CONVEGNO

Terapie Anticoagulanti

EVIDENZE ED OPINIONI A CONFRONTO

Cremona, venerdì 4 marzo 2016

Cremona

4 Marzo 2016

AVK e DOAC in chirurgia: "to bridge or not"?

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Conflitti di Interesse

Letture
Protocolli di Ricerca
Advisory Boards

- Bayer
- BMS/Pfizer
- Boheringer
- Daichii
- Sanofi
- Alfa Wasserman

Pazienti in TAO:

1.000.000-1200000

~ 1/10

Procedura-Intervento/anno

Bridging therapy

Fase
Pre-operatoria

Fase
Post-operatoria

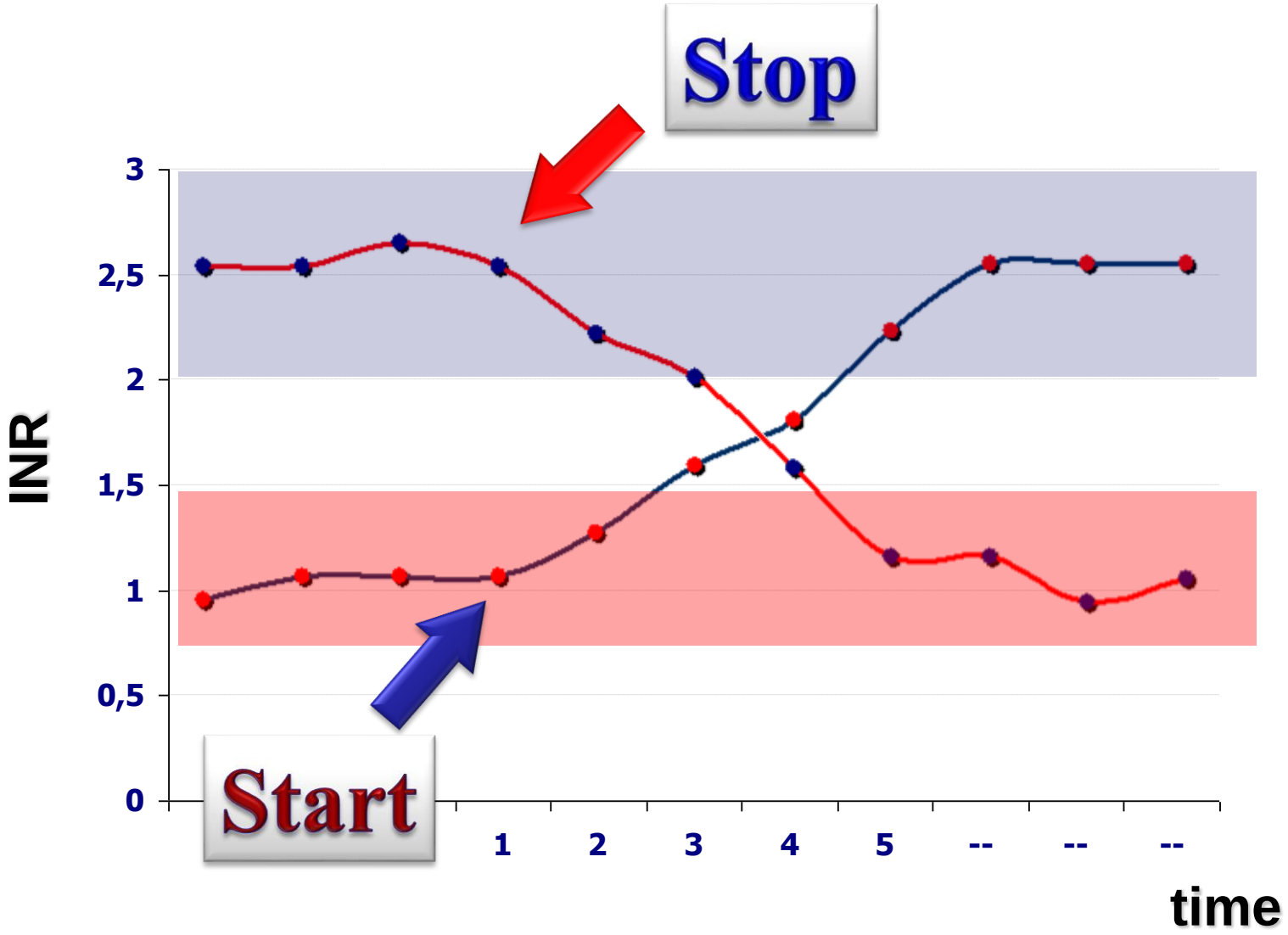
- Procedura invasiva
- Intervento Chirurgico

