption of study drug. In 14 236 participants who received at least 1 dose of study drug, 4692 (33%) experienced TI. Participants with TI were similar to the overall ROCKET AF population in regard to baseline clinical characteristics. Only 6% (n=483) of TI incidences involved bridging therapy. Stroke/systemic embolism rates during the at-risk period were similar in rivaroxaban-treated and warfarin-treated participants (0.30% versus 0.41% per 30 days; hazard ratio [confidence interval]=0.74 [0.36–1.50]; P=0.40). Risk of major bleeding during the at-risk period was also similar in rivaroxaban-treated and warfarin-treated participants (0.99% versus 0.79% per 30 days; hazard ratio [confidence interval]=1.26 [0.80–2.00]; P=0.32).

Conclusions—TI of oral anticoagulation is common and is associated with substantial stroke risks and bleeding risks that were similar among patients treated with rivaroxaban or warfarin. Further investigation is needed to determine the optimal management strategy in patients with atrial fibrillation requiring TI of anticoagulation.

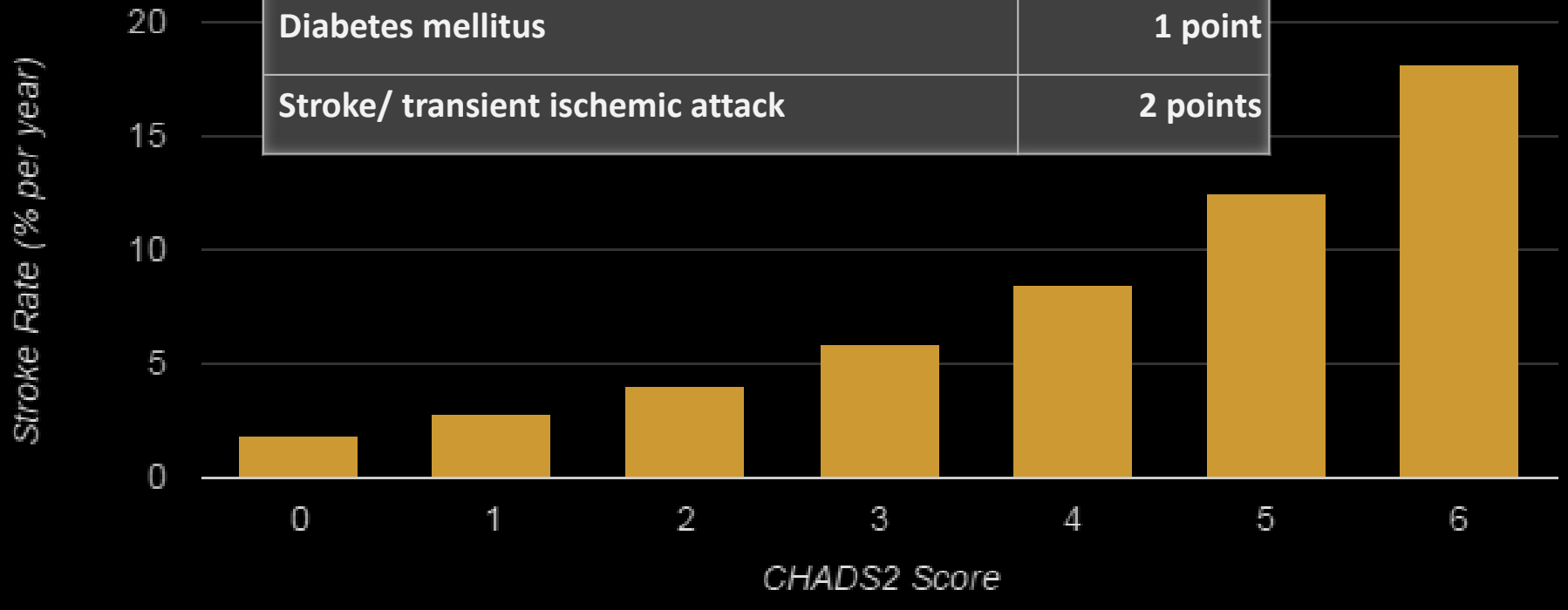
Interventions in anticoagulated patients: types



Sherwood. Circulation. 2014;1850-59

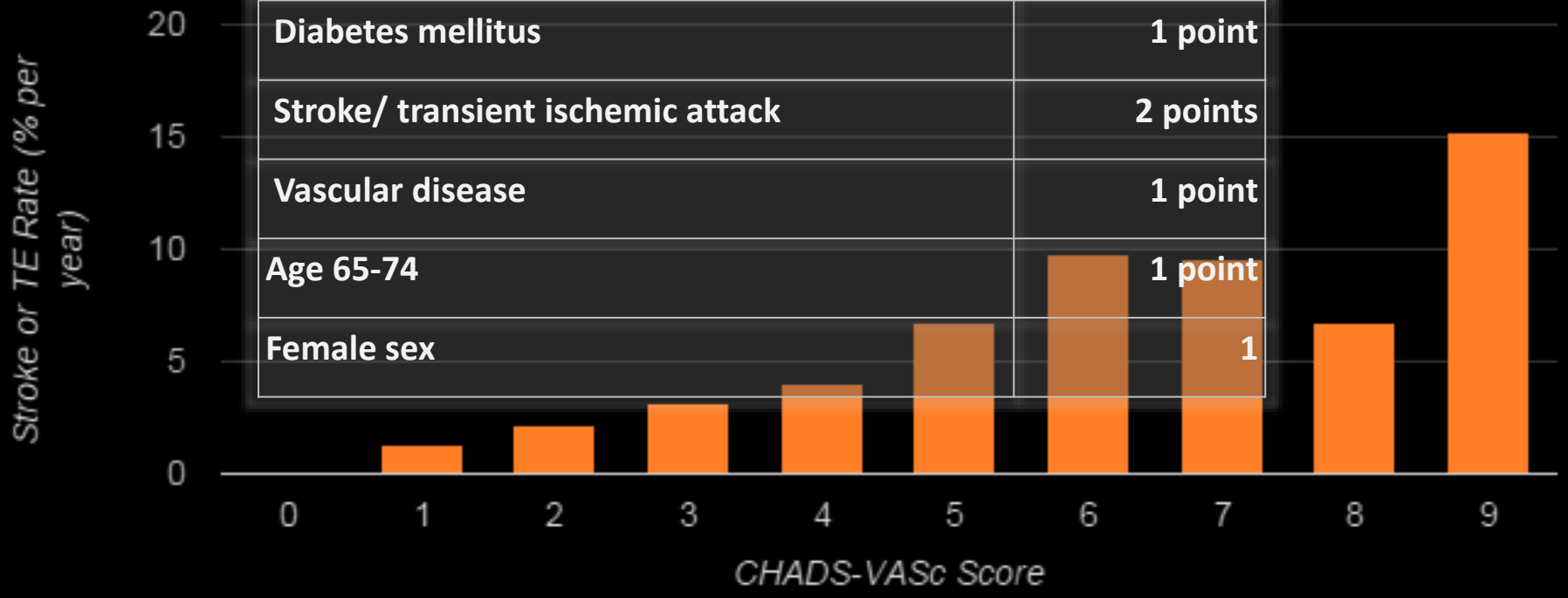
Estimate thromboembolic risk in AF: $CHADS_2$

$CHADS_2$ Risk Criteria	Score
Congestive heart failure	1 point
Hypertension	1 point
Age >75 years	1 point
Diabetes mellitus	1 point
Stroke/ transient ischemic attack	2 points



Estimate thromboembolic risk in AF: $CHA_2DS_2VAS_C$

$CHA_2DS_2Vas_c$ Risk Criteria	Score
Congestive heart failure	1 point
Hypertension	1 point
Age >75 years	2 point
Diabetes mellitus	1 point
Stroke/ transient ischemic attack	2 points
Vascular disease	1 point
Age 65-74	1 point
Female sex	1



Thrombotic risk in patients with mechanical valve

Any mitral-valve prosthesis,
any caged-ball or tilting-disk aortic-valve prosthesis,
multiple mechanical heart valves,
or stroke, TIA, or cardioembolic event.

Bileaflet aortic-valve prosthesis and atrial fibrillation.

Bileaflet aortic-valve prosthesis without atrial fibrillation,
prior stroke or thromboembolic event,
or known intracardiac thrombus.

Douketis. Chest 2012; 141(2)(Suppl):e326S–e350S

Thrombotic risk in patients with VTE

Venous thromboembolism within previous 3 months, severe thrombophilia, unprovoked VTE, or active cancer (cancer diagnosed ≤6 months or patient undergoing cancer therapy).

Venous thromboembolism within previous 3–12 months, non-severe thrombophilia, or recurrent VTE.

Venous thromboembolism >12 months previously and no other risk factor (e.g., provoked and transient).

