Transitions of Care: *Peri-procedural Anticoagulation Management*

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Patient Case

- 78 yo female with a PMH of Atrial fibrillation, HTN, DM and recent CVA (6 months ago) anticoagulated with warfarin therapy.
- She requires a kidney biopsy for suspected glomerularnephritis.
  - New renal injury with eGFR < 30 ml/min
- What is the best approach to peri-procedural management of her anticoagulation?

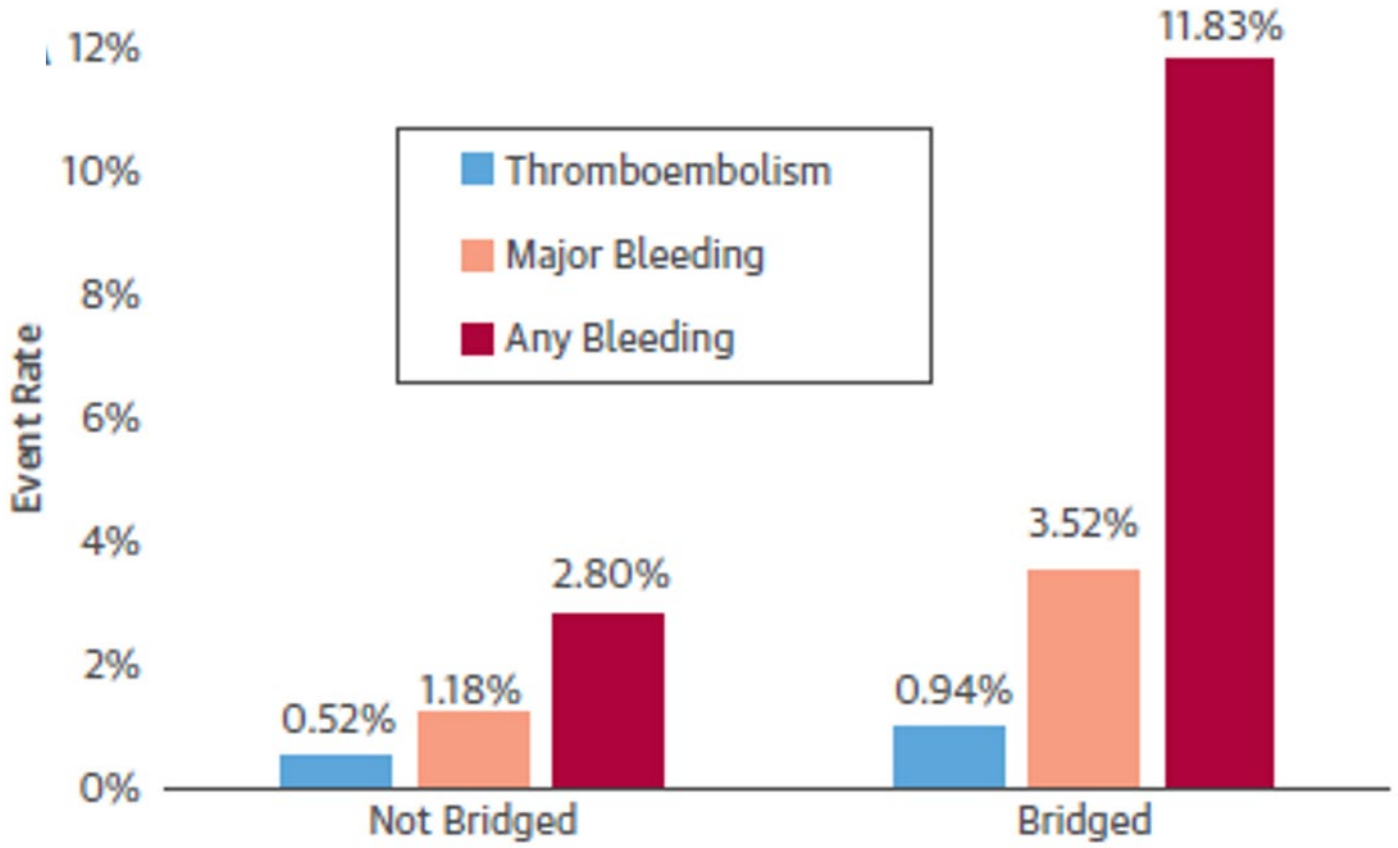
Principles of Bridging

- Do not interrupt chronic anticoagulation for procedures with low bleeding risk
- Bridge therapy has the greatest net benefit when thromboembolism risk is high and bleeding risk is not excessive
- Low thromboembolic risk necessitates an assessment of continued treatment
- Intermediate risk necessitates individual risk benefit assessment