Bridging, la mia posizione attuale…

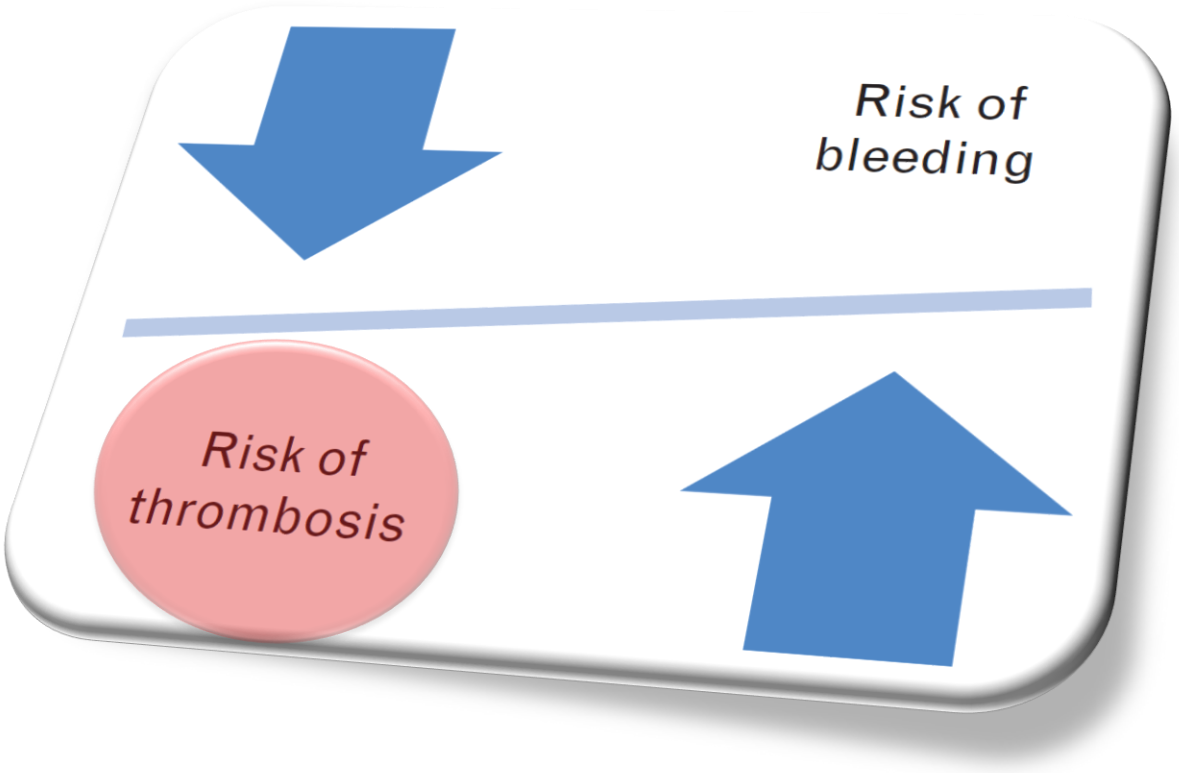
Ma…

F.D. 40 anni
Ex Bridger

Warfarin therapy



‘New’ direct oral anticoagulants in the perioperative setting



Breuer et al. Curr Opin Anesthesiol 2014

EDITORIAL

Perioperative Management of Warfarin Therapy: To Bridge or Not to Bridge, That Is the Question

Although interruption of warfarin is thought to expose patients to a low risk of arterial thromboembolism, such events can have devastating consequences: valve thrombosis is associated with a 15% mortality rate, and an embolic stroke is associated with a 70% rate of major neurologic deficit or death.[3-5]

Douketis et al; Majo Clin Proc 2008

Perioperative management of warfarin and antiplatelet therapy

Major events in perioperative management

Study	Patients (N)	Follow-up (mo)	Reason for anticoagulation	Thromboembolism (%)	Major bleeding (%)
Douketis et al, 2004[9]	650	0.5	AF, MHV	0.6%	1.0%
Kovacs et al, 2004[10]	224	3	AF, MHV	1.3%	6.9%
Dunn et al, 2007[11]	260	1	AF, DVT	2.3%	3.5%
Spyropoulos et al, 2006[12]	901	1	AF, MHV, VTE	1.5%	3.3%
Turpie and Douketis, 2004[13]	220	3	MHV	0.5%	3.5%
Jaffer et al, 2005[14]	493	1	VTE, CVA, AF, MHV	0.8%	3.2%

1.0 % **3.5 %**

Jaffer et al CCJM 2009

Perioperative management of warfarin and antiplatelet therapy

Risk category	Mechanical heart valve
High (>10%/yr risk of ATE or >10%/mo risk of VTE)	Any mechanical mitral valve Older aortic valve Recent (< 6 mo) stroke or TIA
Moderate (4%–10%/yr risk of ATE or 4%–10%/mo risk of VTE)	Bileaflet aortic valve and one of the following: atrial fibrillation, prior stroke/TIA, hypertension, diabetes, heart failure, age > 75 yr
Low (<4%/yr risk of ATE or <2%/mo risk of VTE)	Bileaflet aortic valve without atrial fibrillation and no other risk factors for stroke

Jaffer et al CCJM 2009

Perioperative management of warfarin and antiplatelet therapy

Risk category	Atrial fibrillation
High (>10%/yr risk of ATE or >10%/mo risk of VTE)	$CHADS_2$ score of 5 or 6 Recent (< 3 mo) stroke or TIA Rheumatic valvular heart disease
Moderate (4%–10%/yr risk of ATE or 4%–10%/mo risk of VTE)	$CHADS_2$ score of 3 or 4
Low (<4%/yr risk of ATE or <2%/mo risk of VTE)	$CHADS_2$ score of 0–2 (and no prior stroke or TIA)