Douketis. Chest 2012; 141(2)(Suppl):e326S–e350S

Condition-associated thromboembolic risk

	Clinical Indication for Warfarin Therapy		
Thromboembolic Risk Category	Atrial Fibrillation	Mechanical Heart Valve	Venous Thromboembolism
High risk (annual risk >10%)*	$CHADS_2$ score 5 or 6	Any mechanical mitral valve	Recent (within 3 mo) VTE
	Recent (within 3 mo) stroke/TIA	Older aortic mechanical valve (caged-ball, tilting disk)	High-risk thrombophilia‡
	Rheumatic valvular heart disease	Recent (within 3 mo) stroke or TIA	
Moderate risk (annual risk 5% to 10%)	$CHADS_2$ score 3 or 4	Bileaflet aortic valve prosthesis with ≥1 risk factor†	VTE within 3–12 mo
			Moderate-risk thrombophilia§
			Recurrent VTE
			Active cancer‖
Low risk (annual risk <5%)	$CHADS_2$ score 0–2 (no prior stroke or TIA)	Bileaflet aortic bileaflet without any risk factors†	VTE >12 mo ago

The BRIDGE Study investigators. Circulation. 2012;125:e496-e498

Major bleeding: definition

Major bleeding is generally defined as bleeding that is:

- fatal,
- intracranial,
- requires surgery to correct,
- lowers the hemoglobin by ≥2 g/dL,
- or requires transfusion of ≥2 units packed red cells

Schulman. J Thromb Haemost. 2005;3:692-4.

Periprocedural bleeding risks: high-risk

Procedural bleeding risks
High (2-day risk of major bleed 2%-4%)
Heart valve replacement
Coronary artery bypass
Abdominal aortic aneurysm repair
Neurosurgical/urologic/head and neck/abdominal/breast cancer surgery
Bilateral knee replacement
Laminectomy
Transurethral prostate resection
Kidney biopsy
Polypectomy, variceal treatment, biliary sphincterectomy, pneumatic dilatation
PEG placement
Endoscopically guided fine-needle aspiration
Multiple tooth extractions
Vascular and general surgery
Any major operation (procedure duration > 45 minutes)

Spyropoulos. Blood 2012; 120:2954-62

Procedural bleeding risks

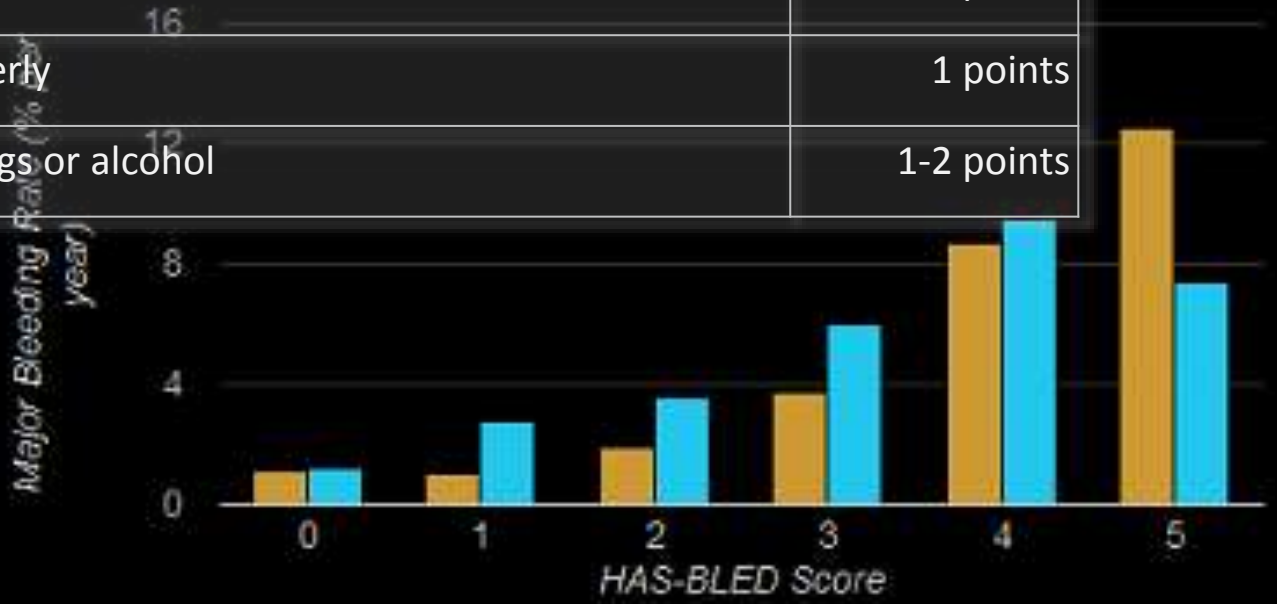
Low (2-day risk of major bleed 0%-2%)

- Cholecystectomy
- Abdominal hysterectomy
- Gastrointestinal endoscopy ± biopsy, enteroscopy, biliary/pancreatic stent without sphincterotomy, endonosonography without fine-needle aspiration
- Pacemaker and cardiac defribillator insertion and electrophysiologic testing
- Simple dental extractions
- Carpal tunnel repair
- Knee/hip replacement and shoulder/foot/hand surgery and arthroscopy
- Dilatation and curettage
- Skin cancer excision
- Abdominal hernia repair
- Hemorrhoidal surgery
- Axillary node dissection
- Hydrocele repair
- Cataract and noncataract eye surgery
- Noncoronary angiography
- Bronchoscopy ± biopsy
- Central venous catheter removal
- Cutaneous and bladder/prostate/thyroid/breast/lymph node biopsies

Baron. NEJM 2013; 368:2113-24

Estimate bleeding risk in AF: **HAS-BLED**

HAS-BLED Risk Criteria	Score
Hypertension	1 point
Abnormal renal/liver tests	1-2 point
Stroke	1 point
Bleeding	1 point
Labile INR	2 points
Elderly	1 points
Drugs or alcohol	1-2 points



Bleeding vs. thromboemblic risk

Bridging VKA with LMWH

Rio-Antirio bridge

Bridging VKA with LMWH

Surgery

“ To bridge or not to bridge? ”

Spyropoulos. Blood 2012; 120:2954-62

Bridge with unfractionated heparin or with LMWH?

Bridge with LMWH or with NOACs?

" To bridge or not to bridge? "

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Heart Association®

Periprocedural Heparin Bridging in Patients Receiving Vitamin K Antagonists : Systematic Review and Meta-Analysis of Bleeding and Thromboembolic Rates

Deborah Siegal, Jovana Yudin, Scott Kaatz, James D. Douketis, Wendy Lim and Alex C. Spyropoulos

Circulation. 2012;126:1630-1639; originally published online August 21, 2012;

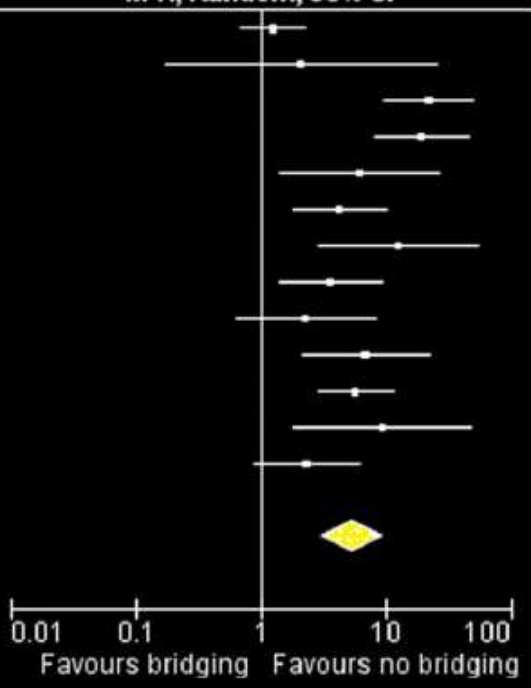
Siegal. Circulation. 2012;126:1630-1639

" To bridge or not to bridge? " - bleeding

Study or Subgroup	Bridging Events	Bridging Total	No bridging Events	No bridging Total	Weight	Odds Ratio M-H, Random, 95% CI
Daniels et al., 2009	36	342	18	213	9.8%	1.27 [0.70, 2.31]
Dotan et al., 2002	2	20	1	20	3.7%	2.11 [0.18, 25.35]
Ercan et al., 2010	11	44	21	1421	9.0%	22.22 [9.92, 49.81]
Garcia et al., 2008	14	108	9	1185	8.8%	19.46 [8.21, 46.14]
Ghanbari et al., 2010	6	29	3	74	6.5%	6.17 [1.43, 26.68]
Jaffer et al., 2010	24	229	7	263	8.8%	4.28 [1.81, 10.14]
Marquie et al., 2006	21	114	2	114	6.4%	12.65 [2.89, 55.34]
McBane et al., 2010	34	514	5	261	8.4%	3.63 [1.40, 9.39]
Robinson et al., 2009	20	113	3	35	7.2%	2.29 [0.64, 8.24]
Tischenko et al., 2009	9	38	5	117	7.6%	6.95 [2.16, 22.33]
Tompkins et al., 2010	23	155	15	513	9.5%	5.78 [2.94, 11.40]
Varkarakis et al., 2005	2	25	7	762	5.9%	9.38 [1.85, 47.64]
Wysokinski et al., 2008	15	204	6	182	8.4%	2.33 [0.88, 6.13]
Total (95% CI)		**1935**		**5160**	**100.0%**	**5.40 [3.00, 9.74]**
Total events	217		102			