Chest 2012;141;e326S-e350S

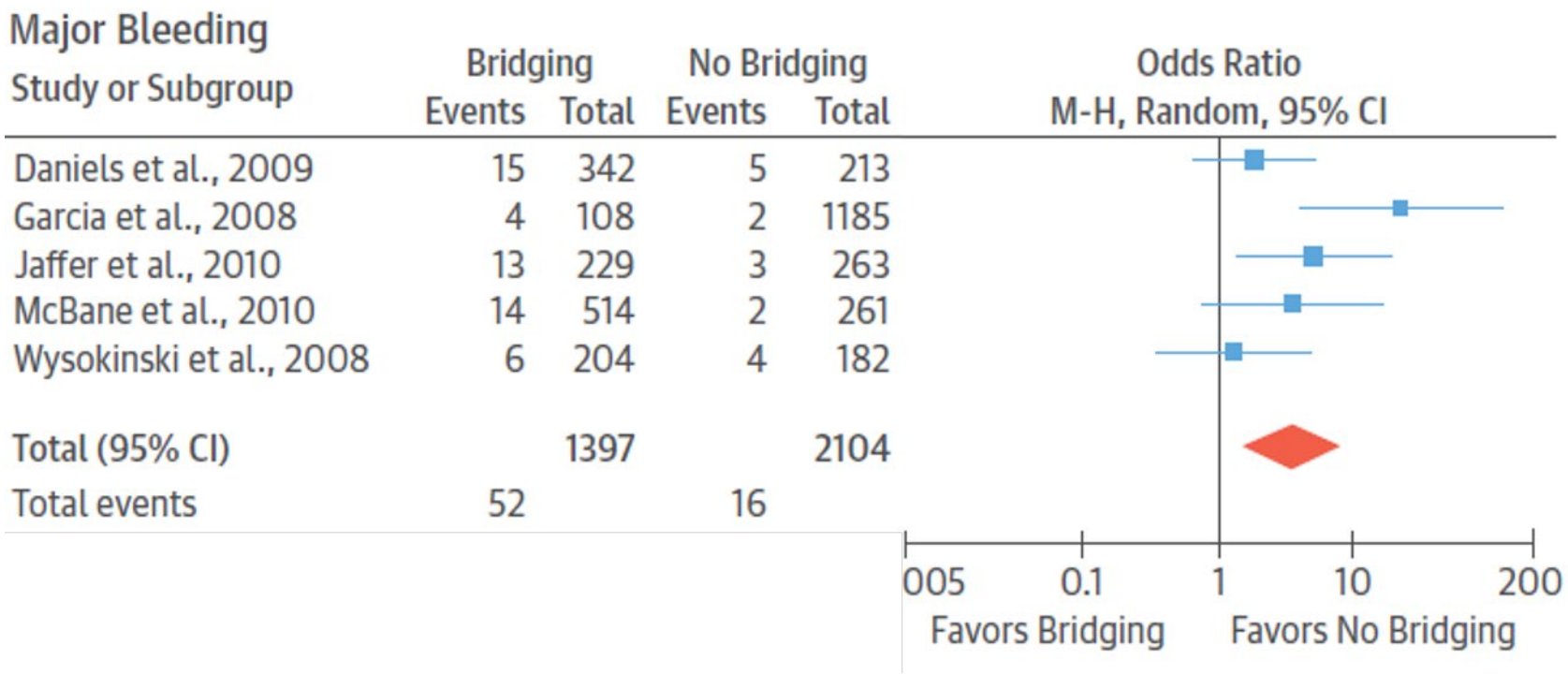
J Am Coll Cardiol 2015;66:1392–403

Periprocedural complications



J Am Coll Cardiol 2015;66:1392–403

Risk of Bleeding



J Am Coll Cardiol 2015;66:1392–403

Will oral anticoagulation need to be discontinued?

- Assess risk of bleeding for the patient and procedure
  - Is the risk of procedural bleeding moderate to high?
  - Does the patient possess any additional bleeding risk factors ?