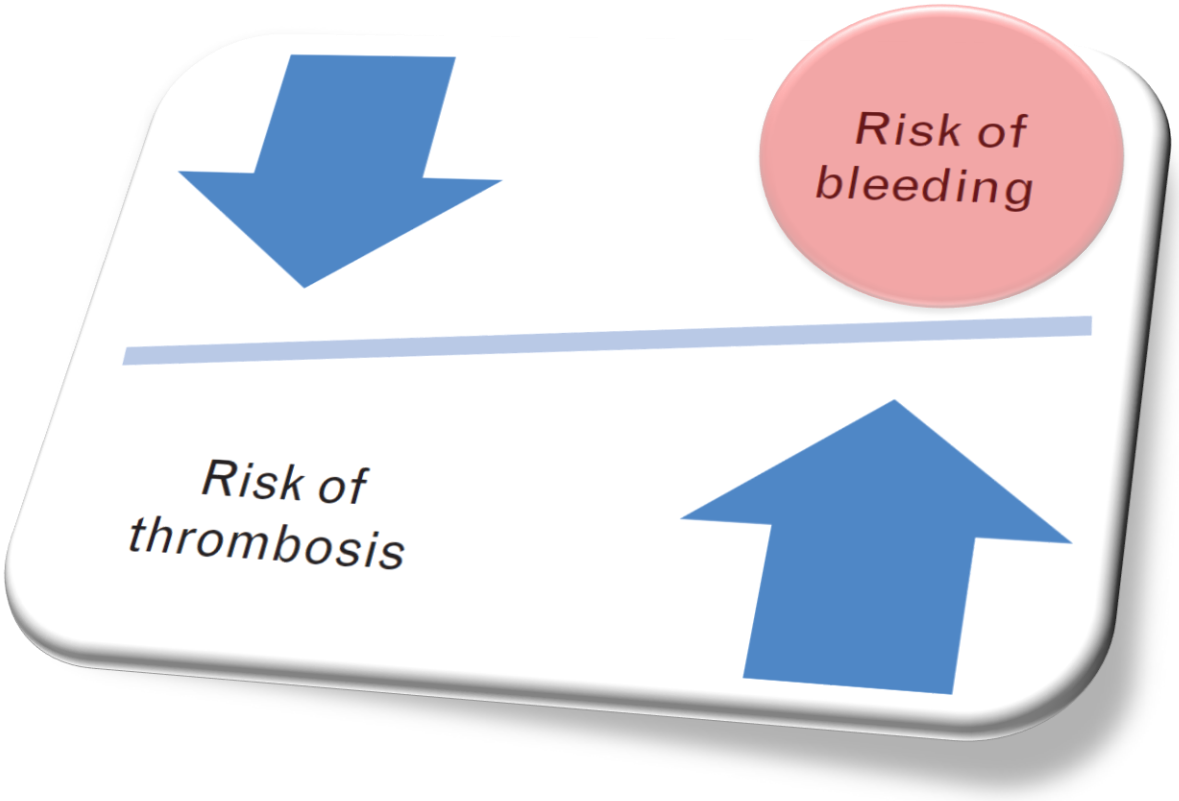
Jaffer et al CCJM 2009

Perioperative management of warfarin and antiplatelet therapy

Risk category	Venous thromboembolism
High (>10%/yr risk of ATE or >10%/mo risk of VTE)	Recent (< 3 mo) VTE Severe thrombophilia
Moderate (4%–10%/yr risk of ATE or 4%–10%/mo risk of VTE)	VTE within past 3–12 mo Recurrent VTE Nonsevere thrombophilic conditions Active cancer
Low (<4%/yr risk of ATE or <2%/mo risk of VTE)	Single VTE within past 12 mo and no other risk factors

Jaffer et al CCJM 2009

‘New’ direct oral anticoagulants in the perioperative setting



Breuer et al. Curr Opin Anesthesiol 2014

Intervento e rischio emorragico correlato

Interventi a basso rischio emorragico	Interventi a moderato rischio emorragico	Interventi ad elevato rischio emorragico
• Estrazioni dentali • Incisioni di ascessi • Cataratta/glaucoma • Endoscopie senza chirurgia • Chirurgia superficiale (dermatologica)	• Endoscopia con biopsia • Studio elettrofisiologico/ablazione • Angiografia • Impianto di pacemaker	• Interventi con anestesia spinale o epidurale • Chirurgia toracica • Chirurgia addominale • Chirurgia ortopedica maggiore • Biopsia del fegato/reni • Resezione della prostata

EHRA Practical Guide, Europace 2013

Periprocedural Heparin Bridging in Patients Receiving Vitamin K Antagonists

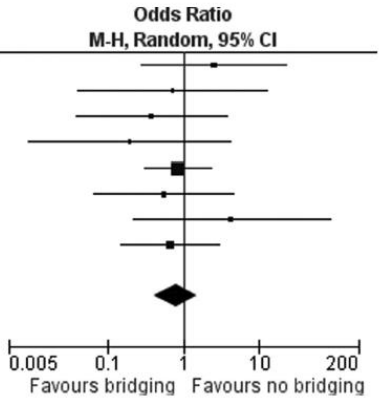
Systematic Review and Meta-Analysis of Bleeding and Thromboembolic Rates

Thromboembolic events

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: $Z = 0.67$ ($P = 0.50$)