Heterogeneity: $Tau^2 = 0.83$; $Chi^2 = 52.47$, $df = 12$ ($P < 0.00001$); $I^2 = 77\%$

Test for overall effect: $Z = 5.61$ ($P < 0.00001$)



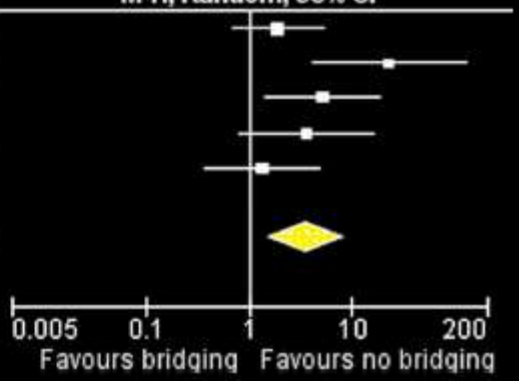
Siegal. Circulation. 2012;126:1630-1639

"To bridge or not to bridge?" – major bleeding

Study or Subgroup	Bridging Events	Bridging Total	No bridging Events	No bridging Total	Weight	Odds Ratio M-H, Random, 95% CI
Daniels et al., 2009	15	342	5	213	24.9%	1.91 [0.68, 5.33]
Garcia et al., 2008	4	108	2	1185	15.3%	22.75 [4.12, 125.68]
Jaffer et al., 2010	13	229	3	263	21.0%	5.22 [1.47, 18.54]
McBane et al., 2010	14	514	2	261	17.9%	3.63 [0.82, 16.08]
Wysokinski et al., 2008	6	204	4	182	20.8%	1.35 [0.37, 4.86]
Total (95% CI)		**1397**		**2104**	**100.0%**	**3.60 [1.52, 8.50]**
Total events	52		16			

Heterogeneity: $Tau^2 = 0.50$; $Chi^2 = 8.41$, df = 4 (P = 0.08); $I^2 = 52\%$

Test for overall effect: Z = 2.92 (P = 0.004)



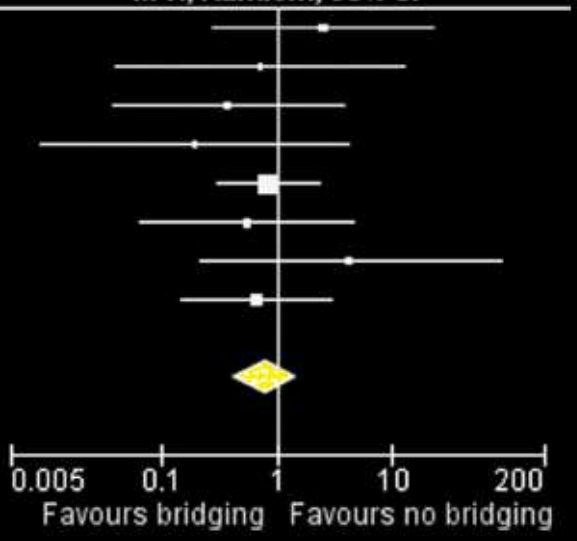
Siegal. Circulation. 2012;126:1630-1639

"To bridge or not to bridge?" – thromboembolism

Study or Subgroup	Bridging Events	Bridging Total	No bridging Events	No bridging Total	Weight	Odds Ratio M-H, Random, 95% CI
Daniels et al., 2009	4	342	1	213	8.8%	2.51 [0.28, 22.60]
Garcia et al., 2008	0	108	7	1185	5.2%	0.72 [0.04, 12.76]
Jaffer et al., 2010	1	229	3	263	8.2%	0.38 [0.04, 3.68]
Marquie et al., 2006	0	114	2	114	4.6%	0.20 [0.01, 4.14]
McBane et al., 2010	10	514	6	261	40.5%	0.84 [0.30, 2.35]
Tompkins et al., 2010	1	155	6	513	9.4%	0.55 [0.07, 4.59]
Varkarakis et al., 2005	0	25	3	762	4.7%	4.25 [0.21, 84.56]
Wysokinski et al., 2008	3	204	4	182	18.6%	0.66 [0.15, 3.01]
Total (95% CI)		**1691**		**3493**	**100.0%**	**0.80 [0.42, 1.54]**
Total events	19		32			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 3.68$, $df = 7$ ($P = 0.82$); $I^2 = 0\%$

Test for overall effect: $Z = 0.67$ ($P = 0.50$)



Siegal. Circulation. 2012;126:1630-1639

" To bridge or not to bridge? "

Circulation
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American Heart Association®

Use and Outcomes Associated with Bridging During Anticoagulation Interruptions in Patients with Atrial Fibrillation: Findings from the Outcomes Registry for Better Informed Treatment of Atrial Fibrillation (ORBIT-AF)

Benjamin A. Steinberg, Eric D. Peterson, Sunghee Kim, Laine Thomas, Bernard J. Gersh, Gregg C. Fonarow, Peter R. Kowey, Kenneth W. Mahaffey, Matthew W. Sherwood, Paul Chang, Jonathan P. Piccini and Jack Ansell
on behalf of the Outcomes Registry for Better Informed Treatment of Atrial Fibrillation (ORBIT-AF) Investigators and Patients

Circulation. published online December 12, 2014:

" To bridge or not to bridge? "

Adjusted 30-day outcomes, by use of bridging anticoagulation.

	Adjusted*	
	Adjusted OR (95% CI), bridging vs. no bridging	**P-value**
Cardiovascular events†		
Bleeding events‡		
Overall composite^		

Steinberg. Circulation. 2015;online early

" To bridge or not to bridge? "