Surgical Procedures
High Bleeding Risk

- Urologic surgery and procedures such as TURP, bladder resection, or tumor ablation; nephrectomy or kidney biopsy
- Pacemaker or implantable cardioverterdefibrillator device implantation
- Colonic polyp resection, typically of large (ie,1-2 cm long) sessile polyps
- Surgery and procedures in highly vascular organs, such as the kidney, liver, and spleen
- Bowel resection
- Major surgery with extensive tissue injury
  - Cancer surgery, joint arthroplasty, reconstructive plastic surgery
- Cardiac, intracranial, or spinal surgery

Chest 2012;141;e326S-e350S

BRUISE Control Trial

- Patients requiring pacemaker or ICD randomized to continue warfarin or bridge with heparin
  - Annual risk of thromboembolic events of 5% or more
- Trial stopped early

Outcome	Heparin Bridging (N=338)	Continued Warfarin (N=343)	Relative Risk (95% CI)	P Value
Primary outcome				
Clinically significant hematoma — no. (%)	54 (16.0)	12 (3.5)	0.19 (0.10–0.36)	<0.001
Components of primary outcome				
Hematoma prolonging hospitalization — no. (%)	16 (4.7)	4 (1.2)	0.24 (0.08–0.72)	0.006
Hematoma requiring interruption of anticoagulation — no. (%)	48 (14.2)	11 (3.2)	0.20 (0.10–0.39)	<0.001
Hematoma requiring evacuation — no. (%)	9 (2.7)	2 (0.6)	0.21 (0.05–1.00)	0.03

N Engl J Med 2013:368:2084-93

Peri-procedural Bleeding Risk Assessment

HAS-BLED Parameters
Hypertension†
Abnormal renal function‡
Abnormal liver function§
Prior stroke
History of or predisposition to (anemia) major bleeding
Labile INR (VKA)‖
Elderly (>65 years)
Concomitant use of an antiplatelet agent or nonsteroidal anti-inflammatory drug
Alcohol or drug usage history (≥8 drinks/week)¶

Additional Parameters included in the algorithm
Prior bleed event within 3 months (including intracranial hemorrhagic)
Quantitative or qualitative platelet abnormality
INR above the therapeutic range at the time of the procedure (VKA)
Bleed history from previous bridging
Bleed history with similar procedure

Surgical Procedures
Low Bleeding Risk

- Minor dental procedure
  - Including tooth extractions and endodontic procedures
  - Continuing VKAs with coadministration of an oral prohemostatic agent OR
  - Stop VKAs 2 to 3 days before the procedure
- Minor dermatologic procedures,
  - Including excision of basal and squamous cell skin cancers, actinic keratoses, and premalignant or cancerous skin nevi
  - Continue VKAs around the time of the procedure and optimizing local hemostasis
- Cataract surgery
  - Continue VKAs around the time of the surgery

Chest 2012;141;e326S-e350S

Will peri-procedural anticoagulation be required?

- Assessment of thrombotic risk:
  - Low – no bridging required
  - Moderate – consider bleeding risk; previous stroke biggest consideration
  - High – bridging should be strongly considered

Thromboembolism Risk

Atrial Fibrillation

Risk Group	Characteristics
High	CHADS2 score 5 or 6 *CHADS VASC ≥ 7* CVA/TIA < 3 months prior Rheumatic valvular heart disease
Moderate	CHADS2 score 3 or 4 *CHADS VASC 5 – 6*
Low	CHADS2 score 2 or less without prior CVA/TIA *CHADS VASC ≤ 4*