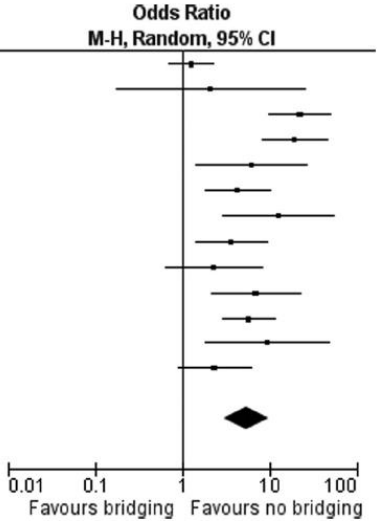


Overall bleeding events

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			

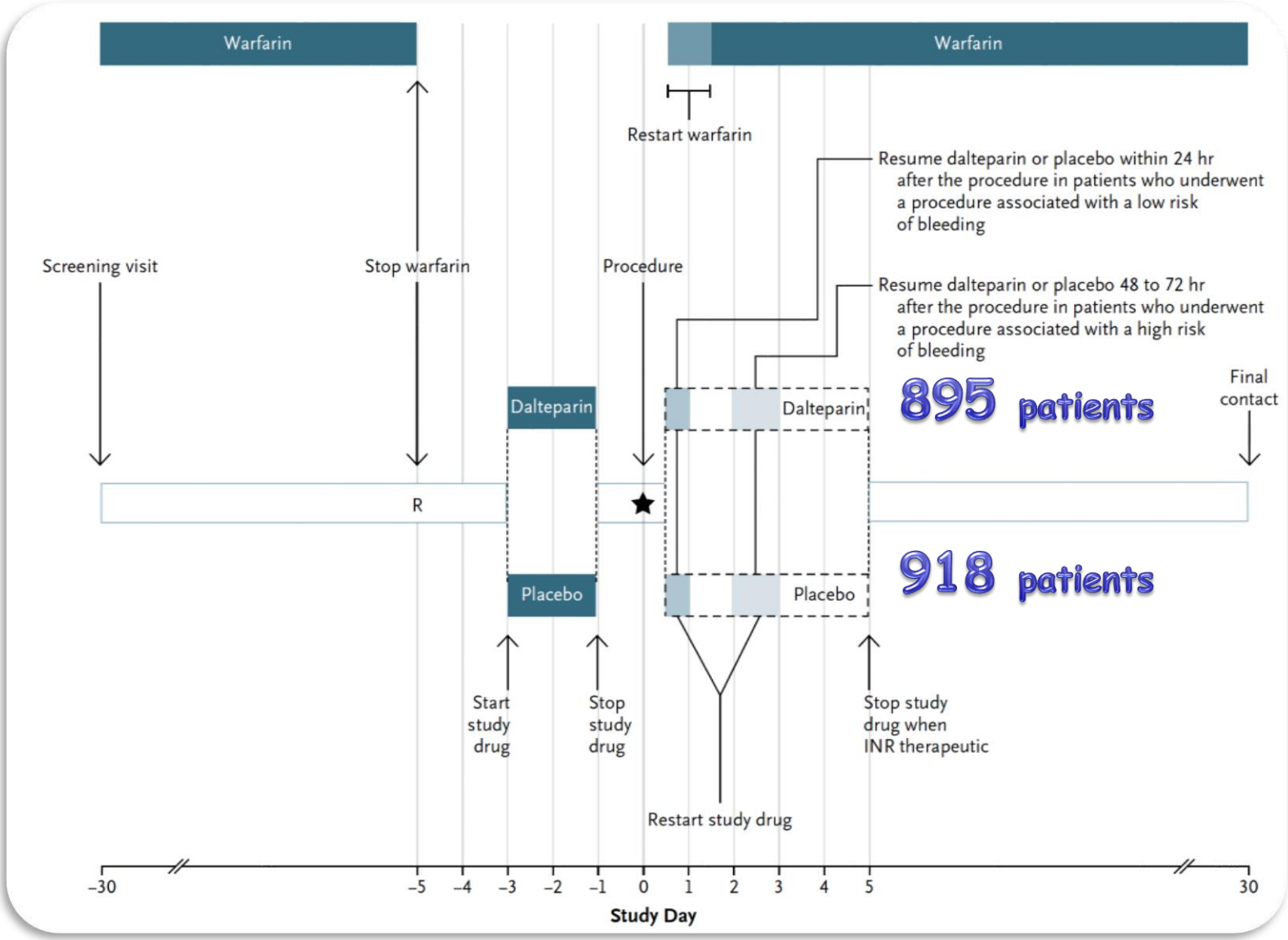
Heterogeneity: $Tau^2 = 0.83$; $Chi^2 = 52.47$, df = 12 ($P < 0.00001$); $I^2 = 77\%$

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



Siegal et al. Circulation 2012

Perioperative Bridging Anticoagulation in Patients with Atrial Fibrillation



Douketis J et al. NEJM 2015; 373:823-33

Perioperative Bridging Anticoagulation in Patients with Atrial Fibrillation

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†
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†

Patients in whom arterial thromboembolism occurred had a mean CHADS2 score of 2.6 (range, 1 to 4)

Five of the seven events occurred after a minor procedure.

Douketis J et al. NEJM 2015; 373:823-33

Perioperative Bridging Anticoagulation in Patients with Atrial Fibrillation

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†

Douketis J et al. NEJM 2015; 373:823-33

The perioperative management of new direct oral anticoagulants: a question without answers

	Apixaban	Rivaroxaban	Dabigatran
Mechanism of action	Direct Xa inhibitor	Direct Xa inhibitor	Direct IIa inhibitor
Protein-binding (%)	35	40–59	> 90
Substrate of transporters (P-gp)	Yes	Yes	Yes
Half-life (h)	8–15	5–9	14–17
Substrate or CYP enzymes	Minor (CYP3A4)	Major (CYP3A4, CYP2J2)	No
Elimination	70% Unchanged 30% Inactive metabolites	50% Unchanged 50% Inactive metabolites	100% Unchanged drug+ active metabolites
Route of elimination	25% Urine 70% Faeces	70% Urine 30% Faeces	80% Urine 20% Faeces

Ferrandis R et al. Thromb Haemost 2013; 110:515-22

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

Table 3 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 et al Europace 2013