The NEW ENGLAND JOURNAL of MEDICINE

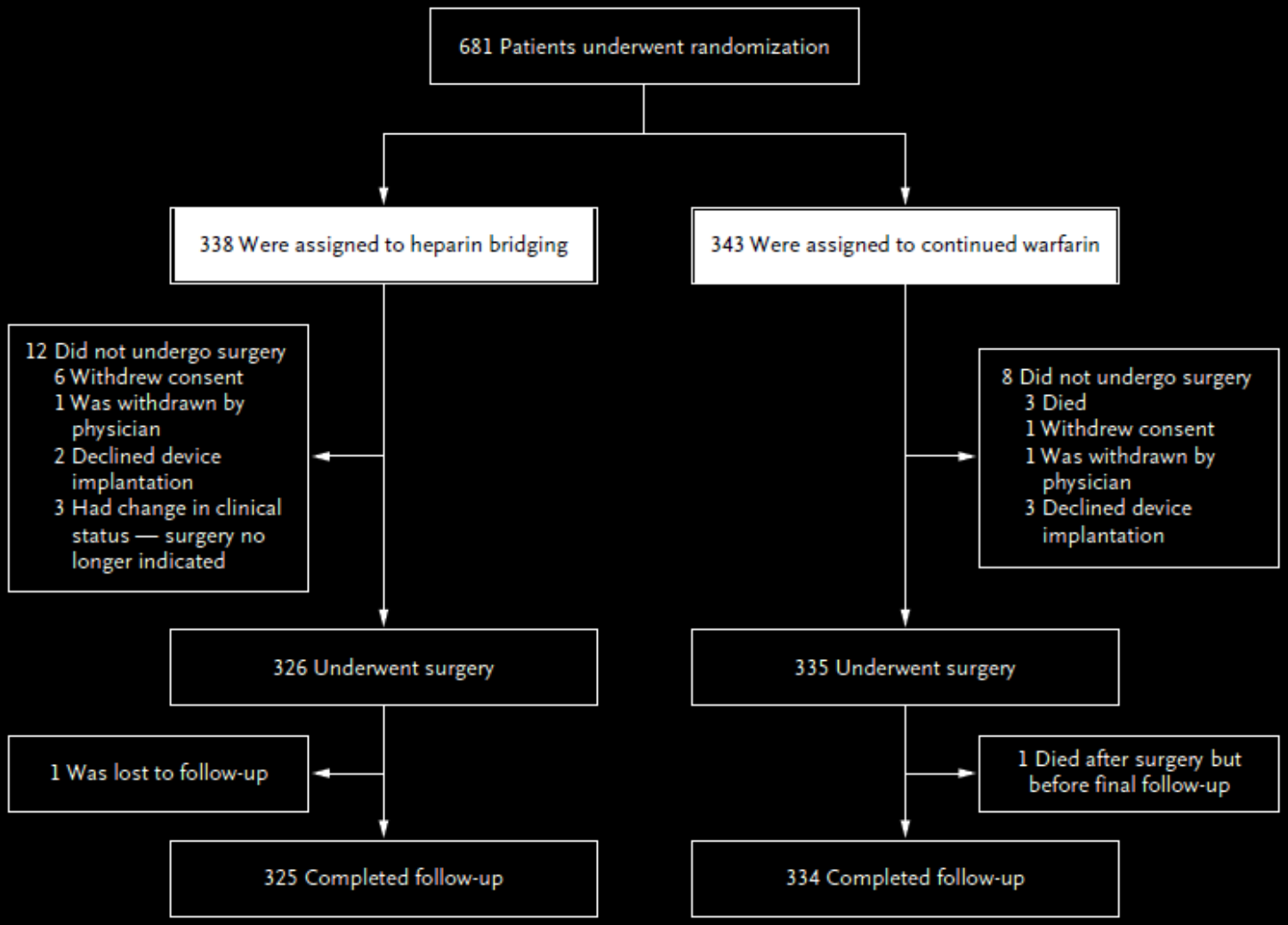
ORIGINAL ARTICLE

Pacemaker or Defibrillator Surgery without Interruption of Anticoagulation

David H. Birnie, M.D., Jeff S. Healey, M.D., George A. Wells, Ph.D., Atul Verma, M.D., Anthony S. Tang, M.D., Andrew D. Krahn, M.D., Christopher S. Simpson, M.D., Felix Ayala-Paredes, M.D., Benoit Coutu, M.D., Tiago L.L. Leiria, M.D., and Vidal Essebag, M.D., Ph.D., for the BRUISE CONTROL Investigators*

Birnie. N Engl J Med 2013;368:2084-93

" To bridge or not to bridge? "

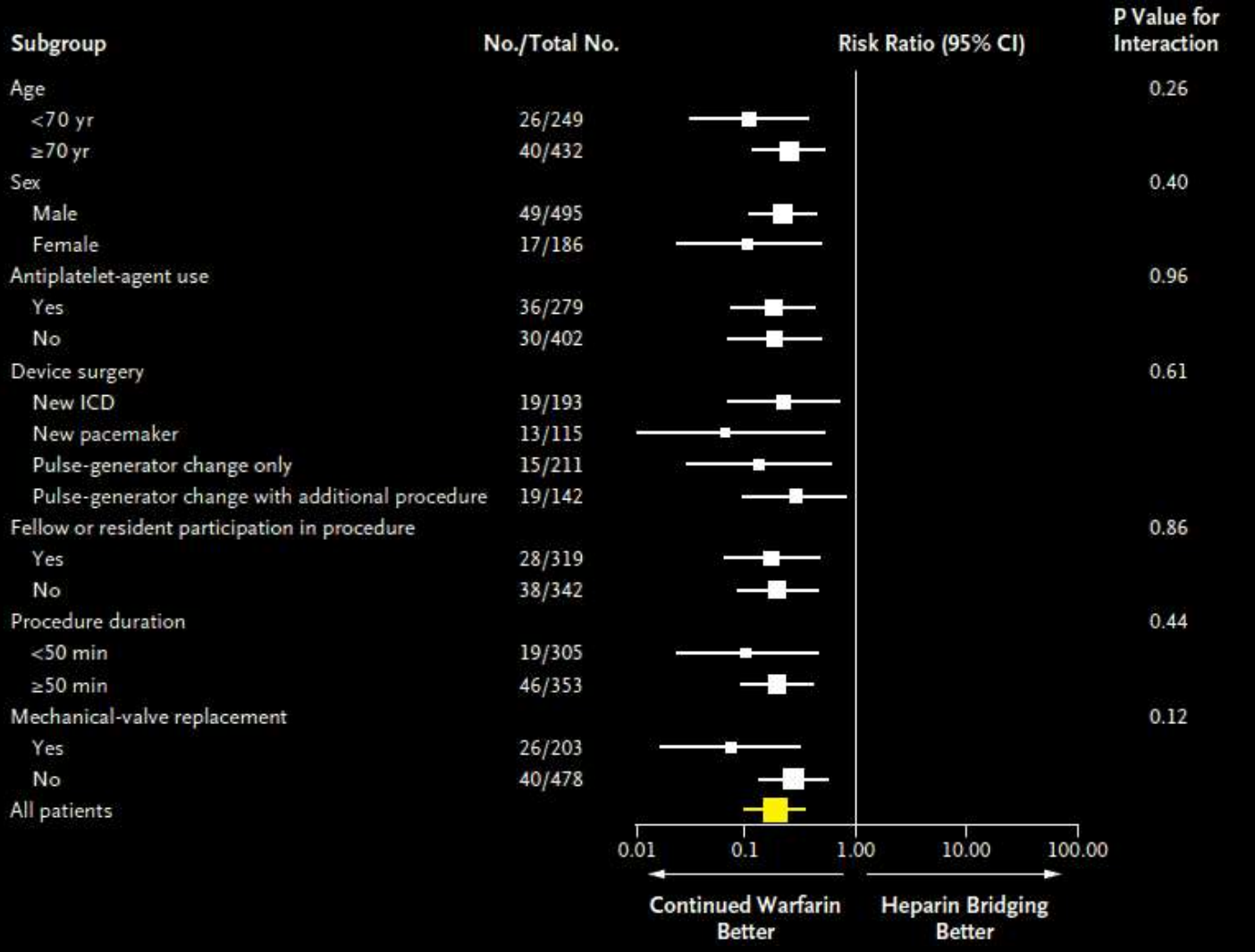


Birnie. N Engl J Med 2013;368:2084-93

“ To bridge or not to bridge? ”

Birnie. N Engl J Med 2013;368:2084-93

" To bridge or not to bridge? "



Birnie. N Engl J Med 2013;368:2084-93

" To bridge or not to bridge? "

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Bridging Anticoagulation in Patients who Require Temporary Interruption of Warfarin Therapy for an Elective Invasive Procedure or Surgery.

Enrollment Ended

December 31, 2014 with 1,884 Subjects!

Enrollment Reports

Enrollment Report for January 2, 2015

https://bridge.dcri.duke.edu/

ClinicalTrials.gov

A service of the U.S. National Institutes of Health

PERIOP 2 - A Safety and Effectiveness Study of LMWH Bridging Therapy Versus Placebo Bridging Therapy for Patients on Long Term Warfarin and Require Temporary Interruption of Their Warfarin.

This study is currently recruiting participants. (see Contacts and Locations)