Chest 2012;141:e326S–50S.
JACC 2017;69:871-98

Stroke Risk Assessment

$CHADS_2$ Score

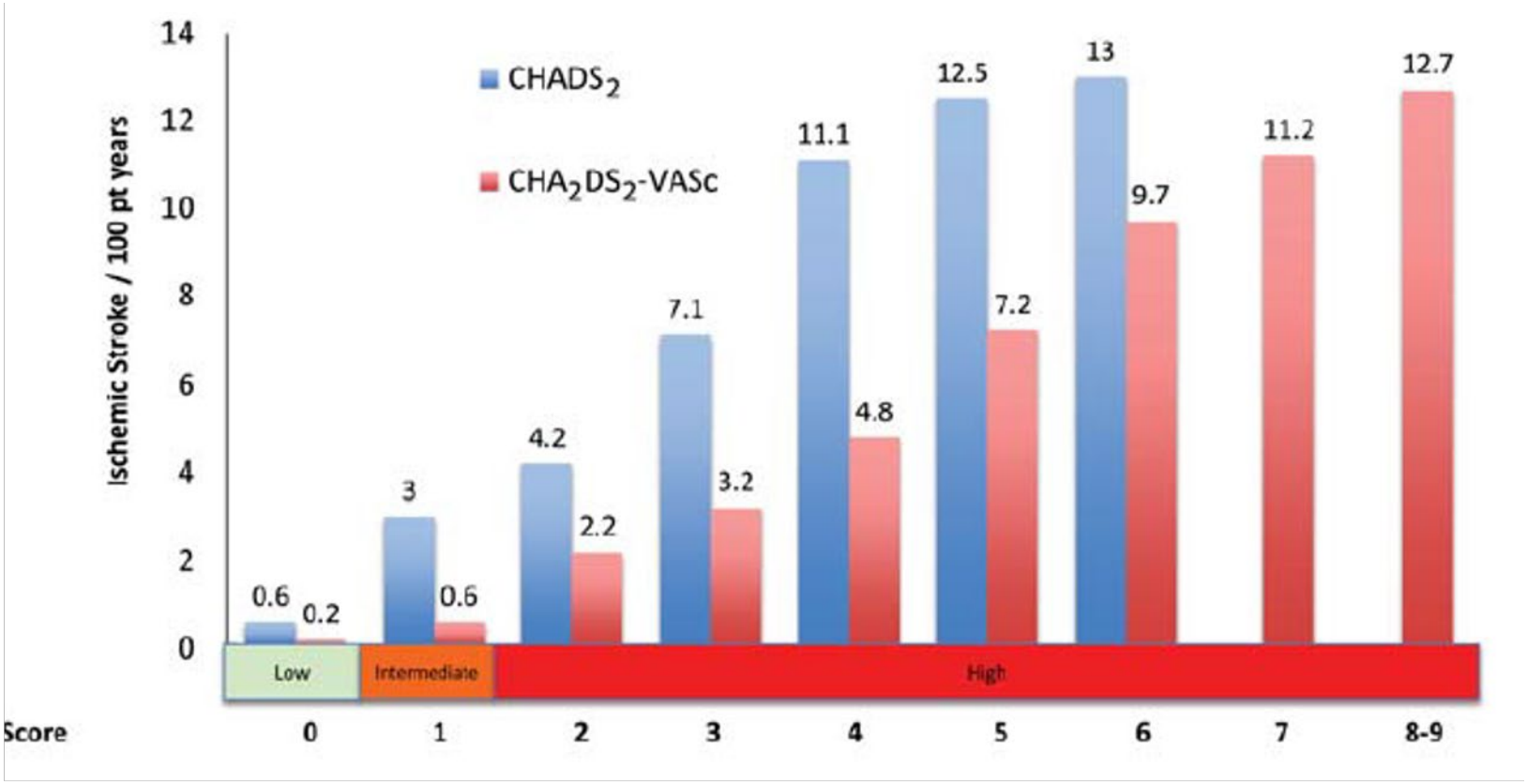
Risk Factor	Score
Congestive heart failure	1
Hypertension	1
Age ≥75 y	1
Diabetes	1
Stroke or TIA history	**2**
MAXIMUM	**6**

CHA_2DS_2-VASc Score

Risk Factor	Score
Congestive heart failure/LV dysfunction	1
Hypertension	1
Age ≥75 y	**2**
Diabetes	1
Stroke/TIA/TE history	**2**
Vascular disease	1
Age 65-74 years	1
Sex **c**ategory, female	1
MAXIMUM	**9**