Peri-interventional management of novel oral anticoagulants in daily care: results from the prospective Dresden NOAC registry

European Heart Journal (2014) **35**, 1888–1896
doi:10.1093/eurheartj/eht557

CLINICAL RESEARCH
Thrombosis and antithrombotic therapy

Peri-interventional management of novel oral anticoagulants in daily care: results from the prospective Dresden NOAC registry

Jan Beyer-Westendorf[1]*, Vera Gelbricht[1], Kati Förster[1], Franziska Ebertz[1], Christina Köhler[1], Sebastian Werth[1], Eberhard Kuhlisch[2], Thoralf Stange[2], Christoph Thieme[1], Katharina Daschkow[1], and Norbert Weiss[1]

Peri-interventional management of novel oral anticoagulants in daily care: results from the prospective Dresden NOAC registry

Outcome at Day 30 ± 5 after procedure	Type of procedures	Procedures without heparin bridging (*N* = 606)	Procedures with heparin bridging (*N* = 257)	*P*-value no bridging vs. bridging
Major cardiovascular events, *n* (%; 95% CI)	Minimal	0 (0.0%; 0.0–0.6)	0 (0.0%; 0.0–1.4)	>0.999
	Minor	4 (0.7%; 0.2–1.7)	1 (0.4%; 0.0–2.1)	0.830
	Major	1 (0.2%; 0.0–0.9)	3 (1.2%; 0.2–3.4)	0.082
	All	5 (0.8%; 0.3–1.9)	4 (1.6%; 0.4–3.9)	0.265
Major bleeding, *n* (%; 95% CI)	Minimal	0 (0.0%; 0.0–0.6)	0 (0.0%; 0.0–1.4)	>0.999
	Minor	2 (0.3%; 0.0–1.2)	1 (0.4%; 0.0–2.1)	[illegible]
	Major	1 (0.2%; 0.0–0.9)	6 (2.3%; 0.9–5.0)	**0.004**
	All	3 (0.5%; 0.1–1.4)	7 (2.7%; 1.1–5.5)	**0.010**

Beyer-Westendorf et al. Eur Heart J 2014

Peri-interventional management of novel oral anticoagulants in daily care: results from the prospective Dresden NOAC registry

Risk factors for cardiovascular events

Table 5 Uni- and multivariate analyses of potential risk factors for cardiovascular events

Risk factor	Univariate analysis			Multivariate analysis		
	OR	95% CI	P-value	OR	95% CI	P-value
Dabigatran vs. rivaroxaban	7.4	0.7–82.2	0.101	–	–	–
Arterial hypertension	n.a.	0–∞	0.996	–	–	–
Diabetes	14.9	1.9–119.9	**0.011**	13.2	1.6–107.3	**0.016**
TIA/stroke in history	1.8	0.4–8.8	0.467	–	–	–
Coronary artery disease	2.0	0.5–8.0	0.337	–	–	–
Impaired renal function (GFR < 50 mL/min)	n.a.	0–∞	0.996	–	–	–
Major vs. non-major procedure	7.4	2.0–28.2	**0.003**	7.3	1.9–28.5	**0.004**
Age >65 years vs. <65 years	1.7	0.2–13.7	0.616	–	–	–
Pre-procedural NOAC interruption >24 h vs. <24 h	0.6	0.2–2.7	0.545	–	–	–
Heparin bridging vs. no bridging	1.9	0.5–7.1	0.341	–	–	–

Beyer-Westendorf et al. Eur Heart J 2014

Peri-interventional management of novel oral anticoagulants in daily care: results from the prospective Dresden NOAC registry

Risk factors for major bleeding events

Table 6 *Uni- and multivariate analyses of potential risk factors for major bleeding events*

Risk factor	Univariate analysis			Multivariate analysis		
	OR	95% CI	P-value	OR	95% CI	P-value
Arterial hypertension	n.a.	0–∞	0.996	–	–	–
Diabetes	1.2	0.3–4.3	0.763	–	–	–
TIA/stroke in history	0.7	0.1–5.5	0.728	–	–	–
Coronary artery disease	2.7	0.7–9.5	0.133	–	–	–
Impaired renal function (GFR < 50 mL/min)	0.67	0.1–5.2	0.687	–	–	–
Major vs. non-major procedure	22.5	5.7–88.9	**<0.001**	16.8	3.8–78.9	**<0.001**
Age >65 years vs. <65 years	0.8	0.2–4.0	0.847	–	–	–
Pre-procedural NOAC interruption >24 h vs. <24 h	n.a.	0–∞	0.955	–	–	–
Heparin bridging vs. no bridging	5.6	1.4–21.9	**0.013**	5.0	1.2–20.4	0.023
HAS-BLED ≥ 3 vs. <3	1.5	0.4–5.7	0.589	–	–	–

Beyer-Westendorf et al. Eur Heart J 2014

Perioperative bridging anticoagulation during dabigatran or warfarin interruption among patients who had an elective surgery or procedure

Substudy of the RE-LY trial

James D. Douketis[1]; Jeff S. Healey[1,2]; Martina Brueckmann[3,4]; John W. Eikelboom[1,2]; Michael D. Ezekowitz[5]; Mandy Fraessdorf[3]; Herbert Noack[3]; Jonas Oldgren[6]; Paul Reilly[7]; Alex C. Spyropoulos[8]; Lars Wallentin[6]; Stuart J. Connolly[1,2]