Verified January 2014 by Lawson Health Research Institute

Sponsor:
Lawson Health Research Institute

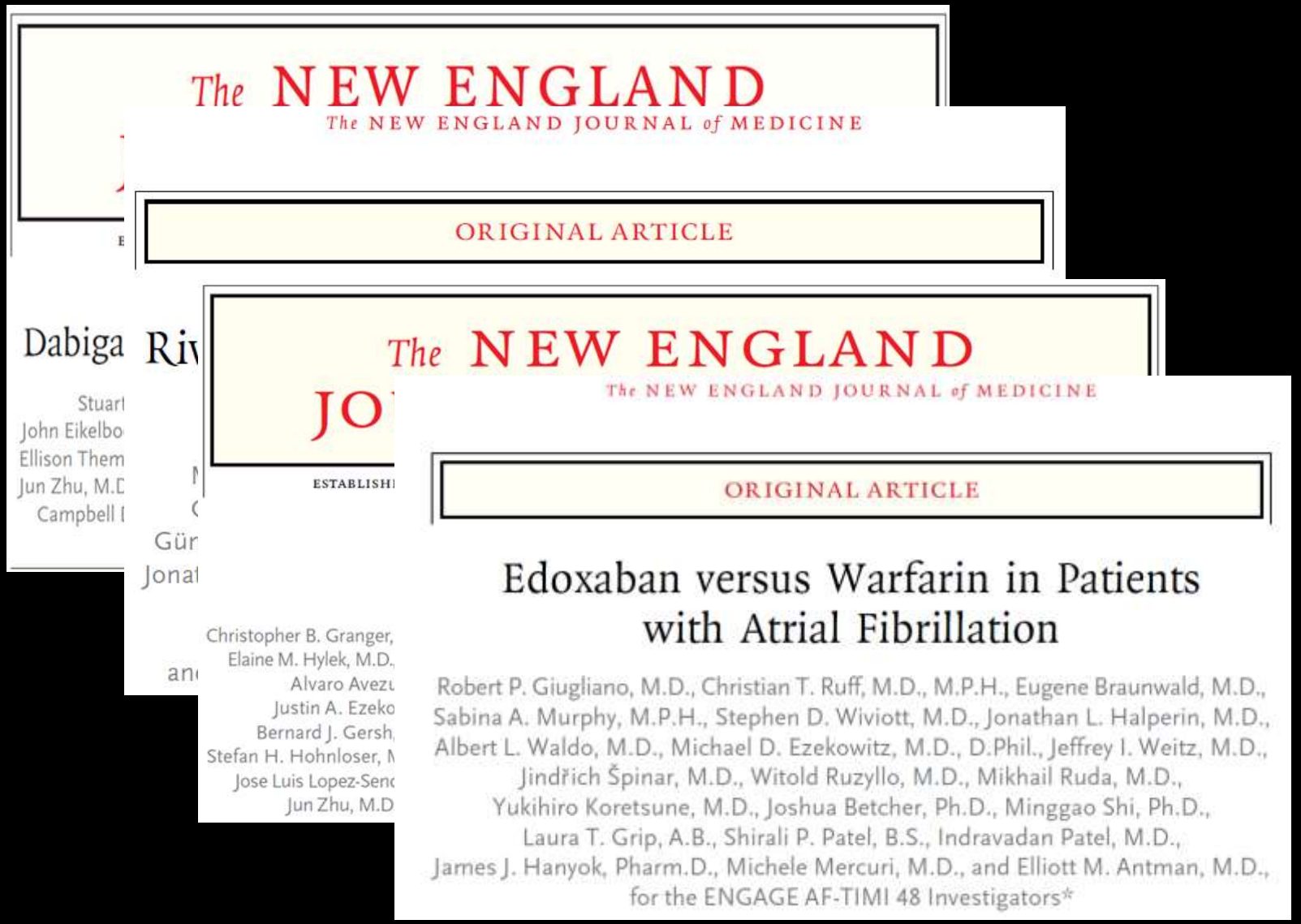
Collaborators:
Canadian Institutes of Health Research (CIHR)
Pfizer

Information provided by (Responsible Party):
Michael Kovacs, Lawson Health Research Institute

ClinicalTrials.gov Identifier:
NCT00432796

First received: February 7, 2007
Last updated: January 15, 2014
Last verified: January 2014
History of Changes

NOACs: New oral anticoagulants



Pre-operative discontinuations of NOACs

Last intake of drug before elective surgical intervention

	Dabigatran		Apixaban		Edoxaban[a]		Rivaroxaban	
	No important bleeding risk and/or adequate local haemostasis possible: perform at trough level (i.e. ≥12 or 24 h after last intake)							
	Low risk (h)	High risk	Low risk	High risk	Low risk	High risk	Low risk	High risk
CrCl ≥80 mL/min	≥24	≥48	≥24	≥48	no data	no data	≥24	≥48
CrCl 50–80 mL/min	**≥36**	**≥72**	≥24	≥48	no data	no data	≥24	≥48
CrCl 30–50 mL/min[b]	**≥48**	**≥96**	≥24	≥48	no data	no data	≥24	≥48
CrCl 15–30 mL/min[b]	not indicated	not indicated	**≥36**	**≥48**	no data	no data	**≥36**	**≥48**
CrCl <15 mL/min	no official indication for use							

Heidbuchel. European Heart Journal 2013

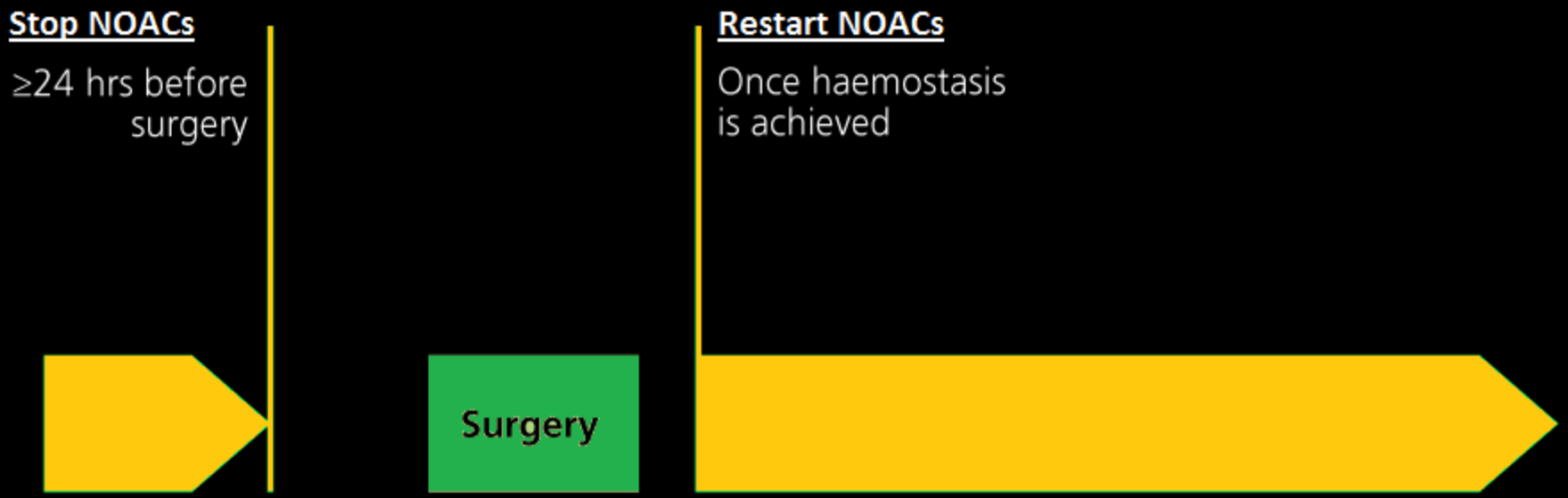
Postoperative resumption of NOACs

Postoperative resumption of new oral anticoagulants

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†

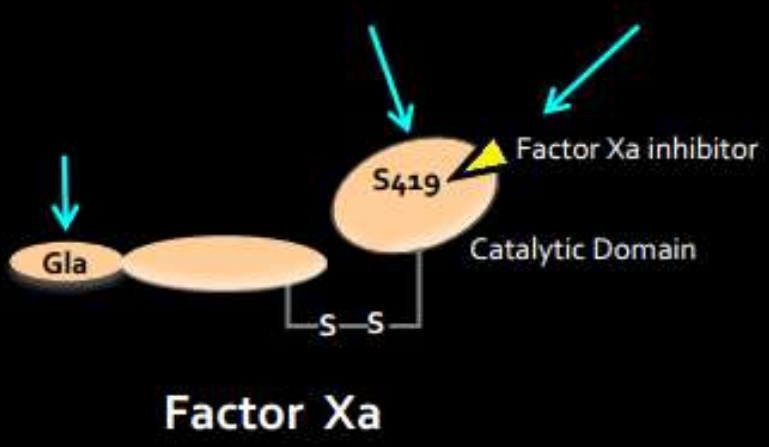
Heidbuchel. European Heart Journal 2013

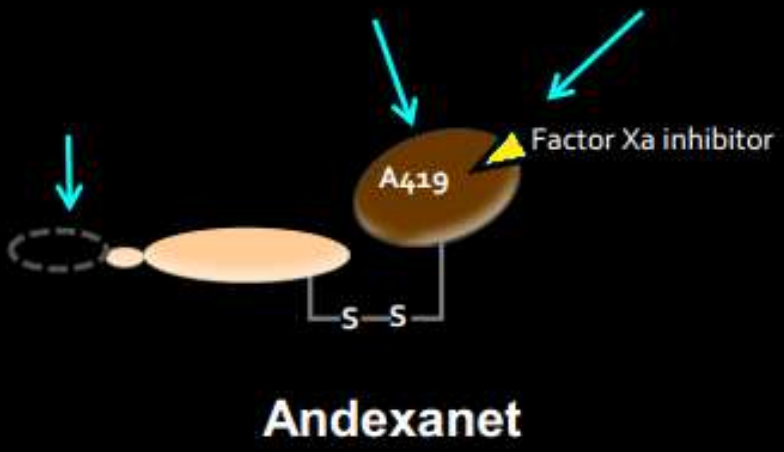
NOACs & elective interventions



www.vatspace.com (modified)