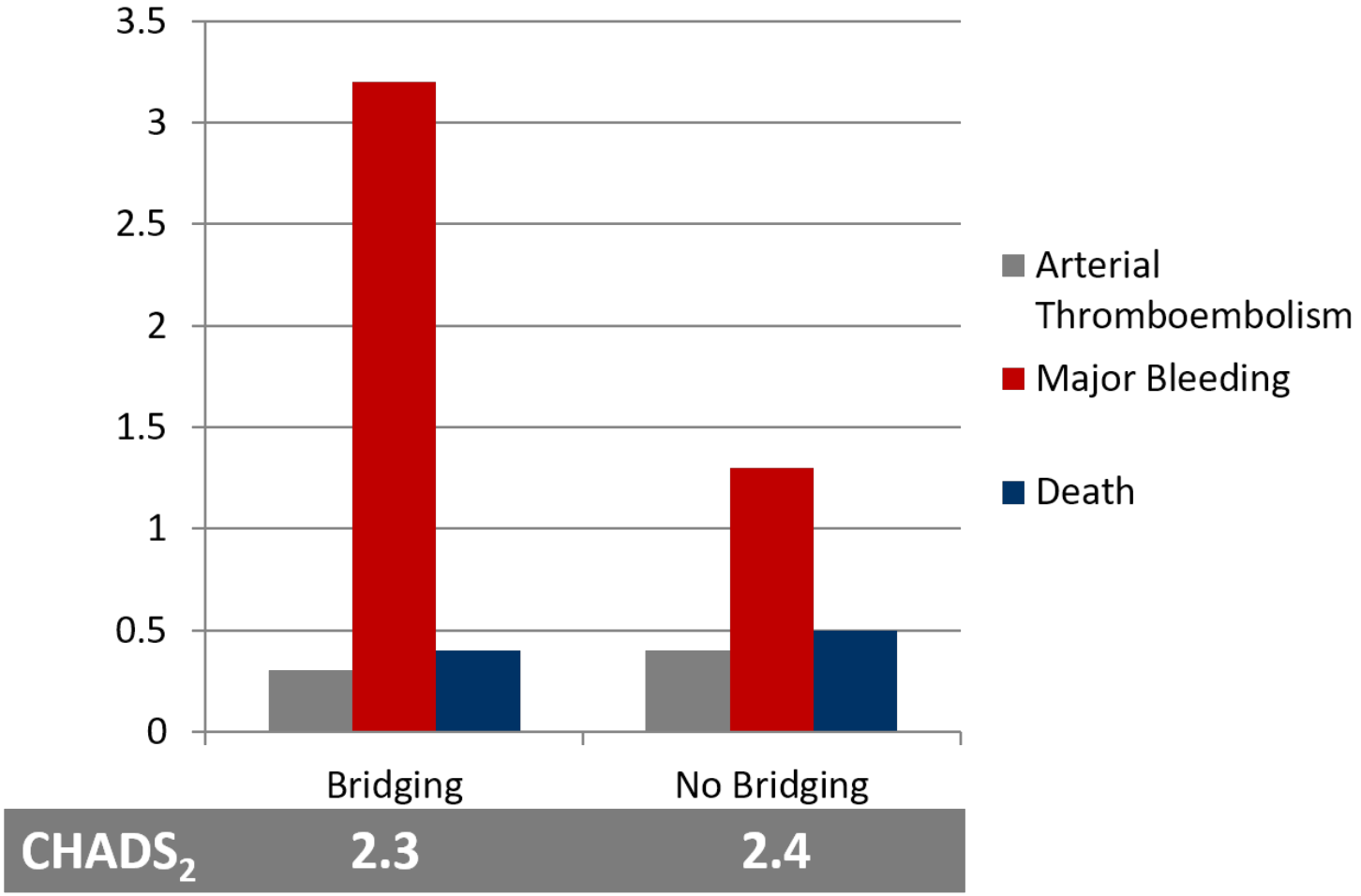
Gage BF et al. *JAMA*. 2001;285:2864-2870.
Lip GY et al. *Chest*. 2010;137:263-272.