Perioperative management	Warfarin-treated (n = 391)		Dabigatran-treated (n = 418)	
	Pre-operative	Post-operative	Pre-operative	Post-operative
Stopping oral anticoagulant: n (%)				
-<1 day before surgery/procedure	12 (3.1)	n/a	43 (10.3)	n/a
-<2 days before surgery/procedure	15 (3.8)		100 (23.9)	
-2–5 days before surgery/procedure	164 (41.9)		167 (40.0)	
->5 days before surgery/procedure	191 (48.8)		98 (23.4)	
-timing data missing	9 (2.3)		10 (2.4)	
Resuming oral anticoagulant: n (%)	n/a		n/a	
-<1 day after surgery/procedure		86 (23.5)		87 (23.8)
-<2 days after surgery/procedure		78 (21.3)		54 (14.8)
-2–5 days after surgery/procedure		90 (24.5)		80 (21.9)
->5 days after surgery/procedure		97 (26.4)		133 (36.3)
-timing data missing		16 (4.4)		12 (3.3)
LMWH bridging regimen: n (%)				
-any LMWH:	246	266	200	265
- once-daily SC	151 (61.4)	159 (59.8)	124 (62.0)	174 (65.7)
- twice-daily SC	92 (37.5)	103 (38.7)	71 (35.5)	82 (30.9)
- dose regimen data missing	3 (1.2)	4 (1.5)	5 (2.5)	9 (3.4)
-timing of 1st post-operative dose:	n/a	80 (30.1)	n/a	92 (34.7)
- day 0		93 (35.0)		81 (30.6)
- day +1		36 (13.6)		21 (7.9)
- day +2 or later		57 (21.4)		71 (26.8)
- timing data missing				
UFH bridging regimen: n (%)				
-any UFH:	58	65	61	70
- intravenous	35 (60.3)	33 (50.8)	40 (65.6)	37 (52.9)
- SC	23 (39.7)	31 (47.7)	21 (34.4)	33 (47.1)
- dose regimen data missing	0	1 (1.5)	0	0

SC, subcutaneous; LMWH, low-molecular-weight heparin; UFH, unfractionated heparin.

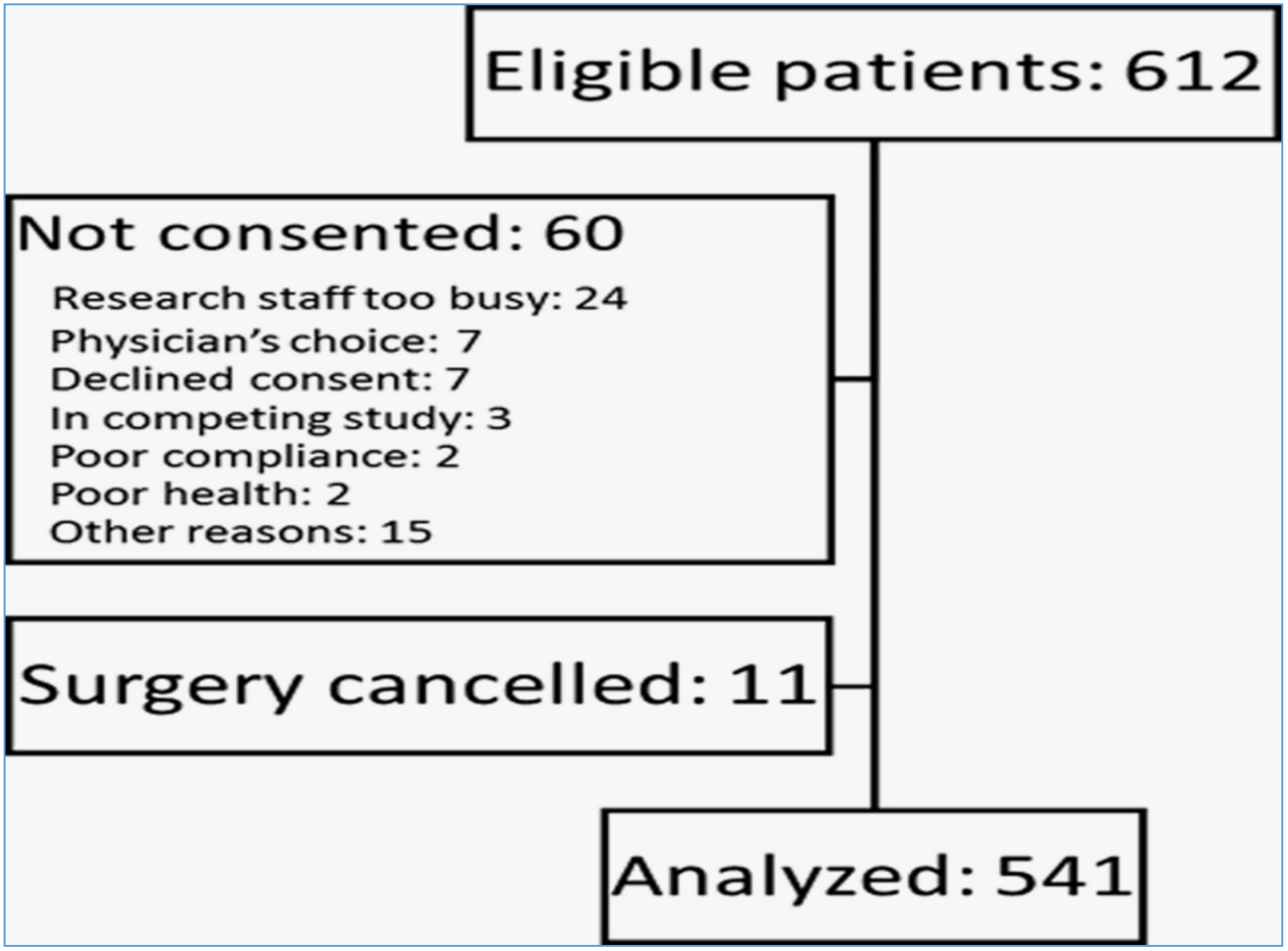
Clinical outcome	Bridging status	Warfarin group (n = 1,415)		Dabigatran group (2,691)	
		% (N) patients with events /(N) patients assessed	OR (95 % CI): bridged vs not bridged‡	% (N) patients with events /(N) patients assessed	OR (95 % CI): bridged vs not bridged‡
Major bleeding	Bridged	6.8 (26/383)	4.62 (2.45–8.72)	6.5 (27/417)	3.68 (2.24–6.04),
	Not bridged	1.6 (16/1,032)	P < 0.001	1.8 (42/2,274)	P < 0.001
	Treatment interaction (warfarin vs. dabigatran) ¶	p = 0.577			
Stroke and systemic embolism	Bridged	0.5 (2/383)	2.70 (0.38–19.3),	0.5 (2/417)	1.82 (0.37–9.06),
	Not bridged	0.2 (2/1,032)	P = 0.321	0.3 (6/2,274)	P = 0.463
	Treatment interaction (warfarin vs. dabigatran) ¶	p = 0.760			
Any thrombo-embolism	Bridged	1.8 (7/383)	6.39 (1.64–24.8),	1.2 (13/417)	2.11 (0.75–5.95),
	Not bridged	0.3 (3/1,032)	P =0.007	0.6 (5/2,274)	P = 0.158
	Treatment interaction (warfarin vs. dabigatran) ¶	p = 0.204			