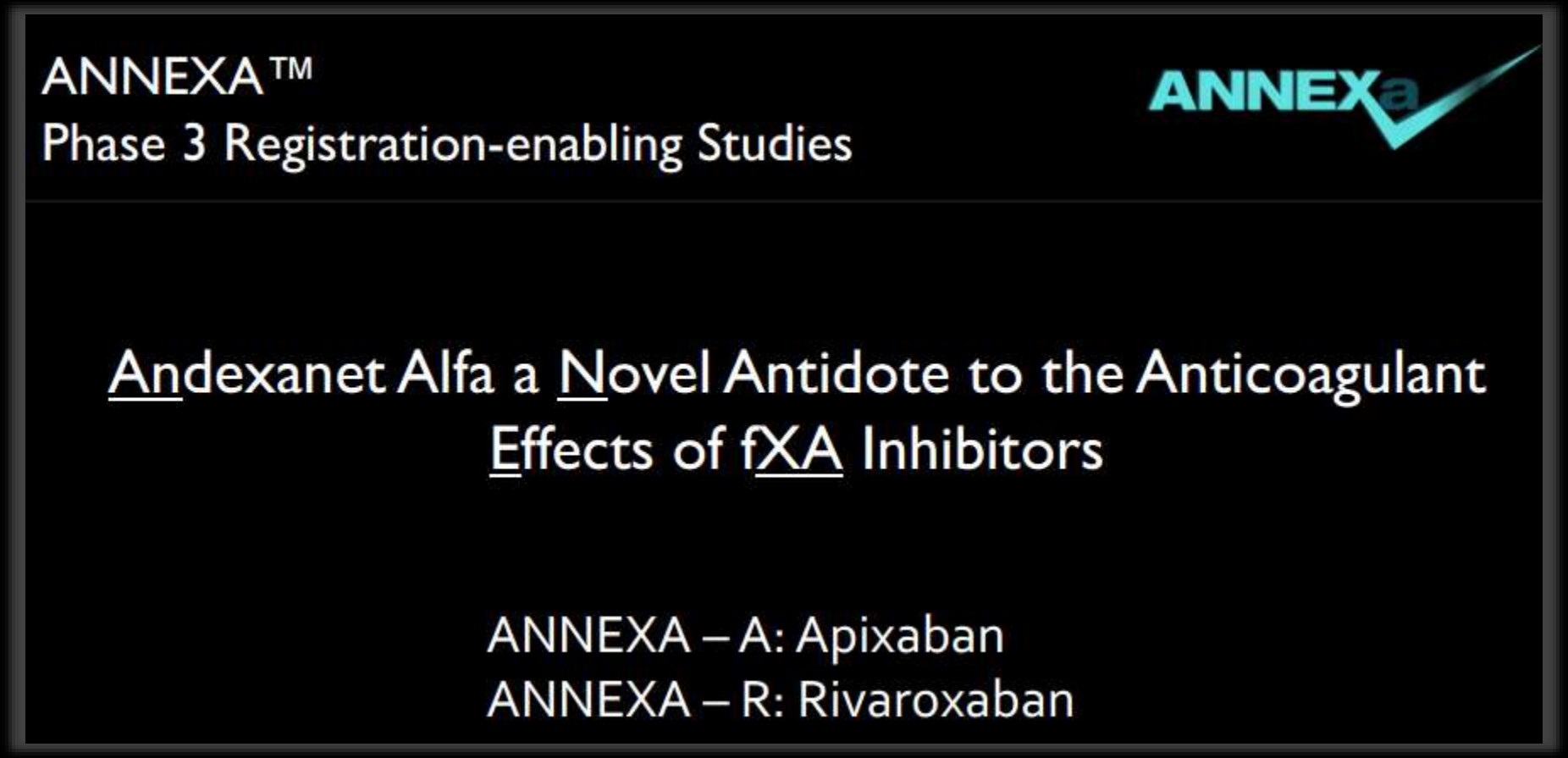
Andexanet: an antidote for Xa inhibitors