$CHADS_2$ & $CHA_2DS_2VAS_C$ Stroke Risk



European Heart Journal (2012) **33**, 1431–1433
doi:10.1093/eurheartj/ehs031

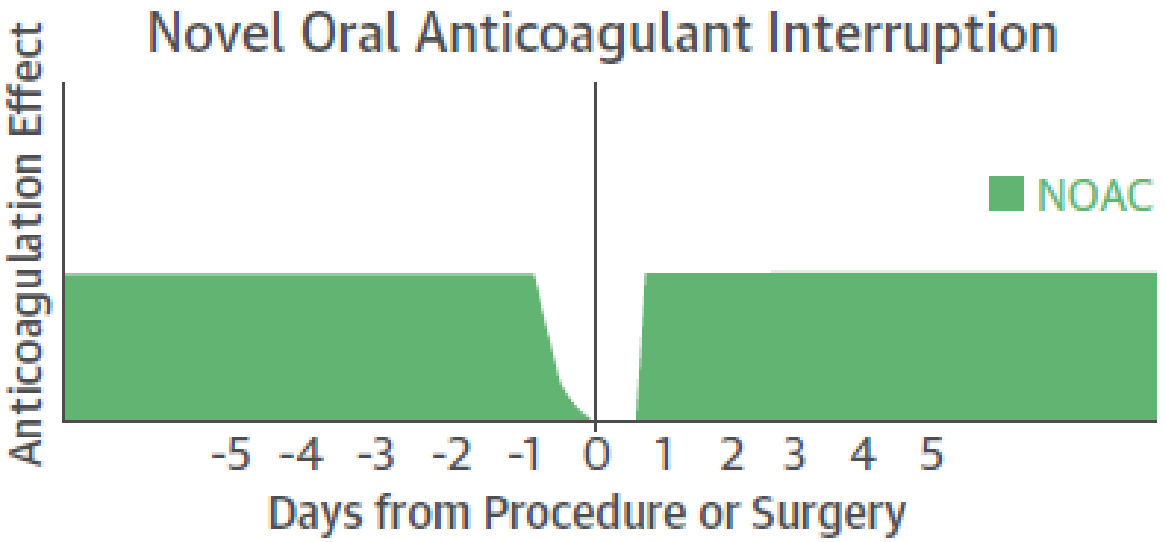
BRIDGE Trial
Results



N Engl J Med 2015;373:823-33.

How would this patient be managed if she was receiving a DOAC?

DOACs



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Dabigatran

CrCl, mL/min	≥80	50-79	30-49	15-29	<15
Estimated drug half-life, h	13	15	18	27	30 (off dialysis)
Procedural bleed risk					
Low	≥24 h	≥36 h	≥48 h	≥72 h	No data. Consider measuring dTT and/or withholding ≥96 h
Uncertain, intermediate, or high	≥48 h	≥72 h	≥96 h	≥120 h	No data. Consider measuring dTT

Apixaban, Edoxaban, Rivaroxaban

CrCl, mL/min	≥30	15-29	<15
Estimated drug half-life, h	6-15	Apixaban: 17 Edoxaban: 17 Rivaroxaban: 9	Apixaban: 17 (off dialysis) Edoxaban: 10-17 (off dialysis) Rivaroxaban: 13 (off dialysis)
Procedural bleed risk			
Low	≥24 h	≥36 h	No data. Consider measuring agent-specific anti Xa level and/or withholding ≥48 h
Uncertain, intermediate, or high	≥48 h	No data. Consider measuring agent-specific anti Xa level and/or withholding ≥72 h	

JACC 2017;69:871-898

How should her peri-procedural anticoagulation be managed?

- Bleeding Risk necessitates temporary interruption of warfarin
  - HAS-BLED > 3
- Thromboembolic risk necessitates consideration of bridging
  - CHADS-VASC : 7
  - History CVA
- Renal Dysfunction impacts treatment choices

Which of the following is the best bridging regimen for this patient?

a) Enoxaparin 1 mg/kg SC q12h
b) Enoxaparin 1.5 mg/kg SC q24h
c) Fondaparinux 2.5 mg SC daily
d) IV UFH post procedure only

Bridging Options

Agent	Route	Dose	Elimination	Half-life
Unfractionated Heparin	IV SC	Protocol 250 units/kg BID	Hepatic / RES Saturable	1 – 2 hrs
LMWH	SC		Renal	
Enoxaparin *CrCl ≥ 30 ml/min* ***CrCl > 30 ml/min*** **Dalteparin**		1 mg/kg BID or 1.5 mg/kg q 24h **1 mg/kg q 24h** 200 units/kg q24h or 100 units/kg BID		4 – 7 hrs 3 – 5 hrs
Fondaparinux	SC	< 50 kg – 5mg 50 – 100 kg – 7.5 mg > 100 kg – 10 mg	Renal	17 – 21 hrs
Argatroban *Normal* *Liver impairment or debilated*	IV	Protocol 2 mcg/kg/min 0.2 - 0.5 mcg/kg/min	Hepatic	30 – 50 min 180 min

Perioperative Anticoagulantion Management

- **Obtain INR** 7 days prior to the surgery
- **Stop VKA** before surgery depending on INR:
  - 3 – 4 days if INR is 1.5 – 1.9
  - 5 days if INR is 2 – 3
  - At least 5 days if INR is > 3
- **Initiate Bridge Therapy** when INR would be anticipated to be less than TR
- **Repeat INR** 24 hours before surgery
- **Discontinue Bridge Therapy** depends on bridging agent
  - LMWH 24 hours ; UFH 4 – 6 hours
- **Resume Anticoagulation**
  - Usually 24 h after surgery but up to 72 hrs if post procedure bleeding risk is high

Chest 2012;141;e326S-e350S; *JACC* 2017 ;69:871-898

Summary / Conclusions

- Net clinical benefit in high risk patients is not fully elucidated
  - Protection against TE events not demonstrated
  - Excessive bleeding has been well described
- Individualized approach to assess:
  - Need to temporarily interrupt anticoagulation
  - Patient-specific bleeding risk factors
  - Thromboembolic risk
  - Complexity of bridging process