†27 patients (9 bridged, 18 not bridged) excluded from total sample (described in Table 1) due to missing creatinine clearance values to enable better comparison of univariate and multivariable logistic regression models; ‡odds ratios obtained from univariate logistic analysis within treatment groups; ¶p-value of interaction from logistic model with treatment, bridging and treatment by bridging interaction; OR, odds ratio; CI, confidence interval. ¥inclusion of 27 patients with missing creatinine clearance values did not significantly affect clinical outcome results in bridged and not bridged patients.

Perioperative Management of Dabigatran

A Prospective Cohort Study

Sam Schulman, MD, PhD; Marc Carrier, MD, MSc; Agnes Y.Y. Lee, MD, MSc; Sudeep Shivakumar, MD; Mark Blostein, MD; Frederick A. Spencer, MD; Susan Solymoss, MD, BSc; Rebecca Barty, MLT, BA, MSc; Grace Wang, MMath; Nancy Heddle, MSc; James D. Douketis, MD; on behalf of the Periop Dabigatran Study Group*



Perioperative Management of Dabigatran

A Prospective Cohort Study

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Renal Function, CL_{CR}, mL/min	Estimated Half-Life, h*	Timing of Last Dose of Dabigatran Before Surgery	
		Standard Risk of Bleeding	High Risk of Bleeding†
>80	13 (11–22)	24 h=morning of day –1	2 d=morning of day –2
>50 to ≤80	15 (12–34)	24 h=morning of day –1	2 d=morning of day –2
>30 to ≤50	18 (13–23)	2 d=morning of day –2	4 d=morning of day –4
≤30‡	27 (22–35)	4 d=morning of day –4	6 d=morning of day –6

CL_{CR} indicates calculated creatinine clearance.

*Data from renal impairment study in healthy volunteers,[10] geometric mean (range).

†Types of surgery associated with a high risk of bleeding (or in major surgery in which complete hemostasis may be required) include but are not limited to cardiac surgery, neurosurgery, abdominal surgery, or surgeries involving a major organ. Other procedures such as spinal anesthesia may also require complete hemostatic function. Other important determinants of bleeding risk include advancing age, comorbidities (eg, major cardiac, respiratory, or liver disease), and concomitant use of antiplatelet therapy. See the online-only Data

Type of surgery/procedure	Time of dabigatran resumption	Dabigatran dose
High risk for bleeding that may be critical		
Major cardiac surgery	evening of POD+1	75 mg first 2 doses
Neurosurgery	no bleed on repeat CT	75 mg first 2 doses
High risk for bleeding		
Large hernia repair	48 hrs or when hemostasis is secured	75 mg first dose
Major cancer surgery	72 hrs or when hemostasis is secured	usual dose
Major urologic surgery (prostate/bladder resection)	when no macroscopic hematuria	usual dose
Major vascular surgery	48 hrs	usual dose
Any other major operation with duration >45 minutes	48 hrs	usual dose
Endoscopic large polyp resection	72 hrs	usual dose
Esophageal variceal treatment, biliary sphincterectomy, pneumatic dilatation	48 hrs	usual dose
Endoscopically-guided fine-needle aspiration; kidney biopsy	48 hrs	usual dose
Pacemaker/ICD insertion*	72 hrs	usual dose
Major dental procedure (multiple extractions)	48 hrs	usual dose
Standard risk for bleeding		
Major orthopedic surgery (joint replacement or laminectomy)†	6-10 hrs	75 mg first dose
Coronary angiography /PCI/electrophysiologic testing	same evening	75 mg first dose
Indwelling catheter for neuraxial anesthesia‡	4 hrs after removal	75 mg first dose
Cholecystectomy, appendectomy	same evening	75 mg first dose
Abdominal hernia repair	same evening	75 mg first dose
Abdominal hysterectomy	same evening	75 mg first dose