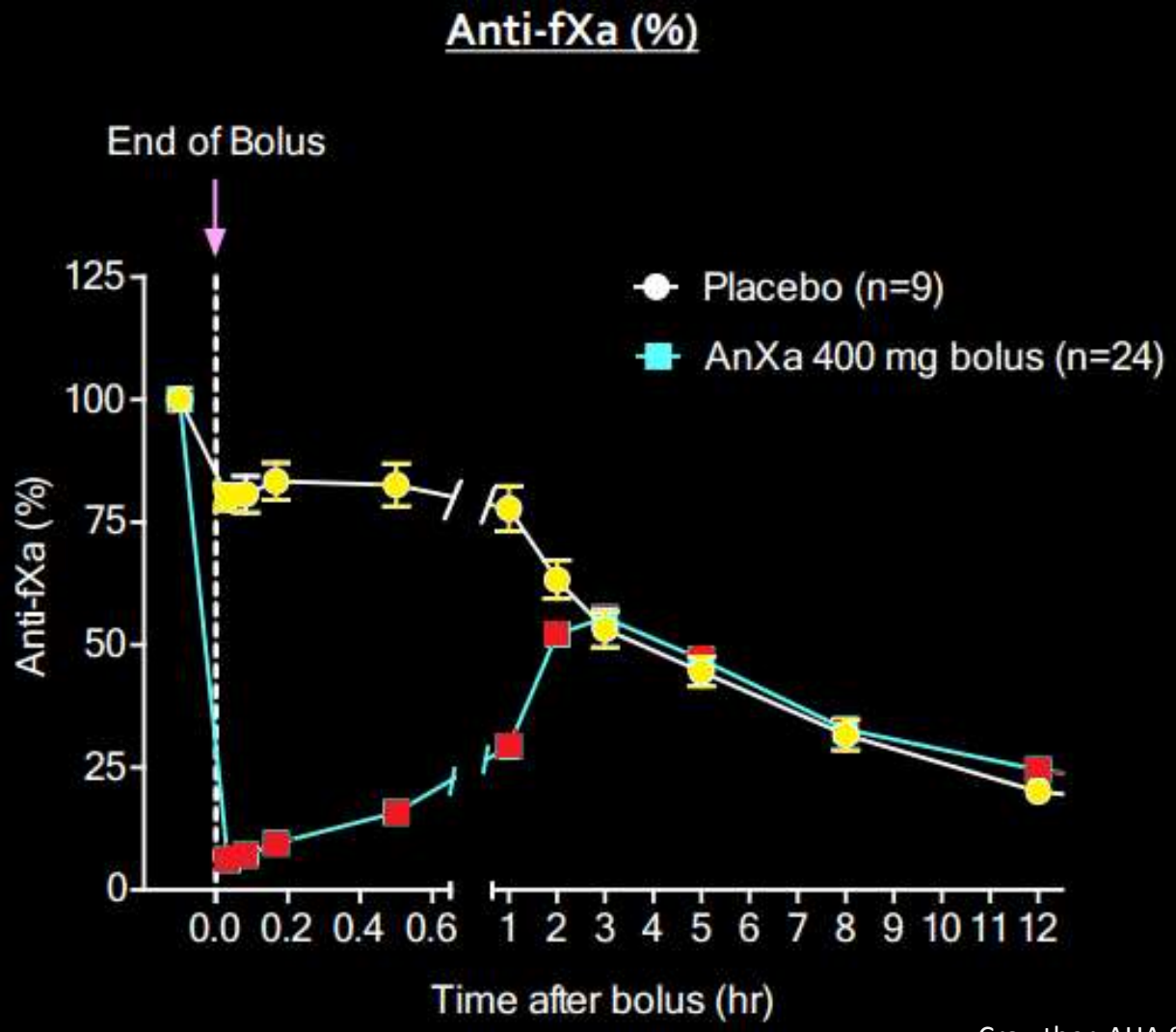
Crowther. AHA Scientific sessions 2014

Andexanet: an antidote for Xa inhibitors



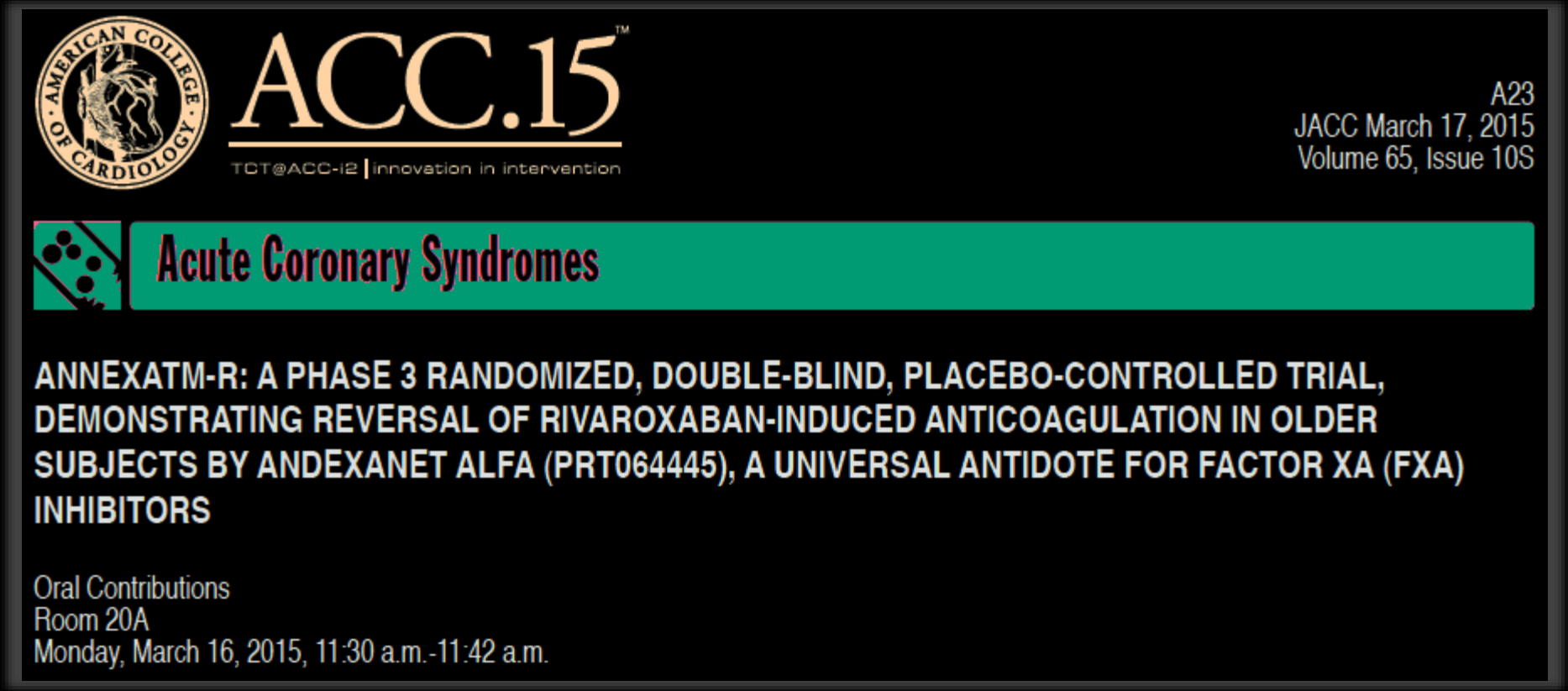
Crowther. AHA Scientific sessions 2014

Andexanet: Annexa-A (*antidote for apixaban*)



Crowther. AHA Scientific sessions 2014

Andexanet: Annexa-R (antidote for *rivaroxaban*)



Gold. JACC, 2 days ago

Idarucizumab: (*antidote for dabigatran*)

Plenary Paper

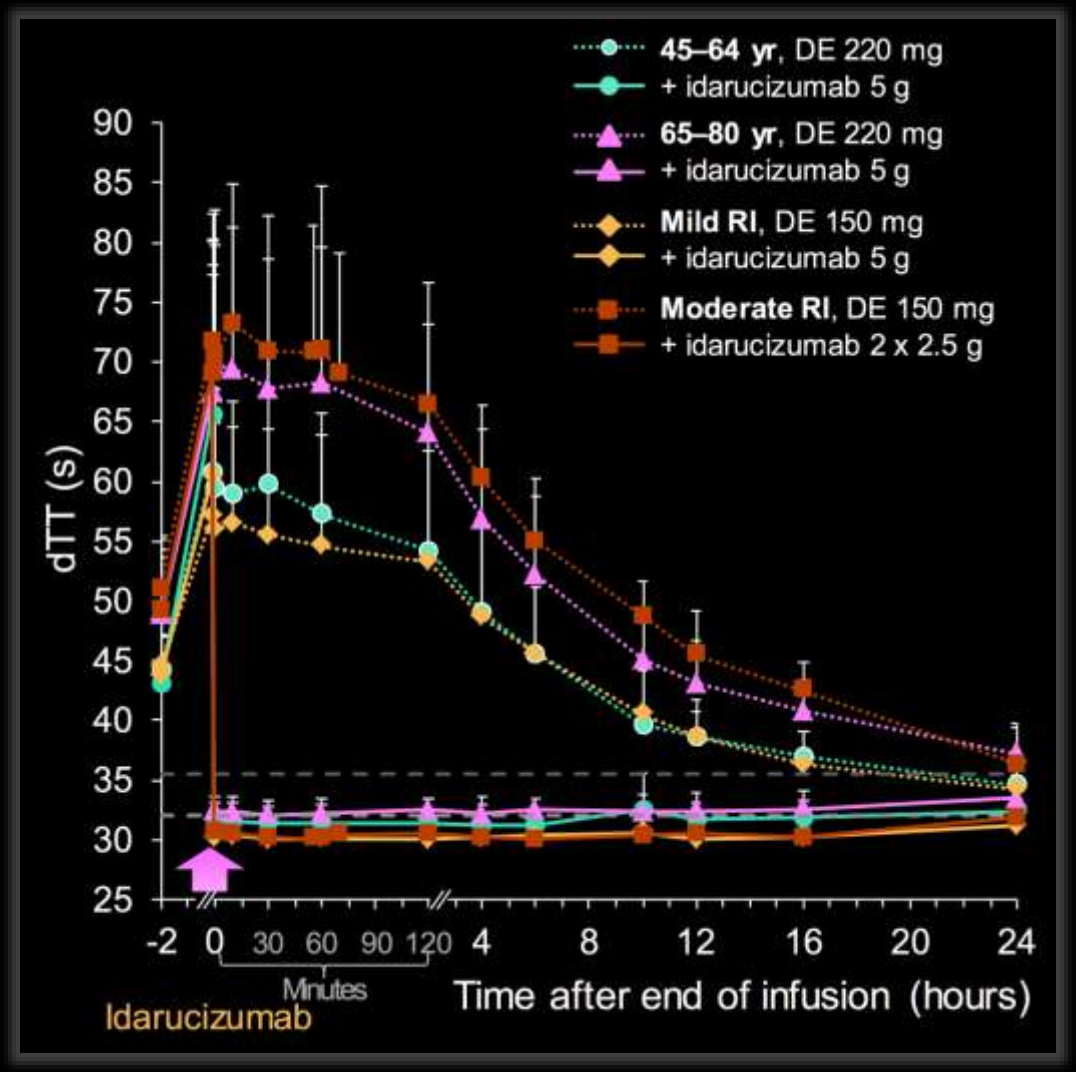
THROMBOSIS AND HEMOSTASIS

A specific antidote for dabigatran: functional and structural characterization

Felix Schiele,[1] Joanne van Ryn,[2] Keith Canada,[3] Corey Newsome,[3] Eliud Sepulveda,[3] John Park,[4] Herbert Nar,[1] and Tobias Litzenburger[4]

Schiele. Blood. 2013;121(18):3554-3562

Idarucizumab: (*antidote for dabigatran*)