Anticoagulation Resumption

Perioperative Management of Dabigatran

A Prospective Cohort Study

Sam Schulman, MD, PhD; Marc Carrier, MD, MSc; Agnes Y.Y. Lee, MD, MSc; Sudeep Shivakumar, MD; Mark Blostein, MD; Frederick A. Spencer, MD; Susan Solymoss, MD, BSc; Rebecca Barty, MLT, BA, MSc; Grace Wang, MMath; Nancy Heddle, MSc; James D. Douketis, MD; on behalf of the Periop Dabigatran Study Group*

			Last Dose Before Procedure			First Dose After Procedure		
CL_{CR} mL/min	n	Planned Stopping Time, h	As Planned, n (%)*	Earlier, n (%)	Later, n (%)	As Planned, n (%)	Earlier, n (%)	Later, n (%)
Procedures with standard risk of bleeding								
>50	274							32 (12)
>30–≤50	47							3 (6)
≤30	3							0
Procedures with high								
>50	177							35 (20)
>30–≤50	39							6 (15)
≤30	1	154	0	0	1 (100)	0	1 (100)	0
Overall	541		479 (89)	30 (6)	21 (4)	415 (77)	16 (3)	77 (14)

CL_{CR} indicates calculated creatinine clearance.

Preoperative bridging was not used at all, but 9 patients (1.7%) received postoperative LMWH or UFH

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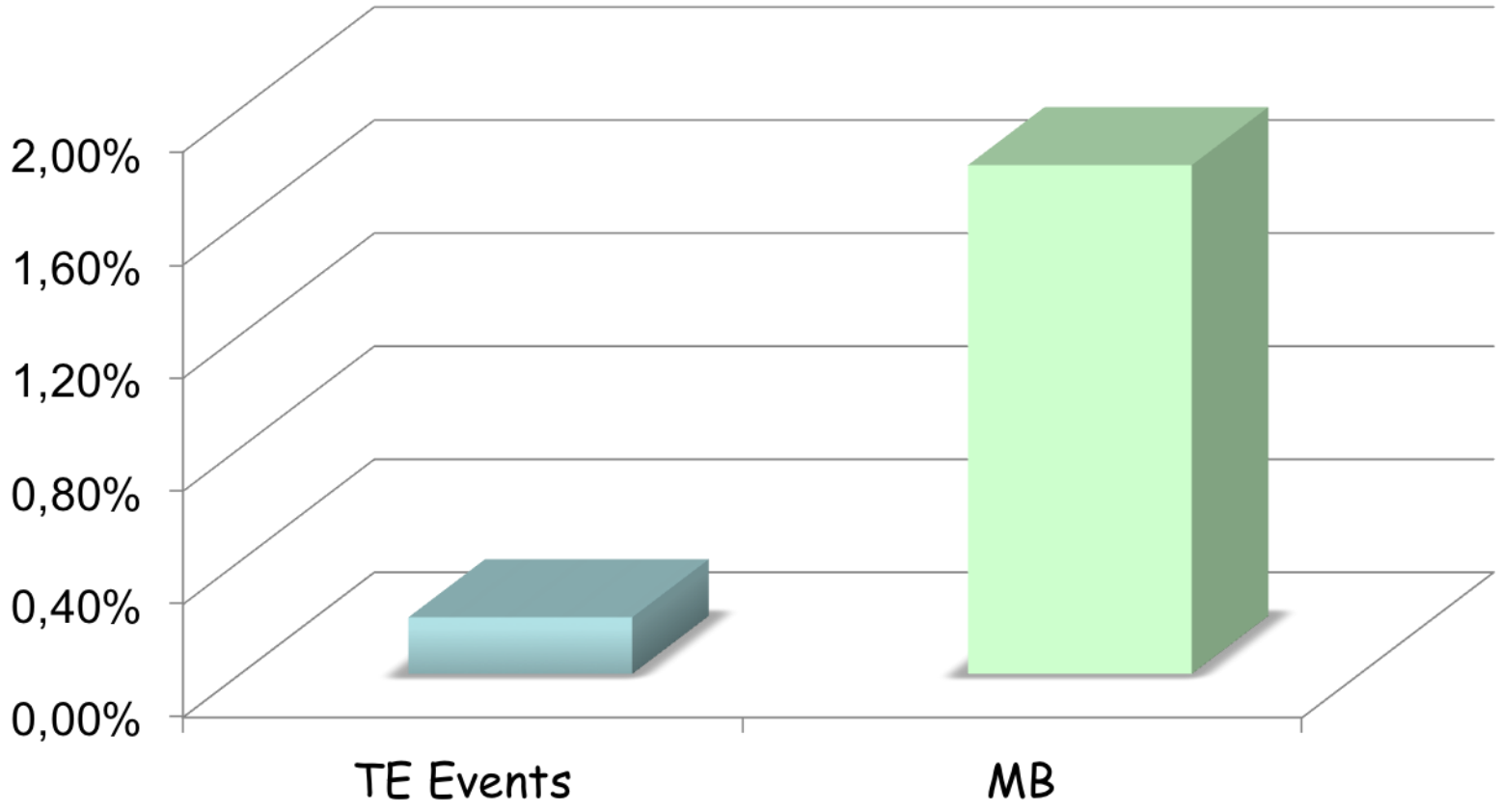

Take home messages

- Bridging aumenta le complicanze emorragiche!
- Riduce le complicanze tromboemboliche?
- DOAC breve emivita
- Costi/scomodità per il paziente