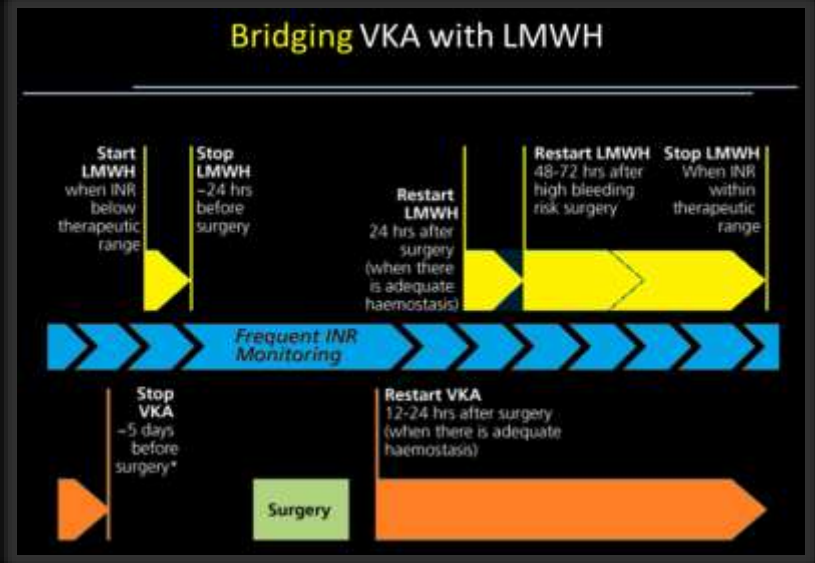


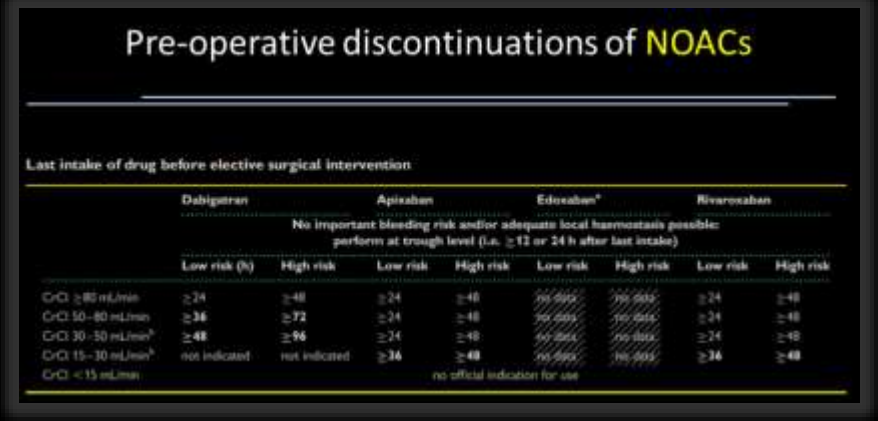
Glund. ASH2014

Question

1. Continue with dabigatran, no need to interrupt it.
2. Stop dabigatran 5 days before the intervention and start it again 1 day after the intervention.
3. Stop dabigatran 1 day before the intervention and start it again 1 day after the intervention.
4. Stop dabigatran 5 days before the intervention and continue with low-dose LMWH; switch back to dabigatran 1 day after the intervention.
5. Stop dabigatran 5 days before the intervention and continue with high-dose LMWH; switch back to dabigatran 1 day after the intervention.
6. Stop dabigatran 5 days before the intervention and continue with acenocoumarol; switch back to dabigatran 1 day after the intervention
7. I don’t know, ask Valeria Caso.

Take-home messages





Postoperative resumption of new oral anticoagulants

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HSO Hellenic Stroke Organization

ESO EUROPEAN STROKE ORGANISATION

Condition-associated thromboembolic risk

High-risk conditions
Atrial fibrillation associated with valvular heart disease (including the presence of a mechanical valve)
Atrial fibrillation associated with congestive heart failure or a left ventricular ejection fraction of <35 percent
Atrial fibrillation associated with a history of a thromboembolic event
Atrial fibrillation associated with hypertension, diabetes, or age >75 years
Mechanical valves in the mitral position
Mechanical valves in patients who have had a prior thromboembolic event
Coronary stents placed within one year
Acute coronary syndrome
Nonstented percutaneous coronary intervention after myocardial infarction
Low-risk conditions
Deep vein thrombosis
Chronic or paroxysmal atrial fibrillation that is not associated with valvular disease
Bioprosthetic valves
Mechanical valves in the aortic position

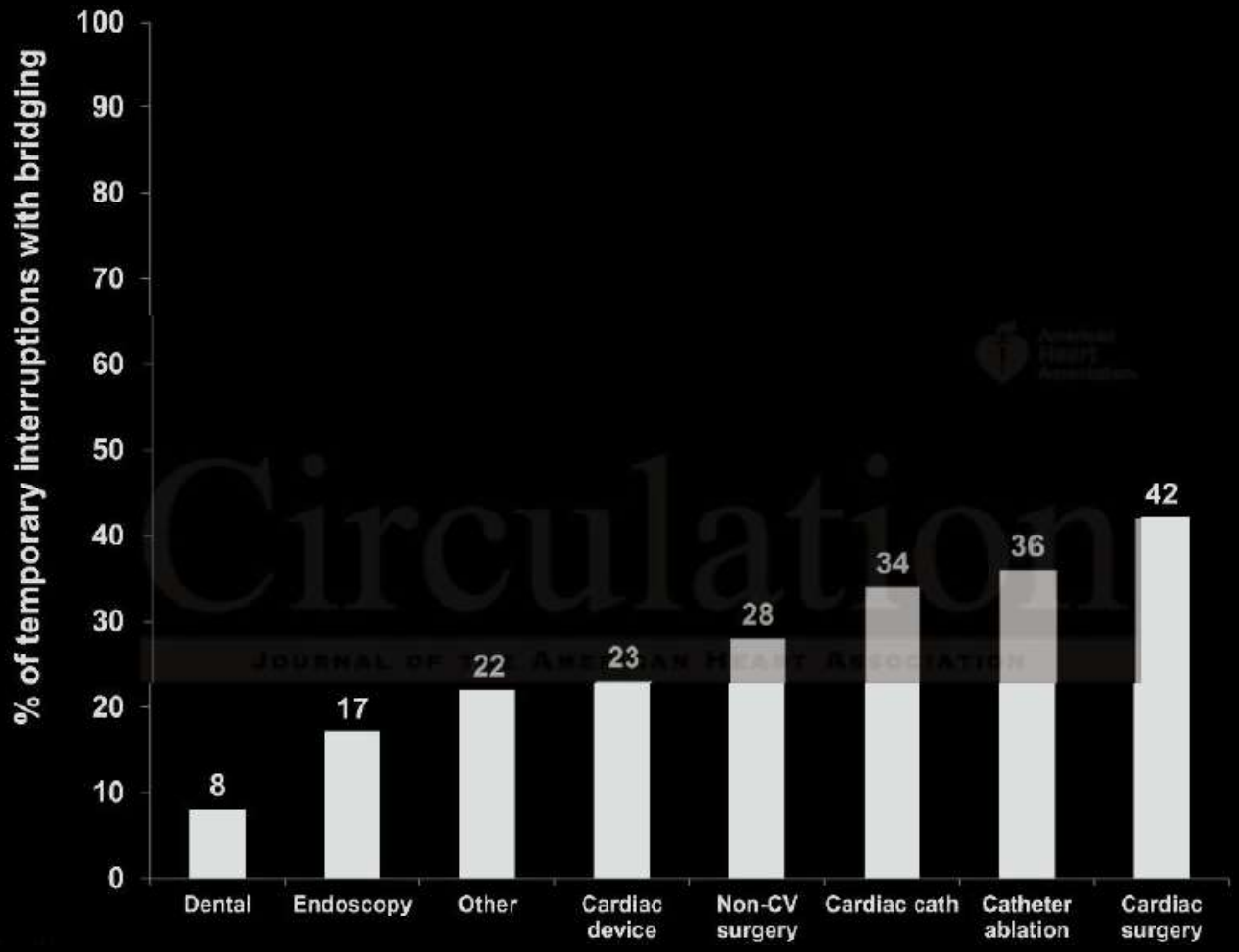
Gan. Gastrointest Endosc 2009; 70:1060

Condition-associated thromboembolic risk

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

Douketis. Chest 2012; 141(2)(Suppl):e326S–e350S

" To bridge or not to bridge? "



Steinberg. Circulation. 2015;online early

Periprocedural thromboembolic risk in AF patients

	% patients		
	Dabigatran 110mg n=1487	Dabigatran 150mg n=1546	Warfarin n=1558
Ischaemic stroke	0.4	0.4	0.4
CV death	0.6	0.5	0.5

Healey. Circulation. 2012;126:343-348

Periprocedural thromboembolic risk in AF patients

	% patients		
	Dabigatran 110mg n=1487	Dabigatran 150mg n=1546	Warfarin n=1558
Systemic embolism	0.1	0.1	0.1

Healey. Circulation. 2012;126:343-348

Bleeding risk of GI interventions

High-risk procedures
Polypectomy or endoscopic resection
Argon plasma coagulation and thermal ablative therapy
Endoscopic sphincterotomy
Pneumatic or bougie dilation of benign or malignant strictures
Percutaneous endoscopic gastrostomy tube placement
Endoscopic ultrasound (EUS)-guided fine-needle aspiration
Endoscopic hemostasis
Therapeutic balloon assisted enteroscopy
Tissue ablation by any technique
Cystgastrostomy
Treatment of varices
Low-risk procedures
Diagnostic upper endoscopy, flexible sigmoidoscopy, and colonoscopy (including biopsies)
Diagnostic endoscopic retrograde cholangiopancreatography (ERCP)
Biliary stent insertion without endoscopic sphincterotomy
Endosonography
Push enteroscopy and diagnostic balloon assisted enteroscopy
Enteral stent deployment without dilation
Capsule endoscopy

Gan. Gastrointest Endosc 2009; 70:1060

Interventions in anticoagulated patients: not rare

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Heart Association®

Use and Outcomes Associated with Bridging During Anticoagulation Interruptions in Patients with Atrial Fibrillation: Findings from the Outcomes Registry for Better Informed Treatment of Atrial Fibrillation (ORBIT-AF)

Benjamin A. Steinberg, Eric D. Peterson, Sunghee Kim, Laine Thomas, Bernard J. Gersh, Gregg C. Fonarow, Peter R. Kowey, Kenneth W. Mahaffey, Matthew W. Sherwood, Paul Chang, Jonathan P. Piccini and Jack Ansell
on behalf of the Outcomes Registry for Better Informed Treatment of Atrial Fibrillation (ORBIT-AF) Investigators and Patients

Circulation. published online December 12, 2014;